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Derivatives of heterocycles with 5 members, their preparation and their use as medicaments

The present invention relates to certain compounds of general formula **(I)** described hereafter, said compounds as medicaments as well as their use for preparing a medicament intended to inhibit the monoamine oxidases (MAO) and/or lipidic peroxidation and/or to act as sodium channel modulators.

The compounds referred to above often have 2 or 3 of the activities mentioned above, which gives them advantageous pharmacological properties.

In fact, given the potential role of the MAO's and ROS's (reactive oxygen species at the origin of lipidic peroxidation) in physiopathology, the new derivatives described corresponding to general formula **(I)** can produce beneficial or favourable effects in the treatment of pathologies where these enzymes and/or these radical species are involved. In particular:

- disorders of the central or peripheral nervous system such as for example neurological diseases where Parkinson's disease, brain and spinal cord trauma, cerebral infarction, subarachnoid haemorrhage, epilepsy, ageing, senile dementia, Alzheimer's disease, Huntington's chorea, amyotrophic lateral sclerosis, peripheral neuropathies, pain can in particular be mentioned;
- schizophrenia, depression, psychoses;
- memory and mood disorders;
- pathologies such as for example migraine;
- behavioural disorders, bulimia and anorexia;
- auto-immune and viral diseases such as for example lupus, AIDS, parasitic and viral infections, diabetes and its complications, multiple sclerosis.
- addiction to toxic substances;
- inflammatory and proliferative pathologies;

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- and more generally all pathologies characterized by an excessive production of ROS's and/or participation of MAO's.

In all these pathologies, experimental evidence exists demonstrating the involvement of the ROS's (*Free Radic. Biol. Med.* (1996) **20**, 675-705; *Antioxid. Health. Dis.* (1997) **4** (Handbook of Synthetic Antioxidants), 1-52) as well as the involvement of MAO's (Goodman & Gilman's: *The pharmacological basis of therapeutics*, 9th ed., 1995, 431-519).

The significance of a combination of the MAO-inhibiting and lipid-peroxidation inhibiting activities is for example well illustrated in Parkinson's disease. This pathology is characterized by a loss of the dopaminergic neurons of the nigrostriatal pathway, the cause of which is partly linked to oxidative stress due to the ROS's. Exogenous dopamine based on L Dopa is used in therapy in order to maintain sufficient dopamine levels. MAO inhibitors are also used with L Dopa to avoid its metabolic degradation but do not act on the ROS's. Compounds acting on both the MAO's and the ROS's therefore have a certain advantage.

Moreover, the sodium channel modulating character is very useful for therapeutic indications such as:

- the treatment or prevention of pain, and in particular:
  - ❖ post-operative pain,
  - ❖ migraine,
  - ❖ neuropathic pain such as trigeminal neuralgia, post-herpetic pain, diabetic neuropathies, glosso-pharyngeal neuralgia, secondary radiculopathies and neuropathies associated with metastatic infiltrations, adiposis dolorosa and pains associated with burns,,
  - ❖ central pains as a result of vascular cerebral incidents, thalamic lesions and multiple sclerosis, and
  - ❖ chronic inflammatory pain or pain linked with a cancer;
- the treatment of epilepsy;
- the treatment of disorders linked with neurodegeneration, and in particular:
  - ❖ vascular cerebral accidents,
  - ❖ cerebral trauma, and
  - ❖ neurodegenerative diseases such Alzheimer's disease, Parkinson's disease and amyotrophic lateral sclerosis;
- the treatment of bipolar disorders and irritable bowel syndrome.

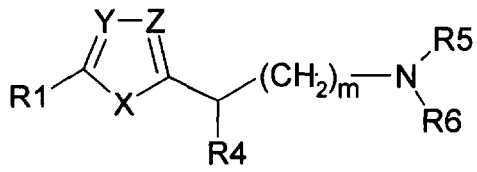
The concrete advantages of the presence in a compound of at least one of these activities is therefore clearly shown by the above.

European Patent Application EP 432,740 describes hydroxyphenylthiazole derivatives, which can be used in the treatment of inflammatory diseases, in particular rheumatic diseases. These hydroxyphenylthiazole derivatives exhibit free radical trapping properties and arachidonic acid metabolism inhibiting properties (they inhibit lipoxygenase and cyclooxygenase).

Other hydroxyphenylthiazole or hydroxyphenyloxazole derivatives are described in Patent Application PCT WO 99/09829. The latter have analgesic properties.

A certain number of imidazole derivatives with structures similar or identical to those of compounds corresponding to general formula **(I)** according to the invention have moreover been described by the Applicant in PCT Patent Application WO 99/64401 as somatostatin agonists or antagonists. However said imidazole derivatives have therapeutic properties in fields different from those indicated above (suppression of growth hormone and treatment of acromegalia, treatment of restenosis, inhibition of gastric acid secretion and prevention of gastro-intestinal bleeding in particular).

Moreover, the compounds of general formula **(A1)**



(A1)

in which

R1 represents one of the aryl, heteroaryl, aralkyl or cycloalkyl radicals optionally substituted by one to three substituents chosen independently from a halogen atom, the CF_3, CN, OH, alkyl or alkoxy, SO_2R9 radical with R9 representing NH_2 or $NHCH_3$,

X represents NR2, R2 representing H or alkyl;

Y represents N or CR3;

Z represents CR3 or N;

on condition however that Y and Z are not both CR3 or N at the same time;

R3 represents H, alkyl, halogen, hydroxyalkyl or phenyl optionally substituted by 1 to 3 substituents chosen from H, CF_3, CN, SO_2NH_2, OH, alkyl or alkoxy;

m represents 0, 1 or 2;

R4 represents H or alkyl;

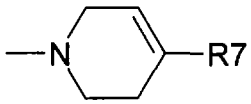
when Z represents CR3, then R3 and R4 can also together represent $-(CH_2)_{n1}-$ with n1 being an integer from 2 to 4 or R2 and R4 can also together represent $-(CH_2)_{n2}-$ with n2 being an integer from 2 to 4;

R5 and R6 represent independently H, alkyl, alkoxy, aryl or aralkyl;

NR5R6 also being able to represent together (in particular):

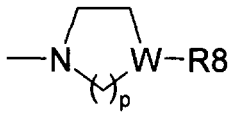
- the optionally substituted 2-(1,2,3,4-tetrahydroquinolyl) radical,

- a



radical in which R7 represents one of the phenyl, benzyl or phenethyl radicals in which the phenyl ring can be substituted;

- a



radical in which p is a an integer from 1 to 3,

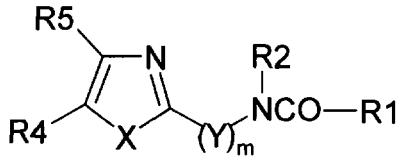
W is N and R8 represents H, CF_3, one of the phenyl, pyridyl or pyrimidinyl radicals optionally substituted from once to twice by radicals chosen from halogen, OH, alkyl or alkoxy, or

W is CH and R8 represents optionally substituted phenyl or aralkyl optionally substituted on the aryl group;

have been described in PCT Patent Application WO 96/16040 as partial agonists or antagonists of the dopamine sub-receptors in the brain or as prodrug forms of such partial agonists or antagonists. These compounds would therefore have useful properties

in the diagnosis and treatment of affective disorders such as schizophrenia and depression as well as certain movement disorders such as Parkinson's disease.

It has also been described in PCT Patent Application WO 98/27108 that certain amides of general formula **(A2)**



(A2)

in which:

R1 represents in particular an optionally substituted alkyl, phenyl radical or optionally substituted heterocyclic aryl radical;

R2 represents H or phenylalkyl;

R4 represents H, quinolyl, 3-4-methylenedioxyphenyl or one of the phenyl or pyridyl radicals, optionally substituted by one or more radicals chosen in particular from alkyl, alkoxy, alkylthio, optionally protected hydroxy, amino, alkylamino, dialkylamino;

R5 represents H or an imidazolyl, phenyl, nitrophenyl, phenylalkyl radical, or also a -CO-N(R7)(R8) radical, in which R7 and R8 represent independently H, phenyl, phenylalkyl, alkyl or alkoxy;

or R4 and R5 in combination form a group of formula -CH=CH-CH=CH-;

Y is a phenylene radical substituted by a phenyl, phenoxy or phenylalkoxy radical, or a group of formula –CH(R3)-, in which R3 represents H or a radical of formula $-(CH_2)_n-$ R6, in which R6 represents an optionally protected hydroxy, acyl, carboxy, acylamino, alkoxy, phenylalkoxy, alkylthio, optionally substituted phenyl, optionally substituted pyridyl, pyrazinyl, pyrimidinyl, furyl, imidazolyl, naphthyl, N-alkylindolyl or 3,4-methylenedioxyphenyl radical and n is an integer from 0 to 3;

R2 and R3 taken together with the carbon atoms which carry them being able to form a phenyl group;

X represents S or NR9;

R9 representing H, an alkyl or cycloalkyl radical, or also a benzyl radical optionally substituted once on its phenyl part by H, alkyl or alkoxy;

are NO synthase inhibitors and can be used to treat diseases which include in particular cardiovascular or cerebral ischemia, cerebral haemorrhage, disorders of the central nervous system, Alzheimer's disease, multiple sclerosis, diabetes, hepatitis, migraine, rheumatoid arthritis and osteoporosis.

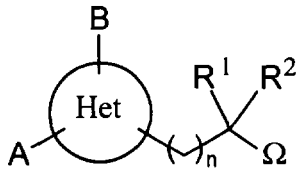
In a different field, the Applicant has itself described previously in PCT Patent Application WO 98/58934 amidine derivatives having the ability to inhibit NO synthases and/or lipidic peroxidation.

The Applicant has more recently described in Patent Application PCT/FR00/02805 that certain intermediates of the first stages of the amidine synthesis described in PCT Patent Application WO 98/58934, and more generally certain derivatives of heterocycles with five members, namely the products of general formula **(I)** defined hereafter, have at least one of the three properties chosen from the following properties (and often even two of these three properties, and sometimes even all three at once):

- MAO inhibiting properties;
- lipidic peroxidation inhibiting properties; and
- sodium channel modulating properties.

These advantageous properties are useful in opening up numerous uses for such compounds, in particular in the treatment of neurodegenerative diseases, and in particular those indicated previously, pain or epilepsy.

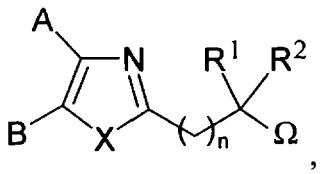
According to PCT Patent Application WO 01/26656, the compounds corresponding to general formula **(I)**



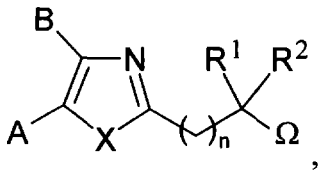
(I)

in racemic, enantiomeric form, or any combination of these forms, in which Het is a heterocycle with 5 members comprising 2 heteroatoms and, like general formula **(I)**

corresponds exclusively to one of the following sub-formulae :

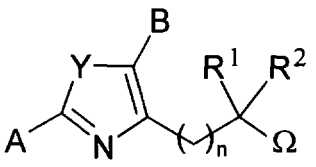


,

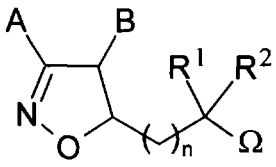


,

$(I)_1$ $(I)_2$



and

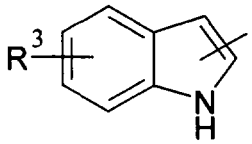


$(I)_3$ $(I)_4$

in which

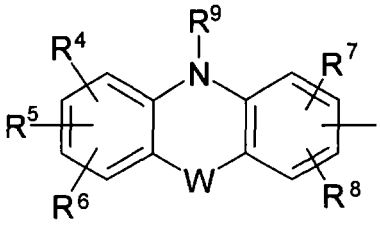
A represents

either a



radical in which R^3 represents a hydrogen atom, the OH group or an alkoxy or alkyl radical,

or a

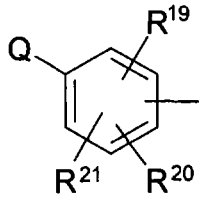


radical in which R^4, R^5, R^6, R^7 and R^8 represent, independently, a hydrogen atom, a halogen, the OH group or an alkyl, alkoxy, cyano, nitro or $NR^{10}R^{11}$ radical,

R^{10} and R^{11} representing, independently, a hydrogen atom, an alkyl radical or a $-COR^{12}$ group, or R^{10} and R^{11} forming together with the nitrogen atom an optionally substituted heterocycle containing 4 to 7 members and 1 to 3 heteroatoms including the nitrogen

atom already present, the additional heteroatoms being chosen independently from the group constituted by the O, N and S atoms, said heterocycle being able to be for example azetidine, pyrrolidine, piperidine, piperazine, morpholine or thiomorpholine,
R^{12} representing a hydrogen atom or an alkyl, alkoxy or $NR^{13}R^{14}$ radical,
R^{13} and R^{14} representing, independently, a hydrogen atom or an alkyl radical, or R^{13} and R^{14} forming together with the nitrogen atom an optionally substituted heterocycle containing 4 to 7 members and 1 to 3 heteroatoms including the nitrogen atom already present, the additional heteroatoms being chosen independently from the group constituted by the O, N and S atoms, said heterocycle being able to be for example azetidine, pyrrolidine, piperidine, piperazine, morpholine or thiomorpholine,
R^9 represents a hydrogen atom, an alkyl radical or a $-COR^{15}$ group,
R^{15} representing a hydrogen atom or an alkyl, alkoxy or $NR^{16}R^{17}$ radical,
R^{16} and R^{17} representing, independently, a hydrogen atom or an alkyl radical, or R^{16} and R^{17} forming together with the nitrogen atom an optionally substituted heterocycle containing 4 to 7 members and 1 to 3 heteroatoms including the nitrogen atom already present, the additional heteroatoms being chosen independently from the group constituted by the O, N and S atoms, said heterocycle being able to be for example azetidine, pyrrolidine, piperidine, piperazine, morpholine or thiomorpholine,
and W does not exist, or represents a bond, or -O-, -S- or $-NR^{18}-$, in which R^{18} represents a hydrogen atom or an alkyl radical;

or a



radical in which Q represents H, $-OR^{22}$, $-SR^{22}$, $-NR^{23}R^{24}$, a phenyl radical optionally substituted by one or more substituents chosen independently from a halogen atom, an OH, cyano, nitro, alkyl, alkoxy or $-NR^{10}R^{11}$ radical and a group of two substituents representing together a methylene dioxy or ethylenedioxy radical, or also Q represents a -COPh, $-SO_2Ph$ or $-CH_2Ph$ radical, said -COPh, $-SO_2Ph$ or $-CH_2Ph$ radical being optionally substituted on its aromatic part by one or more substituents chosen independently from an alkyl or alkoxy radical and a halogen atom,
R^{10} and R^{11} representing, independently, a hydrogen atom, an alkyl radical or a $-COR^{12}$ group, or R^{10} and R^{11} forming together with the nitrogen atom an optionally substituted

heterocycle containing 4 to 7 members and 1 to 3 heteroatoms including the nitrogen atom already present, the additional heteroatoms being chosen independently from the group constituted by the O, N and S atoms, said heterocycle being able to be for example azetidine, pyrrolidine, piperidine, piperazine, morpholine or thiomorpholine,

R^{12} representing a hydrogen atom, an alkyl or alkoxy or $NR^{13}R^{14}$ radical,

R^{13} and R^{14} representing, independently, a hydrogen atom or an alkyl radical, or R^{13} and R^{14} forming together with the nitrogen atom an optionally substituted heterocycle containing 4 to 7 members and 1 to 3 heteroatoms including the nitrogen atom already present, the additional heteroatoms being chosen independently from the group constituted by the O, N and S atoms, said heterocycle being able to be for example azetidine, pyrrolidine, piperidine, piperazine, morpholine or thiomorpholine,

R^{22} representing a hydrogen atom, an alkyl radical or an aryl radical optionally substituted by one or more substituents chosen from the alkyl, OH, halogen, nitro and alkoxy radicals,

R^{23} and R^{24} representing, independently, a hydrogen atom, an alkyl radical or a -CO-R^{25} radical,

R^{25} representing an alkyl radical,

and R^{19}, R^{20} and R^{21} represent, independently, a hydrogen, a halogen, the OH or SR^{26} group, or an alkyl, cycloalkyl, alkenyl, alkoxy, cyano, nitro, $-SO_2NHR^{49}$, $-CONHR^{55}$, $-S(O)_qR^{56}$, $-NH(CO)R^{57}$, $-CF_3$, $-OCF_3$ or $NR^{27}R^{28}$ radical,

R^{26} representing a hydrogen atom or an alkyl radical,

R^{27} and R^{28} representing, independently, a hydrogen atom, an alkyl radical or a $-COR^{29}$ group, or R^{27} and R^{28} forming together with the nitrogen atom an optionally substituted heterocycle containing 4 to 7 members and 1 to 3 heteroatoms including the nitrogen atom already present, the additional heteroatoms being chosen independently from the group constituted by the O, N and S atoms, said heterocycle being able to be for example azetidine, pyrrolidine, piperidine, piperazine, morpholine or thiomorpholine,

R^{49} and R^{55} representing, independently each time they are involved, a hydrogen atom or an alkyl or alkylcarbonyl radical,

q representing an integer from 0 to 2,

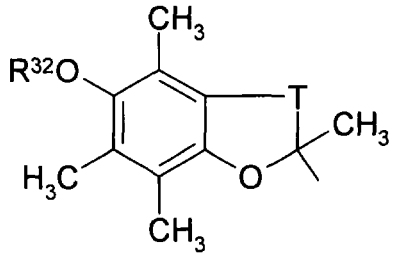
R^{56} and R^{57} representing, independently each time they are involved, a hydrogen atom or an alkyl or alkoxy radical,

R^{29} representing a hydrogen atom, an alkyl, alkoxy or $-NR^{30}R^{31}$ radical,

R^{30} and R^{31} representing, independently, a hydrogen atom or an alkyl radical, or R^{30} and R^{31} forming together with the nitrogen atom an optionally substituted heterocycle containing 4 to 7 members and 1 to 3 heteroatoms including the nitrogen atom already

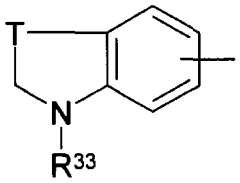
present, the additional heteroatoms being chosen independently from the group constituted by the O, N and S atoms, said heterocycle being able to be for example azetidine, pyrrolidine, piperidine, piperazine, morpholine or thiomorpholine,

or a



radical in which R^{32} represents a hydrogen atom or an alkyl radical, and T represents a $-(CH_2)_m-$ radical with m = 1 or 2,

or finally a



radical in which R^{33} represents a hydrogen atom or an alkyl radical, $-\Sigma-NR^{34}R^{35}$ or $-\Sigma-CHR^{36}R^{37}$,

Σ representing a linear or branched alkylene radical containing 1 to 6 carbon atoms,

R^{34} and R^{35} representing, independently, a hydrogen atom or an alkyl radical,

R^{36} and R^{37} representing, independently, a hydrogen atom or a carbocyclic or heterocyclic aryl radical optionally substituted by one or more substituents chosen from the alkyl, OH, halogen, nitro, alkoxy or $NR^{10}R^{11}$ radicals,

R^{10} and R^{11} representing, independently, a hydrogen atom, an alkyl radical or a $-COR^{12}$ group, or R^{10} and R^{11} forming together with the nitrogen atom an optionally substituted heterocycle containing 4 to 7 members and 1 to 3 heteroatoms including the nitrogen atom already present, the additional heteroatoms being chosen independently from the group constituted by the O, N and S atoms, said heterocycle being able to be for example azetidine, pyrrolidine, piperidine, piperazine, morpholine or thiomorpholine,

R^{12} representing a hydrogen atom or an alkyl, alkoxy or $NR^{13}R^{14}$ radical,

R^{13} and R^{14} representing, independently, a hydrogen atom or an alkyl radical, or R^{13} and R^{14} forming together with the nitrogen atom an optionally substituted heterocycle containing 4 to 7 members and 1 to 3 heteroatoms including the nitrogen atom already present, the additional heteroatoms being chosen independently from the group constituted by the O, N and S atoms, said heterocycle being able to be for example azetidine, pyrrolidine, piperidine, piperazine, morpholine or thiomorpholine,
and T represents a $-(CH_2)_m-$ radical with m = 1 or 2,

or also A represents an alkyl, cycloalkyl or cycloalkylalkyl radical;

X represents S or NR^{38},
R^{38} representing a hydrogen atom or an alkyl, cyanoalkyl, aralkyl, alkylcarbonyl or aralkylcarbonyl radical,

Y represents O or S;

R^1 represents a hydrogen atom, an alkyl, aminoalkyl, alkoxyalkyl, cycloalkyl, cycloalkylalkyl, trifluoromethylalkyl, alkenyl, allenyl, allenylalkyl, alkynyl, cyanoalkyl, $-(CH_2)_g-Z^1R^{39}$, $-(CH_2)_g-COR^{40}$, $-(CH_2)_g-NHCOR^{70}$, aryl, aralkyl, arylcarbonyl, heteroarylalkyl or aralkylcarbonyl radical, the aryl group of the aryl, aralkyl, arylcarbonyl, heteroarylalkyl or aralkylcarbonyl radicals itself being optionally substituted by one or more substituents chosen from the group constituted by the alkyl, halogen, alkoxy, nitro, cyano, cyanoalkyl, amino, alkylamino, dialkylamino, $-(CH_2)_k-Z^2R^{39}$ or $-(CH_2)_k-COR^{40}$ radicals,
Z^1 and Z^2 representing a bond, -O-, $-NR^{41}-$ or -S-,
R^{39} and R^{41} representing, independently each time they are involved, a hydrogen atom or an alkyl, alkenyl, alkynyl or cyanoalkyl radical,
R^{40} representing, independently each time it is involved, a hydrogen atom or an alkyl, allenyl, allenylalkyl, alkenyl, alkynyl, cyanoalkyl, alkoxy or $NR^{42}R^{43}$ radical,
R^{42} and R^{43} representing, independently each time they are involved, a hydrogen atom or an alkyl, allenyl, allenylalkyl, alkenyl, alkynyl or cyanoalkyl radical,
and R^2 represents a hydrogen atom, an alkyl, aminoalkyl, alkoxyalkyl, cycloalkyl, cycloalkylalkyl, trifluoromethylalkyl or $-(CH_2)_g-NHCOR^{71}$ radical, or also one of the aralkyl or heteroarylalkyl radicals optionally substituted on the aryl or heteroaryl group by one or more groups chosen independently from the group comprising a halogen atom and an alkyl, alkoxy, hydroxy, cyano, nitro, amino, alkylamino or dialkylamino radical,

R^{70} and R^{71} independently representing an alkyl or alkoxy radical;

or R^1 and R^2, taken together with the carbon atom which carries them, form a carbocycle with 3 to 7 members;

B represents a hydrogen atom, an alkyl radical, a $-(CH_2)_g-Z^3R^{44}$ radical or a carbocyclic aryl radical optionally substituted from once to 3 times by radicals chosen from the group comprising a halogen atom, a linear or branched alkyl or alkoxy radical containing 1 to 6 carbon atoms, a hydroxy, cyano or nitro radical, an amino, alkylamino or dialkylamino radical and a carbocyclic aryl radical,

Z^3 representing a bond, -O-, $-NR^{45}-$ or -S-,

R^{44} and R^{45} representing, independently, a hydrogen atom or an alkyl, alkenyl, alkynyl, allenyl, allenylalkyl or cyanoalkyl radical;

Ω represents one of the $NR^{46}R^{47}$ or OR^{48} radicals, in which:

R^{46} and R^{47} represent, independently, a hydrogen atom or an alkyl, cycloalkyl, cycloalkylalkyl, alkenyl, alkynyl, allenyl, allenylalkyl, cyanoalkyl, $-(CH_2)_g-Z^4R^{50}$, $-(CH_2)_k-COR^{51}$, $-(CH_2)_k-COOR^{51}$, $-(CH_2)_k-CONHR^{51}$ or $-SO_2R^{51}$ radical, or also a radical chosen from the aryl, aralkyl, aryloxyalkyl, arylcarbonyl, arylimino, aralkylcarbonyl, heteroaryl and in particular pyridinyl, pyridinylalkyl or pyridinylcarbonyl radicals, the aryl or heteroaryl group of said aryl, aralkyl, aryloxyalkyl, arylcarbonyl, arylimino, aralkylcarbonyl, heteroaryl, pyridinylalkyl or pyridinylcarbonyl radicals being optionally substituted by one or more substituents chosen independently from halogen, alkyl, alkoxy, hydroxy, nitro, cyano, cyanoalkyl, amino, alkylamino, dialkylamino, $-(CH_2)_k-Z^5R^{50}$, $-(CH_2)_k-COR^{51}$ and $-(CH_2)_k-COOR^{51}$,

Z^4 and Z^5 representing a bond, -O-, $-NR^{52}-$ or -S-,

or R^{46} and R^{47} taken together form with the nitrogen atom a non-aromatic heterocycle with 4 to 8 members, the elements of the chain being chosen from a group comprising $-CH(R^{53})-$, $-NR^{54}-$, -O-, -S- and -CO-, said heterocycle being able to be for example an azetidine, a piperazine, a homopiperazine, a 3,5-dioxopiperazine, a piperidine, a pyrrolidine, a morpholine or a thiomorpholine,

R^{50} and R^{52}, representing, independently each time they are involved, a hydrogen atom or an alkyl, alkenyl, alkynyl, allenyl, allenylalkyl or cyanoalkyl radical,

R^{51} representing, independently each time it is involved, a hydrogen atom, one of the cycloalkyl or cycloalkylalkyl radicals in which the cycloalkyl radical contains 3 to 7 carbon atoms, a linear or branched alkyl radical containing 1 to 8 carbon atoms, an alkenyl, alkynyl, allenyl, allenylalkyl, cyanoalkyl, alkoxyalkyl or $NR^{58}R^{59}$ radical, or

also an aryl or aralkyl radical, said aryl or aralkyl radical being able to be substituted by one or more substituents chosen independently from a halogen atom and an alkyl or alkoxy radical,

R^{58} and R^{59} representing, independently, a hydrogen atom or an alkyl, alkenyl, alkynyl, allenyl, allenylalkyl or cyanoalkyl radical,

R^{53} and R^{54} representing, independently, a hydrogen atom or a $-(CH_2)_k-Z^7R^{60}$ or $-(CH_2)_k-COR^{61}$ radical,

Z^7 representing a bond, -O-, $-NR^{62}-$ or -S-,

R^{60} and R^{62} representing, independently, a hydrogen atom or an alkyl, alkenyl, allenyl, allenylalkyl, alkynyl, cyanoalkyl, aryl, aralkyl, arylcarbonyl, aralkylcarbonyl, pyridinyl, pyridinylalkyl or pyridinylcarbonyl radical, the aryl or pyridinyl group of the aryl, aralkyl, arylcarbonyl, aralkylcarbonyl, pyridinyl, pyridinylalkyl or pyridinylcarbonyl radicals being optionally substituted by one or more substituents chosen from the group constituted by the alkyl, halogen, nitro, alkoxy, cyano, cyanoalkyl, $-(CH_2)_k-Z^8R^{63}$ and $-(CH_2)_k-COR^{64}$ radicals,

R^{61} representing a hydrogen atom, an alkyl, allenyl, allenylalkyl, alkenyl, alkynyl, cyanoalkyl, alkoxy or $NR^{65}R^{66}$ radical,

R^{65} and R^{66} representing, independently, a hydrogen atom or an alkyl, allenyl, allenylalkyl, alkenyl, alkynyl or cyanoalkyl radical,

Z^8 representing a bond, -O-, $-NR^{67}-$ or -S-,

R^{63} and R^{67} representing, independently, a hydrogen atom, an alkyl, allenyl, allenylalkyl, alkenyl, alkynyl or cyanoalkyl radical,

R^{64} representing a hydrogen atom, an alkyl, allenylalkyl, alkenyl, alkenyl, alkynyl, cyanoalkyl, alkoxy or $NR^{68}R^{69}$ radical,

R^{68} and R^{69} representing, independently, a hydrogen atom or an alkyl, allenyl, allenylalkyl, alkenyl, alkynyl or cyanoalkyl radical,

and R^{48} represents a hydrogen atom or an alkyl, alkynyl or cyanoalkyl radical;

g and p, each time they are involved, being independently integers from 1 to 6, and k and n, each time they are involved, being independently integers from 0 to 6;

it being understood that when Het is such that the compound of general formula **(I)** corresponds to general sub-formula $\mathbf{(I)_4}$, then:

A represents the 4-hydroxy-2, 3-di-tertiobutyl-phenyl radical;

B, R^1 and R^2 all represent H; and finally

Ω represents OH;

or pharmaceutically acceptable salts of compounds of general formula **(I)**;

can be used for preparing a medicament intended to have at least one of the three following activities :

- inhibiting the monoamine oxidases, in particular monoamine oxidase B,
- inhibiting lipidic peroxidation,
- having a modulating activity vis-à-vis the sodium channels.

This allows the compounds of general formula **(I)** to be useful in the treatment of the diseases mentioned previously as being linked with the MAO's, with lipidic peroxidation and with the sodium channels.

By alkyl, unless otherwise specified, is meant a linear or branched alkyl radical containing 1 to 6 carbon atoms. By cycloalkyl, unless otherwise specified, is meant a monocyclic carbon system containing 3 to 7 carbon atoms. By alkenyl, unless otherwise specified, is meant a linear or branched alkyl radical containing 1 to 6 carbon atoms and having at least one unsaturation (double bond). By alkynyl, unless otherwise specified, is meant a linear or branched alkyl radical containing 1 to 6 carbon atoms and having at least one double unsaturation (triple bond). By allenyl, is meant the $-CH=C=CH_2$ radical. By carbocyclic or heterocyclic aryl, is meant a carbocyclic system (in particular, the phenyl radical which can be abbreviated to Ph) or heterocyclic system comprising at least one aromatic ring, a system being referred to as heterocyclic when at least one of the rings composing it comprises a heteroatom (O, N or S). By heterocycle, is meant a mono- or polycyclic system, said system comprising at least one heteroatom chosen from O, N and S and being saturated, partially or totally unsaturated or aromatic. By heteroaryl, is meant a heterocycle as defined previously in which at least one of the rings composing it is aromatic. By haloalkyl, is meant an alkyl radical at least one (and optionally all) of the hydrogen atoms of which is replaced by a halogen atom.

Moreover, unless otherwise specified, by an optionally substituted radical is meant a radical comprising one or more substituents chosen independently from the group comprising a halogen atom and alkyl and alkoxy radicals.

By alkylthio, alkoxy, haloalkyl, alkoxyalkyl, trifluoromethylalkyl, cycloalkylalkyl, haloalkoxy, aminoalkyl, alkenyl, alkynyl, allenylalkyl, cyanoalkyl and aralkyl radicals, is meant respectively the alkylthio, alkoxy, haloalkyl, alkoxyalkyl, trifluoromethylalkyl, cycloalkylalkyl, haloalkoxy, aminoalkyl, alkenyl, alkynyl, allenylalkyl, cyanoalkyl and

aralkyl radicals the alkyl radical (the alkyl radicals) of which has (have) the meaning(s) indicated previously.

By heterocycle, is meant in particular the thiophene, piperidine, piperazine, quinoline, indoline and indole radicals. By linear or branched alkyl having 1 to 6 carbon atoms, is meant in particular the methyl, ethyl, propyl, isopropyl, butyl, isobutyl, sec-butyl and tert-butyl, pentyl, neopentyl, isopentyl, hexyl, isohexyl radicals. Finally, by halogen, is meant fluorine, chlorine, bromine or iodine atoms.

The present invention relates to a selection of compounds of general formula **(I)** represented above, namely the following compounds:

- 2,6-di*tert*-butyl-4-{2-[2-(methylamino)ethyl]-1,3-thiazol-4-yl}phenol (hereafter compound 1);

- 2,6-di*tert*-butyl-4-[4-(hydroxymethyl)-1,3-oxazol-2-yl]phenol (hereafter compound 2);

- 2,6-di*tert*-butyl-4-{2-[1-(methylamino)ethyl]-1,3-thiazol-4-yl}phenol (hereafter compound 3);

- 2,6-di*tert*-butyl-4-[2-(methoxymethyl)-1,3-thiazol-4-yl]phenol (hereafter compound 4);

- 2,6-di*tert*-butyl-4-{4-[(methylamino)methyl]-1,3-oxazol-2-yl}phenol (hereafter compound 5);

- N-{[4-(3,5-di*tert*-butyl-4-hydroxyphenyl)-1,3-thiazol-2-yl]methyl}acetamide (hereafter compound 6);

- ethyl [4-(3,5-di*tert*-butyl-4-hydroxyphenyl)-1,3-thiazol-2-yl]methylcarbamate (hereafter compound 7);

- 2,6-di*tert*-butyl-4-[2-(morpholin-4-ylmethyl)-1,3-thiazol-4-yl]phenol (hereafter compound 8);

- 2,6-di*tert*-butyl-4-[2-(thiomorpholin-4-ylmethyl)-1,3-thiazol-4-yl]phenol (hereafter compound 9);

- 4-[2-(anilinomethyl)-1,3-thiazol-4-yl]-2,6-di*tert*-butylphenol (hereafter compound 10);

- 2,6-di*tert*-butyl-4-(2-{[[2-(dimethylamino)ethyl](methyl)amino]methyl}-1,3-thiazol-4-yl)phenol (hereafter compound 11);

- 2,6-di*tert*-butyl-4-{5-methyl-2-[(methylamino)methyl]-1,3-thiazol-4-yl}phenol (hereafter compound 12);

- 1-[4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]methanamine (hereafter compound 13);

- *N*-{[4-(3,5-di*tert*-butyl-4-hydroxyphenyl)-1,3-thiazol-2-yl]methyl}-*N*-methylacetamide (hereafter compound 14);

- 1-[4-(3,5-di*tert*-butyl-4-methoxyphenyl)-1,3-thiazol-2-yl]-N-methylmethanamine (hereafter compound 15);

- 2,6-di*tert*-butyl-4-{2-[(ethylamino)methyl]-1,3-thiazol-4-yl}phenol (hereafter compound 16);

- 2,6-di*tert*-butyl-4-{2-[(4-phenylpiperazin-1-yl)methyl]-1,3-thiazol-4-yl}phenol (hereafter compound 17);

- 2,6-di*tert*-butyl-4-{2-[(4-methyl-1,4-diazepan-1-yl)methyl]-1,3-thiazol-4-yl}phenol (hereafter compound 18);

- N-{1-[4-(4-anilinophenyl)-1,3-thiazol-2-yl]ethyl}-N-methylamine (hereafter compound 19);

- 2,6-di*tert*-butyl-4-{2-[(isopropylamino)methyl]-1,3-thiazol-4-yl}phenol (hereafter compound 20);

- 2,6-ditert-butyl-4-{2-[(cyclohexylamino)methyl]-1,3-thiazol-4-yl}phenol (hereafter compound 21);

- 2,6-di*tert*-butyl-4-{2-[(4-isopropylpiperazin-1-yl)methyl]-1,3-thiazol-4-yl}phenol (hereafter compound 22);

- *N*-methyl-1-[4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]ethanamine (hereafter compound 23);

- 2,6-di*tert*-butyl-4-{2-[(4-ethylpiperazin-1-yl)methyl]-1,3-thiazol-4-yl}phenol (hereafter compound 24);

- *N*-{[4-(4-anilinophenyl)-1,3-thiazol-2-yl]methyl}-*N*-ethylamine (hereafter compound 25);

- *N*-{[4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]methyl}ethanamine (hereafter compound 26);

- 2,6-di*tert*-butyl-4-(2-{[4-(dimethylamino)piperidin-1-yl]methyl}-1,3-thiazol-4-yl)phenol (hereafter compound 27);

- 1-{[4-(3,5-di*tert*-butyl-4-hydroxyphenyl)-1,3-thiazol-2-yl]methyl}piperidin-4-ol (hereafter compound 28);

- 4-methylpentyl 2-[4-(1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate (hereafter compound 29);

- 3,3-dimethylbutyl 2-[4-(4-pyrrolidin-1-ylphenyl)-1*H*-imidazol-2-yl]ethylcarbamate (hereafter compound 30);

- isopentyl 2-[4-(1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate (hereafter compound 31);

- hexyl 2-[4-(4'-bromo-1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate (hereafter compound 32);

- benzyl 2-[4-(4-*tert*-butylphenyl)-1*H*-imidazol-2-yl]ethylcarbamate (hereafter compound 33);

- 3,3-dimethylbutyl 2-[4-(1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate (hereafter compound 34);

- hexyl 2-[4-(4-pyrrolidin-1-ylphenyl)-1*H*-imidazol-2-yl]ethylcarbamate (hereafter compound 35);

- hexyl 2-[4-(3,5-di*tert*-butyl-4-hydroxyphenyl)-1*H*-imidazol-2-yl]ethylcarbamate (hereafter compound 37);

- 3,3-dimethylbutyl 2-[4-(3,5-di*tert*-butyl-4-hydroxyphenyl)-1*H*-imidazol-2-yl] ethylcarbamate (hereafter compound 38);

- 3,3-dimethylbutyl 2-[4-(4-methoxyphenyl)-1*H*-imidazol-2-yl]ethylcarbamate (hereafter compound 39);

- benzyl 2-[4-(3,5-di*tert*-butyl-4-hydroxyphenyl)-1*H*-imidazol-2-yl]ethylcarbamate (hereafter compound 40);

- benzyl 2-[4-(4-pyrrolidin-1-ylphenyl)-1*H*-imidazol-2-yl]ethylcarbamate (hereafter compound 41);

- 2-phenylethyl 2-[4-(1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate (hereafter compound 42);

- butyl 2-[4-(4'-fluoro-1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate (hereafter compound 43);

- butyl 2-[4-(1,1'-biphenyl-4-yl)-5-methyl-1*H*-imidazol-2-yl]ethylcarbamate (hereafter compound 44);

- butyl 2-[4-(4'-methyl-1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate (hereafter compound 45);

- butyl 2-[4-(4'-chloro-1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate (hereafter compound 46);

- butyl 2-[4-(2'-fluoro-1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate (hereafter compound 47);

- butyl 2-[4-(2',4'-difluoro-1,1'-biphenyl-4-yl)-1H-imidazol-2-yl]ethylcarbamate hereafter compound 49);

- 2,6-di-*tert*-butyl-4-{2-[(propylamino)methyl]-1,3-thiazol-4-yl}phenol (hereafter compound 50);

- *N*-{[4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]methyl}-*N*-propylamine (hereafter compound 51);

- *N*-{[4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]methyl}butan-1-amine (hereafter compound 52);

- *N*-{[4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]methyl}pentan-1-amine (hereafter compound 53);

- 1-{[4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-1,3-thiazol-2-yl]methyl}piperidin-3-ol (hereafter compound 54);

- 1-{[4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-1,3-thiazol-2-yl]methyl}pyrrolidin-3-ol (hereafter compound 55);

- [4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]methanol (hereafter compound 56);

- *N*, *N*-dimethyl-*N*-{[4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]methyl}amine (hereafter compound 57);

- 2-{2-[(4-methylpiperazin-1-yl)methyl]-1,3-thiazol-4-yl}-10*H*-phenothiazine (hereafter compound 58);

- 2-[2-(piperidin-1-ylmethyl)-1,3-thiazol-4-yl]-10*H*-phenothiazine (hereafter compound 59);

- 2-[2-(piperazin-1-ylmethyl)-1,3-thiazol-4-yl]-10*H*-phenothiazine (hereafter compound 60);

- 1-{[4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-1,3-thiazol-2-yl]methyl}azetidin-3-ol (hereafter compound 61);

- 2-[2-(morpholin-4-ylmethyl)-1,3-thiazol-4-yl]-10*H*-phenothiazine (hereafter compound 62);

- 2-[2-(thiomorpholin-4-ylmethyl)-1,3-thiazol-4-yl]-10*H*-phenothiazine (hereafter compound 63);

- 2-{2-[(4-methyl-1,4 -diazepan-1-yl)methyl]-1,3-thiazol-4-yl}-10*H*-phenothiazine (hereafter compound 64);

- (3*R*)-1-{[4-(3,5-di-tert-butyl-4-hydroxyphenyl)-1,3-thiazol-2-yl]methyl}pyrrolidin-3-ol (hereafter compound 65);

- (3*S*)-1-{[4-(3,5-di-tert-butyl-4-hydroxyphenyl)-1,3-thiazol-2-yl]methyl}pyrrolidin-3-ol (hereafter compound 66);

- 2,6-di-*tert*-butyl-4-[2-(pyrrolidin-1-ylmethyl)-1,3-thiazol-4-yl]phenol (hereafter compound 67);

- 2,6-di-tert-butyl-4-{2-[(butylamino)methyl]-1,3-thiazol-4-yl}phenol (hereafter compound 68);

- 2-{2-[(4-ethylpiperazin-1-yl)methyl]-1,3-thiazol-4-yl}-10*H*-phenothiazine (hereafter compound 69);

- *N*-methyl-*N*-{[4-(10*H*-phenothiazin-2-yl)-1*H*-imidazol-2-yl]methyl}amine (hereafter compound 70);

- methyl [4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]methylcarbamate (hereafter compound 71);

- butyl [4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]methylcarbamate (hereafter compound 72);

- *N*-neopentyl-N-{[4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]methyl}amine (hereafter compound 73);

- 1-{[4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]methyl}piperidin-4-ol (hereafter compound 74);

- *N*-{[4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]methyl}acetamide (hereafter compound 75);

- *N*-{[4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]methyl}butanamide (hereafter compound 76);

- 2,6-di-*tert*-butyl-4-{2-[(4-propylpiperazin-1-yl)methyl]-1,3-thiazol-4-yl}phenol (hereafter compound 77);

- 2,6-di-*tert*-butyl-4-{2-[2-methyl-1-(methylamino)propyl]-1,3-thiazol-4-yl}phenol (hereafter compound 78);

- *N*, 2-dimethyl-1-[4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]propan-1-amine (hereafter compound 79);

- *N*-{[4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]methyl}hexanamide (hereafter compound 80);

- (3*R*)-1-{[4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]methyl}pyrrolidin-3-ol (hereafter compound 81);

- (3*S*)-1-{[4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]methyl}pyrrolidin-3-ol (hereafter compound 82);

- 1-{[4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]methyl}azetidin-3-ol (hereafter compound 83);

- 2-{2-[(4-propylpiperazin-1-yl)methyl]-1,3-thiazol-4-yl}-10*H*-phenothiazine (hereafter compound 84);

- 2-{2-[(4-acetylpiperazin-1-yl)methyl]-1,3-thiazol-4-yl}-10*H*-phenothiazine (hereafter compound 85);

- 2-{2-[(4-butylpiperazin-1-yl)methyl]-1,3-thiazol-4-yl}-10*H*-phenothiazine (hereafter compound 86);

- methyl 4-{[4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]methyl}piperazine-1-carboxylate (hereafter compound 87);

- 4-[2-(aminomethyl)-1H-imidazol-4-yl]-2,6-di-*tert*-butylphenol (hereafter compound 88);

- 4-{2-[(benzylamino)methyl]-1,3-thiazol-4-yl}-2,6-di-*tert*-butylphenol (hereafter compound 89);

- 4-{2-[(4-acetylpiperazin-1-yl)methyl]-1,3-thiazol-4-yl}-2,6-di-*tert*-butylphenol (hereafter compound 90);

- *N*-methyl-N-{[4-(10*H*-phenoxazin-2-yl)-1,3-thiazol-2-yl]methyl}amine (hereafter compound 91);

- 4-[2-(azetidin-1-ylmethyl)-1,3-thiazol-4-yl]-2,6-di-*tert*-butylphenol (hereafter compound 92);

- 2,6-di-*tert*-butyl-4-{2-[(4-butylpiperazin-1-yl)methyl]-1,3-thiazol-4-yl}phenol hereafter compound 93);

- butyl 2-[4-(3'-chloro-1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate (hereafter compound 94);

- butyl 2-[4-(3'-fluoro-1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate (hereafter compound 95);

- butyl 2-[4-(4-isobutylphenyl)-1*H*-imidazol-2-yl]ethylcarbamate (hereafter compound 96);

- benzyl 2-[4-(4-isobutylphenyl)-1*H*-imidazol-2-yl]ethylcarbamate (hereafter compound 97);

- butyl 2-[4-(3'-chloro-4'-fluoro-1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate (hereafter compound 98);

- butyl 2-[4-(3', 4'-dichloro-1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate (hereafter compound 99);

- butyl 2-[4-(4-propylphenyl)-1*H*-imidazol-2-yl]ethylcarbamate (hereafter compound 100);

- butyl 2-[4-(4-ethylphenyl)-1*H*-imidazol-2-yl]ethylcarbamate (hereafter compound 101);

- butyl 2-[4-(4'-cyano-1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate (hereafter compound 102);

- butyl 2-[4-(1,1'-biphenyl-4-yl)-5-ethyl-1*H*-imidazol-2-yl]ethylcarbamate (hereafter compound 104);

- butyl 2-[4-(2'-chloro-1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate (hereafter compound 105);

- butyl 2-[4-(2', 3'-difluoro-1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate (hereafter compound 106);

- butyl 2-[4-(2'-bromo-1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate (hereafter compound 107);

- butyl 2-[4-(3',5'-difluoro-1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate (hereafter compound 108);

- butyl 2-[4-(2'-methoxy-1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate (hereafter compound 109);

- butyl 2-[4-(3'-nitro-1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate (hereafter compound 110);

- butyl 2-[4-(2', 5'-difluoro-1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate (hereafter compound 111);

- butyl 2-[4-(3'-methoxy-1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate (hereafter compound 112);

- methyl 4-{[4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-1,3-thiazol-2-yl]methyl}piperazine-1-carboxylate (hereafter compound 113);

- methyl [4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-1,3-thiazol-2-yl]methylcarbamate (hereafter compound 114);

- *N*-{[4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-1,3-thiazol-2-yl]methyl}benzamide (hereafter compound 115);

- *N*-{[4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-1,3-thiazol-2-yl]methyl}-2-phenylacetamide (hereafter compound 116);

- *N*-{[4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-1,3-thiazol-2-yl]methyl}propanamide (hereafter compound 117);

- 1-{[4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-1,3-thiazol-2-yl]methyl}piperidin-4-yl acetate (hereafter compound 118);

- 1-{[4-(3,5-di-tert-butyl-4-hydroxyphenyl)-1,3-thiazol-2-yl]methyl}pyrrolidine-3,4-diol (hereafter compound 119);

and the salts of the latter.

In particular, the invention relates to compounds 1 to 112 and their salts, and in particular compounds 1 to 49 and their salts.

According to preferred variants of the invention, these compounds possess at least two of the activities mentioned above. In particular, they both inhibit the MAO's and trap the ROS's or they both have an antagonist activity vis-à-vis the sodium channels and an ROS trapping activity. In certain cases, the compounds of general formula **(I)** even combine the three activities.

According to a particular variant of the invention, the compounds of the invention are more especially intended to have an MAO and/or ROS inhibiting activity and they are then preferably chosen from compounds 1 to 28, 50 to 93 and 113 to 119 and the salts of these compounds (in particular from compounds 1 to 28 and 50 to 93 and the salts of these compounds, and in particular from compounds 1 to 28 and the salts of these compounds).

More preferentially, the compounds of the invention, when they are intended to have an MAO and/or ROS inhibiting activity, are chosen from compounds 1, 3, 6 to 8, 12, 13, 15, 16, 18 to 20, 22 to 28, 50 to 62, 64 to 71, 73 to 86, 89, 91 to 93 and 119 and the salts of these compounds (in particular from compounds 1, 3, 6 to 8, 12, 13, 15, 16, 18 to 20, 22 to 28, 50 to 62, 64 to 71, 73 to 86, 89 and 91 to 93 and the salts of these compounds, and in particular from compounds 1, 3, 6 to 8, 12, 13, 15, 16, 18 to 20 and 22 to 28 and the salts of these compounds).

Yet more preferentially, the compounds of the invention, when they are intended to have an MAO and/or ROS inhibiting activity, are chosen from compounds 1, 3, 6 to 8, 12, 13, 15, 16, 18 to 20, 22 to 24, 26, 28, 50 to 52, 54, 55, 57, 58, 61, 62, 65 to 69, 73, 75, 77 to 82, 86, 89, 91, 92 and 119 and the salts of these compounds (in particular from compounds 1, 3, 6 to 8, 12, 13, 15, 16, 18 to 20, 22 to 24, 26, 28, 50 to 52, 54, 55, 57, 58, 61, 62, 65 to 69, 73, 75, 77 to 82, 86, 89, 91 and 92 and the salts of these compounds, and in particular from compounds 1, 3, 6 to 8, 12, 13, 15, 16, 18 to 20, 22 to 24, 26 and 28 and the salts of these compounds).

In particular, the compounds of the invention, when they are intended to have an MAO and/or ROS inhibiting activity, are chosen from compounds 1, 3, 6, 15, 16, 18, 20, 23, 24, 26, 28, 50, 52, 55, 61, 65 to 69, 77, 78, 79, 81, 86, 89, 91, 92 and 119 and the salts of these compounds (in particular from compounds 1, 3, 6, 15, 16, 18, 20, 23, 24, 26, 28, 50, 52, 55, 61, 65 to 69, 77, 78, 79, 81, 86, 89, 91 and 92 and the salts of these compounds, and in particular from compounds 1, 3, 6, 15, 16, 18, 20, 23, 24, 26 and 28 and the salts of these compounds).

More particularly, the compounds of the invention, when they are intended to have an MAO and/or ROS inhibiting activity, are chosen from compounds 3, 15, 16, 20, 23, 26, 28, 50, 55, 61, 65 to 68, 78, 79, 91 and 92 and the salts of these compounds (in particular from compounds 3, 15, 16, 20, 23, 26 and 28 and the salts of these compounds).

Yet more particularly, the compounds of the invention, when they are intended to have an MAO and/or ROS inhibiting activity, are chosen from compounds 3, 15, 16, 28, 55, 61, 65, 66 and 79 and the salts of these compounds (in particular from compounds 3, 15, 16 and 28 and the salts of these compounds).

According to another variant of the invention, the compounds of the invention are more especially intended to have a modulating activity on sodium channels and they are then preferably chosen from compounds 1, 3, 5, 12, 15, 16, 29 to 35, 37 to 47, 49, 94 to 102 and 104 to 112 and the salts of these compounds (in particular from compounds 1, 3, 5, 12, 15, 16, 29 to 35, 37 to 47 and 49 and the salts of these compounds).

More preferentially, the compounds of the invention intended to have a modulating activity on sodium channels are chosen from compounds 3, 15, 16, 29 to 35, 37 to 47, 49, 94 to 102 and 104 to 112 and the salts of these compounds (in particular from compounds 1, 3, 5, 12, 15, 16, 29 to 35, 37 to 47 and 49 and the salts of these compounds).

Yet more preferentially, the compounds of general formula **(I)** intended to have a modulating activity on sodium channels are chosen from compounds 30, 37, 42, 44 to 46, 48, 49, 106, 108, 109 and 112 and the salts of these compounds (in particular from compounds 30, 37, 42, 44 to 46, 48 and 49 and the salts of these compounds).

Moreover, the compounds more especially intended to have an inhibiting activity on lipidic peroxidation are preferably chosen from compounds 1 to 28, 37, 38, 40, 50 to 93 and 113 to 119 and the salts of these compounds (in particular from compounds 1 to 28, 37, 38, 40 and 50 to 93 and the salts of these compounds, and in particular from compounds 1 to 28, 37, 38 and 40 and the salts of these compounds).

More preferentially, the compounds more especially intended to have an inhibiting activity on lipidic peroxidation are chosen from compounds 1 to 28, 50 to 62, 64 to 93 and 113 to 119 and the salts of these compounds (in particular from compounds 1 to 28, 50 to 62 and 64 to 93 and the salts of these compounds, and in particular from compounds 1 to 28 and the salts of these compounds).

Yet more preferentially, the compounds more especially intended to have an inhibiting activity on lipidic peroxidation are chosen from compounds 13, 18, 19, 22 to 27, 51 to 53, 55 to 60, 62, 64, 69, 73 to 76, 79, 81 to 86 and 91 and the salts of these compounds (in particular from compounds 13, 18, 19 and 22 to 27 and the salts of these compounds).

In particular, the compounds more especially intended to have an inhibiting activity on lipidic peroxidation are chosen from compounds 13, 23, 58, 64, 81, 82 and 91 and the salts of these compounds (in particular from compounds 13 and 23 and the salts of these compounds).

Moreover, the invention relates, as medicaments, to the selected compounds mentioned previously and their pharmaceutically acceptable salts. The invention also relates to compositions containing, as active ingredient, at least one of the selected compounds mentioned previously or a pharmaceutically acceptable salt of one of these compounds.

A subject of the invention is also the use of one of the selected compounds mentioned previously or of a pharmaceutically acceptable salt of one of these compounds for preparing a medicament intended to have at least one of the three following activities :

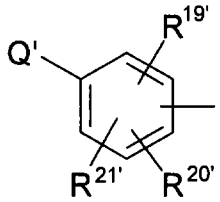
- inhibiting the monoamine oxidases, in particular monoamine oxidase B,
- inhibiting lipidic peroxidation,

- having a modulating activity vis-à-vis the sodium channels.

In particular, the invention relates to the use of one of the selected compounds mentioned previously or of a pharmaceutically acceptable salt of one of these compounds for preparing a medicament intended to treat one of the following disorders or diseases: Parkinson's disease, senile dementia, Alzheimer's disease, Huntington's chorea, amyotrophic lateral sclerosis, schizophrenia, depression, psychoses, migraine or pain and in particular neuropathic pain.

The invention moreover relates to the compounds of general formula **(I')**, a general formula identical to general formula **(I)** except that:

(a) either A is replaced by an A' radical



(A')

in which Q' represents a phenyl radical optionally substituted by one or more substituents chosen independently from a halogen atom, an OH, cyano, nitro, alkyl, haloalkyl, alkoxy, alkylthio or -$NR^{10'}R^{11'}$ radical and a group of two substituents representing together a methylene dioxy or ethylenedioxy radical,

$R^{10'}$ and $R^{11'}$ representing, independently, a hydrogen atom, an alkyl radical or a -$COR^{12'}$ group, or $R^{10'}$ and $R^{11'}$ forming together with the nitrogen atom an optionally substituted heterocycle containing 4 to 7 members and 1 to 3 heteroatoms including the nitrogen atom already present, the additional heteroatoms being chosen independently from the group constituted by the O, N and S atoms, said heterocycle being able to be for example azetidine, pyrrolidine, piperidine, piperazine, morpholine or thiomorpholine,
$R^{12'}$ representing a hydrogen atom, an alkyl or alkoxy or $NR^{13'}R^{14'}$ radical,
$R^{13'}$ and $R^{14'}$ representing, independently, a hydrogen atom or an alkyl radical, or $R^{13'}$ and $R^{14'}$ forming together with the nitrogen atom an optionally substituted heterocycle containing 4 to 7 members and 1 to 3 heteroatoms including the nitrogen atom already present, the additional heteroatoms being chosen independently from the group constituted by the O, N and S atoms, said heterocycle

being able to be for example azetidine, pyrrolidine, piperidine, piperazine, morpholine or thiomorpholine,

and $R^{19'}$, $R^{20'}$ and $R^{21'}$ represent, independently, a hydrogen, a halogen, the OH or $SR^{26'}$ group, or an alkyl, cycloalkyl, alkenyl, alkoxy, alkylthio, cyano, nitro, $-SO_2NHR^{49'}$, $-CONHR^{55'}$, $-S(O)_qR^{56'}$, $-NH(CO)R^{57'}$, $-CF_3$, $-OCF_3$ or $NR^{27'}R^{28'}$ radical,

$R^{26'}$ representing a hydrogen atom or an alkyl radical,

$R^{27'}$ and $R^{28'}$ representing, independently, a hydrogen atom, an alkyl radical or a $-COR^{29'}$ group, or $R^{27'}$ and $R^{28'}$ forming together with the nitrogen atom an optionally substituted heterocycle containing 4 to 7 members and 1 to 3 heteroatoms including the nitrogen atom already present, the additional heteroatoms being chosen independently from the group constituted by the O, N and S atoms, said heterocycle being able to be for example azetidine, pyrrolidine, piperidine, piperazine, morpholine or thiomorpholine,

$R^{49'}$ and $R^{55'}$ representing, independently each time they are involved, a hydrogen atom or an alkyl or alkylcarbonyl radical,

q representing an integer from 0 to 2,

$R^{56'}$ and $R^{57'}$ representing, independently each time they are involved, a hydrogen atom or an alkyl or alkoxy radical,

$R^{29'}$ representing a hydrogen atom, an alkyl, alkoxy or $-NR^{30'}R^{31'}$ radical,

$R^{30'}$ and $R^{31'}$ representing, independently, a hydrogen atom or an alkyl radical, or $R^{30'}$ and $R^{31'}$ forming together with the nitrogen atom an optionally substituted heterocycle containing 4 to 7 members and 1 to 3 heteroatoms including the nitrogen atom already present, the additional heteroatoms being chosen independently from the group constituted by the O, N and S atoms, said heterocycle being able to be for example azetidine, pyrrolidine, piperidine, piperazine, morpholine or thiomorpholine,

R^{51} being moreover replaced by a $R^{51'}$ radical, said $R^{51'}$ radical representing one of the radicals of the definition of R^{51} in general formula **(I)** or a haloalkyl radical,

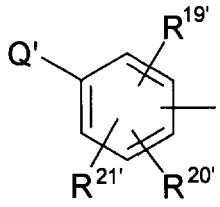
it being understood that either Q' represents a phenyl radical substituted by at least one haloalkyl radical, or at least one of Q', $R^{19'}$, $R^{20'}$ and $R^{21'}$ represents an alkylthio radical;

(b) or Ω is replaced by an Ω' radical, said Ω' radical representing an $NR^{46}R^{47}$ radical in which one of $R^{46'}$ and $R^{47'}$ represents a $-COOR^{51'}$ radical and the other represents a hydrogen atom, $R^{51'}$ representing a haloalkyl radical;

and the salts of said compounds.

In particular, this aspect of the invention relates to the compounds of general formula **(I')**, a general formula identical to general formula **(I)** except that:

(a) either A is replaced by an A' radical



(A')

in which Q' represents a phenyl radical optionally substituted by one or more substituents chosen independently from a halogen atom, an OH, cyano, nitro, alkyl, alkoxy, alkylthio or -$NR^{10'}R^{11'}$ radical and a group of two substituents representing together a methylene dioxy or ethylenedioxy radical,

$R^{10'}$ and $R^{11'}$ representing, independently, a hydrogen atom, an alkyl radical or a -$COR^{12'}$ group, or $R^{10'}$ and $R^{11'}$ forming together with the nitrogen atom an optionally substituted heterocycle containing 4 to 7 members and 1 to 3 heteroatoms including the nitrogen atom already present, the additional heteroatoms being chosen independently from the group constituted by the O, N and S atoms, said heterocycle being able to be for example azetidine, pyrrolidine, piperidine, piperazine, morpholine or thiomorpholine,

$R^{12'}$ representing a hydrogen atom, an alkyl or alkoxy or $NR^{13'}R^{14'}$ radical,

$R^{13'}$ and $R^{14'}$ representing, independently, a hydrogen atom or an alkyl radical, or $R^{13'}$ and $R^{14'}$ forming together with the nitrogen atom an optionally substituted heterocycle containing 4 to 7 members and 1 to 3 heteroatoms including the nitrogen atom already present, the additional heteroatoms being chosen independently from the group constituted by the O, N and S atoms, said heterocycle being able to be for example azetidine, pyrrolidine, piperidine, piperazine, morpholine or thiomorpholine,

and $R^{19'}$, $R^{20'}$ and $R^{21'}$ represent, independently, a hydrogen, a halogen, the OH or $SR^{26'}$ group, or an alkyl, cycloalkyl, alkenyl, alkoxy, alkylthio, cyano, nitro, -$SO_2NHR^{49'}$, -$CONHR^{55'}$, -$S(O)_qR^{56'}$, -$NH(CO)R^{57'}$, -CF_3, -OCF_3 or $NR^{27'}R^{28'}$ radical,

$R^{26'}$ representing a hydrogen atom or an alkyl radical,

$R^{27'}$ and $R^{28'}$ representing, independently, a hydrogen atom, an alkyl radical or a -$COR^{29'}$ group, or $R^{27'}$ and $R^{28'}$ forming together with the nitrogen atom an optionally substituted heterocycle containing 4 to 7 members and 1 to 3 heteroatoms

including the nitrogen atom already present, the additional heteroatoms being chosen independently from the group constituted by the O, N and S atoms, said heterocycle being able to be for example azetidine, pyrrolidine, piperidine, piperazine, morpholine or thiomorpholine,

$R^{49'}$ and $R^{55'}$ representing, independently each time they are involved, a hydrogen atom or an alkyl or alkylcarbonyl radical,

q representing an integer from 0 to 2,

$R^{56'}$ and $R^{57'}$ representing, independently each time they are involved, a hydrogen atom or an alkyl or alkoxy radical,

$R^{29'}$ representing a hydrogen atom, an alkyl, alkoxy or $-NR^{30'}R^{31'}$ radical,

$R^{30'}$ and $R^{31'}$ representing, independently, a hydrogen atom or an alkyl radical, or $R^{30'}$ and $R^{31'}$ forming together with the nitrogen atom an optionally substituted heterocycle containing 4 to 7 members and 1 to 3 heteroatoms including the nitrogen atom already present, the additional heteroatoms being chosen independently from the group constituted by the O, N and S atoms, said heterocycle being able to be for example azetidine, pyrrolidine, piperidine, piperazine, morpholine or thiomorpholine,

R^{51} being moreover replaced by a $R^{51'}$ radical, said $R^{51'}$ radical representing one of the radicals of the definition of R^{51} in general formula **(I)** or a haloalkyl radical,

it being understood that at least one of Q', $R^{19'}$, $R^{20'}$ and $R^{21'}$ represents an alkylthio radical;

(b) or Ω is replaced by an Ω' radical, said Ω' radical representing an $NR^{46}R^{47}$ radical in which one of $R^{46'}$ and $R^{47'}$ represents a $-COOR^{51'}$ radical and the other represents a hydrogen atom, $R^{51'}$ representing a haloalkyl radical;

and the salts of said compounds.

In case (a), the compounds of general formula **(I')** are preferably such that n represents 0 or 1 and Ω represents an $NR^{46}R^{47}$ radical (one of R^{46} and R^{47} preferably representing a $COOR^{51}$ radical when n = 1). Similarly, R^1 and R^2 are preferably chosen independently from the group constituted by a hydrogen atom and an alkyl or cycloalkyl radical (and preferably a methyl radical). Still preferably for case (a), the compounds of general formula **(I')** correspond to one of general sub-formulae $(I)_1$ or $(I)_2$, X preferably representing S or NH, and more preferentially NH. Moreover, the alkylthio radical is preferably an ethylthio or methylthio radical, more preferentially a methylthio radical.

In case (b), the compounds of general formula **(I')** are preferably such that n represents 0 or 1 (and preferably 1). Similarly, R^1 and R^2 are preferably hydrogen atoms.

Moreover, still in case (b), the haloalkyl radical is preferably a radical exclusively substituted by one or more fluorine atoms (for example the 4,4,4-trifluorobutyl radical) . Still preferably for case (b), the compounds of general formula **(I')** correspond to one of general sub-formulae $(I)_1$ or $(I)_2$, X preferably representing S or NH, and more preferentially NH.

The invention therefore also relates in particular to the following compounds of general formula **(I')** :

- butyl 2-{4-[4'-(methylthio)-1,1'-biphenyl-4-yl]-1H-imidazol-2-yl}ethylcarbamate;

- 4,4,4-trifluorobutyl 2-[4-(4-pyrrolidin-1-ylphenyl)-1*H*-imidazol-2-yl]ethylcarbamate;

- butyl 2-{4-[4'-(trifluoromethyl)-1,1'-biphenyl-4-yl]-1H-imidazol-2-yl}ethylcarbamate;

and the salts of said compounds;

and in particular:

- butyl 2-{4-[4'-(methylthio)-1,1'-biphenyl-4-yl]-1H-imidazol-2-yl}ethylcarbamate;

- 4,4,4-trifluorobutyl 2-[4-(4-pyrrolidin-1-ylphenyl)-1*H*-imidazol-2-yl]ethylcarbamate;

and the salts of said compounds;

Moreover, the invention relates, as medicaments, to the compounds of general formula **(I')** defined previously and their pharmaceutically acceptable salts. The invention also relates to compositions containing, as active ingredient, at least one of the compounds of general formula **(I')** defined previously or a pharmaceutically acceptable salt of one of these compounds.

A subject of the invention is also the use of one of the compounds of general formula **(I')** defined previously or of a pharmaceutically acceptable salt of one of these compounds for preparing a medicament intended to have at least one of the three following activities :

- inhibiting the monoamine oxidases, in particular monoamine oxidase B,
- inhibiting lipidic peroxidation,
- having a modulating activity vis-à-vis the sodium channels.

In particular, the invention relates to the use of one of the compounds of general formula **(I')** defined previously or of a pharmaceutically acceptable salt of one of these compounds for preparing a medicament intended to treat one of the following disorders

or diseases: Parkinson's disease, senile dementia, Alzheimer's disease, Huntington's chorea, amyotrophic lateral sclerosis, schizophrenia, depression, psychoses, migraine or pain and in particular neuropathic pain.

In certain cases, the compounds according to the present invention can contain asymmetrical carbon atoms. As a result, the compounds according to the present invention have two possible enantiomeric forms, i.e. the "R" and "S" configurations. The present invention includes the two enantiomeric forms and all combinations of these forms, including the "RS" racemic mixtures. In an effort to simplify matters, when no specific configuration is indicated in the structural formulae or names of the compounds, it should be understood that the two enantiomeric forms and their mixtures are represented.

The invention also relates, as medicaments, to the compounds mentioned previously or their pharmaceutically acceptable salts. It relates similarly to pharmaceutical compositions containing, as active ingredient, said compounds or their pharmaceutically acceptable salts as well as the use of these same compounds or of their pharmaceutically acceptable salts for preparing a medicament intended to inhibit the monoamine oxidases, in particular monoamine oxidase B, to inhibit lipidic peroxidation, having a modulating activity vis-à-vis the sodium channels or to possess two of the three, or the three abovementioned activities.

In particular, the compounds of the invention can be used for preparing a medicament intended to treat one of the following disorders or diseases: Parkinson's disease, senile dementia, Alzheimer's disease, Huntington's chorea, amyotrophic lateral sclerosis, schizophrenia, depression, psychoses, migraine or pain and in particular neuropathic pain. More particularly, the compounds presented as inhibiting the MAO's and/or the ROS's can be used for treating one of the following disorders or diseases: Parkinson's disease, senile dementia, Alzheimer's disease, Huntington's chorea, amyotrophic lateral sclerosis, schizophrenia, depression and psychoses; and the compounds presented as having a modulating activity 0n sodium channels can be used for treating one of the following disorders or diseases: Parkinson's disease, Alzheimer's disease, amyotrophic lateral sclerosis, migraine or pain and in particular neuropathic pain.

By salt, is meant in particular in the present Application the addition salts of inorganic or organic acids as well as the salts formed from bases.

By pharmaceutically acceptable salt, is meant in particular addition salts of inorganic acids such as hydrochloride, hydrobromide, hydroiodide, sulphate, phosphate, diphosphate and nitrate or organic acids such as acetate, maleate, fumarate, tartrate,

succinate, citrate, lactate, methanesulphonate, p-toluenesulphonate, pamoate and stearate. The salts formed from bases such as sodium or potassium hydroxide also fall within the scope of the present invention, when they can be used. For other examples of pharmaceutically acceptable salts, reference can be made to "Salt selection for basic drugs", *Int. J. Pharm.* (1986), **33**, 201-217.

The pharmaceutical composition can be in the form of a solid, for example powders, granules, tablets, gelatin capsules, liposomes or suppositories. Appropriate solid supports can be, for example, calcium phosphate, magnesium stearate, talc, the sugars, lactose, dextrin, starch, gelatin, cellulose, methyl cellulose, sodium carboxymethyl cellulose, polyvinylpyrrolidine and wax.

The pharmaceutical compositions containing a compound of the invention can also be presented in liquid form, for example, solutions, emulsions, suspensions or syrups. Appropriate liquid supports can be, for example, water, organic solvents such as glycerol or the glycols, as well as their mixtures, in varying proportions, in water.

The administration of a medicament according to the invention can be done by topical, oral, parenteral route, by intramuscular injection, etc.

The administration dose envisaged for medicaments according to the invention is comprised between 0.1 mg to 10 g depending on the type of active compound used.

According to the invention, the compounds of general formula **(I)** can be prepared by the processes described below.

PREPARATION OF THE COMPOUNDS OF THE INVENTION:

General information

The preparations of the compounds of the invention in which Ω represents OH are carried out in an analogous manner to those described in PCT Patent Application WO 99/09829 and European Patent Application EP 432,740.

With respect to the compounds of the invention in which Het is an imidazole ring, a person skilled in the art can also usefully consult PCT Patent Application WO 99/64401.

The preparations of the other compounds of the invention are carried out in an analogous manner to those described in PCT Patent Application WO 98/58934 (*cf. in particular on pages 39 to 45 of this document the syntheses of the intermediates of general formulae (XXV) and (XXVIII)*) or according to the procedures described hereafter.

Moreover, the compounds of general formula **(I')** are prepared in an analogous manner to that of the compounds of general formula **(I)**; the teaching of the disclosure which follows for the compounds of general formula **(I)** can generally be extended to the synthesis of the compounds of general formula **(I')**.

Preparation of the compounds of general formula (I)

The compounds of general formula **(I)** can be prepared by the 8 synthesis routes illustrated below (Diagram 1) from the intermediates of general formulae **(IV)**, **(V)**, **(VI)**, **(VII)**, **(VIII)**, **(IX)**, **(X)** and **(I)*a*** in which A, B, Ω, R^1, R^2, Het and n are as defined above, L is a leaving group such as for example a halogen, Alk is an alkyl radical, Gp is a protective group for an amine function, for example a 2-(trimethylsilyl)ethoxymethyl (SEM) group, and Gp' a protective group for an alcohol function, for example a benzyl, acetate or also silyl type group such as *tert*-butyldimethylsilyl, and finally Λ represents a bond or a $-(CH_2)_x-$, $-CO-(CH_2)_x-$, $-(CH_2)_y-O-$ or –C(=NH)- radical. Of course, a person skilled in the art can choose to use other protective groups Gp and Gp' from those known to him, and in particular those mentioned in: *Protective groups in organic synthesis*, 2nd ed., (John Wiley & Sons Inc., 1991).

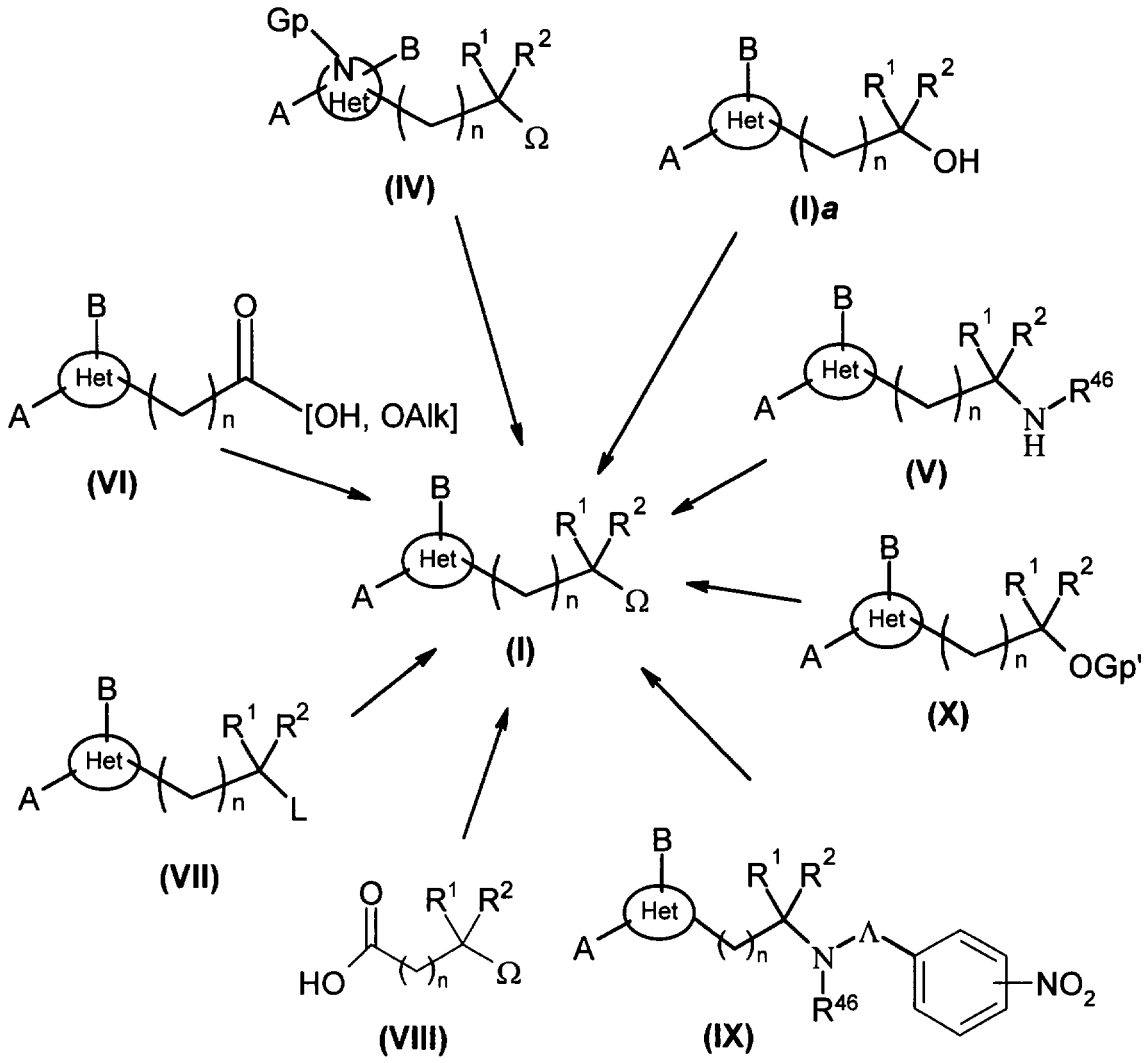


Diagram 1

Route 1: Het is imidazole and Ω is $NR^{46}R^{47}$ but not a carbamate type radical

The amines and the carboxamides of general formula **(I)**, Diagram 2, in which A, B, R^1, R^2, R^{46}, R^{47}, Het and n are as defined above, are prepared by deprotection for example, in the case where Gp represents SEM, with *tert*-butylammonium fluoride (TBAF) in THF, of the amine of general formula **(IV)** in order to release the amine from the heterocycle of the compound of general formula **(I)**. The protected amines of general formula **(IV)** are accessible by a general synthesis route described in *Biorg. and Med. Chem. Lett.*, 1993, **3,** 915 and *Tetrahedron Lett.*, 1993. **34**, 1901 and more particularly in PCT Patent Application WO 98/58934.

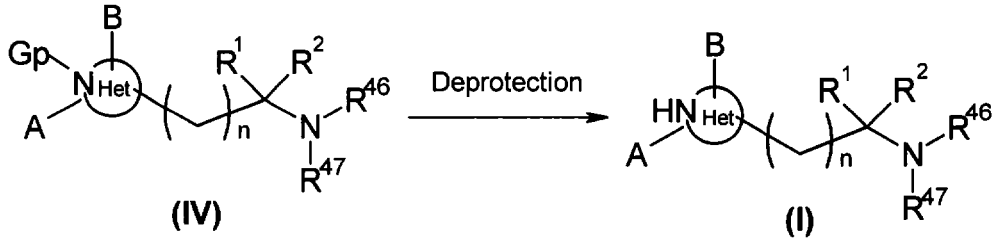


Diagram 2

Route 2: Het is imidazole, oxazole or thiazole and Ω is $NR^{46}R^{47}$

The amines and the carboxamides of general formula **(I)**, Diagram 3, in which A, B, R^1, R^2, R^{46}, Het, g, k and n are as defined above, Δ represents an alkyl, cycloalkylalkyl, arylalkyl, aryl, allenyl, allenylalkyl, alkenyl, alkynyl, cyanoalkyl or hydroxyalkyl radical and Δ' represents an alkyl, cycloalkylalkyl, arylalkyl or aryl radical when g or k does not represent 0, or Δ' represents an alkyl, cycloalkylalkyl, arylalkyl radical or an aryl radical preferably deactivated (i.e. an aryl radical substituted by an electron-attracting group such as for example a nitro or cyano group) when g or k represents 0, are prepared by condensation of the amines of general formula **(V)** with the carboxylic acids (or the corresponding acid chlorides) of general formula **(XIII)** under standard peptide synthesis conditions, with the aldehydes of general formula **(XII)** in the presence of a reducing agent such as sodium triacetoxyborohydride or sodium borohydride, in a lower aliphatic alcohol such as methanol and optionally in the presence of molecular sieves, or with the halogenated derivatives (Hal = halogen atom) of general formula **(XI)**. In particular, when Δ represents an allenyl, allenylalkyl, alkenyl, alkynyl, cyanoalkyl or hydroxyalkyl radical, the compounds of general formula **(V)** are converted to the corresponding compounds of general formula **(I)** by reaction with the halogenated derivatives of general formula **(XI)** in a solvent such as acetonitrile, dichloromethane or acetone and in the presence of a base such as for example triethylamine or potassium carbonate at a temperature comprised between ambient temperature and the reflux temperature of the solvent.

The derivatives of general formula **(V)** are in particular accessible by a general synthesis route described in *Biorg. and Med. Chem. Lett.*, 1993, **3**, 915 and *Tetrahedron Lett.*, 1993. **34**, 1901, and more particularly in Patent Application WO 98/58934. When R^{46} = H, the compounds of general formula **(V)** can be prepared, for example, according to a protocol described in Patent Application WO 98/58934 (using the appropriate amino acid in the place of N-Boc-sarcosinamide).

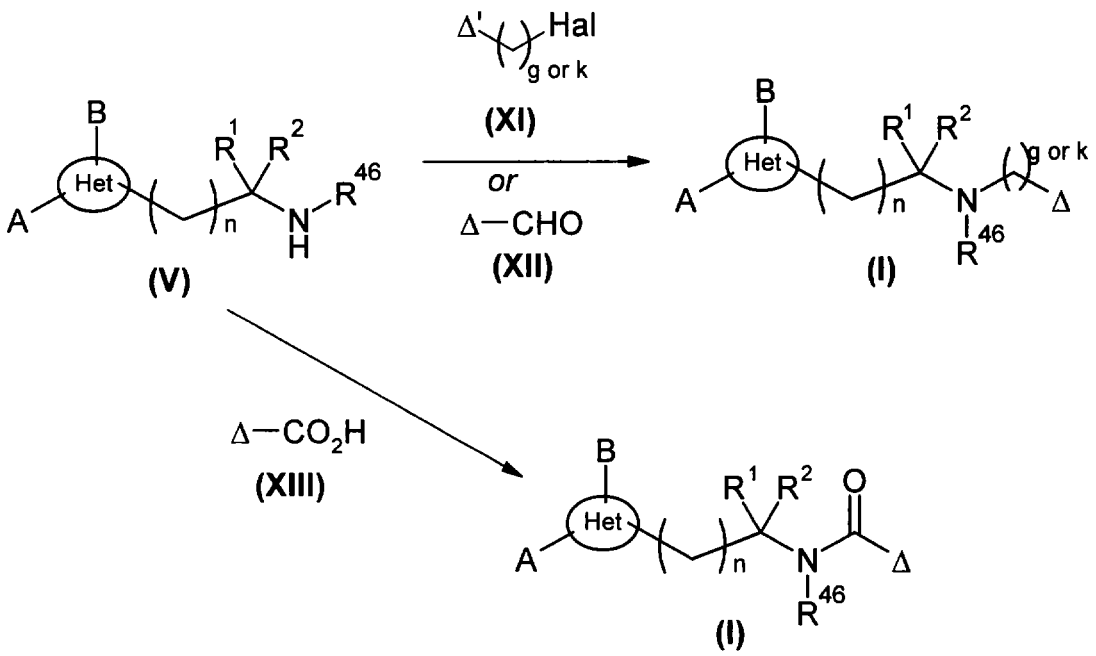


Diagram 3

In the particular case where R^{47} represents a cycloalkyl radical, the amines of general formula **(I)**, Diagram 3*a*, in which A, B, R^1, R^2, R^{46}, Het and n are as defined above and i represents an integer from 0 to 4 are prepared by condensation of the amines of general formula **(V)** with the cycloalkylketones of general formula **(XIV)** in the presence of a reducing agent such as sodium triacetoxyborohydride or sodium borohydride in a lower aliphatic alcohol such as methanol and optionally in the presence of molecular sieves at ambient temperature.

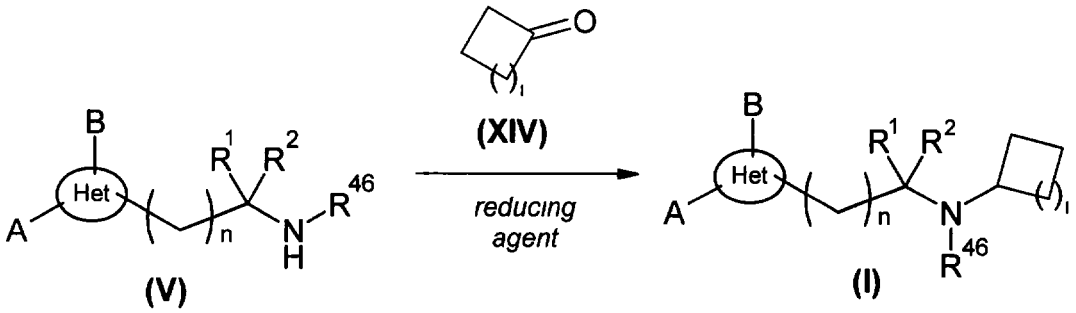


Diagram 3*a*

The sulphonamides of general formula **(I)**, Diagram 3*b*, in which A, B, R^1, R^2, R^{46}, Het and n are as defined above, R^{47} represents an $-SO_2-\Delta$ radical and Δ represents an alkyl, cycloalkyl, cycloalkylalkyl or arylalkyl radical, are prepared by condensation of the amines of general formula **(V)** with the sulphochlorides of general formula **(XV)** under

standard conditions, for example in a solvent such as dimethylformamide at ambient temperature.

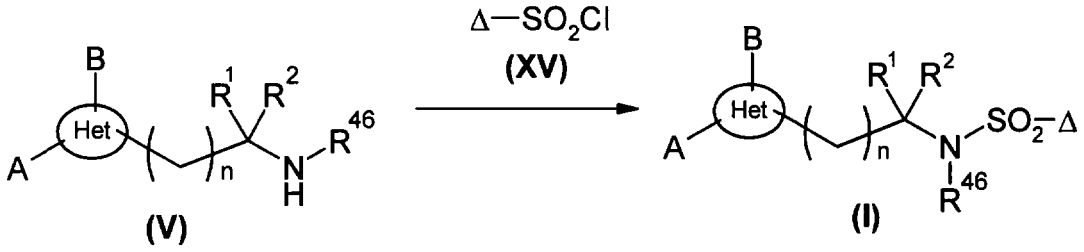


Diagram 3*b*

The ureas of general formula **(I)**, Diagram 3*c*, in which A, B, R^1, R^2, R^{46}, Het and n are as defined above, R^{47} represents a -CO-NH-Δ radical and Δ represents an alkyl, cycloalkyl, cycloalkylalkyl or arylalkyl radical, are prepared by reaction of the amines of general formula **(V)** with the isocyanates of general formula **(XVI)** in an inert solvent such as dichloromethane or 1,2-dichloroethane.

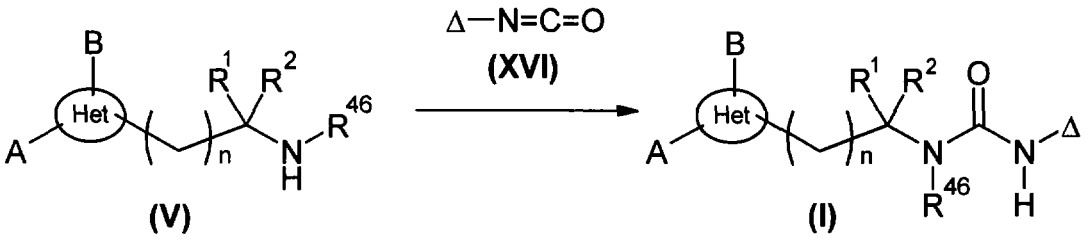


Diagram 3*c*

Route 3: Het is oxazole or thiazole, R^1 and R^2 are both H and Ω is OH.

The alcohol derivatives of general formula **(I)**, Diagram 4, in which A, B, Het and n are as defined above and R^1 and R^2 are hydrogen atoms are obtained by reduction of the acids or esters of general formula **(VI)** (accessible by a general synthesis route described in *J.Med Chem.*, 1996, **39,** 237-245 and PCT Patent Application WO 99/09829). This reduction can, for example, be carried out by the action of boron or lithium aluminium hydride or also of diisobutylaluminium hydride in an aprotic polar solvent such as tetrahydrofuran.

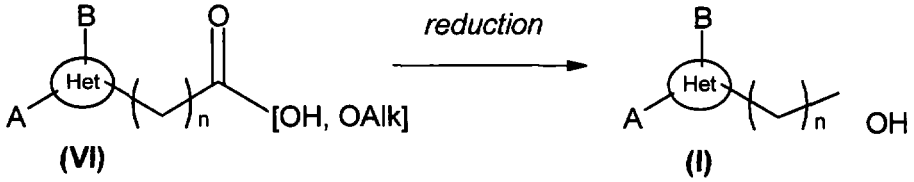


Diagram 4

Route 4: Het is oxazole or thiazole and Ω is $NR^{46}R^{47}$

The amines of general formula **(I)**, Diagram 5, in which A, B, R^1, R^2, R^{46}, R^{47}, Het, and n are as defined above, are prepared by condensation of the primary or secondary amines of general formula R^{46}-NHR^{47} with the compounds of general formula **(VII)** (in which L preferably represents a halogen atom Hal, but can also represent a mesylate or tosylate group) according to a general synthesis route described in *J. Med. Chem.*, 1996, **39,** 237-245 and PCT Patent Application WO 99/09829 or US Patent 4,123,529. This synthesis route can in particular be used when R^{46} and R^{47} taken together form with the nitrogen atom which carries them a non-aromatic heterocycle with 4 to 8 members. The reaction typically takes place in an anhydrous solvent (for example dimethylformamide, dichloromethane, tetrahydrofuran or acetone) in the presence of a base (for example Na_2CO_3 or K_2CO_3 in the presence of triethylamine), and preferably while heating.



Diagram 5

Route 5: Het is imidazole and Ω is a carbamate-type radical

When Ω is a carbamate-type radical, the acids of general formula **(VIII)** can be cyclized in the form of imidazole derivatives of general formula **(I)**, Diagram 6, by the addition of caesium carbonate followed by condensation with an α-halogenoketone of formula A-CO-CH(B)-[Br, Cl] followed by the addition of a large excess of ammonium acetate (for example 15 or 20 equivalents per equivalent of acid of general formula **(VIII)**). This reaction is preferably carried out in a mixture of xylenes and while heating (it is also possible, if appropriate, to simultaneously eliminate the water formed during the reaction).

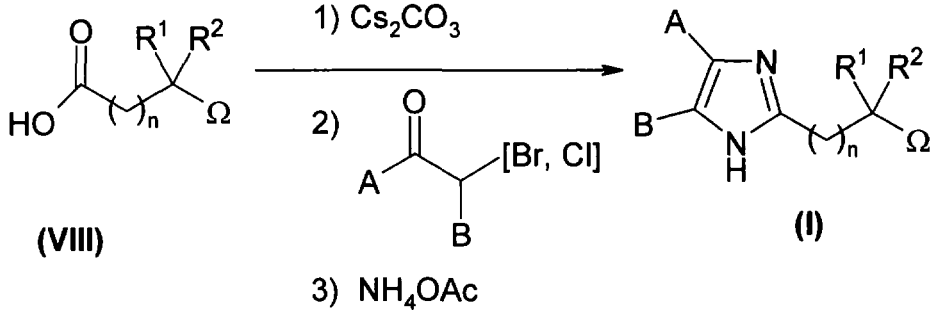


Diagram 6

Route 6: Het is imidazole, oxazole or thiazole and Ω is $NR^{46}R^{47}$

When Ω is an $NR^{46}R^{47}$ radical in which R^{47} is a radical comprising an aminophenylene, alkylaminophenylene or dialkylaminophenylene type termination, the compounds of general formula **(I)**, in which A, B, Het, n, R^1, R^2 and R^{46} are as defined above and Λ represents a bond or a $-(CH_2)_x-$, $-CO-(CH_2)_x-$, $-(CH_2)_y-O-$ or $-C(=NH)-$ radical, x and y being integers from 0 to 6, can be obtained, Diagram 7, by reduction of the compound of general formula **(IX)**, for example by the action of hydrogen in the presence of a palladium on carbon type catalyst in a solvent such as for example methanol, ethanol, dichloromethane or tetrahydrofuran. The reduction of the nitro function can also be carried out, for example, while heating the product in an appropriate solvent such as ethyl acetate with a little ethanol in the presence of $SnCl_2$ (*J. Heterocyclic Chem.* (1987), **24**, 927-930; *Tetrahedron Letters* (1984), **25** (8), 839-842) or in the presence of $SnCl_2$ / Zn (*Synthesis* (1996), 9.1076-1078), using $NaBH_4$-$BiCl_3$ (*Synth. Com.* (1995) 25 (23), 3799-3803) in a solvent such as ethanol, or then by using Raney Ni to which hydrazine hydrate has been added (*Monatshefte für Chemie*, (1995), 126, 725-732), or also using indium in a mixture of ethanol and ammonium chloride at reflux (*Synlett (1998) 9,* 1028).

When R^{47} is an aminophenylene, alkylaminophenylene or dialkylaminophenylene type radical (Alk and Alk' are identical or different alkyl radicals), the compound of general formula **(IX)** is reduced in order to produce the aniline derivative of general formula **(I)** and optionally mono- or di-alkylated according to standard reactions known to a person skilled in the art. The mono-alkylation is carried out by reducing amination with an aldehyde or by nucleophilic substitution by reaction with a equivalent of halogenoalkyl Alk-Hal. A second alkylation can then be optionally carried out by means of a halogenoalkyl Alk'-Hal.

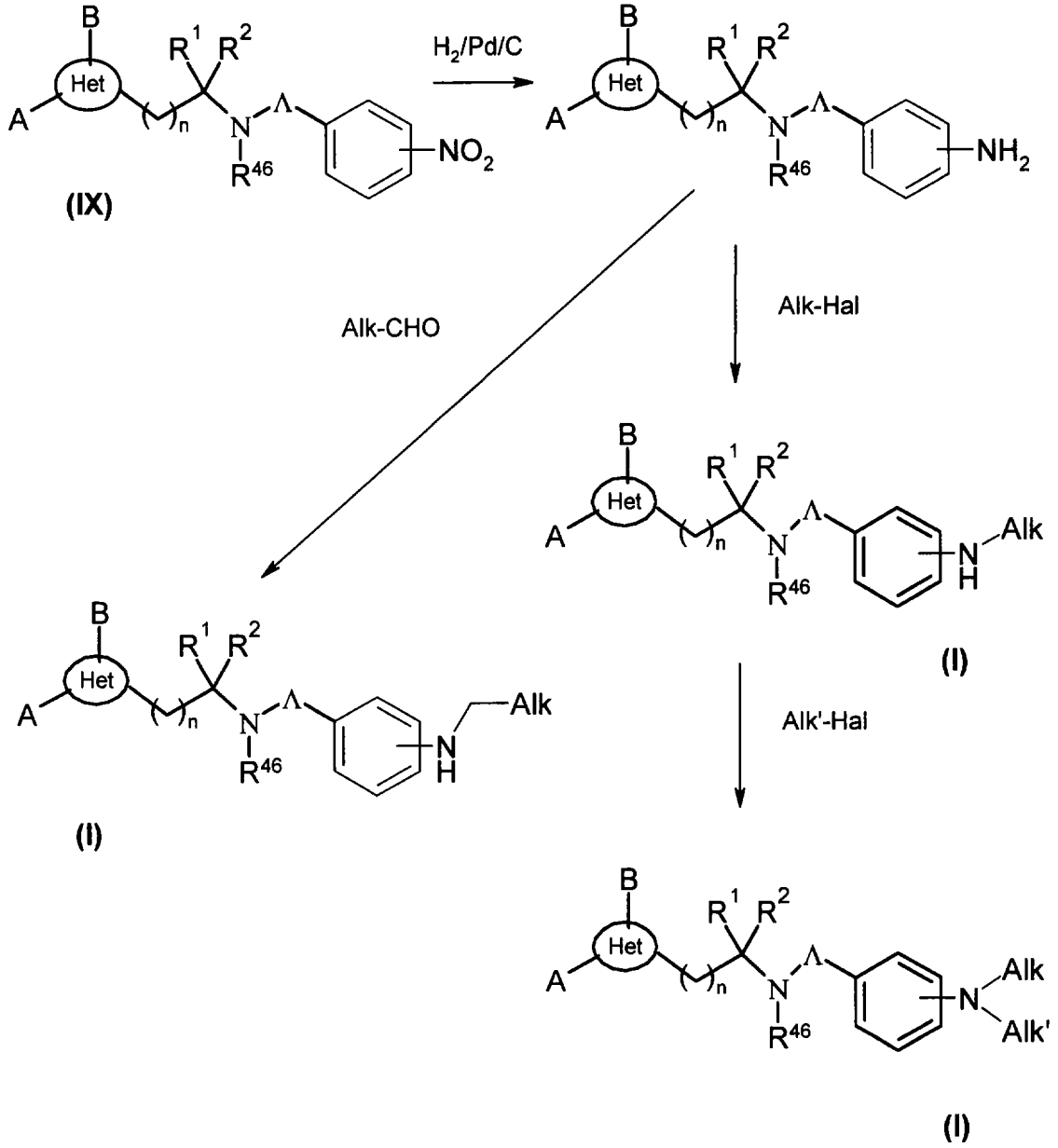


Diagram 7

In the particular case where Alk = Alk' = $-CH_3$ and where Λ does not represent $-CH_2-$, the nitro derivative of general formula **(IX)** is treated with appropriate quantities of paraformaldehyde under a flow of hydrogen in a solvent such as ethanol and in the presence of a palladium on carbon type catalyst (Diagram 7*a*).

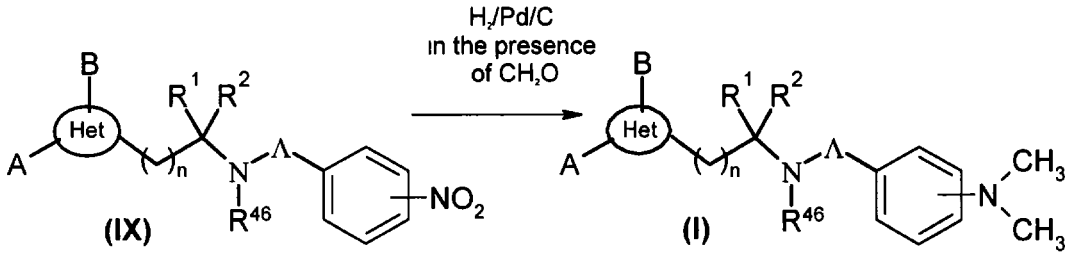


Diagram 7*a*

Route 7: Het is imidazole, oxazole or thiazole and Ω is OH

This route can be used when Ω is OH. Unlike Route 3, R^1 and R^2 cannot be hydrogen atoms. In this case, the compounds of general formula **(I)** can be obtained, Diagram 8, by deprotection of the protected alcohol of general formula **(X)**.

In the case where Gp' is a silyl-type protective group, the deprotection can be carried out, for example, by adding tetra-*tert*-butylammonium fluoride to a solvent such as tetrahydrofuran. In the case where Gp' is a benzyl-type protective group, the deprotection is carried out by hydrogenation in a solvent such as for example methanol, ethanol, dichloromethane or tetrahydrofuran. In the case where Gp' is an acetate-type protective group, the deprotection can be carried out, for example, using sodium or potassium carbonate in an alcoholic solvent such as methanol. In other cases, a person skilled in the art will usefully consult the following document: *Protective groups in organic synthesis*, 2nd ed., (John Wiley & Sons Inc., 1991).

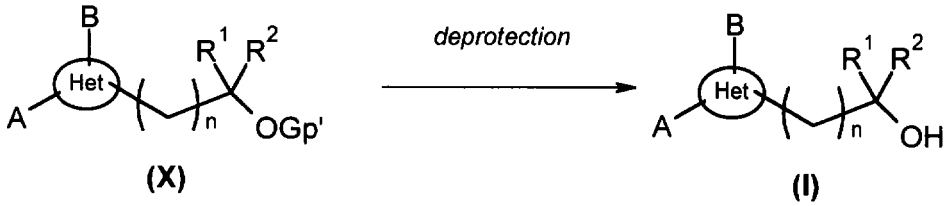


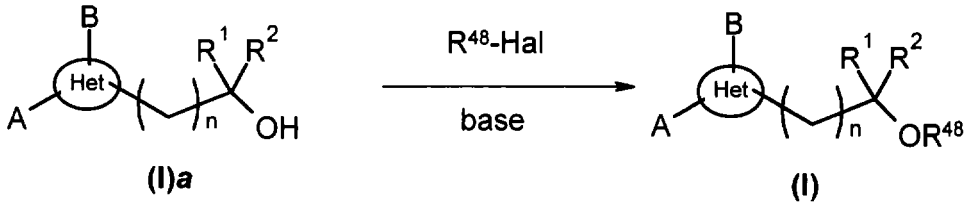
Diagram 8

Route 8: Het is imidazole, oxazole or thiazole and Ω is OR^{48} with $R^{48} \neq H$

The compounds of general formula **(I)** in which Ω is an OR^{48} radical with $R^{48} \neq H$ are obtained, for example, Diagram 9, from the alcohols of general formula **(I)*a*** (which are compounds of general formula **(I)** as defined previously in which Ω represents OH) by reaction of the latter with a halide of general formula R^{48}-Hal (Hal = Br, Cl or I) in a solvent such as dichloromethane, acetonitrile,

anhydrous tetrahydrofuran or anhydrous ether and in the presence of a base such as potassium or sodium carbonate, sodium hydride or triethylamine.

In the case where the A, B, R^1 and R^2 radicals comprise alcohol, phenol, amine or aniline functions, it can be necessary to add protection / deprotection stages of these functions according to standard methods known to a person skilled in the art (stages not represented in Diagram 9).



(I)*a* **(I)**

Diagram 9

Preparation of synthesis intermediates

Preparation of the imidazoles and thiazoles of general formula (V)

General Diagram

The non-commercial ketone derivative of general formula **(V.i)** or $(\mathbf{V.i})_2$ in which A and B are as defined in general formula **(I)** is converted, Diagram 3.1, to the corresponding α-bromo-ketone of general formula **(V.ii)** or $(\mathbf{V.ii})_2$ by reaction with a bromination agent such as $CuBr_2$ (*J. Org. Chem.* (1964), **29**, 3459), bromine (*J. Het. Chem.* (1988), **25**, 337), N-bromosuccinimide (*J. Amer. Chem. Soc.* (1980), **102**, 2838) in the presence of acetic acid in a solvent such as ethyl acetate or dichloromethane, HBr or Br_2 in ether, ethanol or acetic acid (*Biorg. Med. Chem. Lett.* (1996), **6**(3), 253-258; *J. Med. Chem.* (1988), **31**(10), 1910-1918; *J. Am. Chem. Soc.* (1999), **121**, 24) or also using a bromination resin (*J. Macromol. Sci. Chem.* (1977), **A11**, (3) 507-514). In the particular case where A is a p-dimethylaminophenyl radical, it is possible to use the operating method figuring in the publication *Tetrahedron Lett.*, 1998, **39** (28), 4987. The amine of general formula **(V)** is then obtained according to the procedures represented in Diagrams 3.2 (imidazoles) and 3.3 (thiazoles) hereafter.

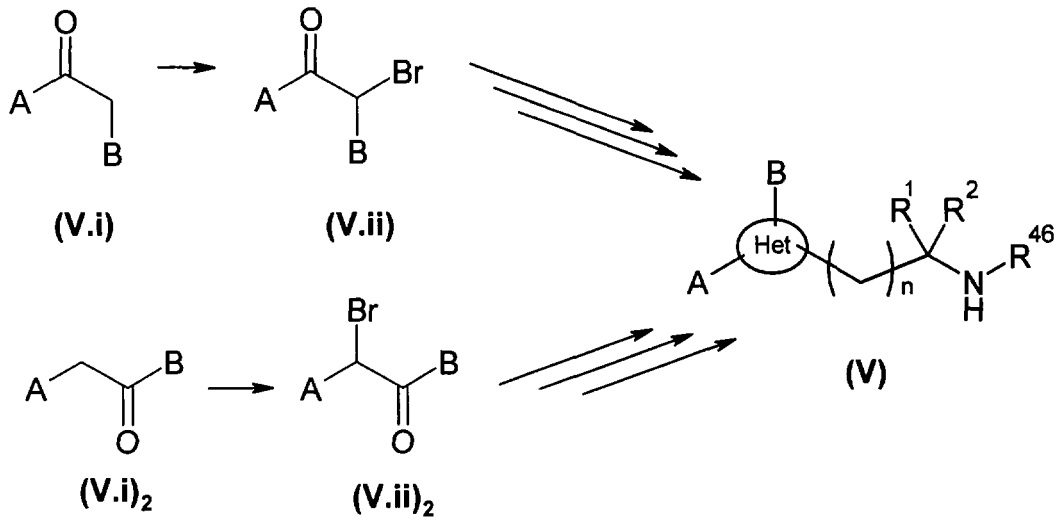


Diagram 3.1

Alternatively to the synthesis presented in Diagram 3.1, a person skilled in the art can optionally use an α-chloro-ketone in the place of an α-bromo-ketone.

Obtaining the imidazoles of general formula (V)

The acid of general formula **(V.iii),** in which Gp represents a protective group for an amine function, for example a protective group of carbamate type, is treated, Diagram 3.2, with Cs_2CO_3 in a solvent such as methanol or ethanol. The α-halogeno-ketone of general formula **(V.ii)** in an inert solvent such as dimethylformamide is added. to the caesium salt recovered. The intermediate ketoester cyclized by heating to reflux in xylene (mixture of isomers) in the presence of a large excess of ammonium acetate (15 or 20 equivalents for example) in order to produce the imidazole derivative of general formula **(V.iv)** (the water formed being optionally eliminated during the reaction).

In the case where R^{38} is not H, the amine function of the imidazole ring of the compound of general formula **(V.iv)** is substituted by reaction with the halogenated derivative R^{38}-Hal (Hal = halogen atom); the protected amine function is then deprotected under standard conditions (for example: trifluoroacetic acid or HCl in an organic solvent when it is a carbamate-type protective group, or also hydrogenation in the presence of palladium on carbon when the protective group is a benzyl carbamate).

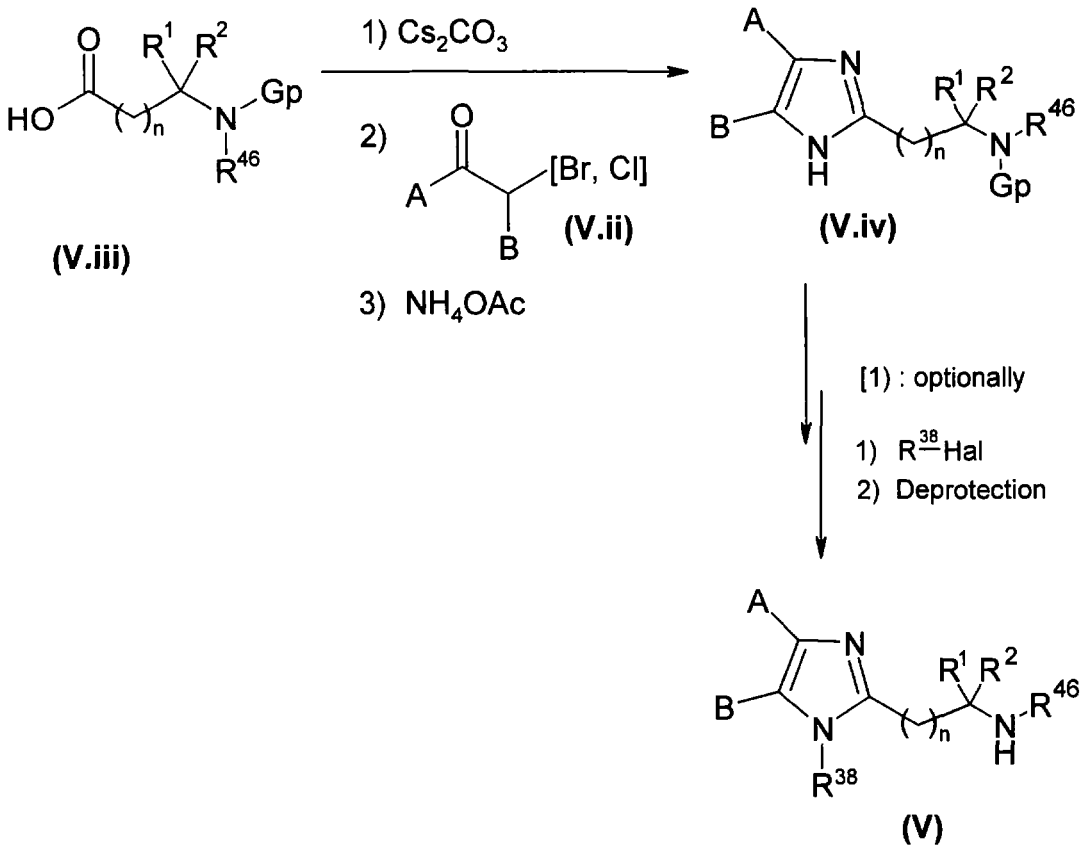


Diagram 3.2

Obtaining the thiazoles of general formula (V) intended for the preparation of compounds of general formula $(I)_1$ or $(I)_2$:

The thiocarboxamide of general formula **(V.v)**, in which Gp represents a protective group for an amine function, for example a carbamate-type protective group, obtained for example by reaction of the corresponding carboxamide with Lawesson's reagent or with $(P_2S_5)_2$, is reacted, Diagram 3.3, with the α-bromo-ketone of general formula **(V.ii)** or $\mathbf{(V.ii)_2}$ according to an experimental protocol described in the literature (*J. Org. Chem.*, (1995), **60**, 5638-5642). The protected amine function is then deprotected under standard conditions in a strong acid medium (for example: trifluoroacetic acid or HCl in an organic solvent when it is a carbamate-type protective group), releasing the amine of general formula **(V)**.

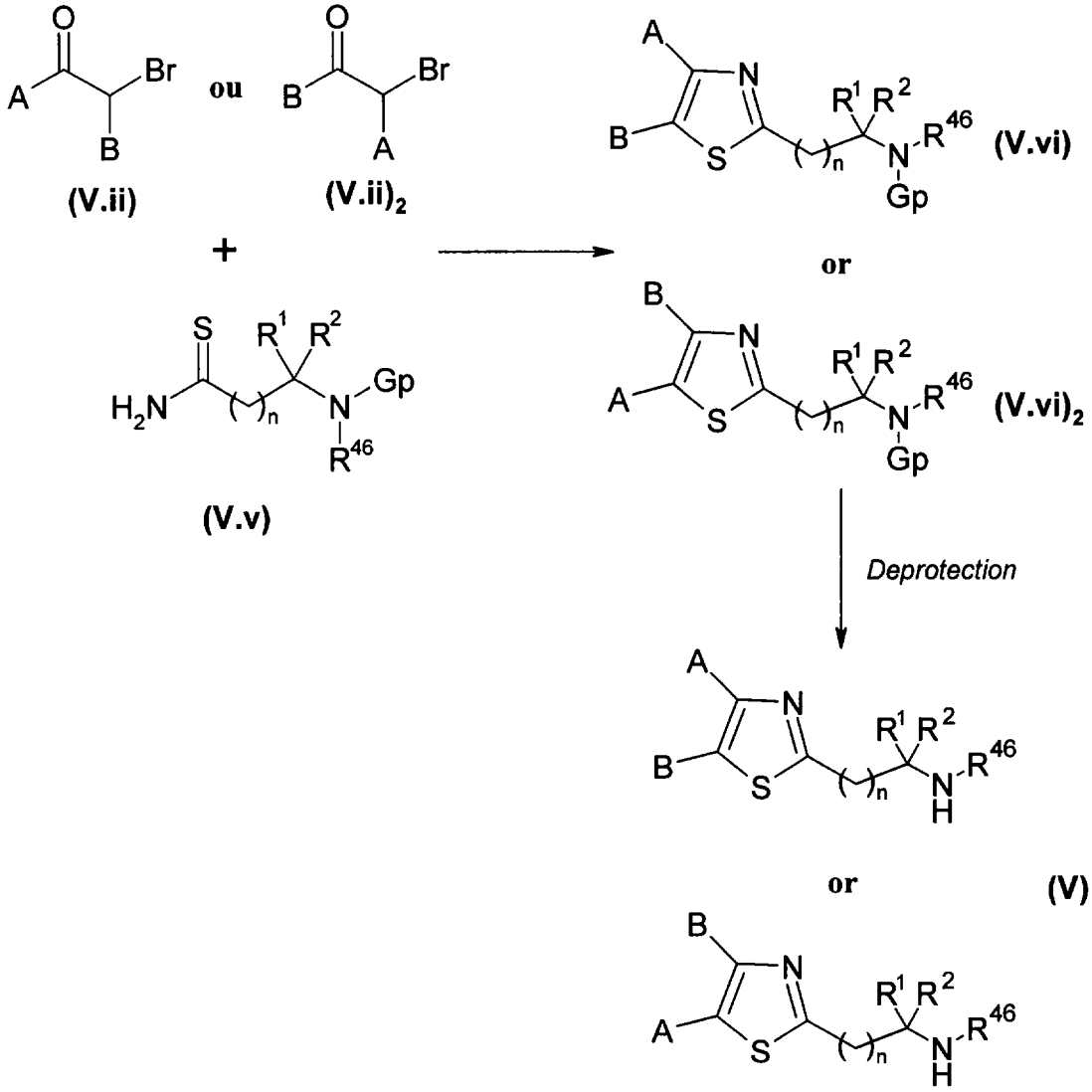


Diagram 3.3

Obtaining the thiazoles of general formula (V) intended for the preparation of compounds of general formula (I)3:

These compounds are obtained according to a method summarized in Diagram 3.4 below. The carboxamide of general formula **(VII.ii)** is first treated, for example, with Lawesson's reagent or with $(P_2S_5)_2$ then the thiocarboxamide of general formula **(VII.iii)** obtained is reacted with the halogenated derivative of general formula **(V.vii)** (cf. *Biorg. Med. Chem. Lett.* (1996), **6**(3), 253-258; *J. Med. Chem.* (1988), **31**(10), 1910-1918; *Tetrahedron Lett.*, (1993), **34** (28), 4481-4484; or *J. Med. Chem.* (1974), 17, 369-371; or also *Bull. Acd. Sci. USSR Div. Chem. Sci.* (Engl Transl) (1980) **29**, 1830-1833). The protected amine of general formula **(V.viii)** thus obtained is then deprotected under standard conditions for a person skilled in the art (for example:

trifluoroacetic acid or HCl in an organic solvent when Gp is a carbamate-type protective group).

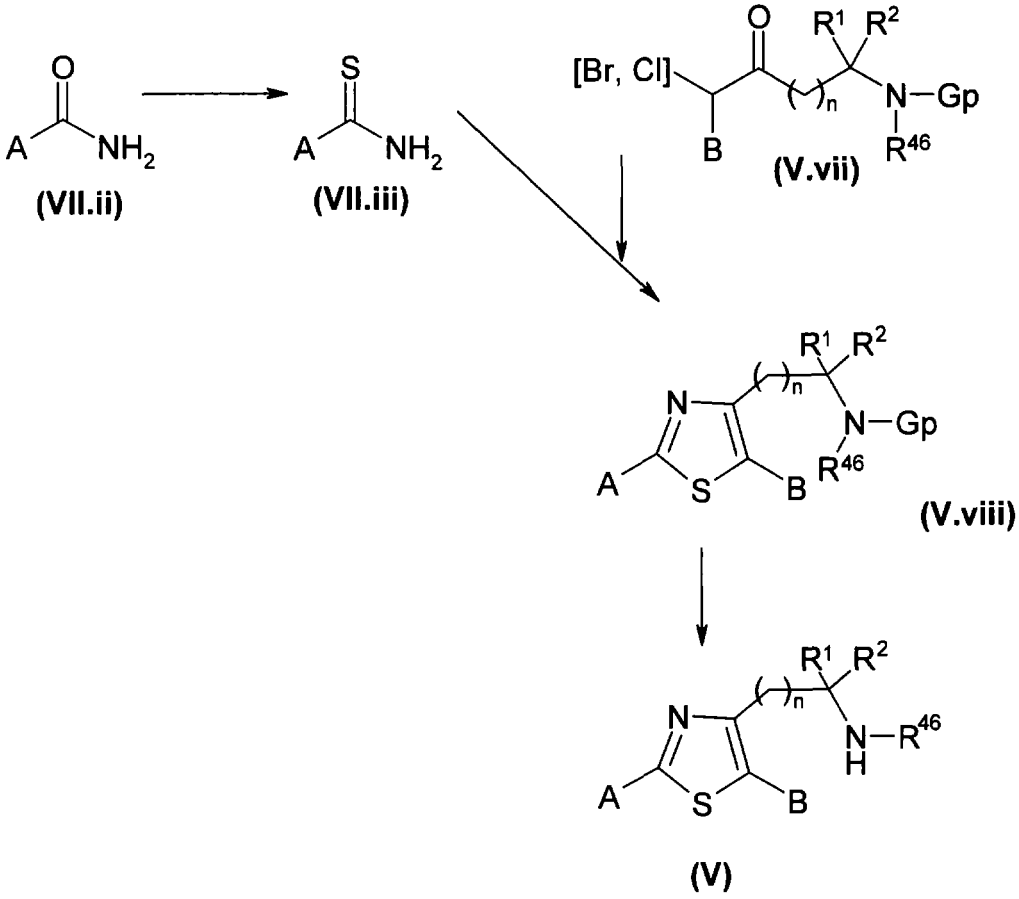


Diagram 3.4

Obtaining the oxazoles of general formula (V) intended for the preparation of compounds of general formula (I)$_3$:

These compounds are obtained according to a method summarized in Diagram 3.5 below. The carboxamide of general formula **(VII.ii)** is reacted with the halogenated derivative of general formula **(V.vii)**. The protected amine of general formula **(V.ix)** thus obtained is then deprotected under standard conditions for a person skilled in the art in order to produce the compound of general formula **(V)** (for example: trifluoroacetic acid or HCl in an organic solvent when Gp is a carbamate-type protective group) .

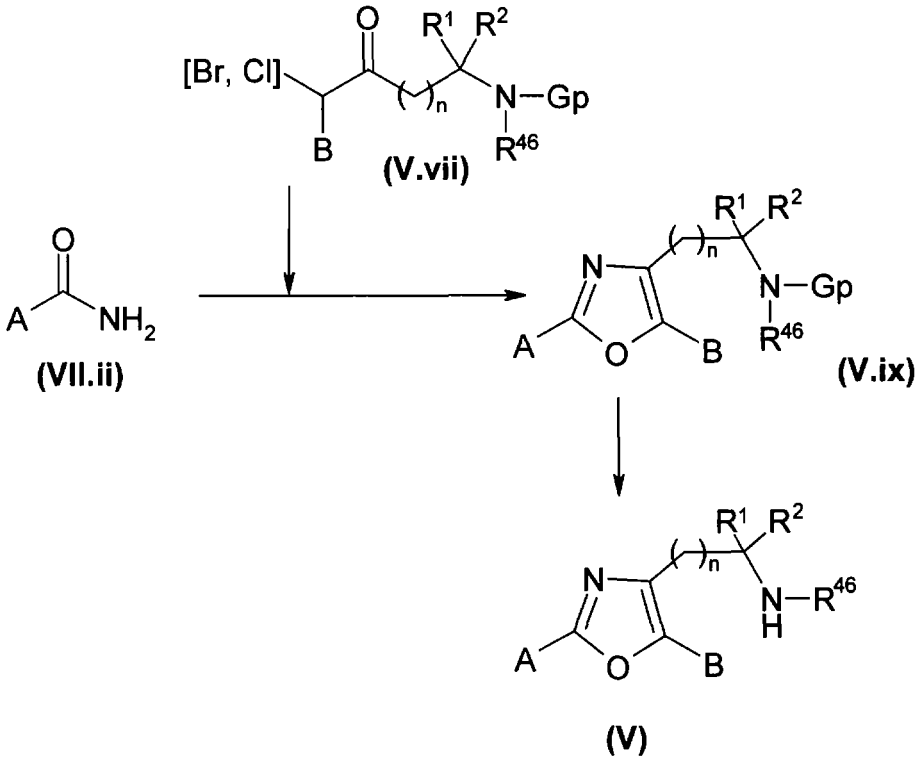


Diagram 3.5

Preparation of the ketone derivatives of general formula (V.i) and of certain α-bromoketone derivatives of general formula (V.ii), $(V.ii)_2$ or (V.vii)

The non-commercial ketone derivatives of general formula **(V.i)** or their α-bromoketone homologues are accessible from methods in the literature or similar methods adapted by a person skilled in the art. In particular:

- when A represents an indolinyl or tetrahydroquinolyl radical, the compounds of general formula **(V.i)** are accessible from methods in the literature such as, for example, *J. Med. Chem.* (1986), **29**, (6), 1009-1015 or *J. Chem. Soc., Perkin Trans. 1* (1992), **24**, 3401-3406.

Alternatively, the compounds of general formula **(V.ii)** in which A represents an indolinyl or tetrahydroquinolyl radical in which R^{33} represents H can be synthesized according to a protocol which is slightly modified with respect to that described in *J. Chem. Soc., Perkin Trans 1* (1992), **24**, 3401-3406. This protocol is summarized in Diagram 3.6 hereafter.

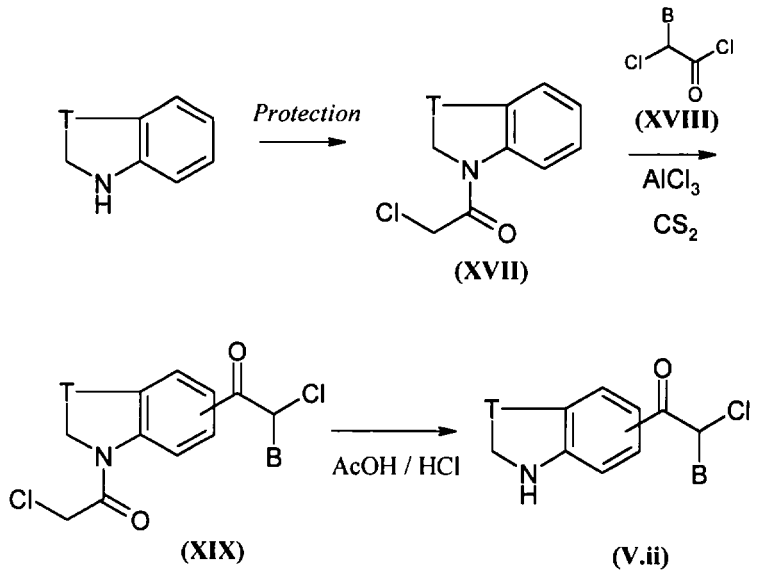


Diagram 3.6

The indoline or the tetrahydroquinoline (T represents $-CH_2-$ or $-(CH_2)_2-$) is protected using chloroacetyl chloride in order to produce the compound of general formula **(XVII)** which is subjected to a Friedel-Crafts reaction (substituted chloroacetyl chloride of general formula **(XVIII)**, in which B has the meaning indicated previously, in a solvent such as carbon disulphide and in the presence of aluminium chloride) in order to produce the compound of general formula **(XIX)**. Then the compound of general formula **(XIX)** is hydrolyzed in the presence of an acid, for example an acetic acid/HCl mixture, in order to produce the compounds of general formula **(V.ii)** in the form of a mixture of the meta and para isomers. These isomers can be separated by fractionated crystallisation in a solvent such as glacial acetic acid.

A person skilled in the art can adapt the syntheses described previously to the case where A represents an indolinyl or tetrahydroquinolyl radical in which R^{33} does not represent H. For example, when R^{33} represents an alkyl or aralkyl radical, the protection and deprotection stages are unnecessary.

- when A represents a 4-(4-hydroxyphenyl)-phenyl type radical, the compounds of general formula **(V.i)** are accessible from methods in the literature such as for example *J. Org. Chem.*, (1994), **59**(16), 4482-4489.

Alternatively, the compounds of general formula **(V.i)** and **(V.ii)** in which A represents a 4-(4-hydroxyphenyl)-phenyl type radical are accessible for example by the method illustrated in Diagram 3.7 hereafter.

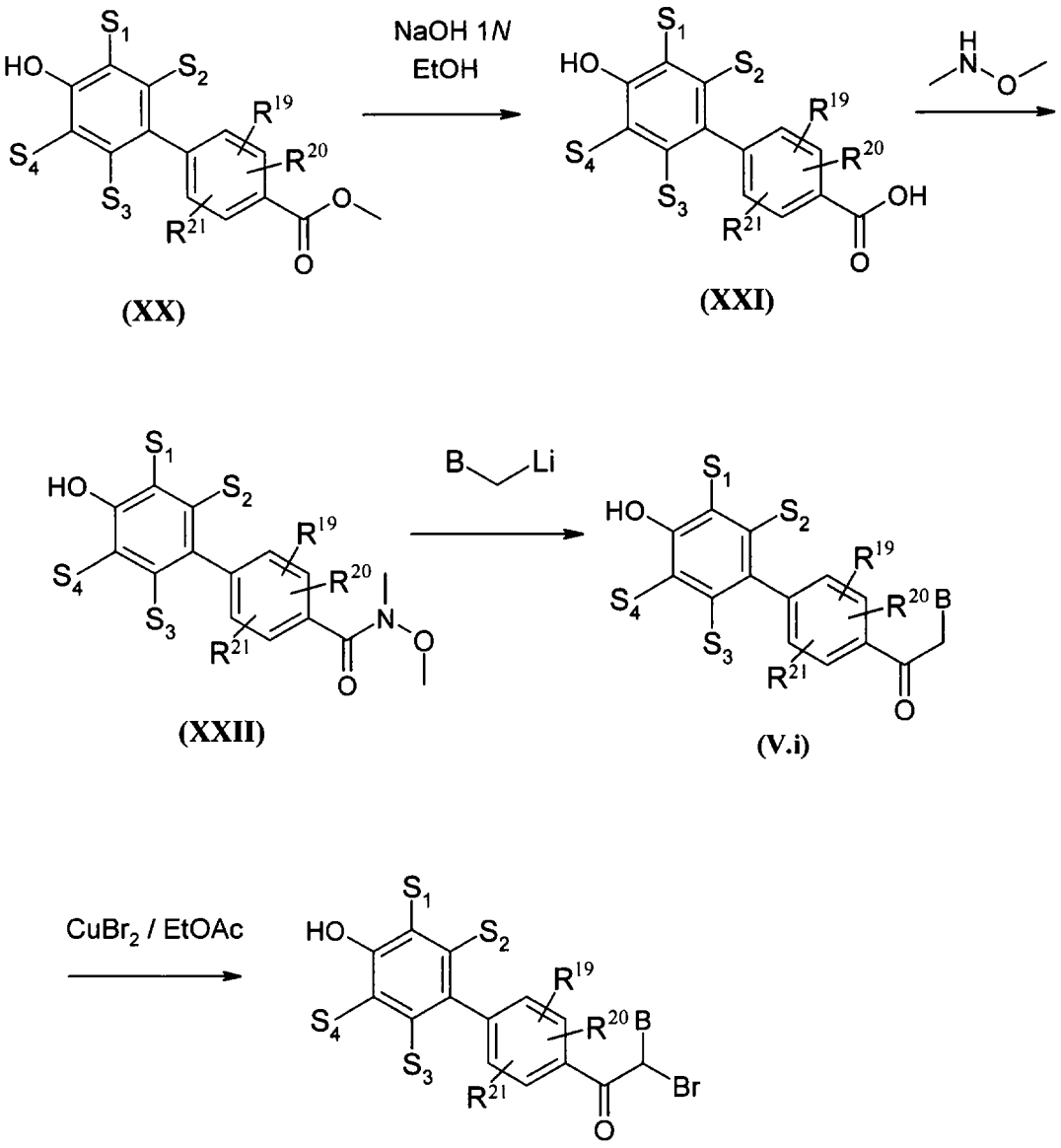


Diagram 3.7

The compounds of general formula **(V.i)** or **(V.ii)**, in which S_1, S_2, S_3 and S_4 are chosen independently from a hydrogen atom and OH, cyano, nitro, alkyl, alkoxy or $-NR^{10}R^{11}$ as defined in general formula **(I)**, are prepared, Diagram 3.7, from the esters of general formula **(XX)** (cf. in particular *Chem. Lett.* (1998), **9**, 931-932 and *Synthesis* (1993), **8**, 788-790). Of course, the phenol or aniline functions resulting from the nature of the substituents R^{19}, R^{20}, R^{21}, S_1, S_2, S_3 and S_4 can lead a person skilled in the art to add to the stages represented in Diagram 3.7, stages of protection (and, subsequently in the synthesis of the compounds of general formula **(I)**, of deprotection) of these functions so that they do not interfere with the remainder of the chemical synthesis. The esters of general formula **(XX)** are hydrolyzed in order

to produce the acids of general formula **(XXI)**. The latter are then subjected to coupling with N,O-dimethylhydroxylamine (*Syn. Commun.* (1995), **25**(8), 1255; *Tetrahedron Lett.* (1999), **40**(3), 411-414) in a solvent such as dimethylformamide or dichloromethane, in the presence of a base such as triethylamine with dicyclohexylcarbodiimide or 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride and hydroxybenzotriazole, in order to produce the intermediates of general formula **(XXII)**. The compounds of general formula **(V.i)** are prepared from the compounds of general formula **(XXII)** by a substitution reaction with MeLi (*J. Med. Chem.* (1992), **35**(13), 2392). The bromoacetophenones of general formula **(V.ii)** are now accessible from the acetophenone of general formula **(V.i)** under conditions previously described.

- when A represents a carbazolyl radical, the compounds of general formula **(V.i)** are accessible from methods in the literature such as for example *J. Org. Chem.*, (1951), **16**, 1198 or *Tetrahedron* (1980), **36**, 3017.

Alternatively, the compounds of general formula **(V.ii)** in which A represents a carbazolyl radical in which R^9 represents H can be synthesized according to a protocol which is slightly modified with respect to that described for A = carbazolyl in *Tetrahedron* (1980), **36**, 3017. This method is summarized in Diagram 3.8 hereafter:

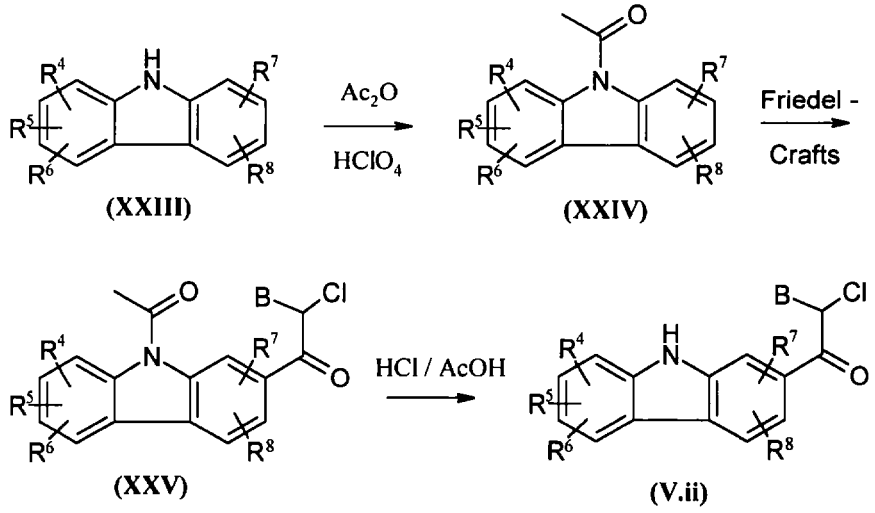


Diagram 3.8

The carbazole of general formula **(XXIII)** is protected using acetic anhydride in order to produce the compound of general formula **(XXIV)**, which is subjected to a Friedel-Crafts reaction (substituted chloroacetyl chloride of general formula **(XVIII)** as defined previously in a solvent such as carbon disulphide and in the presence of

aluminium chloride) in order to produce the compound of general formula **(XXV)**. Then the acyl group protecting the amine function is hydrolyzed in the presence of an acid, for example an AcOH/HCl mixture, in order to produce the compound of general formula **(V.ii)**. When A represents a carbazolyl radical in which R^9 represents alkyl or a $-COR^{15}$ group (case not represented in Diagram 3.8), the initial acylation stage is unnecessary and the last two stages in Diagram 3.8 make it possible to obtain the compounds of general formula **(V.ii)**. Of course, the phenol or aniline functions resulting from the nature of the substituents R^4, R^5, R^6, R^7 and R^8 can lead a person skilled in the art to add to the stages represented in Diagram 3.8, stages of protection (and, subsequently in the synthesis of the compounds of general formula **(I)**, of deprotection) of these functions so that they do not interfere with the remainder of the chemical synthesis.

- when A represents a phenothiazinyl radical, the intermediates of general formula **(V.i)** and **(V.ii)** are accessible from methods in the literature: *J. Heterocyclic. Chem.* (1978), **15**, 175-176 and *Arzneimittel Forschung* (1962), **12**, 48.

  Alternatively, the intermediates of general formula **(V.ii)** in which A represents a phenothiazinyl radical can be prepared according to a protocol which is slightly modified with respect to that described for the phenothiazinyl radical in *Arzneimittel Forschung* (1962), **12**, 48, which is summarized in Diagram 3.9 hereafter (see also the examples). The phenothiazine of general formula **(XXVI)** is protected using chloroacetyl chloride in order to produce the compound of general formula **(XXVII)**, which is then subjected to a Friedel-Crafts reaction (compound of general formula **(XVIII)** in a solvent such as carbon disulphide in the presence of aluminium chloride) in order to produce the compound of general formula **(XXVIII)**. During the last stage of the process, the hydrolysis with HCl/acetic acid is accompanied by a halogen exchange and makes it possible to obtain the chloroketone of general formula **(V.ii)**. Of course, the phenol or aniline functions resulting from the nature of the substituents R^4, R^5, R^6, R^7 and R^8 can lead a person skilled in the art to add to the stages represented in Diagram 3.9 stages of protection (and, subsequently in the synthesis of the compounds of general formula **(I)**, of deprotection) of these functions so that they do not interfere with the remainder of the chemical synthesis.

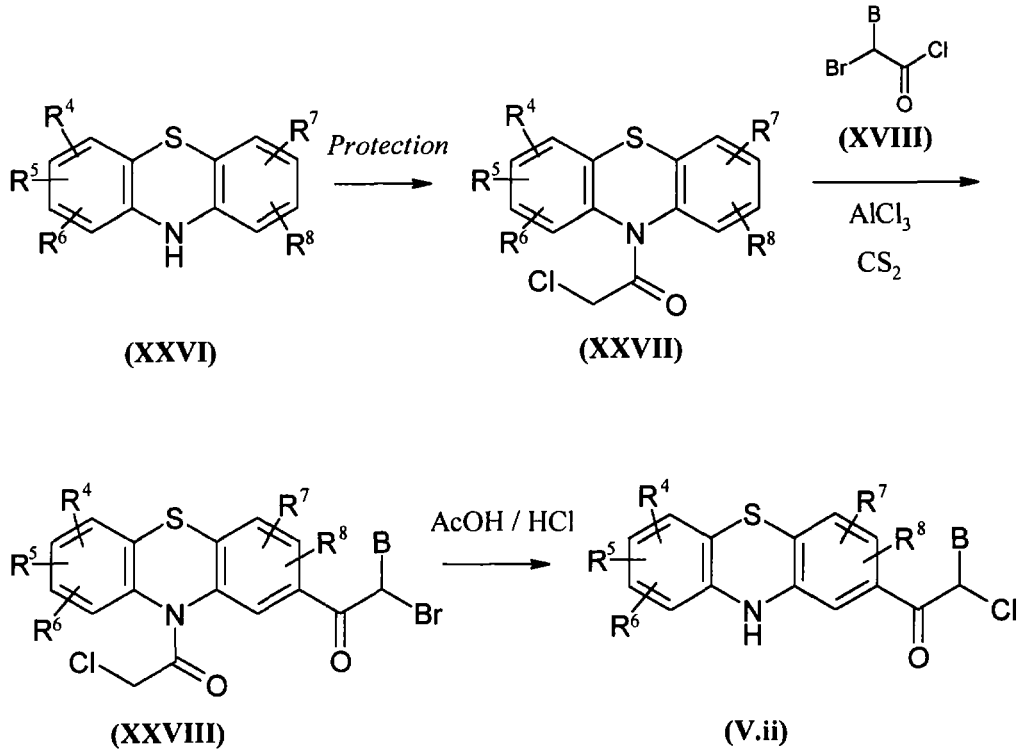


Diagram 3.9

- when A represents a phenylaminophenyl radical, the compounds of general formula **(V.i)** are accessible from methods in the literature such as for example *Chem. Commun.*, (1998), **15**, (6) 1509-1510 or *Chem Ber.*, (1986), **119**, 3165-3197, or similar methods adapted by a person skilled in the art.

For example, the intermediates of general formula **(V.i)*a*** and **(V.ii)*a*** in which A represents a phenylaminophenyl radical (which correspond to the corresponding compounds of general formula **(V.i)** and **(V.ii)** the aniline function of which has been acetylated), can be prepared according to a protocol which is slightly modified with respect to that described for the phenylaminophenyl radical in *Chem Ber.* (1986), **119**, 3165-3197. This protocol is summarized in Diagram 3.10 hereafter.

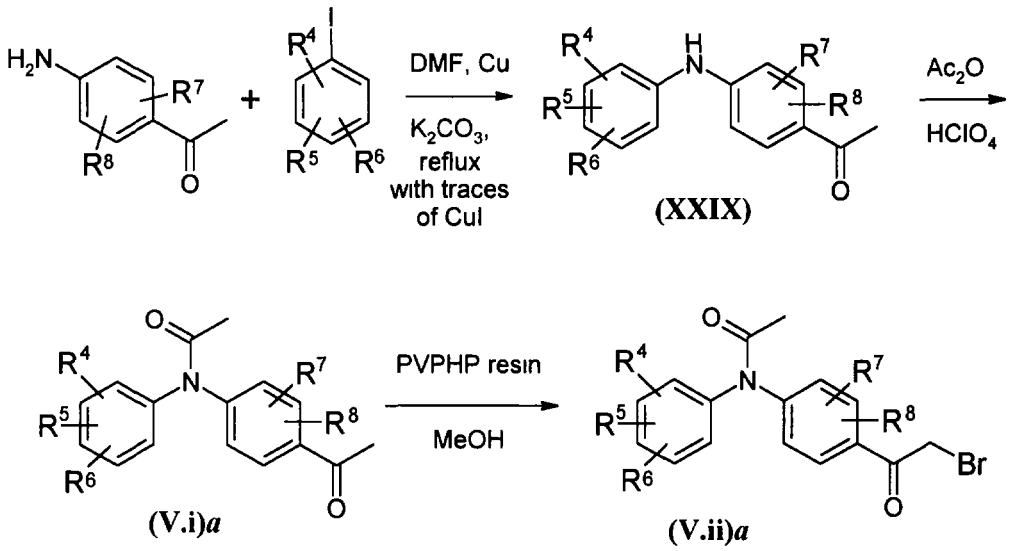


Diagram 3.10

In the case (represented in Diagram 3.10) where the R^9 radical of the compound of general formula **(I)** to be synthesized is a hydrogen atom or an acetyl group, the diphenylamine of general formula **(XXIX)** formed after the coupling reaction in the presence of CuI is protected by acetylation using, for example, acetic anhydride in order to produce the compound of general formula **(V.i)*a***. In the case (not represented in Diagram 3.10) where the R^9 radical of the compound of general formula **(I)** to be synthesized is not a hydrogen atom or an acetyl radical, the acetylation stage is replaced by a stage of substitution on the aniline according to standard methods known to a person skilled in the art in order to produce the corresponding compound of general formula **(V.i)**. The compound of general formula **(V.i)*a*** (or **(V.i)**, in the case not represented in Diagram 3.10) is then subjected to a bromination reaction using a bromination resin, PVPHP (Poly(VinylPyridinium Hydrobromide Perbromide) resin, described in *J. Macromol. Sci. Chem.* (1977), **A11**, (3), 507-514, in order to produce the compound of general formula **(V.ii)*a*** (or **(V.ii)**, in the case not represented in Diagram 3.10). Of course, the phenol or aniline functions resulting from the nature of the substituents R^4, R^5, R^6, R^7 and R^8 can lead a person skilled in the art to add to the stages represented in Diagram 3.10, stages of protection (and, subsequently in the synthesis of the compounds of general formula **(I)**, of deprotection) of these functions so that they do not interfere with the remainder of the chemical synthesis. The deprotection of the acetylated aniline function is carried out in principle during the last stage of the synthesis of the compounds of general formula **(I)**.

- when A represents a radical benzopyrane or benzofurane such as defined in general formula **(I)** with R^{32} representing a hydrogen atom, the intermediates of general formula **(V.i)** and **(V.ii)** are accessible by the methods illustrated in Diagram 3.11 hereafter.

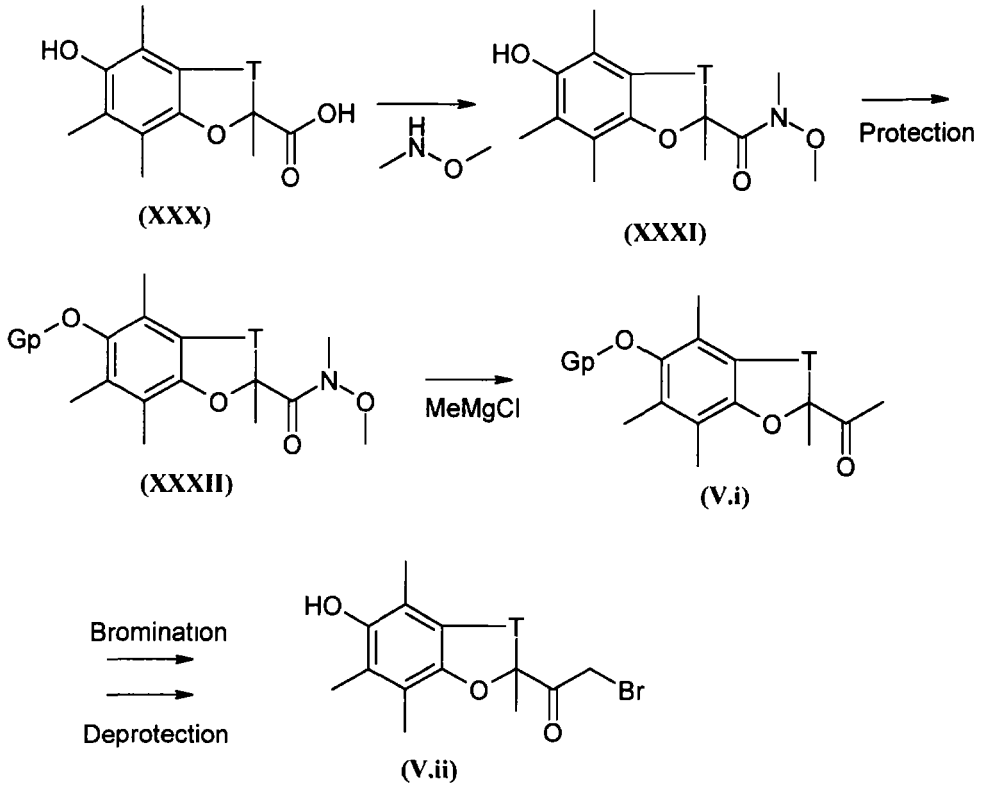
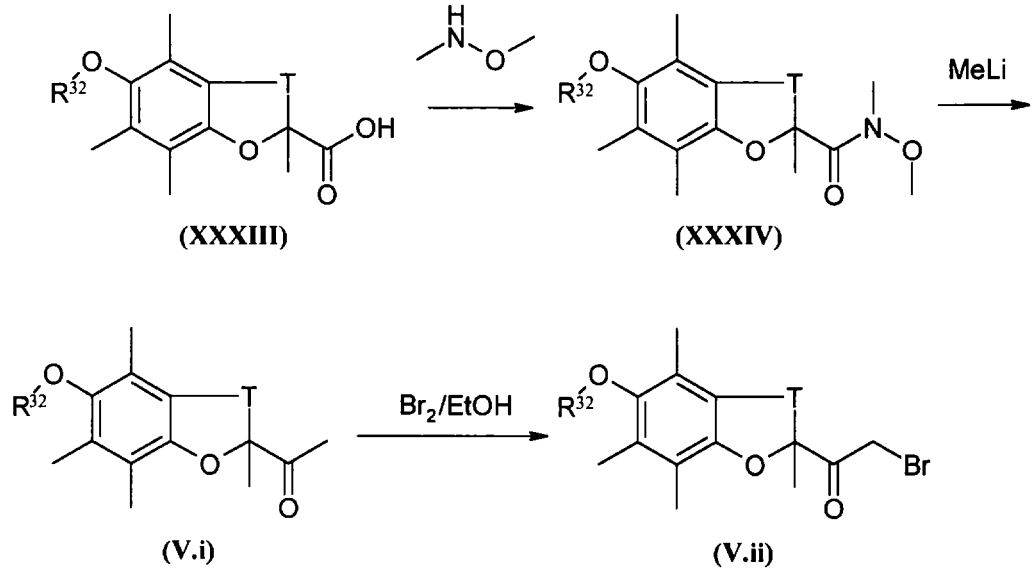


Diagram 3.11

The compounds of general formulae **(V.i)** and **(V.ii)**, Diagram 3.11, in which T is as defined above and Gp = protective group, are prepared from the acids of general formula **(XXX)**. The acids of general formula **(XXX)** are subjected to coupling with N,O-dimethylhydroxylamine (*Syn. Commun.* (1995), **25**, (8), 1255; *Tetrahedron Lett.* (1999), **40**, (3), 411-414) in a solvent such as dimethylformamide or dichloromethane, in the presence of a base such as triethylamine with dicyclohexylcarbodiimide or 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride and hydroxybenzotriazole, in order to produce the intermediates of general formula **(XXXI)**. The protection of the phenol function in the form of a benzylated or *tert*-butyldimethylsilylated derivative or by other protective groups (Gp) known to a person skilled in the art is then carried out in order to produce the compounds of general formula **(XXXII)**. The compounds of general formula **(V.i)**

are prepared from the compounds of general formula **(XXXII)** by a substitution reaction with Grignard's reagent, MeMgCl (*J. Het. Chem.* (1990), **27**, 1709-1712) or with MeLi (*J. Med. Chem.* (1992), **35**, 13). The bromoacetophenones of general formula **(V.ii)** are now accessible from the acetophenone of general formula **(V.i)** under conditions described previously.

Alternatively, the compound of general formula **(V.ii)** in which R^{32} represents a hydrogen atom or an alkyl radical can be prepared according to a process in only 3 stages (cf. Diagram 3.12 - see also the examples). In this process, the bromination in the last stage of the compound of general formula **(V.i)** in order to produce the compound of general formula **(V.ii)** is preferably carried out according to *J. Am. Chem. Soc.* (1999), **121**, 24.



(XXXIII) **(XXXIV)**

(V.i) **(V.ii)**

Diagram 3.12

- when A represents a substituted biphenyl radical, the intermediate ketones of general formula **(V.i)** are in particular accessible using a Suzuki synthesis (cf. Baroni et al., *J.Org. Chem.* 1997, **62**, 7170-7173; cf. also Example 44 of the present Application, stage 44.1).

When A represents a substituted phenol radical, it may be necessary to use intermediates of general formula **(V.ii)** as defined previously, the phenol function of which has been acetylated (hereafter designated as compounds of general formula **(V.ii)*b***). In particular:

- when A represents a 4-hydroxy-3,5-diisopropylphenyl radical, the homologous α-bromoketone derivatives of the compound of formula **(V.ii)** the phenol function of

which is protected by an acetyl radical can be prepared as summarized in Diagram 3.13 hereafter.

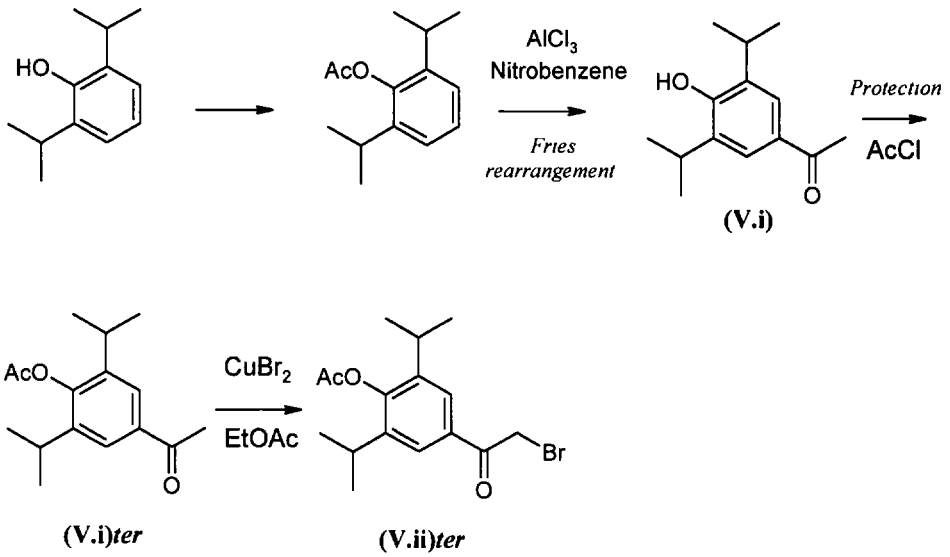
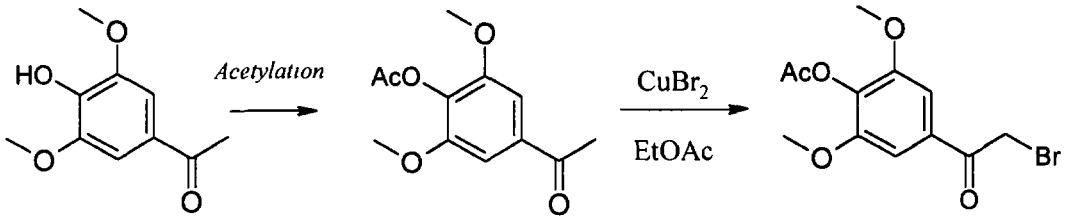


Diagram 3.13

The 2,6-diisopropylphenol is acetylated according to methods known to a person skilled in the art, for example by reacting it with acetic acid in the presence of trifluoroacetic acid anhydride or with acetyl chloride in the presence of a base such as for example K_2CO_3. The acetylated homologue of 2,6-diisopropylphenol is then subjected to a Fries rearrangement in the presence of aluminium chloride in a solvent such as nitrobenzene in order to produce the compound of formula **(V.i)**. Then the compound of formula **(V.i)** is acetylated in order to produce the compound of formula **(V.i)*b***. Bromination is then carried out with $CuBr_2$ as described previously in order to produce the compound of formula **(V.ii)*b***. The deprotection stage to release the phenol function will occur subsequently in the synthesis of the compounds of general formula **(I)** (at a time deemed the most appropriate by a person skilled in the art).

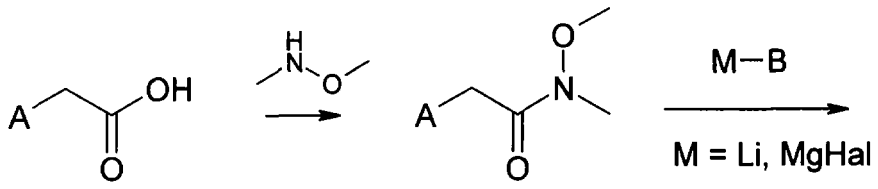
- when A represents a dimethoxyphenol-type radical, the compounds of general formula **(V.ii)*b*** can be prepared in analogous manner to the synthesis described for the compound of formula **(V.ii)*b*** derived from 2,6-diisopropylphenol, optionally with a few minor modifications within the scope of a person skilled in the art. For example, when A represents the 3,5-dimethoxy-4-hydroxyphenyl radical, the corresponding α-bromoketone derivative of formula **(V.ii)*b*** can be prepared, for example, as indicated in Diagram 3.13 from the commercial compound of formula **(XXXV)**:



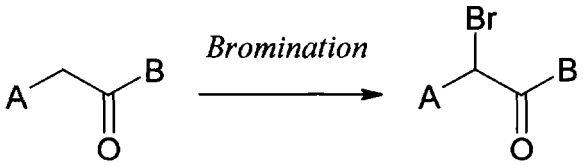
(XXXV) **(V.i)*b*** **(V.ii)*b***

Diagram 3.14

The compounds of general formula **(V.ii)$_2$** in which A and B are as defined previously can be prepared according to the method summarized in Diagram 3.15 hereafter.



(XXXVI) **(XXXVII)**



(V.i)$_2$ **(V.ii)$_2$**

Diagram 3.15

The acids of general formula **(XXXVI)** are subjected to coupling with N,O-dimethylhydroxylamine (*Syn. Commun.* (1995), **25**, (8), 1255; *Tetrahedron Lett.* (1999), **40**, (3), 411-414) in a solvent such as dimethylformamide or dichloromethane, in the presence of a base such as triethylamine with dicyclohexylcarbodiimide or 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride and hydroxybenzotriazole, in order to produce the intermediates of general formula **(XXXVII).** The compounds of general formula **(V.i)$_2$** are prepared from the compounds of general formula **(XXXVII)** by a substitution reaction of lithium or magnesium derivatives of general formula B-M in which M represents Li or MgHal (Hal = I, Br or Cl) in solvents such as ether or anhydrous tetrahydrofuran. The α-bromo- or α-chloroketones of general formula

(V.ii)$_2$ are now accessible from the ketones of general formula **(V.i)$_2$** under conditions described previously.

Moreover, the non-commercial α-halogenoketone derivatives of general formula **(V.vii)** are accessible using methods from the literature. In particular, they can be obtained according to a procedure summarized in Diagram 3.16.

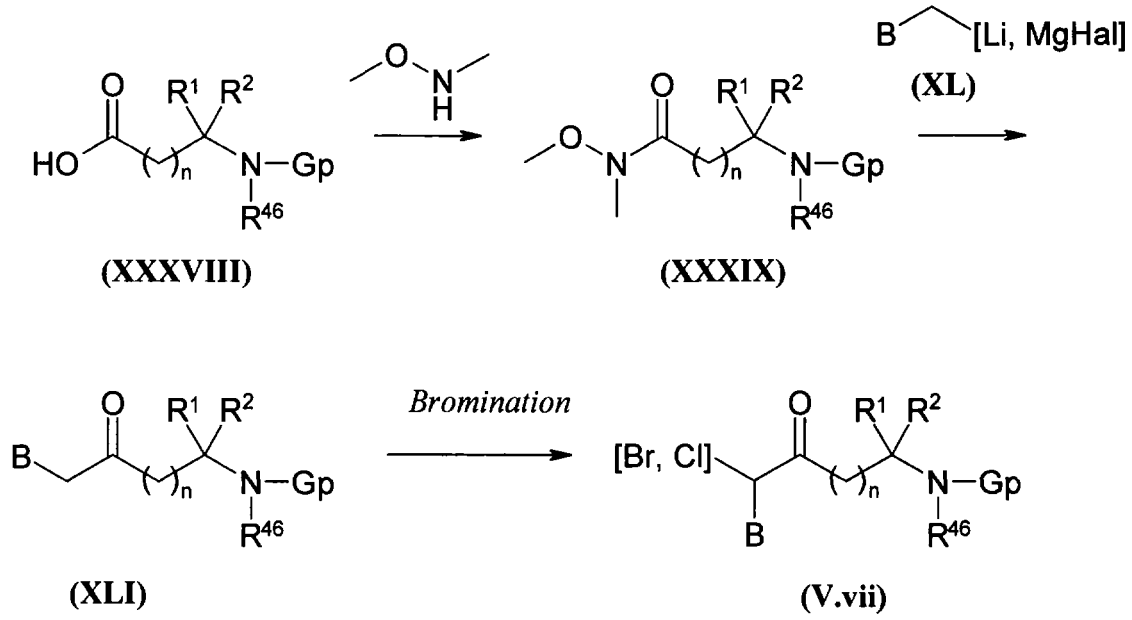


Diagram 3.16

The protected amino acids of general formula **(XXXVIII)** are obtained by the protection of the corresponding amino acids by a carbamate-type group according to methods known to a person skilled in the art. The acids of general formula **(XXXVIII)** are then subjected to coupling with N,O-dimethylhydroxylamine (*Syn. Commun.* (1995), **25**, (8), 1255; *Tetrahedron Lett.* (1999), **40**, (3), 411-414) in a solvent such as dimethylformamide or dichloromethane, in the presence of a base such as triethylamine with dicyclohexylcarbodiimide or 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride and hydroxybenzotriazole, in order to produce the intermediates of general formula **(XXXIX).** The compounds of general formula **(XLI)** are prepared from the compounds of general formula **(XXXIX)** by a substitution reaction with lithium or magnesium derivatives of general formula **(XL)** (in which Hal = I, Br or Cl) in solvents such as ether or anhydrous tetrahydrofuran The bromo or chloroacetophenones of general formula **(V.vii)** are now accessible from the acetophenone of general formula **(XLI)** under conditions previously described.

Alternatively, a person skilled in the art can also use or adapt the syntheses described in *Angew. Chem. Int.* (1998), **37** (10), 411-414, *Liebigs Ann. Chem.* (1995), 1217 or *Chem. Pharm. Bull.* (1981), **29**(11), 3249-3255.

Preparation of the acid derivatives of general formula (V.iii)

The acid derivatives of general formula **(V.iii)** can be obtained, Diagram 3.17, directly by reaction of the commercial amino acid of general formula **(V.vi)** with (ar)alkylchloroformate or di(ar)alkylcarbonate type compounds (Δ represents an alkyl or benzyl radical) under standard conditions known to a person skilled in the art.

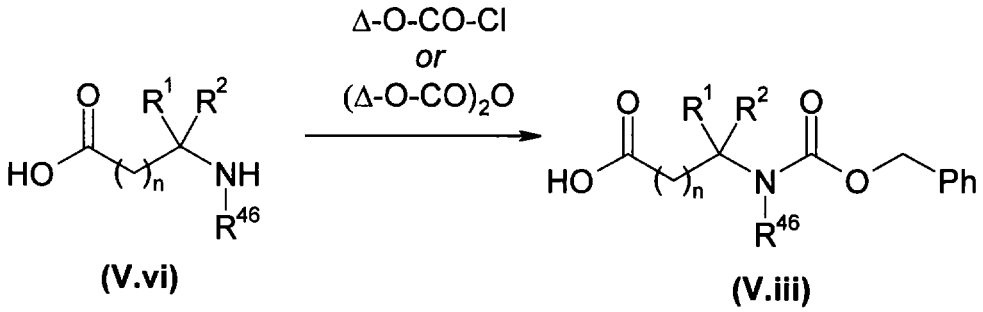


Diagram 3.17

Preparation of the compounds of general formula (V.v)

The thiocarboxamides of general formula **(V.v)** can be obtained in three stages from the compounds of general formula **(V.vi)** as indicated in Diagram 3.18 below. The amine function of the amino acid of general formula **(V.vi)** is first protected under standard conditions with tBu-O-CO-Cl or $(tBu\text{-}O\text{-}CO)_2O$ (or other protective groups known to a person skilled in the art), then the intermediate obtained is converted to its corresponding amide by methods described in the literature (cf. for example, *J. Chem. Soc., Perkin Trans. 1*, (1998), **20,** 3479-3484 or PCT Patent Application WO 99/09829). Finally, the carboxamide is converted to thiocarboxamide of general formula **(V.v)**, for example by reaction with Lawesson's reagent in a solvent such as dioxane or tetrahydrofuran at a temperature preferably comprised between ambient temperature and that of the reflux of the mixture, or also using $(P_2S_5)_2$ under standard conditions for a person skilled in the art.

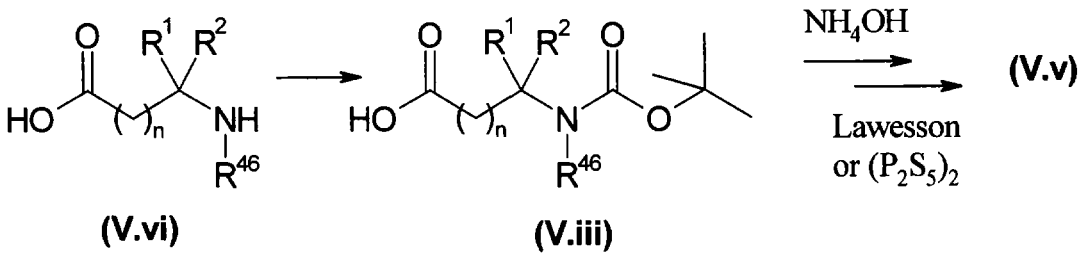


Diagram 3.18

Alternatively, the thiocarboxamides of general formula **(V.v)** can also be obtained, Diagram 3.19, by adding H_2S to the corresponding cyano derivatives of general formula **(V.x)** under standard conditions known to a person skilled in the art.

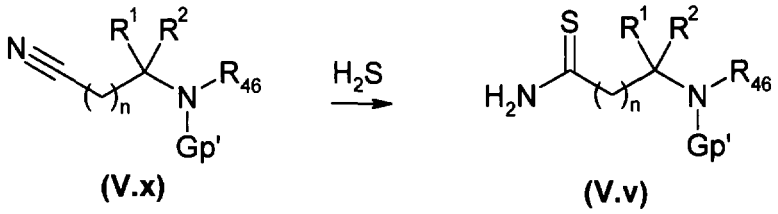


Diagram 3.19

5 Preparation of the acids of general formula (VI)

Preparation of the acids derived from thiazoles of general formula (VI)

The acids of general formula **(VI)** derived from thiazoles can be prepared according to procedures represented in Diagram 4.1 below.

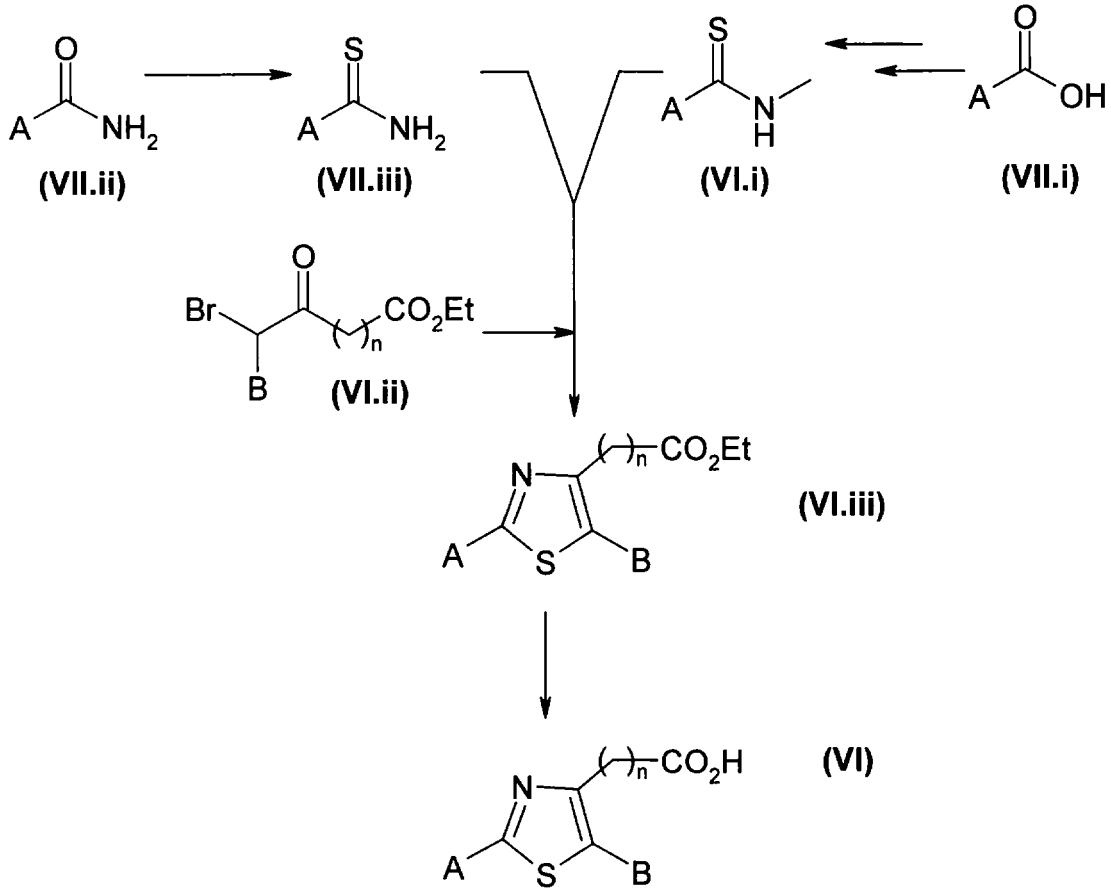


Diagram 4.1

The carboxamides of general formula **(VII.ii)** are treated under standard conditions in order to produce the thiocarboxamide of general formula **(VII.iii)**, for example by Lawesson's reagent or also using $(P_2S_5)_2$ under standard conditions for a person skilled in the art. Alternatively, the acid of general formula **(VII.i)** is activated by the action of 1,1'-carbonyldiimidazole then treated with methylamine in an aprotic polar solvent such as for example tetrahydrofuran. The intermediate carboxamide obtained is converted to the thiocarboxamide of general formula **(VI.i)** under standard conditions, for example using Lawesson's reagent or also using $(P_2S_5)_2$ under standard conditions for a person skilled in the art. The thiocarboxamide of general formula **(VII.iii)** or **(VI.i)** is then reacted with the compound of general formula **(VI.ii)**, for example by heating to reflux in a solvent such as benzene, dioxane or dimethylformamide. The ester of general formula **(VI.iii)** obtained can then be saponified by the action of a base such as for example potash in alcoholic medium or LiOH in tetrahydrofuran in order to produce the acid of general formula **(VI)**.

Preparation of the acids derived from oxazoles of general formula (VI)

The acids of general formula **(VI)** derived from oxazoles can be prepared according to a procedure represented in Diagram 4.2 below.

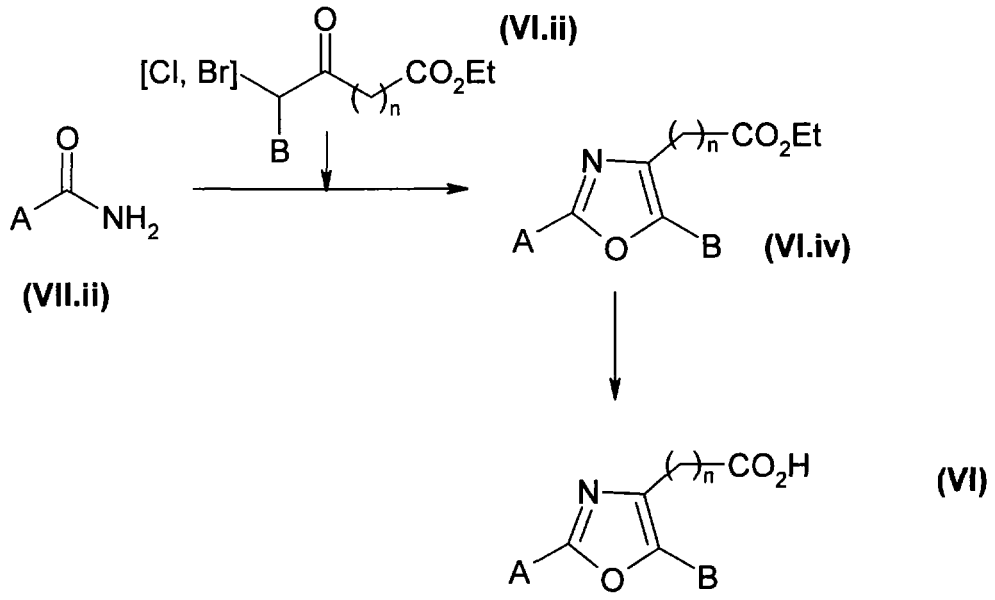


Diagram 4.2

The carboxamides of general formula **(VII.ii)** are reacted with the compound of general formula **(VI.ii)** by heating, for example under reflux, in the absence or in the presence of a solvent such as dimethylformamide. The ester of general formula **(VI.iv)** obtained can then be saponified by the action of a base such as for example potash in alcoholic medium or LiOH in tetrahydrofuran in order to produce the acid of general formula **(VI)**.

Preparation of the acids derived from isoxazolines of general formula (VI)

The acids derived from isoxazolines of general formula **(VI)**, which are useful in the preparation of compounds of general formula $(I)_4$, can be prepared according to a procedure represented in Diagram 4.3 hereafter.

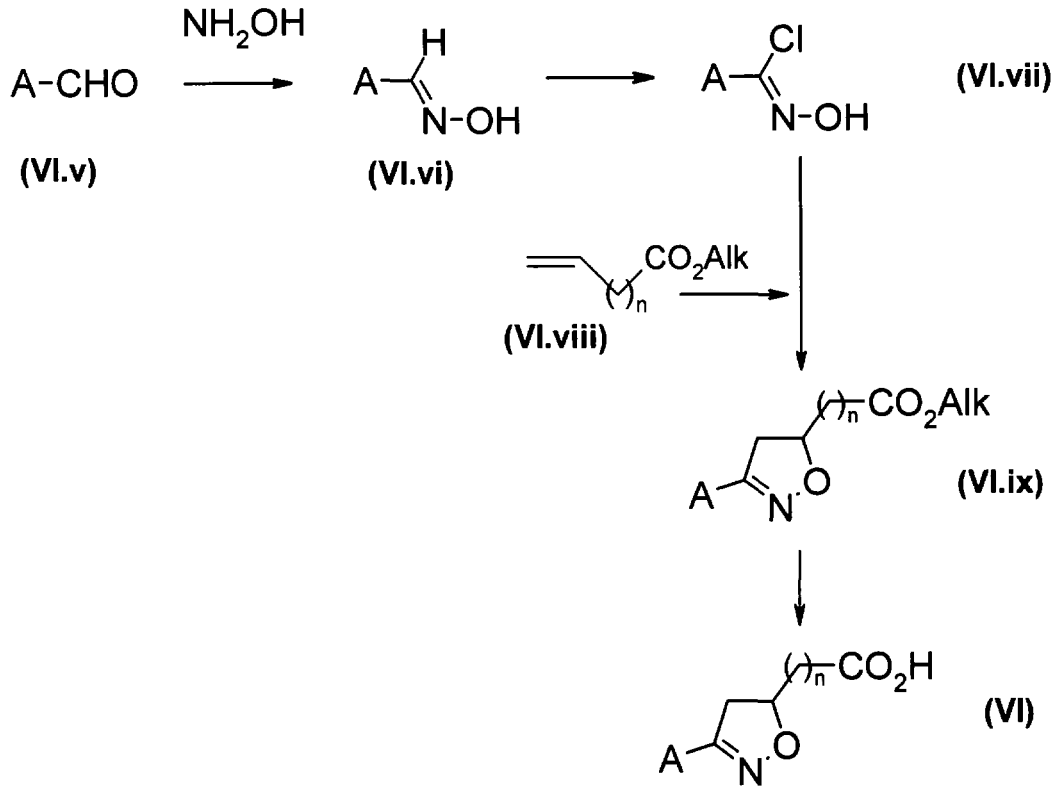


Diagram 4.3

The acids of general formula **(VI)** derived from isoxazolines can be prepared as follows: the commercial aldehydes of general formula **(VI.v)** are reacted with hydroxylamine hydrochloride. The oxime of general formula **(VI.vi)** thus obtained is activated in the form of oxime chloride, of general formula **(VI.vii)**, by reaction with N-chlorosuccinimide in DMF before being reacted with the esters of general formula **(VI.viii)** (in which Alk represents an alkyl radical) in order to produce the isoxazoline derivatives according to an experimental protocol described in the literature (*Tetrahedron Lett.*, 1996, **37** (26), 4455; *J. Med. Chem.*, 1997, **40**, 50-60 and 2064-2084). The saponification of the isoxazolines of general formula **(VI.ix)** is then carried out in a standard fashion (for example by the action of KOH in an alcoholic solvent or LiOH in a solvent such as tetrahydrofuran) in order to produce the acid derivative of general formula **(VI)**.

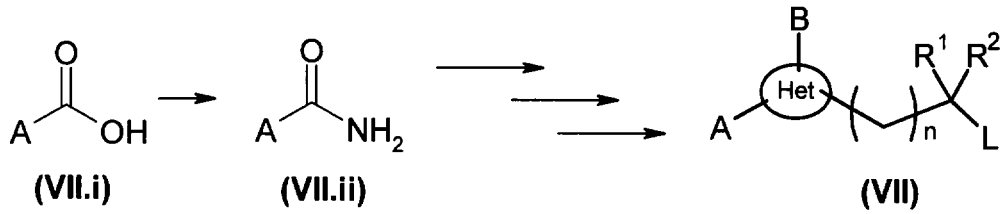
The non-commercial unsaturated esters of general formula **(VI.x)** can be prepared according to methods described in the literature (*J. Med. Chem.*, 1987, **30**, 193; *J. Org. Chem.*, 1980, **45**, 5017).

Preparation of the thiazoles and oxazoles of general formula (VII)

General diagram

The acids of general formula **(VII.i)**, Diagram 5.1, are converted to the corresponding carboxamides of general formula **(VII.ii)** by methods described in the literature (cf. for example, *J. Chem. Soc., Perkin Trans. 1*, (1998), **20,** 3479-3484 or PCT Patent Application WO 99/09829). The compounds of general formula **(VII)** can then obtained in a standard fashion according to the procedures represented in Diagrams 5.2 and 5.3 (thiazoles) and the Diagram 5.4 (oxazoles) hereafter.

This synthesis route is useful for then preparing compounds corresponding to general sub-formulae $(I)_1$ and $(I)_3$.



(VII.i) **(VII.ii)** **(VII)**

Diagram 5.1

Obtaining the thiazoles of general formula (VII)

When R^1 and R^2 both represent H, the thiazoles of general formula **(VII)** intended for the preparation of compounds of general formula $(I)_3$ can be prepared according to the method summarized in Diagram 5.2. The carboxamide of general formula **(VII.ii)** is converted to the corresponding thiocarboxamide of general formula **(VII.iii)** in the presence of Lawesson's reagent in a solvent such as dioxane or benzene at a temperature preferably comprised between ambient temperature and that of the reflux of the mixture. The thiocarboxamide of general formula **(VII.iii)** is then treated with the α-halogenoketoester of general formula **(VII.iv)** in which Alk represents an alkyl radical (for example methyl, ethyl or *tert*-butyl), in order to produce the ester of general formula **(VII.v)**, which is reduced to the corresponding alcohol of general formula **(VII.vi)**, for example by the action of lithium aluminium hydride or diisobutylaluminium hydride in a solvent such as tetrahydrofuran. The latter can then be converted to a halogenated derivative of general formula **(VII)** according to methods known to a person skilled in the art, for example, in the case of a brominated derivative (L = Br), by reaction with CBr_4 in the presence of triphenylphosphine in dichloromethane at ambient temperature.

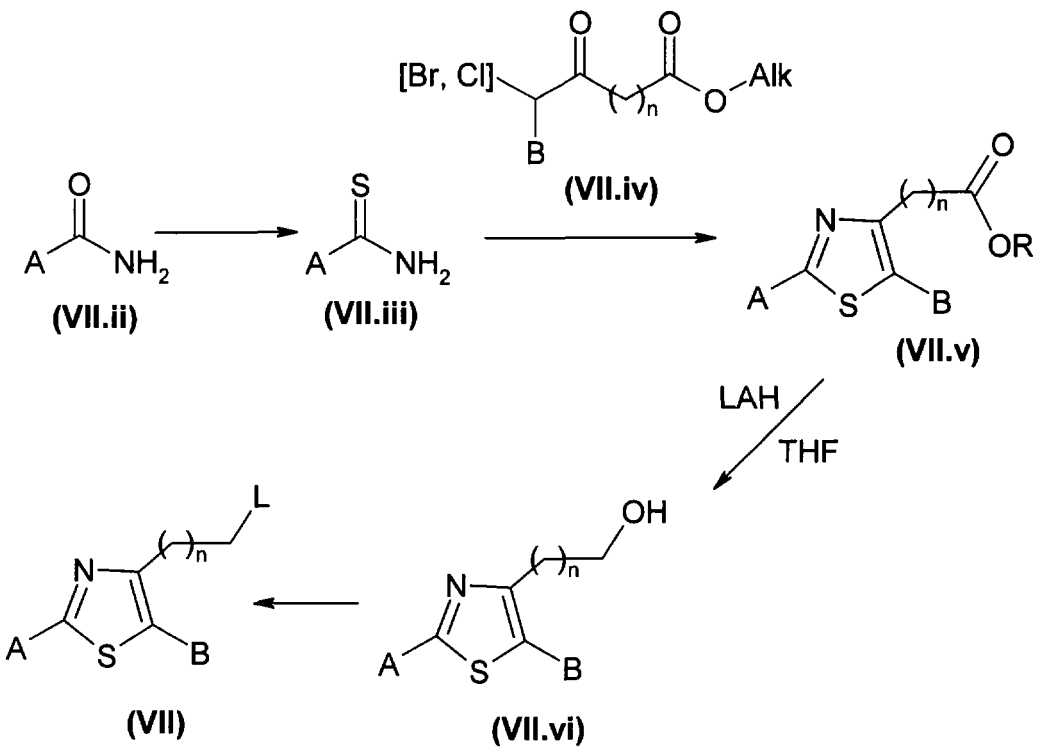


Diagram 5.2

The thiazoles of general formula **(VII)** intended for the preparation of compounds of general formula $(I)_I$ can be prepared according to the method summarized in Diagram 5.3. The cyano derivative of general formula **(VII.vii)** in which Gp' is a protective group for an alcohol function (for example a benzyl or –CO-ρ group in which ρ represents alkyl, for example methyl or *tert*-butyl) is converted to the corresponding thiocarboxamide of general formula **(VII.viii)** by the action of H_2S in a solvent such as ethanol in the presence of triethanolamine at a temperature preferably comprised between ambient temperature and that of the reflux of the mixture. The thiocarboxamide of general formula **(VII.viii)** is then treated with the α-halogenoketone of general formula **(VII.ix)** in order to produce the compound of general formula **(VII.x)**, which is deprotected in order to produce the corresponding alcohol of general formula **(VII.xi)** according to methods known to a person skilled in the art (for example when Gp' is an acetate-type protective group, the latter is extracted *in situ* by the action of an aqueous sodium carbonate solution) . The latter can then be converted to a halogenated derivative of general formula **(VII)** according to methods known to a person skilled in the art, for example, in the case of a brominated derivative (L = Br), by reaction with CBr_4 in the presence of triphenylphosphine in dichloromethane at ambient temperature.

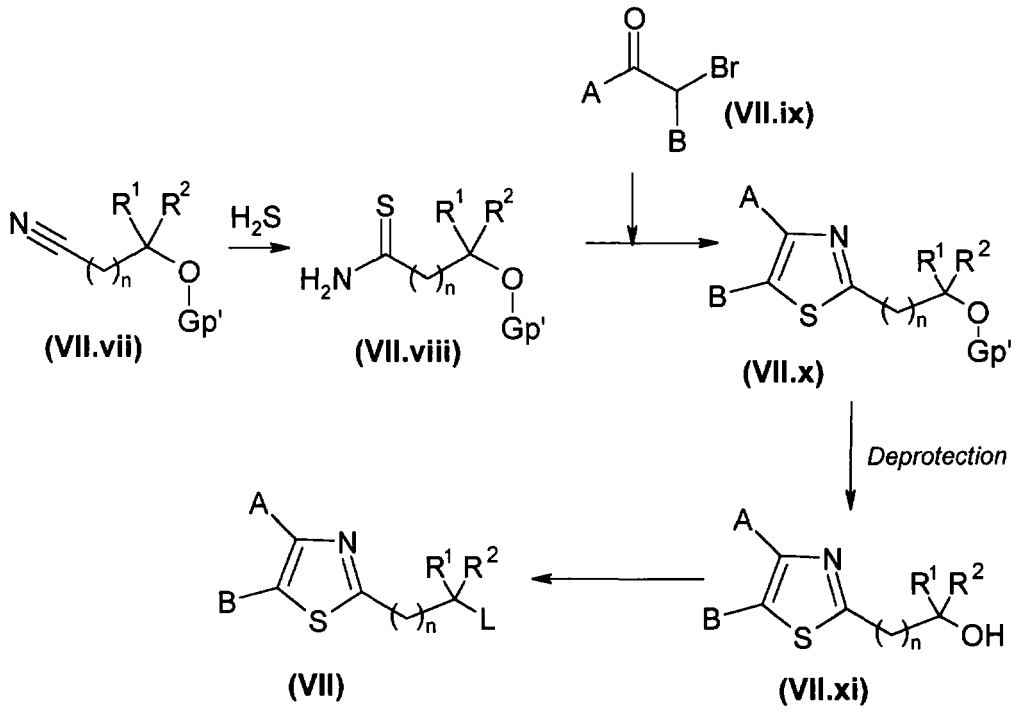


Diagram 5.3

Obtaining the oxazoles of general formula (VII)

When R^1 and R^2 both represent H, the oxazoles of general formula **(VII)** intended for the preparation of compounds of general formula $(I)_3$ can be prepared according to the method summarized in Diagram 5.4. The carboxamide of general formula **(VII.ii)** is treated with the α-halogenoketoester of general formula **(VII.iv)** in which Alk represents an alkyl radical (for example methyl, ethyl or *tert*-butyl), in order to produce the ester / the acid of general formula **(VII.xii)**. The latter is reduced to the corresponding alcohol of general formula **(VII.xiii)**, for example by the action of lithium and aluminium hydride or diisobutylaluminium hydride in a solvent such as tetrahydrofuran when starting with the ester or by the action of diborane in tetrahydrofuran when starting with the acid. The latter can then be converted to a halogenated derivative of general formula **(VII)** according to methods known to a person skilled in the art, for example, in the case of a brominated derivative (L = Br), by reaction with CBr_4 in the presence of triphenylphosphine in dichloromethane at ambient temperature.

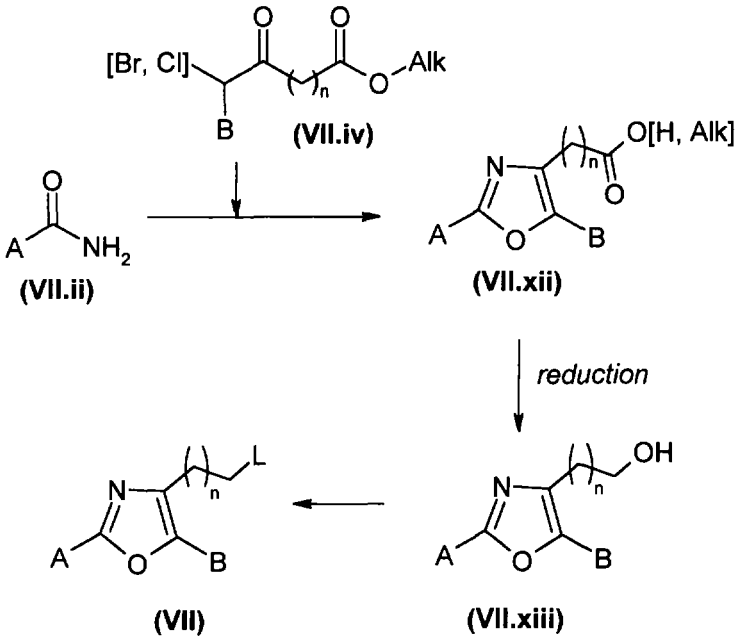


Diagram 5.4

Preparation of the acids of general formula (VII.i)

The non-commercial acids of general formula **(VII.i)** are accessible from methods in the literature. In particular:

- when A represents a phenothiazinyl radical, the acids of general formula **(VII.i)** are accessible from methods in the literature such as for example *J. Med. Chem.* (1992), **35**, 716-724, *J. Med. Chem.* (1998), **41**, 148 –156; *Synthesis* (1988) 215-217; or *J. Chem. Soc. Perkin. Trans. 1* (1998), 351-354;

- when A represents an indolinyl radical, the acids of general formula **(VII.i)** are accessible from methods in the literature such as for example *J. Het. Chem.* (1993), **30**, 1133-1136 or *Tetrahedron* (1967), **23**, 3823;

- when A represents a phenylaminophenyl radical, the acids of general formula **(VII.i)** are accessible from methods in the literature such as for example *J. Amer. Chem Soc.* (1940), **62**, 3208; *Zh. Obshch. Khim.* (1953), **23**, 121-122 or *J. Org. Chem.* (1974), 1239-1243;

- when A represents a carbazolyl radical, the acids of general formula **(VII.i)** are accessible from methods in the literature such as for example *J. Amer. Chem Soc.*, (1941), **63**, 1553-1555; *J. Chem. Soc.* (1934), 1142-1144; *J. Chem. Soc.* (1945), 945-956; or *Can. J. Chem. Soc.* (1982), 945-956; and

- when A represents a 4-(4-hydroxyphenyl)-phenyl type radical, reference will be made for example to the following publication: *Synthesis*, (1993) 788-790.

Preparation of the compounds of general formula (VIII)

When R^1 and R^2 both represent H, the protected amino acids of general formula **(VIII)** are either commercial, or obtained by protection of commercial amino acids by a carbamate-type group according to methods known to a person skilled in the art.

When at least one of R^1 and R^2 is not H, and n = 0, the protected amino acids of general formula **(VIII)** are obtained in one stage, Diagram 6.1, by alkylation, in a solvent such as tetrahydrofuran and at a low temperature, of commercial compound of general formula **(VIII.i)** using 3 equivalents of butyllithium and approximately one equivalent of halogenated derivative of general formula **(VIII.ii)** in which R^1 represents an alkyl, cycloalkyl, cycloalkylalkyl or arylalkyl type radical and Hal a halogen atom. According to the case, a second alkylation (not represented in Diagram 6.1) can be carried out in similar fashion, thus making it possible to obtain the compounds of general formula **(VIII)** in which neither R^1 nor R^2 represents H.

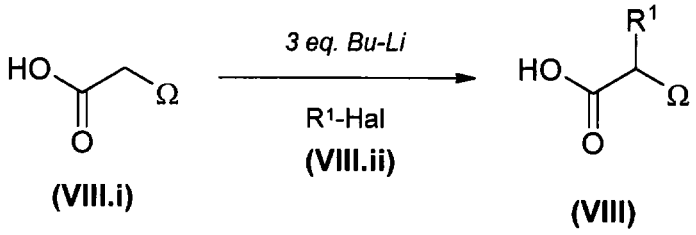


Diagram 6.1

Preparation of the imidazoles, thiazoles and oxazoles of general formula (IX)

The preparation of the intermediates of general formula **(IX)** is described in Patent Application WO 98/58934 (cf. in particular pages 10 to 50 and the examples in this document) or carried out by analogy using commercial starting products.

Preparation of the protected alcohols of general formula (X)

Preparation of the compounds of general formula (X) derived from imidazoles

The acid of general formula **(X.i)** is successively treated, Diagram 8.1, by Cs_2CO_3, the compound of general formula **(V.ii)** and by NH_4OAc, in order to produce the compound of general formula **(X)**. The reaction conditions are analogous to those described above for this type of synthesis.

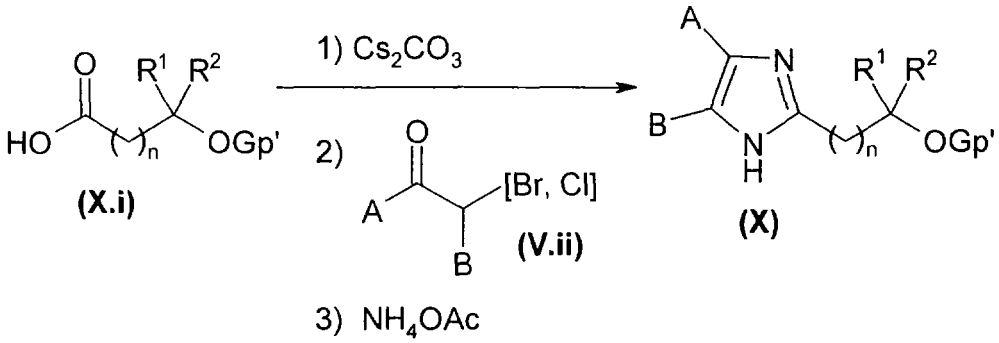


Diagram 8.1

Preparation of the compounds of general formula (X) derived from thiazoles

The cyano derivative of general formula **(X.ii)** is treated, Diagram 8.2, by H_2S in order to produce the thiocarboxamide of general formula **(X.iii)**, which, condensed with the compound of general formula **(V.ii)**, makes it possible to obtain the compound of general formula **(X)**. The reaction conditions are analogous to those described above (Diagram 5.3) for this type of synthesis.

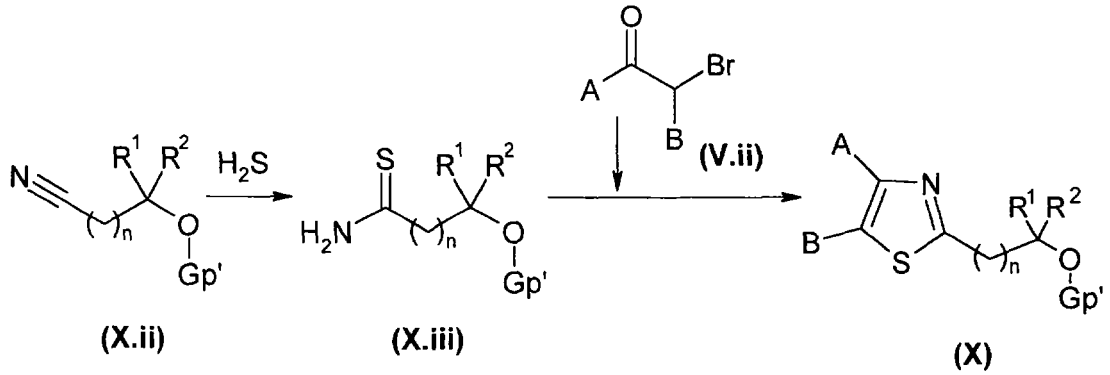


Diagram 8.2

Preparation of the acids of general formula (XXXVI)

The non commercial acids of general formula **(XXXVI)** are accessible from methods in the literature or similar methods adapted by a person skilled in the art. In particular:

- when A represents a phenothiazinyl radical, the acids of general formula **(XXXVI)** are accessible from methods in the literature: *J. Org. Chem.*, (1956), **21**, 1006; *Chem. Abstr.*, **89**, 180029 and *Arzneimittel Forschung* (1969), **19**, 1193.

- when A represents a diphenylamine radical, the acids of general formula **(XXXVI)** are accessible from methods in the literature: *Chem Ber.*, (1986), **119**, 3165-3197; *J. Heterocyclic. Chem.* (1982), **15**, 1557-1559; *Chem. Abstr.*, (1968), **68**, 68730x; or by adaptation of these methods by a person skilled in the art;
- when A represents a 4-(4-hydroxyphenyl)-phenyl type radical, the acids of general formula **(XXXVI)** are accessible from methods in the literature such as for example *Tetrahedron Lett.* (1968), 4739 or *J. Chem. Soc.* (1961), 2898.
- when A represents a carbazolyl radical, the acids of general formula **(XXXVI)** are accessible from methods in the literature such as for example *J. Amer. Chem.*, (1946), **68**, 2104 or *J. Het. Chem* (1975), **12**, 547-549.
- when A represents a benzopyrane or benzofurane type radical, the acids of general formula **(XXXVI)** are accessible by methods in the literature such as for example *Syn. Commun.* (1982), **12**(8), 57-66; *J. Med. Chem.* (1995), **38**(15), 2880-2886; or *Helv. Chim. Acta.* (1978), **61**, 837-843.
- when A represents an indolinyl or tetrahydroquinolyl radical, the acids of general formula **(XXXVI)** are accessible from methods in the literature such as, for example, *J. Med. Chem.* (1997), **40**, (7), 1049-1062; *Bioorg. Med. Chem. Lett.* (1997), 1519-1524; *Chem. Abstr.* (1968), **69**, 43814k; or *Chem. Abstr.* (1966), **66**, 17538c.

Of course, the phenol, amine or aniline functions resulting from the nature of the substituents on the A radical of the compounds of general formula **(XXXVI)** can lead a person skilled in the art to add to the stages described, stages of protection / deprotection of these functions so that they do not interfere with the remainder of the chemical synthesis.

Unless otherwise specified, all the technical and scientific terms used here have the same meaning as that usually understood by an ordinary specialist of the field to which this invention belongs. Similarly, all the publications, patent applications, all the patents and all other references mentioned here are incorporated by way of reference.

The following examples are presented in order to illustrate the above procedures and should in no event be considered as a limit to the scope of the invention.

EXAMPLES

Example 1: 2,6-di*tert*-butyl-4-{2-[2-(methylamino)ethyl]-1,3-thiazol-4-yl}phenol hydrochloride :

1.1) *Tert-butyl 2-cyanoethyl(methyl)carbamate :*

0.1 mol of N-methyl-β-alaninenitrile is solubilized in dichloromethane (100 ml) containing 20.9 ml (0.12 mol) of diisopropylethylamine. The mixture is cooled down to 0 °C then Boc-O-Boc (26.2 g; 0.12 mol) is added by fractions and the mixture is stirred overnight at ambient temperature. The reaction medium is then poured over iced water and extracted with dichloromethane. The organic phase is washed successively with a 10% aqueous sodium bicarbonate solution and with water, then finally with a saturated sodium chloride solution. The organic phase is then dried over magnesium sulphate, filtered and concentrated under vacuum. The brown-red oil obtained is used as it is in the following stage.

1.2) *Tert-butyl 3-amino-3-thioxopropyl(methyl)carbamate:*

43.4 mmol of intermediate 1.1 are dissolved in ethanol (40 ml) containing triethylamine (6.1 ml). H_2S is then bubbled through the mixture for 3 hours before the solvents are evaporated to dryness. The expected product is obtained after chromatography on a silica column (eluent: 50% of ethyl acetate in heptane) in the form of light orange oil. Crystallization of this oil from diisopropyl ether produces a white solid with a yield of 15% Melting point: 104 °C.

1.3) *4-[3,5-bis(1, 1-dimethylethyl)-4-hydroxyphenyl]-N-[(1, 1-dimethylethoxy)-carbonyl]-N-methyl-2-thiazoleethanamine:*

Intermediate 1.2 (2.11 mmol) and bromo-1-(3,5-di*tert*-butyl-4-hydroxyphenyl)ethanone (6.9 g; 2.11 mmol) are dissolved in toluene (75 ml) under an argon atmosphere then the mixture is stirred at ambient temperature for 12 hours. The reaction medium is taken to reflux for 4 hours. After evaporation of the solvents, the residue is diluted with dichloromethane and washed with a saturated NaCl solution. The organic phase is separated, dried over magnesium sulphate, filtered and concentrated under vacuum. The expected product is crystallized in the form of a white solid. Melting point: 204 °C.

1.4) *2,6-ditert-butyl-4-{2-[2-(methylamino)ethyl]-1,3-thiazol-4-yl}phenol hydrochloride :*

1.95 mmol of intermediate 1.3 are dissolved in ethyl acetate (20 ml). The solution is cooled down to 0 °C then HCl gas is bubbled through for 10 minutes. The mixture is allowed to return to ambient temperature while stirring is maintained. After filtration and drying under vacuum, the expected product is recovered in the form of white crystals that are washed with ether. Quantitative yield. Melting point: 206-208 °C.

Example 2: 2,6-di*tert*-butyl-4-[4-(hydroxymethyl)-1,3-oxazol-2-yl]phenol:

This compound can be obtained according to a procedure analogous to that described for intermediate 1.C of the PCT Application WO 99/09829 in which ethyl bromopyruvate replaces 4-chloroacetoacetate and the isolated intermediate ester is then reduced using DIBAL in dichloromethane at 0 °C. The reaction mixture is then treated with an aqueous solution of NH_4Cl and filtered on celite, followed by extraction with a 50/50 mixture of dichloromethane and ethyl acetate. After decantation, drying over magnesium sulphate, filtration and evaporation of the filtrate, crystallisation from the ethanol makes it possible to obtain the expected product in the form of a white powder. Melting point: 167-168 °C.

Example 3: 2,6-di*tert*-butyl-4-{2-[1-(methylamino)ethyl]-1,3-thiazol-4-yl}phenol hydrochloride :

3.1) *N'-(tert-butoxycarbonyl)-N'-methylalaninamide:*

12 mmol of Boc-N-Me-DL-Ala-OH are dissolved in dimethoxyethane. N-methylmorpholine is added dropwise, then *iso*-butyl chloroformate. After stirring the mixture for 15 minutes at –15 °C, ammonia (NH_3) is bubbled through, then continuous stirring of the mixture is maintained at this temperature overnight. The precipitate obtained is filtered. The product, once dried, is used as it is in the following stage.

3.2) *Tert-butyl 2-amino-1-methyl-2-thioxoethyl(methyl)carbamate :*

This compound is obtained by reaction with P_2S_5 under the conditions described in Example 12, Stage 12.2.

3.3) *Tert-butyl 1-[4-(3,5-ditert-butyl-4-hydroxyphenyl)-1,3-thiazol-2-yl]ethyl(methyl)carbamate:*

Intermediate 3.2 and bromo-1-(3,5-di*tert*-butyl-4-hydroxyphenyl)ethanone are condensed according to a protocol analogous to that described in Stage 1.3.

3.4) *2,6-ditert-butyl-4-{2-[1-(methylamino)ethyl]-1,3-thiazol-4-yl}phenol hydrochloride :*

The experimental protocol used is the same as that described in Stage 1.4 of Example 1, with intermediate 3.3 replacing intermediate 1.3. The expected product is obtained in the form of a white powder. Melting point: 236-237 °C.

Example 4: 2,6-di*tert*-butyl-4-[2-(methoxymethyl)-1,3-thiazol-4-yl]phenol:

4.1) *[4-(3,5-ditert-butyl-4-hydroxyphenyl)-1,3-thiazol-2-yl]methyl pivalate :*

Intermediate 4.1 is prepared according to a protocol identical to that described for Example 1, Stage 1.3, using 2-(*tert*-butylcarbonyloxy)thioacetamide instead of intermediate 1.2 and with toluene replacing benzene. The expected compound is obtained in the form of a white solid with a yield of 100%. Melting point: 114.6-116.0 °C.

4.2) *2,6-ditert-butyl-4-[2-(hydroxymethyl)-1,3-thiazol-4-yl]phenol:*

Intermediate 4.1 (1.25 mmol) is dissolved in methanol (20 ml). The solution is cooled down using an ice bath then a 1*N* solution of NaOH is added dropwise. The mixture is allowed to return to ambient temperature whilst being stirred. After evaporation to dryness and dilution of the residue with water, the solution is neutralized using citric acid and extracted with dichloromethane. The organic phase is washed with a saturated aqueous solution of sodium chloride before being dried over magnesium sulphate, filtered and concentrated under vacuum. A white solid is obtained with a yield of 88%. Melting point: 126.4-127.4 °C.

4.3) *2,6-ditert-butyl-4-[2-(methoxymethyl)-1,3-thiazol-4-yl]phenol:*

Intermediate 4.2 (1 equivalent) is methylated by reaction with 1.1 equivalent of iodomethyl in the presence of 2 equivalents of triethylamine, the reaction being carried out in tetrahydrofuran. A dark cream powder is obtained. Melting point: 115.8-117 °C.

Example 5: 2,6-di*tert*-butyl-4-{4-[(methylamino)methyl]-1,3-oxazol-2-yl}phenol hydrochloride :

5.1) *2,6-ditert-butyl-4-[4-(bromomethyl)-1,3-oxazol-2-yl]phenol:*

The compound of Example 2 (4.70 mmol) was dissolved in dichloromethane (30 ml). After the addition of CBr_4 (2.02 g; 6.10 mmol), the reaction medium is cooled down to 0 °C. PPh_3 (1.48 g; 5.63 mmol) is added by fractions then the mixture is allowed to return to ambient temperature. The reaction medium is then poured over iced water before being extracted with dichloromethane. The organic phase is washed with salt water before being dried over magnesium sulphate, filtered and concentrated under vacuum. The crude oil obtained is sufficiently pure to be able to be used directly in the following stage.

5.2) *2,6-ditert-butyl-4-{4-[(methylamino)methyl]-1,3-oxazol-2-yl}phenol hydrochloride :*

33 mmol of methylamine (2*M* solution in THF) are dissolved in acetonitrile (50 ml). 5.48 mmol of intermediate 5.1 dissolved in acetonitrile (50 ml) are added at 0 °C then the mixture is stirred at ambient temperature for 3 hours. The solvents are evaporated off then the residue is divided between ethyl acetate and a 10% aqueous solution of $NaHCO_3$. The organic phase is washed with salt water before being dried over magnesium sulphate, filtered and concentrated under vacuum. The hydrochloride is then obtained by solubilizing the base in ether and adding 1.2 ml of a 1*N* solution of HCl in ether. After filtration and washing the solid formed with ether, a dark orange powder is obtained. Melting point: decomposes at 150 °C.

Example 6: N-{[4-(3,5-di*tert*-butyl-4-hydroxyphenyl)-1,3-thiazol-2-yl]methyl}acetamide:

6.1) *Benzyl {4-[3,5-di(tert-butyl)-4-hydroxyphenyl]-1,3-thiazol-2-yl}methylcarbamate:*

This compound is prepared according to an experimental protocol described in Patent Application WO 98/58934 (see preparation of intermediates 26.1 and 26.2), using Z-Gly-NH_2 instead of N-Boc sarcosinamide. Expected compound is obtained in the form of a pale yellow oil with a yield of 99%. MH+ = 453.20

6.2) *4-[2-(aminomethyl)-1,3-thiazol-4-yl]-2,6-di(tert-butyl)phenol:*

0.1 ml of a 40% solution of potassium hydroxide is added dropwise to a solution of 0.106 g (1.1 mmol) of intermediate 6.1 in 10 ml of methanol. After stirring overnight under reflux, the reaction mixture is concentrated under vacuum and the residue is diluted with dichloromethane and washed with a 1*N* solution of HCl then 50 ml of a saturated solution of NaCl. The organic phase is separated and dried over magnesium sulphate, filtered and concentrated under vacuum. The expected product is obtained after chromatography on a silica column (eluent: 5% ethanol in dichloromethane) in the form of a brown foam with a yield of 76%.
MH+ = 319.29.

6.3) *N-{[4-(3,5-ditert-butyl-4-hydroxyphenyl)-1,3-thiazol-2-yl]methyl}acetamide:*

Intermediate 6.2 (2 mmol) is dissolved in dichloromethane (20 ml). Triethylamine (3 mmol) is added and the mixture cooled down to 0 °C. Acetyl chloride (3 mmol) is then added dropwise. Once the addition is completed, the mixture is taken to ambient temperature and stirred overnight at this temperature before being poured over iced water. The aqueous phase is extracted with dichloromethane, and the organic phase obtained is washed with salt water before being dried over magnesium sulphate. After filtration and evaporation of the solvents, the expected product is obtained, after chromatography on a silica column (eluent: 3% ethanol in dichloromethane), with a yield of 79%. Dark cream foam. MH+ = 361.2.

Example 7: Ethyl [4-(3,5-di*tert*-butyl-4-hydroxyphenyl)-1,3-thiazol-2-yl]methylcarbamate:

A solution containing intermediate 6.2 described above (5 mmol) and 5 ml of a 1N solution of sodium hydroxide is cooled down to 10 °C. Ethyl chloroformate (5 mmol)

and 2.5 ml of a 2 N solution of sodium hydroxide are added simultaneously. After stirring for 16 hours at 23 °C, approximately 0.5 ml of a solution of concentrated hydrochloric acid (approximately 11 N) is added in order to adjust the pH to 4-5. The oil obtained is extracted with ethyl acetate (2 x 5 ml), washed with water then dried over magnesium sulphate. The solvents are evaporated off and the expected product is recovered in the form of white crystals. MH+ =391.2.

Example 8: 2,6-di*tert*-butyl-4-[2-(morpholin-4-ylmethyl)-1,3-thiazol-4-yl]phenol:

8.1) *4-[2-(bromomethyl)-1,3-thiazol-4-yl]-2,6-ditert-butylphenol:*

1.5 g (4.70 mmol) of intermediate 4.2, (2,6-ditert-butyl-4-[2-(hydroxymethyl)-1,3-thiazol-4-yl]phenol is dissolved in dichloromethane (30 ml). After the addition of CBr_4 (2.02 g; 6.10 mmol), the reaction medium is cooled down to 0 °C. PPh_3 (1.48 g; 5.63 mmol) is added by fractions then the mixture is allowed to return to ambient temperature. The reaction medium is then poured over iced water before being extracted with dichloromethane. The organic phase is washed with salt water before being dried over magnesium sulphate, filtered and concentrated under vacuum. The expected product is obtained after chromatography on a silica column (eluent: 30% ethyl acetate in heptane), in order to produce a brown oil with a yield of 92%. This product is sufficiently pure to be able to be used directly in the following stage. MH+ = 382.20.

8.2) *2,6-ditert-butyl-4-[2-(morpholin-4-ylmethyl)-1,3-thiazol-4-yl]phenol:*

1.57 mmol of morpholine and 0.4 ml (2.62 mmol) of triethylamine are dissolved in dimethylformamide (15 ml). 0.400 g (1.05 mmol) of intermediate 8.1 dissolved in dimethylformamide (5 ml) are added then the mixture is stirred at ambient temperature for 18 hours. The reaction medium is then poured over iced water and extracted with ethyl acetate. The organic phase is washed with salt water before being dried over magnesium sulphate, filtered and concentrated under vacuum. The expected product is obtained after chromatography on a silica column (eluent: 50% ethyl acetate in heptane), in order to produce an orange oil with a yield of 92%. Light cream crystals are obtained. Melting point: 136.7-137.2 °C.

Example 9: 2,6-di*tert*-butyl-4-[2-(thiomorpholin-4-ylmethyl)-1,3-thiazol-4-yl]phenol:

The experimental protocol used is the same as that described for Example 8, with thiomorpholine replacing morpholine in the second stage. The expected product is obtained in the form of a light orange solid. Melting point: 153.4-154.6 °C.

Example 10: 4-[2-(anilinomethyl)-1,3-thiazol-4-yl]-2,6-di*tert*-butylphenol:

The experimental protocol used is the same as that described for Example 8, with aniline replacing morpholine in the second stage. The expected product is obtained in the form of brown crystals. Melting point: 147.2-148.0 °C.

Example 11: 2,6-di*tert*-butyl-4-(2-{[[2-(dimethylamino)ethyl]-(methyl)amino]methyl}-1,3-thiazol-4-yl)phenol:

11.1) *4-[3,5-bis(1, 1-dimethylethyl)-4-hydroxyphenyl]-N-methyl-2-thiazolemethanamine hydrochloride :*

This compound is obtained using an experimental protocol identical to that of Stages 14.1 to 14.4 of Example 14 (see below).

11.2) *2,6-ditert-butyl-4-(2-{[[2-(dimethylamino)ethyl]-(methyl)amino]methyl}-1, 3-thiazol-4-yl)phenol:*

5 mmol of triethylamine and a slight excess (1.2 mmol) of N-dimethyl-N-(2-chloroethyl)amine are added dropwise to a solution of 1 mmol of intermediate 11.1 in 20 ml of dimethylformamide at ambient temperature under an argon atmosphere. After stirring for 24 hours at 80 °C, the reaction mixture is poured over iced water, then extracted with ethyl acetate, washed with a saturated solution of NaCl, dried over magnesium sulphate and the solution is concentrated. The expected product is obtained after chromatography on a silica column (eluent: dichloromethane containing 5% ethanol with traces of ammonia in dichloromethane containing 5% ethanol with traces of ammonia). After evaporation, the pure fractions produce a brown viscous oil. MH+ = 404.26.

Example 12: 2,6-di*tert*-butyl-4-{5-methyl-2-[(methylamino)methyl]-1,3-thiazol-4-yl}phenol hydrochloride :

12.1) *N-Boc-sarcosinamide:*

15.0 g (0.120 mol) of sarcosinamide hydrochloride (N-Me-Gly-NH_2.HCl) are solubilized in dichloromethane containing 46.2 ml (0.265 mol) of diisopropylethylamine. The mixture is cooled down to 0 °C then Boc-O-Boc (28.8 g; 0.132 mol) is added by fractions and stirring of the mixture is maintained overnight at ambient temperature. The reaction medium is then poured over iced water and extracted with dichloromethane. The organic phase is washed successively with a 10% aqueous solution of sodium bicarbonate and water, then finally with a saturated solution of sodium chloride. The organic phase is then dried over magnesium sulphate, filtered and concentrated under vacuum. The product obtained is purified by crystallisation from diisopropyl ether in order to produce a white solid with a yield of 72%. Melting point: 103 °C.

12.2) *2-{[(1, 1-dimethylethoxy)carbonyl]methyl}amino-ethanethioamide:*

16.0 g (0.085 mol) of intermediate 12.1 are dissolved in dimethoxyethane (500 ml) and the solution obtained is cooled down to 5 °C. Sodium bicarbonate (28.5 g; 0.34 mol) then, by small portions, $(P_2S_5)_2$ (38.76 g; 0.17 mol) are added. The reaction medium is allowed to return to ambient temperature whilst being stirred over 24 hours. After evaporation of the solvents under vacuum, a 10% aqueous solution of sodium bicarbonate is added to the residue and the solution is extracted using ethyl acetate. The organic phase is washed successively with a 10% aqueous solution of sodium bicarbonate and water, then finally with a saturated solution of sodium chloride. The organic phase is then dried over magnesium sulphate, filtered and concentrated under vacuum. The product obtained is purified by crystallisation from ether in order to produce a white-coloured solid with a yield of 65%. Melting point: 150-151 °C.

12.3) *bromo-1-(3,5-ditert-butyl-4-hydroxyphenyl)propan-1-one:*

This compound is obtained in a simple fashion by reaction of 1-(3,5-ditert-butyl-4-hydroxyphenyl)propan-1-one (prepared from 2,6-ditertbutylphenol according to *Russ. J. Org. Chem.* (1997), **33**, 1409-1416) with bromine in acetic acid or also according to a protocol described in one of the following references: *Biorg. Med. Chem. Lett.*

(1996), **6**(3), 253-258; *J. Med. Chem.* (1988), **31**(10), 1910-1918; *J. Am. Chem. Soc.* (1999), **121**, 24.

12.4) *5-methyl-4-[3,5-bis(1, 1-dimethylethyl)-4-hydroxyphenyl]-N-[(1, 1-dimethylethoxy)-carbonyl]-N-methyl-2-thiazolemethanamine:*

Intermediate 12.2 (4.3 g; 2.11 mmol) and intermediate 12.3 (2.11 mmol) are dissolved in toluene (75 ml) under an argon atmosphere then the mixture is stirred at ambient temperature for 12 hours. The reaction medium is taken to reflux for 4 hours. After evaporation of the solvents, the residue is diluted with ethyl acetate and washed with a 10% solution of $NaHCO_3$ then with a saturated solution of NaCl. The organic phase is separated, dried over magnesium sulphate, filtered and concentrated under vacuum. The expected product is obtained after chromatography on a silica column (eluent: 30% ethyl acetate in heptane). The oil recovered is used as it is in the stage which follows.

12.5) *2,6-ditert-butyl-4-{5-methyl-2-[(methylamino)methyl]-1, 3-thiazol-4-yl}phenol hydrochloride:*

This compound is obtained in the form of a white powder by an experimental protocol analogous to that of Stage 1.4 of Example 1. Melting point: 140-142 °C.

<u>Example 13:</u> 1-[4-(10H-phenothiazin-2-yl)-1,3-thiazol-2-yl]methanamine hydrochloride :

13.1) *2-chloro-1-(10H-phenothiazin-2-yl)ethanone:*

2-chloro-1-[10-(chloroacetyl)-10*H*-phenothiazin-2-yl)ethanone is prepared from phenothiazine according to a protocol described in the literature (*J. Heterocyclic. Chem.* (1978), **15,** 175 and *Arzneimittel Forschung*, (1962), **12**, 48), which is followed by a deprotection reaction in an acid medium (acetic acid and hydrochloric acid) of the chloroacetyl group (which has served to protect position 10 of the phenothiazine during the Friedel-Crafts reaction) .

13.2) *Benzyl 2-amino-2-thioxoethylcarbamate :*

85 mmol of Z-Gly-NH_2 are dissolved in dimethoxyethane (500 ml) and the solution obtained is cooled down to 5 °C. Sodium bicarbonate (28.5 g; 0.34 mol) then, by small portions, $(P_2S_5)_2$ (38.76 g; 0.17 mol) are added. The reaction medium is allowed to return to ambient temperature whilst being stirred over 24 hours. After evaporation

under vacuum of the solvents, a 10% aqueous solution of sodium bicarbonate is added to the residue and the solution is extracted using ethyl acetate. The organic phase is washed successively with a 10% aqueous solution of sodium bicarbonate and water, then finally with a saturated solution of sodium chloride. The organic phase is then dried over magnesium sulphate, filtered and concentrated under vacuum. The product obtained is then purified by crystallisation from ether.

13.3) *Benzyl [4-(10H-phenothiazin-2-yl)-1,3-thiazol-2-yl]methylcarbamate :*

Intermediates 13.1 and 13.2 are coupled according to a protocol analogous to that described in Stage 1.3 of Example 1.

13.4) *1-[4-(10H-phenothiazin-2-yl)-1,3-thiazol-2-yl]methanamine hydrochloride*

The experimental protocol used is the same as that described in Stage 1.4 of Example 1, with intermediate 13.3 replacing intermediate 1.3. After drying under vacuum, the expected product is obtained in the form of a dark green powder. Melting point: > 275 °C.

Example 14: ***N*-{[4-(3,5-di*tert*-butyl-4-hydroxyphenyl)-1,3-thiazol-2-yl]methyl}-*N*-methylacetamide:**

14.1) *N-Boc-sarcosinamide:*

The preparation of this compound has already been described in Stage 12.1 of Example 12.

14.2) *2-{[(1, 1-dimethylethoxy)carbonyl]methyl}amino-ethanethioamide:*

The preparation of this compound has already been described in Stage 12.2 of Example 12.

14.3) *4-[3,5-bis(1, 1-dimethylethyl)-4-hydroxyphenyl]-N-[(1, 1-dimethylethoxy)-carbonyl]-N-methyl-2-thiazolemethanamine:*

Intermediate 14.2 (4.3 g; 2.11 mmol) and bromo-1-(3,5-di*tert*-butyl-4-hydroxyphenyl)ethanone (6.9g; 2.11 mmol) are dissolved in benzene (75 ml) under an argon atmosphere, then the mixture is stirred at ambient temperature for 12 hours. The reaction medium is taken to reflux for 4 hours. After evaporation of the solvents, the residue is diluted with dichloromethane and washed with a saturated solution of NaCl. The organic phase is separated, dried over magnesium sulphate, filtered and

concentrated under vacuum. The expected product is obtained after chromatography on a silica column (eluent: 20% of ethyl acetate in heptane) in the form of an oil which crystallizes very slowly in the refrigerator with a yield of 28%. Melting point: 126.5-127.3 °C.

14.4) *4-[3,5-bis(1, 1-dimethylethyl)-4-hydroxyphenyl]-N-methyl-2-thiazolemethanamine hydrochloride :*

1.95 mmol of intermediate 14.3 are dissolved in ethyl acetate (20 ml). The solution is cooled down to 0 °C then HCl gas is bubbled through for 10 minutes. The mixture is allowed to return to ambient temperature whilst stirring is maintained. After filtration and drying under vacuum, the expected product is recovered (quantitative yield).

14.5) *N-{[4-(3,5-ditert-butyl-4-hydroxyphenyl)-1,3-thiazol-2-yl]methyl}-N-methylacetamide:*

This compound is obtained according to a protocol identical to that described in Stage 6.3 of Example 6, with intermediate 14.5 replacing intermediate 6.2. White crystals. Melting point: 132.3-133.1 °C.

<u>Example 15:</u> 1-[4-(3,5-di*tert*-butyl-4-methoxyphenyl)-1, 3-thiazol-2-yl]-N-methylmethanamine hydrochloride :

15.1) *4-[3,5-bis(1, 1-dimethylethyl)-4-methoxyphenyl]-N-[(1, 1-dimethylethoxy)-carbonyl]-N-methyl-2-thiazolemethanamine:*

Intermediate 14.3 is methylated by the action of methyl iodide in the presence of NaH in tetrahydrofuran in order to produce the expected product. The brown oil which is obtained is used as it is in the following stage.

15.2) *1-[4-(3,5-ditert-butyl-4-methoxyphenyl)-1,3-thiazol-2-yl]-N-methylmethanamine hydrochloride*

The operating method is analogous to that of Stage 14.4 of Example 14, with intermediate 15.1 replacing intermediate 14.3 and the ethyl acetate being replaced by a mixture of ethyl acetate and ether. The expected product is recovered in the form of light cream crystals. Melting point: 218.4-219.6 °C.

<u>Example 16:</u> 2,6-di*tert*-butyl-4-{2-[(ethylamino)methyl]-1, 3-thiazol-4-yl}phenol hydrochloride :

The experimental protocol is identical to that used in Stages 14.1 to 14.4 of Example 14, with N-ethylglycineamide (*J. Med. Chem.* (1995), **38**(21), 4244-4256) replacing N-sarcosinamide in the first stage. White crystals. Melting point: 232.4-234.6 °C.

Example 17: 2,6-di*tert*-butyl-4-{2-[(4-phenylpiperazin-1-yl)methyl]-1,3-thiazol-4-yl}phenol hydrochloride :

The experimental protocol used is the same as that described for Example 8, with 4-phenylpiperazine replacing morpholine in the second stage. Light cream crystals. Melting point: 225.3-226.9 °C.

Example 18: 2,6-di*tert*-butyl-4-{2-[(4-methyl-1,4 -diazepan-1-yl)methyl]-1,3-thiazol-4-yl}phenol hydrochloride :

The experimental protocol used is the same as that described for Example 8, with N-methylhomopiperazine replacing morpholine in the second stage. White crystals. Melting point: 222.1-225.4 °C.

Example 19: N-{1-[4-(4-anilinophenyl)-1,3-thiazol-2-yl]ethyl}-N-methylamine hydrochloride :

19.1) *1-(4-anilinophenyl)ethanone*

4-amino-acetophenone (4.87 g; 36.0 mmol) is dissolved in dimethylformamide (75 ml). 15 g (0.108 mol) of potassium carbonate (previously dried at 170 °C under an argon atmosphere), 7.236 g (36.0 mmol) of iodobenzene, 0.4 g of copper in powder form and a catalytic quantity of copper iodide are added. The reaction mixture is taken to reflux for 12 hours. After the reaction medium has been allowed to return to ambient temperature, the latter is filtered on celite and poured over iced water. After extraction with ethyl acetate, the organic phase is washed with water before being dried over magnesium sulphate, filtered and concentrated under vacuum. The product obtained is purified by crystallisation from heptane in order to produce a yellow solid with a yield of 53.4%. Melting point: 105 °C.

19.2) *N-(4-acetylphenyl)-N-phenylacetamide:*

This compound is obtained according to a method inspired by *Tetrahedron* (1980), **36**, 3017-3019. Intermediate 19.1 (60 mmol) is suspended in 150 ml of acetic anhydride. 70% perchloric acid (0.5 ml) is added. After heating for 15 minutes at 70 °C, the mixture is poured over ice and the precipitate formed is filtered. After drying under vacuum, redissolution in dichloromethane and treatment with bone black, the

suspension is filtered on celite and the solvents are evaporated off. After crystallisation from heptane, a yellow solid is obtained with a yield of 54.2%. Melting point: 118-120 °C (value in the literature: 122-123 °C).

19.3) *N-[4-(bromoacetyl)phenyl]-N-phenylacetamide*

Intermediate 19.2 (0.633 g; 2.5 mmol) is dissolved in methanol (20 ml) and 1 g (2.0 mmol) of bromination resin PVPHP (*J. Macromol. Sci. Chem.* (1977), **A11**, (3), 507-514) is added. After stirring under an argon atmosphere for 4 hours, the resins are filtered and rinsed with methanol. After evaporation of the filtrate solvents and crystallisation from methanol, a white solid is obtained with a yield of 59%. Melting point: 152-153 °C.

19.4) *Tert-butyl (4-{4-[acetyl(phenyl)amino]phenyl}-1,3-thiazol-2-yl)methyl(methyl)carbamate:*

Intermediate 19.3 (2.11 mmol) and intermediate 3.2 (2.11 mmol) are dissolved in toluene (75 ml) under an argon atmosphere, then the mixture is stirred at ambient temperature for 12 hours. The reaction medium is taken to reflux for 4 hours. After evaporation of the solvents, the residue is diluted with dichloromethane and washed with a saturated solution of NaCl. The organic phase is separated, dried over magnesium sulphate, filtered and concentrated under vacuum. The expected product is obtained and used as it is in the following stage.

19.5) *N-{1-[4-(4-anilinophenyl)-1,3-thiazol-2-yl]ethyl}-N-methylamine hydrochloride*

Intermediate 19.4 (1.5 mmol) is treated with concentrated HCl (15 ml) and acetic acid (30 ml). After refluxing for 24 hours and evaporation of the solvents, the residue is taken up in toluene, the solvents are again evaporated then the product crystallizes from a little water. A grey powder is obtained. Melting point: > 250 °C.

<u>Example 20:</u> 2,6-di*tert*-butyl-4-{2-[(isopropylamino)methyl]-1, 3-thiazol-4-yl}phenol hydrochloride :

Intermediate 6.2 (2 mmol), in solution in methanol (20 ml), is reacted with acetone (2.2 mmol), $NaBH_4$ (2.2 mmol) in the presence of molecular sieves. The reaction product is then converted to the hydrochloride according to an operating method analogous to that of Stage 1.4 of Example 1. White crystals. Melting point: 197.1-198.8 °C.

Example 21: 2,6-ditert-butyl-4-{2-[(cyclohexylamino)methyl]-1,3-thiazol-4-yl}phenol hydrochloride :

The experimental protocol used is the same as that described for Example 20, with cyclohexanone replacing acetone. White crystals. Melting point: 202.1-203.4 °C.

Example 22: 2,6-di*tert*-butyl-4-{2-[(4-isopropylpiperazin-1-yl)methyl]-1,3-thiazol-4-yl}phenol hydrochloride :

The experimental protocol used is the same as that described for Example 8, with N-isopropylpiperazine replacing morpholine in the second stage. White crystals. Melting point: 238.4-239.7 °C.

Example 23: *N*-methyl-1-[4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]ethanamine hydrochloride :

The experimental protocol used is the same as that described in Stage 19.4 of Example 19, with intermediate 13.1 replacing intermediate 19.3, this stage being followed by a stage analogous to that of Stage 1.4 of Example 1 in order to obtain the hydrochloride. Dark green powder. Melting point: > 250 °C.

Example 24: 2,6-di*tert*-butyl-4-{2-[(4-ethylpiperazin-1-yl)methyl]-1,3-thiazol-4-yl}phenol hydrochloride :

The experimental protocol used is the same as that described for Example 8, with N-ethylpiperazine replacing morpholine in the second stage. White crystals. Melting point: 247.0-248.8 °C.

Example 25: *N*-{[4-(4-anilinophenyl)-1,3-thiazol-2-yl]methyl}-*N*-ethylamine hydrochloride :

The experimental protocol used is the same as that described for Stages 14.1 to 14.4 of Example 14, with N-ethyl-glycineamide (*J. Med. Chem.* (1995), **38**(21), 4244-56) replacing sarcosinamide and intermediate 19.3 replacing bromo-1-(3,5-di*tert*-butyl-4-hydroxyphenyl)ethanone. Dark green powder. Melting point: > 250 °C.

Example 26: *N*-{[4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]methyl}ethanamine hydrochloride :

The experimental protocol used is the same as that described for Stages 14.1 to 14.4 of Example 14, with N-ethyl-glycineamide (*J. Med. Chem.* (1995), **38**(21), 4244-56)

replacing sarcosinamide and intermediate 13.1 replacing bromo-1-(3,5-di*tert*-butyl-4-hydroxyphenyl)ethanone. Dark green powder. Melting point: > 250 °C.

Example 27: 2,6-di*tert*-butyl-4-(2-{[4-(dimethylamino)piperidin-1-yl]methyl}-1,3-thiazol-4-yl)phenol hydrochloride :

The experimental protocol used is the same as that described for Example 8, with 4-dimethylaminopiperidine (*J. Med. Chem.* (1983), **26**, 1218-1223 or *J. Chem. Soc.* (1957), 3165-3172) replacing morpholine in the second stage. Dark green powder. Melting point: 113.0-113.4 °C.

Example 28: 1-{[4-(3,5-di*tert*-butyl-4-hydroxyphenyl)-1,3-thiazol-2-yl]methyl}piperidin-4-ol hydrochloride :

28.1) *1-{[4-(3,5-ditert-butyl-4-hydroxyphenyl)-1,3-thiazol-2-yl]methyl}piperidin-4-ol*

The experimental protocol used is the same as that described for Example 8, with piperidin-4-one hydrochloride (*J. Org. Chem.* (1949), **14**, 530-535) replacing morpholine and 2 additional equivalents of triethylamine being used in the second stage. The product obtained is used as it is in the following stage.

28.2) *1-{[4-(3,5-ditert-butyl-4-hydroxyphenyl)-1,3-thiazol-2-yl]methyl}piperidin-4-ol hydrochloride :*

Intermediate 28.1 is reduced to an alcohol by the action of $NaBH_4$ in methanol. Once the reaction is completed, dichloromethane and salt water are added to the reaction medium. The aqueous phase is extracted with dichloromethane and washed with salt water. The combined organic phases are dried over magnesium sulphate and the solvents evaporated off.

The product obtained previously is solubilized in ethyl acetate and the solution cooled down to 0 °C. A 1*N* solution of HCl in ether (3 equivalents) is added slowly, the mixture being maintained at a temperature of 0 °C for the addition then allowed to return to ambient temperature, stirring being maintained thus for 12 hours. The expected product is recovered in the form of a white solid. Melting point: 215.4-218.2 °C.

Example 29: 4-methylpentyl 2-[4-(1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate:

29.1) *N-{[(4-methylpentyl)oxy]carbonyl}-β-alanine:*

Triphosgene at 23 °C (5.3 g; 0.019 mol) is added to a solution containing 4-methyl-1-pentanol (5 g; 0.049 mol) in 80 ml of dichloromethane. The mixture is cooled down to 0 °C then pyridine (3.8 g; 0.049 mol) is added dropwise. The mixture is taken to 23 °C and stirring maintained for 2 hours. The solvents are evaporated off using a rotary evaporator. The white solid recovered is filtered on frit after having been triturated in ether. The filtrate ether is evaporated.

A mixture containing β-alanine (4.4 g, 0.049 mol) and 50 ml of a 1*N* solution of sodium hydroxide is cooled down to 10 °C. 4-methylpentylcarbonate chloride freshly prepared previously and 50 ml of a 1*N* solution of sodium hydroxide at 5 °C are added simultaneously to the mixture of β-alanine and sodium hydroxide prepared above. After stirring for 16 hours at 23 °C, approximately 80 ml of a hydrochloric acid solution (approximately 1*N*) is added in order to adjust the pH to 4-5 until a light white precipitate is obtained. The reaction mixture is extracted with ethyl acetate (2 x 50 ml) and the extract washed with water then dried over magnesium sulphate. A colourless oil is obtained (7.2 g; yield of 68%).

NMR H^1 (δ ppm, DMSO): 0.85 (dq, 6H); 1.15 (m, 2H); 1.49-1.53 (m, 3H); 2.35 (t, 2H); 3.14-3.19 (m, 2H); 3.88-3.91 (m, 2H); 7.04 (se, 1H).; 12 (se, 1H)

29.2) *4-methylpentyl 2-[4-(1,1'-biphenyl-4-yl)-1H-imidazol-2-yl]ethylcarbamate:*

A mixture of intermediate 29.1 (4.52 g; 0.021 mol) and of caesium carbonate (3.4 g; 0.0105 mol) in 35 ml of methanol is stirred at 23 °C for 1 hour. The methanol is eliminated by evaporation under reduced pressure in a rotary evaporator. The mixture obtained is dissolved in 70 ml of dimethylformamide then 2-bromo-4-phenylacetophenone (5.7 g; 0.021 mol) is added. After stirring for 16 hours, the solvent is evaporated off under reduced pressure. The mixture obtained is taken up in ethyl acetate then the caesium bromide is filtered. The ethyl acetate of the filtrate is evaporated and the reaction oil is taken up in a mixture of xylenes (300 ml) and ammonium acetate (32 g; 0.42 mol). The reaction medium is heated to reflux for approximately an hour and a half, evacuating the water using a Dean-Stark apparatus, then, after cooling down, a mixture of iced water and ethyl acetate is poured into the reaction medium. After decantation, the organic phase is washed with a saturated solution of sodium bicarbonate, dried over magnesium sulphate then evaporated under vacuum. After purification on a silica column (eluent: ethyl acetate-heptane / 5-5 to 10-

0), a white-coloured powder is obtained (yield of 10%). Melting point: 128.3 °C. MH+ = 392.3.

The compounds of Examples 30 to 43 are obtained according to procedures analogues to that described for Example 29 or above in the part entitled "Preparation of the compounds of general formula (I)".

Example 30: 3,3-dimethylbutyl 2-[4-(4-pyrrolidin-1-ylphenyl)-1*H*-imidazol-2-yl]ethylcarbamate:

Melting point: 119.2 °C. MH+ = 385.3.

Example 31: Isopentyl 2-[4-(1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate:

Melting point: 128-130 °C. MH+ = 378.3.

Example 32: Hexyl 2-[4-(4'-bromo-1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate :

Melting point: 138-140 °C. MH+ = 470.2.

Example 33: Benzyl 2-[4-(4-*tert*-butylphenyl)-1*H*-imidazol-2-yl]ethylcarbamate :

Melting point: 173 °C. MH+ = 378.2.

Example 34: 3,3-dimethylbutyl 2-[4-(1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate:

Melting point: 98.4 °C. MH+ = 392.15.

Example 35: Hexyl 2-[4-(4-pyrrolidin-1-ylphenyl)-1*H*-imidazol-2-yl]ethylcarbamate :

Melting point: 110-114 °C. MH+ = 385.3.

Example 36: 4,4,4-trifluorobutyl 2-[4-(4-pyrrolidin-1-ylphenyl)-1*H*-imidazol-2-yl]ethylcarbamate :

Melting point: 148.3 °C. MH+ = 411.3.

Example 37: Hexyl 2-[4-(3,5-di*tert*-butyl-4-hydroxyphenyl)-1*H*-imidazol-2-yl]ethylcarbamate:

Melting point: 197.4 °C. MH+ = 444.4.

Example 38: 3,3-dimethylbutyl 2-[4-(3,5-di*tert*-butyl-4-hydroxyphenyl)-1*H*-imidazol-2-yl]ethylcarbamate:

Melting point: 118-120 °C. MH+ = 441.3.

Example 39: 3,3-dimethylbutyl 2-[4-(4-methoxyphenyl)-1*H*-imidazol-2-yl]ethylcarbamate:

Melting point: 116.8 °C. MH+ = 346.2.

Example 40: Benzyl 2-[4-(3,5-di*tert*-butyl-4-hydroxyphenyl)-1*H*-imidazol-2-yl]ethylcarbamate:

Melting point: 177.5 °C. MH+ = 450.3.

Example 41: Benzyl 2-[4-(4-pyrrolidin-1-ylphenyl)-1*H*-imidazol-2-yl]ethylcarbamate:

Melting point: 122.4 °C. MH+ = 391.2.

Example 42: 2-phenylethyl 2-[4-(1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate:

Melting point: 142-143 °C. MH+ = 412.2.

Example 43: Butyl 2-[4-(4'-fluoro-1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate:

Melting point: 149.3 °C. MH+ = 382.2.

Example 44: Butyl 2-[4-(1,1'-biphenyl-4-yl)-5-methyl-1*H*-imidazol-2-yl]ethylcarbamate:

44.1) *1-(1,1'-biphenyl-4-yl)propan-1-one:*

A mixture containing phenylboric acid (6.1 g; 50 mmol), 4'-bromopropiophenone (10.65 g; 50 mmol), sodium carbonate (5.3 g; 50 mmol) and palladium chloride (500 mg, 2.8 mmol) in 300 ml of water is heated under reflux for 4 hours. Boric acid (1 g;

0.8 mmol) is then added followed by heating for a further 30 minutes. Once the mixture has returned to 23 °C, 250 ml of ethyl acetate is added, followed by filtration on frit then on GFA paper. The filtrate is decanted and the organic phase washed with a saturated solution of NaCl before being dried over $MgSO_4$ and concentrated using a rotary evaporator. The precipitate is stirred for 30 minutes in 100 ml of isopentane and 5 ml of dichloromethane. After filtration on frit, the solid is rinsed with isopentane. A cream-coloured powder (8.7 g; 83%) is obtained. Melting point: 98-99 °C. MH+ = 211.1

44.2) *1-(1,1'-biphenyl-4-yl)-2-bromopropan-1-one:*

Intermediate 43.1 prepared previously is stirred with PVPHP bromination resin (30 g; 2 mmol Br_3/g) in 120 ml of toluene for 3 hours at a temperature of approximately 5°C. Approximately 15 g of bromination resin are added, then stirring is continued for a further 3 hours at 23 °C. Once again approximately 15 g of resin are added, then the mixture is stirred for 16 hours. The resin is recovered by filtration on frit followed by rinsing with toluene then with dichloromethane. The filtrate is concentrated to dryness and the precipitate obtained is stirred in isopropyl acetate for 30 minutes, followed by filtration on frit and rinsing with isopentane. A cream coloured powder is obtained (9.58 g; 87%). Melting point: 102-104 °C. MH+ = 398.2.

44.3) *N-(butoxycarbonyl)-β-alanine:*

A solution containing the β-alanine (8.9 g; 0.1 mol) and 100 ml of a 1N solution of sodium hydroxide is cooled down to 10 °C. *N*-butyl chloroformate (13.66 g; 0.1 mol) and 50 ml of a 2*N* solution of hydroxide of sodium are added simultaneously. After stirring for 16 hours at 23 °C, approximately 10 ml of a solution of concentrated hydrochloric acid (approximately 11 N) is added to adjust the pH to 4-5. The oil obtained is extracted with ethyl acetate (2 x 50 ml), washed with water then dried over magnesium sulphate. The product crystallizes from isopentane in the form of a white powder (yield of 68%). Melting point: 50.5 °C.

44.4) *Butyl 2-[4-(1,1'-biphenyl-4-yl)-5-methyl-1H-imidazol-2-yl]ethylcarbamate:*

A mixture of N-(butoxycarbonyl)-β-alanine (prepared in Stage 44.3; 3.27 g; 0.0173 mol) and caesium carbonate (2.81 g; 0.0087 mol) in 50 ml of methanol is stirred at 23 °C for 1 hour. The methanol is eliminated by evaporation under reduced pressure in a rotary evaporator. The mixture obtained is dissolved in 50 ml of dimethylformamide then intermediate 44.2 (5 g; 0.0173 mol) is added. After stirring for 16 hours, the solvent is evaporated off under reduced pressure. The mixture obtained is

taken up in ethyl acetate then the caesium bromide is filtered. The ethyl acetate of the filtrate is evaporated and the reaction oil is taken up in a mixture of xylene (80 ml) and ammonium acetate (26.6 g; 0.35 mol). The reaction medium is heated to reflux for approximately an hour and a half, whilst evacuating the water using a Dean-Stark apparatus then, after cooling down, a mixture of iced water and ethyl acetate is poured into the reaction medium. After decantation, the organic phase is washed with a saturated solution of sodium bicarbonate, dried over magnesium sulphate then evaporated under vacuum. After purification on a silica column (eluent: CH_2Cl_2-ethanol / 9-1), a colourless oil is obtained which crystallizes from a mixture of isopentane and isopropyl ether. After filtration and drying a white-coloured powder is obtained (3.31 g, yield of 50%). Melting point: 143-144 °C. MH+ = 378.2.

The compounds of Examples 45 to 49 are obtained according to procedures analogous to that described for Example 44 or above in the part entitled "Preparation of the compounds of general formula (I)".

Example 45: Butyl 2-[4-(4'-methyl-1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate:

Melting point: 168.4 °C. MH+ = 378.2.

Example 46: Butyl 2-[4-(4'-chloro-1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate:

Melting point: 164.2 °C. MH+ = 398.2.

Example 47: Butyl 2-[4-(2'-fluoro-1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate:

Melting point: 113.8 °C. MH+ = 382.2.

Example 48: Butyl 2-{4-[4'-(methylthio)-1,1'-biphenyl-4-yl]-1*H*-imidazol-2-yl}ethylcarbamate:

Melting point: 167.9 °C. MH+ = 410.3.

Example 49: Butyl 2-[4-(2', 4'-difluoro-1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate :

Melting point: 105.7 °C. MH+ = 430.2.

Example 50: 2,6-di-*tert*-butyl-4-{2-[(propylamino)methyl]-1, 3-thiazol-4-yl}phenol hydrochloride :

50.1) *2,6-di-tert-butyl-4-{2-[(propylamino)methyl]-1,3-thiazol-4-yl}phenol:*

0.636 g (2.0 mmol) of intermediate 6.2, 0.16 ml (2.2 mmol) of propionaldehyde and 1 g of previously activated pulverulent 4 Å molecular sieve are successively added to a flask containing 20 ml of anhydrous MeOH, under an inert atmosphere. The reaction mixture is stirred vigorously for 18 hours before the addition, by portions, of 0.083 g (2.2 mmol) of $NaBH_4$. Stirring is maintained for an additional 4 hours then 5 ml of water are added. A quarter of an hour later, the sieve is filtered and the reaction mixture is extracted twice with 100 ml of CH_2Cl_2. The organic phase is washed successively with 50 ml of water and 50 ml of salt water before being dried over sodium sulphate, filtered and concentrated under vacuum. The residue is purified on a silica column (eluent: 30% ethyl acetate in heptane). A yellow oil is obtained, used as it is in the following stage.

50.2) *2,6-di-tert-butyl-4-{2-[(propylamino)methyl]-1,3-thiazol-4-yl}phenol hydrochloride :*

Intermediate 50.1 is dissolved in anhydrous ether (15 ml). The solution is cooled down to 0 °C then an excess of 1*N* HCl solution in ether (0.6 ml) is added dropwise. The mixture is allowed to return to ambient temperature whilst stirring is maintained. After filtration, washing with ether then isopentane and drying under vacuum, a white-grey solid is recovered with a yield of 4%. MH+ = 361.2.

Example 51: *N*-{[4-(10H-phenothiazin-2-yl)-1,3-thiazol-2-yl]methyl}-*N*-propylamine hydrochloride :

The experimental protocol used is the same as that described in Stage 50.1 of Example 50, with the compound of Example 13 replacing intermediate 6.2. A yellow-green solid is obtained with a yield of 32%. MH+ = 354.2.

Example 52: *N*-{[4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]methyl}butan-1-amine:

The experimental protocol used is the same as that described for Example 8, with butylamine replacing morpholine in Stage 8.2. A yellow solid is obtained with a yield of 25.6%. Melting point: 139.0-141.0 °C.

Example 53: ***N*-{[4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]methyl}pentan-1-amine hydrochloride :**

The experimental protocol used is the same as that described in Stage 50.1 of Example 50, with the compound of Example 13 and valeraldehyde replacing intermediate 6.2 and propionaldehyde respectively. A dark-coloured solid is obtained with a yield of 38%. MH+ = 382.2.

Example 54: **(*R,S*)-1-{[4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-1, 3-thiazol-2-yl]methyl}piperidin-3-ol hydrochloride :**

The experimental protocol used is the same as that described for Example 8, with (*R,S*)-3-hydroxypiperidine replacing morpholine in Stage 8.2. The product obtained in base form is salified according to the protocol described in Stage 50.2 in order to produce a light cream solid with a yield of 81%. Melting point: 126.9-130.1 °C.

Example 55: **(*R,S*)-1-{[4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-1, 3-thiazol-2-yl]methyl}pyrrolidin-3-ol hydrochloride :**

The experimental protocol used is the same as that described for Example 8, with (*R,S*)-3-hydroxypyrrolidine replacing morpholine in Stage 8.2. The product obtained in base form is salified according to the protocol described in Stage 50.2 in order to produce a light cream solid with a yield of 93%. Melting point: 79.8-83.3 °C.

Example 56: **[4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]methanol:**

56.1) *[4-(10H-phenothiazin-2-yl)-1,3-thiazol-2-yl]methyl pivalate :*

This compound is prepared according to a protocol identical to that described in Stage 1.3 of Example 1, using 2-(tert-butylcarbonyloxy)thioacetamide and 2-bromo-1-[10-(chloroacetyl)-10H-phenothiazin-2-yl)ethanone respectively instead of intermediate 1.2 and bromo-1-(3,5-ditert-butyl-4-hydroxyphenyl)ethanone. The expected compound is obtained in the form of a greenish solid with a yield of 63.2%. Melting point: 120.0-122.0 °C.

56.2) *[4-(10H-phenothiazin-2-yl)-1,3-thiazol-2-yl]methanol:*

This compound is prepared from intermediate 56.1 according to a protocol identical to that described in Stage 4.2 of Example 4. The expected compound is obtained in the form of a greenish solid with a yield of 61%. Melting point: 145.0-147.0 °C.

Example 57: ***N*, *N*-dimethyl-*N*-{[4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]methyl}amine:**

57.1) *2-[2-(bromomethyl)-1,3-thiazol-4-yl]-10H-phenothiazine:*

This compound is prepared according to a protocol identical to that described in Stage 8.1 of Example 8, using intermediate 56.2 instead of intermediate 4.2. Expected compound is obtained in the form of bright golden yellow-green crystals with a yield of 42%. Melting point: 165-170 °C (decomp.).

57.2) *N,N-dimethyl-N-{[4-(10H-phenothiazin-2-yl)-1,3-thiazol-2-yl]methyl}amine:*

This compound is prepared according to a protocol identical to that described in Stage 8.2 of Example 8 using intermediate 57.1 and N,N-dimethylamine respectively instead of intermediate 8.1 and morpholine. The expected compound is obtained in the form of a yellow solid with a yield of 41.8%. Melting point: 155.0-157.0 °C.

Example 58: 2-{2-[(4-methylpiperazin-1-yl)methyl]-1,3-thiazol-4-yl}-10*H*-phenothiazine hydrochloride :

The experimental protocol used is the same as that described for Example 8, with intermediate 57.1 and N-methylpiperazine replacing intermediate 8.1 and the morpholine in Stage 8.2 respectively. The product obtained in base form is salified according to the protocol described in Stage 50.2 in order to produce a grey solid with a yield of 67%. Melting point: 210.0-212.0 °C.

Example 59: 2-[2-(piperidin-1-ylmethyl)-1,3-thiazol-4-yl]-10*H*-phenothiazine:

The experimental protocol used is the same as that described for Example 8, with intermediate 57.1 and piperidine replacing intermediate 8.1 and the morpholine in Stage 8.2 respectively. The product obtained in base form is salified according to the protocol described in Stage 50.2 in order to produce a grey-yellow solid with a yield of 67%. Melting point: 186.0-188.0 °C.

Example 60: 2-[2-(piperazin-1-ylmethyl)-1,3-thiazol-4-yl]-10*H*-phenothiazine hydrochloride :

60.1) *Tert-butyl 4-{[4-(10H-phenothiazin-2-yl)-1,3-thiazol-2-yl]methyl}piperazine-1-carboxylate:*

This compound is prepared according to a protocol identical to that described for Example 8, using intermediate 57.1 and N-*tert*-butoxycarbonylpiperazine respectively

instead of intermediate 8.1 and morpholine. The expected compound is obtained with a yield of 81.2%. MH+ = 481.2.

60.2) *2-[2-(piperazin-1-ylmethyl)-1,3-thiazol-4-yl]-10H-phenothiazine hydrochloride :*

This compound is prepared according to a protocol identical to that described in Stage 1.4 of Example 1, with intermediate 60.1 replacing intermediate 1.3. The expected compound is obtained in the form of a grey-green solid with a yield of 78.9%. Melting point: 210.0-215.0 °C.

Example 61: 1-{[4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-1, 3-thiazol-2-yl]methyl}azetidin-3-ol hydrochloride :

61.1) *1-(diphenylmethyl)-3-hydroxyazetidine hydrochloride :*

Aminodiphenylmethane (55 g; 0.3 mol) and epichlorhydrin (23.5 ml; 0.3 mol) are mixed in methanol (200 ml). The mixture is taken to reflux for 5 days. The methanol is then evaporated off in order to produce a beige solid. The latter is filtered and washed with ether in order to produce a white solid with a yield of 45%. Melting point: 186.0-186.4 °C.

61.2) *Azetidin-3-ol:*

Intermediate 61.1 is solubilized in an ethanol / THF mixture (7:3) to which water is added in order to obtain good solubilization. The atmosphere is purged with argon then hydrogen before placing the mixture at ambient temperature under a pressure of 3 bars of hydrogen. After filtration and washing with ethanol, the solvents are evaporated off and the residual paste taken up in ether. The solid formed is filtered and rinsed with ether in order to produce a white solid (yield of 86%). Melting point: 74.0-76.8 °C.

61.3) *1-{[4-(3,5-di-tert-butyl-4-hydroxyphenyl)-1,3-thiazol-2-yl]methyl}azetidin-3-ol hydrochloride :*

This compound is prepared according to a protocol identical to that described for Example 8, with intermediate 61.2 replacing morpholine in Stage 8.2. The product obtained in base form is salified according to the protocol described in Stage 50.2 in order to produce a light cream solid with a yield of 74%. Melting point: 124.2-126.5 °C.

Example 62: 2-[2-(morpholin-4-ylmethyl)-1,3-thiazol-4-yl]-10*H*-phenothiazine:

This compound is prepared according to a protocol identical to that described for Example 8, with intermediate 57.1 replacing intermediate 8.1 in Stage 8.2 in order to produce an off-white solid with a yield of 86.0%. Melting point: 203.0-205.0 °C.

Example 63: 2-[2-(thiomorpholin-4-ylmethyl)-1,3-thiazol-4-yl]-10*H*-phenothiazine:

This compound is prepared according to a protocol identical to that described for Example 8, with intermediate 57.1 and thiomorpholine replacing respectively intermediate 8.1 and morpholine in Stage 8.2. The expected product is obtained in the form of a yellow solid with a yield of 80.8%. Melting point: 229.0-231.0 °C.

Example 64: 2-{2-[(4-methyl-1,4 -diazepan-1-yl)methyl]-1,3-thiazol-4-yl}-10*H*-phenothiazine:

This compound is prepared according to a protocol identical to that described for Example 8, with intermediate 57.1 and homopiperazine replacing respectively intermediate 8.1 and morpholine in Stage 8.2. The expected product is obtained in the form of a yellow solid with a yield of 27.0%. Melting point: 135-137 °C.

Example 65: (3*R*)-1-{[4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-1, 3-thiazol-2-yl]methyl}pyrrolidin-3-ol hydrochloride :

This compound is prepared according to a protocol identical to that described for Example 8, with (*R*)-3-pyrrolidinol replacing morpholine in Stage 8.2. The product obtained in base form is salified according to the protocol described in Stage 50.2 in order to produce a white solid with a yield of 93%. Melting point: 162.0-164.6 °C.

Example 66: (3*S*)-1-{[4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-1, 3-thiazol-2-yl]methyl}pyrrolidin-3-ol hydrochloride :

This compound is prepared according to a protocol identical to that described for Example 8, with (*S*)-3-pyrrolidinol replacing morpholine in Stage 8.2. The product obtained in base form is salified according to the protocol described in Stage 50.2 in order to produce a white solid with a yield of 93%. Melting point: 162.8-165.9 °C.

Example 67: 2,6-di-*tert*-butyl-4-[2-(pyrrolidin-1-ylmethyl)-1, 3-thiazol-4-yl]phenol hydrochloride :

This compound is prepared according to a protocol identical to that described for Example 8, with pyrrolidine replacing morpholine in Stage 8.2. The product obtained in base form is salified according to the protocol described in Stage 50.2 in order to produce an off-white solid with a yield of 73%. Melting point: 188.0-195.0 °C.

Example 68: 2,6-di-tert-butyl-4-{2-[(butylamino)methyl]-1, 3-thiazol-4-yl}phenol hydrochloride :

This compound is prepared according to a protocol identical to that described for Example 8, with butylamine replacing morpholine in Stage 8.2. The product obtained in base form is salified according to the protocol described in Stage 50.2 in order to produce an off-white solid with a yield of 72%. Melting point: 179.7-180.2 °C.

Example 69: 2-{2-[(4-ethylpiperazin-1-yl)methyl]-1,3-thiazol-4-yl}-10*H*-phenothiazine:

This compound is prepared according to a protocol identical to that described for Example 8, with intermediate 57.1 and N-ethylpiperazine replacing respectively intermediate 8.1 and morpholine in Stage 8.2. The expected product is obtained in the form of a white solid with a yield of 57.7%. Melting point: 182.0-184.0 °C.

Example 70: *N*-methyl-*N*-{[4-(10*H*-phenothiazin-2-yl)-1*H*-imidazol-2-yl]methyl}amine hydrochloride :

70.1) *Tert-butyl methyl{[4-(10H-phenothiazin-2-yl)-1H-imidazol-2-yl]methyl}carbamate:*

This compound is prepared according to a protocol identical to that described in Stage 44.4 of Example 44, with Boc-Sar-OH and 2-chloro-1-[10-(chloroacetyl)-10*H*-phenothiazin-2-yl)ethanone (cf. stage 13.1 of Example 13) replacing respectively *N*-(butoxycarbonyl)-*β*-alanine and intermediate 44.2 whilst ethanol replaces methanol in Stage 44.4. The expected product is obtained with a yield of 81.6% and used as it is in the following stage.

70.2) *N-methyl-N-{[4-(10H-phenothiazin-2-yl)-1H-imidazol-2-yl]methyl}amine hydrochloride :*

Intermediate 70.1 is deprotected before being converted to the hydrochloride according to an operating method analogous to that of Stage 1.4 of Example 1. The expected product is obtained in the form of a brown powder with a yield of 53.7%. Melting point: 190.0-195.0 °C.

Example 71: Methyl [4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]methylcarbamate:

The compound of Example 13 (0.622 g; 2.0 mmol) is solubilized in dioxane (100 ml) cooled down to 0 °C. Triethylamine is added, then, dropwise, methylchloroformate (2.5 mmol). The reaction medium is then stirred for 3 hours at ambient temperature before being poured over iced water and extracted with ethyl acetate. The organic phase is dried over magnesium sulphate, filtered and concentrated under vacuum. The expected product is purified on a silica column (eluent: 10% acetone in dichloromethane). The pure fractions are collected and the solvents evaporated off in order to produce an off-white solid with a yield of 46.0%. Melting point: 151-153 °C.

Example 72: Butyl [4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]methylcarbamate:

This compound is prepared according to a protocol identical to that described for Example 71, using *n*-butylchloroformate instead of methylchloroformate. The expected product is obtained in the form of a yellow solid with a yield of 61.0%. Melting point: 186.0-188.0 °C.

Example 73: *N*-neopentyl-N-{[4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]methyl}amine:

This compound is prepared according to a protocol identical to that described in Stage 50.1 of Example 50, with the compound of Example 13 and pivaldehyde replacing respectively intermediate 6.2 and propionaldehyde. The expected product is obtained in the form of an off-white solid with a yield of 40.6%. Melting point: 172.0-174.0 °C.

Example 74: 1-{[4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]methyl}piperidin-4-ol:

This compound is prepared according to a protocol identical to that described for Example 8, with intermediate 57.1 and 4-hydroxy-piperidine replacing respectively intermediate 8.1 and morpholine in Stage 8.2. The expected product is obtained in the form of a white solid with a yield of 52.5%. Melting point: 205.0-207.0 °C.

Example 75: *N*-{[4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]methyl}acetamide:

This compound is prepared according to a protocol identical to that described for Example 6, with the compound of Example 13 replacing intermediate 6.2 in Stage 6.3. The expected product is obtained in the form of a yellow solid with a yield of 25.0%. Melting point: 219.0-221.0 °C.

Example 76: *N*-{[4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]methyl}butanamide:

This compound is prepared according to a protocol identical to that described for Example 6, with the compound of Example 13 and butanoyl chloride replacing respectively intermediate 6.2 and acetyl chloride in Stage 6.3. The expected product is obtained in the form of a yellow solid with a yield of 47.2%. Melting point: 218.0-220.0 °C.

Example 77: 2,6-di-*tert*-butyl-4-{2-[(4-propylpiperazin-1-yl)methyl]-1,3-thiazol-4-yl}phenol:

77.1) *tert-butyl 4-{[4-(3,5-ditert-butyl-4-hydroxyphenyl)-1,3-thiazol-2-yl]methyl}piperazine-1-carboxylate hydrochloride :*

This compound is prepared according to a protocol identical to that described for Example 8, with *N*-Boc-piperazine replacing morpholine in Stage 8.2. A pale orange solid is obtained with a yield of 64%. Melting point: 108-109 °C.

77.2) *2,6-ditert-butyl-4-[2-(piperazin-1-ylmethyl)-1,3-thiazol-4-yl]phenol hydrochloride :*

This compound is prepared according to a protocol identical to that described in Stage 1.4, with intermediate 77.1 replacing intermediate 1.3. A white solid is obtained with a yield of 86%. Melting point: 255.4-257.7 °C.

77.3) *2,6-di-tert-butyl-4-{2-[(4-propylpiperazin-1-yl)methyl]-1,3-thiazol-4-yl}phenol:*

This compound is prepared according to a protocol identical to that described in Stage 50.1 of Example 50, with intermediate 77.2 replacing intermediate 6.2 and an excess of triethylamine being added initially in order to convert intermediate 77.2 to the corresponding base. The expected product is obtained in the form of an off-white solid with a yield of 45%. Melting point: 236.5-238.2 °C.

Example 78: 2,6-di-*tert*-butyl-4-{2-[2-methyl-1-(methylamino)propyl]-1,3-thiazol-4-yl}phenol hydrochloride :

78.1) *N-(tert-butoxycarbonyl)-N-methylvaline:*

N-methyl-*D,L*-valine (10.0 g; 0.0763 mol) is solubilized in a dioxane-water mixture (9:1) (100 ml) containing triethylamine (13 ml). The mixture is cooled down to 0 °C then Boc-O-Boc (18.32 g; 0.0763 mol) is added, by portions, and the mixture is maintained under stirring overnight at ambient temperature. The reaction medium is then poured over iced water and extracted with ethyl acetate. The organic phase is washed successively with a 10% aqueous solution of sodium bicarbonate and water, then finally with a saturated solution of sodium chloride. The organic phase is then dried over magnesium sulphate, filtered and concentrated under vacuum in order to produce an oily product which crystallizes from petroleum ether. The expected product is recovered with a yield of 67% before being used as it is in the following stage. Melting point: 83-85 °C.

78.2) *N^2-(tert-butoxycarbonyl)-N^2-methylvalinamide:*

1-(3-dimethylaminopropyl)-3-ethyl-carbodiimide hydrochloride (9.777 g; 0.051 mol) and hydroxybenzotriazole (7.8 g; 0.051 mol) are added successively to intermediate 78.1 (11.8 g; 0.051 mol) in dichloromethane (200 ml). Triethylamine (13 ml) is then added dropwise then the mixture is stirred for 12 hours at ambient temperature. The reaction medium is then poured into a 10% aqueous solution of sodium bicarbonate. After decantation, the organic phase is washed with water then with a saturated solution of sodium chloride. The organic phase is then dried over magnesium sulphate, filtered and concentrated under vacuum. The residue is taken up in methanol previously saturated with ammonia gas (150 ml). The mixture is placed in an autoclave oven at 50 °C and stirred for 4 days at this temperature. The methanol is evaporated off and the product is taken up in dichloromethane before being washed with a saturated solution of sodium chloride. The organic phase is dried over magnesium sulphate, filtered and

concentrated under vacuum. The product is purified by trituration in ether in order to produce a white solid with a yield of 23.5%. Melting point: 181-183 °C.

78.3) *Tert-butyl 1-(aminocarbonothioyl)-2-methylpropyl(methyl)carbamate:*

This compound is prepared by reaction of intermediate 78.2 with P_2S_5 under the conditions described in Example 12, stage 12.2. The expected product is purified by chromatography on a silica column (eluent = 5% methanol in dichloromethane) in order to produce an off-white solid with a yield of 32.5%. Melting point: 199.0-201.0 °C.

78.4) *2,6-di-tert-butyl-4-{2-[2-methyl-1-(methylamino)propyl]-1, 3-thiazol-4-yl}phenol hydrochloride :*

This compound is prepared according to a protocol identical to that described in Stage 1.3 of Example 1, with intermediate 78.3 replacing intermediate 1.2. The intermediate compound obtained is deprotected by hydrobromic acid released *in situ* in order to produce the expected product in the form of the free base, which is purified by chromatography on a silica column (eluent: 30% ethyl acetate in heptane). The free base is then salified by dissolution in ethyl acetate through which as stream of HCl gas is passed for 10 minutes. After stirring the mixture for one hour, the latter is evaporated to dryness and the residue taken up in ether. After filtration, a pale pink solid is recovered with a yield of 92%. Melting point: 248.6-250.0 °C.

<u>Example 79:</u> *N*,2-dimethyl-1-[4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]propan-1-amine hydrochloride :

79.1) *Tert-butyl methyl{2-methyl-1-[4-(10H-phenothiazin-2-yl)-1,3-thiazol-2-yl]propyl}carbamate:*

Intermediates 78.3 and 13.1 are coupled according to a protocol analogous to that described in Stage 1.3 of Example 1. The expected compound is obtained in the form of an oil which is purified by chromatography on a silica column (eluent: pure dichloromethane) . The expected product is obtained in the form of a white solid with a yield of 72.4%. The latter is used as it is in the following stage.

79.2) *N,2-dimethyl-1-[4-(10H-phenothiazin-2-yl)-1,3-thiazol-2-yl]propan-1-amine hydrochloride:*

This compound is prepared according to a protocol identical to that described in Stage 1.4 of Example 1, with intermediate 79.1 replacing intermediate 1.3. After washing with ether and isopentane then drying, the expected compound is obtained in the form of a dark green powder with a yield of 62%. MH+ = 368.1.

Example 80: ***N*-{[4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]methyl}hexanamide:**

This compound is prepared according to a protocol identical to that described for Example 6, with the compound of Example 13 and hexanoyl chloride replacing respectively intermediate 6.2 and acetyl chloride in Stage 6.3. The expected product is obtained in the form of a brown solid with a yield of 40.7%. Melting point: 192.0-194.0 °C.

Example 81: **(3*R*)-1-{[4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]methyl}pyrrolidin-3-ol:**

This compound is prepared according to a protocol identical to that described for Example 8, with intermediate 57.1 and (*R*)-3-pyrrolidinol replacing respectively intermediate 8.1 and morpholine in Stage 8.2. The expected product is obtained in the form of a white solid with a yield of 49.5%. Melting point: 180.0-182.0 °C.

Example 82: **(3*S*)-1-{[4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]methyl}pyrrolidin-3-ol:**

This compound is prepared according to a protocol identical to that described for Example 8, with intermediate 57.1 and (*S*)-3-pyrrolidinol replacing respectively intermediate 8.1 and morpholine in Stage 8.2. The expected product is obtained in the form of a white solid with a yield of 49.5%. Melting point: 178.0-180.0 °C.

Example 83: **1-{[4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]methyl}azetidin-3-ol:**

This compound is prepared according to a protocol identical to that described for Example 8, with intermediate 57.1 and azetidine-3-ol (intermediate 61.2) replacing respectively intermediate 8.1 and morpholine in Stage 8.2. The expected product is obtained in the form of an off-white solid with a yield of 20.4%. Melting point: 240.0-242.0 °C.

Example 84: 2-{2-[(4-propylpiperazin-1-yl)methyl]-1,3-thiazol-4-yl}-10*H*-phenothiazine:

This compound is prepared according to a protocol identical to that described for Example 8, with intermediate 57.1 and *N*-propylpiperazine replacing respectively intermediate 8.1 and morpholine in Stage 8.2. The expected product is obtained in the form of a white solid with a yield of 42.6%. Melting point: 189.0-190.0 °C.

Example 85: 2-{2-[(4-acetylpiperazin-1-yl)methyl]-1,3-thiazol-4-yl}-10*H*-phenothiazine:

This compound is prepared according to a protocol identical to that described for Example 8, with intermediate 57.1 and N-acetyl-piperazine replacing respectively intermediate 8.1 and morpholine in Stage 8.2. The expected product is obtained in the form of an off-white solid with a yield of 53.5%. Melting point: 218.0-220.0 °C.

Example 86: 2-{2-[(4-butylpiperazin-1-yl)methyl]-1,3-thiazol-4-yl}-10*H*-phenothiazine:

This compound is prepared according to a protocol identical to that described for Example 8, with intermediate 57.1 and *N*-butylpiperazine replacing respectively intermediate 8.1 and morpholine in Stage 8.2. The expected product is obtained in the form of a white solid with a yield of 69.3%. Melting point: 188.0-190.0 °C.

Example 87: Methyl 4-{[4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]methyl}piperazine-1-carboxylate:

Intermediate 60.2 (0.380 g; 1 mmol) is dissolved in THF. Triethylamine (1 ml) to the solution thus obtained then, methylchloroformate (0.1 ml) is added dropwise. Once the reaction is completed, the reaction mixture is poured over iced water and extracted with ethyl acetate. The organic phase recovered is filtered and the solvents are evaporated off. After crystallisation from *iso*-propanol, the expected product is obtained in the form of a white solid with a yield of 66.1%. Melting point: 180.0-182.0 °C.

<u>Example 88:</u> 4-[2-(aminomethyl)-1H-imidazol-4-yl]-2,6-di-*tert*-butylphenol hydrochloride :

88.1) *Benzyl [4-(3,5-di-tert-butyl-4-hydroxyphenyl)-1H-imidazol-2-yl]methylcarbamate :*

This compound is prepared according to a protocol similar to that described in Stage 44.4 of Example 44, with carbobenzyloxyglycine and bromo-1-(3,5-di*tert*-butyl-4-hydroxyphenyl)ethanone replacing respectively N-(butoxycarbonyl)-β-alanine and intermediate 44.2. The expected product is obtained with a yield of 55%. Melting point: 212.1-213.4 °C.

88.2) *4-[2-(aminomethyl)-1H-imidazol-4-yl]-2,6-di-tert-butylphenol hydrochloride :*

Intermediate 88.1 (2.2 g; 5.05 mmol) is dissolved in a 50/50 mixture of ethanol and THF (70 ml). 0.7 g of palladium on carbon (10 %) is added and the mixture is placed under a hydrogen atmosphere (3.5 bars of pressure). The catalyst is filtered then the solvent is evaporated off under reduced pressure. The base obtained is solubilized in ether and the hydrochloride is prepared by the addition of a 1*N* solution of HCl in ether (20 ml). After filtration and drying under vacuum, the expected product is recovered in the form of a white to slightly grey solid which is washed with ether then with *iso*-pentane (yield of 56%). Melting point: 225-228.3 °C.

<u>Example 89:</u> 4-{2-[(benzylamino)methyl]-1,3-thiazol-4-yl}-2,6-di-*tert*-butylphenol hydrochloride :

This compound is prepared according to a protocol identical to that described for Example 8, with benzylamine replacing morpholine in Stage 8.2. The expected product is obtained in the form of a white solid with a yield of 62%. Melting point: 166.4-167.8 °C.

<u>Example 90:</u> 4-{2-[(4-acetylpiperazin-1-yl)methyl]-1,3-thiazol-4-yl}-2,6-di-*tert*-butylphenol hydrochloride :

This compound is prepared according to a protocol identical to that described for Example 8, with *N*-acetyl-piperazine replacing morpholine in Stage 8.2. The expected product is obtained in the form of a white solid with a yield of 64%. Melting point: 199.0-200.4 °C.

Example 91: ***N*-methyl-N-{[4-(10*H*-phenoxazin-2-yl)-1,3-thiazol-2-yl]methyl}amine hydrochloride :**

This compound is prepared according to a protocol identical to that described for Example 12, with 2-chloro-1-(10*H*-phenoxazin-2-yl)ethanone replacing bromo-1-(3,5-di*tert*-butyl-4-hydroxyphenyl)propan-1-one (the 2-chloro-1-(10*H*-phenoxazine-2-yl)ethanone being prepared in an analogous manner to that used for intermediate 13.1 – cf. *J. Org. Chem.* (1960), **25**, 747-753). The expected product is obtained after coupling and deprotection and salification in the form of a green solid. Melting point: 218-220 °C.

Example 92: **4-[2-(azetidin-1-ylmethyl)-1,3-thiazol-4-yl]-2,6-di-*tert*-butylphenol hydrochloride :**

This compound is prepared according to a protocol identical to that described for Example 8, with azetidine replacing morpholine in Stage 8.2. The expected product is obtained in the form of a white solid with a yield of 90%. Melting point: 141.7-144.2 °C.

Example 93: **2,6-di-*tert*-butyl-4-{2-[(4-butylpiperazin-1-yl)methyl]-1,3-thiazol-4-yl}phenol hydrochloride:**

This compound is prepared according to a protocol identical to that described for Example 8, *N*-butyl-piperazine replacing morpholine in Stage 8.2. The expected product is obtained in the form of an off-white solid with a yield of 68%. Melting point: 229.9-230.5 °C.

The compounds of Examples 94 to 112 are obtained according to procedures analogous to that described for Example 29 *or above in the part entitled "Preparation of the compounds of general formula (I)".*

Example 94: **Butyl 2-[4-(3'-chloro-1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate:**

Melting point: 142.6 °C. MH+ = 398.3.

Example 95: **Butyl 2-[4-(3'-fluoro-1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate:**

Melting point: 141.5 °C. MH+ = 381.2.

Example 96: **Butyl 2-[4-(4-isobutylphenyl)-1*H*-imidazol-2-yl]ethylcarbamate :**

Melting point: 95.5 °C. MH+ = 344.2.

Example 97: **Benzyl 2-[4-(4-isobutylphenyl)-1*H*-imidazol-2-yl]ethylcarbamate :**

Melting point: 125.2 °C. MH+ = 378.4.

Example 98: **Butyl 2-[4-(3'-chloro-4'-fluoro-1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate :**

Melting point: 132.4 °C. MH+ = 416.3.

Example 99: **Butyl 2-[4-(3', 4'-dichloro-1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate :**

Melting point: 137.5 °C. MH+ = 432.2.

Example 100: **Butyl 2-[4-(4-propylphenyl)-1*H*-imidazol-2-yl]ethylcarbamate :**

Melting point: 83.2 °C. MH+ = 330.4.

Example 101: **Butyl 2-[4-(4-ethylphenyl)-1*H*-imidazol-2-yl]ethylcarbamate :**

Melting point: 92.4 °C. MH+ = 316.3.

Example 102: **Butyl 2-[4-(4'-cyano-1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate :**

Melting point: 147 °C. MH+ = 389.2.

Example 103: **Butyl 2-{4-[4'-(trifluoromethyl)-1,1'-biphenyl-4-yl]-1*H*-imidazol-2-yl}ethylcarbamate:**

Melting point: 168.5 °C. MH+ = 432.3.

Example 104: **Butyl 2-[4-(1,1'-biphenyl-4-yl)-5-ethyl-1*H*-imidazol-2-yl]ethylcarbamate :**

Melting point: 127-128 °C. MH+ = 392.2.

Example 105: Butyl 2-[4-(2'-chloro-1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate :

Melting point: 99.7 °C. MH+ = 398.1.

Example 106: Butyl 2-[4-(2', 3'-difluoro-1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate :

Melting point: 90 °C. MH+ = 400.1.

Example 107: Butyl 2-[4-(2'-bromo-1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate :

Melting point: 109.6 °C. MH+ = 442.1.

Example 108: Butyl 2-[4-(3', 5'-difluoro-1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate :

Melting point: 111.1 °C. MH+ = 400.2.

Example 109: Butyl 2-[4-(2'-methoxy-1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate :

Melting point: 116-121 °C. MH+ = 394.3.

Example 110: Butyl 2-[4-(3'-nitro-1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate :

Melting point: 100, 5-101.5 °C. MH+ = 409.2.

Example 111: Butyl 2-[4-(2', 5'-difluoro-1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate:

Melting point: 109.5 °C. MH+ = 400.2.

Example 112: Butyl 2-[4-(3'-methoxy-1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate :

Melting point: 112-113 °C. MH+ = 394.2.

Example 113: Methyl 4-{[4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-1, 3-thiazol-2-yl]methyl}piperazine-1-carboxylate hydrochloride :

This compound is prepared according to a protocol identical to that described for Example 8, with the methyl ester of piperazine-1-carboxylic acid replacing morpholine in Stage 8.2. The expected product is obtained in the form of white crystals with a yield of 51%. Melting point: 240.6-241.4 °C.

Example 114: Methyl [4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-1,3-thiazol-2-yl]methylcarbamate :

This compound is prepared according to a protocol identical to that described for Example 71, with intermediate 6.2 replacing the compound of Example 13. The expected product is obtained in the form of a crystalline white solid with a yield of 18%. Melting point: 94.0-95.9 °C.

Example 115: *N*-{[4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-1,3-thiazol-2-yl]methyl}benzamide:

This compound is prepared according to a protocol identical to that described for Example 71, with intermediate 6.2 replacing the compound of Example 13 and benzoyl chloride replacing methylchloroformate. The expected product is obtained in the form of a crystalline white solid with a yield of 84%. Melting point: 200.4-201.2 °C.

Example 116: *N*-{[4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-1,3-thiazol-2-yl]methyl}-2-phenylacetamide:

This compound is prepared according to a protocol identical to that described for Example 71, with intermediate 6.2 replacing the compound of Example 13 and phenylacetyl chloride replacing methylchloroformate. The expected product is obtained in the form of a crystalline white solid with a yield of 45%. Melting point: 123.5-125.4 °C.

Example 117: *N*-{[4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-1,3-thiazol-2-yl]methyl}propanamide:

This compound is prepared according to a protocol identical to that described for Example 71, with intermediate 6.2 replacing the compound of Example 13 and propionyl chloride replacing methylchloroformate. The expected product is obtained in the form of a crystalline white solid with a yield of 45%. Melting point: 82.0-83.5 °C.

Example 118: 1-{[4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-1,3-thiazol-2-yl]methyl}piperidin-4-yl acetate :

This compound is prepared according to a protocol identical to that described for Example 8, with 1-acetyl-piperazine replacing morpholine in Stage 8.2. The expected product is obtained in the form of a crystalline orange solid with a yield of 50%. Melting point: 160.3-160.6 °C.

Example 119: 1-{[4-(3,5-di-tert-butyl-4-hydroxyphenyl)-1,3-thiazol-2-yl]methyl}pyrrolidine-3, 4-diol:

This compound is prepared according to a protocol identical to that described for Example 8, with 3,4-dihydroxypyrrolidine replacing morpholine in Stage 8.2. The expected product is obtained in the form of a brown foam with a yield of 29%. MH+ = 405.20.

Pharmacological study of the products of the invention

Study of the effects on the binding of a specific ligand of MAO-B, [^{3}H]Ro 19-6327

The inhibiting activity of the products of the invention is determined by measuring their effects on the binding of a specific ligand of MAO-B, [^{3}H]Ro 19-6327.

a) *Mitochondrial preparation of rat cortex*

The mitochondrial preparation of rat cortex is carried out according to the method described in Cesura A M, Galva M D, Imhof R and Da Prada M, *J. Neurochem.* **48** (1987)0, 170-176. The rats are decapitated and their cortices removed, homogenized in 9 volumes of a 0.32 M sucrose buffer, buffered at pH 7.4 with 5 mM of HEPES, then centrifuged at 800 g for 20 minutes. The supernatants are recovered and the pellets washed twice with the 0.32 M sucrose buffer as previously. The supernatants collected are centrifuged at 10,000 g for 20 minutes. The pellets obtained are suspended in a Tris buffer (50 mM Tris, 130 mM NaCl, 5 mM KCl, 0.5 mM EGTA, 1 mM $MgCl_2$, pH 7.4) and centrifuged at 10,000 g for 20 minutes. This stage is repeated twice, and the final pellet, corresponding to the mitochondrial fraction, is kept at –80 °C in the Tris buffer.

The protein content of the preparation is determined by Lowry's method.

b) *Binding of [^{3}H]Ro 19-6327*

In an Eppendorf tube, 100 µl of the mitochondrial preparation (2 mg protein/ml) are incubated for 1 hour at 37 °C in the presence of 100 µl of [^{3}H] Ro 19-6327 (33 nM, final concentration) and 100 µl of Tris buffer containing or not containing the inhibitors. The reaction is stopped by the addition of 1 ml of unlabelled Tris buffer to each tube, then the samples are centrifuged for 2 minutes at 12,000 g. The supernatants are aspirated and the pellets washed with 1 ml of Tris buffer. The pellets are then solubilized in 200 µl of sodium dodecyl sulphate (20% weight/volume) for 2 hours at 70 °C. The radioactivity is determined by liquid scintillation counting of the samples.

c) *Results*

The compounds of Examples 1, 3, 5, 11 and 18 described above have an IC_{50} below or equal to 10 µM.

Study of the effects on lipidic peroxidation of the cerebral cortex of the rat

The inhibitory activity of the products of the invention is determined by measuring their effects on the degree of lipidic peroxidation, determined by the concentration of malondialdehyde (MDA). The MDA produced by peroxidation of unsaturated fatty acids is a good indication of lipidic peroxidation (H Esterbauer and KH Cheeseman, *Meth. Enzymol.* (1990) **186**: 407-421). Male Sprague Dawley rats weighing 200 to 250 g (Charles River) were sacrificed by decapitation. The cerebral cortex is removed, then homogenized using a Thomas potter in a 20 mM Tris-HCl buffer, pH = 7.4. The homogenate is centrifuged twice at 50000 g for 10 minutes at 4°C. The pellet is kept at -80°C. On the day of the experiment, the pellet is replaced in suspension at a concentration of 1 g/ 15 ml and centrifuged at 515 g for 10 minutes at 4°C. The supernatant is used immediately to determine the lipidic peroxidation. The homogenate of rat's cerebral cortex (500 µl) is incubated at 37° C for 15 minutes in the presence of the compounds to be tested or of solvent (10 µl). The lipidic peroxidation reaction is initiated by adding 50 µl of $FeCl_2$ at 1 mM, EDTA at 1 mM and ascorbic acid at 4 mM. After incubation for 30 minutes at 37°C, the reaction is stopped by adding 50 µl of a solution of hydroxylated di tertio butyl toluene (BHT, 0.2 %). The MDA is quantified using a colorimetric test, by reacting a chromogenic reagent (R), N-methyl-2-phenylindol (650 µl) with 200 µl of the homogenate for 1 hour at 45°C. The condensation of an MDA molecule with two molecules of reagent R produces a stable chromophore the maximum absorbence wavelength of which is equal to 586 nm.

(Caldwell et al. *European J. Pharmacol.* (1995) **285**, 203-206). The compounds of Examples 1, 3 to 28, 50 to 62, 64 to 86, 88 to 93 and 114 to 118 described above have a IC_{50} below or equal to 10 μM.

Binding test on the sodium channels of rat cerebral cortices

The test consists in measuring the interaction of the compounds vis-à-vis the binding of tritiated batrachotoxin on the voltage-dependent sodium channels according to the protocol described by Brown (*J. Neurosci.* (1986), **6**, 2064-2070).

Preparation of homogenates of cerebral cortices of the rat

The cerebral cortices of Sprague-Dawley rats weighing 230-250 g (Charles River, France) are removed, weighed and homogenized using a Potter grinder provided with a teflon piston (10 strokes) in 10 volumes of isolation buffer the composition of which is as follows (sucrose 0.32 M, K_2HPO_4 5 mM, pH 7.4). The homogenate is subjected to a first centrifugation at 1000 g for 10 minutes. The supernatant is removed and centrifuged at 20000 g for 15 minutes. The pellet is taken up in the isolation buffer and centrifuged at 20000 g for 15 minutes. The pellet obtained is resuspended in incubation buffer (HEPES 50 mM, KCl 5.4 mM, $MgSO_4$ 0.8 mM, glucose 5.5 mM, choline chloride 130 mM pH 7.4) then aliquoted and stored at –80 °C until the day of assay. The final protein concentration is comprised between 4 and 8 mg/ml. The assay of proteins is carried out using a kit marketed by BioRad (France).

Measurement of the binding of tritiated batrachotoxin

The binding reaction is carried out by incubating for 1 hour 30 minutes at 25 °C 100 μl of homogenate of rat cortex containing 75 μg of proteins with 100 μl of [^{3}H] batrachotoxin-A 20-alpha benzoate (37.5 Ci/mmol, NEN) at 5 nM (final concentration), 200 μl of tetrodotoxin at 1 μM (final concentration) and scorpion venom at 40 μg/ml (final concentration) and 100 μl of incubation buffer alone or in the presence of the products to be tested at different concentrations. The non-specific binding is determined in the presence of 300 μM of veratridine and the value of this non-specific binding is subtracted from all the other values. The samples are then filtered using a Brandel (Gaithersburg, Maryland, USA) using Unifilter GF/C plates pre-incubated with 0.1 % of polyethylene imine (20 μl/well) and rinsed twice with 2 ml of filtration buffer (HEPES 5 mM, $CaCl_2$ 1.8 mM, $MgSO_4$ 0.8 mM, choline chloride 130 mM, BSA 0.01 %, pH 7.4). After having added 20 μl of Microscint 0 ®, the radioactivity is counted using a liquid scintillation counter (Topcount, Packard). The measurement is carried

out in duplicate. The results are expressed as a % of the specific binding of tritiated batrachotoxin relative to the control.

Results

The compounds of Examples 1, 3, 5, 12, 15, 16, 18, 20, 28 to 47, 49, 52, 61, 65 to 69, 89 and 94 to 112 described above all have a IC_{50} below or equal to 1 μM.

Claims

1. Compound characterized in that it is chosen from the following compounds:

- 2,6-di*tert*-butyl-4-{2-[2-(methylamino)ethyl]-1,3-thiazol-4-yl}phenol;
- 2,6-di*tert*-butyl-4-[4-(hydroxymethyl)-1,3-oxazol-2-yl]phenol;
- 2,6-di*tert*-butyl-4-{2-[1-(methylamino)ethyl]-1,3-thiazol-4-yl}phenol;
- 2,6-di*tert*-butyl-4-[2-(methoxymethyl)-1,3-thiazol-4-yl]phenol;
- 2,6-di*tert*-butyl-4-{4-[(methylamino)methyl]-1,3-oxazol-2-yl}phenol;
- N-{[4-(3,5-di*tert*-butyl-4-hydroxyphenyl)-1,3-thiazol-2-yl]methyl}acetamide;
- ethyl [4-(3,5-di*tert*-butyl-4-hydroxyphenyl)-1,3-thiazol-2-yl]methylcarbamate;
- 2,6-di*tert*-butyl-4-[2-(morpholin-4-ylmethyl)-1,3-thiazol-4-yl]phenol;
- 2,6-di*tert*-butyl-4-[2-(thiomorpholin-4-ylmethyl)-1,3-thiazol-4-yl]phenol;
- 4-[2-(anilinomethyl)-1,3-thiazol-4-yl]-2,6-di*tert*-butylphenol;
- 2,6-di*tert*-butyl-4-(2-{[[2-(dimethylamino)ethyl](methyl)amino]methyl}-1,3-thiazol-4-yl)phenol;
- 2,6-di*tert*-butyl-4-{5-methyl-2-[(methylamino)methyl]-1,3-thiazol-4-yl}phenol;
- 1-[4-(10H-phenothiazin-2-yl)-1,3-thiazol-2-yl]methanamine;
- *N*-{[4-(3,5-di*tert*-butyl-4-hydroxyphenyl)-1,3-thiazol-2-yl]methyl}-*N*-methylacetamide;
- 1-[4-(3,5-di*tert*-butyl-4-methoxyphenyl)-1,3-thiazol-2-yl]-N-methylmethanamine;
- 2,6-di*tert*-butyl-4-{2-[(ethylamino)methyl]-1,3-thiazol-4-yl}phenol;
- 2,6-di*tert*-butyl-4-{2-[(4-phenylpiperazin-1-yl)methyl]-1,3-thiazol-4-yl}phenol;
- 2,6-di*tert*-butyl-4-{2-[(4-methyl-1,4 -diazepan-1-yl)methyl]-1,3-thiazol-4-yl}phenol;
- N-{1-[4-(4-anilinophenyl)-1,3-thiazol-2-yl]ethyl}-N-methylamine;
- 2,6-di*tert*-butyl-4-{2-[(isopropylamino)methyl]-1,3-thiazol-4-yl}phenol;
- 2,6-ditert-butyl-4-{2-[(cyclohexylamino)methyl]-1,3-thiazol-4-yl}phenol;
- 2,6-di*tert*-butyl-4-{2-[(4-isopropylpiperazin-1-yl)methyl]-1,3-thiazol-4-yl}phenol;

- *N*-methyl-1-[4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]ethanamine;
- 2,6-di*tert*-butyl-4-{2-[(4-ethylpiperazin-1-yl)methyl]-1,3-thiazol-4-yl}phenol;
- *N*-{[4-(4-anilinophenyl)-1,3-thiazol-2-yl]methyl}-*N*-ethylamine;
- *N*-{[4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]methyl}ethanamine;
- 2,6-di*tert*-butyl-4-(2-{[4-(dimethylamino)piperidin-1-yl]methyl}-1,3-thiazol-4-yl)phenol;
- 1-{[4-(3,5-di*tert*-butyl-4-hydroxyphenyl)-1,3-thiazol-2-yl]methyl}piperidin-4-ol;
- 4-methylpentyl 2-[4-(1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate;
- 3,3-dimethylbutyl 2-[4-(4-pyrrolidin-1-ylphenyl)-1*H*-imidazol-2-yl]ethylcarbamate;
- isopentyl 2-[4-(1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate;
- hexyl 2-[4-(4'-bromo-1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate;
- benzyl 2-[4-(4-*tert*-butylphenyl)-1*H*-imidazol-2-yl]ethylcarbamate;
- 3,3-dimethylbutyl 2-[4-(1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate;
- hexyl 2-[4-(4-pyrrolidin-1-ylphenyl)-1*H*-imidazol-2-yl]ethylcarbamate;
- hexyl 2-[4-(3,5-di*tert*-butyl-4-hydroxyphenyl)-1*H*-imidazol-2-yl]ethylcarbamate;
- 3,3-dimethylbutyl 2-[4-(3,5-di*tert*-butyl-4-hydroxyphenyl)-1*H*-imidazol-2-yl]ethylcarbamate;
- 3,3-dimethylbutyl 2-[4-(4-methoxyphenyl)-1*H*-imidazol-2-yl]ethylcarbamate;
- benzyl 2-[4-(3,5-di*tert*-butyl-4-hydroxyphenyl)-1*H*-imidazol-2-yl]ethylcarbamate;
- benzyl 2-[4-(4-pyrrolidin-1-ylphenyl)-1*H*-imidazol-2-yl]ethylcarbamate;
- 2-phenylethyl 2-[4-(1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate;
- butyl 2-[4-(4'-fluoro-1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate;
- butyl 2-[4-(1,1'-biphenyl-4-yl)-5-methyl-1*H*-imidazol-2-yl]ethylcarbamate;
- butyl 2-[4-(4'-methyl-1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate;
- butyl 2-[4-(4'-chloro-1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate;
- butyl 2-[4-(2'-fluoro-1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate;
- butyl 2-[4-(2', 4'-difluoro-1,1'-biphenyl-4-yl)-1H-imidazol-2-yl]ethylcarbamate;
- 2,6-di-*tert*-butyl-4-{2-[(propylamino)methyl]-1,3-thiazol-4-yl}phenol;

- *N*-{[4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]methyl}-*N*-propylamine;
- *N*-{[4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]methyl}butan-1-amine;
- *N*-{[4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]methyl}pentan-1-amine;
- 1-{[4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-1,3-thiazol-2-yl]methyl}piperidin-3-ol;
- 1-{[4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-1,3-thiazol-2-yl]methyl}pyrrolidin-3-ol;
- [4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]methanol;
- *N*, *N*-dimethyl-*N*-{[4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]methyl}amine;
- 2-{2-[(4-methylpiperazin-1-yl)methyl]-1,3-thiazol-4-yl}-10*H*-phenothiazine;
- 2-[2-(piperidin-1-ylmethyl)-1,3-thiazol-4-yl]-10*H*-phenothiazine;
- 2-[2-(piperazin-1-ylmethyl)-1,3-thiazol-4-yl]-10*H*-phenothiazine;
- 1-{[4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-1,3-thiazol-2-yl]methyl}azetidin-3-ol;
- 2-[2-(morpholin-4-ylmethyl)-1,3-thiazol-4-yl]-10*H*-phenothiazine;
- 2-[2-(thiomorpholin-4-ylmethyl)-1,3-thiazol-4-yl]-10*H*-phenothiazine;
- 2-{2-[(4-methyl-1,4 -diazepan-1-yl)methyl]-1,3-thiazol-4-yl}-10*H*-phenothiazine;
- (3R)-1-{[4-(3,5-di-tert-butyl-4-hydroxyphenyl)-1,3-thiazol-2-yl]methyl}pyrrolidin-3-ol;
- (3S)-1-{[4-(3,5-di-tert-butyl-4-hydroxyphenyl)-1,3-thiazol-2-yl]methyl}pyrrolidin-3-ol;
- 2,6-di-*tert*-butyl-4-[2-(pyrrolidin-1-ylmethyl)-1,3-thiazol-4-yl]phenol;
- 2,6-di-tert-butyl-4-{2-[(butylamino)methyl]-1,3-thiazol-4-yl}phenol;
- 2-{2-[(4-ethylpiperazin-1-yl)methyl]-1,3-thiazol-4-yl}-10*H*-phenothiazine;
- *N*-methyl-*N*-{[4-(10*H*-phenothiazin-2-yl)-1*H*-imidazol-2-yl]methyl}amine;
- methyl [4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]methylcarbamate;
- butyl [4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]methylcarbamate;
- *N*-neopentyl-N-{[4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]methyl}amine;
- 1-{[4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]methyl}piperidin-4-ol;
- *N*-{[4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]methyl}acetamide;
- *N*-{[4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]methyl}butanamide;
- 2,6-di-*tert*-butyl-4-{2-[(4-propylpiperazin-1-yl)methyl]-1,3-thiazol-4-yl}phenol;

- 2,6-di-*tert*-butyl-4-{2-[2-methyl-1-(methylamino)propyl]-1,3-thiazol-4-yl}phenol;
- *N*, 2-dimethyl-1-[4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]propan-1-amine;
- *N*-{[4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]methyl}hexanamide;
- (3*R*)-1-{[4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]methyl}pyrrolidin-3-ol;
- (3*S*)-1-{[4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]methyl}pyrrolidin-3-ol;
- 1-{[4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]methyl}azetidin-3-ol;
- 2-{2-[(4-propylpiperazin-1-yl)methyl]-1,3-thiazol-4-yl}-10*H*-phenothiazine;
- 2-{2-[(4-acetylpiperazin-1-yl)methyl]-1,3-thiazol-4-yl}-10*H*-phenothiazine;
- 2-{2-[(4-butylpiperazin-1-yl)methyl]-1,3-thiazol-4-yl}-10*H*-phenothiazine;
- methyl 4-{[4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]methyl}piperazine-1-carboxylate;
- 4-[2-(aminomethyl)-1H-imidazol-4-yl]-2,6-di-*tert*-butylphenol;
- 4-{2-[(benzylamino)methyl]-1,3-thiazol-4-yl}-2,6-di-*tert*-butylphenol;
- 4-{2-[(4-acetylpiperazin-1-yl)methyl]-1,3-thiazol-4-yl}-2,6-di-*tert*-butylphenol;
- *N*-methyl-N-{[4-(10*H*-phenoxazin-2-yl)-1,3-thiazol-2-yl]methyl}amine;
- 4-[2-(azetidin-1-ylmethyl)-1,3-thiazol-4-yl]-2,6-di-*tert*-butylphenol;
- 2,6-di-*tert*-butyl-4-{2-[(4-butylpiperazin-1-yl)methyl]-1,3-thiazol-4-yl}phenol;
- butyl 2-[4-(3'-chloro-1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate;
- butyl 2-[4-(3'-fluoro-1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate;
- butyl 2-[4-(4-isobutylphenyl)-1*H*-imidazol-2-yl]ethylcarbamate;
- benzyl 2-[4-(4-isobutylphenyl)-1*H*-imidazol-2-yl]ethylcarbamate;
- butyl 2-[4-(3'-chloro-4'-fluoro-1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate;
- butyl 2-[4-(3', 4'-dichloro-1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate;
- butyl 2-[4-(4-propylphenyl)-1*H*-imidazol-2-yl]ethylcarbamate;
- butyl 2-[4-(4-ethylphenyl)-1*H*-imidazol-2-yl]ethylcarbamate;
- butyl 2-[4-(4'-cyano-1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate;
- butyl 2-[4-(1,1'-biphenyl-4-yl)-5-ethyl-1*H*-imidazol-2-yl]ethylcarbamate;
- butyl 2-[4-(2'-chloro-1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate;

- butyl 2-[4-(2', 3'-difluoro-1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate;

- butyl 2-[4-(2'-bromo-1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate;

- butyl 2-[4-(3', 5'-difluoro-1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate;

- butyl 2-[4-(2'-methoxy-1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate;

- butyl 2-[4-(3'-nitro-1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate;

- butyl 2-[4-(2', 5'-difluoro-1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate;

- butyl 2-[4-(3'-methoxy-1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate;

- methyl 4-{[4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-1,3-thiazol-2-yl]methyl}piperazine-1-carboxylate;

- methyl [4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-1,3-thiazol-2-yl]methylcarbamate;

- *N*-{[4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-1,3-thiazol-2-yl]methyl}benzamide;

- *N*-{[4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-1,3-thiazol-2-yl]methyl}-2-phenylacetamide;

- *N*-{[4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-1,3-thiazol-2-yl]methyl}propanamide;

- 1-{[4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-1,3-thiazol-2-yl]methyl}piperidin-4-yl acetate;

- 1-{[4-(3,5-di-tert-butyl-4-hydroxyphenyl)-1,3-thiazol-2-yl]methyl}pyrrolidine-3, 4-diol;

or salt of such a compound.

2. As a medicament, a compound characterized in that it is chosen from the following compounds:

- 2,6-di*tert*-butyl-4-{2-[2-(methylamino)ethyl]-1,3-thiazol-4-yl}phenol;

- 2,6-di*tert*-butyl-4-[4-(hydroxymethyl)-1,3-oxazol-2-yl]phenol;

- 2,6-di*tert*-butyl-4-{2-[1-(methylamino)ethyl]-1,3-thiazol-4-yl}phenol;

- 2,6-di*tert*-butyl-4-[2-(methoxymethyl)-1,3-thiazol-4-yl]phenol;

- 2,6-di*tert*-butyl-4-{4-[(methylamino)methyl]-1,3-oxazol-2-yl}phenol;

- N-{[4-(3,5-di*tert*-butyl-4-hydroxyphenyl)-1,3-thiazol-2-yl]methyl}acetamide;

- ethyl [4-(3,5-di*tert*-butyl-4-hydroxyphenyl)-1,3-thiazol-2-yl]methylcarbamate;

- 2,6-di*tert*-butyl-4-[2-(morpholin-4-ylmethyl)-1,3-thiazol-4-yl]phenol;

- 2,6-di*tert*-butyl-4-[2-(thiomorpholin-4-ylmethyl)-1,3-thiazol-4-yl]phenol;

- 4-[2-(anilinomethyl)-1,3-thiazol-4-yl]-2,6-di*tert*-butylphenol;

- 2,6-di*tert*-butyl-4-(2-{[[2-(dimethylamino)ethyl](methyl)amino]methyl}-1,3-thiazol-4-yl)phenol;

- 2,6-di*tert*-butyl-4-{5-methyl-2-[(methylamino)methyl]-1,3-thiazol-4-yl}phenol;

- 1-[4-(10H-phenothiazin-2-yl)-1,3-thiazol-2-yl]methanamine;

- *N*-{[4-(3,5-di*tert*-butyl-4-hydroxyphenyl)-1,3-thiazol-2-yl]methyl}-*N*-methylacetamide;

- 1-[4-(3,5-di*tert*-butyl-4-methoxyphenyl)-1,3-thiazol-2-yl]-N-methylmethanamine;

- 2,6-di*tert*-butyl-4-{2-[(ethylamino)methyl]-1,3-thiazol-4-yl}phenol;

- 2,6-di*tert*-butyl-4-{2-[(4-phenylpiperazin-1-yl)methyl]-1,3-thiazol-4-yl}phenol;

- 2,6-di*tert*-butyl-4-{2-[(4-methyl-1,4 -diazepan-1-yl)methyl]-1,3-thiazol-4-yl}phenol;

- N-{1-[4-(4-anilinophenyl)-1,3-thiazol-2-yl]ethyl}-N-methylamine;

- 2,6-di*tert*-butyl-4-{2-[(isopropylamino)methyl]-1,3-thiazol-4-yl}phenol;

- 2,6-ditert-butyl-4-{2-[(cyclohexylamino)methyl]-1,3-thiazol-4-yl}phenol;

- 2,6-di*tert*-butyl-4-{2-[(4-isopropylpiperazin-1-yl)methyl]-1,3-thiazol-4-yl}phenol;

- *N*-methyl-1-[4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]ethanamine;

- 2,6-di*tert*-butyl-4-{2-[(4-ethylpiperazin-1-yl)methyl]-1,3-thiazol-4-yl}phenol;

- *N*-{[4-(4-anilinophenyl)-1,3-thiazol-2-yl]methyl}-*N*-ethylamine;

- *N*-{[4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]methyl}ethanamine;

- 2,6-di*tert*-butyl-4-(2-{[4-(dimethylamino)piperidin-1-yl]methyl}-1,3-thiazol-4-yl)phenol;

- 1-{[4-(3,5-di*tert*-butyl-4-hydroxyphenyl)-1,3-thiazol-2-yl]methyl}piperidin-4-ol;

- 4-methylpentyl 2-[4-(1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate;

- 3,3-dimethylbutyl 2-[4-(4-pyrrolidin-1-ylphenyl)-1*H*-imidazol-2-yl]ethylcarbamate;

- isopentyl 2-[4-(1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate;

- hexyl 2-[4-(4'-bromo-1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate;

- benzyl 2-[4-(4-*tert*-butylphenyl)-1*H*-imidazol-2-yl]ethylcarbamate;

- 3,3-dimethylbutyl 2-[4-(1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate;

- hexyl 2-[4-(4-pyrrolidin-1-ylphenyl)-1*H*-imidazol-2-yl]ethylcarbamate;

- hexyl 2-[4-(3,5-di*tert*-butyl-4-hydroxyphenyl)-1*H*-imidazol-2-yl]ethylcarbamate;

- 3,3-dimethylbutyl 2-[4-(3,5-di*tert*-butyl-4-hydroxyphenyl)-1*H*-imidazol-2-yl]ethylcarbamate;

- 3,3-dimethylbutyl 2-[4-(4-methoxyphenyl)-1*H*-imidazol-2-yl]ethylcarbamate;

- benzyl 2-[4-(3,5-di*tert*-butyl-4-hydroxyphenyl)-1*H*-imidazol-2-yl]ethylcarbamate;

- benzyl 2-[4-(4-pyrrolidin-1-ylphenyl)-1*H*-imidazol-2-yl]ethylcarbamate;

- 2-phenylethyl 2-[4-(1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate;

- butyl 2-[4-(4'-fluoro-1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate;

- butyl 2-[4-(1,1'-biphenyl-4-yl)-5-methyl-1*H*-imidazol-2-yl]ethylcarbamate;

- butyl 2-[4-(4'-methyl-1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate;

- butyl 2-[4-(4'-chloro-1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate;

- butyl 2-[4-(2'-fluoro-1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate;

- butyl 2-[4-(2', 4'-difluoro-1,1'-biphenyl-4-yl)-1H-imidazol-2-yl]ethylcarbamate;

- 2,6-di-*tert*-butyl-4-{2-[(propylamino)methyl]-1,3-thiazol-4-yl}phenol;

- *N*-{[4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]methyl}-*N*-propylamine;

- *N*-{[4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]methyl}butan-1-amine;

- *N*-{[4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]methyl}pentan-1-amine;

- 1-{[4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-1,3-thiazol-2-yl]methyl}piperidin-3-ol;

- 1-{[4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-1,3-thiazol-2-yl]methyl}pyrrolidin-3-ol;

- [4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]methanol;

- *N*, *N*-dimethyl-*N*-{[4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]methyl}amine;

- 2-{2-[(4-methylpiperazin-1-yl)methyl]-1,3-thiazol-4-yl}-10*H*-phenothiazine;

- 2-[2-(piperidin-1-ylmethyl)-1,3-thiazol-4-yl]-10*H*-phenothiazine;

- 2-[2-(piperazin-1-ylmethyl)-1,3-thiazol-4-yl]-10*H*-phenothiazine;

- 1-{[4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-1,3-thiazol-2-yl]methyl}azetidin-3-ol;

- 2-[2-(morpholin-4-ylmethyl)-1,3-thiazol-4-yl]-10*H*-phenothiazine;

- 2-[2-(thiomorpholin-4-ylmethyl)-1,3-thiazol-4-yl]-10*H*-phenothiazine;

- 2-{2-[(4-methyl-1,4-diazepan-1-yl)methyl]-1,3-thiazol-4-yl}-10*H*-phenothiazine;

- (3R)-1-{[4-(3,5-di-tert-butyl-4-hydroxyphenyl)-1,3-thiazol-2-yl]methyl}pyrrolidin-3-ol;

- (3S)-1-{[4-(3,5-di-tert-butyl-4-hydroxyphenyl)-1,3-thiazol-2-yl]methyl}pyrrolidin-3-ol;

- 2,6-di-*tert*-butyl-4-[2-(pyrrolidin-1-ylmethyl)-1,3-thiazol-4-yl]phenol;

- 2,6-di-tert-butyl-4-{2-[(butylamino)methyl]-1,3-thiazol-4-yl}phenol;

- 2-{2-[(4-ethylpiperazin-1-yl)methyl]-1,3-thiazol-4-yl}-10*H*-phenothiazine;

- *N*-methyl-*N*-{[4-(10*H*-phenothiazin-2-yl)-1*H*-imidazol-2-yl]methyl}amine;

- methyl [4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]methylcarbamate;

- butyl [4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]methylcarbamate;

- *N*-neopentyl-N-{[4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]methyl}amine;

- 1-{[4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]methyl}piperidin-4-ol;

- *N*-{[4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]methyl}acetamide;

- *N*-{[4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]methyl}butanamide;

- 2,6-di-*tert*-butyl-4-{2-[(4-propylpiperazin-1-yl)methyl]-1,3-thiazol-4-yl}phenol;

- 2,6-di-*tert*-butyl-4-{2-[2-methyl-1-(methylamino)propyl]-1,3-thiazol-4-yl}phenol;

- *N*, 2-dimethyl-1-[4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]propan-1-amine;

- *N*-{[4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]methyl}hexanamide;

- (3*R*)-1-{[4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]methyl}pyrrolidin-3-ol;

- (3*S*)-1-{[4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]methyl}pyrrolidin-3-ol;

- 1-{[4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]methyl}azetidin-3-ol;

- 2-{2-[(4-propylpiperazin-1-yl)methyl]-1,3-thiazol-4-yl}-10*H*-phenothiazine;

- 2-{2-[(4-acetylpiperazin-1-yl)methyl]-1,3-thiazol-4-yl}-10*H*-phenothiazine;

- 2-{2-[(4-butylpiperazin-1-yl)methyl]-1,3-thiazol-4-yl}-10*H*-phenothiazine;

- methyl 4-{[4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]methyl}piperazine-1-carboxylate;

- 4-[2-(aminomethyl)-1H-imidazol-4-yl]-2,6-di-*tert*-butylphenol;

- 4-{2-[(benzylamino)methyl]-1,3-thiazol-4-yl}-2,6-di-*tert*-butylphenol;

- 4-{2-[(4-acetylpiperazin-1-yl)methyl]-1,3-thiazol-4-yl}-2,6-di-*tert*-butylphenol;

- *N*-methyl-N-{[4-(10*H*-phenoxazin-2-yl)-1,3-thiazol-2-yl]methyl}amine;
- 4-[2-(azetidin-1-ylmethyl)-1,3-thiazol-4-yl]-2,6-di-*tert*-butylphenol;
- 2,6-di-*tert*-butyl-4-{2-[(4-butylpiperazin-1-yl)methyl]-1,3-thiazol-4-yl}phenol;
- butyl 2-[4-(3'-chloro-1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate;
- butyl 2-[4-(3'-fluoro-1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate;
- butyl 2-[4-(4-isobutylphenyl)-1*H*-imidazol-2-yl]ethylcarbamate;
- benzyl 2-[4-(4-isobutylphenyl)-1*H*-imidazol-2-yl]ethylcarbamate;
- butyl 2-[4-(3'-chloro-4'-fluoro-1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate;
- butyl 2-[4-(3', 4'-dichloro-1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate;
- butyl 2-[4-(4-propylphenyl)-1*H*-imidazol-2-yl]ethylcarbamate;
- butyl 2-[4-(4-ethylphenyl)-1*H*-imidazol-2-yl]ethylcarbamate;
- butyl 2-[4-(4'-cyano-1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate;
- butyl 2-[4-(1,1'-biphenyl-4-yl)-5-ethyl-1*H*-imidazol-2-yl]ethylcarbamate;
- butyl 2-[4-(2'-chloro-1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate;
- butyl 2-[4-(2', 3'-difluoro-1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate;
- butyl 2-[4-(2'-bromo-1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate;
- butyl 2-[4-(3',5'-difluoro-1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate;
- butyl 2-[4-(2'-methoxy-1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate;
- butyl 2-[4-(3'-nitro-1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate;
- butyl 2-[4-(2',5'-difluoro-1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate;
- butyl 2-[4-(3'-methoxy-1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate;
- methyl 4-{[4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-1,3-thiazol-2-yl]methyl}piperazine-1-carboxylate;
- methyl [4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-1,3-thiazol-2-yl]methylcarbamate;
- *N*-{[4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-1,3-thiazol-2-yl]methyl}benzamide;
- *N*-{[4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-1,3-thiazol-2-yl]methyl}-2-phenylacetamide;
- *N*-{[4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-1,3-thiazol-2-yl]methyl}propanamide;

- 1-{[4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-1,3-thiazol-2-yl]methyl}piperidin-4-yl acetate;

- 1-{[4-(3,5-di-tert-butyl-4-hydroxyphenyl)-1,3-thiazol-2-yl]methyl}pyrrolidine-3,4-diol;

or a pharmaceutically acceptable salt of such a compound.

3. Pharmaceutical composition containing, as active ingredient, at least one of the compounds according to claim 2.

4. Use of a compound characterized in that it is chosen from the following compounds:

- 2,6-di*tert*-butyl-4-{2-[2-(methylamino)ethyl]-1,3-thiazol-4-yl}phenol;

- 2,6-di*tert*-butyl-4-[4-(hydroxymethyl)-1,3-oxazol-2-yl]phenol;

- 2,6-di*tert*-butyl-4-{2-[1-(methylamino)ethyl]-1,3-thiazol-4-yl}phenol;

- 2,6-di*tert*-butyl-4-[2-(methoxymethyl)-1,3-thiazol-4-yl]phenol;

- 2,6-di*tert*-butyl-4-{4-[(methylamino)methyl]-1,3-oxazol-2-yl}phenol;

- N-{[4-(3,5-di*tert*-butyl-4-hydroxyphenyl)-1,3-thiazol-2-yl]methyl}acetamide;

- ethyl [4-(3,5-di*tert*-butyl-4-hydroxyphenyl)-1,3-thiazol-2-yl]methylcarbamate;

- 2,6-di*tert*-butyl-4-[2-(morpholin-4-ylmethyl)-1,3-thiazol-4-yl]phenol;

- 2,6-di*tert*-butyl-4-[2-(thiomorpholin-4-ylmethyl)-1,3-thiazol-4-yl]phenol;

- 4-[2-(anilinomethyl)-1,3-thiazol-4-yl]-2,6-di*tert*-butylphenol;

- 2,6-di*tert*-butyl-4-(2-{[[2-(dimethylamino)ethyl](methyl)amino]methyl}-1,3-thiazol-4-yl)phenol;

- 2,6-di*tert*-butyl-4-{5-methyl-2-[(methylamino)methyl]-1,3-thiazol-4-yl}phenol;

- 1-[4-(10H-phenothiazin-2-yl)-1,3-thiazol-2-yl]methanamine;

- *N*-{[4-(3,5-di*tert*-butyl-4-hydroxyphenyl)-1,3-thiazol-2-yl]methyl}-*N*-methylacetamide;

- 1-[4-(3,5-di*tert*-butyl-4-methoxyphenyl)-1,3-thiazol-2-yl]-N-methylmethanamine;

- 2,6-di*tert*-butyl-4-{2-[(ethylamino)methyl]-1,3-thiazol-4-yl}phenol;

- 2,6-di*tert*-butyl-4-{2-[(4-phenylpiperazin-1-yl)methyl]-1,3-thiazol-4-yl}phenol;

- 2,6-di*tert*-butyl-4-{2-[(4-methyl-1,4 -diazepan-1-yl)methyl]-1,3-thiazol-4-yl}phenol;

- N-{1-[4-(4-anilinophenyl)-1,3-thiazol-2-yl]ethyl}-N-methylamine;
- 2,6-di*tert*-butyl-4-{2-[(isopropylamino)methyl]-1,3-thiazol-4-yl}phenol;
- 2,6-ditert-butyl-4-{2-[(cyclohexylamino)methyl]-1,3-thiazol-4-yl}phenol;
- 2,6-di*tert*-butyl-4-{2-[(4-isopropylpiperazin-1-yl)methyl]-1,3-thiazol-4-yl}phenol;
- *N*-methyl-1-[4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]ethanamine;
- 2,6-di*tert*-butyl-4-{2-[(4-ethylpiperazin-1-yl)methyl]-1,3-thiazol-4-yl}phenol;
- *N*-{[4-(4-anilinophenyl)-1,3-thiazol-2-yl]methyl}-*N*-ethylamine;
- *N*-{[4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]methyl}ethanamine;
- 2,6-di*tert*-butyl-4-(2-{[4-(dimethylamino)piperidin-1-yl]methyl}-1,3-thiazol-4-yl)phenol;
- 1-{[4-(3,5-di*tert*-butyl-4-hydroxyphenyl)-1,3-thiazol-2-yl]methyl}piperidin-4-ol;
- 4-methylpentyl 2-[4-(1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate;
- 3,3-dimethylbutyl 2-[4-(4-pyrrolidin-1-ylphenyl)-1*H*-imidazol-2-yl]ethylcarbamate;
- isopentyl 2-[4-(1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate;
- hexyl 2-[4-(4'-bromo-1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate;
- benzyl 2-[4-(4-*tert*-butylphenyl)-1*H*-imidazol-2-yl]ethylcarbamate;
- 3,3-dimethylbutyl 2-[4-(1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate;
- hexyl 2-[4-(4-pyrrolidin-1-ylphenyl)-1*H*-imidazol-2-yl]ethylcarbamate;
- hexyl 2-[4-(3,5-di*tert*-butyl-4-hydroxyphenyl)-1*H*-imidazol-2-yl]ethylcarbamate;
- 3,3-dimethylbutyl 2-[4-(3,5-di*tert*-butyl-4-hydroxyphenyl)-1*H*-imidazol-2-yl]ethylcarbamate;
- 3,3-dimethylbutyl 2-[4-(4-methoxyphenyl)-1*H*-imidazol-2-yl]ethylcarbamate;
- benzyl 2-[4-(3,5-di*tert*-butyl-4-hydroxyphenyl)-1*H*-imidazol-2-yl]ethylcarbamate;
- benzyl 2-[4-(4-pyrrolidin-1-ylphenyl)-1*H*-imidazol-2-yl]ethylcarbamate;
- 2-phenylethyl 2-[4-(1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate;
- butyl 2-[4-(4'-fluoro-1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate;
- butyl 2-[4-(1,1'-biphenyl-4-yl)-5-methyl-1*H*-imidazol-2-yl]ethylcarbamate;
- butyl 2-[4-(4'-methyl-1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate;
- butyl 2-[4-(4'-chloro-1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate;

- butyl 2-[4-(2'-fluoro-1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate;
- butyl 2-[4-(2', 4'-difluoro-1,1'-biphenyl-4-yl)-1H-imidazol-2-yl]ethylcarbamate;
- 2,6-di-*tert*-butyl-4-{2-[(propylamino)methyl]-1,3-thiazol-4-yl}phenol;
- *N*-{[4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]methyl}-*N*-propylamine;
- *N*-{[4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]methyl}butan-1-amine;
- *N*-{[4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]methyl}pentan-1-amine;
- 1-{[4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-1,3-thiazol-2-yl]methyl}piperidin-3-ol;
- 1-{[4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-1,3-thiazol-2-yl]methyl}pyrrolidin-3-ol;
- [4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]methanol;
- *N*, *N*-dimethyl-*N*-{[4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]methyl}amine;
- 2-{2-[(4-methylpiperazin-1-yl)methyl]-1,3-thiazol-4-yl}-10*H*-phenothiazine;
- 2-[2-(piperidin-1-ylmethyl)-1,3-thiazol-4-yl]-10*H*-phenothiazine;
- 2-[2-(piperazin-1-ylmethyl)-1,3-thiazol-4-yl]-10*H*-phenothiazine;
- 1-{[4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-1,3-thiazol-2-yl]methyl}azetidin-3-ol;
- 2-[2-(morpholin-4-ylmethyl)-1,3-thiazol-4-yl]-10*H*-phenothiazine;
- 2-[2-(thiomorpholin-4-ylmethyl)-1,3-thiazol-4-yl]-10*H*-phenothiazine;
- 2-{2-[(4-methyl-1,4 -diazepan-1-yl)methyl]-1,3-thiazol-4-yl}-10*H*-phenothiazine;
- (3R)-1-{[4-(3,5-di-tert-butyl-4-hydroxyphenyl)-1,3-thiazol-2-yl]methyl}pyrrolidin-3-ol;
- (3S)-1-{[4-(3,5-di-tert-butyl-4-hydroxyphenyl)-1,3-thiazol-2-yl]methyl}pyrrolidin-3-ol;
- 2,6-di-*tert*-butyl-4-[2-(pyrrolidin-1-ylmethyl)-1,3-thiazol-4-yl]phenol;
- 2,6-di-tert-butyl-4-{2-[(butylamino)methyl]-1,3-thiazol-4-yl}phenol;
- 2-{2-[(4-ethylpiperazin-1-yl)methyl]-1,3-thiazol-4-yl}-10*H*-phenothiazine;
- *N*-methyl-*N*-{[4-(10*H*-phenothiazin-2-yl)-1*H*-imidazol-2-yl]methyl}amine;
- methyl [4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]methylcarbamate;
- butyl [4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]methylcarbamate;
- *N*-neopentyl-N-{[4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]methyl}amine;
- 1-{[4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]methyl}piperidin-4-ol;

- *N*-{[4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]methyl}acetamide;
- *N*-{[4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]methyl}butanamide;
- 2,6-di-*tert*-butyl-4-{2-[(4-propylpiperazin-1-yl)methyl]-1,3-thiazol-4-yl}phenol;
- 2,6-di-*tert*-butyl-4-{2-[2-methyl-1-(methylamino)propyl]-1,3-thiazol-4-yl}phenol;
- *N*, 2-dimethyl-1-[4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]propan-1-amine;
- *N*-{[4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]methyl}hexanamide;
- (3*R*)-1-{[4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]methyl}pyrrolidin-3-ol;
- (3*S*)-1-{[4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]methyl}pyrrolidin-3-ol;
- 1-{[4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]methyl}azetidin-3-ol;
- 2-{2-[(4-propylpiperazin-1-yl)methyl]-1,3-thiazol-4-yl}-10*H*-phenothiazine;
- 2-{2-[(4-acetylpiperazin-1-yl)methyl]-1,3-thiazol-4-yl}-10*H*-phenothiazine;
- 2-{2-[(4-butylpiperazin-1-yl)methyl]-1,3-thiazol-4-yl}-10*H*-phenothiazine;
- methyl 4-{[4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]methyl}piperazine-1-carboxylate;
- 4-[2-(aminomethyl)-1H-imidazol-4-yl]-2,6-di-*tert*-butylphenol;
- 4-{2-[(benzylamino)methyl]-1,3-thiazol-4-yl}-2,6-di-*tert*-butylphenol;
- 4-{2-[(4-acetylpiperazin-1-yl)methyl]-1,3-thiazol-4-yl}-2,6-di-*tert*-butylphenol;
- *N*-methyl-N-{[4-(10*H*-phenoxazin-2-yl)-1,3-thiazol-2-yl]methyl}amine;
- 4-[2-(azetidin-1-ylmethyl)-1,3-thiazol-4-yl]-2,6-di-*tert*-butylphenol;
- 2,6-di-*tert*-butyl-4-{2-[(4-butylpiperazin-1-yl)methyl]-1,3-thiazol-4-yl}phenol;
- butyl 2-[4-(3'-chloro-1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate;
- butyl 2-[4-(3'-fluoro-1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate;
- butyl 2-[4-(4-isobutylphenyl)-1*H*-imidazol-2-yl]ethylcarbamate;
- benzyl 2-[4-(4-isobutylphenyl)-1*H*-imidazol-2-yl]ethylcarbamate;
- butyl 2-[4-(3'-chloro-4'-fluoro-1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate;
- butyl 2-[4-(3', 4'-dichloro-1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate;
- butyl 2-[4-(4-propylphenyl)-1*H*-imidazol-2-yl]ethylcarbamate;
- butyl 2-[4-(4-ethylphenyl)-1*H*-imidazol-2-yl]ethylcarbamate;
- butyl 2-[4-(4'-cyano-1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate;

- butyl 2-[4-(1,1'-biphenyl-4-yl)-5-ethyl-1*H*-imidazol-2-yl]ethylcarbamate;

- butyl 2-[4-(2'-chloro-1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate;

- butyl 2-[4-(2', 3'-difluoro-1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate;

- butyl 2-[4-(2'-bromo-1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate;

- butyl 2-[4-(3', 5'-difluoro-1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate;

- butyl 2-[4-(2'-methoxy-1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate;

- butyl 2-[4-(3'-nitro-1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate;

- butyl 2-[4-(2', 5'-difluoro-1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate;

- butyl 2-[4-(3'-methoxy-1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate;

- methyl 4-{[4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-1,3-thiazol-2-yl]methyl}piperazine-1-carboxylate;

- methyl [4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-1,3-thiazol-2-yl]methylcarbamate;

- *N*-{[4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-1,3-thiazol-2-yl]methyl}benzamide;

- *N*-{[4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-1,3-thiazol-2-yl]methyl}-2-phenylacetamide;

- *N*-{[4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-1,3-thiazol-2-yl]methyl}propanamide;

- 1-{[4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-1,3-thiazol-2-yl]methyl}piperidin-4-yl acetate;

- 1-{[4-(3,5-di-tert-butyl-4-hydroxyphenyl)-1,3-thiazol-2-yl]methyl}pyrrolidine-3, 4-diol;

or of a pharmaceutically acceptable salt of one of the latter

for preparing a medicament intended to have at least one of the three following activities :

- inhibiting the monoamine oxidases, in particular monoamine oxidase B,
- inhibiting lipidic peroxidation,
- having a modulating activity vis-à-vis the sodium channels.

5. Use according to claim 4, characterized in that the medicament prepared is intended to treat one of the following disorders or diseases: Parkinson's disease, senile dementia, Alzheimer's disease, Huntington's chorea, amyotrophic lateral sclerosis, schizophrenia, depression, psychoses, migraine or pain and in particular neuropathic pain.

6. Use of one of the following compounds:

- 2,6-di*tert*-butyl-4-{2-[2-(methylamino)ethyl]-1,3-thiazol-4-yl}phenol;
- 2,6-di*tert*-butyl-4-[4-(hydroxymethyl)-1,3-oxazol-2-yl]phenol;
- 2,6-di*tert*-butyl-4-{2-[1-(methylamino)ethyl]-1,3-thiazol-4-yl}phenol;
- 2,6-di*tert*-butyl-4-[2-(methoxymethyl)-1,3-thiazol-4-yl]phenol;
- 2,6-di*tert*-butyl-4-{4-[(methylamino)methyl]-1,3-oxazol-2-yl}phenol;
- N-{[4-(3,5-di*tert*-butyl-4-hydroxyphenyl)-1,3-thiazol-2-yl]methyl}acetamide;
- ethyl [4-(3,5-di*tert*-butyl-4-hydroxyphenyl)-1,3-thiazol-2-yl]methylcarbamate;
- 2,6-di*tert*-butyl-4-[2-(morpholin-4-ylmethyl)-1,3-thiazol-4-yl]phenol;
- 2,6-di*tert*-butyl-4-[2-(thiomorpholin-4-ylmethyl)-1,3-thiazol-4-yl]phenol;
- 4-[2-(anilinomethyl)-1,3-thiazol-4-yl]-2,6-di*tert*-butylphenol;
- 2,6-di*tert*-butyl-4-(2-{[[2-(dimethylamino)ethyl](methyl)amino]methyl}-1,3-thiazol-4-yl)phenol;
- 2,6-di*tert*-butyl-4-{5-methyl-2-[(methylamino)methyl]-1,3-thiazol-4-yl}phenol;
- 1-[4-(10H-phenothiazin-2-yl)-1,3-thiazol-2-yl]methanamine;
- *N*-{[4-(3,5-di*tert*-butyl-4-hydroxyphenyl)-1,3-thiazol-2-yl]methyl}-*N*-methylacetamide;
- 1-[4-(3,5-di*tert*-butyl-4-methoxyphenyl)-1,3-thiazol-2-yl]-N-methylmethanamine;
- 2,6-di*tert*-butyl-4-{2-[(ethylamino)methyl]-1,3-thiazol-4-yl}phenol;
- 2,6-di*tert*-butyl-4-{2-[(4-phenylpiperazin-1-yl)methyl]-1,3-thiazol-4-yl}phenol;
- 2,6-di*tert*-butyl-4-{2-[(4-methyl-1,4 -diazepan-1-yl)methyl]-1,3-thiazol-4-yl}phenol;
- N-{1-[4-(4-anilinophenyl)-1,3-thiazol-2-yl]ethyl}-N-methylamine;
- 2,6-di*tert*-butyl-4-{2-[(isopropylamino)methyl]-1,3-thiazol-4-yl}phenol;
- 2,6-ditert-butyl-4-{2-[(cyclohexylamino)methyl]-1,3-thiazol-4-yl}phenol;
- 2,6-di*tert*-butyl-4-{2-[(4-isopropylpiperazin-1-yl)methyl]-1,3-thiazol-4-yl}phenol;

- *N*-methyl-1-[4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]ethanamine;
- 2,6-di*tert*-butyl-4-{2-[(4-ethylpiperazin-1-yl)methyl]-1,3-thiazol-4-yl}phenol;
- *N*-{[4-(4-anilinophenyl)-1,3-thiazol-2-yl]methyl}-*N*-ethylamine;
- *N*-{[4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]methyl}ethanamine;
- 2,6-di*tert*-butyl-4-(2-{[4-(dimethylamino)piperidin-1-yl]methyl}-1,3-thiazol-4-yl)phenol;
- 1-{[4-(3,5-di*tert*-butyl-4-hydroxyphenyl)-1,3-thiazol-2-yl]methyl}piperidin-4-ol;
- 2,6-di-*tert*-butyl-4-{2-[(propylamino)methyl]-1,3-thiazol-4-yl}phenol;
- *N*-{[4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]methyl}-*N*-propylamine;
- *N*-{[4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]methyl}butan-1-amine;
- *N*-{[4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]methyl}pentan-1-amine;
- 1-{[4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-1,3-thiazol-2-yl]methyl}piperidin-3-ol;
- 1-{[4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-1,3-thiazol-2-yl]methyl}pyrrolidin-3-ol;
- [4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]methanol;
- *N*, *N*-dimethyl-*N*-{[4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]methyl}amine;
- 2-{2-[(4-methylpiperazin-1-yl)methyl]-1,3-thiazol-4-yl}-10*H*-phenothiazine;
- 2-[2-(piperidin-1-ylmethyl)-1,3-thiazol-4-yl]-10*H*-phenothiazine;
- 2-[2-(piperazin-1-ylmethyl)-1,3-thiazol-4-yl]-10*H*-phenothiazine;
- 1-{[4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-1,3-thiazol-2-yl]methyl}azetidin-3-ol;
- 2-[2-(morpholin-4-ylmethyl)-1,3-thiazol-4-yl]-10*H*-phenothiazine;
- 2-[2-(thiomorpholin-4-ylmethyl)-1,3-thiazol-4-yl]-10*H*-phenothiazine;
- 2-{2-[(4-methyl-1,4 -diazepan-1-yl)methyl]-1,3-thiazol-4-yl}-10*H*-phenothiazine;
- (3R)-1-{[4-(3,5-di-tert-butyl-4-hydroxyphenyl)-1,3-thiazol-2-yl]methyl}pyrrolidin-3-ol;
- (3S)-1-{[4-(3,5-di-tert-butyl-4-hydroxyphenyl)-1,3-thiazol-2-yl]methyl}pyrrolidin-3-ol;
- 2,6-di-*tert*-butyl-4-[2-(pyrrolidin-1-ylmethyl)-1,3-thiazol-4-yl]phenol;
- 2,6-di-tert-butyl-4-{2-[(butylamino)methyl]-1,3-thiazol-4-yl}phenol;
- 2-{2-[(4-ethylpiperazin-1-yl)methyl]-1,3-thiazol-4-yl}-10*H*-phenothiazine;

- *N*-methyl-*N*-{[4-(10*H*-phenothiazin-2-yl)-1*H*-imidazol-2-yl]methyl}amine;
- methyl [4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]methylcarbamate;
- butyl [4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]methylcarbamate;
- *N*-neopentyl-N-{[4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]methyl}amine;
- 1-{[4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]methyl}piperidin-4-ol;
- *N*-{[4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]methyl}acetamide;
- *N*-{[4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]methyl}butanamide;
- 2,6-di-*tert*-butyl-4-{2-[(4-propylpiperazin-1-yl)methyl]-1,3-thiazol-4-yl}phenol;
- 2,6-di-*tert*-butyl-4-{2-[2-methyl-1-(methylamino)propyl]-1,3-thiazol-4-yl}phenol;
- *N*, 2-dimethyl-1-[4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]propan-1-amine;
- *N*-{[4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]methyl}hexanamide;
- (3*R*)-1-{[4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]methyl}pyrrolidin-3-ol;
- (3*S*)-1-{[4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]methyl}pyrrolidin-3-ol;
- 1-{[4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]methyl}azetidin-3-ol;
- 2-{2-[(4-propylpiperazin-1-yl)methyl]-1,3-thiazol-4-yl}-10*H*-phenothiazine;
- 2-{2-[(4-acetylpiperazin-1-yl)methyl]-1,3-thiazol-4-yl}-10*H*-phenothiazine;
- 2-{2-[(4-butylpiperazin-1-yl)methyl]-1,3-thiazol-4-yl}-10*H*-phenothiazine;
- methyl 4-{[4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]methyl}piperazine-1-carboxylate;
- 4-[2-(aminomethyl)-1H-imidazol-4-yl]-2,6-di-*tert*-butylphenol;
- 4-{2-[(benzylamino)methyl]-1,3-thiazol-4-yl}-2,6-di-*tert*-butylphenol;
- 4-{2-[(4-acetylpiperazin-1-yl)methyl]-1,3-thiazol-4-yl}-2,6-di-*tert*-butylphenol;
- *N*-methyl-N-{[4-(10*H*-phenoxazin-2-yl)-1,3-thiazol-2-yl]methyl}amine;
- 4-[2-(azetidin-1-ylmethyl)-1,3-thiazol-4-yl]-2,6-di-*tert*-butylphenol;
- 2,6-di-*tert*-butyl-4-{2-[(4-butylpiperazin-1-yl)methyl]-1,3-thiazol-4-yl}phenol;
- methyl 4-{[4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-1,3-thiazol-2-yl]methyl}piperazine-1-carboxylate;
- methyl [4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-1,3-thiazol-2-yl]methylcarbamate;
- *N*-{[4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-1,3-thiazol-2-yl]methyl}benzamide;

- *N*-{[4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-1,3-thiazol-2-yl]methyl}-2-phenylacetamide;

- *N*-{[4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-1,3-thiazol-2-yl]methyl}propanamide;

- 1-{[4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-1,3-thiazol--yl]methyl}piperidin-4-yl acetate;

- 1-{[4-(3,5-di-tert-butyl-4-hydroxyphenyl)-1,3-thiazol-2-yl]methyl}pyrrolidine-3, 4-diol;

or of a pharmaceutically acceptable salt of one of the latter

for preparing a medicament intended to inhibit the monoamine oxidases and/or to inhibit lipidic peroxidation.

7. Use according to claim 6, characterized in that the compound used is chosen from one of the following compounds:

- 2,6-di*tert*-butyl-4-{2-[1-(methylamino)ethyl]-1,3-thiazol-4-yl}phenol;

- 1-[4-(3,5-di*tert*-butyl-4-methoxyphenyl)-1,3-thiazol-2-yl]-N-methylmethanamine;

- 2,6-di*tert*-butyl-4-{2-[(ethylamino)methyl]-1,3-thiazol-4-yl}phenol;

- 1-{[4-(3,5-di*tert*-butyl-4-hydroxyphenyl)-1,3-thiazol-2-yl]methyl}piperidin-4-ol;

- 1-{[4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-1,3-thiazol-2-yl]methyl}pyrrolidin-3-ol;

- 1-{[4-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-1,3-thiazol-2-yl]methyl}azetidin-3-ol;

- (3*R*)-1-{[4-(3,5-di-tert-butyl-4-hydroxyphenyl)-1,3-thiazol-2-yl]methyl}pyrrolidin-3-ol;

- (3*S*)-1-{[4-(3,5-di-tert-butyl-4-hydroxyphenyl)-1,3-thiazol-2-yl]methyl}pyrrolidin-3-ol;

- *N*, 2-dimethyl-1-[4-(10*H*-phenothiazin-2-yl)-1,3-thiazol-2-yl]propan-1-amine;

and the pharmaceutically acceptable salts of the latter.

8. Use according to claim 6 or 7, characterized in that the medicament prepared is intended to treat one of the following disorders or diseases: Parkinson's disease, senile dementia, Alzheimer's disease, Huntington's chorea, amyotrophic lateral sclerosis, schizophrenia, depression and psychoses.

9. Use of one of the following compounds

- 2,6-di*tert*-butyl-4-{2-[2-(methylamino)ethyl]-1,3-thiazol-4-yl}phenol;
- 2,6-di*tert*-butyl-4-{2-[1-(methylamino)ethyl]-1,3-thiazol-4-yl}phenol;
- 2,6-di*tert*-butyl-4-{4-[(methylamino)methyl]-1,3-oxazol-2-yl}phenol;
- 2,6-di*tert*-butyl-4-{5-methyl-2-[(methylamino)methyl]-1,3-thiazol-4-yl}phenol;
- 1-[4-(3,5-di*tert*-butyl-4-methoxyphenyl)-1,3-thiazol-2-yl]-N-methylmethanamine;
- 2,6-di*tert*-butyl-4-{2-[(ethylamino)methyl]-1,3-thiazol-4-yl}phenol;
- 4-methylpentyl 2-[4-(1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate;
- 3,3-dimethylbutyl 2-[4-(4-pyrrolidin-1-ylphenyl)-1*H*-imidazol-2-yl]ethylcarbamate;
- isopentyl 2-[4-(1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate;
- hexyl 2-[4-(4'-bromo-1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate;
- benzyl 2-[4-(4-*tert*-butylphenyl)-1*H*-imidazol-2-yl]ethylcarbamate;
- 3,3-dimethylbutyl 2-[4-(1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate;
- hexyl 2-[4-(4-pyrrolidin-1-ylphenyl)-1*H*-imidazol-2-yl]ethylcarbamate;
- hexyl 2-[4-(3,5-di*tert*-butyl-4-hydroxyphenyl)-1*H*-imidazol-2-yl]ethylcarbamate;
- hexyl 2-[4-(3,5-di*tert*-butyl-4-hydroxyphenyl)-1*H*-imidazol-2-yl]ethylcarbamate;
- 3,3-dimethylbutyl 2-[4-(4-methoxyphenyl)-1*H*-imidazol-2-yl]ethylcarbamate;
- benzyl 2-[4-(3,5-di*tert*-butyl-4-hydroxyphenyl)-1*H*-imidazol-2-yl]ethylcarbamate;
- benzyl 2-[4-(4-pyrrolidin-1-ylphenyl)-1*H*-imidazol-2-yl]ethylcarbamate;
- 2-phenylethyl 2-[4-(1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate;
- butyl 2-[4-(4'-fluoro-1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate;
- butyl 2-[4-(1,1'-biphenyl-4-yl)-5-methyl-1*H*-imidazol-2-yl]ethylcarbamate;
- butyl 2-[4-(4'-methyl-1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate;
- butyl 2-[4-(4'-chloro-1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate;
- butyl 2-[4-(2'-fluoro-1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate;
- butyl 2-[4-(2', 4'-difluoro-1,1'-biphenyl-4-yl)-1H-imidazol-2-yl]ethylcarbamate;
- butyl 2-[4-(3'-chloro-1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate;
- butyl 2-[4-(3'-fluoro-1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate;

- butyl 2-[4-(4-isobutylphenyl)-1*H*-imidazol-2-yl]ethylcarbamate;
- benzyl 2-[4-(4-isobutylphenyl)-1*H*-imidazol-2-yl]ethylcarbamate;
- butyl 2-[4-(3'-chloro-4'-fluoro-1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate;
- butyl 2-[4-(3', 4'-dichloro-1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate;
- butyl 2-[4-(4-propylphenyl)-1*H*-imidazol-2-yl]ethylcarbamate;
- butyl 2-[4-(4-ethylphenyl)-1*H*-imidazol-2-yl]ethylcarbamate;
- butyl 2-[4-(4'-cyano-1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate;
- butyl 2-[4-(1,1'-biphenyl-4-yl)-5-ethyl-1*H*-imidazol-2-yl]ethylcarbamate;
- butyl 2-[4-(2'-chloro-1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate;
- butyl 2-[4-(2', 3'-difluoro-1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate;
- butyl 2-[4-(2'-bromo-1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate;
- butyl 2-[4-(3', 5'-difluoro-1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate;
- butyl 2-[4-(2'-methoxy-1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate;
- butyl 2-[4-(3'-nitro-1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate;
- butyl 2-[4-(2', 5'-difluoro-1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate;
- butyl 2-[4-(3'-methoxy-1,1'-biphenyl-4-yl)-1*H*-imidazol-2-yl]ethylcarbamate;

or of a pharmaceutically acceptable salt of one of the latter

for preparing a medicament intended to modulate the sodium channels.

10. Use according to claim 9, characterized in that the medicament prepared is intended to treat one of the following disorders or diseases: Parkinson's disease, Alzheimer's disease, amyotrophic lateral sclerosis, migraine or pain and in particular neuropathic pain.