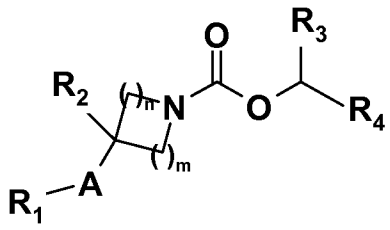
Alkyl-heterocycle carbamate derivatives, their preparation and their therapeutic application

A subject-matter of the invention is alkyl-heterocycle carbamate derivatives, their preparation and their therapeutic application.

There still exists a need to find and develop products which are inhibitors of the enzyme FAAH (Fatty Acid Amide Hydrolase). The compounds of the invention meet this objective.

Furthermore, these compounds have to exhibit metabolic and pharmacokinetic properties and a safety index which allow them to be used as medicaments.

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



(I)

in which:

- R_2 represents a hydrogen or fluorine atom or a hydroxyl, cyano, trifluoromethyl, C_{1-6}-alkyl, C_{1-6}-alkoxy or $-NR_8R_9$ group;
- n and m represent, independently of one another, an integer equal to 1, 2 or 3, it being understood that the sum m+n is at most equal to 5;
- A represents a covalent bond, an oxygen atom, a C_{1-6}-alkylene group or an $-O-C_{1-6}$-alkylene group in which the end represented by an oxygen atom is bonded to the R_1 group;
- R_1 represents an R_5 group optionally substituted by one or more R_6 and/or R_7 groups;

R_5 representing a group chosen from a phenyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, triazinyl, naphthyl, quinolinyl, isoquinolinyl, phthalazinyl, quinazolinyl, quinoxalinyl, cinnolinyl, naphthyridinyl, benzothiazolyl, benzisothiazolyl, benzoxazolyl, benzisoxazolyl, benzimidazolyl, isobenzofuranyl, benzofuranyl, benzothiophenyl, benzothiadiazolyl, benzoxadiazolyl, indazolyl, indolizinyl, indolyl, isoindolyl, imidazopyridinyl, imidazopyrimidinyl, imidazopyrazinyl, imidazopyridazinyl, triazolopyridinyl, pyrrolopyridinyl, pyrrolopyrimidinyl, pyrrolopyrazinyl, pyrrolopyridazinyl, pyrrolotriazinyl, pyrazolopyridinyl, pyrazolopyrimidinyl, pyrazolopyrazinyl, pyrazolopyridazinyl, furopyridinyl, furopyrimidinyl, furopyrazinyl, furopyridazinyl, furotriazinyl, oxazolopyridinyl, oxazolopyrimidinyl, oxazolopyrazinyl, oxazolopyridazinyl, isoxazolopyridinyl, isoxazolopyrimidinyl, isoxazolopyrazinyl, isoxazolopyridazinyl, oxadiazolopyridinyl, thienopyridinyl, thienopyrimidinyl, thienopyrazinyl, thienopyridazinyl, thienotriazinyl, thiazolopyridinyl, thiazolopyrimidinyl, thiazolopyrazinyl, thiazolopyridazinyl, isothiazolopyridinyl, isothiazolopyrimidinyl, isothiazolopyrazinyl, isothiazolopyridazinyl or thiadiazolopyridinyl;

R_6 representing a halogen atom or a cyano, $-CH_2CN$, nitro, hydroxyl, C_{1-8}-alkyl, C_{1-6}-alkoxy, C_{1-6}-thioalkyl, C_{1-6}-haloalkyl, C_{1-6}-haloalkoxy, C_{1-6}-halothioalkyl, C_{3-7}-cycloalkyl, C_{3-7}-cycloalkyl-C_{1-3}-alkylene, C_{3-7}-cycloalkyl-C_{1-3}-alkylene-O-, $-(CH_2)_p-NR_8R_9$, $-NR_8COR_9$, $-NR_8CO_2R_9$, $-NR_8SO_2R_9$, $-NR_8SO_2NR_8R_9$, $-COR_8$, $-CO_2R_8$, $-(CH_2)_p-CONR_8R_9$, $-SO_2R_8$, $-SO_2NR_8R_9$ or $-O-(C_{1-3}$-alkylene)-O- group;

R_7 representing a group chosen from a phenyl, phenyl-C_{1-4}-alkylene-, phenyl-$(CH_2)_p$-O-, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, triazinyl, furanyl, thienyl, imidazolyl, oxazolyl, isoxazolyl, pyrrolyl, pyrazolyl,

tetrazolyl, thiazolyl, isothiazolyl, oxadiazolyl, thiadiazolyl, imidazopyrimidinyl, thienopyrimidinyl, benzofuranyl, benzothienyl, benzimidazolyl, benzoxazolyl, benzisoxazolyl, benzothiazolyl, benzisothiazolyl, indolyl, isoindolyl, indazolyl, pyrrolopyridinyl, furopyridinyl, thienopyridinyl, imidazopyridinyl, pyrazolopyridinyl, oxazolopyridinyl, isoxazolopyridinyl or thiazolopyridinyl; it being possible for the R_7 group or groups to be substituted by one or more R_6 groups which are identical to or different from one another;

p representing a number which can have the value 0, 1, 2 or 3;

- R_3 represents a hydrogen or fluorine atom, a C_{1-6}-alkyl group or a trifluoromethyl group;
- R_4 represents a 5-membered heterocycle chosen from a furanyl, pyrrolyl, thienyl, thiazolyl, isothiazolyl, oxazolyl, isoxazolyl, pyrazolyl, oxadiazolyl, thiadiazolyl, imidazolyl, triazolyl or tetrazolyl;

this heterocycle optionally being substituted by one or more substituents chosen from a halogen atom or a C_{1-6}-alkyl, C_{1-6}-haloalkyl, C_{3-7}-cycloalkyl, C_{3-7}-cycloalkyl-C_{1-3}-alkylene, C_{1-6}-haloalkoxy, cyano, $-NR_8R_9$, $-NR_8C(O)R_9$, $-NR_8CO_2R_9$, $-NR_8SO_2R_9$, $-NR_8SO_2NR_8R_9$, $-C(O)R_8$, $-CO_2R_8$, $-C(O)NR_8R_9$, $-C(O)N(R_8)(C_{1-3}\text{-alkylene-}NR_{10}R_{11})$, $-SO_2R_8$, $-SO_2NR_8R_9$ or $-O-(C_{1-3}$-alkylene$)-O-$ group;

R_8 and R_9 representing, independently of one another, a hydrogen atom or a C_{1-6}-alkyl group,

or forming, with the nitrogen atom or atoms which carry them,

in the case of NR_8R_9, a ring chosen from the azetidine, pyrrolidine, piperidine, morpholine, thiomorpholine, azepine, oxazepine or piperazine rings, this ring optionally being substituted by a C_{1-6}-alkyl or benzyl group;

in the case of NR_8COR_9, a lactam ring;

in the case of $NR_8CO_2R_9$, an oxazolidinone, oxazinone or

oxazepinone ring;

in the case of $NR_8SO_2R_9$, a sultam ring;

in the case of $NR_8SO_2NR_8R_9$, a thiazolidine dioxide or thiadiazinane dioxide ring;

R_{10} and R_{11} representing, independently of one another, a hydrogen atom or a C_{1-6}-alkyl group;

with the exclusion of the following compound:

5-methylisoxazol-3-ylmethyl 4-hydroxy-4-(4-chlorophenyl)-piperidine-1-carboxylate.

Among the compounds of general formula (I), a first subgroup of compounds is composed of the compounds for which R_2 represents a hydrogen atom.

Among the compounds of general formula (I), a second subgroup of compounds is composed of the compounds for which m and n represent, independently of one another, the value 1 or 2.

Among the compounds of general formula (I), a third subgroup of compounds is composed of the compounds for which m and n each represent the value 2.

Among the compounds of general formula (I), a fourth subgroup of compounds is composed of the compounds for which A represents an $-O-C_{1-6}$-alkylene group in which the end represented by an oxygen atom is bonded to the R_1 group, in particular an $-O-(CH_2)_2-$ group, also known as an ethyleneoxy group.

Among the compounds of general formula (I), a fifth subgroup of compounds is composed of the compounds for which A represents an $-O-C_{1-6}$-alkylene group in which the end represented by an oxygen atom is bonded to the R_1 group, in particular an $-O-CH_2-$ group, also known as a methyleneoxy

group.

Among the compounds of general formula (I), a sixth subgroup of compounds is composed of the compounds for which R_1 represents an R_5 group optionally substituted by one or more R_6 and/or R_7 groups;

R_5 representing a group chosen from a phenyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, triazinyl, naphthyl, quinolinyl, isoquinolinyl, phthalazinyl, quinoxalinyl, quinazolinyl, cinnolinyl, naphthyridinyl, benzothiazolyl, benzisothiazolyl, benzoxazolyl, benzisoxazolyl, benzimidazolyl, isobenzofuranyl, benzofuranyl, benzothiophenyl, indazolyl, indolizinyl, indolyl, isoindolyl, pyrrolopyridinyl, furopyridinyl or thienopyridinyl;

R_6 representing a halogen atom or a cyano, $-CH_2CN$, nitro, hydroxyl, C_{1-8}-alkyl, C_{1-6}-alkoxy, C_{1-6}-thioalkyl, C_{1-6}-haloalkyl, C_{1-6}-haloalkoxy, C_{1-6}-halothioalkyl, C_{3-7}-cycloalkyl, C_{3-7}-cycloalkyl-C_{1-3}-alkylene, C_{3-7}-cycloalkyl-C_{1-3}-alkylene-O-, $-(CH_2)_p-NR_8R_9$, $-NR_8COR_9$, $-NR_8CO_2R_9$, $-NR_8SO_2R_9$, $-NR_8SO_2NR_8R_9$, $-COR_8$, $-CO_2R_8$, $-(CH_2)_p-CONR_8R_9$, $-SO_2R_8$, $-SO_2NR_8R_9$ or $-O-(C_{1-3}$-alkylene)-O- group;

R_7 representing a group chosen from a phenyl, phenyl-C_{1-4}-alkylene-, phenyl-$(CH_2)_p$-O-, pyridinyl, pyridazinyl, isoxazolyl, benzothiazolyl, pyrrolyl, pyrazolyl, tetrazolyl, pyrimidinyl, thiazolyl, pyrazinyl, triazinyl or benzoxazolyl; it being possible for the R_7 group or groups to be substituted by one or more R_6 groups, which are identical to or different from one another, as defined above;

p representing a number which can have the value 0, 1, 2 or 3;

R_8 and R_9 representing, independently of one another, a hydrogen atom or a C_{1-6}-alkyl group;

or forming, with the nitrogen atom(s) which carry them,

in the case of NR_8R_9, a ring chosen from the azetidine,

pyrrolidine, piperidine, morpholine, thiomorpholine, azepine, oxazepine or piperazine rings, this ring optionally being substituted by a C_{1-6}-alkyl or benzyl group;

in the case of NR_8COR_9, a lactam ring;

in the case of $NR_8CO_2R_9$, an oxazolidinone, oxazinone or oxazepinone ring;

in the case of $NR_8SO_2R_9$, a sultam ring;

in the case of $NR_8SO_2NR_8R_9$, a thiazolidine dioxide or thiadiazinane dioxide ring.

Among the compounds of general formula (I), a seventh subgroup of compounds is composed of the compounds for which R_1 represents an R_5 group optionally substituted by one or more R_6 and/or R_7 groups;

R_5 representing a group chosen from a phenyl, benzothiazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, triazinyl, naphthyl, quinolinyl, isoquinolinyl, phthalazinyl, quinoxalinyl, cinnolinyl, naphthyridinyl or indolyl;

R_6 representing a halogen atom or a cyano, $-CH_2CN$, nitro, hydroxyl, C_{1-8}-alkyl, C_{1-6}-alkoxy, C_{1-6}-thioalkyl, C_{1-6}-haloalkyl, C_{1-6}-haloalkoxy, C_{1-6}-halothioalkyl, C_{3-7}-cycloalkyl, C_{3-7}-cycloalkyl-C_{1-3}-alkylene, C_{3-7}-cycloalkyl-C_{1-3}-alkylene-O-, $-(CH_2)_p-NR_8R_9$, $-NR_8COR_9$, $-NR_8CO_2R_9$, $-NR_8SO_2R_9$, $-NR_8SO_2NR_8R_9$, $-COR_8$, $-CO_2R_8$, $-(CH_2)_p-CONR_8R_9$, $-SO_2R_8$, $-SO_2NR_8R_9$ or $-O-(C_{1-3}$-alkylene)-O- group;

R_7 representing a group chosen from a phenyl, phenyl-C_{1-4}-alkylene-, phenyl-$(CH_2)_p$-O-, pyridinyl, pyridazinyl, isoxazolyl, benzothiazolyl, pyrrolyl, pyrazolyl, tetrazolyl, pyrimidinyl, thiazolyl, pyrazinyl, triazinyl or benzoxazolyl; it being possible for the R_7 group or groups to be substituted by one or more R_6 groups which are identical to or different from one another;

p representing a number which can have the value 0, 1, 2 or

3;

R_8 and R_9 representing, independently of one another, a hydrogen atom or a C_{1-6}-alkyl group,

or forming, with the nitrogen atom which carries them,

in the case of NR_8R_9, a ring chosen from azetidine, pyrrolidine, piperidine, morpholine, thiomorpholine, azepine, oxazepine or piperazine rings, this ring optionally being substituted by a C_{1-6}-alkyl or benzyl group;

in the case of NR_8COR_9, a lactam ring;

in the case of $NR_8CO_2R_9$, an oxazolidinone, oxazinone or oxazepinone ring;

in the case of $NR_8SO_2R_9$, a sultam ring;

in the case of $NR_8SO_2NR_8R_9$, a thiazolidine dioxide or thiadiazinane dioxide ring.

Among the compounds of general formula (I), an eighth subgroup of compounds is composed of the compounds for which R_1 represents a group chosen from a phenyl, benzothiazolyl, naphthyl, quinolinyl, isoquinolinyl or indolyl, optionally substituted by one or more R_6 and/or R_7 groups;

R_6 representing a halogen atom or a cyano, C_{1-8}-alkyl, C_{1-6}-alkoxy, C_{1-6}-haloalkyl, C_{1-6}-haloalkoxy, C_{3-7}-cycloalkyl, $-(CH_2)_p-NR_8R_9$, $-NR_8COR_9$, $-CO_2R_8$, $-(CH_2)_p-CONR_8R_9$, $-SO_2R_8$ or $-SO_2NR_8R_9$ group;

R_7 representing a group chosen from a phenyl, phenyl-C_{1-4}-alkylene-, phenyl-$(CH_2)_p$-O-, isoxazolyl, benzothiazolyl, pyrrolyl, pyrazolyl, tetrazolyl, thiazolyl or benzoxazolyl; it being possible for the R_7 group or groups to be substituted by one or more R_6 groups, which are identical to or different from one another, as defined above;

p representing a number which can have the value 0 or 1;

R_8 and R_9 representing, independently of one another, a hydrogen atom or a C_{1-6}-alkyl group; or else

R_8 and R_9 forming, with the nitrogen atom which carries

them,

in the case of $-NR_8R_9$, a morpholine ring;

in the case of $-NR_8COR_9$, a lactam ring.

Among the compounds of general formula (I), a ninth subgroup of compounds is composed of the compounds for which R_3 represents a hydrogen atom.

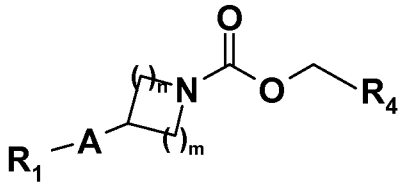
Among the compounds of general formula (I), a tenth subgroup of compounds is composed of the compounds for which R_4 represents a 5-membered heterocycle chosen from a pyrazolyl, imidazolyl, thiazolyl, isothiazolyl, oxazolyl or isoxazolyl;

this heterocycle optionally being substituted by one or more $-C(O)NR_8R_9$ substituents in which R_8 and R_9 each represent a hydrogen atom.

Among the compounds of general formula (I), an eleventh subgroup of compounds is composed of the compounds for which R_4 represents a 5-membered heterocycle chosen from a thiazolyl or isoxazolyl;

this heterocycle optionally being substituted by one or more $-C(O)NR_8R_9$ substituents in which R_8 and R_9 each represent a hydrogen atom.

Among the compounds of general formula (I), mention may be made of a twelfth subgroup represented by the compounds of formula (Ii):



(Ii)

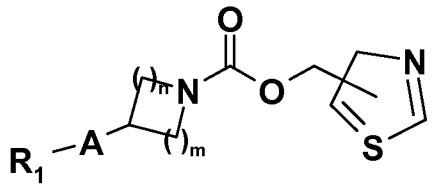
in which R_1, A, R_4, n and m are as defined above.

Other subgroups composed of the compounds of formula (Ii) also come within the present invention.

Thus, among the compounds of abovementioned general formula (Ii), a subgroup of compounds is composed of the compounds for which A represents an $-O-(CH_2)_2-$ group.

Among the compounds of abovementioned general formula (Ii), a subgroup of compounds is composed of the compounds for which A represents an $-O-CH_2-$ group.

Among the compounds of general formula (I), mention may be made of a thirteenth subgroup represented by the compounds of formula (Iii):



(Iii)

in which R_1, A, n and m are as defined above.

Other subgroups composed of the compounds of formula (Iii) also come within the present invention.

Thus, among the compounds of abovementioned general formula (Iii), a subgroup of compounds is composed of the compounds for which A represents an $-O-(CH_2)_2-$ group.

Thus, among the compounds of abovementioned general formula (Iii), a subgroup of compounds is composed of the compounds for which A represents an $-O-CH_2-$ group.

Among the compounds of general formula (I), a fourteenth

subgroup is composed of the compounds of general formula (I) in which:

- R_2 represents a hydrogen atom;
- m and n represent, independently of one another, the value 1 or 2;
- A represents an $-O-C_{1-6}$-alkylene group in which the end represented by an oxygen atom is bonded to the R_1 group, in particular an ethyleneoxy ou methyleneoxy group;
- R_1 represents a group chosen from a phenyl, benzothiazolyl, naphthyl, quinolinyl, isoquinolinyl or indolyl, optionally substituted by one or more R_6 and/or R_7 groups;

R_6 representing:

- a halogen atom, in particular a chlorine, fluorine or bromine;
- a cyano group;
- a C_{1-8}-alkyl group, in particular a methyl, isopropyl, 1,1,3,3-tetramethylbutyl or tert-butyl;
- a C_{1-6}-alkoxy group, in particular a methoxy, hexyloxy, butoxy, ethoxy;
- a C_{1-6}-haloalkyl group, in particular a trifluoromethyl, pentafluoroethyl;
- a C_{1-6}-haloalkoxy group, in particular a trifluoromethoxy or difluoromethoxy;
- a C_{3-7}-cycloalkyl group, in particular a cyclopentyl;
- a $-(CH_2)_p-NR_8R_9$ group, in which p has the value 0 or 1; R_8 and R_9 each represent a hydrogen atom or R_8 and R_9 each represent a methyl, or else R_8 and R_9 form, with the nitrogen atom which carries them, a morpholine ring;
- an $-NR_8COR_9$ group, in which R_8 represents a hydrogen atom and R_9 represents a methyl, or else R_8 and R_9 form, with the nitrogen atom which carries them, a lactam ring, in particular a β-lactam ring;
- a $-CO_2R_8$ group, in which R_8 represents a methyl;
- a $-(CH_2)_p-CONR_8R_9$ group, in which p has the value 0 or 1

and R_8 and R_9 each represent a hydrogen atom;

- an $-SO_2R_8$ group, in which R_8 represents a methyl;

- an $-SO_2NR_8R_9$ group, in which R_8 and R_9 each represent a hydrogen atom;

R_7 representing a group chosen from a phenyl group; a phenyl-C_{1-4}-alkylene- group, in particular a 1,1-dimethyl-1-phenylmethylene or a benzyl; a phenyl-$(CH_2)_p$-O- group in which p has a value of 0 or 1; or an isoxazolyl, benzothiazolyl, pyrrolyl, pyrazolyl, tetrazolyl, thiazolyl or benzoxazolyl group; it being possible for the R_7 group or groups to be substituted by one or more R_6 groups, which are identical to or different from one another, as defined above, such as a halogen atom or a cyano group;

- R_3 represents a hydrogen atom;

- R_4 represents a 5-membered heterocycle chosen from a thiazolyl or isoxazolyl; this heterocycle optionally being substituted by one or more $-C(O)NR_8R_9$ substituents in which R_8 and R_9 each represent a hydrogen atom.

Among the compounds of general formula (I), a fifteenth subgroup of compounds is composed of the compounds of general formula (I) in which, simultaneously, R_1 and/or R_2 and/or R_3 and/or R_4 and/or n and/or m and/or A are as defined in the above subgroups.

Among the compounds of general formula (I), the following compounds may be cited (IUPAC nomenclature generated by the AutoNom software):

1. Thiazol-2-ylmethyl 4-[2-(4-chloronaphth-1-yloxy)ethyl]-piperidine-1-carboxylate

2. Thiazol-2-ylmethyl 4-[2-(4-fluorophenoxy)ethyl]piperidine-1-carboxylate

3. Thiazol-4-ylmethyl 4-[2-(4-fluorophenoxy)ethyl]piperidine-1-carboxylate

4. Thiazol-4-ylmethyl 4-[2-(4-{trifluoromethyl}phenoxy)-ethyl]piperidine-1-carboxylate

5. Thiazol-4-ylmethyl 4-[2-(4-chlorophenoxy)ethyl]piperidine-1-carboxylate

6. Thiazol-5-ylmethyl 4-[2-(4-fluorophenoxy)ethyl]piperidine-1-carboxylate

7. Thiazol-5-ylmethyl 4-[2-(4-chlorophenoxy)ethyl]piperidine-1-carboxylate

8. Thiazol-5-ylmethyl 4-[2-(4-{trifluoromethyl}phenoxy)-ethyl]piperidine-1-carboxylate

9. Thiazol-4-ylmethyl 4-[2-(7-methoxynaphth-2-yloxy)ethyl]-piperidine-1-carboxylate

10. Thiazol-4-ylmethyl 4-[2-(4-cyanophenoxy)ethyl]-piperidine-1-carboxylate

11. Thiazol-4-ylmethyl (+/-)-3-(6-methoxynaphth-2-yloxy-methyl)pyrrolidine-1-carboxylate

12. Thiazol-4-ylmethyl (+/-)-3-(7-methoxynaphth-2-yloxy-methyl)pyrrolidine-1-carboxylate

13. Thiazol-4-ylmethyl (+/-)-3-(3,4-dichlorophenoxy-methyl)pyrrolidine-1-carboxylate

14. Thiazol-4-ylmethyl 4-[2-(6-methoxynaphth-2-yloxy)-ethyl]piperidine-1-carboxylate

15. Thiazol-4-ylmethyl 4-[2-(naphth-2-yloxy)ethyl]-piperidine-1-carboxylate

16. Thiazol-4-ylmethyl (+/-)-3-(4-chloronaphth-1-yloxy-methyl)pyrrolidine-1-carboxylate

17. Thiazol-4-ylmethyl (+/-)-3-(naphth-2-yloxymethyl)-pyrrolidine-1-carboxylate

18. Thiazol-4-ylmethyl 4-[2-(4'-fluorobiphenyl-4-yloxy)-ethyl]piperidine-1-carboxylate

19. Thiazol-4-ylmethyl 4-[2-(quinolin-6-yloxy)ethyl]-piperidine-1-carboxylate and its hydrochloride

20. Thiazol-4-ylmethyl 4-[2-(isoquinolin-6-yloxy)ethyl]-piperidine-1-carboxylate and its hydrochloride

21. Thiazol-4-ylmethyl (+/-)-3-(3'-cyanobiphenyl-3-yloxymethyl)pyrrolidine-1-carboxylate

22. Thiazol-4-ylmethyl (+/-)-3-(4'-fluorobiphenyl-4-yloxymethyl)pyrrolidine-1-carboxylate

23. Thiazol-4-ylmethyl (+/-)-3-(5-chloronaphth-2-yloxy-methyl)pyrrolidine-1-carboxylate

24. Thiazol-4-ylmethyl (+/-)-3-(3-{trifluoromethoxy}-phenoxymethyl)pyrrolidine-1-carboxylate

25. Thiazol-4-ylmethyl (+/-)-3-[4-(1-methyl-1-phenyl-ethyl)phenoxymethyl]pyrrolidine-1-carboxylate

26. Thiazol-4-ylmethyl (+/-)-3-(quinolin-3-yloxymethyl)-pyrrolidine-1-carboxylate

27. Thiazol-4-ylmethyl (+/-)-3-(isoquinolin-6-yloxy-methyl)pyrrolidine-1-carboxylate

28. Thiazol-4-ylmethyl (+/-)-3-(quinolin-7-yloxymethyl)-pyrrolidine-1-carboxylate

29. Thiazol-4-ylmethyl (+/-)-3-(isoquinolin-7-yloxy-methyl)pyrrolidine-1-carboxylate

30. Thiazol-4-ylmethyl (+/-)-3-(4-chloro-3-{trifluoro-methyl}phenoxymethyl)pyrrolidine-1-carboxylate

31. Thiazol-4-ylmethyl (+/-)-3-(5-fluoronaphth-2-yloxy-methyl)pyrrolidine-1-carboxylate

32. Thiazol-2-ylmethyl 4-[2-(2,4-dimethylphenoxy)ethyl]-piperidine-1-carboxylate

33. Thiazol-2-ylmethyl 4-[2-(2,3-dichlorophenoxy)ethyl]-piperidine-1-carboxylate

34. Thiazol-2-ylmethyl 4-[2-(2,4-dichlorophenoxy)ethyl]-piperidine-1-carboxylate

35. Thiazol-2-ylmethyl 4-[2-(2,5-dichlorophenoxy)ethyl]-piperidine-1-carboxylate

36. Thiazol-2-ylmethyl 4-[2-(3,4-dichlorophenoxy)ethyl]-piperidine-1-carboxylate

37. Thiazol-2-ylmethyl 4-[2-(3,5-dichlorophenoxy)ethyl]-piperidine-1-carboxylate

38. Thiazol-2-ylmethyl 4-[2-(4-cyclopentylphenoxy)-ethyl]piperidine-1-carboxylate

39. Thiazol-2-ylmethyl 4-[2-(2-{benzoxazol-2-yl}phenoxy)-ethyl]piperidine-1-carboxylate

40. Thiazol-2-ylmethyl 4-[2-(4-{benzyloxy}phenoxy)ethyl]-piperidine-1-carboxylate

41. Thiazol-2-ylmethyl 4-[2-(4-{carbamoylmethyl}phenoxy)-ethyl]piperidine-1-carboxylate

42. Thiazol-2-ylmethyl 4-[2-(quinolin-7-yloxy)ethyl]-piperidine-1-carboxylate and its trifluoroacetate

43. Thiazol-2-ylmethyl 4-[2-(quinolin-6-yloxy)ethyl]-piperidine-1-carboxylate and its trifluoroacetate

44. Thiazol-2-ylmethyl 4-[2-(4-cyano-3-fluorophenoxy)-ethyl]piperidine-1-carboxylate

45. Thiazol-2-ylmethyl 4-[2-(biphenyl-2-yloxy)ethyl]-piperidine-1-carboxylate

46. Thiazol-2-ylmethyl 4-[2-(2-isopropyl-5-methyl-phenoxy)ethyl]piperidine-1-carboxylate

47. Thiazol-2-ylmethyl 4-[2-(3-{trifluoromethyl}-phenoxy)ethyl]piperidine-1-carboxylate

48. Thiazol-2-ylmethyl 4-{2-[4-(1,1,3,3-tetramethyl-butyl)phenoxy]ethyl}piperidine-1-carboxylate

49. Thiazol-2-ylmethyl 4-[2-(4-benzylphenoxy)ethyl]-piperidine-1-carboxylate

50. Thiazol-2-ylmethyl 4-[2-(4-{pyrrol-1-yl}phenoxy)-ethyl]piperidine-1-carboxylate and its trifluoroacetate

51. Thiazol-2-ylmethyl 4-[2-(4-carbamoylphenoxy)ethyl]-piperidine-1-carboxylate

52. Thiazol-2-ylmethyl 4-[2-(3-cyanophenoxy)ethyl]-piperidine-1-carboxylate

53. Thiazol-2-ylmethyl 4-[2-(3,5-di{tert-butyl}phenoxy)-ethyl]piperidine-1-carboxylate

54. Thiazol-2-ylmethyl 4-[2-(2-benzylphenoxy)ethyl]-piperidine-1-carboxylate

55. Thiazol-2-ylmethyl 4-[2-(8-{acetylamino}naphth-2-yloxy)ethyl]piperidine-1-carboxylate

56. Thiazol-2-ylmethyl 4-[2-(3-{methoxycarbonyl}naphth-2-yloxy)ethyl]piperidine-1-carboxylate

57. Thiazol-2-ylmethyl 4-[2-(3-phenoxyphenoxy)ethyl]-piperidine-1-carboxylate

58. Thiazol-2-ylmethyl 4-[2-(isoquinolin-7-yloxy)ethyl]-piperidine-1-carboxylate and its trifluoroacetate

59. Thiazol-2-ylmethyl 4-[2-(4-hexyloxyphenoxy)ethyl]-piperidine-1-carboxylate

60. Thiazol-2-ylmethyl 4-[2-(3-butoxyphenoxy)ethyl]-piperidine-1-carboxylate

61. Thiazol-2-ylmethyl 4-[2-(quinolin-5-yloxy)ethyl]-piperidine-1-carboxylate and its trifluoroacetate

62. Thiazol-2-ylmethyl 4-[2-(3-{pentafluoroethyl}-phenoxy)ethyl]piperidine-1-carboxylate

63. Thiazol-2-ylmethyl 4-[2-(5-{acetylamino}naphth-2-yloxy)ethyl]piperidine-1-carboxylate

64. Thiazol-2-ylmethyl 4-[2-(5-bromo-2-chlorophenoxy)-ethyl]piperidine-1-carboxylate

65. Thiazol-2-ylmethyl 4-[2-(2-methylquinolin-6-yloxy)-ethyl]piperidine-1-carboxylate and its trifluoroacetate

66. Thiazol-2-ylmethyl 4-[2-(4'-cyanobiphenyl-3-yloxy)-ethyl]piperidine-1-carboxylate

67. Thiazol-2-ylmethyl 4-[2-(6-cyanonaphth-2-yloxy)-ethyl]piperidine-1-carboxylate

68. Thiazol-2-ylmethyl 4-[2-(4-{thiazol-2-yl}phenoxy)-ethyl]piperidine-1-carboxylate

69. Thiazol-2-ylmethyl 4-[2-(biphenyl-3-yloxy)ethyl]-piperidine-1-carboxylate

70. Thiazol-2-ylmethyl 4-[2-(biphenyl-4-yloxy)ethyl]-piperidine-1-carboxylate

71. Thiazol-2-ylmethyl 4-[2-(2-cyanoquinolin-8-yloxy)-ethyl]piperidine-1-carboxylate and its trifluoroacetate

72. Thiazol-2-ylmethyl 4-[2-(4-chloro-2-cyanophenoxy)-ethyl]piperidine-1-carboxylate and its trifluoroacetate

73. Thiazol-2-ylmethyl 4-[2-(2-methylbenzothiazol-5-yloxy)ethyl]piperidine-1-carboxylate

74. Thiazol-2-ylmethyl 4-[2-(4'-cyanobiphenyl-4-yloxy)-ethyl]piperidine-1-carboxylate

75. Thiazol-2-ylmethyl 4-[2-(2-{morpholin-4-yl}phenoxy)-ethyl]piperidine-1-carboxylate

76. Thiazol-2-ylmethyl 4-[2-(4-chloro-2-{isoxazol-5-yl}-phenoxy)ethyl]piperidine-1-carboxylate

77. Thiazol-4-ylmethyl 4-[2-(2,4-dimethylphenoxy)ethyl]-piperidine-1-carboxylate

78. Thiazol-4-ylmethyl 4-[2-(2,3-dichlorophenoxy)ethyl]-piperidine-1-carboxylate

79. Thiazol-4-ylmethyl 4-[2-(naphth-1-yloxy)ethyl]-piperidine-1-carboxylate

80. Thiazol-4-ylmethyl 4-[2-(3-{dimethylamino}phenoxy)-ethyl]piperidine-1-carboxylate and its trifluoroacetate

81. Thiazol-4-ylmethyl 4-[2-(3-{trifluoromethyl}-phenoxy)ethyl]piperidine-1-carboxylate

82. Thiazol-4-ylmethyl 4-[2-(4-benzylphenoxy)ethyl]-piperidine-1-carboxylate

83. Thiazol-4-ylmethyl 4-[2-(2-ethoxyphenoxy)ethyl]-piperidine-1-carboxylate

84. Thiazol-4-ylmethyl 4-{2-[4-(1-methyl-1-phenylethyl)-phenoxy]ethyl}piperidine-1-carboxylate

85. Thiazol-4-ylmethyl 4-[2-(4-phenoxyphenoxy)ethyl]-piperidine-1-carboxylate

86. Thiazol-4-ylmethyl 4-[2-(2-bromo-4-fluorophenoxy)-ethyl]piperidine-1-carboxylate

87. Thiazol-4-ylmethyl 4-[2-(2-benzylphenoxy)ethyl]-piperidine-1-carboxylate

88. Thiazol-4-ylmethyl 4-[2-(3-phenoxyphenoxy)ethyl]-piperidine-1-carboxylate

89. Thiazol-4-ylmethyl 4-[2-(4-{hexyloxy}phenoxy)ethyl]-piperidine-1-carboxylate

90. Thiazol-4-ylmethyl 4-[2-(3-butoxyphenoxy)ethyl]-piperidine-1-carboxylate

91. Thiazol-4-ylmethyl 4-[2-(4-chloro-5-isopropyl-2-methylphenoxy)ethyl]piperidine-1-carboxylate

92. Thiazol-4-ylmethyl 4-[2-(3-{pentafluoroethyl}-phenoxy)ethyl]piperidine-1-carboxylate

93. Thiazol-4-ylmethyl 4-[2-(5-{acetylamino}naphth-2-yloxy)ethyl]piperidine-1-carboxylate

94. Thiazol-4-ylmethyl 4-[2-(5-bromo-2-chlorophenoxy)-ethyl]piperidine-1-carboxylate

95. Thiazol-4-ylmethyl 4-[2-(4'-cyanobiphenyl-3-yloxy)-ethyl]piperidine-1-carboxylate

96. Thiazol-4-ylmethyl 4-[2-(6-cyanonaphth-2-yloxy)-ethyl]piperidine-1-carboxylate

97. Thiazol-4-ylmethyl 4-[2-(4-{thiazol-2-yl}phenoxy)-ethyl]piperidine-1-carboxylate

98. Thiazol-4-ylmethyl 4-[2-(biphenyl-3-yloxy)ethyl]-piperidine-1-carboxylate

99. Thiazol-4-ylmethyl 4-[2-(biphenyl-4-yloxy)ethyl]-piperidine-1-carboxylate

100. Thiazol-4-ylmethyl 4-[2-(4-chloro-2-cyanophenoxy)-ethyl]piperidine-1-carboxylate

101. Thiazol-4-ylmethyl 4-[2-(2-methylbenzothiazol-5-yloxy)ethyl]piperidine-1-carboxylate

102. Thiazol-4-ylmethyl 4-[2-(4'-cyanobiphenyl-4-yloxy)-ethyl]piperidine-1-carboxylate

103. Thiazol-4-ylmethyl 4-[2-(2-{morpholin-4-yl}phenoxy)-ethyl]piperidine-1-carboxylate and its trifluoroacetate

104. Thiazol-4-ylmethyl 4-[2-(4-chloro-2-{isoxazol-5-yl}-phenoxy)ethyl]piperidine-1-carboxylate

105. Thiazol-2-ylmethyl 4-[2-(4-{dimethylaminomethyl}-phenoxy)ethyl]piperidine-1-carboxylate and its trifluoro-acetate

106. Thiazol-2-ylmethyl 4-[2-(naphth-2-yloxy)ethyl]-piperidine-1-carboxylate

107. Thiazol-2-ylmethyl 4-[2-(naphth-1-yloxy)ethyl]-piperidine-1-carboxylate

108. Thiazol-2-ylmethyl 4-[2-(7-methoxynaphth-2-yloxy)-ethyl]piperidine-1-carboxylate

109. Thiazol-4-ylmethyl 4-[2-(2-cyclopentylphenoxy)-ethyl]piperidine-1-carboxylate

110. Thiazol-4-ylmethyl 4-[2-(2-benzyloxyphenoxy)ethyl]-piperidine-1-carboxylate

111. Thiazol-4-ylmethyl 4-[2-(isoquinolin-7-yloxy)ethyl]-piperidine-1-carboxylate and its trifluoroacetate

112. Thiazol-4-ylmethyl 4-[2-(quinolin-5-yloxy)ethyl]-piperidine-1-carboxylate and its trifluoroacetate

113. Thiazol-4-ylmethyl 4-[2-(2-methylquinolin-6-yloxy)-ethyl]piperidine-1-carboxylate and its trifluoroacetate

114. Thiazol-4-ylmethyl 4-[2-(2-cyanoquinolin-8-yloxy)-ethyl]piperidine-1-carboxylate and its trifluoroacetate

115. Thiazol-4-ylmethyl 4-[2-(2,4-dichlorophenoxy)ethyl]-piperidine-1-carboxylate

116. Thiazol-4-ylmethyl 4-[2-(4-cyclopentylphenoxy)-ethyl]piperidine-1-carboxylate

117. Thiazol-4-ylmethyl 4-[2-(2-{benzoxazol-2-yl}-phenoxy)ethyl]piperidine-1-carboxylate

118. Thiazol-4-ylmethyl 4-[2-(4-cyano-3-fluorophenoxy)-ethyl]piperidine-1-carboxylate

119. Thiazol-4-ylmethyl 4-{2-[4-(1,1,3,3-tetramethyl-butyl)phenoxy]ethyl}piperidine-1-carboxylate

120. Thiazol-4-ylmethyl 4-[2-(4-{pyrrol-1-yl}phenoxy)-ethyl]piperidine-1-carboxylate and its trifluoroacetate

121. Thiazol-4-ylmethyl 4-[2-(3,5-di{tert-butyl}phenoxy)-ethyl]piperidine-1-carboxylate

122. Thiazol-4-ylmethyl 4-[2-(4-{dimethylaminomethyl}-phenoxy)ethyl]piperidine-1-carboxylate and its trifluoroacetate

123. Thiazol-4-ylmethyl 4-[2-(2-methylquinolin-8-yloxy)-ethyl]piperidine-1-carboxylate and its trifluoroacetate

124. Thiazol-4-ylmethyl 4-[2-(3-cyanophenoxy)ethyl]-piperidine-1-carboxylate

125. Thiazol-5-ylmethyl 4-(2-phenoxyethyl)piperidine-1-carboxylate

126. Thiazol-5-ylmethyl 4-[2-(biphenyl-4-yloxy)ethyl]-piperidine-1-carboxylate

127. Thiazol-5-ylmethyl 4-[2-(4-carbamoylphenoxy)ethyl]-piperidine-1-carboxylate

128. Thiazol-5-ylmethyl 4-[2-(4-fluorophenoxy)ethyl]-piperidine-1-carboxylate

129. Thiazol-5-ylmethyl 4-[2-(2,4-dimethylphenoxy)ethyl]-piperidine-1-carboxylate

130. Thiazol-5-ylmethyl 4-[2-(4-{dimethylaminomethyl}-phenoxy)ethyl]piperidine-1-carboxylate and its trifluoroacetate

131. Thiazol-5-ylmethyl 4-[2-(2,3-dichlorophenoxy)ethyl]-piperidine-1-carboxylate

132. Thiazol-5-ylmethyl 4-[2-(2,4-dichlorophenoxy)ethyl]-piperidine-1-carboxylate

133. Thiazol-5-ylmethyl 4-[2-(2,5-dichlorophenoxy)ethyl]-piperidine-1-carboxylate

134. Thiazol-5-ylmethyl 4-[2-(3,5-dichlorophenoxy)ethyl]-piperidine-1-carboxylate

135. Thiazol-5-ylmethyl 4-[2-(4-cyclopentylphenoxy)-ethyl]piperidine-1-carboxylate

136. Thiazol-5-ylmethyl 4-[2-(naphth-2-yloxy)ethyl]-piperidine-1-carboxylate

137. Thiazol-5-ylmethyl 4-[2-(naphth-1-yloxy)ethyl]-piperidine-1-carboxylate

138. Thiazol-5-ylmethyl 4-[2-(2-methylquinolin-8-yloxy)-ethyl]piperidine-1-carboxylate

139. Thiazol-5-ylmethyl 4-[2-(2-{benzoxazol-2-yl}-phenoxy)ethyl]piperidine-1-carboxylate

140. Thiazol-5-ylmethyl 4-[2-(4-{benzyloxy}phenoxy)ethyl]-piperidine-1-carboxylate

141. Thiazol-5-ylmethyl 4-[2-(4-sulphamoylphenoxy)ethyl]-piperidine-1-carboxylate

142. Thiazol-5-ylmethyl 4-[2-(isoquinolin-5-yloxy)ethyl]-piperidine-1-carboxylate

143. Thiazol-5-ylmethyl 4-[2-(4-{carbamoylmethyl}-phenoxy)ethyl]piperidine-1-carboxylate

144. Thiazol-5-ylmethyl 4-[2-(quinolin-7-yloxy)ethyl]-piperidine-1-carboxylate

145. Thiazol-5-ylmethyl 4-[2-(quinolin-6-yloxy)ethyl]-piperidine-1-carboxylate

146. Thiazol-5-ylmethyl 4-[2-(quinolin-8-yloxy)ethyl]-piperidine-1-carboxylate

147. Thiazol-5-ylmethyl 4-[2-(3-{dimethylamino}phenoxy)-ethyl]piperidine-1-carboxylate and its trifluoroacetate

148. Thiazol-5-ylmethyl 4-[2-(4-cyano-3-fluorophenoxy)-ethyl]piperidine-1-carboxylate

149. Thiazol-5-ylmethyl 4-[2-(biphenyl-2-yloxy)ethyl]-piperidine-1-carboxylate

150. Thiazol-5-ylmethyl 4-[2-(biphenyl-3-yloxy)ethyl]-piperidine-1-carboxylate

151. Thiazol-5-ylmethyl 4-[2-(3-{trifluoromethyl}-phenoxy)ethyl]piperidine-1-carboxylate

152. Thiazol-5-ylmethyl 4-[2-(4-benzylphenoxy)ethyl]-piperidine-1-carboxylate

153. Thiazol-5-ylmethyl 4-[2-(2-ethoxyphenoxy)ethyl]-piperidine-1-carboxylate

154. Thiazol-5-ylmethyl 4-[2-(2-cyclopentylphenoxy)ethyl]-piperidine-1-carboxylate

155. Thiazol-5-ylmethyl 4-{2-[4-(1-methyl-1-phenylethyl)-phenoxy]ethyl}piperidine-1-carboxylate

156. Thiazol-5-ylmethyl 4-[2-(4-phenoxyphenoxy)ethyl]-piperidine-1-carboxylate

157. Thiazol-5-ylmethyl 4-[2-(2-bromo-4-fluorophenoxy)-ethyl]piperidine-1-carboxylate

158. Thiazol-5-ylmethyl 4-[2-(4-{pyrrol-1-yl}phenoxy)-ethyl]piperidine-1-carboxylate

159. Thiazol-5-ylmethyl 4-[2-(3-cyanophenoxy)ethyl]-piperidine-1-carboxylate

160. Thiazol-5-ylmethyl 4-[2-(3,5-di{tert-butyl}phenoxy)-ethyl]piperidine-1-carboxylate

161. Thiazol-5-ylmethyl 4-[2-(2-benzylphenoxy)ethyl]-piperidine-1-carboxylate

162. Thiazol-5-ylmethyl 4-[2-(2-{benzyloxy}phenoxy)ethyl]-piperidine-1-carboxylate

163. Thiazol-5-ylmethyl 4-[2-(2-cyanoquinolin-8-yloxy)-ethyl]piperidine-1-carboxylate

164. Thiazol-5-ylmethyl 4-[2-(3-{methoxycarbonyl}naphth-2-yloxy)ethyl]piperidine-1-carboxylate

165. Thiazol-5-ylmethyl 4-[2-(3-phenoxyphenoxy)ethyl]-piperidine-1-carboxylate

166. Thiazol-5-ylmethyl 4-[2-(4-chloro-2-cyanophenoxy)-ethyl]piperidine-1-carboxylate

167. Thiazol-5-ylmethyl 4-[2-(isoquinolin-7-yloxy)ethyl]-piperidine-1-carboxylate

168. Thiazol-5-ylmethyl 4-[2-(4-{hexyloxy}phenoxy)ethyl]-piperidine-1-carboxylate

169. Thiazol-5-ylmethyl 4-[2-(3-butoxyphenoxy)ethyl]-piperidine-1-carboxylate

170. Thiazol-5-ylmethyl 4-[2-(4-chloro-5-isopropyl-2-methylphenoxy)ethyl]piperidine-1-carboxylate

171. Thiazol-5-ylmethyl 4-[2-(2-methylbenzothiazol-5-yloxy)ethyl]piperidine-1-carboxylate

172. Thiazol-5-ylmethyl 4-[2-(quinolin-5-yloxy)ethyl]-piperidine-1-carboxylate

173. Thiazol-5-ylmethyl 4-[2-(3-{pentafluoroethyl}-phenoxy)ethyl]piperidine-1-carboxylate

174. Thiazol-5-ylmethyl 4-[2-(5-bromo-2-chlorophenoxy)-ethyl]piperidine-1-carboxylate

175. Thiazol-5-ylmethyl 4-[2-(4-{difluoromethoxy}phenoxy)-ethyl]piperidine-1-carboxylate

176. Thiazol-5-ylmethyl 4-[2-(4'-cyanobiphenyl-3-yloxy)-ethyl]piperidine-1-carboxylate

177. Thiazol-5-ylmethyl 4-[2-(6-cyanonaphth-2-yloxy)-ethyl]piperidine-1-carboxylate

178. Thiazol-5-ylmethyl 4-[2-(4-{thiazol-2-yl}phenoxy)-ethyl]piperidine-1-carboxylate

179. Thiazol-5-ylmethyl 4-[2-(7-methoxynaphth-2-yloxy)-ethyl]piperidine-1-carboxylate

180. Thiazol-5-ylmethyl 4-[2-(4-chloro-2-{isoxazol-5-yl}-phenoxy)ethyl]piperidine-1-carboxylate

181. Thiazol-5-ylmethyl 4-[2-(2-carbamoyl-4-chloro-phenoxy)ethyl]piperidine-1-carboxylate

182. Thiazol-5-ylmethyl 4-[2-(5-{acetylamino}naphth-2-yloxy)ethyl]piperidine-1-carboxylate

183. Thiazol-5-ylmethyl 4-[2-(4'-cyanobiphenyl-4-yloxy)-ethyl]piperidine-1-carboxylate

184. Thiazol-5-ylmethyl 4-[2-(4-{methanesulphonyl}-phenoxy)ethyl]piperidine-1-carboxylate

185. Thiazol-5-ylmethyl 4-[2-(5-acetylamino-2-propyl-phenoxy)ethyl]piperidine-1-carboxylate

186. Thiazol-5-ylmethyl 4-[2-(1H-indol-6-yloxy)ethyl]-piperidine-1-carboxylate

187. Thiazol-5-ylmethyl 4-{2-[4-fluoro-2-(1H-pyrazol-3-yl)phenoxy]ethyl}piperidine-1-carboxylate

188. Thiazol-5-ylmethyl 4-[2-(4-cyano-2-fluorophenoxy)-ethyl]piperidine-1-carboxylate

189. Thiazol-5-ylmethyl 4-[2-(2-isopropyl-5-methyl-phenoxy)ethyl]piperidine-1-carboxylate

190. Thiazol-5-ylmethyl 4-[2-(2-{morpholin-4-yl}phenoxy)-ethyl]piperidine-1-carboxylate and its trifluoroacetate

191. Thiazol-5-ylmethyl 4-[2-(2-methylquinolin-6-yloxy)-ethyl]piperidine-1-carboxylate

192. Thiazol-5-ylmethyl 4-{2-[4-(2-oxopyrrolidin-1-yl)-phenoxy]ethyl}piperidine-1-carboxylate

193. Thiazol-5-ylmethyl 4-[2-(3-{tetrazol-1-yl}phenoxy)-ethyl]piperidine-1-carboxylate

194. Thiazol-2-ylmethyl (R)-3-(naphth-2-yloxymethyl)-pyrrolidine-1-carboxylate (enantiomer I)

195. Thiazol-2-ylmethyl (S)-3-(naphth-2-yloxymethyl)-pyrrolidine-1-carboxylate (enantiomer II)

196. Thiazol-2-ylmethyl (+/-)-3-(5-chloronaphth-2-yloxymethyl)pyrrolidine-1-carboxylate

197. Thiazol-2-ylmethyl (+/-)-3-(4'-fluorobiphenyl-4-yloxymethyl)pyrrolidine-1-carboxylate

198. 3-Carbamoylisoxazol-5-ylmethyl 4-[2-(4-fluorophenoxy)ethyl]piperidine-1-carboxylate

199. 3-Carbamoylisoxazol-5-ylmethyl 4-[2-(4-{trifluoromethoxy}phenoxy)ethyl]piperidine-1-carboxylate

200. 3-Carbamoylisoxazol-5-ylmethyl (-)-(R)-3-(naphth-2-yloxymethyl)pyrrolidine-1-carboxylate (enantiomer I)

201. 3-Carbamoylisoxazol-5-ylmethyl (+/-)-3-(6-methoxynaphth-2-yloxymethyl)pyrrolidine-1-carboxylate

202. 3-Carbamoylisoxazol-5-ylmethyl (+)-(S)-3-(naphth-2-yloxymethyl)pyrrolidine-1-carboxylate (enantiomer II).

The compounds of general formulae (I), (Ii) and (Iii) can comprise one or more asymmetric carbon atoms. They can exist in the form of enantiomers or diastereoisomers. These enantiomers and diastereoisomers and their mixtures, including the racemic mixtures, come within the invention.

The compounds of formulae (I), (Ii) and (Iii) can exist in the form of bases or of addition salts with acids. Such addition salts come within the invention.

These salts are advantageously prepared with pharmaceutically acceptable acids but the salts of other acids, for example of use in the purification or the isolation of the compounds of formulae (I), (Ii) and (Iii), also come within the invention.

The compounds of formulae (I), (Ii) and (Iii) and/or salts thereof may form solvates or hydrates and the invention

includes all such solvates and hydrates.

The term « hydrates » and « solvates » mean that the compounds of formulae (I), (Ii) and (Iii) according to the invention can be combined or associated with one or more water or solvent molecules. This is only a chemical characteristic of such compounds, which can be applied for all organic compounds of this type.

In the context of the invention:

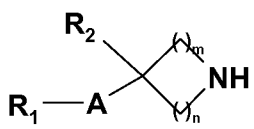
- C_{t-z}, where t and z can take the values from 1 to 8, is understood to mean a carbon-comprising chain which can have from t to z carbon atoms, for example C_{1-3} is understood to mean a carbon-comprising chain which can have from 1 to 3 carbon atoms;
- alkyl is understood to mean a saturated and linear or branched aliphatic group; for example, a C_{1-6}-alkyl group represents a linear or branched carbon-comprising chain of 1 to 6 carbon atoms, more particularly a methyl, ethyl, propyl, isopropyl, butyl, isobutyl, *tert*-butyl, pentyl or hexyl;
- alkylene is understood to mean a saturated and linear or branched divalent alkyl group; for example, a C_{1-3}-alkylene group represents a linear or branched divalent carbon-comprising chain of 1 to 3 carbon atoms, more particularly a methylene, ethylene, 1-methylethylene or propylene;
- cycloalkyl is understood to mean a cyclic alkyl group; for example, a C_{3-7}-cycloalkyl group represents a cyclic carbon-comprising group of 3 to 7 carbon atoms, more particularly a cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl or cycloheptyl;
- alkoxy is understood to mean an -O-alkyl group comprising a saturated and linear or branched aliphatic chain;
- thioalkyl is understood to mean an -S-alkyl group comprising a saturated and linear or branched aliphatic chain;

- haloalkyl is understood to mean an alkyl group, one or more hydrogen atoms of which have been replaced by a halogen atom;
- haloalkoxy is understood to mean an alkoxy group, one or more hydrogen atoms of which have been replaced by a halogen atom;
- halothioalkyl is understood to mean a thioalkyl group, one or more hydrogen atoms of which have been replaced by a halogen atom;
- halogen atom is understood to mean a fluorine, a chlorine, a bromine or an iodine;
- TFA is understood to mean trifluoroacetic acid;
- ACN is understood to mean acetonitrile.

Within the meaning of the present invention, it should be noted that the terms "ranging from … to …" and "between … and …" mean that the limits are also considered.

The term « preventing », as used herein, means reducing the risk of onset or slowing the occurrence of a given phenomenom, namely in the present invention, a pathology in which endogenous cannabinoids and/or other substrates metabolized by the enzyme FAAH are involved such as the pathologies as defined below.

Another subject-matter of the invention is targeted at a process for the preparation of the compounds of formula (I) according to the invention, comprising the stage consisting in reacting an amine derivative, a compound of following general formula (II):

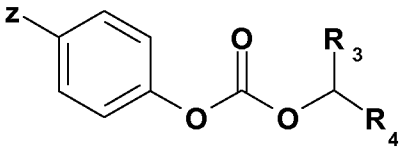


(II)

in which R_1, R_2, A, n and m are as defined in the formula (I)

defined above,

with a carbonate of following general formula (III):



(III)

in which Z represents a hydrogen atom or a nitro group and R_3 and R_4 are as defined in the general formula (I) defined above,

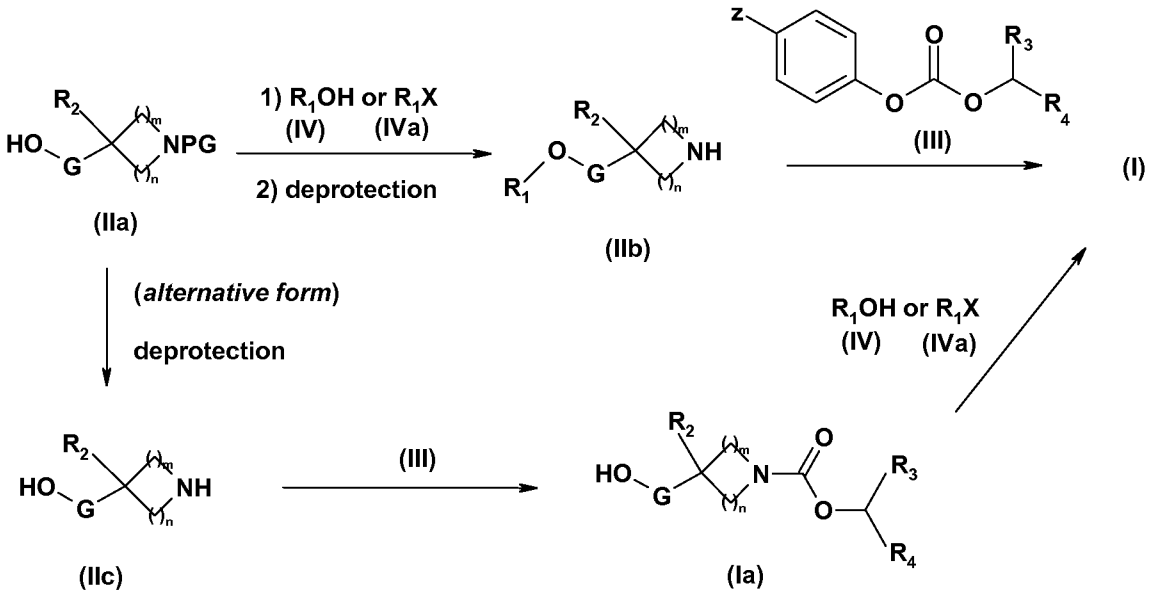
in the presence of a base, such as triethylamine, pyridine, *N*,*N*-dimethylaminopyridine or *N*,*N*-diisopropylethylamine, in an organic solvent, such as toluene, acetonitrile or dichloroethane, at a temperature between ambient temperature and the reflux temperature of the solvent.

In addition, the compounds of the invention can be prepared according to different methods illustrated by the following schemes. These methods and the intermediate compounds used are also a subject-matter of the present invention.

If appropriate, a compound of formula (II) can be protected, in particular at its amine functional group, according to methods well known to a person skilled in the art.
Mention may be made, as examples of protective groups and also of protecting and deprotecting methods, of the work "*Protective Groups in Organic Synthesis*", Green et al., 2nd Edition (John Wiley & Sons, Inc., New York).
A preparation process employing a protected compound of formula (II) is, for example, described in the following Scheme 1.

As regards more particularly the compounds of general formula (I) in which A more particularly represents an oxygen atom or an $-O-C_{1-6}$-alkylene group, they can also be prepared according to the procedure described in the following Scheme 1.

Scheme 1



This preparation method (Scheme 1) consists in reacting, in a first step, an alcohol of general formula (IIa), in which R_2, m and n are as defined in the general formula (I) as defined above, G represents a portion of the group A as defined in the general formula (I), namely either a covalent bond or the C_{1-6}-alkylene portion of the -O-C_{1-6}-alkylene group, and PG represents a protective group, such as a Boc (*tert*-butyloxycarbonyl), a Cbz (benzyloxycarbonyl), a benzyl or a benzhydryl;

- either with an alcohol derivative of general formula (IV), in which R_1 is as defined above, using the Mitsunobu reaction conditions (*Synthesis*, 1981, 1-28),
- or with a halogenated derivative of general formula (IVa), in which R_1 is as defined above and X represents a fluorine, chlorine, bromine or iodine atom, using aromatic or heteroaromatic nucleophilic substitution reactions or Buchwald *O*-arylation or *O*-heteroarylation reactions, for example using a palladium or copper catalyst;

followed by a deprotection reaction, for example in the presence of trifluoroacetic acid or of a solution of

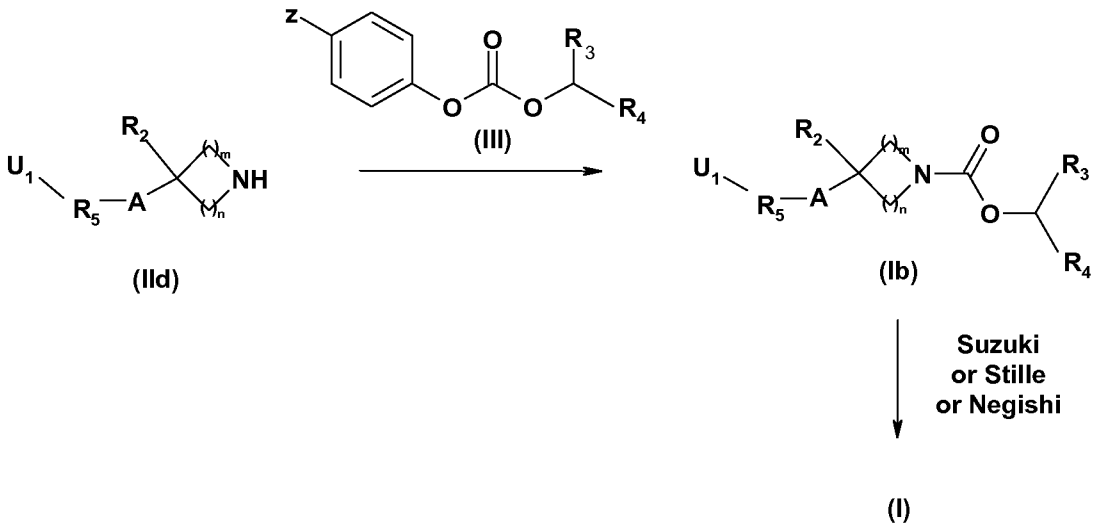
hydrochloric acid in isopropanol or dioxane, to result in the amine of general formula (IIb) in which G, R_2, m and n are as defined in the amine of formula (IIa) above and R_1 is as defined in the general formula (I) as defined above. An alternative to the Mitsunobu reaction consists in reacting an alcohol derivative of general formula (IV) with a compound said to be of general formula (IIe) and deriving from the activation by a tosylate group of the alcohol functional group of a compound of general formula (IIa). The derivative of general formula (IIb) thus obtained is subsequently converted to the compound of general formula (I) according to a condensation reaction with a carbonate of general formula (III) as defined above, under the conditions described above.

An alternative form of producing the compounds of general formula (I) (Scheme 1) in which A more particularly represents an oxygen atom or an $-O-C_{1-6}$-alkylene group consists in deprotecting an alcohol of general formula (IIa) as defined above, according to a deprotection reaction as defined above, in order to obtain an aminoalcohol of general formula (IIc), and in then reacting this aminoalcohol of general formula (IIc) in which R_2, m and n are as defined in the general formula (I) defined above and G represents a portion of the group A as defined in the general formula (I), namely either a covalent bond or the C_{1-6}-alkylene portion of the $-O-C_{1-6}$-alkylene group, with a carbonate of general formula (III) as defined above under the conditions described above, to result in the carbamate derivative of general formula (Ia) in which R_2, R_3, R_4, m and n are as defined in the general formula (I) defined above and G represents a portion of the group A as defined in the general formula (I), namely either a covalent bond or the C_{1-6}-alkylene portion of the $-O-C_{1-6}$-alkylene group. The carbamate derivative (Ia) thus obtained is subsequently converted to the compound of general formula (I) by the action

of an alcohol of general formula R_1OH (IV) as defined above by using the Mitsunobu reaction conditions or by the action of a halogenated derivative of general formula R_1X (IVa) as defined above by using aromatic or heteroaromatic nucleophilic substitution reactions or Buchwald *O*-arylation or *O*-heteroarylation reactions, for example using a palladium or copper catalyst.

As regards more particularly the compounds of general formula (I) in which R_1 represents an R_5 group substituted in particular by an R_6 group of C_{1-6}-alkyl, C_{3-7}-cycloalkyl or C_{3-7}-cycloalkyl-C_{1-3}-alkylene type or by an R_7 group as defined in the general formula (I) defined above, they can also be prepared according to the procedure described in the following Scheme 2.

Scheme 2



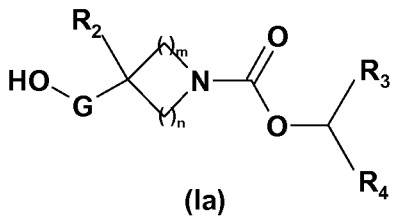
Thus, the first stage consists in reacting an amine of general formula (IId), in which A, R_2, R_5, m and n are as defined in the general formula (I) defined above and U_1 represents a chlorine, bromine or iodine atom or a triflate group, with a carbonate of general formula (III) as defined above under the conditions described above, to result in the carbamate

derivative of general formula (Ib) in which A, R_2, R_3, R_4, R_5, m and n are as defined in the general formula (I) defined above and U_1 is as defined above. The coupling reaction catalysed by means of a transition metal, such as palladium(0), is subsequently carried out on the key intermediate of general formula (Ib) as defined above, U_1 being in the position where it is desired to introduce the R_6 or R_7 group (Scheme 2):

- either by a reaction of Suzuki type, for example using an alkyl-, cycloalkyl-, aryl- or heteroarylboronic acid,
- or according to a reaction of Stille type, for example using a trialkylaryltin or trialkylheteroaryltin derivative,
- or by a reaction of Negishi type, for example using an alkyl-, cycloalkyl-, aryl- or heteroarylzinc halide derivative.

Alternatively, the other compounds of general formulae (II), (IIa), (IIb), (IIc), (IId), (III), (IV) and (IVa) and the other reactants are commercially available or are described in the literature or else can be prepared according to methods which are described therein or which are known to a person skilled in the art.

Another subject-matter of the present invention is the compounds of general formula (Ia):



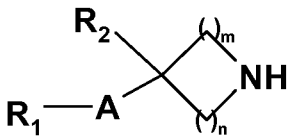
(Ia)

in which R_2, R_3, R_4, m and n are as defined in the general formula (I) and G represents a portion of the group A as defined in the general formula (I), namely either a covalent bond or the C_{1-6}-alkylene portion of the -O-C_{1-6}-alkylene group.

Mention may be made, among these compounds, of:

- thiazol-2-ylmethyl 4-(2-hydroxyethyl)piperidine-1-carboxylate
- thiazol-4-ylmethyl 3-(hydroxymethyl)pyrrolidine-1-carboxylate.

Another subject-matter of the present invention is the compounds of general formula (II):



(II)

in which A, R_1, R_2, m and n are as defined in the general formula (I).

Mention may be made, among these compounds, of:

- 4-[2-(4-chloronaphth-1-yloxy)ethyl]piperidine
- 3-(6-methoxynaphth-2-yloxymethyl)pyrrolidine
- 3'-(pyrrolidin-3-ylmethoxy)biphenyl-3-carbonitrile
- 3-(5-chloronaphth-2-yloxymethyl)pyrrolidine
- 3-(3-{trifluoromethoxy}phenoxymethyl)pyrrolidine
- 3-[4-(1-methyl-1-phenylethyl)phenoxymethyl]pyrrolidine
- 7-(pyrrolidin-3-ylmethoxy)quinoline
- 3-(pyrrolidin-3-ylmethoxy)quinoline
- 3-(4-chloro-3-{trifluoromethyl}phenoxymethyl)pyrrolidine
- 7-(pyrrolidin-3-ylmethoxy)isoquinoline
- 3-(5-fluoronaphth-2-yloxymethyl)pyrrolidine
- 3-(4'-fluorobiphenyl-4-yloxymethyl)pyrrolidine

The following examples illustrate the preparation of some compounds of the invention. These examples are not limiting and serve only to illustrate the invention. The NMR spectra and/or the LC-MS (Liquid Chromatography-Mass Spectroscopy)

confirm the structures and the purities of the compounds obtained.

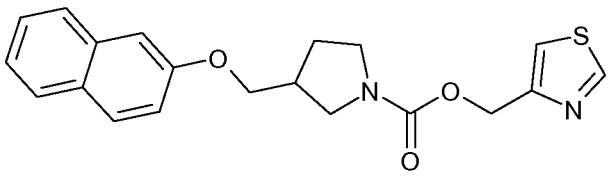
M.p.(°C) represents the melting point in degrees Celsius.

R_f indicates the retention time obtained by TLC (Thin Layer Chromatography) analysis.

The numbers shown in brackets in the titles of the examples correspond to those in the 1st column of the tables below.

The IUPAC (International Union of Pure and Applied Chemistry) nomenclature was used in the naming of the compounds in the examples below.

Example 1 (Compound No. 17)
Thiazol-4-ylmethyl 3-(naphth-2-yloxymethyl)pyrrolidine-1-carboxylate



1.1 Thiazol-4-ylmethyl 3-(hydroxymethyl)pyrrolidine-1-carboxylate

A solution of 3.00 g (10.70 mmol) of thiazol-4-ylmethyl 4-nitrophenyl carbonate in 20 ml of dichloromethane is added at ambient temperature, via a dropping funnel, to a solution of 1.13 g (11.24 mmol) of pyrrolidin-3-ylmethanol (commercial) in 20 ml of methanol. The solution is stirred for 15 hours. Water is subsequently added to the reaction medium. After extraction of the aqueous phase with dichloromethane, the organic phases are successively washed with a 1M aqueous sodium hydroxide solution and then with a saturated aqueous sodium chloride solution. After having dried the organic phases over sodium

sulphate, the mixture is filtered and the filtrate is evaporated to dryness. 0.56 g of the desired product is thus obtained in the form of an oil after purification on a column of silica gel, elution being carried out with a dichloromethane/methanol (97/3 to 95/5) mixture.

1.2 Thiazol-4-ylmethyl 3-(naphth-2-yloxymethyl)pyrrolidine-1-carboxylate

0.25 g (1.03 mmol) of thiazol-4-ylmethyl 3-(hydroxymethyl)pyrrolidine-1-carboxylate is dissolved in 8 ml of toluene. 0.35 g (1.34 mmol) of triphenylphosphine and 0.16 g (1.13 mmol) of naphth-2-ol are added and then the medium is cooled to 0°C for slow addition of a solution of 0.27 g (1.34 mmol) of diisopropyl azodicarboxylate in 2 ml of toluene. The medium is stirred at ambient temperature for 14 hours. The residue obtained is taken up in water and extracted twice with dichloromethane. The combined organic phases are washed with a saturated aqueous sodium chloride solution, dried over sodium sulphate, filtered and concentrated under vacuum. The residue is purified by chromatography on silica gel, elution being carried out with a 99/1 to 98/2 mixture of dichloromethane and methanol. 0.15 g of the expected product is obtained in the form of a powder.

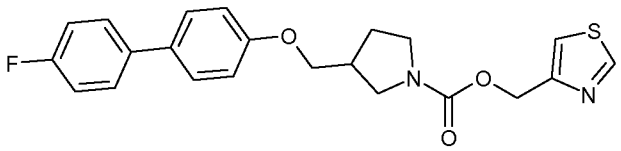
M.p.(°C): 90-92

LC-MS: M+H = 369

^{1}H NMR (d_6-DMSO) δ (ppm): 9.10 (s, 1H); 7.85 (m, 3H); 7.70 (m, 1H); 7.50 (m, 1H); 7.35 (m, 2H); 7.20 (m, 1H); 5.20 (s, 2H); 4.10 (m, 2H); 3.60 (m, 1H); 3.50 (m, 1H); 3.40 (m, 1H); 3.30 (m, 1H); 2.70 (m, 1H); 2.10 (m, 1H); 1.80 (m, 1H)

Example 2 (Compound No. 22)

Thiazol-4-ylmethyl 3-(4'-fluorobiphenyl-4-yloxymethyl)-pyrrolidine-1-carboxylate



2.1 tert-Butyl 3-(4'-fluorobiphenyl-4-yloxymethyl)pyrrolidine-1-carboxylate

The procedure is the same as for Example 1 (Stage 1.2) starting from 1.50 g (7.45 mmol) of tert-butyl 3-(hydroxymethyl)pyrrolidine-1-carboxylate (commercial), 2.15 g (11.18 mmol) of 4'-fluorobiphenyl-4-ol, 2.93 g (11.18 mmol) of triphenylphosphine and 2.26 g (11.18 mmol) of diisopropyl azodicarboxylate. After purification by chromatography on a column of silica gel, elution being carried out with dichloromethane, 1.55 g of the expected product are obtained in the form of an oil.

2.2 3-(4'-Fluorobiphenyl-4-yloxymethyl)pyrrolidine

1.55 g (4.17 mmol) of tert-butyl 3-(4'-fluorobiphenyl-4-yloxymethyl)pyrrolidine-1-carboxylate are dissolved in 40 ml of dichloromethane and then, at 0°C, 6.00 ml (80.77 mmol) of trifluoroacetic acid are subsequently added. After stirring at ambient temperature for two hours, the mixture is concentrated to dryness and then the residue is taken up in water and dichloromethane. A saturated sodium hydrogencarbonate solution is added and then the aqueous phase is extracted with dichloromethane. The combined organic phases are washed with a saturated aqueous sodium chloride solution, dried over sodium sulphate, filtered and concentrated under vacuum. 0.98 g of product is obtained in the form of an oil, used as is in the following stage.

2.3 Thiazol-4-ylmethyl 3-(4'-fluorobiphenyl-4-yloxymethyl)-pyrrolidine-1-carboxylate

0.30 g (1.07 mmol) of thiazol-4-ylmethyl 4-nitrophenyl carbonate, 0.34 g (1.28 mmol) of 3-(4'-fluorobiphenyl-4-

yloxymethyl)pyrrolidine, 0.20 g (1.61 mmol) of *N,N*-diisopropylethylamine and 0.01 g (0.11 mmol) of dimethylaminopyridine are dissolved in 10 ml of 1,2-dichloroethane. The mixture is stirred at 70°C for 4 hours. After returning to ambient temperature, water is added to the reaction medium. After extraction of the aqueous phase with dichloromethane, the organic phases are successively washed three times with a 1M aqueous sodium hydroxide solution and then twice with a saturated aqueous ammonium chloride solution. After having dried the organic phases over sodium sulphate, they are filtered and the filtrate is evaporated to dryness. After purification by chromatography on a column of silica gel, elution being carried out with dichloromethane and methanol (98/2), 0.16 g of the expected product is obtained in the form of a powder.

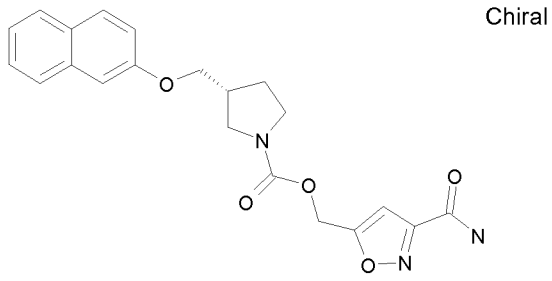
M.p.(°C): 115-117

LC-MS: M+H = 413

^{1}H NMR (d_6-DMSO) δ (ppm): 9.10 (s, 1H); 7.70 (m, 3H); 7.60 (d, 2H); 7.30 (m, 2H); 7.05 (m, 2H); 5.20 (s, 2H); 4.05 (m, 2H); 3.60 (m, 1H); 3.50 (m, 1H); 3.35 (m, 1H); 3.20 (m, 1H); 2.70 (m, 1H); 2.10 (m, 1H); 1.80 (m, 1H)

Example 3 (Compound No. 200)

3-Carbamoylisoxazol-5-ylmethyl (-)-(R)-3-(naphth-2-yloxymethyl)pyrrolidine-1-carboxylate



3.1 tert-Butyl (R)-3-(naphth-2-yloxymethyl)pyrrolidine-1-carboxylate

The procedure is the same as for Example 1 (Stage 1.2)

starting from 2.00 g (9.94 mmol) of tert-butyl (R)-3-(hydroxymethyl)pyrrolidine-1-carboxylate (commercial), 2.00 g (13.91 mmol) of naphth-2-ol, 3.90 g (14.91 mmol) of triphenylphosphine and 3.01 g (14.91 mmol) of diisopropyl azodicarboxylate. 1.75 g of product are obtained in the form of an oil after purification on a column of silica gel, elution being carried out with dichloromethane.

3.2 (R)-3-(naphth-2-yloxymethyl)pyrrolidine

The procedure is the same as for Example 2 (Stage 2.2) starting from 1.75 g (5.34 mmol) of tert-butyl (R)-3-(naphth-2-yloxymethyl)pyrrolidine-1-carboxylate and 5.00 ml (67.31 mmol) of trifluoroacetic acid. 1.20 g of product are obtained in the form of an oil.

3.3 3-Carbamoylisoxazol-5-ylmethyl 4-nitrophenyl carbonate

2.84 g (14.07 mmol) of 4-nitrophenyl chloroformate are added in small portions to a solution, cooled to approximately 0°C, of 2.00 g (14.07 mmol) of 3-carbamoylisoxazol-5-ylmethanol, 1.71 ml (21.11 mmol) of pyridine and 0.17 g (1.41 mmol) of *N,N*-dimethylaminopyridine in 15 ml of dichloromethane. The medium is kept stirred at 0°C for 1 hour and then at ambient temperature for 1 hour. The precipitate formed is filtered off and then copiously rinsed with diisopropyl ether. After drying under vacuum at approximately 60°C, 3.12 g (72%) of the expected product are obtained in the form of a white solid used as is in the following stage.

M.p.(°C): 143-145

^{1}H NMR (d_6-DMSO, 400 MHz) δ (ppm): 8.40 (d, 2H); 8.25 (broad s, 1H); 7.90 (broad s, 1H); 7.65 (d, 2H); 7.0 (s, 1H); 5.50 (s, 2H).

3.4 3-Carbamoylisoxazol-5-ylmethyl (-)-(R)-3-(naphth-2-yloxymethyl)pyrrolidine-1-carboxylate

0.21 g (0.92 mmol) of (R)-3-(naphth-2-yloxymethyl)pyrrolidine is dissolved in 3.80 ml of dichloromethane and then 0.31 g (1.01 mmol) of 3-carbamoylisoxazol-5-ylmethyl 4-nitrophenyl carbonate and 0.15 ml (1.38 mmol) of N-methylmorpholine are added. The mixture is stirred at ambient temperature for 20 hours and then water is added to the reaction medium. After extraction of the aqueous phase with dichloromethane, the organic phases are successively washed three times with a 1M aqueous sodium hydroxide solution and then twice with a saturated aqueous ammonium chloride solution. After having dried the organic phases over sodium sulphate, they are filtered and the filtrate is evaporated to dryness. 0.14 g of the desired product is thus obtained in the form of a white solid after purification on a column of silica gel, elution being carried out with a dichloromethane/methanol mixture, and then taken up in isopropyl ether.

M.p.(°C): 138-140

LC-MS: M+H = 396

^{1}H NMR (d_6-DMSO) δ (ppm): 8.15 (broad s, 1H); 7.80 (m, 4H); 7.50 (m, 1H); 7.35 (m, 2H); 7.20 (m, 1H); 6.80 (s, 1H); 5.30 (s, 2H); 4.10 (m, 2H); 3.65 (m, 1H); 3.50 (m, 1H); 3.40 (m, 1H); 3.30 (m, 1H); 2.80 (m, 1H); 2.10 (m, 1H); 1.85 (m, 1H)

$[\alpha]^{20°C}$ -7.917° (c = 0.312; DMSO, 589 nm)

Example 4 (Compound No. 202)
3-Carbamoylisoxazol-5-ylmethyl (+)-(S)-3-(naphth-2-yloxymethyl)pyrrolidine-1-carboxylate

4.1 tert-Butyl (S)-3-(naphth-2-yloxymethyl)pyrrolidine-1-carboxylate

The procedure is the same as for Example 1 (Stage 1.2) starting from 2.00 g (9.94 mmol) of tert-butyl (S)-3-(hydroxymethyl)pyrrolidine-1-carboxylate (commercial), 2.00 g (13.91 mmol) of naphth-2-ol, 3.90 g (14.91 mmol) of

triphenylphosphine and 3.01 g (14.91 mmol) of diisopropyl azodicarboxylate. 2.80 g of product are obtained in the form of an oil after purification on a column of silica gel, elution being carried out with dichloromethane.

4.2 (S)-3-(Naphth-2-yloxymethyl)pyrrolidine

The procedure is the same as for Example 2 (Stage 2.2) starting from 1.75 g (5.34 mmol) of tert-butyl (S)-3-(naphth-2-yloxymethyl)pyrrolidine-1-carboxylate and 5.00 ml (67.31 mmol) of trifluoroacetic acid. The product is obtained in the form of an oil after purification on a column of silica gel, elution being carried out with a dichloromethane/methanol/aqueous ammonia (90/9/1) mixture.

4.3 3-Carbamoylisoxazol-5-ylmethyl (+)-(S)-3-(naphth-2-yloxymethyl)pyrrolidine-1-carboxylate

The procedure is the same as for Example 3 (Stage 3.4) starting from 0.21 g (0.95 mmol) of (S)-3-(naphth-2-yloxymethyl)pyrrolidine, 0.32 g (1.04 mmol) of 3-carbamoylisoxazol-5-ylmethyl 4-nitrophenyl carbonate (Stage 4.3) and 0.16 ml (1.42 mmol) of N-methylmorpholine. 0.21 g of a powder is obtained after purification on a column of silica gel, elution being carried out with a dichloromethane/methanol mixture, and trituration from isopropyl ether.

M.p.(°C): 139-141

LC-MS: M+H = 396

^{1}H NMR (d_6-DMSO) δ (ppm): 8.15 (broad s, 1H); 7.80 (m, 4H); 7.50 (m, 1H); 7.35 (m, 2H); 7.20 (m, 1H); 6.80 (s, 1H); 5.30 (s, 2H); 4.10 (m, 2H); 3.65 (m, 1H); 3.50 (m, 1H); 3.40 (m, 1H); 3.30 (m, 1H); 2.80 (m, 1H); 2.10 (m, 1H); 1.85 (m, 1H)

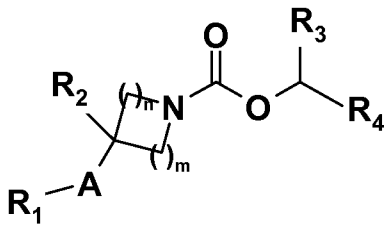
$[\alpha]^{20°C}$ +9.944° (c = 0.036; DMSO, 589 nm)

The chemical structures and the physical properties of some compounds according to the invention are illustrated in the

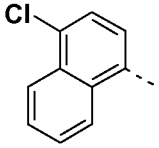
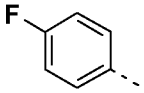
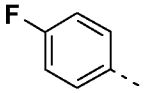
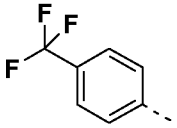
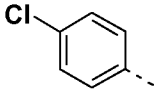
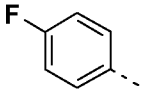
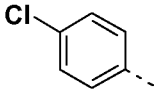
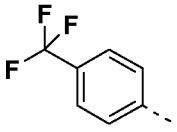
following Table 1. In this table, the compounds are in the free base or salt form.

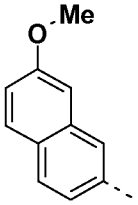
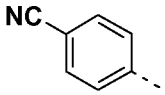
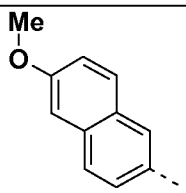
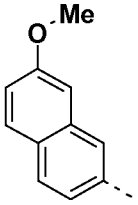
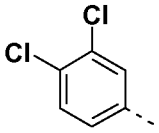
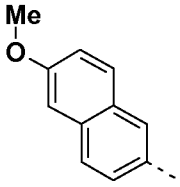
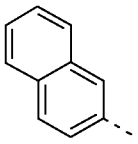
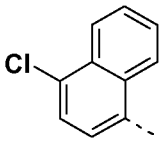
* A represents an $-O-C_{1-6}$-alkylene group in which the end represented by an oxygen atom is bonded to the R_1 group.

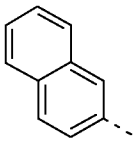
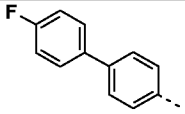
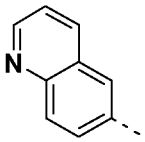
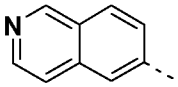
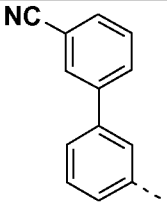
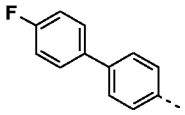
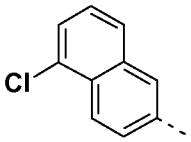
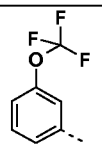
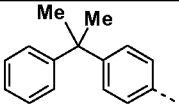
Table 1

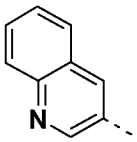
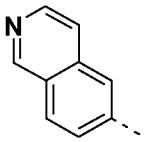
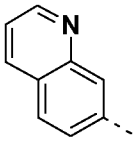
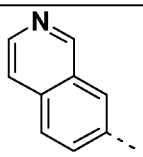
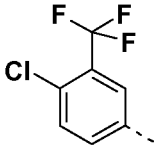
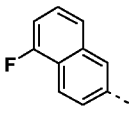
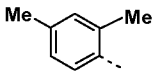
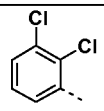
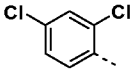
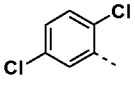


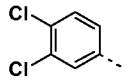
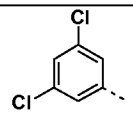
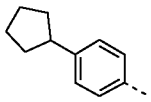
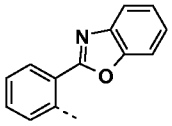
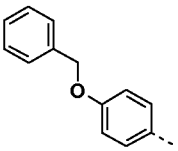
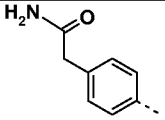
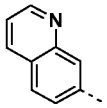
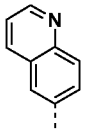
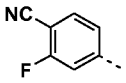
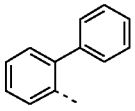
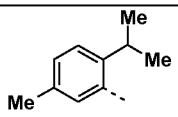
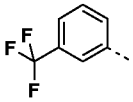
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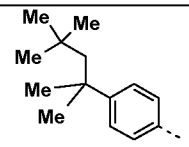
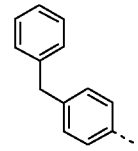
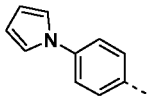
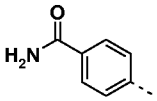
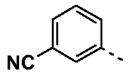
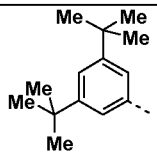
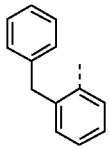
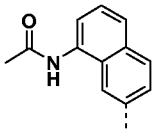
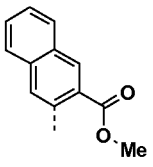
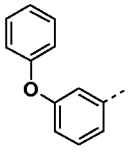
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2.		2	2	$-OCH_2CH_2-$	H	H		base
3.		2	2	$-OCH_2CH_2-$	H	H		base
4.		2	2	$-OCH_2CH_2-$	H	H		base
5.		2	2	$-OCH_2CH_2-$	H	H		base
6.		2	2	$-OCH_2CH_2-$	H	H		base
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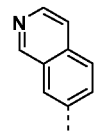
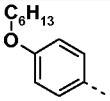
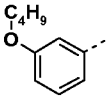
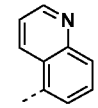
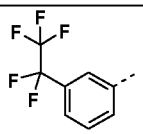
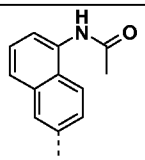
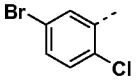
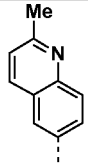
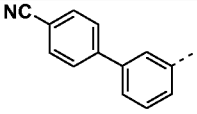
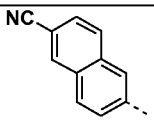
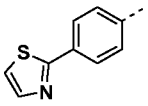
N°	R_1	m	n	A*	R_2	R_3	R_4	Base or salt
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10.		2	2	$-OCH_2CH_2-$	H	H		base
11.		2	1	$-OCH_2-$	H	H	 (+/−)	base
12.		2	1	$-OCH_2-$	H	H	 (+/−)	base
13.		2	1	$-OCH_2-$	H	H	 (+/−)	base
14.		2	2	$-OCH_2CH_2-$	H	H		base
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16.		1	2	$-OCH_2-$	H	H	 (+/−)	base

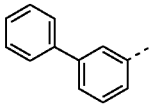
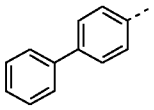
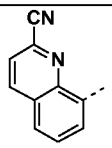
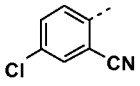
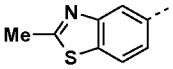
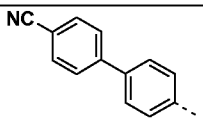
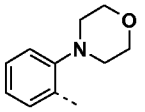
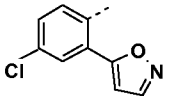
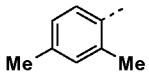
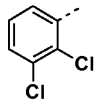
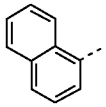
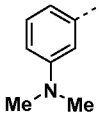
N°	R_1	m	n	A*	R_2	R_3	R_4	Base or salt
17.		1	2	$-OCH_2-$	H	H	 (+/−)	base
18.		2	2	$-OCH_2CH_2-$	H	H		base
19.		2	2	$-OCH_2CH_2-$	H	H		HCl
20.		2	2	$-OCH_2CH_2-$	H	H		HCl
21.		1	2	$-OCH_2-$	H	H	 (+/−)	base
22.		1	2	$-OCH_2-$	H	H	 (+/−)	base
23.		1	2	$-OCH_2-$	H	H	 (+/−)	base
24.		1	2	$-OCH_2-$	H	H	 (+/−)	base
25.		1	2	$-OCH_2-$	H	H	 (+/−)	base

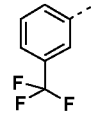
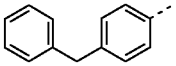
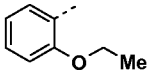
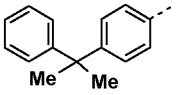
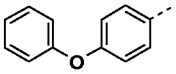
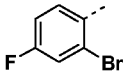
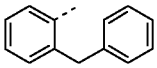
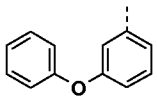
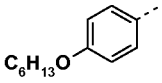
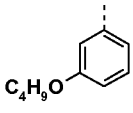
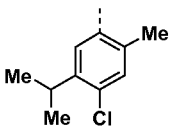
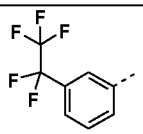
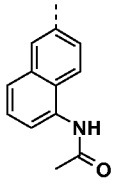
N°	R_1	m	n	A*	R_2	R_3	R_4	Base or salt
26.		1	2	$-OCH_2-$	H	H	 (+/−)	base
27.		1	2	$-OCH_2-$	H	H	 (+/−)	base
28.		1	2	$-OCH_2-$	H	H	 (+/−)	base
29.		1	2	$-OCH_2-$	H	H	 (+/−)	base
30.		1	2	$-OCH_2-$	H	H	 (+/−)	base
31.		1	2	$-OCH_2-$	H	H	 (+/−)	base
32.		2	2	$-OCH_2CH_2-$	H	H		base
33.		2	2	$-OCH_2CH_2-$	H	H		base
34.		2	2	$-OCH_2CH_2-$	H	H		base
35.		2	2	$-OCH_2CH_2-$	H	H		base

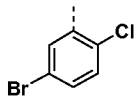
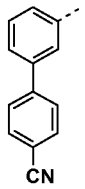
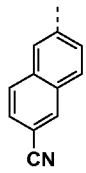
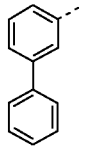
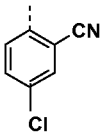
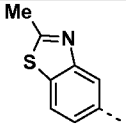
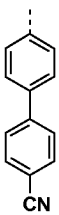
N°	R_1	m	n	A*	R_2	R_3	R_4	Base or salt
36.		2	2	$-OCH_2CH_2-$	H	H		base
37.		2	2	$-OCH_2CH_2-$	H	H		base
38.		2	2	$-OCH_2CH_2-$	H	H		base
39.		2	2	$-OCH_2CH_2-$	H	H		base
40.		2	2	$-OCH_2CH_2-$	H	H		base
41.		2	2	$-OCH_2CH_2-$	H	H		base
42.		2	2	$-OCH_2CH_2-$	H	H		CF_3CO_2H
43.		2	2	$-OCH_2CH_2-$	H	H		CF_3CO_2H
44.		2	2	$-OCH_2CH_2-$	H	H		base
45.		2	2	$-OCH_2CH_2-$	H	H		base
46.		2	2	$-OCH_2CH_2-$	H	H		base
47.		2	2	$-OCH_2CH_2-$	H	H		base

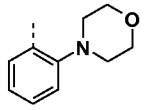
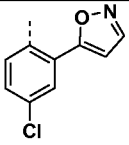
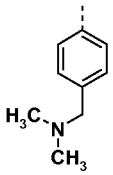
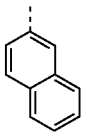
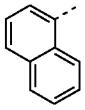
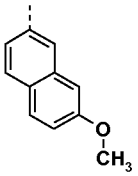
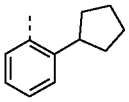
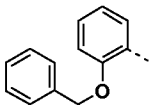
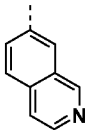
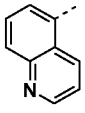
N°	R_1	m	n	A*	R_2	R_3	R_4	Base or salt
48.		2	2	$-OCH_2CH_2-$	H	H		base
49.		2	2	$-OCH_2CH_2-$	H	H		base
50.		2	2	$-OCH_2CH_2-$	H	H		CF_3CO_2H
51.		2	2	$-OCH_2CH_2-$	H	H		base
52.		2	2	$-OCH_2CH_2-$	H	H		base
53.		2	2	$-OCH_2CH_2-$	H	H		base
54.		2	2	$-OCH_2CH_2-$	H	H		base
55.		2	2	$-OCH_2CH_2-$	H	H		base
56.		2	2	$-OCH_2CH_2-$	H	H		base
57.		2	2	$-OCH_2CH_2-$	H	H		base

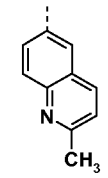
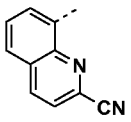
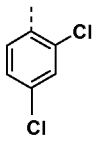
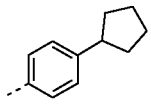
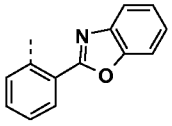
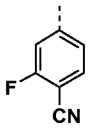
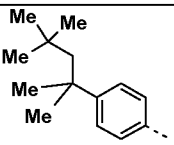
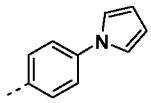
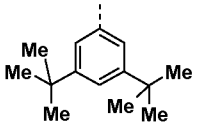
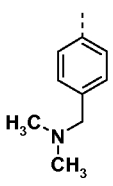
N°	R_1	m	n	A*	R_2	R_3	R_4	Base or salt
58.		2	2	$-OCH_2CH_2-$	H	H		CF_3CO_2H
59.		2	2	$-OCH_2CH_2-$	H	H		base
60.		2	2	$-OCH_2CH_2-$	H	H		base
61.		2	2	$-OCH_2CH_2-$	H	H		CF_3CO_2H
62.		2	2	$-OCH_2CH_2-$	H	H		base
63.		2	2	$-OCH_2CH_2-$	H	H		base
64.		2	2	$-OCH_2CH_2-$	H	H		base
65.		2	2	$-OCH_2CH_2-$	H	H		CF_3CO_2H
66.		2	2	$-OCH_2CH_2-$	H	H		base
67.		2	2	$-OCH_2CH_2-$	H	H		base
68.		2	2	$-OCH_2CH_2-$	H	H		base

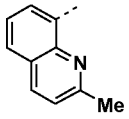
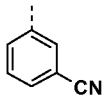
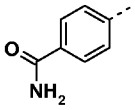
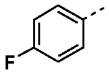
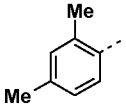
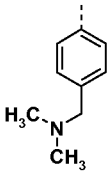
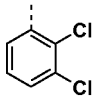
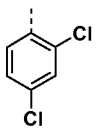
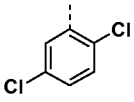
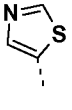
N°	R_1	m	n	A*	R_2	R_3	R_4	Base or salt
69.		2	2	$-OCH_2CH_2-$	H	H		base
70.		2	2	$-OCH_2CH_2-$	H	H		base
71.		2	2	$-OCH_2CH_2-$	H	H		CF_3CO_2H
72.		2	2	$-OCH_2CH_2-$	H	H		CF_3CO_2H
73.		2	2	$-OCH_2CH_2-$	H	H		base
74.		2	2	$-OCH_2CH_2-$	H	H		base
75.		2	2	$-OCH_2CH_2-$	H	H		base
76.		2	2	$-OCH_2CH_2-$	H	H		base
77.		2	2	$-OCH_2CH_2-$	H	H		base
78.		2	2	$-OCH_2CH_2-$	H	H		base
79.		2	2	$-OCH_2CH_2-$	H	H		base
80.		2	2	$-OCH_2CH_2-$	H	H		CF_3CO_2H

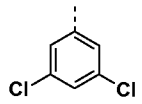
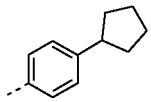
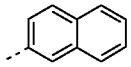
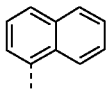
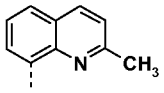
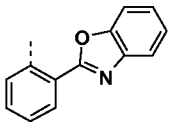
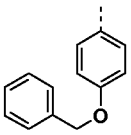
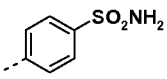
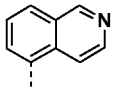
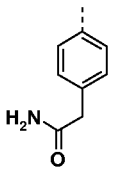
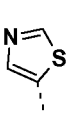
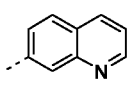
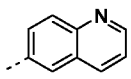
N°	R_1	m	n	A*	R_2	R_3	R_4	Base or salt
81.		2	2	$-OCH_2CH_2-$	H	H		base
82.		2	2	$-OCH_2CH_2-$	H	H		base
83.		2	2	$-OCH_2CH_2-$	H	H		base
84.		2	2	$-OCH_2CH_2-$	H	H		base
85.		2	2	$-OCH_2CH_2-$	H	H		base
86.		2	2	$-OCH_2CH_2-$	H	H		base
87.		2	2	$-OCH_2CH_2-$	H	H		base
88.		2	2	$-OCH_2CH_2-$	H	H		base
89.		2	2	$-OCH_2CH_2-$	H	H		base
90.		2	2	$-OCH_2CH_2-$	H	H		base
91.		2	2	$-OCH_2CH_2-$	H	H		base
92.		2	2	$-OCH_2CH_2-$	H	H		base
93.		2	2	$-OCH_2CH_2-$	H	H		base

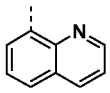
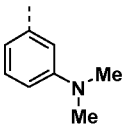
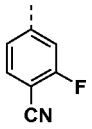
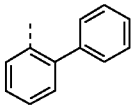
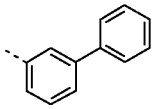
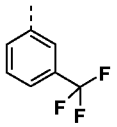
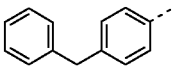
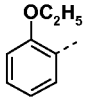
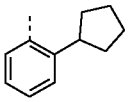
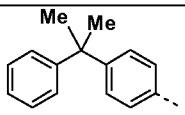
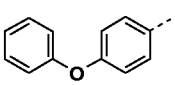
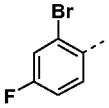
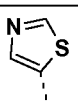
N°	R_1	m	n	A*	R_2	R_3	R_4	Base or salt
94.		2	2	$-OCH_2CH_2-$	H	H		base
95.		2	2	$-OCH_2CH_2-$	H	H		base
96.		2	2	$-OCH_2CH_2-$	H	H		base
97.		2	2	$-OCH_2CH_2-$	H	H		base
98.		2	2	$-OCH_2CH_2-$	H	H		base
99.		2	2	$-OCH_2CH_2-$	H	H		base
100.		2	2	$-OCH_2CH_2-$	H	H		base
101.		2	2	$-OCH_2CH_2-$	H	H		base
102.		2	2	$-OCH_2CH_2-$	H	H		base

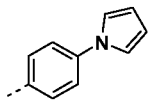
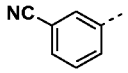
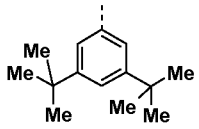
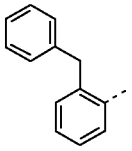
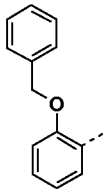
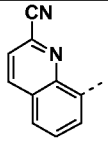
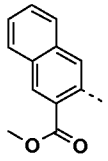
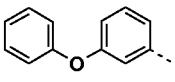
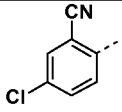
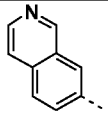
N°	R_1	m	n	A*	R_2	R_3	R_4	Base or salt
103.		2	2	$-OCH_2CH_2-$	H	H		CF_3CO_2H
104.		2	2	$-OCH_2CH_2-$	H	H		base
105.		2	2	$-OCH_2CH_2-$	H	H		CF_3CO_2H
106.		2	2	$-OCH_2CH_2-$	H	H		base
107.		2	2	$-OCH_2CH_2-$	H	H		base
108.		2	2	$-OCH_2CH_2-$	H	H		base
109.		2	2	$-OCH_2CH_2-$	H	H		base
110.		2	2	$-OCH_2CH_2-$	H	H		base
111.		2	2	$-OCH_2CH_2-$	H	H		CF_3CO_2H
112.		2	2	$-OCH_2CH_2-$	H	H		CF_3CO_2H

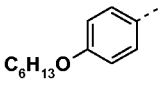
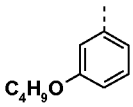
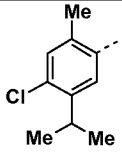
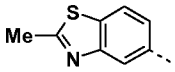
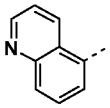
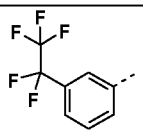
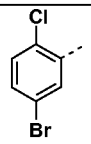
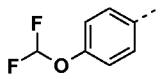
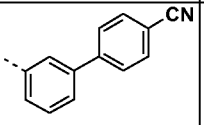
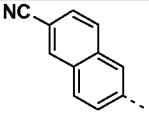
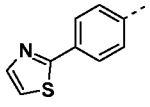
N°	R_1	m	n	A*	R_2	R_3	R_4	Base or salt
113.		2	2	$-OCH_2CH_2-$	H	H		CF_3CO_2H
114.		2	2	$-OCH_2CH_2-$	H	H		CF_3CO_2H
115.		2	2	$-OCH_2CH_2-$	H	H		base
116.		2	2	$-OCH_2CH_2-$	H	H		base
117.		2	2	$-OCH_2CH_2-$	H	H		base
118.		2	2	$-OCH_2CH_2-$	H	H		base
119.		2	2	$-OCH_2CH_2-$	H	H		base
120.		2	2	$-OCH_2CH_2-$	H	H		CF_3CO_2H
121.		2	2	$-OCH_2CH_2-$	H	H		base
122.		2	2	$-OCH_2CH_2-$	H	H		CF_3CO_2H

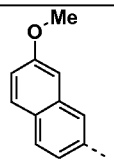
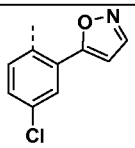
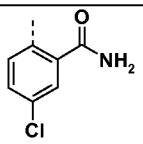
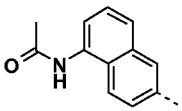
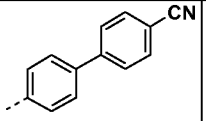
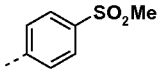
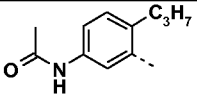
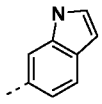
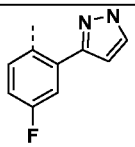
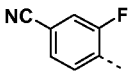
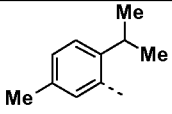
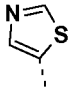
N°	R_1	m	n	A*	R_2	R_3	R_4	Base or salt
123.		2	2	$-OCH_2CH_2-$	H	H		CF_3CO_2H
124.		2	2	$-OCH_2CH_2-$	H	H		base
125.		2	2	$-OCH_2CH_2-$	H	H		base
126.		2	2	$-OCH_2CH_2-$	H	H		base
127.		2	2	$-OCH_2CH_2-$	H	H		base
128.		2	2	$-OCH_2CH_2-$	H	H		base
129.		2	2	$-OCH_2CH_2-$	H	H		base
130.		2	2	$-OCH_2CH_2-$	H	H		CF_3CO_2H
131.		2	2	$-OCH_2CH_2-$	H	H		base
132.		2	2	$-OCH_2CH_2-$	H	H		base
133.		2	2	$-OCH_2CH_2-$	H	H		base

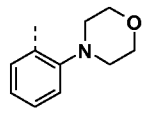
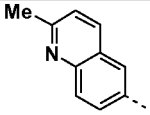
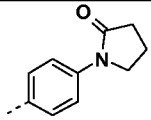
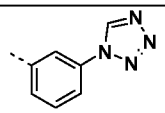
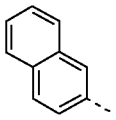
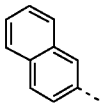
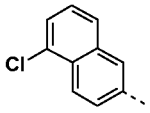
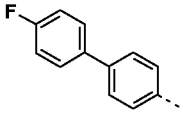
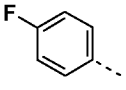
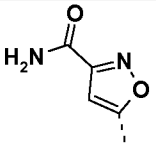
N°	R_1	m	n	A*	R_2	R_3	R_4	Base or salt
134.		2	2	$-OCH_2CH_2-$	H	H		base
135.		2	2	$-OCH_2CH_2-$	H	H		base
136.		2	2	$-OCH_2CH_2-$	H	H		base
137.		2	2	$-OCH_2CH_2-$	H	H		base
138.		2	2	$-OCH_2CH_2-$	H	H		base
139.		2	2	$-OCH_2CH_2-$	H	H		base
140.		2	2	$-OCH_2CH_2-$	H	H		base
141.		2	2	$-OCH_2CH_2-$	H	H		base
142.		2	2	$-OCH_2CH_2-$	H	H		base
143.		2	2	$-OCH_2CH_2-$	H	H		base
144.		2	2	$-OCH_2CH_2-$	H	H		base
145.		2	2	$-OCH_2CH_2-$	H	H		base

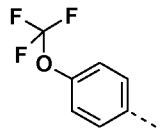
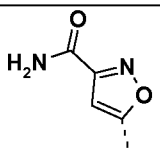
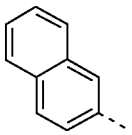
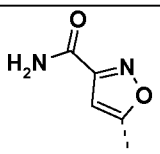
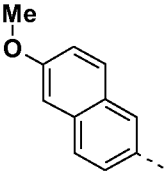
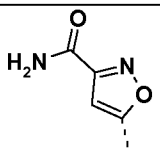
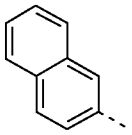
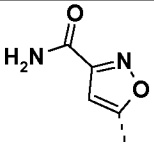
N°	R_1	m	n	A*	R_2	R_3	R_4	Base or salt
146.		2	2	$-OCH_2CH_2-$	H	H		base
147.		2	2	$-OCH_2CH_2-$	H	H		CF_3CO_2H
148.		2	2	$-OCH_2CH_2-$	H	H		base
149.		2	2	$-OCH_2CH_2-$	H	H		base
150.		2	2	$-OCH_2CH_2-$	H	H		base
151.		2	2	$-OCH_2CH_2-$	H	H		base
152.		2	2	$-OCH_2CH_2-$	H	H		base
153.		2	2	$-OCH_2CH_2-$	H	H		base
154.		2	2	$-OCH_2CH_2-$	H	H		base
155.		2	2	$-OCH_2CH_2-$	H	H		base
156.		2	2	$-OCH_2CH_2-$	H	H		base
157.		2	2	$-OCH_2CH_2-$	H	H		base

N°	R_1	m	n	A*	R_2	R_3	R_4	Base or salt
158.		2	2	$-OCH_2CH_2-$	H	H		base
159.		2	2	$-OCH_2CH_2-$	H	H		base
160.		2	2	$-OCH_2CH_2-$	H	H		base
161.		2	2	$-OCH_2CH_2-$	H	H		base
162.		2	2	$-OCH_2CH_2-$	H	H		base
163.		2	2	$-OCH_2CH_2-$	H	H		base
164.		2	2	$-OCH_2CH_2-$	H	H		base
165.		2	2	$-OCH_2CH_2-$	H	H		base
166.		2	2	$-OCH_2CH_2-$	H	H		base
167.		2	2	$-OCH_2CH_2-$	H	H		base

N°	R_1	m	n	A*	R_2	R_3	R_4	Base or salt
168.		2	2	$-OCH_2CH_2-$	H	H		base
169.		2	2	$-OCH_2CH_2-$	H	H		base
170.		2	2	$-OCH_2CH_2-$	H	H		base
171.		2	2	$-OCH_2CH_2-$	H	H		base
172.		2	2	$-OCH_2CH_2-$	H	H		base
173.		2	2	$-OCH_2CH_2-$	H	H		base
174.		2	2	$-OCH_2CH_2-$	H	H		base
175.		2	2	$-OCH_2CH_2-$	H	H		base
176.		2	2	$-OCH_2CH_2-$	H	H		base
177.		2	2	$-OCH_2CH_2-$	H	H		base
178.		2	2	$-OCH_2CH_2-$	H	H		base

N°	R_1	m	n	A*	R_2	R_3	R_4	Base or salt
179.		2	2	$-OCH_2CH_2-$	H	H		base
180.		2	2	$-OCH_2CH_2-$	H	H		base
181.		2	2	$-OCH_2CH_2-$	H	H		base
182.		2	2	$-OCH_2CH_2-$	H	H		base
183.		2	2	$-OCH_2CH_2-$	H	H		base
184.		2	2	$-OCH_2CH_2-$	H	H		base
185.		2	2	$-OCH_2CH_2-$	H	H		base
186.		2	2	$-OCH_2CH_2-$	H	H		base
187.		2	2	$-OCH_2CH_2-$	H	H		base
188.		2	2	$-OCH_2CH_2-$	H	H		base
189.		2	2	$-OCH_2CH_2-$	H	H		base

N°	R_1	m	n	A*	R_2	R_3	R_4	Base or salt
190.		2	2	$-OCH_2CH_2-$	H	H		CF_3CO_2H
191.		2	2	$-OCH_2CH_2-$	H	H		base
192.		2	2	$-OCH_2CH_2-$	H	H		base
193.		2	2	$-OCH_2CH_2-$	H	H		base
194.		1	2	$-OCH_2-$	H	H	 (R) Enantiomer I	base
195.		1	2	$-OCH_2-$	H	H	 (S) Enantiomer II	base
196.		1	2	$-OCH_2-$	H	H	 (+/-)	base
197.		1	2	$-OCH_2-$	H	H	 (+/-)	base
198.		2	2	$-OCH_2CH_2-$	H	H		base

N°	R_1	m	n	A*	R_2	R_3	R_4	Base or salt
199.		2	2	$-OCH_2CH_2-$	H	H		base
200.		2	1	$-OCH_2-$	H	H	 (R) (-) Enantiomer I	base
201.		2	1	$-OCH_2-$	H	H	 (+/-)	base
202.		2	1	$-OCH_2-$	H	H	 (S) (+) Enantiomer II	base

The results of the ^1H NMR analyses and the melting points (M.p.) for the compounds in Table 1 are given in the following Table 2.

Table 2

N°	^1H NMR 400 MHz d_6-DMSO/$CDCl_3$	M.p. (°C)
1	8.25 (m, 2H); 7.80 (d, 1H); 7.60 (m, 2H); 7.50 (d, 1H); 7.40 (d, 1H); 6.70 (d, 1H); 5.45 (s, 2H); 4.20 (m, 4H); 2.90 (m, 2H); 1.80 (m; 5H); 1.30 (m, 2H)	oil

2	7.80 (d, 1H); 7.70 (d, 1H); 7.10 (m, 2H); 6.90 (m, 2H); 5.35 (s, 2H); 4.00 (m, 2H); 2.85 (m, 2H); 1.70 (m, 5H); 1.10 (m, 2H)	oil
3	8.80 (s, 1H); 7.40 (s, 1H); 7.00 (m, 2H); 6.85 (m, 2H); 5.30 (s, 2H); 4.20 (m, 2H); 4.00 (m, 2H); 2.80 (m, 2H); 1.70 (m, 5H); 1.25 (m, 2H)	76-78
4	9.10 (s, 1H), 7.65 (s, 1H); 7.60 (d, 2H); 7.10 (d, 2H); 5.20 (s, 2H); 4.10 (m, 2H); 4.00 (m, 2H); 2.80 (m, 2H); 1.70 (m, 5H); 1.15 (m, 2H)	oil
5	9.10 (s, 1H); 7.65 (s, 1H); 7.30 (d, 2H); 6.90 (d, 2H); 5.10 (s, 2H); 3.90 (m, 4H); 2.80 (m, 2H); 1.70 (m, 4H); 1.10 (m, 2H)	53-55
6	8.80 (s, 1H); 7.90 (s, 1H); 7.00 (m, 2H); 6.80 (m, 2H); 5.30 (s, 2H); 4.20 (m, 2H); 4.00 (m, 2H); 2.80 (m, 2H); 1.75 (m, 6H); 1.20 (m, 2H)	96-98
7	9.10 (s, 1H); 7.90 (s, 1H); 7.30 (d, 2H); 6.95 (d, 2H); 5.30 (s, 2H); 3.90 (m, 4H); 2.80 (m, 2H); 1.60 (m, 6H); 1.10 (m, 2H)	93-97
8	9.10 (s, 1H); 7.95 (s, 1H); 7.60 (d, 2H); 7.10 (d, 2H); 5.30 (s, 2H); 4.10 (m, 2H); 3.95 (m, 2H); 2.80 (m, 2H); 1.65 (m, 6H); 1.10 (m, 2H)	47-49
9	9.10 (s, 1H); 7.75 (s, 1H); 7.70 (m, 2H); 7.20 (m, 2H); 6.95 (m, 2H); 5.15 (s, 2H); 4.10 (m, 2H); 4.00 (m, 2H); 3.80 (s, 3H); 2.80 (m, 2H); 1.70 (m, 5H); 1.15 (m, 2H)	95-97
10	8.80 (s, 1H); 7.60 (d, 2H); 7.40 (s, 1H); 6.95 (d, 2H); 5.30 (s, 2H); 4.20 (m, 2H); 4.05 (m, 2H); 2.80 (m, 2H); 1.75 (m, 5H); 1.20 (m, 2H)	108-110
11	8.80 (s, 1H); 7.65 (m, 2H); 7.40 (s, 1H); 7.10 (m, 4H), 5.30 (s, 2H); 4.05 (m, 2H); 3.90 (s, 3H); 3.80-3.35 (m, 4H); 2.80 (m, 1H); 2.20 (m, 1H); 1.90 (m, 1H)	128-130
12	8.80 (s, 1H); 7.70 (m, 2H); 7.40 (s, 1H); 7.05 (m, 4H), 5.35 (s, 2H); 4.10 (m, 2H); 3.90 (s, 3H); 3.80 (m, 1H); 3.65 (m, 1H); 3.55 (m, 1H); 3.40 (m, 1H); 2.80 (m, 1H); 2.20 (m, 1H); 1.90 (m, 1H)	112-114
13	8.80 (s, 1H); 7.40 (s, 1H); 7.35 (d, 1H); 7.00 (s, 1H); 6.75 (d, 1H); 5.30 (s, 2H); 3.90 (m, 2H); 3.70 (m, 1H); 3.60 (m, 1H); 3.50 (m, 1H); 3.30 (m, 1H); 2.70 (m, 1H); 2.10 (m, 1H); 1.80 (m, 1H)	78-80
14	8.80 (s, 1H); 7.65 (m, 2H); 7.40 (s, 1H); 7.10 (m, 4H); 5.30 (s, 2H); 4.20 (m, 2H); 4.10 (m, 2H); 3.90 (s, 3H); 2.80 (m, 2H); 1.80 (m, 5H); 1.25 (m, 2H)	100-102

15	8.80 (s, 1H); 7.80 (m, 3H); 7.45 (m, 1H); 7.40 (m, 2H); 7.15 (m, 2H); 5.30 (s, 2H); 4.25 (m, 2H); 4.20 (m, 2H); 2.90 (m, 2H); 1.85 (m, 5H); 1.25 (m, 2H)	88-90
16	9.10 (m, 1H); 8.50 (m, 2H); 7.95 (m, 1H); 7.85 (m, 1H); 7.75 (d, 1H); 7.70 (m, 1H); 7.00 (d, 1H); 5.60 (s, 2H); 4.40 (m, 2H); 4.10 (m, 1H); 4.00 (m, 1H); 3.85 (m, 1H); 3.70 (m, 1H); 3.20 (m, 1H); 2.50 (m, 1H); 2.30 (m, 1H)	84-86
17	9.10 (s, 1H); 7.85 (m, 3H); 7.70 (m, 1H); 7.50 (m, 1H); 7.35 (m, 2H); 7.20 (m, 1H); 5.20 (s, 2H); 4.10 (m, 2H); 3.60 (m, 1H); 3.50 (m, 1H); 3.40 (m, 1H); 3.30 (m, 1H); 2.70 (m, 1H); 2.10 (m, 1H); 1.80 (m, 1H)	90-92
18	8.80 (s, 1H); 7.50 (m, 4H); 7.40 (s, 1H); 7.10 (m, 2H); 6.95 (d, 2H); 5.30 (s, 2H); 4.20 (m, 2H); 4.10 (m, 2H); 2.85 (m, 2H); 1.80 (m, 5H); 1.25 (m, 2H)	62-64
19	9.10 (s, 1H); 9.05 (m, 1H); 8.80 (d, 1H); 8.20 (d, 1H); 7.90 (m, 1H); 7.70 (m, 3H); 5.20 (s, 2H); 4.25 (m, 2H); 4.00 (m, 2H); 2.85 (m, 2H); 1.80 (m, 5H); 1.15 (m, 2H)	140-150
20	9.70 (s, 1H); 9.10 (s, 1H); 8.60 (d, 1H); 8.45 (d, 1H); 8.30 (d, 1H); 7.80 (s, 1H); 7.70 (m, 2H); 5.20 (s, 2H); 4.35 (m, 2H); 4.00 (m, 2H); 2.85 (m, 2H); 1.80 (m, 5H); 1.20 (m, 2H)	150-160
21	9.10 (s, 1H); 8.20 (s, 1H); 8.10 (d, 1H); 7.85 (d, 1H); 7.70 (m, 2H); 7.40 (m, 1H); 7.30 (m, 2H); 7.00 (m, 1H); 5.20 (s, 2H); 4.10 (m, 2H); 3.60 (m, 1H); 3.50 (m, 1H); 3.40 (m, 1H); 3.20 (m, 1H); 2.70 (m, 1H); 2.10 (m, 1H); 1.80 (m, 1H)	oil
22	9.10 (s, 1H); 7.70 (m, 3H); 7.60 (d, 2H); 7.30 (m, 2H); 7.05 (m, 2H); 5.20 (s, 2H); 4.05 (m, 2H); 3.60 (m, 1H); 3.50 (m, 1H); 3.35 (m, 1H); 3.20 (m, 1H); 2.70 (m, 1H); 2.10 (m, 1H); 1.80 (m, 1H)	115-117
23	9.10 (s, 1H); 8.10 (d, 1H); 7.80 (d, 1H); 7.70 (m, 1H); 7.50 (m, 3H); 7.30 (d, 1H); 5.20 (s, 2H); 4.15 (m, 2H); 3.60 (m, 1H); 3.50 (m, 1H); 3.40 (m, 1H); 3.25 (m, 1H); 2.80 (m, 1H); 2.10 (m, 1H); 1.80 (m, 1H)	89-91
24	9.10 (s, 1H); 7.70 (s, 1H); 7.40 (m, 1H); 7.05 (m, 1H); 6.95 (m, 2H); 5.20 (s, 2H); 4.05 (m, 2H); 3.60 (m, 1H); 3.50 (m, 1H); 3.35 (m, 1H); 3.20 (m, 1H); 2.70 (m, 1H); 2.10 (m, 1H); 1.80 (m, 1H)	54-56
25	9.10 (s, 1H); 7.70 (s, 1H); 7.30-7.10 (m, 7H); 6.90 (m, 2H); 5.20 (s, 2H); 4.00 (m, 2H); 3.60 (m, 1H); 3.50 (m, 1H); 3.35 (m, 1H); 3.20 (m, 1H); 2.70 (m, 1H); 2.05 (m, 1H); 1.75 (m, 1H); 1.60 (s, 6H)	76-78
26	9.10 (s, 1H); 8.70 (s, 1H); 8.00 (d, 1H); 7.90 (m, 1H); 7.80 (m, 1H); 7.70 (m, 1H); 7.60 (m, 2H); 5.20 (s, 2H); 4.20 (m, 2H); 3.65 (m, 1H); 3.55 (m, 1H); 3.40 (m, 1H); 3.30 (m, 1H); 2.80 (m, 1H); 2.10 (m, 1H); 1.85 (m, 1H)	83-85
27	9.20 (s, 1H); 9.10 (m, 1H); 8.40 (d, 1H); 8.05 (d, 1H); 7.70 (m, 2H); 7.40 (m, 1H); 7.30 (d, 1H); 5.20 (s, 2H); 4.20 (m, 2H); 3.60 (m, 1H); 3.50 (m, 1H); 3.40 (m, 1H); 3.30 (m, 1H); 2.75 (m, 1H); 2.10 (m, 1H); 1.80 (m, 1H)	122-124

28	9.10 (s, 1H); 8.80 (s, 1H); 8.30 (d, 1H); 7.90 (d, 1H); 7.70 (m, 1H); 7.40 (m, 2H); 7.30 (d, 1H); 5.20 (s, 2H); 4.20 (m, 2H); 3.60 (m, 1H); 3.50 (m, 1H); 3.40 (m, 1H); 3.30 (m, 1H); 2.80 (m, 1H); 2.10 (m, 1H); 1.80 (m, 1H)	94-96
29	9.20 (s, 1H); 9.10 (s, 1H); 8.40 (d, 1H); 7.90 (d, 1H); 7.80 (d, 1H); 7.70 (m, 1H); 7.55 (s, 1H); 7.45 (d, 1H); 5.20 (s, 2H); 4.20 (m, 2H); 3.60 (m, 1H); 3.50 (m, 1H); 3.40 (m, 1H); 3.30 (m, 1H); 2.80 (m, 1H); 2.10 (m, 1H); 1.80 (m, 1H)	121-123
30	9.10 (s, 1H); 7.65 (m, 2H); 7.40 (s, 1H); 7.30 (d, 1H); 5.20 (s, 2H); 4.10 (m, 2H); 3.60 (m, 1H); 3.50 (m, 1H); 3.40 (m, 1H); 3.20 (m, 1H); 2.70 (m, 1H); 2.10 (m, 1H); 1.80 (m, 1H)	60-62
31	9.10 (s, 1H); 8.00 (d, 1H); 7.70 (m, 2H); 7.50 (m, 2H); 7.30 (d, 1H); 7.15 (m, 1H); 5.20 (s, 2H); 4.15 (m, 2H); 3.60 (m, 1H); 3.50 (m, 1H); 3.40 (m, 1H); 3.30 (m, 1H); 2.80 (m, 1H); 2.10 (m, 1H); 1.85 (m, 1H)	76-78
194	7.90 (m, 4H); 7.75 (d, 1H); 7.50 (m, 1H); 7.35 (m, 2H); 7.20 (d, 1H); 5.35 (s, 2H); 4.15 (m, 2H); 3.65 (m, 1H); 3.55 (m, 1H); 3.45 (m, 1H); 3.30 (m, 1H); 2.80 (m, 1H); 2.15 (m, 1H); 1.85 (m, 1H)	100-112
195	7.90 (m, 4H); 7.75 (d, 1H); 7.50 (m, 1H); 7.35 (m, 2H); 7.20 (d, 1H); 5.35 (s, 2H); 4.15 (m, 2H); 3.65 (m, 1H); 3.55 (m, 1H); 3.45 (m, 1H); 3.30 (m, 1H); 2.80 (m, 1H); 2.15 (m, 1H); 1.85 (m, 1H)	112-114
196	8.10 (d, 1H); 7.85 (m, 2H); 7.75 (d, 1H); 7.50 (m, 3H); 7.40 (d, 1H); 5.35 (s, 2H); 4.20 (m, 2H); 3.65 (m, 1H); 3.55 (m, 1H); 3.45 (m, 1H); 3.30 (m, 1H); 2.80 (m, 1H); 2.15 (m, 1H); 1.85 (m, 1H)	100-102
197	7.85 (m, 1H); 7.75 (m, 1H); 7.65 (m, 2H); 7.60 (d, 2H); 7.30 (m, 2H); 7.05 (d, 2H); 5.40 (s, 2H); 4.10 (m, 2H); 3.60 (m, 1H); 3.50 (m, 1H); 3.40 (m, 1H); 3.30 (m, 1H); 2.70 (m, 1H); 2.10 (m, 1H); 1.80 (m, 1H)	81-83
198	8.15 (bs, 1H); 7.85 (bs, 1H); 7.15 (m, 2H); 7.00 (m, 2H); 6.80 (s, 1H); 5.25 (s, 2H); 4.00 (m, 4H); 2.90 (m, 2H); 1.70 (m, 5H); 1.10 (m, 2H)	106-108
199	8.15 (bs, 1H); 7.85 (bs, 1H); 7.30 (d, 2H); 7.05 (d, 2H); 6.80 (s, 1H); 5.25 (s, 2H); 4.05 (m, 4H); 2.85 (m, 2H); 1.70 (m, 5H); 1.10 (m, 2H)	112-115
200	8.15 (bs, 1H); 7.80 (m, 4H); 7.50 (m, 1H); 7.35 (m, 2H); 7.20 (m, 1H); 6.80 (s, 1H); 5.30 (s, 2H); 4.10 (m, 2H); 3.65 (m, 1H); 3.50 (m, 1H); 3.40 (m, 1H); 3.30 (m, 1H); 2.80 (m, 1H); 2.10 (m, 1H); 1.85 (m, 1H)	138-140
201	8.15 (bs, 1H); 8.85 (bs, 1H); 8.75 (m, 2H); 7.30 (m, 2H); 7.20 (m, 2H); 6.80 (s, 1H); 5.30 (s, 2H); 4.10 (m, 2H); 3.90 (s, 3H); 3.60 (m, 1H); 3.50 (m, 1H); 3.40 (m, 1H); 3.30 (m, 1H); 2.80 (m, 1H); 2.10 (m, 1H); 1.85 (m, 1H)	193-195
202	8.15 (bs, 1H); 7.80 (m, 4H); 7.50 (m, 1H); 7.35 (m, 2H); 7.20 (m, 1H); 6.80 (s, 1H); 5.30 (s, 2H); 4.10 (m, 2H); 3.65 (m, 1H); 3.50 (m, 1H); 3.40 (m, 1H); 3.30 (m, 1H); 2.80 (m, 1H); 2.10 (m, 1H); 1.85 (m, 1H)	139-141

The results for the masses M+H measured by LC-MS and the retention times for the compounds in Table 1 are given in the following Table 3.

LC-MS conditions:

Method A:

HPLC/ZQ - Gradient 10 min

Mobile phases: Phase A: CH_3COONH_4 + 3% ACN

Phase B: ACN

Stationary phase/column: Kromasil C18 column

Dimensions: 50*2.1 mm; 3.5 µm

Flow rate: D = 0.8 ml/min

Temperature of the column: T = 40°C

Injection volume: V = 5 µl

Gradient: T = 0 min: 100% of A, from T = 5.5 min to T = 7 min: 100% of B, from T = 7.1 min to T = 10 min: 100% of A.

Method B:

UPLC/TOF - Gradient 3 min

Mobile phases: Phase A: H_2O + 0.05% of TFA

Phase B: ACN + 0.035% of TFA

Stationary phase/column: Acquity BEH C18 column

Dimensions: 50*2.1 mm; 1.7 µm

Flow rate: D = 1.0 ml/min

Temperature of the column: T = 40°C

Injection volume: V = 2 µl

Gradient: T = 0 min: 98% of A and 2% of B, from T = 1.6 min to T = 2.1 min: 100% of B, from T = 2.5 min to T = 3 min: 98% of A and 2% of B.

Method C:

LC/TRAP - Gradient 20 min

Mobile phases: H_2O/CH_3COONH_4/ACN

Stationary phase/column: Kromasil C18 column

Method D:

LC/ZQ - Gradient 20 min

Mobile phases: TFA/ACN

Stationary phase/column: Kromasil C18 column

Method E:

LC/TOF - Gradient 20 min

Mobile phases: $H_2O/CH_3COONH_4/ACN$

Stationary phase/column: Kromasil C18 column

Method F:

Stationary phase/column: Jsphere

Dimensions: 33*2 mm; 4 µm

Gradient: H_2O + 0.05% TFA:ACN + 0.05% TFA; 2:98 (1 min) to 95:5 (5.0 min) to 95:5 (6.25 min).

Method G:

Stationary phase/column: Waters XBridge C18

Dimensions: 4.6*50 mm; 2.5 µm

Gradient: H_2O + 0.05% TFA:ACN + 0.05% TFA; 95:5 (0 min) to 95:5 (0.3 min) to 5:95 (3.5 min) to 5:95 (4 min).

Method H:

YMC

Stationary phase/column: Jsphere

Dimensions: 33*2 mm; 4 µm

Gradient: H_2O + 0.1% TFA:ACN + 0.08% TFA; 95:5 (0 min) to 5:95 (2.5 min) to 5:95 (3 min).

Table 3

N°	Method	M+H	Retention time
1.	D	431	10.40
2.	A	365	9.70
3.	D	365	8.80
4.	D	415	10.00
5.	D	381	9.80
6.	D	365	9.00
7.	D	381	9.70
8.	C	415	10.50
9.	D	427	10.00
10.	D	372	8.30
11.	E	399	8.50
12.	D	387	10.50
13.	D	387.01	10.00
14.	D	427	11.10
15.	D	397	11.50
16.	D	403	10.00
17.	D	369	8.90
18.	D	441	10.70
19.	D	398	5.70
20.	D	398	5.80
21.	D	420	9.40
22.	D	413	10.00
23.	D	403	10.40
24.	D	403	9.60
25.	D	437	11.00
26.	D	370	6.00
27.	D	370	5.30
28.	D	370	5.20
29.	D	370	5.30
30.	D	421	10.10
31.	D	387	9.90
32.	F	375.12	4.20
33.	F	414.98	4.10
34.	F	414.98	4.19
35.	F	414.97	4.11
36.	F	414.99	4.17
37.	F	415.03	4.30
38.	F	415.16	4.60

39.	F	464.05	3.95
40.	F	453.10	4.17
41.	F	404.09	2.81
42.	F	398.09	2.52
43.	F	398.07	2.50
44.	F	390.04	3.55
45.	F	423.09	4.14
46.	F	403.15	4.44
47.	F	415.06	4.07
48.	F	459.19	4.90
49.	F	437.16	4.29
50.	F	412.09	3.93
51.	F	390.10	2.86
52.	F	372.07	3.72
53.	F	459.21	5.15
54.	F	437.15	4.27
55.	H	454.41	2.01
56.	F	455.09	3.89
57.	F	439.09	4.19
58.	F	398.08	2.51
59.	F	447.16	4.73
60.	F	419.15	4.29
61.	F	398.07	2.55
62.	F	465.04	4.27
63.	F	454.08	3.17
64.	F	460.92	4.14
65.	F	412.08	2.51
66.	F	448.07	4.04
67.	F	422.06	3.78
68.	F	430.01	3.65
69.	F	423.12	4.24
70.	F	423.11	4.22
71.	F	423.05	3.39
72.	F	406.01	3.66
73.	F	418.03	3.56
74.	F	448.07	3.94
75.	F	432.10	2.82
76.	F	448.00	3.92
77.	F	375.12	4.04

78.	F	415.00	3.91
79.	F	397.11	4.08
80.	F	390.13	2.59
81.	F	415.06	3.97
82.	F	437.11	4.19
83.	F	391.12	3.55
84.	F	465.20	4.44
85.	F	439.09	4.17
86.	F	442.97	3.80
87.	G	437.11	3.87
88.	G	439.10	3.77
89.	G	447.11	4.16
90.	G	419.12	3.85
91.	G	437.03	4.26
92.	G	465.01	3.79
93.	G	454.11	2.85
94.	G	460.94	3.76
95.	F	448.11	3.56
96.	G	422.09	4.31
97.	G	430.04	3.23
98.	G	423.10	3.79
99.	G	423.10	3.78
100.	G	406.03	3.33
101.	G	418.05	3.15
102.	G	448.09	3.51
103.	G	432.12	2.57
104.	G	448.03	3.53
105.	F	404.13	2.55
106.	F	397.07	3.99
107.	F	397.08	4.13
108.	F	427.08	4.03
109.	G	415.11	4.08
110.	G	453.13	3.63
111.	G	398.11	2.39
112.	G	398.11	2.37
113.	G	412.14	2.38
114.	G	423.08	3.08
115.	H	415.27	2.49
116.	H	415.27	2.49

117.	H	464.38	2.34
118.	H	390.33	2.12
119.	H	459.45	3.04
120.	H	412.36	2.37
121.	H	459.45	2.92
122.	H	404.39	1.35
123.	H	412.36	1.36
124.	H	372.32	2.10
125.	F	347.16	3.55
126.	F	423.20	4.12
127.	F	390.2	2.71
128.	F	365.15	3.60
129.	F	375.20	4.06
130.	F	404.24	2.49
131.	G	415.04	3.95
132.	F	415.10	4.01
133.	F	415.09	3.99
134.	F	415.12	4.15
135.	H	415.11	4.38
136.	F	397.20	3.94
137.	F	397.19	3.97
138.	F	412.20	2.43
139.	F	464.19	3.85
140.	F	453.21	4.09
141.	F	426.16	2.82
142.	F	398.18	2.48
143.	F	404.20	2.81
144.	F	398.19	2.47
145.	F	398.19	2.50
146.	F	398.17	2.40
147.	F	390.22	2.57
148.	F	390.16	3.46
149.	F	423.18	4.06
150.	F	423.20	4.09
151.	F	415.12	3.88
152.	F	437.22	4.13
153.	F	391.20	3.53
154.	F	415.27	4.41
155.	F	465.29	4.42

156.	F	439.20	4.08
157.	F	443.06	3.87
158.	F	412.21	3.85
159.	F	372.17	3.43
160.	F	459.33	4.84
161.	F	437.23	4.15
162.	F	453.21	3.89
163.	F	423.18	3.37
164.	F	455.2	3.70
165.	F	439.20	4.05
166.	F	406.13	3.55
167.	F	398.18	2.49
168.	F	447.29	4.55
169.	F	419.27	4.25
170.	F	437.23	4.56
171.	F	418.15	3.37
172.	F	398.18	2.52
173.	F	465.15	4.07
174.	F	461.03	4.08
175.	F	413.15	3.69
176.	F	448.20	3.86
177.	F	422.07	3.76
178.	F	430.14	3.53
179.	F	427.21	3.88
180.	F	448.15	3.81
181.	F	424.15	3.04
182.	F	454.23	3.11
183.	F	448.20	3.99
184.	F	425.16	3.00
185.	F	446.13	3.44
186.	F	386.2	3.36
187.	F	431.19	3.19
188.	F	390.15	3.36
189.	F	403.28	4.34
190.	F	432.22	2.72
191.	F	412.20	2.49
192.	F	430.21	3.05
193.	F	415.20	3.17
194.	D	369	4.70

195.	D	369	4.73
196.	A	403	5.08
197.	A	413	5.00
198.	B	392	1.14
199.	B	458	1.28
200.	B	396	1.15
201.	A	426	1.13
202.	B	396	1.15

The compounds of the invention form the subject of pharmacological trials which make it possible to determine their inhibitory effect on the enzyme FAAH (Fatty Acid Amide Hydrolase).

1/ Radioenzymatic test

The inhibitory activity was demonstrated in a radioenzymatic test based on the measurement of the product of hydrolysis of anandamide [ethanolamine 1-^{3}H] by FAAH (*Life Sciences (1995), 56, 1999-2005* and *Journal of Biochemical* and *Biophysical Methods (2004)*, 60(2), 171-177). Thus, mouse brains (minus the cerebellum) are removed and stored at -80°C. The membrane homogenates are prepared at the time of use by homogenization of the tissues using a Precellys® device in the reaction buffer (Tris-HCl 10 mM pH=8, NaCl 150 mM and ethylenediaminetetraacetic acid (EDTA) 1 mM). The enzymatic reaction is carried out in 96-well MultiScreen filtration plates in a final volume of 70 µl. Reaction buffer supplemented with bovine serum albumin free from fatty acids (BSA, 1 mg/ml) is used for the enzymatic reaction, the dilution of the compounds and the dilution of the anandamide [ethanolamine 1-^{3}H]. Reaction buffer comprising the BSA (43 µl/well), the diluted test compounds at different concentrations (7 µl/well comprising 1% of DMSO) and the

membrane preparation (10 µl/well, i.e. 200 µg of tissue per trial) are successively added to the wells. After preincubating the compounds with the enzyme at 25°C for 20 minutes, the reaction is initiated by the addition of anandamide [ethanolamine 1-^{3}H] (specific activity of 15-20 Ci/mmol) diluted with cold anandamide (10 µl/well, final concentration of 10 µM, 0.01 µCi, per trial). After incubating at 25°C for 20 minutes, the enzymatic reaction is halted by addition of a 5M active charcoal solution prepared in a 1.5M NaCl and 0.5M HCl buffer (50 µl/well). The mixture is stirred for 10 minutes and then the aqueous phase comprising the [1-^{3}H]ethanolamine is recovered by filtration under vacuum and counted by liquid scintillation.

Under these conditions, the most active compounds of the invention exhibit CI_{50} values (concentration which inhibits the control enzymatic activity of FAAH by 50%) of between 0.1 and 1000 nM, preferably between 0.1 and 500 nM, preferably between 0.2 and 100 nM, indeed even between 0.2 and 50 nM. For example, compounds No. 26, No. 38, No. 39, No. 49, No. 60, No. 90, No. 196, No. 199, No. 200 and No. 202 have respective CI_{50} values of 86 nM, 14 nM, 13 nM, 19 nM, 95 nM, 92 nM, 252 nM, 350 nM, 122 nM and 8 nM.

It is thus apparent that the compounds according to the invention have an inhibitory activity on the enzyme FAAH.

The *in vivo* activity of the compounds of the invention can be evaluated in a test for analgesia.

2/ Test for analgesia

The intraperitoneal (i.p.) administration of PBQ (phenylbenzoquinone, 2 mg/kg in a 0.9% sodium chloride solution comprising 5% of ethanol) to male OF1 mice weighing

25 to 30 g causes abdominal tractions, on average 30 twisting or contracting motions during the period from 5 to 15 minutes after injection. The test compounds are administered, orally (p.o.) or intraperitoneally (i.p.) in suspension in 0.5% Tween 80, 60 minutes or 120 minutes before the administration of PBQ. Under these conditions, the most powerful compounds reduce by 30 to 80% the number of tractions induced by the PBQ, within a range of doses of between 1 and 30 mg/kg.

The enzyme FAAH (*Chemistry and Physics of Lipids*, (2000), 108, 107-121) catalyses the hydrolysis of endogenous derivatives of amides and esters of various fatty acids, such as *N*-arachidonoylethanolamine (anandamide), *N*-palmitoyl-ethanolamine, *N*-oleoylethanolamine, oleamide or 2-arachidonoylglycerol. These derivatives exert various pharmacological activities by interacting, *inter alia*, with the cannabinoid and vanilloid receptors.

The compounds of the invention block this decomposition pathway and increase the tissue level of these endogenous substances. They can therefore be used in the prevention and treatment of pathologies in which endogenous cannabinoids and/or any other substrate metabolized by the enzyme FAAH are involved. Mention may be made, for example, of the following diseases and conditions:
pain, in particular acute or chronic pain of neurogenic type: migraine, neuropathic pain, including forms associated with the herpes virus and with diabetes and with chemotherapy; acute or chronic pain associated with inflammatory diseases: arthritis, rheumatoid arthritis, osteoarthritis, spondylitis, gout, vasculitis, Crohn's disease, irritable bowel syndrome; acute or chronic peripheral pain; dizziness, vomiting, nausea, in particular resulting from chemotherapy; eating disorders, in particular anorexia and cachexia of various natures;

neurological and psychiatric pathologies: tremors, dyskinesias, dystonias, spasticity, obsessive-compulsive behaviour, Tourette's syndrome, all forms of depression and of anxiety of any nature and origin, mood disorders, psychoses; acute or chronic neurodegenerative diseases: Parkinson's disease, Alzheimer's disease, senile dementia, Huntington's chorea, lesions related to cerebral ischaemia and to cranial and medullary trauma; epilepsy; sleep disorders, including sleep apnoea; cardiovascular diseases, in particular hypertension, cardiac arrhythmias, arteriosclerosis, heart attack, cardiac ischaemia; renal ischaemia; cancers: benign skin tumours, brain tumours and papillomas, prostate tumours, cerebral tumours (glioblastomas, medulloepitheliomas, medulloblastomas, neuroblastomas, tumours of embryonic origin, astrocytomas, astroblastomas, ependymomas, oligodendrogliomas, plexus tumour, neuroepitheliomas, epiphyseal tumour, ependymoblastomas, malignant meningiomas, sarcomatosis, malignant melanomas, schwannomas); disorders of the immune system, in particular autoimmune diseases: psoriasis, lupus erythematosus, diseases of the connective tissue or collagen diseases, Sjögren's syndrome, ankylosing spondylitis, undifferentiated spondylitis, Behcet's disease, autoimmune haemolytic anaemia, multiple sclerosis, amyotrophic lateral sclerosis, amyloidosis, graft rejection, diseases affecting the plasmocytic line; allergic diseases: immediate or delayed hypersensitivity, allergic rhinitis or conjunctivitis, contact dermatitis; parasitic, viral or bacterial infectious diseases: AIDS, meningitis; inflammatory diseases, in particular joint diseases: arthritis, rheumatoid arthritis, osteoarthritis, spondylitis, gout, vasculitis, Crohn's disease, irritable bowel syndrome; osteoporosis; eye conditions: ocular hypertension, glaucoma; pulmonary conditions: diseases of the respiratory tract, bronchospasm, coughing, asthma, chronic bronchitis, chronic obstruction of the respiratory tract,

emphysema; gastrointestinal diseases: irritable bowel syndrome, inflammatory intestinal disorders, ulcers, diarrhoea; urinary incontinence and bladder inflammation.

The use of the compounds according to the invention, in the form of the base, of an addition salt with an acid, of a hydrate or of a solvate which is pharmaceutically acceptable, in the preparation of a medicament intended to treat the abovementioned pathologies forms an integral part of the invention.

Compounds according to the invention, in the form of the base, of an addition salt with an acid, of a hydrate or of a solvate which is pharmaceutically acceptable, for their use in the preparation of a medicament intended to treat the abovementioned pathologies forms an integral part of the invention.

Another subject-matter of the invention is medicaments which comprise a compound of formula (I), (Ii) or (Iii), or an addition salt with an acid, or a hydrate or a solvate which is pharmaceutically acceptable of the compound of formula (I), (Ii) or (Iii). These medicaments are used therapeutically, in particular in the treatment of the abovementioned pathologies.

According to another of its aspects, the present invention relates to pharmaceutical compositions including, as active principle, at least one compound according to the invention. These pharmaceutical compositions comprise an effective dose of a compound according to the invention, or an addition salt with an acid, or a hydrate, or a solvate which is pharmaceutically acceptable of the said compound, and optionally one or more pharmaceutically acceptable excipients.

The said excipients are chosen, depending on the pharmaceutical form and the method of administration desired, from the usual excipients which are known to a person skilled in the art.

In the pharmaceutical compositions of the present invention for oral, sublingual, subcutaneous, intramuscular, intravenous, topical, local, intrathecal, intranasal, transdermal, pulmonary, ocular or rectal administration, the active principle of formula (I), (Ii) or (Iii) above or its optional addition salt with an acid, solvate or hydrate can be administered in a unit administration form, as a mixture with conventional pharmaceutical excipients, to animals and to man for the prophylaxis or the treatment of the above disorders or diseases.

Appropriate unit administration forms comprise oral forms, such as tablets, soft or hard gelatin capsules, powders, granules, chewing gums and oral solutions or suspensions, forms for sublingual, buccal, intratracheal, intraocular or intranasal administration or for administration by inhalation, forms for subcutaneous, intramuscular or intravenous administration and forms for rectal or vaginal administration. For topical application, the compounds according to the invention can be used in creams, ointments or lotions.

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

Compound according to the invention	50.0 mg
Mannitol	223.75 mg
Croscarmellose sodium	6.0 mg
Maize starch	15.0 mg
Hydroxypropylmethylcellulose	2.25 mg

Magnesium stearate	3.0 mg

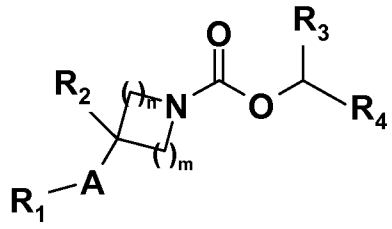
The said unit forms comprise a dose which makes possible a daily administration of 0.01 to 20 mg of active principle per kg of body weight, depending upon the pharmaceutical dosage form.

There may be specific cases where higher or lower dosages are appropriate; such dosages also come within the invention. According to the usual practice, the dosage appropriate to each patient is determined by the doctor according to the method of administration and the weight and the response of the said patient.

According to another of its aspects, the invention also relates to a method for the treatment of the pathologies indicated above which comprises the administration of an effective dose of a compound according to the invention, of one of its addition salts with a pharmaceutically acceptable acid or of a solvate or of a hydrate of the said compound.

Claims

1. Compound corresponding to the general formula (I):



(I)

in which:

- R_2 represents a hydrogen or fluorine atom or a hydroxyl, cyano, trifluoromethyl, C_{1-6}-alkyl, C_{1-6}-alkoxy or $-NR_8R_9$ group;
- n and m represent, independently of one another, an integer equal to 1, 2 or 3, it being understood that the sum m+n is at most equal to 5;
- A represents a covalent bond, an oxygen atom, a C_{1-6}-alkylene group or an $-O-C_{1-6}$-alkylene group in which the end represented by an oxygen atom is bonded to the R_1 group;
- R_1 represents an R_5 group optionally substituted by one or more R_6 and/or R_7 groups;

R_5 representing a group chosen from a phenyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, triazinyl, naphthyl, quinolinyl, isoquinolinyl, phthalazinyl, quinazolinyl, quinoxalinyl, cinnolinyl, naphthyridinyl, benzothiazolyl, benzisothiazolyl, benzoxazolyl, benzisoxazolyl, benzimidazolyl, isobenzofuranyl, benzofuranyl, benzothiophenyl, benzothiadiazolyl, benzoxadiazolyl, indazolyl, indolizinyl, indolyl, isoindolyl, imidazopyridinyl, imidazopyrimidinyl, imidazopyrazinyl, imidazopyridazinyl, triazolopyridinyl, pyrrolopyridinyl, pyrrolopyrimidinyl, pyrrolopyrazinyl, pyrrolopyridazinyl, pyrrolotriazinyl, pyrazolopyridinyl, pyrazolopyrimidinyl, pyrazolopyrazinyl, pyrazolopyridazinyl, furopyridinyl, furopyrimidinyl, furopyrazinyl, furopyridazinyl, furotriazinyl, oxazolopyridinyl, oxazolopyrimidinyl, oxazolopyrazinyl,

oxazolopyridazinyl, isoxazolopyridinyl, isoxazolopyrimidinyl, isoxazolopyrazinyl, isoxazolopyridazinyl, oxadiazolopyridinyl, thienopyridinyl, thienopyrimidinyl, thienopyrazinyl, thienopyridazinyl, thienotriazinyl, thiazolopyridinyl, thiazolopyrimidinyl, thiazolopyrazinyl, thiazolopyridazinyl, isothiazolopyridinyl, isothiazolopyrimidinyl, isothiazolopyrazinyl, isothiazolopyridazinyl or thiadiazolopyridinyl;

R_6 representing a halogen atom or a cyano, $-CH_2CN$, nitro, hydroxyl, C_{1-8}-alkyl, C_{1-6}-alkoxy, C_{1-6}-thioalkyl, C_{1-6}-haloalkyl, C_{1-6}-haloalkoxy, C_{1-6}-halothioalkyl, C_{3-7}-cycloalkyl, C_{3-7}-cycloalkyl-C_{1-3}-alkylene, C_{3-7}-cycloalkyl-C_{1-3}-alkylene-O-, $-(CH_2)_p-NR_8R_9$, $-NR_8COR_9$, $-NR_8CO_2R_9$, $-NR_8SO_2R_9$, $-NR_8SO_2NR_8R_9$, $-COR_8$, $-CO_2R_8$, $-(CH_2)_p-CONR_8R_9$, $-SO_2R_8$, $-SO_2NR_8R_9$ or $-O-(C_{1-3}$-alkylene)-O- group;

R_7 representing a group chosen from a phenyl, phenyl-C_{1-4}-alkylene-, phenyl-$(CH_2)_p$-O-, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, triazinyl, furanyl, thienyl, imidazolyl, oxazolyl, isoxazolyl, pyrrolyl, pyrazolyl, tetrazolyl, thiazolyl, isothiazolyl, oxadiazolyl, thiadiazolyl, imidazopyrimidinyl, thienopyrimidinyl, benzofuranyl, benzothienyl, benzimidazolyl, benzoxazolyl, benzisoxazolyl, benzothiazolyl, benzisothiazolyl, indolyl, isoindolyl, indazolyl, pyrrolopyridinyl, furopyridinyl, thienopyridinyl, imidazopyridinyl, pyrazolopyridinyl, oxazolopyridinyl, isoxazolopyridinyl or thiazolopyridinyl; it being possible for the R_7 group or groups to be substituted by one or more R_6 groups which are identical to or different from one another;

p representing a number which can have the value 0, 1, 2 or 3;

- R_3 represents a hydrogen or fluorine atom, a C_{1-6}-alkyl group or a trifluoromethyl group;

- R_4 represents a 5-membered heterocycle chosen from a furanyl, pyrrolyl, thienyl, thiazolyl, isothiazolyl, oxazolyl, isoxazolyl, pyrazolyl, oxadiazolyl, thiadiazolyl, imidazolyl, triazolyl or tetrazolyl;

this heterocycle optionally being substituted by one or more substituents chosen from a halogen atom or a C_{1-6}-alkyl, C_{1-6}-haloalkyl, C_{3-7}-cycloalkyl, C_{3-7}-cycloalkyl-C_{1-3}-alkylene, C_{1-6}-haloalkoxy, cyano, $-NR_8R_9$, $-NR_8C(O)R_9$, $-NR_8CO_2R_9$, $-NR_8SO_2R_9$, $-NR_8SO_2NR_8R_9$, $-C(O)R_8$, $-CO_2R_8$, $-C(O)NR_8R_9$, $-C(O)N(R_8)(C_{1-3}$-alkylene-$NR_{10}R_{11})$, $-SO_2R_8$, $-SO_2NR_8R_9$ or $-O-(C_{1-3}$-alkylene)-O- group;

R_8 and R_9 representing, independently of one another, a hydrogen atom or a C_{1-6}-alkyl group,

or forming, with the nitrogen atom or atoms which carry them,

in the case of NR_8R_9, a ring chosen from the azetidine, pyrrolidine, piperidine, morpholine, thiomorpholine, azepine, oxazepine or piperazine rings, this ring optionally being substituted by a C_{1-6}-alkyl or benzyl group;

in the case of NR_8COR_9, a lactam ring;

in the case of $NR_8CO_2R_9$, an oxazolidinone, oxazinone or oxazepinone ring;

in the case of $NR_8SO_2R_9$, a sultam ring;

in the case of $NR_8SO_2NR_8R_9$, a thiazolidine dioxide or thiadiazinane dioxide ring;

R_{10} and R_{11} representing, independently of one another, a hydrogen atom or a C_{1-6}-alkyl group;

with the exclusion of the following compound:

5-methylisoxazol-3-ylmethyl 4-hydroxy-4-(4-chlorophenyl)-piperidine-1-carboxylate,

in the form of the base or of an addition salt with an acid.

2. Compound of formula (I) according to Claim 1, characterized in that R_2 represents a hydrogen atom;

in the form of the base or of an addition salt with an acid.

3. Compound of formula (I) according to Claim 1 or 2, characterized in that m and n represent, independently of one another, the value 1 or 2;
in the form of the base or of an addition salt with an acid.

4. Compound of formula (I) according to any one of the preceding claims, characterized in that A represents an $-O-C_{1-6}$-alkylene group in which the end represented by an oxygen atom is bonded to the R_1 group;
in the form of the base or of an addition salt with an acid.

5. Compound of formula (I) according to any one of the preceding claims, characterized in that R_1 represents an R_5 group optionally substituted by one or more R_6 and/or R_7 groups;

R_5 representing a group chosen from a phenyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, triazinyl, naphthyl, quinolinyl, isoquinolinyl, phthalazinyl, quinoxalinyl, quinazolinyl, cinnolinyl, naphthyridinyl, benzothiazolyl, benzisothiazolyl, benzoxazolyl, benzisoxazolyl, benzimidazolyl, isobenzofuranyl, benzofuranyl, benzothiophenyl, indazolyl, indolizinyl, indolyl, isoindolyl, pyrrolopyridinyl, furopyridinyl or thienopyridinyl;

R_6 representing a halogen atom or a cyano, $-CH_2CN$, nitro, hydroxyl, C_{1-8}-alkyl, C_{1-6}-alkoxy, C_{1-6}-thioalkyl, C_{1-6}-haloalkyl, C_{1-6}-haloalkoxy, C_{1-6}-halothioalkyl, C_{3-7}-cycloalkyl, C_{3-7}-cycloalkyl-C_{1-3}-alkylene, C_{3-7}-cycloalkyl-C_{1-3}-alkylene-O-, $-(CH_2)_p-NR_8R_9$, $-NR_8COR_9$, $-NR_8CO_2R_9$, $-NR_8SO_2R_9$, $-NR_8SO_2NR_8R_9$, $-COR_8$, $-CO_2R_8$, $-(CH_2)_p-CONR_8R_9$, $-SO_2R_8$, $-SO_2NR_8R_9$ or $-O-(C_{1-3}$-alkylene)-O- group;

R_7 representing a group chosen from a phenyl, phenyl-C_{1-4}-alkylene-, phenyl-$(CH_2)_p$-O-, pyridinyl, pyridazinyl, isoxazolyl, benzothiazolyl, pyrrolyl, pyrazolyl, tetrazolyl,

pyrimidinyl, thiazolyl, pyrazinyl, triazinyl or benzoxazolyl; it being possible for the R_7 group or groups to be substituted by one or more R_6 groups, which are identical to or different from one another, as defined above;

p representing a number which can have the value 0, 1, 2 or 3;

R_8 and R_9 representing, independently of one another, a hydrogen atom or a C_{1-6}-alkyl group;

or forming, with the nitrogen atom or atoms which carry them,

in the case of NR_8R_9, a ring chosen from the azetidine, pyrrolidine, piperidine, morpholine, thiomorpholine, azepine, oxazepine or piperazine rings, this ring optionally being substituted by a C_{1-6}-alkyl or benzyl group;

in the case of NR_8COR_9, a lactam ring;

in the case of $NR_8CO_2R_9$, an oxazolidinone, oxazinone or oxazepinone ring;

in the case of $NR_8SO_2R_9$, a sultam ring;

in the case of $NR_8SO_2NR_8R_9$, a thiazolidine dioxide or thiadiazinane dioxide ring;

in the form of the base or of an addition salt with an acid.

6. Compound of formula (I) according to any one of the preceding claims, characterized in that R_3 represents a hydrogen atom;

in the form of the base or of an addition salt with an acid.

7. Compound of formula (I) according to any one of the preceding claims, characterized in that R_4 represents a 5-membered heterocycle chosen from a thiazolyl or isoxazolyl;

this heterocycle optionally being substituted by one or more -$C(O)NR_8R_9$ substituents in which R_8 and R_9 each represent a hydrogen atom;

in the form of the base or of an addition salt with an acid.

8. Compound of formula (I) according to claim 1 which is chosen among the following compounds :

Thiazol-2-ylmethyl 4-[2-(4-chloronaphth-1-yloxy)ethyl]-piperidine-1-carboxylate

Thiazol-2-ylmethyl 4-[2-(4-fluorophenoxy)ethyl]piperidine-1-carboxylate

Thiazol-4-ylmethyl 4-[2-(4-fluorophenoxy)ethyl]piperidine-1-carboxylate

Thiazol-4-ylmethyl 4-[2-(4-{trifluoromethyl}phenoxy)-ethyl]piperidine-1-carboxylate

Thiazol-4-ylmethyl 4-[2-(4-chlorophenoxy)ethyl]piperidine-1-carboxylate

Thiazol-5-ylmethyl 4-[2-(4-fluorophenoxy)ethyl]piperidine-1-carboxylate

Thiazol-5-ylmethyl 4-[2-(4-chlorophenoxy)ethyl]piperidine-1-carboxylate

Thiazol-5-ylmethyl 4-[2-(4-{trifluoromethyl}phenoxy)-ethyl]piperidine-1-carboxylate

Thiazol-4-ylmethyl 4-[2-(7-methoxynaphth-2-yloxy)ethyl]-piperidine-1-carboxylate

Thiazol-4-ylmethyl 4-[2-(4-cyanophenoxy)ethyl]piperidine-1-carboxylate

Thiazol-4-ylmethyl (+/-)-3-(6-methoxynaphth-2-yloxy-methyl)pyrrolidine-1-carboxylate

Thiazol-4-ylmethyl (+/-)-3-(7-methoxynaphth-2-yloxy-methyl)pyrrolidine-1-carboxylate

Thiazol-4-ylmethyl (+/-)-3-(3,4-dichlorophenoxy-methyl)pyrrolidine-1-carboxylate

Thiazol-4-ylmethyl 4-[2-(6-methoxynaphth-2-yloxy)-ethyl]piperidine-1-carboxylate

Thiazol-4-ylmethyl 4-[2-(naphth-2-yloxy)ethyl]piperidine-1-carboxylate

Thiazol-4-ylmethyl (+/-)-3-(4-chloronaphth-1-yloxy-methyl)pyrrolidine-1-carboxylate

Thiazol-4-ylmethyl (+/-)-3-(naphth-2-yloxymethyl)pyrrolidine-1-carboxylate

Thiazol-4-ylmethyl 4-[2-(4'-fluorobiphenyl-4-yloxy)-ethyl]piperidine-1-carboxylate

Thiazol-4-ylmethyl 4-[2-(quinolin-6-yloxy)ethyl]piperidine-1-carboxylate and its hydrochloride

Thiazol-4-ylmethyl 4-[2-(isoquinolin-6-yloxy)ethyl]piperidine-1-carboxylate and its hydrochloride

Thiazol-4-ylmethyl (+/-)-3-(3'-cyanobiphenyl-3-yloxymethyl)pyrrolidine-1-carboxylate

Thiazol-4-ylmethyl (+/-)-3-(4'-fluorobiphenyl-4-yloxymethyl)pyrrolidine-1-carboxylate

Thiazol-4-ylmethyl (+/-)-3-(5-chloronaphth-2-yloxy-methyl)pyrrolidine-1-carboxylate

Thiazol-4-ylmethyl (+/-)-3-(3-{trifluoromethoxy}-phenoxymethyl)pyrrolidine-1-carboxylate

Thiazol-4-ylmethyl (+/-)-3-[4-(1-methyl-1-phenyl-ethyl)phenoxymethyl]pyrrolidine-1-carboxylate

Thiazol-4-ylmethyl (+/-)-3-(quinolin-3-yloxymethyl)pyrrolidine-1-carboxylate

Thiazol-4-ylmethyl (+/-)-3-(isoquinolin-6-yloxy-methyl)pyrrolidine-1-carboxylate

Thiazol-4-ylmethyl (+/-)-3-(quinolin-7-yloxymethyl)pyrrolidine-1-carboxylate

Thiazol-4-ylmethyl (+/-)-3-(isoquinolin-7-yloxy-methyl)pyrrolidine-1-carboxylate

Thiazol-4-ylmethyl (+/-)-3-(4-chloro-3-{trifluoro-methyl}phenoxymethyl)pyrrolidine-1-carboxylate

Thiazol-4-ylmethyl (+/-)-3-(5-fluoronaphth-2-yloxy-methyl)pyrrolidine-1-carboxylate

Thiazol-2-ylmethyl 4-[2-(2,4-dimethylphenoxy)ethyl]piperidine-1-carboxylate

Thiazol-2-ylmethyl 4-[2-(2,3-dichlorophenoxy)ethyl]piperidine-1-carboxylate

Thiazol-2-ylmethyl 4-[2-(2,4-dichlorophenoxy)ethyl]piperidine-1-carboxylate

Thiazol-2-ylmethyl 4-[2-(2,5-dichlorophenoxy)ethyl]piperidine-1-carboxylate

Thiazol-2-ylmethyl 4-[2-(3,4-dichlorophenoxy)ethyl]piperidine-1-carboxylate

Thiazol-2-ylmethyl 4-[2-(3,5-dichlorophenoxy)ethyl]piperidine-1-carboxylate

Thiazol-2-ylmethyl 4-[2-(4-cyclopentylphenoxy)ethyl]piperidine-1-carboxylate

Thiazol-2-ylmethyl 4-[2-(2-{benzoxazol-2-yl}phenoxy)-ethyl]piperidine-1-carboxylate

Thiazol-2-ylmethyl 4-[2-(4-{benzyloxy}phenoxy)ethyl]piperidine-1-carboxylate

Thiazol-2-ylmethyl 4-[2-(4-{carbamoylmethyl}phenoxy)-ethyl]piperidine-1-carboxylate

Thiazol-2-ylmethyl 4-[2-(quinolin-7-yloxy)ethyl]piperidine-1-carboxylate and its trifluoroacetate

Thiazol-2-ylmethyl 4-[2-(quinolin-6-yloxy)ethyl]piperidine-1-carboxylate and its trifluoroacetate

Thiazol-2-ylmethyl 4-[2-(4-cyano-3-fluorophenoxy)-ethyl]piperidine-1-carboxylate

Thiazol-2-ylmethyl 4-[2-(biphenyl-2-yloxy)ethyl]piperidine-1-carboxylate

Thiazol-2-ylmethyl 4-[2-(2-isopropyl-5-methyl-phenoxy)ethyl]piperidine-1-carboxylate

Thiazol-2-ylmethyl 4-[2-(3-{trifluoromethyl}-phenoxy)ethyl]piperidine-1-carboxylate

Thiazol-2-ylmethyl 4-{2-[4-(1,1,3,3-tetramethyl-butyl)phenoxy]ethyl}piperidine-1-carboxylate

Thiazol-2-ylmethyl 4-[2-(4-benzylphenoxy)ethyl]piperidine-1-carboxylate

Thiazol-2-ylmethyl 4-[2-(4-{pyrrol-1-yl}phenoxy)-ethyl]piperidine-1-carboxylate and its trifluoroacetate

Thiazol-2-ylmethyl 4-[2-(4-carbamoylphenoxy)ethyl]piperidine-1-carboxylate

Thiazol-2-ylmethyl 4-[2-(3-cyanophenoxy)ethyl]piperidine-1-carboxylate

Thiazol-2-ylmethyl 4-[2-(3,5-di{tert-butyl}phenoxy)-ethyl]piperidine-1-carboxylate

Thiazol-2-ylmethyl 4-[2-(2-benzylphenoxy)ethyl]piperidine-1-carboxylate

Thiazol-2-ylmethyl 4-[2-(8-{acetylamino}naphth-2-yloxy)ethyl]piperidine-1-carboxylate

Thiazol-2-ylmethyl 4-[2-(3-{methoxycarbonyl}naphth-2-yloxy)ethyl]piperidine-1-carboxylate

Thiazol-2-ylmethyl 4-[2-(3-phenoxyphenoxy)ethyl]piperidine-1-carboxylate

Thiazol-2-ylmethyl 4-[2-(isoquinolin-7-yloxy)ethyl]piperidine-1-carboxylate and its trifluoroacetate

Thiazol-2-ylmethyl 4-[2-(4-hexyloxyphenoxy)ethyl]piperidine-1-carboxylate

Thiazol-2-ylmethyl 4-[2-(3-butoxyphenoxy)ethyl]piperidine-1-carboxylate

Thiazol-2-ylmethyl 4-[2-(quinolin-5-yloxy)ethyl]piperidine-1-carboxylate and its trifluoroacetate

Thiazol-2-ylmethyl 4-[2-(3-{pentafluoroethyl}-phenoxy)ethyl]piperidine-1-carboxylate

Thiazol-2-ylmethyl 4-[2-(5-{acetylamino}naphth-2-yloxy)ethyl]piperidine-1-carboxylate

Thiazol-2-ylmethyl 4-[2-(5-bromo-2-chlorophenoxy)-ethyl]piperidine-1-carboxylate

Thiazol-2-ylmethyl 4-[2-(2-methylquinolin-6-yloxy)-ethyl]piperidine-1-carboxylate and its trifluoroacetate

Thiazol-2-ylmethyl 4-[2-(4'-cyanobiphenyl-3-yloxy)-ethyl]piperidine-1-carboxylate

Thiazol-2-ylmethyl 4-[2-(6-cyanonaphth-2-yloxy)ethyl]piperidine-1-carboxylate

Thiazol-2-ylmethyl 4-[2-(4-{thiazol-2-yl}phenoxy)-ethyl]piperidine-1-carboxylate

Thiazol-2-ylmethyl 4-[2-(biphenyl-3-yloxy)ethyl]piperidine-1-carboxylate

Thiazol-2-ylmethyl 4-[2-(biphenyl-4-yloxy)ethyl]piperidine-1-carboxylate

Thiazol-2-ylmethyl 4-[2-(2-cyanoquinolin-8-yloxy)-ethyl]piperidine-1-carboxylate and its trifluoroacetate

Thiazol-2-ylmethyl 4-[2-(4-chloro-2-cyanophenoxy)-ethyl]piperidine-1-carboxylate and its trifluoroacetate

Thiazol-2-ylmethyl 4-[2-(2-methylbenzothiazol-5-yloxy)ethyl]piperidine-1-carboxylate

Thiazol-2-ylmethyl 4-[2-(4'-cyanobiphenyl-4-yloxy)-ethyl]piperidine-1-carboxylate

Thiazol-2-ylmethyl 4-[2-(2-{morpholin-4-yl}phenoxy)-ethyl]piperidine-1-carboxylate

Thiazol-2-ylmethyl 4-[2-(4-chloro-2-{isoxazol-5-yl}-phenoxy)ethyl]piperidine-1-carboxylate

Thiazol-4-ylmethyl 4-[2-(2,4-dimethylphenoxy)ethyl]piperidine-1-carboxylate

Thiazol-4-ylmethyl 4-[2-(2,3-dichlorophenoxy)ethyl]piperidine-1-carboxylate

Thiazol-4-ylmethyl 4-[2-(naphth-1-yloxy)ethyl]piperidine-1-carboxylate

Thiazol-4-ylmethyl 4-[2-(3-{dimethylamino}phenoxy)-ethyl]piperidine-1-carboxylate and its trifluoroacetate

Thiazol-4-ylmethyl 4-[2-(3-{trifluoromethyl}-phenoxy)ethyl]piperidine-1-carboxylate

Thiazol-4-ylmethyl 4-[2-(4-benzylphenoxy)ethyl]piperidine-1-carboxylate

Thiazol-4-ylmethyl 4-[2-(2-ethoxyphenoxy)ethyl]piperidine-1-carboxylate

Thiazol-4-ylmethyl 4-{2-[4-(1-methyl-1-phenylethyl)-phenoxy]ethyl}piperidine-1-carboxylate

Thiazol-4-ylmethyl 4-[2-(4-phenoxyphenoxy)ethyl]piperidine-1-carboxylate

Thiazol-4-ylmethyl 4-[2-(2-bromo-4-fluorophenoxy)-ethyl]piperidine-1-carboxylate

Thiazol-4-ylmethyl 4-[2-(2-benzylphenoxy)ethyl]piperidine-1-carboxylate

Thiazol-4-ylmethyl 4-[2-(3-phenoxyphenoxy)ethyl]piperidine-1-carboxylate

Thiazol-4-ylmethyl 4-[2-(4-{hexyloxy}phenoxy)ethyl]piperidine-1-carboxylate

Thiazol-4-ylmethyl 4-[2-(3-butoxyphenoxy)ethyl]piperidine-1-carboxylate

Thiazol-4-ylmethyl 4-[2-(4-chloro-5-isopropyl-2-methylphenoxy)ethyl]piperidine-1-carboxylate

Thiazol-4-ylmethyl 4-[2-(3-{pentafluoroethyl}-phenoxy)ethyl]piperidine-1-carboxylate

Thiazol-4-ylmethyl 4-[2-(5-{acetylamino}naphth-2-yloxy)ethyl]piperidine-1-carboxylate

Thiazol-4-ylmethyl 4-[2-(5-bromo-2-chlorophenoxy)-ethyl]piperidine-1-carboxylate

Thiazol-4-ylmethyl 4-[2-(4'-cyanobiphenyl-3-yloxy)-ethyl]piperidine-1-carboxylate

Thiazol-4-ylmethyl 4-[2-(6-cyanonaphth-2-yloxy)ethyl]piperidine-1-carboxylate

Thiazol-4-ylmethyl 4-[2-(4-{thiazol-2-yl}phenoxy)-ethyl]piperidine-1-carboxylate

Thiazol-4-ylmethyl 4-[2-(biphenyl-3-yloxy)ethyl]piperidine-1-carboxylate

Thiazol-4-ylmethyl 4-[2-(biphenyl-4-yloxy)ethyl]piperidine-1-carboxylate

Thiazol-4-ylmethyl 4-[2-(4-chloro-2-cyanophenoxy)-ethyl]piperidine-1-carboxylate

Thiazol-4-ylmethyl 4-[2-(2-methylbenzothiazol-5-yloxy)ethyl]piperidine-1-carboxylate

Thiazol-4-ylmethyl 4-[2-(4'-cyanobiphenyl-4-yloxy)-ethyl]piperidine-1-carboxylate

Thiazol-4-ylmethyl 4-[2-(2-{morpholin-4-yl}phenoxy)-ethyl]piperidine-1-carboxylate and its trifluoroacetate

Thiazol-4-ylmethyl 4-[2-(4-chloro-2-{isoxazol-5-yl}-phenoxy)ethyl]piperidine-1-carboxylate

Thiazol-2-ylmethyl 4-[2-(4-{dimethylaminomethyl}-phenoxy)ethyl]piperidine-1-carboxylate and its trifluoroacetate

Thiazol-2-ylmethyl 4-[2-(naphth-2-yloxy)ethyl]piperidine-1-carboxylate

Thiazol-2-ylmethyl 4-[2-(naphth-1-yloxy)ethyl]piperidine-1-carboxylate

Thiazol-2-ylmethyl 4-[2-(7-methoxynaphth-2-yloxy)-ethyl]piperidine-1-carboxylate

Thiazol-4-ylmethyl 4-[2-(2-cyclopentylphenoxy)ethyl]piperidine-1-carboxylate

Thiazol-4-ylmethyl 4-[2-(2-benzyloxyphenoxy)ethyl]piperidine-1-carboxylate

Thiazol-4-ylmethyl 4-[2-(isoquinolin-7-yloxy)ethyl]piperidine-1-carboxylate and its trifluoroacetate

Thiazol-4-ylmethyl 4-[2-(quinolin-5-yloxy)ethyl]piperidine-1-carboxylate and its trifluoroacetate

Thiazol-4-ylmethyl 4-[2-(2-methylquinolin-6-yloxy)-ethyl]piperidine-1-carboxylate and its trifluoroacetate

Thiazol-4-ylmethyl 4-[2-(2-cyanoquinolin-8-yloxy)-ethyl]piperidine-1-carboxylate and its trifluoroacetate

Thiazol-4-ylmethyl 4-[2-(2,4-dichlorophenoxy)ethyl]piperidine-1-carboxylate

Thiazol-4-ylmethyl 4-[2-(4-cyclopentylphenoxy)ethyl]piperidine-1-carboxylate

Thiazol-4-ylmethyl 4-[2-(2-{benzoxazol-2-yl}-phenoxy)ethyl]piperidine-1-carboxylate

Thiazol-4-ylmethyl 4-[2-(4-cyano-3-fluorophenoxy)-ethyl]piperidine-1-carboxylate

Thiazol-4-ylmethyl 4-{2-[4-(1,1,3,3-tetramethyl-butyl)phenoxy]ethyl}piperidine-1-carboxylate

Thiazol-4-ylmethyl 4-[2-(4-{pyrrol-1-yl}phenoxy)-ethyl]piperidine-1-carboxylate and its trifluoroacetate

Thiazol-4-ylmethyl 4-[2-(3,5-di{tert-butyl}phenoxy)-ethyl]piperidine-1-carboxylate

Thiazol-4-ylmethyl 4-[2-(4-{dimethylaminomethyl}-phenoxy)ethyl]piperidine-1-carboxylate and its trifluoroacetate

Thiazol-4-ylmethyl 4-[2-(2-methylquinolin-8-yloxy)-ethyl]piperidine-1-carboxylate and its trifluoroacetate

Thiazol-4-ylmethyl 4-[2-(3-cyanophenoxy)ethyl]piperidine-1-carboxylate

Thiazol-5-ylmethyl 4-(2-phenoxyethyl)piperidine-1-carboxylate

Thiazol-5-ylmethyl 4-[2-(biphenyl-4-yloxy)ethyl]piperidine-1-carboxylate

Thiazol-5-ylmethyl 4-[2-(4-carbamoylphenoxy)ethyl]piperidine-1-carboxylate

Thiazol-5-ylmethyl 4-[2-(4-fluorophenoxy)ethyl]piperidine-1-carboxylate

Thiazol-5-ylmethyl 4-[2-(2,4-dimethylphenoxy)ethyl]piperidine-1-carboxylate

Thiazol-5-ylmethyl 4-[2-(4-{dimethylaminomethyl}-phenoxy)ethyl]piperidine-1-carboxylate and its trifluoroacetate

Thiazol-5-ylmethyl 4-[2-(2,3-dichlorophenoxy)ethyl]piperidine-1-carboxylate

Thiazol-5-ylmethyl 4-[2-(2,4-dichlorophenoxy)ethyl]piperidine-1-carboxylate

Thiazol-5-ylmethyl 4-[2-(2,5-dichlorophenoxy)ethyl]piperidine-1-carboxylate

Thiazol-5-ylmethyl 4-[2-(3,5-dichlorophenoxy)ethyl]piperidine-1-carboxylate

Thiazol-5-ylmethyl 4-[2-(4-cyclopentylphenoxy)ethyl]piperidine-1-carboxylate

Thiazol-5-ylmethyl 4-[2-(naphth-2-yloxy)ethyl]piperidine-1-carboxylate

Thiazol-5-ylmethyl 4-[2-(naphth-1-yloxy)ethyl]piperidine-1-carboxylate

Thiazol-5-ylmethyl 4-[2-(2-methylquinolin-8-yloxy)-ethyl]piperidine-1-carboxylate

Thiazol-5-ylmethyl 4-[2-(2-{benzoxazol-2-yl}-phenoxy)ethyl]piperidine-1-carboxylate

Thiazol-5-ylmethyl 4-[2-(4-{benzyloxy}phenoxy)ethyl]piperidine-1-carboxylate

Thiazol-5-ylmethyl 4-[2-(4-sulphamoylphenoxy)ethyl]piperidine-1-carboxylate

Thiazol-5-ylmethyl 4-[2-(isoquinolin-5-yloxy)ethyl]piperidine-1-carboxylate

Thiazol-5-ylmethyl 4-[2-(4-{carbamoylmethyl}-phenoxy)ethyl]piperidine-1-carboxylate

Thiazol-5-ylmethyl 4-[2-(quinolin-7-yloxy)ethyl]piperidine-1-carboxylate

Thiazol-5-ylmethyl 4-[2-(quinolin-6-yloxy)ethyl]piperidine-1-carboxylate

Thiazol-5-ylmethyl 4-[2-(quinolin-8-yloxy)ethyl]piperidine-1-carboxylate

Thiazol-5-ylmethyl 4-[2-(3-{dimethylamino}phenoxy)-ethyl]piperidine-1-carboxylate and its trifluoroacetate

Thiazol-5-ylmethyl 4-[2-(4-cyano-3-fluorophenoxy)-ethyl]piperidine-1-carboxylate

Thiazol-5-ylmethyl 4-[2-(biphenyl-2-yloxy)ethyl]piperidine-1-carboxylate

Thiazol-5-ylmethyl 4-[2-(biphenyl-3-yloxy)ethyl]piperidine-1-carboxylate

Thiazol-5-ylmethyl 4-[2-(3-{trifluoromethyl}-phenoxy)ethyl]piperidine-1-carboxylate

Thiazol-5-ylmethyl 4-[2-(4-benzylphenoxy)ethyl]piperidine-1-carboxylate

Thiazol-5-ylmethyl 4-[2-(2-ethoxyphenoxy)ethyl]piperidine-1-carboxylate

Thiazol-5-ylmethyl 4-[2-(2-cyclopentylphenoxy)ethyl]piperidine-1-carboxylate

Thiazol-5-ylmethyl 4-{2-[4-(1-methyl-1-phenylethyl)-phenoxy]ethyl}piperidine-1-carboxylate

Thiazol-5-ylmethyl 4-[2-(4-phenoxyphenoxy)ethyl]piperidine-1-carboxylate

Thiazol-5-ylmethyl 4-[2-(2-bromo-4-fluorophenoxy)-ethyl]piperidine-1-carboxylate

Thiazol-5-ylmethyl 4-[2-(4-{pyrrol-1-yl}phenoxy)-ethyl]piperidine-1-carboxylate

Thiazol-5-ylmethyl 4-[2-(3-cyanophenoxy)ethyl]piperidine-1-carboxylate

Thiazol-5-ylmethyl 4-[2-(3,5-di{tert-butyl}phenoxy)-ethyl]piperidine-1-carboxylate

Thiazol-5-ylmethyl 4-[2-(2-benzylphenoxy)ethyl]piperidine-1-carboxylate

Thiazol-5-ylmethyl 4-[2-(2-{benzyloxy}phenoxy)ethyl]piperidine-1-carboxylate

Thiazol-5-ylmethyl 4-[2-(2-cyanoquinolin-8-yloxy)-ethyl]piperidine-1-carboxylate

Thiazol-5-ylmethyl 4-[2-(3-{methoxycarbonyl}naphth-2-yloxy)ethyl]piperidine-1-carboxylate

Thiazol-5-ylmethyl 4-[2-(3-phenoxyphenoxy)ethyl]piperidine-1-carboxylate

Thiazol-5-ylmethyl 4-[2-(4-chloro-2-cyanophenoxy)-ethyl]piperidine-1-carboxylate

Thiazol-5-ylmethyl 4-[2-(isoquinolin-7-yloxy)ethyl]piperidine-1-carboxylate

Thiazol-5-ylmethyl 4-[2-(4-{hexyloxy}phenoxy)ethyl]piperidine-1-carboxylate

Thiazol-5-ylmethyl 4-[2-(3-butoxyphenoxy)ethyl]piperidine-1-carboxylate

Thiazol-5-ylmethyl 4-[2-(4-chloro-5-isopropyl-2-methylphenoxy)ethyl]piperidine-1-carboxylate

Thiazol-5-ylmethyl 4-[2-(2-methylbenzothiazol-5-yloxy)ethyl]piperidine-1-carboxylate

Thiazol-5-ylmethyl 4-[2-(quinolin-5-yloxy)ethyl]piperidine-1-carboxylate

Thiazol-5-ylmethyl 4-[2-(3-{pentafluoroethyl}-phenoxy)ethyl]piperidine-1-carboxylate

Thiazol-5-ylmethyl 4-[2-(5-bromo-2-chlorophenoxy)-ethyl]piperidine-1-carboxylate

Thiazol-5-ylmethyl 4-[2-(4-{difluoromethoxy}phenoxy)-ethyl]piperidine-1-carboxylate

Thiazol-5-ylmethyl 4-[2-(4'-cyanobiphenyl-3-yloxy)-ethyl]piperidine-1-carboxylate

Thiazol-5-ylmethyl 4-[2-(6-cyanonaphth-2-yloxy)ethyl]piperidine-1-carboxylate

Thiazol-5-ylmethyl 4-[2-(4-{thiazol-2-yl}phenoxy)-ethyl]piperidine-1-carboxylate

Thiazol-5-ylmethyl 4-[2-(7-methoxynaphth-2-yloxy)-ethyl]piperidine-1-carboxylate

Thiazol-5-ylmethyl 4-[2-(4-chloro-2-{isoxazol-5-yl}-phenoxy)ethyl]piperidine-1-carboxylate

Thiazol-5-ylmethyl 4-[2-(2-carbamoyl-4-chloro-phenoxy)ethyl]piperidine-1-carboxylate

Thiazol-5-ylmethyl 4-[2-(5-{acetylamino}naphth-2-yloxy)ethyl]piperidine-1-carboxylate

Thiazol-5-ylmethyl 4-[2-(4'-cyanobiphenyl-4-yloxy)-ethyl]piperidine-1-carboxylate

Thiazol-5-ylmethyl 4-[2-(4-{methanesulphonyl}-phenoxy)ethyl]piperidine-1-carboxylate

Thiazol-5-ylmethyl 4-[2-(5-acetylamino-2-propyl-phenoxy)ethyl]piperidine-1-carboxylate

Thiazol-5-ylmethyl 4-[2-(1H-indol-6-yloxy)ethyl]piperidine-1-carboxylate

Thiazol-5-ylmethyl 4-{2-[4-fluoro-2-(1H-pyrazol-3-yl)phenoxy]ethyl}piperidine-1-carboxylate

Thiazol-5-ylmethyl 4-[2-(4-cyano-2-fluorophenoxy)-ethyl]piperidine-1-carboxylate

Thiazol-5-ylmethyl 4-[2-(2-isopropyl-5-methyl-phenoxy)ethyl]piperidine-1-carboxylate

Thiazol-5-ylmethyl 4-[2-(2-{morpholin-4-yl}phenoxy)-ethyl]piperidine-1-carboxylate and its trifluoroacetate

Thiazol-5-ylmethyl 4-[2-(2-methylquinolin-6-yloxy)-ethyl]piperidine-1-carboxylate

Thiazol-5-ylmethyl 4-{2-[4-(2-oxopyrrolidin-1-yl)-phenoxy]ethyl}piperidine-1-carboxylate

Thiazol-5-ylmethyl 4-[2-(3-{tetrazol-1-yl}phenoxy)-ethyl]piperidine-1-carboxylate

Thiazol-2-ylmethyl (R)-3-(naphth-2-yloxymethyl)pyrrolidine-1-carboxylate (enantiomer I)

Thiazol-2-ylmethyl (S)-3-(naphth-2-yloxymethyl)pyrrolidine-1-carboxylate (enantiomer II)

Thiazol-2-ylmethyl (+/-)-3-(5-chloronaphth-2-yloxymethyl)pyrrolidine-1-carboxylate

Thiazol-2-ylmethyl (+/-)-3-(4'-fluorobiphenyl-4-yloxymethyl)pyrrolidine-1-carboxylate

3-Carbamoylisoxazol-5-ylmethyl 4-[2-(4-fluorophenoxy)ethyl]piperidine-1-carboxylate

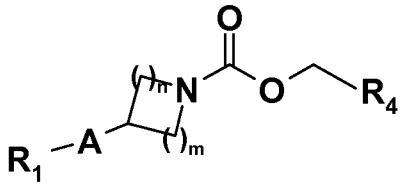
3-Carbamoylisoxazol-5-ylmethyl 4-[2-(4-{trifluoromethoxy}phenoxy)ethyl]piperidine-1-carboxylate

3-Carbamoylisoxazol-5-ylmethyl (-)-(R)-3-(naphth-2-yloxymethyl)pyrrolidine-1-carboxylate (enantiomer I)

3-Carbamoylisoxazol-5-ylmethyl (+/-)-3-(6-methoxynaphth-2-yloxymethyl)pyrrolidine-1-carboxylate

3-Carbamoylisoxazol-5-ylmethyl (+)-(S)-3-(naphth-2-yloxymethyl)pyrrolidine-1-carboxylate (enantiomer II).

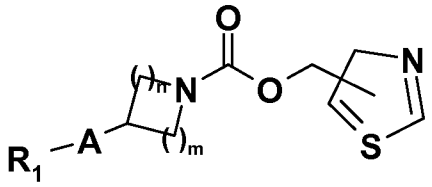
9. Compound according to any one of the preceding claims, characterized in that the compound is of formula (Ii):



(Ii)

in which R_1, A, R_4, n and m are as defined in one of the preceding claims;
in the form of the base or of an addition salt with an acid.

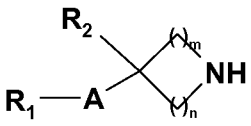
10. Compound according to any one of the preceding claims, characterized in that the compound is of formula (Iii):



(Iii)

in which R_1, A, n and m are as defined in one of Claims 1 to 9; in the form of the base or of an addition salt with an acid.

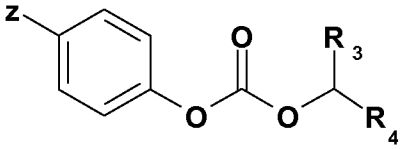
11. Process for the preparation of a compound according to any one of Claims 1 to 10, comprising the stage consisting in reacting an amine derivative, a compound of following general formula (II):



(II)

in which R_1, R_2, A, n and m are as defined in one of the preceding claims,

with a carbonate of following general formula (III):



(III)

in which Z represents a hydrogen atom or a nitro group and R_3 and R_4 are as defined in one of the preceding claims,

in the presence of a base, such as triethylamine, pyridine, *N*,*N*-dimethylaminopyridine or *N*,*N*-diisopropyl-ethylamine, in an organic solvent, such as toluene, acetonitrile or dichloroethane, at a temperature between ambient temperature and the reflux temperature of the solvent.

12. Compound according to any one of Claims 1 to 10, in the form of a base or of an addition salt with a pharmaceutically acceptable acid, for the use thereof as medicament.

13. Pharmaceutical composition comprising at least one compound according to any one of Claims 1 to 10, in the form of the base or of an addition salt with a pharmaceutically acceptable acid, and optionally one or more pharmaceutically acceptable excipients.

14. Compound according to any one of Claims 1 to 10 in the form of the base or of an addition salt with a pharmaceutically acceptable acid, for its use in the preparation of a medicament intended to prevent or to treat a pathology in which endogenous cannabinoids and/or any other substrate metabolized by the enzyme FAAH are involved.

15. Compound according to any one of Claims 1 to 10, in the form of the base or of an addition salt with a pharmaceutically acceptable acid, for its use in the preparation of a medicament intended to prevent or treat acute or chronic pain of neurogenic type, acute or chronic pain associated with inflammatory diseases, acute or chronic peripheral pain, dizziness, vomiting, nausea, eating disorders, neurological and psychiatric pathologies, acute or chronic neurodegenerative diseases, epilepsy, sleep disorders, cardiovascular diseases, renal ischaemia, cancers, disorders of the immune system, allergic diseases, parasitic, viral or bacterial infectious diseases, inflammatory diseases, osteoporosis, eye conditions, pulmonary conditions, gastrointestinal diseases, urinary incontinence or bladder inflammation.