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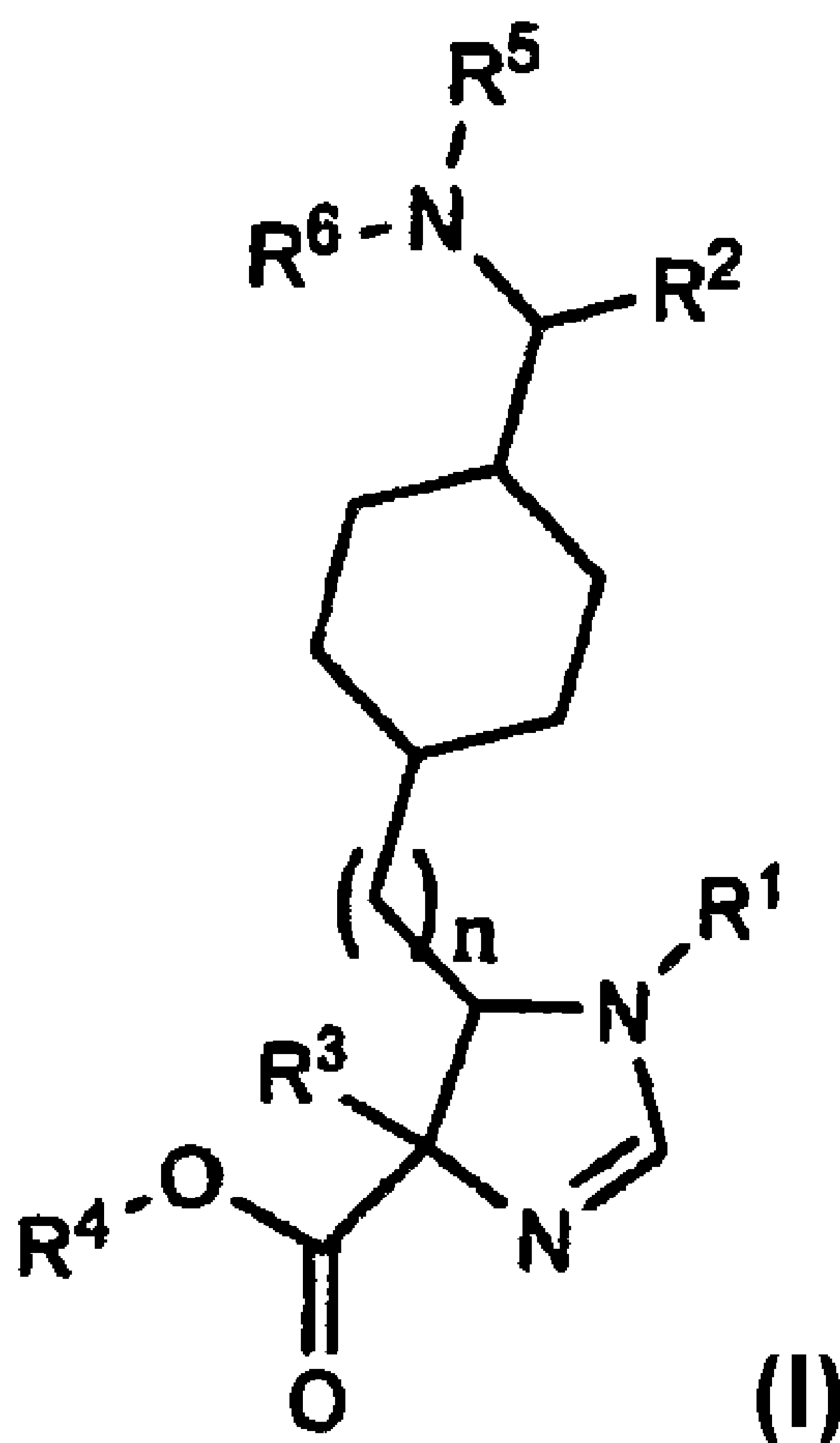
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(54) Titre : DERIVES IMIDAZOLINE SUBSTITUES  
(54) Title: SUBSTITUTED IMIDAZOLINE DERIVATIVES



(57) Abrégé/Abstract:

The invention relates to substituted imidazoline derivatives of formula (I), to a method for their production, to medicaments containing said compounds and to the use of substituted imidazoline derivatives for producing medicaments.

Abstract

The invention relates to substituted imidazoline derivatives of formula (I), to a method for their production, to medicaments containing said compounds and to  
5 the use of substituted imidazoline derivatives for producing medicaments.

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Aachen

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### Substituted imidazoline derivatives

The present invention relates to substituted imidazoline derivatives, processes for their preparation, medicaments  
10 containing these compounds, and the use of substituted imidazoline derivatives for the preparation of medicaments.

The treatment of chronic and non-chronic pain states is extremely important in medicine. There is therefore a  
15 widespread need for highly effective pain treatments. The urgent need for a patient-friendly and targeted treatment of chronic and non-chronic pain states, which from the patient's point of view is hereinafter understood to mean the successful and satisfactory handling and treatment of  
20 pain, is well documented in the large number of scientific papers and articles that have appeared in recent years in the field of applied analgesics and in basic research on nociception.

25 Conventional opioids such as morphine are highly effective in the treatment of severe to extremely severe pain. Their use is however limited by their known side effects, for example respiratory depression, nausea, vomiting, sedation, constipation and development of tolerance. Also, they are  
30 less effective in neuropathic or incidental pain, including in particular tumour patients.

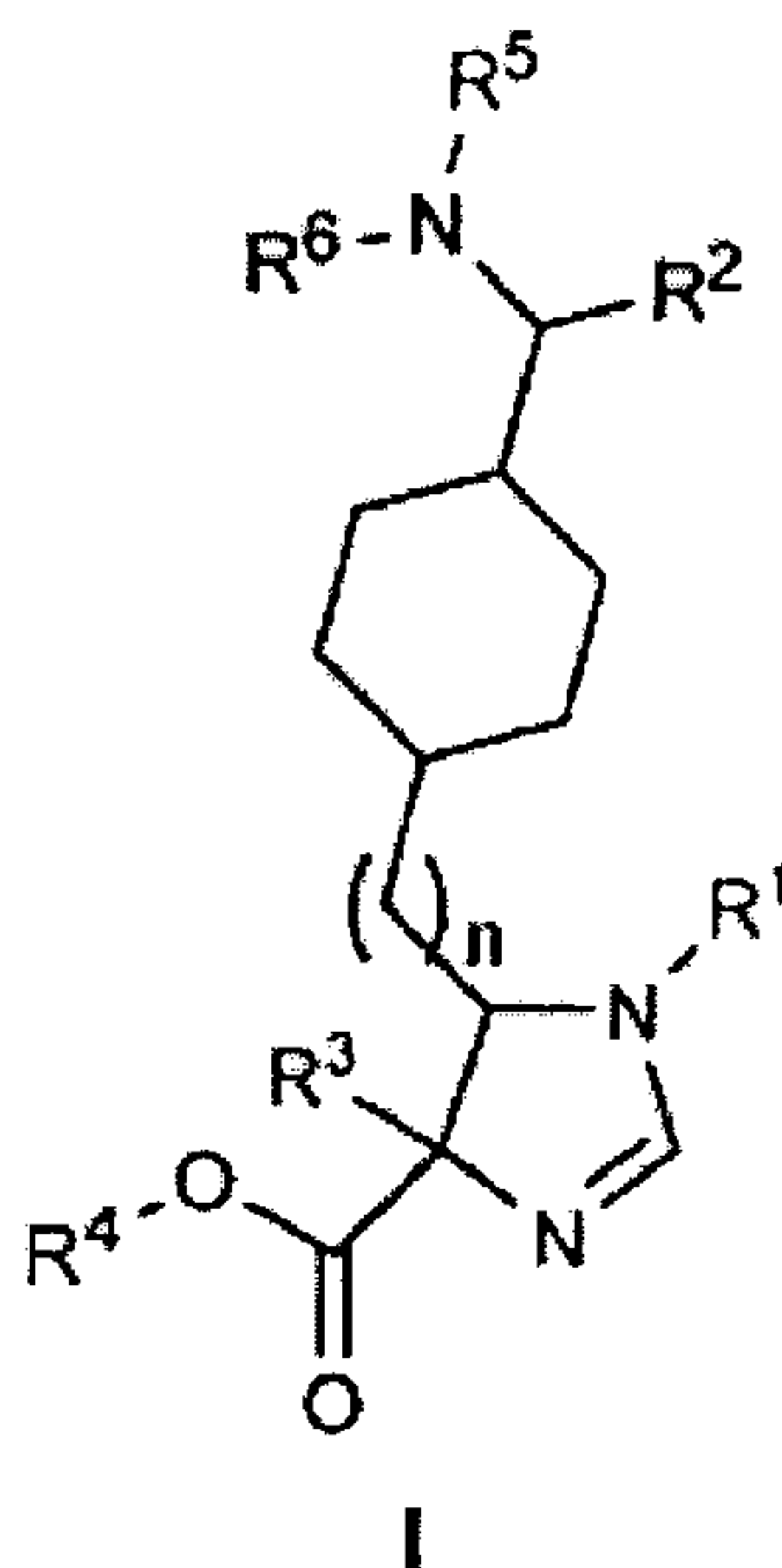
In Org. Lett. 2003, 5, 3759-3762 substituted imidazolines with a carboxylic acid/carboxylic acid ester group are likewise disclosed, which however are not coupled to an aminomethyl-substituted cyclohexane ring.

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A basic object of the invention was to provide new analgesically effective substances that are suitable for treating pain, in particular also chronic and neuropathic pain.

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The invention accordingly provides substituted imidazoline derivatives of the general Formula I



, wherein

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n is 0, 1 or 2;

R<sup>1</sup> denotes C<sub>1-8</sub>-alkyl, saturated or unsaturated, branched or unbranched, unsubstituted or monosubstituted or polysubstituted; C<sub>3-8</sub>-cycloalkyl, saturated or unsaturated, unsubstituted or monosubstituted or polysubstituted; an aryl or heteroaryl radical bonded via a C<sub>1-3</sub>-alkyl chain, in

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each case unsubstituted or monosubstituted or polysubstituted;

5  $R^2$  denotes aryl or heteroaryl, in each case unsubstituted or monosubstituted or polysubstituted; an aryl radical bonded via a  $C_{1-3}$ -alkyl chain, in each case unsubstituted or monosubstituted or polysubstituted;

10  $R^3$  denotes  $C_{1-8}$ -alkyl, saturated or unsaturated, branched or unbranched, unsubstituted or monosubstituted or polysubstituted; an aryl radical bonded via a  $C_{1-3}$ -alkyl chain, in each case unsubstituted or monosubstituted or polysubstituted;

15  $R^4$  denotes H,  $C_{1-4}$ -alkyl, or an aryl radical bonded via a  $C_{1-3}$ -alkyl chain;

$R^5$  and  $R^6$  independently of one another denote H;  $C_{1-6}$ -alkyl, in each case saturated or unsaturated, branched or  
20 unbranched, wherein  $R^5$  and  $R^6$  do not simultaneously denote H,

or the radicals  $R^5$  and  $R^6$  together denote  $CH_2CH_2OCH_2CH_2$  or  $(CH_2)_{3-6}$ ,

25

in the form of the racemate; in the form of the enantiomers, diastereomers, mixtures of the enantiomers or diastereomers or in the form of an individual enantiomer or diastereomer; in the form of the bases and/or salts of  
30 physiological compatible acids.

The compounds have an affinity for the  $\mu$ -opioid receptor.

The expressions "C<sub>1-8</sub>-alkyl", "C<sub>1-3</sub>-alkyl", "C<sub>1-4</sub>-alkyl" and "C<sub>1-6</sub>-alkyl" include in the context of the present invention acyclic saturated or unsaturated hydrocarbon radicals, which can be branched or straight-chain, as well as  
5 unsubstituted or monosubstituted or polysubstituted, with 1 to 8 or 1 to 3 C atoms or 1 to 4 C atoms or 1 to 6 C atoms, i.e. C<sub>1-8</sub>-alkanyls, C<sub>2-8</sub>-alkenyls and C<sub>2-8</sub>-alkinyls, or C<sub>1-3</sub>-alkanyls, C<sub>2-3</sub>-alkenyls and C<sub>2-3</sub>-alkinyls, or C<sub>1-4</sub>-alkanyls, C<sub>2-4</sub>-alkenyls and C<sub>2-4</sub>-alkinyls, or C<sub>1-6</sub>-alkanyls, C<sub>2-6</sub>-  
10 alkenyls and C<sub>2-6</sub>-alkinyls. In this connection alkenyls have at least one C-C double bond and alkinyls have at least one C-C triple bond. Advantageously the alkyl is selected from the group comprising methyl, ethyl, n-propyl, 2-propyl, n-butyl, iso-butyl, sec.-butyl, tert.-butyl,  
15 n-pentyl, iso-pentyl, neo-pentyl, n-hexyl, 2-hexyl, n-heptyl, n-octyl, 1,1,3,3-tetramethylbutyl; ethylenyl (vinyl), ethinyl, propenyl (-CH<sub>2</sub> CH=CH<sub>2</sub>, -CH=CH-CH<sub>3</sub>, -C(=CH<sub>2</sub>)-CH<sub>3</sub>), propinyl (-CH-C≡CH, -C≡C-CH<sub>3</sub>), butenyl, butinyl, pentenyl, pentinyl, hexenyl, hexinyl, heptenyl,  
20 heptinyl, octenyl and octinyl. Particularly preferred are methyl, ethyl, n-propyl, n-butyl, sec-butyl, iso-butyl.

The expression "cycloalkyl" or "C<sub>3-8</sub>-cycloalkyl" denotes, for the purposes of the present invention, cyclic  
25 hydrocarbons with 3, 4, 5, 6, 7 or 8 carbon atoms, in which the hydrocarbon radicals can be saturated or unsaturated (but not aromatic), unsubstituted or monosubstituted or polysubstituted. With regard to cycloalkyl the expression also includes saturated or unsaturated (but not aromatic)  
30 cycloalkyls in which one or two carbon atoms is/are replaced by a heteroatom S, N or O. Advantageously the C<sub>3-8</sub>-cycloalkyl is selected from the group comprising cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl,

cycloheptyl, cyclooctyl, cyclopentenyl, cyclohexenyl, cycloheptenyl and cyclooctenyl, but also tetrahydropyranyl, dioxanyl, dioxolanyl, morpholinyl, piperidinyl, piperazinyl, pyrazolinonyl and pyrrolidinyl.

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The expression "aryl" denotes within the meaning of the present invention aromatic hydrocarbons, inter alia phenyls and naphthyls. The aryl radicals can also be condensed with further saturated, (partially) unsaturated or aromatic  
10 ring systems. Each aryl radical can be unsubstituted or monosubstituted or polysubstituted, wherein the aryl substituents can be identical or different and can be in any arbitrary and possible position of the aryl radical. Advantageously aryl is selected from the group containing  
15 phenyl, 1-naphthyl, 2-naphthyl, which can in each case be unsubstituted or monosubstituted or polysubstituted. The phenyl radical is particularly advantageous.

The expression "heteroaryl" denotes a 5-, 6- or 7-membered  
20 cyclic aromatic radical that contains at least 1, possibly also 2, 3, 4 or 5 heteroatoms, in which the heteroatoms are identical or different and the heterocycle can be unsubstituted or monosubstituted or polysubstituted; in the case of the substitution on the heterocycle, the  
25 substituents can be identical or different and can be in any arbitrary and possible position of the heteroaryl. The heterocycle can also be part of a bicyclic or polycyclic system. Preferred heteroatoms are nitrogen, oxygen and sulfur. It is preferred that the heteroaryl radical is  
30 selected from the group containing pyrrolyl, indolyl, furyl (furanlyl), benzofuranlyl, thienyl (thiophenyl), benzothienyl, benzothiadiazolyl, benzothiazolyl, benzotriazolyl, benzodioxolanyl, benzodioxanyl,

phthalazinyl, pyrazolyl, imidazolyl, thiazolyl, oxazolyl, isoxazolyl, pyridyl, pyridazinyl, pyrimidinyl, pyrazinyl, pyranyl, indazolyl, purinyl, indolizinyl, quinolinyl, isoquinolinyl, quinazolinyl, carbazolyl, phenazinyl, phenothiazinyl or oxadiazolyl, wherein the bonding to the compounds of the general structure I can be effected via any arbitrary and possible ring member of the heteroaryl radical. Pyridyl, furyl, thienyl and indolyl are particularly preferred.

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The expression "aryl or heteroaryl bonded via C<sub>1-3</sub>-alkyl" denotes, for the purposes of the present invention, that C<sub>1-3</sub>-alkyl and aryl or heteroaryl have the meanings defined above and that the aryl or heteroaryl radical is bonded via a C<sub>1-3</sub>-alkyl group to the compound of the general structure I. Within the context of the present invention benzyl and phenethyl are particularly advantageous.

In connection with "alkyl" or "cycloalkyl", the term "substituted" is understood within the context of the present invention to denote the substitution of a hydrogen atom by F, Cl, Br, I, -CN, NH<sub>2</sub>, NH-C<sub>1-6</sub>-alkyl, NH-C<sub>1-6</sub>-alkyl-OH, N(C<sub>1-6</sub>-alkyl)<sub>2</sub>, N(C<sub>1-6</sub>-alkyl-OH)<sub>2</sub>, NO<sub>2</sub>, SH, S-C<sub>1-6</sub>-alkyl, S-benzyl, O-C<sub>1-6</sub>-alkyl, OH, O-C<sub>1-6</sub>-alkyl-OH, =O, C<sub>1-6</sub>-alkyl, benzyl, O-benzyl, C(=O)C<sub>1-6</sub>-alkyl, CO<sub>2</sub>H, CO<sub>2</sub>-C<sub>1-6</sub>-alkyl, wherein polysubstituted radicals are understood to be those radicals that are polysubstituted, for example disubstituted or trisubstituted, either on different atoms or on the same atoms, for example trisubstituted on the same C atom as in the case of CF<sub>3</sub> or -CH<sub>2</sub>CF<sub>3</sub>, or at different sites as in the case of -CH(OH)-CH=CH-CHCl<sub>2</sub>. The polysubstitution can take place with the same or with different substituents. For the purposes of the present

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invention "monosubstituted or polysubstituted" in connection with alkyl particularly preferably denotes S-CH<sub>3</sub>, S-benzyl or COOCH<sub>3</sub>.

5 With regard to "aryl" and "heteroaryl", within the context of the present invention "monosubstituted or polysubstituted" denotes monosubstitution or polysubstitution, for example disubstitution, trisubstitution or tetrasubstitution of one or more  
10 hydrogen atoms of the ring system by F, Cl, Br, I, CN, NH<sub>2</sub>, NH-C<sub>1-6</sub>-alkyl, NH-C<sub>1-6</sub>-alkyl-OH, N(C<sub>1-6</sub>-alkyl)<sub>2</sub>, N(C<sub>1-6</sub>-alkyl-OH)<sub>2</sub>, NO<sub>2</sub>, SH, S-C<sub>1-6</sub>-alkyl, OH, O-C<sub>1-6</sub>-alkyl, O-C<sub>1-6</sub>-alkyl-OH, C(=O)C<sub>1-6</sub>-alkyl, CO<sub>2</sub>H, CO<sub>2</sub>-C<sub>1-6</sub>-alkyl, CF<sub>3</sub>, C<sub>1-6</sub>-alkyl, on one or possibly different atoms (in which connection a  
15 substituent can optionally for its part be substituted). The polysubstitution can in this connection be carried out with the same or with different substituents. For "aryl" and "heteroaryl", preferred substituents in this case are F, -Cl, -CF<sub>3</sub>, -O-CH<sub>3</sub>, methyl, ethyl, n-propyl, nitro,  
20 tert.-butyl, and -CN. Particularly preferred are -F and -Cl.

The expression "salt formed with a physiologically compatible acid" is understood within the context of the  
25 present invention to mean salts of the respective active substance with inorganic or organic acids which are physiologically compatible, especially when used in humans and/or mammals. The hydrochloride is particularly preferred. Examples of physiologically compatible acids  
30 are: hydrochloric acid, hydrobromic acid, sulphuric acid, methanesulfonic acid, formic acid, acetic acid, oxalic acid, succinic acid, tartaric acid, mandelic acid, fumaric acid, lactic acid, citric acid, glutamic acid, 1,1-dioxo-

1,2-dihydro-1 $\lambda$ <sup>6</sup>-benzo[d]isothiazol-3-one (saccharinic acid), monomethylsebacic acid, 5-oxo-proline, hexane-1-sulfonic acid, nicotinic acid, 2-, 3- or 4-aminobenzoic acid, 2,4,6-trimethylbenzoic acid,  $\alpha$ -lipoic acid, acetylglycine, hippuric acid, phosphoric acid and/or aspartic acid. Hydrochloric acid is particularly preferred.

The groups (CH<sub>2</sub>)<sub>3-6</sub> and (CH<sub>2</sub>)<sub>4-5</sub> are understood to denote -CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-, -CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>- and CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-, and -CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>- and -CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>.

Preferred within the meaning of the present invention are those substituted imidazoline derivatives in which

R<sup>1</sup> denotes C<sub>1-8</sub>-alkyl, branched or unbranched, saturated or unsaturated, unsubstituted or monosubstituted or polysubstituted with F, Cl, -CN, NH-C<sub>1-6</sub>-alkyl, NH-C<sub>1-6</sub>-alkyl-OH, N(C<sub>1-6</sub>-alkyl)<sub>2</sub>, N(C<sub>1-6</sub>-alkyl-OH)<sub>2</sub>, NO<sub>2</sub>, SH, S-C<sub>1-6</sub>-alkyl, S-benzyl, OH, O-C<sub>1-6</sub>-alkyl-OH, O-C<sub>1-6</sub>-alkyl, O-benzyl, benzyl, C(=O)C<sub>1-6</sub>-alkyl, CO<sub>2</sub>H, CO<sub>2</sub>-C<sub>1-6</sub>-alkyl; C<sub>3-8</sub>-cycloalkyl, in each case unsubstituted or monosubstituted or polysubstituted with F, Cl, -CN, NH-C<sub>1-6</sub>-alkyl, NH-C<sub>1-6</sub>-alkyl-OH, N(C<sub>1-6</sub>-alkyl)<sub>2</sub>, N(C<sub>1-6</sub>-alkyl-OH)<sub>2</sub>, NO<sub>2</sub>, SH, S-C<sub>1-6</sub>-alkyl, S-benzyl, benzyl, C<sub>1-6</sub>-alkyl, OH, O-C<sub>1-6</sub>-alkyl-OH, O-benzyl, C(=O)C<sub>1-6</sub>-alkyl, CO<sub>2</sub>H, CO<sub>2</sub>-C<sub>1-6</sub>-alkyl; a phenyl, furyl, thienyl or indolyl radical bonded via a C<sub>1-3</sub>-alkyl chain, in each case unsubstituted or monosubstituted or polysubstituted with F, Cl, CN, NH-C<sub>1-6</sub>-alkyl, NH-C<sub>1-6</sub>-alkyl-OH, N(C<sub>1-6</sub>-alkyl)<sub>2</sub>, N(C<sub>1-6</sub>-alkyl-OH)<sub>2</sub>, NO<sub>2</sub>, SH, S-C<sub>1-6</sub>-alkyl, OH, O-C<sub>1-6</sub>-alkyl, O-C<sub>1-6</sub>-alkyl-OH, C(=O)C<sub>1-6</sub>-alkyl, CO<sub>2</sub>H, CO<sub>2</sub>-C<sub>1-6</sub>-alkyl, CF<sub>3</sub>, C<sub>1-6</sub>-alkyl;

preferably

R<sup>1</sup> denotes C<sub>1-8</sub>-alkyl, branched or unbranched, unsubstituted or monosubstituted or polysubstituted with F, Cl, -CN, SH, S-C<sub>1-6</sub>-alkyl, S-benzyl, OH, O-benzyl, O-C<sub>1-6</sub>-alkyl, CO<sub>2</sub>H, CO<sub>2</sub>-C<sub>1-6</sub>-alkyl; C<sub>3-8</sub>-cycloalkyl, in each case unsubstituted or monosubstituted or polysubstituted with F, Cl, -CN, SH, S-C<sub>1-6</sub>-alkyl, C<sub>1-6</sub>-alkyl, S-benzyl, OH, O-benzyl, O-C<sub>1-6</sub>-alkyl, CO<sub>2</sub>H, CO<sub>2</sub>-C<sub>1-6</sub>-alkyl; a phenyl radical bonded via a C<sub>1-3</sub>-alkyl chain, in each case unsubstituted or monosubstituted or polysubstituted with F, Cl, CN, NO<sub>2</sub>, SH, S-C<sub>1-6</sub>-alkyl, OH, O-C<sub>1-6</sub>-alkyl, CO<sub>2</sub>H, CO<sub>2</sub>-C<sub>1-6</sub>-alkyl, CF<sub>3</sub>, C<sub>1-6</sub>-alkyl;

in particular

R<sup>1</sup> denotes C<sub>1-8</sub>-alkyl, branched or unbranched; C<sub>3-8</sub>-cycloalkyl; a phenyl radical bonded via a C<sub>1-3</sub>-alkyl chain.

Particularly preferred are imidazoline derivatives in which R<sup>1</sup> denotes cyclohexyl, n-propyl, n-butyl, phenethyl or benzyl.

Preferred within the context of the present invention are also substituted imidazoline derivatives in which

R<sup>2</sup> denotes phenyl, thienyl or pyridyl, in each case unsubstituted or monosubstituted or polysubstituted with F, Cl, CN, NH-C<sub>1-6</sub>-alkyl, NH-C<sub>1-6</sub>-alkyl-OH, N(C<sub>1-6</sub>-alkyl)<sub>2</sub>, N(C<sub>1-6</sub>-alkyl-OH)<sub>2</sub>, NO<sub>2</sub>, SH, S-C<sub>1-6</sub>-alkyl, OH, O-C<sub>1-6</sub>-alkyl, O-C<sub>1-6</sub>-alkyl-OH, C(=O)C<sub>1-6</sub>-alkyl, CO<sub>2</sub>H, CO<sub>2</sub>-C<sub>1-6</sub>-alkyl, CF<sub>3</sub>, C<sub>1-6</sub>-alkyl; an aryl radical bonded via a C<sub>1-3</sub>-alkyl chain, in each case unsubstituted or monosubstituted or

polysubstituted with F, Cl, CN, NH-C<sub>1-6</sub>-alkyl, NH-C<sub>1-6</sub>-alkyl  
-OH, N(C<sub>1-6</sub>-alkyl)<sub>2</sub>, N(C<sub>1-6</sub>-alkyl-OH)<sub>2</sub>, NO<sub>2</sub>, SH, S-C<sub>1-6</sub>-alkyl,  
OH, O-C<sub>1-6</sub>-alkyl, O-C<sub>1-6</sub>-alkyl-OH, C(=O)C<sub>1-6</sub>-alkyl, CO<sub>2</sub>H, CO<sub>2</sub>-  
C<sub>1-6</sub>-alkyl, CF<sub>3</sub>, C<sub>1-6</sub>-alkyl;

5

preferably

R<sup>2</sup> denotes phenyl or thienyl, in each case unsubstituted or  
monosubstituted or polysubstituted with F, Cl, CN, NO<sub>2</sub>, SH,  
10 S-C<sub>1-6</sub>-alkyl, OH, O-C<sub>1-6</sub>-alkyl, CO<sub>2</sub>H, CO<sub>2</sub>-C<sub>1-6</sub>-alkyl, CF<sub>3</sub>, C<sub>1-6</sub>-  
alkyl; a phenyl radical bonded via a C<sub>1-3</sub>-alkyl chain, in  
each case unsubstituted or monosubstituted or  
polysubstituted with F, Cl, CN, NO<sub>2</sub>, SH, S-C<sub>1-6</sub>-alkyl, OH,  
O-C<sub>1-6</sub>-alkyl, CO<sub>2</sub>H, CO<sub>2</sub>-C<sub>1-6</sub>-alkyl, CF<sub>3</sub>, C<sub>1-6</sub>-alkyl;

15

in particular

R<sup>2</sup> denotes phenyl, unsubstituted or monosubstituted or  
polysubstituted with F, Cl, OH, OCH<sub>3</sub>, CF<sub>3</sub> or CH<sub>3</sub>; thienyl; or  
20 a phenyl radical bonded via a C<sub>1-3</sub>-alkyl chain,  
unsubstituted or monosubstituted or polysubstituted with F,  
Cl, CN, OH, OCH<sub>3</sub>, CF<sub>3</sub> or CH<sub>3</sub>.

Most particularly preferred are imidazoline derivates in  
25 which R<sup>2</sup> denotes phenyl, unsubstituted or monosubstituted  
with Cl or F, or denotes thienyl or phenethyl.

Also preferred within the meaning of the present invention  
are substituted imidazoline derivatives in which

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R<sup>3</sup> denotes C<sub>1-8</sub>-alkyl, saturated or unsaturated, branched or  
unbranched, unsubstituted or monosubstituted or  
polysubstituted with F, Cl, -CN, SH, S-C<sub>1-6</sub>-alkyl, S-benzyl,

benzyl, OH, O-benzyl, O-C<sub>1-6</sub>-alkyl, CO<sub>2</sub>H, CO<sub>2</sub>-C<sub>1-6</sub>-alkyl; a phenyl radical bonded via a C<sub>1-3</sub>-alkyl chain, in each case unsubstituted or monosubstituted or polysubstituted with F, Cl, CN, NH-C<sub>1-6</sub>-alkyl, NH-C<sub>1-6</sub>-alkyl-OH, N(C<sub>1-6</sub>-alkyl)<sub>2</sub>, N(C<sub>1-6</sub>-alkyl-OH)<sub>2</sub>, NO<sub>2</sub>, SH, S-C<sub>1-6</sub>-alkyl, OH, O-C<sub>1-6</sub>-alkyl, O-C<sub>1-6</sub>-alkyl-OH, C(=O)C<sub>1-6</sub>-alkyl, CO<sub>2</sub>H, CO<sub>2</sub>-C<sub>1-6</sub>-alkyl, CF<sub>3</sub>, C<sub>1-6</sub>-alkyl,

preferably

10

R<sup>3</sup> denotes C<sub>1-8</sub>-alkyl, branched or unbranched, unsubstituted or monosubstituted or polysubstituted with F, Cl, -CN, SH, S-C<sub>1-6</sub>-alkyl, S-benzyl, OH, O-benzyl, O-C<sub>1-6</sub>-alkyl, CO<sub>2</sub>H, CO<sub>2</sub>-C<sub>1-6</sub>-alkyl; a phenyl radical bonded via a C<sub>1-3</sub>-alkyl chain, in each case unsubstituted or monosubstituted or polysubstituted with F, Cl, CN, NO<sub>2</sub>, SH, S-C<sub>1-6</sub>-alkyl, OH, O-C<sub>1-6</sub>-alkyl, CO<sub>2</sub>H, CO<sub>2</sub>-C<sub>1-6</sub>-alkyl, CF<sub>3</sub>, C<sub>1-6</sub>-alkyl;

in particular

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R<sup>3</sup> denotes C<sub>1-8</sub>-alkyl, branched or unbranched, unsubstituted or monosubstituted or polysubstituted with S-CH<sub>3</sub>, S-benzyl or COOCH<sub>3</sub>; a phenyl radical bonded via a C<sub>1-3</sub>-alkyl chain, in each case unsubstituted or monosubstituted or polysubstituted with F, Cl, CN, OH, O-CH<sub>3</sub>, CF<sub>3</sub>, CH<sub>3</sub>.

Particularly preferred are imidazoline derivatives in which R<sup>3</sup> denotes sec-butyl, iso-butyl, n-butyl, n-propyl, CH<sub>3</sub>, CH<sub>2</sub>-CH<sub>2</sub> COOCH<sub>3</sub>, CH<sub>2</sub>-S-benzyl, CH<sub>2</sub>CH<sub>2</sub>-S-CH<sub>3</sub>, CH<sub>2</sub>-S-CH<sub>3</sub> or 4-Cl-benzyl.

Also preferred within the context of the present invention are imidazoline derivatives in which R<sup>4</sup> denotes C<sub>1-4</sub>-alkyl.

Particularly preferred are imidazoline derivatives in which  $R^4$  denotes  $CH_3$ .

- 5 Also preferred within the meaning of the present invention are imidazoline derivatives in which  $R^5$  and  $R^6$  independently of one another denote H or  $C_{1-6}$ -alkyl, wherein  $R^5$  and  $R^6$  do not simultaneously denote H.
- 10 Furthermore preferred are imidazoline derivatives in which the radicals  $R^5$  and  $R^6$  together denote  $CH_2CH_2OCH_2CH_2$  or  $(CH_2)_{4-5}$ .

Preferably n is 0 or 1.

15

Particularly preferred are imidazoline derivatives in which  $R^5$  and  $R^6$  denote  $CH_3$ .

- Most particularly preferred are substituted imidazoline
- 20 derivatives from the group

1-cyclohexyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexyl}-4-isobutyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester

- 25 4-(4-chlorobenzyl)-1-cyclohexyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexyl}-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester

- 4-butyl-1-cyclohexyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexyl}-4,5-dihydro-1H-imidazole-4-carboxylic
- 30 acid methyl ester

- 5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexyl}-1-cyclohexyl-4-isobutyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 4-(4-chlorobenzyl)-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexyl}-1-cyclohexyl-4,5-dihydro-1H-imidazole-carboxylic acid methyl ester
- 4-butyl-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexyl}-1-cyclohexyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 10 5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexylmethyl}-1-cyclohexyl-4-isobutyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 4-(4-chlorobenzyl)-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexylmethyl}-1-cyclohexyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 15 4-butyl-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexylmethyl}-1-cyclohexyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 4-(4-chlorobenzyl)-1-cyclohexyl-5-[4-(dimethylamino-thiophen-2-yl-methyl)-cyclohexylmethyl]-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 20 5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexyl}-4-isobutyl-1-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 25 4-(4-chlorobenzyl)-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexyl}-1-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester

- 4-butyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexyl}-1-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexyl}-4-isobutyl-1-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 4-(4-chlorobenzyl)-5-{4-[(4-chlorophenyl)-dimethylamino-methyl]-cyclohexyl}-1-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 10 5-(4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexylmethyl)-4-isobutyl-1-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 4-(4-chlorobenzyl)-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexylmethyl}-1-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 15 4-butyl-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexylmethyl}-1-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 1-butyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexyl}-4-isobutyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 20 1-butyl-4-(4-chlorobenzyl)-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexyl}-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 25 1-butyl-5-{4-[(chlorophenyl)-dimethylaminomethyl]-cyclohexyl}-4-isobutyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester

- 1-butyl-4-(4-chlorobenzyl)-5-{4-[(4-chlorophenyl)-  
dimethylaminomethyl]-cyclohexyl}-4,5-dihydro-1H-imidazole-  
4-carboxylic acid methyl ester
- 1,4-dibutyl-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-  
5 cyclohexyl}-4,5-dihydro-1H-imidazole-4-carboxylic acid  
methyl ester
- 1-butyl-5-{4-[(chlorophenyl)-dimethylaminomethyl]-  
cyclohexylmethyl}-4-isobutyl-4,5-dihydro-1H-imidazole-4-  
carboxylic acid methyl ester
- 10 1-butyl-4-(4-chlorobenzyl)-5-{4-[(4-chlorophenyl)-  
dimethylaminomethyl]-cyclohexylmethyl}-4,5-dihydro-1H-  
imidazole-4-carboxylic acid methyl ester
- 1,4-dibutyl-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-  
cyclohexylmethyl}-4,5-dihydro-1H-imidazole-4-carboxylic  
15 acid methyl ester
- 5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexyl}-4-  
isobutyl-1-phenethyl-4,5-dihydro-1H-imidazole-4-carboxylic  
acid methyl ester
- 4-(4-chlorobenzyl)-5-{4-[dimethylamino-(3-fluorophenyl)-  
20 methyl]-cyclohexyl}-1-phenethyl-4,5-dihydro-1H-imidazole-4-  
carboxylic acid methyl ester
- 4-butyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-  
cyclohexyl}-1-phenethyl-4,5-dihydro-1H-imidazole-4-  
carboxylic acid methyl ester
- 25 5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexyl}-4-  
isobutyl-1-phenethyl-4,5-dihydro-1H-imidazole-4-carboxylic  
acid methyl ester

- 4-(4-chlorobenzyl)-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexyl}-1-phenethyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 4-butyl-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexyl}-1-phenethyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexylmethyl}-4-isobutyl-1-phenethyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 10 4-(4-chlorobenzyl)-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexylmethyl}-1-phenethyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 4-butyl-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexylmethyl}-1-phenethyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 15 1-benzyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexyl}-4-isobutyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 1-benzyl-4-(4-chlorobenzyl)-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexyl}-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 20 1-benzyl-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexyl}-4-isobutyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 25 1-benzyl-4-(4-chlorobenzyl)-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexyl}-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester

- 1-benzyl-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexylmethyl}-4-isobutyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexyl}-1-cyclohexyl-4-(2-methoxycarbonyl-ethyl)-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 4-benzylsulfanylmethyl-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexyl}-1-cyclohexyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 10 5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexylmethyl}-1-cyclohexyl-4-(2-methoxycarbonyl-ethyl)-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 1-benzyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexylmethyl}-4-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 15 5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexylmethyl}-1-cyclohexyl-4-methylsulfanylmethyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 4-benzylsulfanylmethyl-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexylmethyl}-1-cyclohexyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 20 5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexyl}-4-methylsulfanylmethyl-1-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 25 4-benzylsulfanylmethyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexyl}-1-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester

- 5- {4- [(4-chlorophenyl)-dimethylaminomethyl]-cyclohexyl}-4-(2-methoxycarbonylethyl)-1-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 4-benzylsulfanylmethyl-5- {4- [(4-chlorophenyl)-dimethylaminomethyl]-cyclohexyl}-1-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 5- {4- [(4-chlorophenyl)-dimethylaminomethyl]-cyclohexylmethyl}-4-(2-methoxycarbonylethyl)-1-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 10 4-sec-butyl-5- {4- [(4-chlorophenyl)-dimethylaminomethyl]-cyclohexylmethyl}-1-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 5- {4- [(4-chlorophenyl)-dimethylaminomethyl]-cyclohexylmethyl}-4-methylsulfanylmethyl-1-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 15 4-benzylsulfanylmethyl-5- {4- [(4-chlorophenyl)-dimethylaminomethyl]-cyclohexylmethyl}-1-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 1-butyl-5- {4- [dimethylamino-(3-fluorophenyl)-methyl]-cyclohexyl}-4-(2-methoxycarbonylethyl)-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 20 1-butyl-5- {4- [dimethylamino-(3-fluorophenyl)-methyl]-cyclohexyl}-4-methylsulfanylmethyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 25 4-benzylsulfanylmethyl-1-butyl-5- {4- [dimethylamino-(3-fluorophenyl)-methyl]-cyclohexyl}-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester

- 1-butyl-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexyl}-4-(2-methoxycarbonylethyl)-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 4-benzylsulfanylmethyl-1-butyl-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexyl}-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 1-butyl-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexylmethyl}-4-(2-methoxycarbonylethyl)-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 10 5-[4-(1-dimethylamino-3-phenylpropyl)-cyclohexylmethyl]-4-(2-methoxycarbonylethyl)-1-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 1-butyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexylmethyl}-4-(2-methoxycarbonylethyl)-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 15 1-butyl-4-sec-butyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexylmethyl}-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 1-butyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexylmethyl}-4-methylsulfanylmethyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 20 4-benzylsulfanylmethyl-1-butyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexylmethyl}-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 25 1-butyl-5-{4-[dimethylamino-(4-fluorophenyl)-methyl]-cyclohexylmethyl}-4-(2-methoxycarbonylethyl)-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester

1-butyl-5-{4-[dimethylamino-(4-fluorophenyl)-methyl]-  
cyclohexylmethyl}-4-methylsulfanylmethyl-4,5-dihydro-1H-  
imidazole-4-carboxylic acid methyl ester

1-butyl-5-[4-(1-dimethylamino-3-phenylpropyl)-cyclohexyl  
5 methyl]-4-(2-methoxycarbonylethyl)-4,5-dihydro-1H-  
imidazole-4-carboxylic acid methyl ester

4-benzylsulfanylmethyl-1-butyl-5-[4-(1-dimethylamino-3-  
phenylpropyl)-cyclohexylmethyl]-4,5-dihydro-1H-imidazole-4-  
carboxylic acid methyl ester

10 5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-  
cyclohexylmethyl}-4-(2-methoxycarbonylethyl)-1-phenethyl-  
4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester

4-sec-butyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-  
cyclohexylmethyl}-1-phenethyl-4,5-dihydro-1H-imidazole-4-  
15 carboxylic acid methyl ester

4-benzylsulfanylmethyl-5-{4-[dimethylamino-(3-  
fluorophenyl)-methyl]-cyclohexylmethyl}-1-phenethyl-4,5-  
dihydro-1H-imidazole-4-carboxylic acid methyl ester

5-{4-[dimethylamino-(4-fluorophenyl)-methyl]-  
20 cyclohexylmethyl}-4-(2-methoxycarbonylethyl)-1-phenethyl-  
4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester

5-[4-(1-dimethylamino-3-phenylpropyl)-cyclohexylmethyl]-4-  
(2-methoxycarbonylethyl)-1-phenethyl-4,5-dihydro-1H-  
imidazole-4-carboxylic acid methyl ester

25 1-benzyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-  
cyclohexylmethyl}-4-(2-methoxycarbonylethyl)-4,5-dihydro-  
1H-imidazole-4-carboxylic acid methyl ester

- 1-benzyl-4-benzylsulfanylmethyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexylmethyl}-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 1-benzyl-5-{4-[dimethylamino-(4-fluorophenyl)-methyl]-cyclohexylmethyl}-4-(2-methoxycarbonylethyl)-4,5-dihydro-1H-imidazole-carboxylic acid methyl ester
- 1-butyl-4-sec-butyl-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexylmethyl}-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 10 1-butyl-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexylmethyl}-4-methylsulfanylmethyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 4-benzylsulfanylmethyl-1-butyl-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexylmethyl}-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 15 5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexyl}-4-(2-methoxycarbonylethyl)-1-phenethyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 4-benzylsulfanylmethyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexyl}-1-phenethyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 20 4-benzylsulfanylmethyl-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexyl}-1-phenethyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 25 5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexylmethyl}-4-(2-methoxycarbonylethyl)-1-phenethyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester

- 1-benzyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexyl}-4-(2-methoxycarbonylethyl)-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 1-benzyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexyl}-4-methylsulfanylmethyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 1-benzyl-4-benzylsulfanylmethyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexyl}-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 10 1-benzyl-4-benzylsulfanylmethyl-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexyl}-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 1-benzyl-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexylmethyl}-4-(2-methoxycarbonylethyl)-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 15 1-benzyl-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexylmethyl}-4-methylsulfanylmethyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 1-benzyl-4-benzylsulfanylmethyl-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexylmethyl}-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 20 1-cyclohexyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexylmethyl}-4-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 25 1-cyclohexyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexylmethyl}-4-(2-methylsulfanylethyl)-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester

- 1-cyclohexyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexylmethyl}-4-methyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 1-cyclohexyl-5-{4-[dimethylamino-(4-fluorophenyl)-methyl]-cyclohexylmethyl}-4-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 1-cyclohexyl-5-{4-[dimethylamino-(4-fluorophenyl)-methyl]-cyclohexylmethyl}-4-(2-methylsulfanylethyl)-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 10 1-cyclohexyl-5-{4-[dimethylamino-(4-fluorophenyl)-methyl]-cyclohexylmethyl}-4-methyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 1-cyclohexyl-5-[4-(1-dimethylamino-3-phenylpropyl)-cyclohexylmethyl]-4-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 15 1-cyclohexyl-5-[4-(1-dimethylamino-3-phenylpropyl)-cyclohexylmethyl]-4-(2-methylsulfanylethyl)-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 1-cyclohexyl-5-[4-(1-dimethylamino-3-phenylpropyl)-cyclohexylmethyl]-4-methyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 20 5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexylmethyl}-1,4-dipropyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 25 5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexylmethyl}-4-(2-methylsulfanylethyl)-1-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester

- 1-benzyl-4-(4-chlorobenzyl)-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexylmethyl}-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 1-benzyl-4-butyl-5-{4-[(chlorophenyl)-dimethylaminomethyl]-cyclohexylmethyl}-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 1-cyclohexyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexyl}-4-(2-methoxycarbonyl ethyl)-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 10 4-benzylsulfanylmethyl-1-cyclohexyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexyl}-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexylmethyl}-4-methyl-1-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 15 5-{4-[dimethylamino-(4-fluorophenyl)-methyl]-cyclohexylmethyl}-1,4-dipropyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 5-{4-[dimethylamino-(4-fluorophenyl)-methyl]-cyclohexylmethyl}-4-(2-methylsulfanylethyl)-1-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 20 5-[4-(1-dimethylamino-3-phenylpropyl)-cyclohexylmethyl]-1,4-dipropyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 25 5-[4-(1-dimethylamino-3-phenylpropyl)-cyclohexylmethyl]-4-(2-methylsulfanylethyl)-1-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester

- 1-butyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexylmethyl}-4-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 1-butyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexylmethyl}-4-(2-methylsulfanylethyl)-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 1-butyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexylmethyl}-4-methyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 10 1-butyl-5-{4-[dimethylamino-(4-fluorophenyl)-methyl]-cyclohexylmethyl}-4-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 1-butyl-5-{4-[dimethylamino-(4-fluorophenyl)-methyl]-cyclohexylmethyl}-4-(2-methylsulfanylethyl)-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 15 1-butyl-5-[4-(1-dimethylamino-3-phenylpropyl)-cyclohexylmethyl]-4-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 1-butyl-5-[4-(1-dimethylamino-3-phenylpropyl)-cyclohexylmethyl]-4-(2-methylsulfanylethyl)-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 20 5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexylmethyl}-1-phenethyl-4-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 25 5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexylmethyl}-4-(2-methylsulfanylethyl)-1-phenethyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester

- 5- {4- [dimethylamino- (3-fluorophenyl) -methyl] -  
cyclohexylmethyl} -4-methyl-1-phenethyl-4,5-dihydro-1H-  
imidazole-4-carboxylic acid methyl ester
- 5- {4- [dimethylamino- (4-fluorophenyl) -methyl] -  
5 cyclohexylmethyl} -1-phenethyl-4-propyl-4,5-dihydro-1H-  
imidazole-4-carboxylic acid methyl ester
- 5- {4- [dimethylamino- (4-fluorophenyl) -methyl] -  
cyclohexylmethyl} -4- (2-methylsulfanylethyl) -1-phenethyl-  
4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 10 5- {4- [dimethylamino- (4-fluorophenyl) -methyl] -  
cyclohexylmethyl} -4-methyl-1-phenethyl-4,5-dihydro-1H-  
imidazole-4-carboxylic acid methyl ester
- 5- [4- (1-dimethylamino-3-phenylpropyl) -cyclohexylmethyl] -1-  
phenethyl-4-propyl-4,5-dihydro-1H-imidazole-4-carboxylic  
15 acid methyl ester
- 5- [4- (1-dimethylamino-3-phenylpropyl) -cyclohexylmethyl] -4-  
(2-methylsulfanylethyl) -1-phenethyl-4,5-dihydro-1H-  
imidazole-4-carboxylic acid methyl ester
- 5- [4- (1-dimethylamino-3-phenylpropyl) -cyclohexylmethyl] -4-  
20 methyl-1-phenethyl-4,5-dihydro-1H-imidazole-4-carboxylic  
acid methyl ester
- 1-benzyl-5- {4- [dimethylamino- (3-fluorophenyl) -methyl] -  
cyclohexylmethyl} -4-propyl-4,5-dihydro-1H-imidazole-4-  
carboxylic acid methyl ester
- 25 1-benzyl-5- {4- [dimethylamino- (3-fluorophenyl) -methyl] -  
cyclohexylmethyl} -4- (2-methylsulfanylethyl) -4,5-dihydro-1H-  
imidazole-4-carboxylic acid methyl ester

- 1-benzyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexylmethyl}-4-methyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 1-benzyl-5-{4-[dimethylamino-(4-fluorophenyl)-methyl]-cyclohexylmethyl}-4-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 1-benzyl-5-{4-[dimethylamino-(4-fluorophenyl)-methyl]-cyclohexylmethyl}-4-(2-methylsulfanylethyl)-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 10 1-benzyl-5-{4-[dimethylamino-(4-fluorophenyl)-methyl]-cyclohexylmethyl}-4-methyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 1-benzyl-5-[4-(1-dimethylamino-3-phenylpropyl)-cyclohexylmethyl]-4-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 15 1-benzyl-5-[4-(1-dimethylamino-3-phenylpropyl)-cyclohexylmethyl]-4-(2-methylsulfanylethyl)-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 1-benzyl-5-[4-(1-dimethylamino-3-phenylpropyl)-cyclohexylmethyl]-4-methyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 20 1-cyclohexyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexylmethyl}-4-(2-methoxycarbonylethyl)-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 25 4-sec-butyl-1-cyclohexyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexylmethyl}-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester

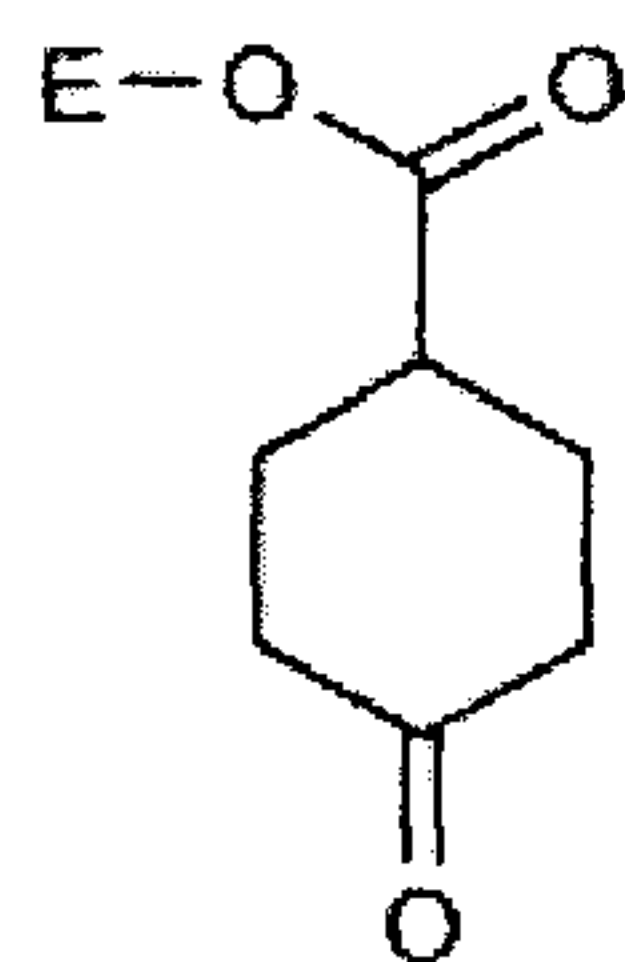
- 1-cyclohexyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexylmethyl}-4-methylsulfanylmethyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 4-benzylsulfanylmethyl-1-cyclohexyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexylmethyl}-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 1-cyclohexyl-5-{4-[dimethylamino-(4-fluorophenyl)-methyl]-cyclohexylmethyl}-4-(2-methoxycarbonylethyl)-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 10 4-sec-butyl-1-cyclohexyl-5-{4-[dimethylamino-(4-fluorophenyl)-methyl]-cyclohexylmethyl}-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 1-cyclohexyl-5-{4-[dimethylamino-(4-fluorophenyl)-methyl]-cyclohexylmethyl}-4-methylsulfanylmethyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 15 1-cyclohexyl-5-[4-(1-dimethylamino-3-phenylpropyl)-cyclohexylmethyl]-4-(2-methoxycarbonylethyl)-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 1-cyclohexyl-5-[4-(1-dimethylamino-3-phenylpropyl)-cyclohexylmethyl]-4-methylsulfanylmethyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 20 4-benzylsulfanylmethyl-1-cyclohexyl-5-[4-(1-dimethylamino-3-phenylpropyl)-cyclohexylmethyl]-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 25 5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexylmethyl}-4-(2-methoxycarbonylethyl)-1-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester

- 5- {4- [dimethylamino- (3-fluorophenyl) -methyl] -  
cyclohexylmethyl} -4-methylsulfanylmethyl-1-propyl-4,5-  
dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 5- {4- [dimethylamino- (4-fluorophenyl) -methyl] -  
5 cyclohexylmethyl} -4- (2-methoxycarbonylethyl) -1-propyl-4,5-  
dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 5- {4- [dimethylamino- (4-fluorophenyl) -methyl] -  
cyclohexylmethyl} -4-methylsulfanylmethyl-1-propyl-4,5-  
dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 10 4-benzylsulfanylmethyl-5- {4- [dimethylamino- (4-  
fluorophenyl) -methyl] -cyclohexylmethyl} -1-propyl-4,5-  
dihydro-1H-imidazole-4-carboxylic acid methyl ester
- methyl-4-sec-butyl-5- ( (4- (4-  
chlorophenyl) (dimethylamino)methyl)cyclohexyl)methyl) -1-  
15 cyclohexyl-4,5-dihydro-1H-imidazole-4-carboxylate

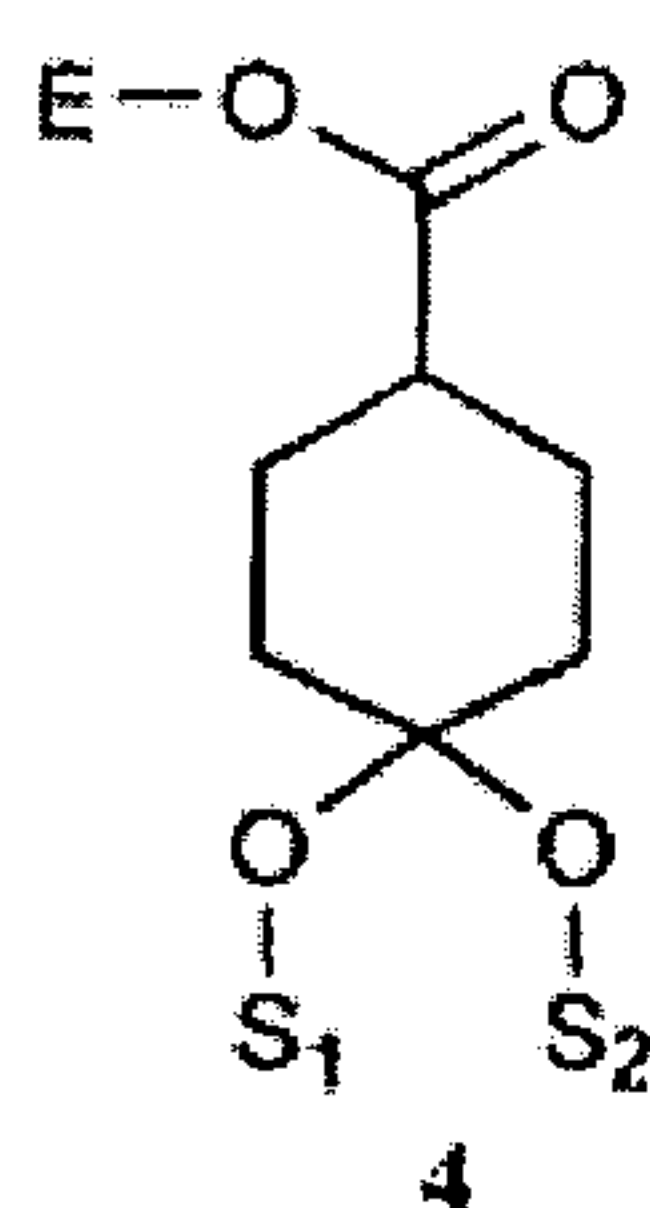
in the form of the racemate; in the form of the  
enantiomers, diastereomers, mixtures of the enantiomers or  
diastereomers or in the form of an individual enantiomer or  
20 diastereomer; in the form of the bases and/or salts of  
physiologically compatible acids.

The invention also provides a process for the preparation  
of an imidazoline derivative according to the invention.  
25 In this connection the keto function of  
4-oxocyclohexanecarboxylic acid esters

30

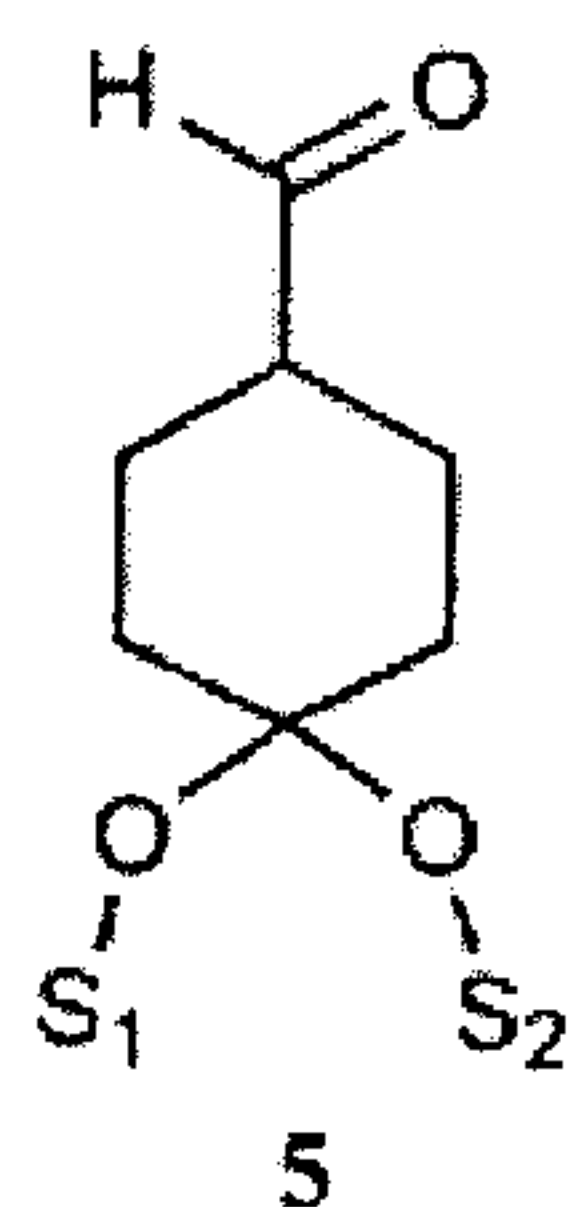


wherein E denotes a C<sub>1-6</sub>-alkyl radical, preferably ethyl, is protected by methods known to the person skilled in the art



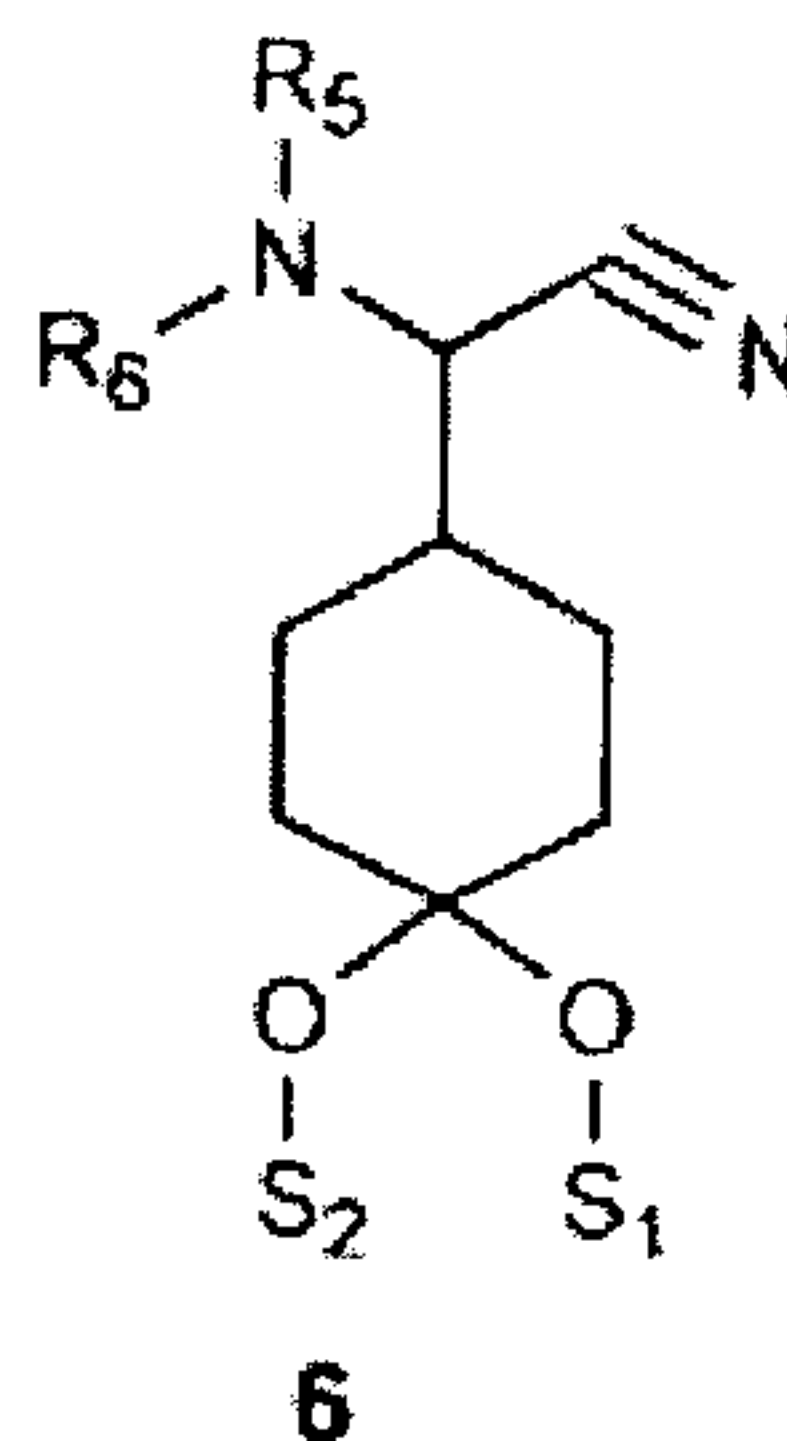
5

Here S1 and S2 denote in each case a protective group, preferably form a ring, and together denote -CH<sub>2</sub>-CH<sub>2</sub>-. The ester **4** is reduced with a reducing agent, for example diisobutyl aluminium hydride, to form the aldehyde **5**

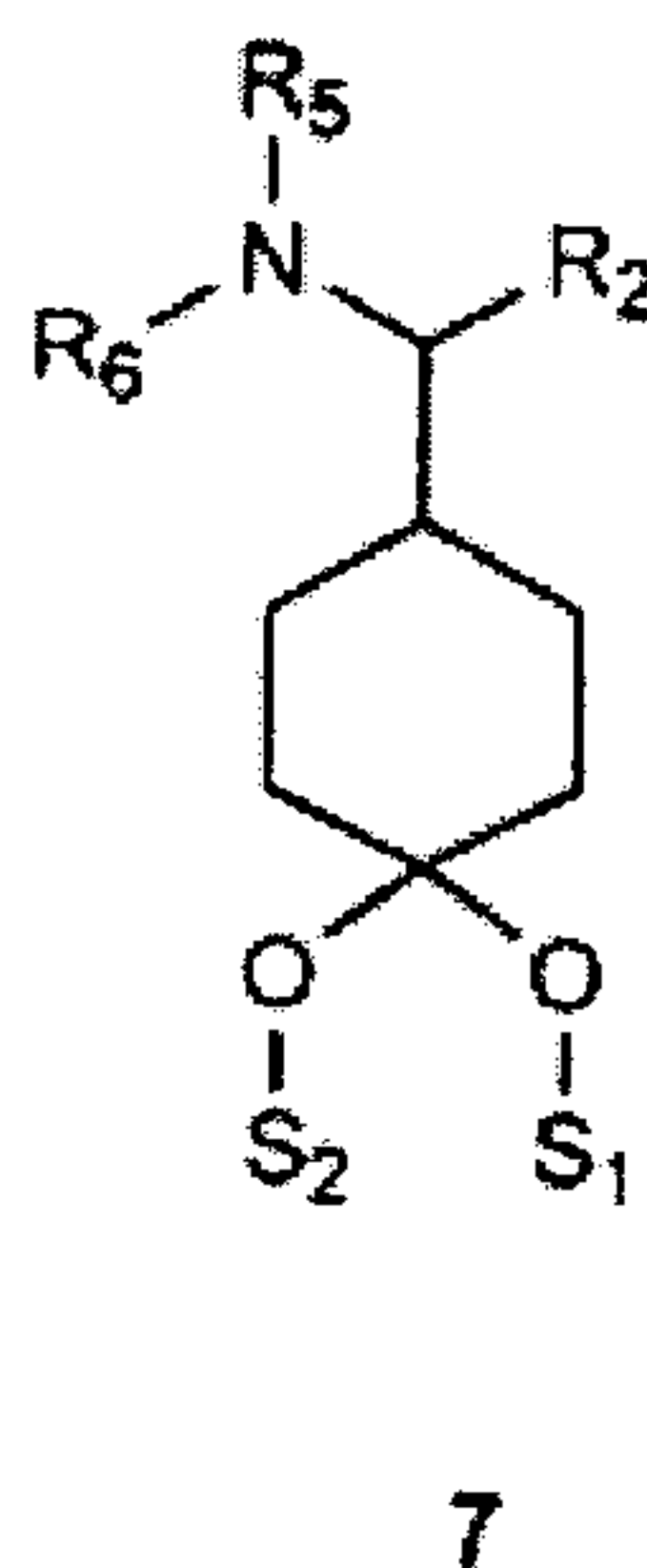


By adding an amine of the general Formula R<sup>5</sup>R<sup>6</sup>NH and a cyanide, for example KCN or NaCN, the aldehyde **5** is converted under the addition of an acid, for example hydrochloric acid, in an organic solvent, for example methanol or ethanol, to the nitrile **6**.

31

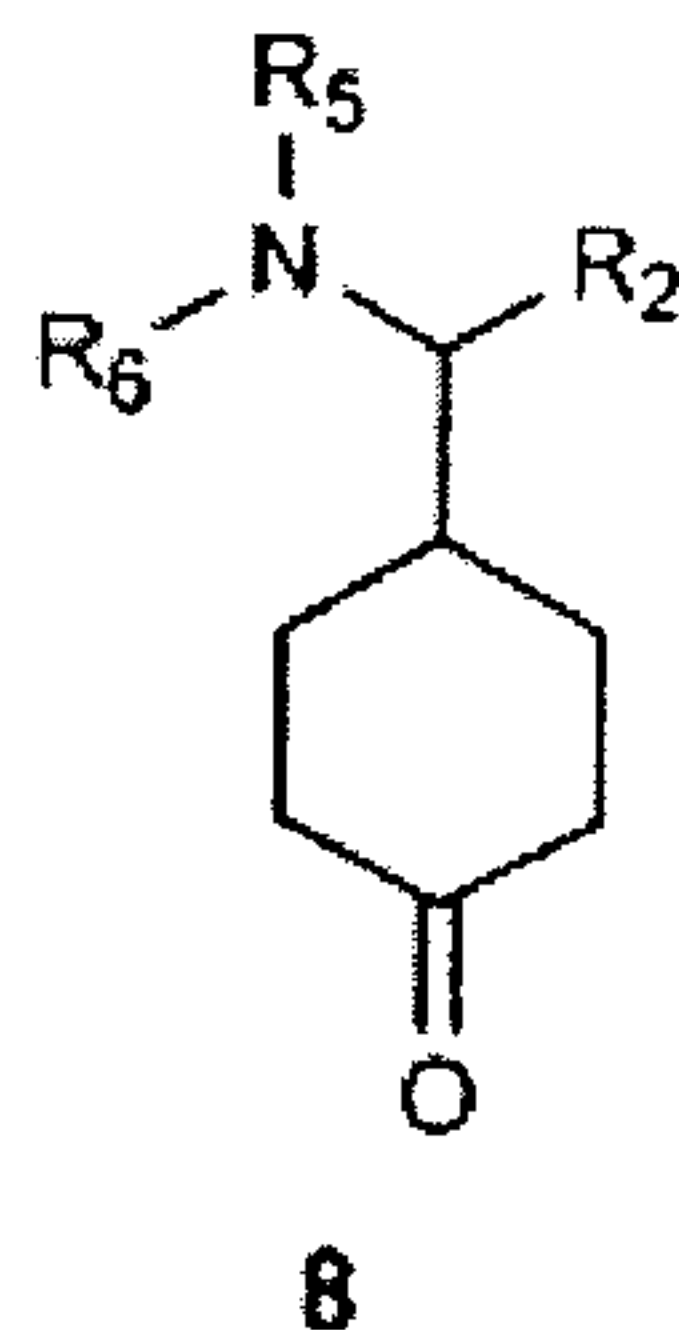


The nitrile **6** is reacted with a Grignard reagent of the general formula  $R^2MgHal$ , wherein Hal denotes Br, Cl or I, or an organometallic compound of the general formula  $R^2Li$  in an organic solvent, for example diethyl ether, dioxane or tetrahydrofuran, to form a compound of the general Formula **7**

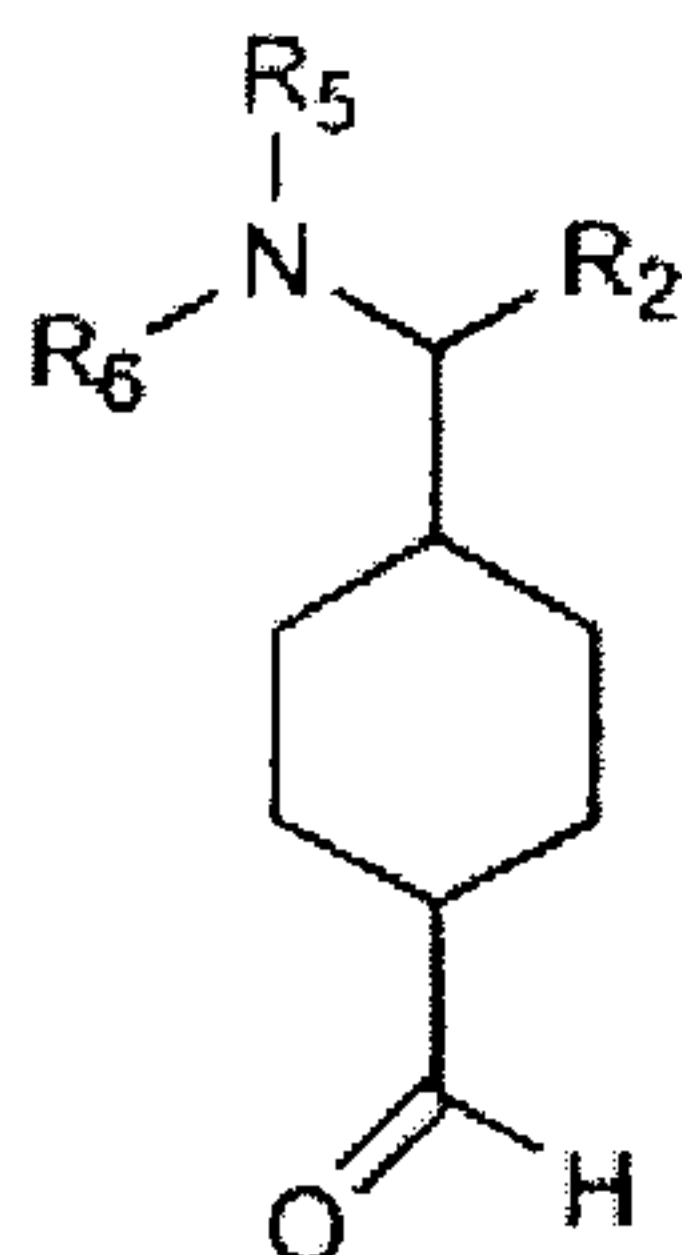


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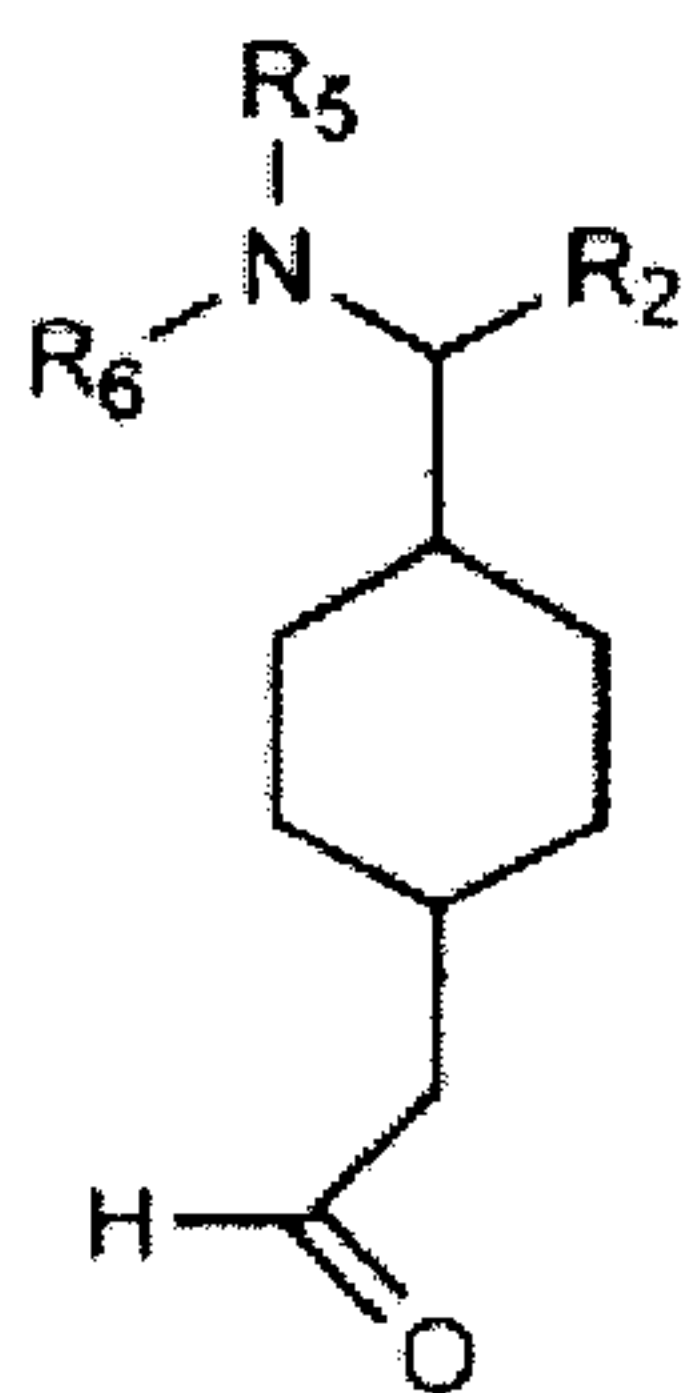
The protective groups are split off by conventional methods, the ketone **8** thereby being obtained.



The aldehyde **9**

**9**

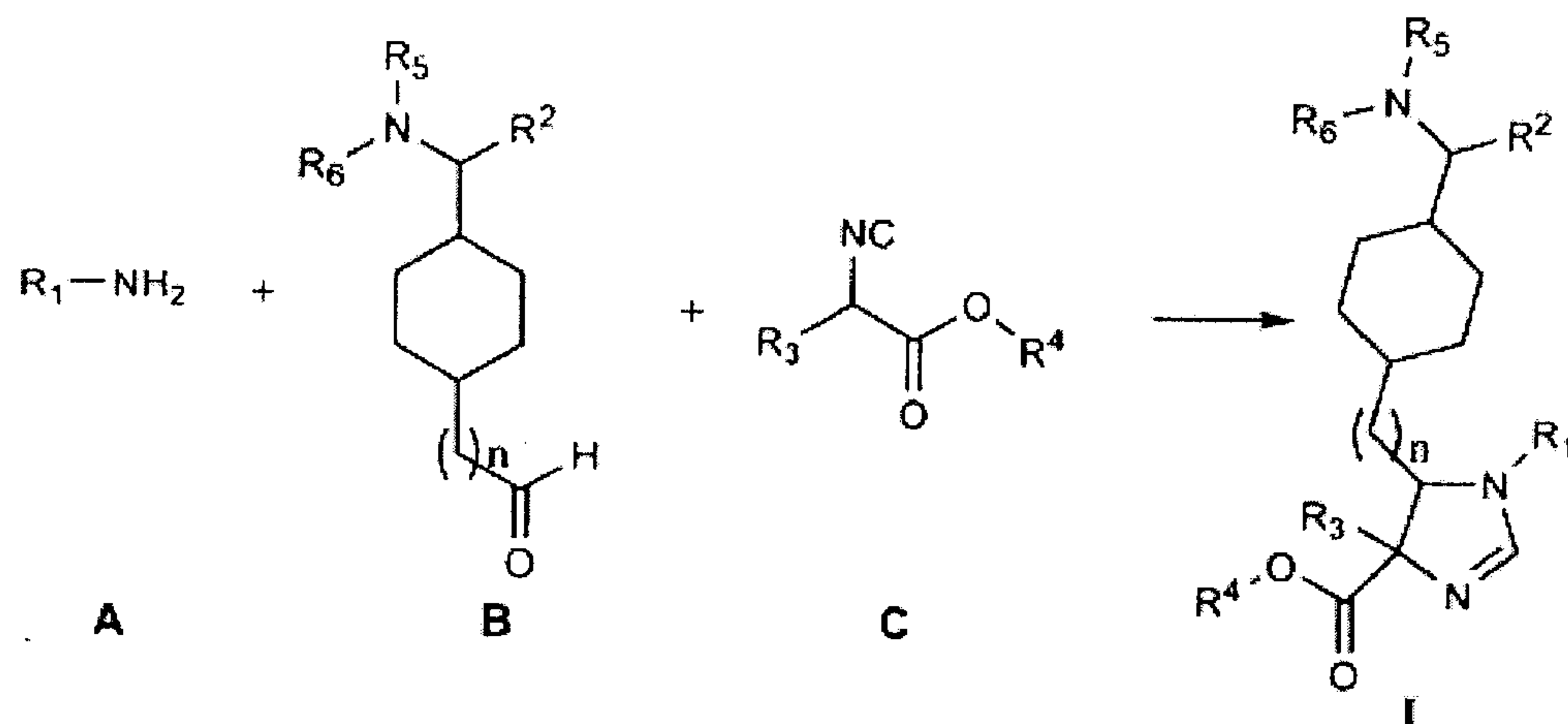
is obtained by reacting the ketone **8** with (methoxymethyl)triphenylphosphonium chloride and a strong  
 5 base, for example potassium tert-butyrate, at a temperature from -20°C to +30°C. By reacting the aldehyde **9** with (methoxymethyl)triphenylphosphonium chloride and a strong base, for example potassium tert-butyrate at a temperature from -20°C to +30°C, an aldehyde of the general Formula **10**  
 10 is obtained.

**10**

By repeating the last reaction step aldehydes can be obtained in which n is 2.

15 The aldehydes of the general Formula **B** are reacted with amines of the general Formula **A** and isonitrile esters of the general Formula **C** in an organic solvent, for example methanol or ethanol, at a temperature of 20°-100°C according to the following synthesis reaction scheme, to

form substituted imidazoline derivatives of the general Formula I



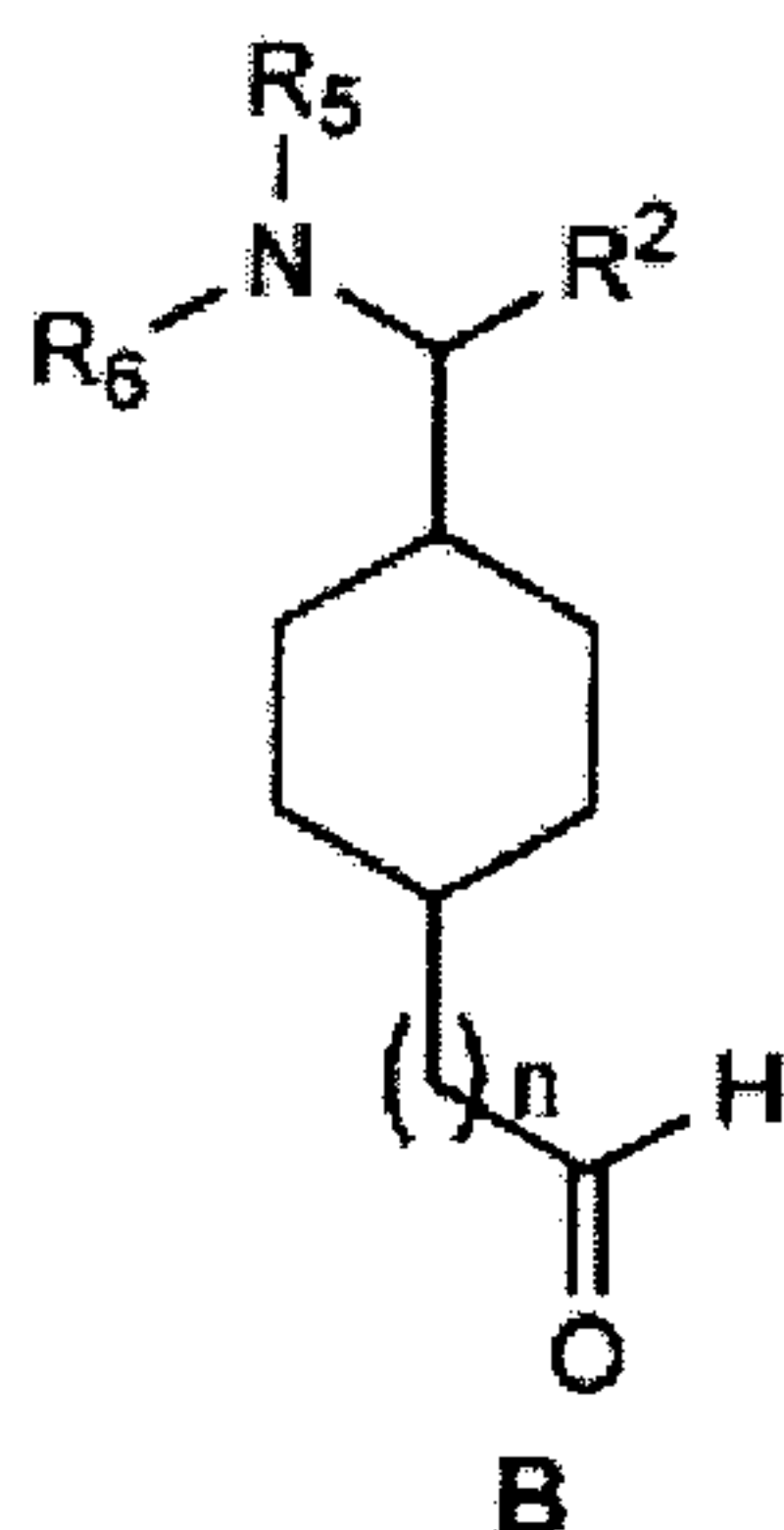
- 5 The amines of the general Formula **A** are commercially obtainable or can be prepared by methods known to the person skilled in the art. The isonitrile esters of the general Formula **C** are either commercially obtainable or can be prepared according to the method of R.S. Bon *et al.*,  
 10 Org. Lett. 2003, 5, 20, 3759-3762.

The separation of diastereomers and/or enantiomers is carried out by methods known to the person skilled in the art, for example by recrystallisation, chromatography or in  
 15 particular HPLC chromatography, or crystallisation with an optionally chiral acid or base and separation of the salts or chiral HPLC chromatography (Fogassy *et al.*, Optical resolution methods, Org. Biomol. Chem 2006, 4, 3011-3030).

- 20 In the case of compounds in which  $R^4$  denotes  $C_{1-4}$ -alkyl or an aryl radical bonded via a  $C_{1-3}$ -alkyl chain,  $R^4$  can be split off according to the following method:

The ester is dissolved or suspended in a small amount of dioxane or THF and is heated under reflux with 1 N sodium hydroxide or potassium hydroxide (10 ml/g) until it has completely dissolved. For working-up, the reaction mixture  
5 is first of all concentrated by evaporation to dryness, following which sufficient water is added so that the residue just dissolves. The solution is carefully acidified with concentrated HCl (pH1) and the acid is extracted several times with diethyl ether or  
10 dichloromethane. The combined organic phases are washed with a small amount of saturated sodium chloride solution, dried, and concentrated by evaporation.

The aldehydes of the general Formula **B** are new and  
15 surprisingly exhibit a good binding to the  $\mu$ -opioid receptor as well as an inhibition of noradrenaline and also serotonin reuptake. The invention therefore also provides an aldehyde of the general Formula **B**



20 wherein the radicals  $\text{R}^2$ ,  $\text{R}^5$ ,  $\text{R}^6$  as well as  $n$  have the meanings given above.

Preferred are aldehydes according to the invention of the general Formula **B** from the following group

4- [dimethylamino- (4-fluorophenyl) -methyl] -  
cyclohexanecarbaldehyde

4- (1-dimethylamino-3-phenylpropyl) -cyclohexanecarbaldehyde

4- [dimethylamino- (3-fluorophenyl) -methyl] -  
5 cyclohexanecarbaldehyde

4- [(4-chlorophenyl) -dimethylaminomethyl] -  
cyclohexanecarbaldehyde

{4- [(4-chlorophenyl) -dimethylaminomethyl] -cyclohexyl} -  
acetaldehyde

10 {4- [dimethylamino- (3-fluorophenyl) -methyl] -cyclohexyl} -  
acetaldehyde

4- (dimethylamino-thiophen-2-yl-methyl) -  
cyclohexanecarbaldehyde

{4- [dimethylamino- (4-fluorophenyl) -methyl] -cyclohexyl} -  
15 acetaldehyde

[4- (dimethylamino-thiophen-2-yl-methyl) -cyclohexyl] -  
acetaldehyde

[4- (1-dimethylamino-3-phenylpropyl) -cyclohexyl] -  
acetaldehyde

20

in the form of the racemates; in the form of the  
enantiomers, diastereomers, mixtures of the enantiomers or  
diastereomers or in the form of an individual enantiomer or  
diastereomer; in the form of the bases and/or salts of  
25 physiologically compatible acids.

The substances according to the invention are suitable as  
pharmaceutical active substances in medicaments. The  
invention accordingly also provides medicaments containing

at least one substituted imidazoline derivative according to the invention of the general Formula **I** and a substituted aldehyde of the invention of the general Formula **B**, as well as optionally suitable additives and/or auxiliary  
5 substances and/or optionally further active substances.

The medicaments according to the invention contain, apart from at least one substituted imidazoline derivative according to the invention or a substituted aldehyde  
10 according to the invention, optionally also suitable additives and/or auxiliary substances, thus also carrier materials, fillers, solvents, diluents, colourants and/or binders, and can be administered as liquid medicament in the form of injection solutions, drops or juices, as semi-  
15 solid medicament in the form of granules, tablets, pellets, patches, capsules, plasters or aerosols. The choice of the auxiliary substances, etc. as well as the amounts thereof to be employed depends on whether the medicament is to be administered orally, parenterally, intravenously,  
20 intraperitoneally, intradermally, intramuscularly, intranasally, buccally, rectally or topically, for example to the skin, mucus membranes or to the eyes. For oral application suitable preparations are in the form of tablets, pills, capsules, granules, drops, juices and  
25 syrups, while for parenteral, topical and inhalative application suitable preparations are solutions, suspensions, easily reconstitutable dry preparations as well as sprays. Imidazoline derivatives according to the invention in a depot form, in dissolved form or in a  
30 plaster, optionally with the addition of agents promoting penetration of the skin, are suitable percutaneous application forms. Orally or percutaneously employable preparation forms can release the imidazoline derivatives

or aldehydes according to the invention in a delayed manner. In principle other active substances known to the person skilled in the art can also be added to the medicaments according to the invention.

5

The amount of active substance to be administered to the patient varies depending on the patient's weight, type of application, medical indications and the severity of the disease. Normally 0.005 to 20 mg/kg, preferably 0.05 to  
10 5 mg/kg of at least one imidazoline derivative or aldehyde according to the invention are administered.

In the medicament a contained imidazoline derivative according to the invention or contained aldehyde according  
15 to the invention can be present as pure diastereomer and/or enantiomer, as racemate, or as a non-equimolar or equimolar mixture of the diastereomers and/or enantiomers.

The invention also provides for the use of an imidazoline  
20 derivative or substituted aldehyde according to the invention for the preparation of a medicament for treating pain, in particular acute, neuropathic or chronic pain.

The invention also provides for the use of an imidazoline  
25 derivative or substituted aldehyde according to the invention for the preparation of a medicament for treating depression and/or anxiety.

The substituted imidazoline derivatives or substituted  
30 aldehydes of the general Formula I and of the general Formula B are also suitable for treating urinary incontinence, diarrhea, pruritus, alcohol and drug misuse, drug dependency and lack of drive.

The invention therefore also provides for the use of a substituted imidazoline derivative of the general formula I and of a substituted aldehyde of the general formula B for the preparation of a medicament for treating urinary  
5 incontinence, diarrhea, pruritus, alcohol and drug misuse, drug dependency and lack of drive.

Particularly preferably the substituted imidazoline derivatives or substituted aldehydes according to the  
10 invention that are used for the preparation of the medicament for treating pain, in particular acute, neuropathic or chronic pain, depression and/or anxiety, for treating urinary incontinence, diarrhea, pruritus, alcohol and drug misuse, drug dependency and lack of drive, are  
15 selected from the following group:

4-[dimethylamino-(4-fluorophenyl)-methyl]-  
cyclohexanecarbaldehyde

4-(1-dimethylamino-3-phenylpropyl)-cyclohexanecarbaldehyde

20 4-[dimethylamino-(3-fluorophenyl)-methyl]-  
cyclohexanecarbaldehyde

4-[(4-chlorophenyl)-dimethylaminomethyl]-  
cyclohexanecarbaldehyde

{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexyl}-  
25 acetaldehyde

{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexyl}-  
acetaldehyde

4-(dimethylaminothiophen-2-yl-methyl)-  
cyclohexanecarbaldehyde

- {4-[dimethylamino-(4-fluorophenyl)-methyl]-cyclohexyl}-  
acetaldehyde
- [4-(dimethylaminothiophen-2-yl-methyl)-cyclohexyl]-  
acetaldehyde
- 5 [4-(1-dimethylamino-3-phenylpropyl)-cyclohexyl]-  
acetaldehyde
- 1-cyclohexyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-  
cyclohexyl}-4-isobutyl-4,5-dihydro-1H-imidazole-4-  
carboxylic acid methyl ester
- 10 4-(4-chlorobenzyl)-1-cyclohexyl-5-{4-[dimethylamino-(3-  
fluorophenyl)-methyl]-cyclohexyl}-4,5-dihydro-1H-imidazole-  
4-carboxylic acid methyl ester
- 4-butyl-1-cyclohexyl-5-{4-[dimethylamino-(3-fluorophenyl)-  
methyl]-cyclohexyl}-4,5-dihydro-1H-imidazole-4-carboxylic  
15 acid methyl ester
- 5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexyl}-1-  
cyclohexyl-4-isobutyl-4,5-dihydro-1H-imidazole-4-carboxylic  
acid methyl ester
- 4-(4-chlorobenzyl)-5-{4-[(4-chlorophenyl)-  
20 dimethylaminomethyl]-cyclohexyl}-1-cyclohexyl-4,5-dihydro-  
1H-imidazole-4-carboxylic acid methyl ester
- 4-butyl-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-  
cyclohexyl}-1-cyclohexyl-4,5-dihydro-1H-imidazole-4-  
carboxylic acid methyl ester
- 25 5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-  
cyclohexylmethyl}-1-cyclohexyl-4-isobutyl-4,5-dihydro-1H-  
imidazole-4-carboxylic acid methyl ester

- 4- (4-chlorobenzyl) -5- {4- [(4-chlorophenyl) -  
dimethylaminomethyl] -cyclohexylmethyl} -1-cyclohexyl-4,5-  
dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 4-butyl-5- {4- [(4-chlorophenyl) -dimethylaminomethyl] -  
5 cyclohexylmethyl} -1-cyclohexyl-4,5-dihydro-1H-imidazole-4-  
carboxylic acid methyl ester
- 4- (4-chlorobenzyl) -1-cyclohexyl-5- [4-  
(dimethylaminothiophen-2-yl-methyl) -cyclohexylmethyl] -4,5-  
dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 10 5- {4- [dimethylamino- (3-fluorophenyl) -methyl] -cyclohexyl} -4-  
isobutyl-1-propyl-4,5-dihydro-1H-imidazole-4-carboxylic  
acid methyl ester
- 4- (4-chlorobenzyl) -5- {4- [dimethylamino- (3-fluorophenyl) -  
methyl] -cyclohexyl} -1-propyl-4,5-dihydro-1H-imidazole-4-  
15 carboxylic acid methyl ester
- 4-butyl-5- {4- [dimethylamino- (3-fluorophenyl) -methyl] -  
cyclohexyl} -1-propyl-4,5-dihydro-1H-imidazole-4-carboxylic  
acid methyl ester
- 5- {4- [(4-chlorophenyl) -dimethylaminomethyl] -cyclohexyl} -4-  
20 isobutyl-1-propyl-4,5-dihydro-1H-imidazole-4-carboxylic  
acid methyl ester
- 4- (4-chlorobenzyl) -5- {4- [(4-chlorophenyl) -  
dimethylaminomethyl] -cyclohexyl} -1-propyl-4,5-dihydro-1H-  
imidazole-4-carboxylic acid methyl ester
- 25 5- {4- [(4-chlorophenyl) -dimethylaminomethyl] -  
cyclohexylmethyl} -4-isobutyl-1-propyl-4,5-dihydro-1H-  
imidazole-4-carboxylic acid methyl ester

- 4-(4-chlorobenzyl)-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexylmethyl}-1-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 4-butyl-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexylmethyl}-1-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 1-butyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexyl}-4-isobutyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 10 1-butyl-4-(4-chlorobenzyl)-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexyl}-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 1-butyl-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexyl}-4-isobutyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 15 1-butyl-4-(4-chlorobenzyl)-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexyl}-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 1-butyl-4-(4-chlorobenzyl)-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexyl}-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 1,4-dibutyl-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexyl}-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 20 1-butyl-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexylmethyl}-4-isobutyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 1-butyl-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexylmethyl}-4-isobutyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 25 1-butyl-4-(4-chlorobenzyl)-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexylmethyl}-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester

- 1,4-dibutyl-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexylmethyl}-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexyl}-4-isobutyl-1-phenethyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 4-(4-chlorobenzyl)-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexyl}-1-phenethyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 10 4-butyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexyl}-1-phenethyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexyl}-4-isobutyl-1-phenethyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 15 4-(4-chlorobenzyl)-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexyl}-1-phenethyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 4-butyl-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexyl}-1-phenethyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 20 4-butyl-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexyl}-1-phenethyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexylmethyl}-4-isobutyl-1-phenethyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 25 4-(4-chlorobenzyl)-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexylmethyl}-1-phenethyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester

- 4-butyl-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexylmethyl}-1-phenethyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 1-benzyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexyl}-4-isobutyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 1-benzyl-4-(4-chlorobenzyl)-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexyl}-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 10 1-benzyl-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexyl}-4-isobutyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 1-benzyl-4-(4-chlorobenzyl)-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexyl}-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 15 4-carboxylic acid methyl ester
- 1-benzyl-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexylmethyl}-4-isobutyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexyl}-1-cyclohexyl-4-(2-methoxycarbonyl-ethyl)-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 20 4-benzylsulfanylmethyl-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexyl}-1-cyclohexyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 25 5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexylmethyl}-1-cyclohexyl-4-(2-methoxycarbonyl-ethyl)-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester

- 1-benzyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexylmethyl}-4-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 5- {4- [(4-chlorophenyl)-dimethylaminomethyl]-cyclohexylmethyl}-1-cyclohexyl-4-methylsulfanylmethyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 4-benzylsulfanylmethyl-5-{4- [(4-chlorophenyl)-dimethylaminomethyl]-cyclohexylmethyl}-1-cyclohexyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 10 5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexyl}-4-methylsulfanylmethyl-1-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 4-benzylsulfanylmethyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexyl}-1-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 15 5-{4- [(4-chlorophenyl)-dimethylaminomethyl]-cyclohexyl}-4-(2-methoxycarbonylethyl)-1-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 4-benzylsulfanylmethyl-5-{4- [(4-chlorophenyl)-dimethylaminomethyl]-cyclohexyl}-1-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 20 5-{4- [(4-chlorophenyl)-dimethylaminomethyl]-cyclohexylmethyl}-4-(2-methoxycarbonylethyl)-1-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 25 4-sec-butyl-5-{4- [(4-chlorophenyl)-dimethylaminomethyl]-cyclohexylmethyl}-1-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester

- 5- {4- [(4-chlorophenyl)-dimethylaminomethyl]-  
cyclohexylmethyl}-4-methylsulfanylmethyl-1-propyl-4,5-  
dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 4-benzylsulfanylmethyl-5- {4- [(4-chlorophenyl)-  
5 dimethylaminomethyl]-cyclohexylmethyl}-1-propyl-4,5-  
dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 1-butyl-5- {4- [dimethylamino- (3-fluorophenyl)-methyl]-  
cyclohexyl}-4- (2-methoxycarbonylethyl)-4,5-dihydro-1H-  
imidazole-4-carboxylic acid methyl ester
- 10 1-butyl-5- {4- [dimethylamino- (3-fluorophenyl)-methyl]-  
cyclohexyl}-4-methylsulfanylmethyl-4,5-dihydro-1H-  
imidazole-4-carboxylic acid methyl ester
- 4-benzylsulfanylmethyl-1-butyl-5- {4- [dimethylamino- (3-  
fluorophenyl)-methyl]-cyclohexyl}-4,5-dihydro-1H-imidazole-  
15 4-carboxylic acid methyl ester
- 1-butyl-5- {4- [(4-chlorophenyl)-dimethylaminomethyl]-  
cyclohexyl}-4- (2-methoxycarbonylethyl)-4,5-dihydro-1H-  
imidazole-4-carboxylic acid methyl ester
- 4-benzylsulfanylmethyl-1-butyl-5- {4- [(4-chlorophenyl)-  
20 dimethylaminomethyl]-cyclohexyl}-4,5-dihydro-1H-imidazole-  
4-carboxylic acid methyl ester
- 1-butyl-5- {4- [(4-chlorophenyl)-dimethylaminomethyl]-  
cyclohexylmethyl}-4- (2-methoxycarbonylethyl)-4,5-dihydro-  
1H-imidazole-4-carboxylic acid methyl ester
- 25 5- [4- (1-dimethylamino-3-phenylpropyl)-cyclohexylmethyl]-4-  
(2-methoxycarbonylethyl)-1-propyl-4,5-dihydro-1H-imidazole-  
4-carboxylic acid methyl ester

- 1-butyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexylmethyl}-4-(2-methoxycarbonylethyl)-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 1-butyl-4-sec-butyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexylmethyl}-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 1-butyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexylmethyl}-4-methylsulfanylmethyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 10 4-benzylsulfanylmethyl-1-butyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexylmethyl}-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 1-butyl-5-{4-[dimethylamino-(4-fluorophenyl)-methyl]-cyclohexylmethyl}-4-(2-methoxycarbonylethyl)-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 15 1-butyl-5-{4-[dimethylamino-(4-fluorophenyl)-methyl]-cyclohexylmethyl}-4-methylsulfanylmethyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 1-butyl-5-[4-(1-dimethylamino-3-phenylpropyl)-cyclohexylmethyl]-4-(2-methoxycarbonylethyl)-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 20 4-benzylsulfanylmethyl-1-butyl-5-[4-(1-dimethylamino-3-phenylpropyl)-cyclohexylmethyl]-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 25 5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexylmethyl}-4-(2-methoxycarbonylethyl)-1-phenethyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester

- 4-sec-butyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexylmethyl}-1-phenethyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 4-benzylsulfanylmethyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexylmethyl}-1-phenethyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 5-{4-[dimethylamino-(4-fluorophenyl)-methyl]-cyclohexylmethyl}-4-(2-methoxycarbonylethyl)-1-phenethyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 10 5-[4-(1-dimethylamino-3-phenylpropyl)-cyclohexylmethyl]-4-(2-methoxycarbonylethyl)-1-phenethyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 1-benzyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexylmethyl}-4-(2-methoxycarbonylethyl)-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 15 1-benzyl-4-benzylsulfanylmethyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexylmethyl}-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 1-benzyl-5-{4-[dimethylamino-(4-fluorophenyl)-methyl]-cyclohexylmethyl}-4-(2-methoxycarbonylethyl)-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 20 1-butyl-4-sec-butyl-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexylmethyl}-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 25 1-butyl-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexylmethyl}-4-methylsulfanylmethyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester

- 4-benzylsulfanylmethyl-1-butyl-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexylmethyl}-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexyl}-4-(2-methoxycarbonylethyl)-1-phenethyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 4-benzylsulfanylmethyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexyl}-1-phenethyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 10 4-benzylsulfanylmethyl-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexyl}-1-phenethyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexylmethyl}-4-(2-methoxycarbonylethyl)-1-phenethyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 15 1-benzyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexyl}-4-(2-methoxycarbonylethyl)-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 1-benzyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexyl}-4-methylsulfanylmethyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 20 1-benzyl-4-benzylsulfanylmethyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexyl}-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 1-benzyl-4-benzylsulfanylmethyl-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexyl}-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 25 1-benzyl-4-benzylsulfanylmethyl-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexyl}-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester

- 1-benzyl-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexylmethyl}-4-(2-methoxycarbonylethyl)-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 1-benzyl-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexylmethyl}-4-methylsulfanylmethyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 1-benzyl-4-benzylsulfanylmethyl-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexylmethyl}-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 10 1-cyclohexyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexylmethyl}-4-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 1-cyclohexyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexylmethyl}-4-(2-methylsulfanylethyl)-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 15 1-cyclohexyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexylmethyl}-4-methyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 1-cyclohexyl-5-{4-[dimethylamino-(4-fluorophenyl)-methyl]-cyclohexylmethyl}-4-methyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 20 1-cyclohexyl-5-{4-[dimethylamino-(4-fluorophenyl)-methyl]-cyclohexylmethyl}-4-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 1-cyclohexyl-5-{4-[dimethylamino-(4-fluorophenyl)-methyl]-cyclohexylmethyl}-4-(2-methylsulfanylethyl)-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 25 1-cyclohexyl-5-{4-[dimethylamino-(4-fluorophenyl)-methyl]-cyclohexylmethyl}-4-methyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester

- 1-cyclohexyl-5-[4-(1-dimethylamino-3-phenylpropyl)-  
cyclohexylmethyl]-4-propyl-4,5-dihydro-1H-imidazole-4-  
carboxylic acid methyl ester
- 1-cyclohexyl-5-[4-(1-dimethylamino-3-phenylpropyl)-  
5 cyclohexylmethyl]-4-(2-methylsulfanylethyl)-4,5-dihydro-1H-  
imidazole-4-carboxylic acid methyl ester
- 1-cyclohexyl-5-[4-(1-dimethylamino-3-phenylpropyl)-  
cyclohexylmethyl]-4-methyl-4,5-dihydro-1H-imidazole-4-  
carboxylic acid methyl ester
- 10 5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-  
cyclohexylmethyl}-1,4-dipropyl-4,5-dihydro-1H-imidazole-4-  
carboxylic acid methyl ester
- 5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-  
cyclohexylmethyl}-4-(2-methylsulfanylethyl)-1-propyl-4,5-  
15 dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 1-benzyl-4-(4-chlorobenzyl)-5-{4-[(4-chlorophenyl)-  
dimethylaminomethyl]-cyclohexylmethyl}-4,5-dihydro-1H-  
imidazole-4-carboxylic acid methyl ester
- 1-benzyl-4-butyl-5-{4-[(4-chlorophenyl)-  
20 dimethylaminomethyl]-cyclohexylmethyl}-4,5-dihydro-1H-  
imidazole-4-carboxylic acid methyl ester
- 1-cyclohexyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-  
cyclohexyl}-4-(2-methoxycarbonylethyl)-4,5-dihydro-1H-  
imidazole-4-carboxylic acid methyl ester
- 25 4-benzylsulfanylmethyl-1-cyclohexyl-5-{4-[dimethylamino-(3-  
fluorophenyl)-methyl]-cyclohexyl}-4,5-dihydro-1H-imidazole-  
4-carboxylic acid methyl ester

- 5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexylmethyl}-4-methyl-1-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 5-{4-[dimethylamino-(4-fluorophenyl)-methyl]-cyclohexylmethyl}-1,4-dipropyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 5-{4-[dimethylamino-(4-fluorophenyl)-methyl]-cyclohexylmethyl}-4-(2-methylsulfanylethyl)-1-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 10 5-[4-(1-dimethylamino-3-phenylpropyl)-cyclohexylmethyl]-1,4-dipropyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 5-[4-(1-dimethylamino-3-phenylpropyl)-cyclohexylmethyl]-4-(2-methylsulfanylethyl)-1-propyl-4,5-dihydro-1H-imidazole-
- 15 4-carboxylic acid methyl ester
- 1-butyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexylmethyl}-4-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 1-butyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexylmethyl}-4-(2-methylsulfanylethyl)-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 20 1-butyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexylmethyl}-4-methyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 1-butyl-5-{4-[dimethylamino-(4-fluorophenyl)-methyl]-cyclohexylmethyl}-4-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 25 1-butyl-5-{4-[dimethylamino-(4-fluorophenyl)-methyl]-cyclohexylmethyl}-4-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester

- 1-butyl-5-{4-[dimethylamino-(4-fluorophenyl)-methyl]-  
cyclohexylmethyl}-4-(2-methylsulfanylethyl)-4,5-dihydro-1H-  
imidazole-4-carboxylic acid methyl ester
- 1-butyl-5-[4-(1-dimethylamino-3-phenylpropyl)-  
5 cyclohexylmethyl]-4-propyl-4,5-dihydro-1H-imidazole-4-  
carboxylic acid methyl ester
- 1-butyl-5-[4-(1-dimethylamino-3-phenylpropyl)-  
cyclohexylmethyl]-4-(2-methylsulfanylethyl)-4,5-dihydro-1H-  
imidazole-4-carboxylic acid methyl ester
- 10 5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-  
cyclohexylmethyl}-1-phenethyl-4-propyl-4,5-dihydro-1H-  
imidazole-4-carboxylic acid methyl ester
- 5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-  
cyclohexylmethyl}-4-(2-methylsulfanylethyl)-1-phenethyl-  
15 4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-  
cyclohexylmethyl}-4-methyl-1-phenethyl-4,5-dihydro-1H-  
imidazole-4-carboxylic acid methyl ester
- 5-{4-[dimethylamino-(4-fluorophenyl)-methyl]-  
20 cyclohexylmethyl}-1-phenethyl-4-propyl-4,5-dihydro-1H-  
imidazole-4-carboxylic acid methyl ester
- 5-{4-[dimethylamino-(4-fluorophenyl)-methyl]-  
cyclohexylmethyl}-4-(2-methylsulfanylethyl)-1-phenethyl-  
4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 25 5-{4-[dimethylamino-(4-fluorophenyl)-methyl]-  
cyclohexylmethyl}-4-methyl-1-phenethyl-4,5-dihydro-1H-  
imidazole-4-carboxylic acid methyl ester

- 5- [4-dimethylamino-3-phenylpropyl)-cyclohexylmethyl]-1-phenethyl-4-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 5- [4-(1-dimethylamino-3-phenylpropyl)-cyclohexylmethyl]-4-(2-methylsulfanylethyl)-1-phenethyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 5- [4-(1-dimethylamino-3-phenylpropyl)-cyclohexylmethyl]-4-methyl-1-phenethyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 10 1-benzyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexylmethyl}-4-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 1-benzyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexylmethyl}-4-(2-methylsulfanylethyl)-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 15 1-benzyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexylmethyl}-4-methyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 1-benzyl-5-{4-[dimethylamino-(4-fluorophenyl)-methyl]-cyclohexylmethyl}-4-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 20 1-benzyl-5-{4-[dimethylamino-(4-fluorophenyl)-methyl]-cyclohexylmethyl}-4-(2-methylsulfanylethyl)-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 1-benzyl-5-{4-[dimethylamino-(4-fluorophenyl)-methyl]-cyclohexylmethyl}-4-methyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 25 1-benzyl-5-{4-[dimethylamino-(4-fluorophenyl)-methyl]-cyclohexylmethyl}-4-methyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester

1-benzyl-5-[4-(1-dimethylamino-3-phenylpropyl)-  
cyclohexylmethyl]-4-propyl-4,5-dihydro-1H-imidazole-4-  
carboxylic acid methyl ester

1-benzyl-5-[4-(1-dimethylamino-3-phenylpropyl)-  
5 cyclohexylmethyl]-4-(2-methylsulfonyl-ethyl)-4,5-dihydro-1H-  
imidazole-4-carboxylic acid methyl ester

1-benzyl-5-[4-(1-dimethylamino-3-phenylpropyl)-  
cyclohexylmethyl]-4-methyl-4,5-dihydro-1H-imidazole-4-  
carboxylic acid methyl ester

10 1-cyclohexyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-  
cyclohexylmethyl}-4-(2-methoxycarbonyl-ethyl)-4,5-dihydro-  
1H-imidazole-4-carboxylic acid methyl ester

4-sec-butyl-1-cyclohexyl-5-{4-[dimethylamino-(3-  
fluorophenyl)-methyl]-cyclohexylmethyl}-4,5-dihydro-1H-  
15 imidazole-4-carboxylic acid methyl ester

1-cyclohexyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-  
cyclohexylmethyl}-4-methylsulfonylmethyl-4,5-dihydro-1H-  
imidazole-4-carboxylic acid methyl ester

4-benzylsulfonylmethyl-1-cyclohexyl-5-{4-[dimethylamino-(3-  
20 fluorophenyl)-methyl]-cyclohexylmethyl}-4,5-dihydro-1H-  
imidazole-4-carboxylic acid methyl ester

1-cyclohexyl-5-{4-[dimethylamino-(4-fluorophenyl)-methyl]-  
cyclohexylmethyl}-4-(2-methoxycarbonyl-ethyl)-4,5-dihydro-  
1H-imidazole-4-carboxylic acid methyl ester

25 4-sec-butyl-1-cyclohexyl-5-{4-[dimethylamino-(4-  
fluorophenyl)-methyl]-cyclohexylmethyl}-4,5-dihydro-1H-  
imidazole-4-carboxylic acid methyl ester

- 1-cyclohexyl-5-{4-[dimethylamino-(4-fluorophenyl)-methyl]-cyclohexylmethyl}-4-methylsulfanylmethyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 1-cyclohexyl-5-[4-(1-dimethylamino-3-phenylpropyl)-cyclohexylmethyl]-4-(2-methoxycarbonylethyl)-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 1-cyclohexyl-5-[4-(1-dimethylamino-3-phenylpropyl)-cyclohexylmethyl]-4-methylsulfanylmethyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 4-benzylsulfanylmethyl-1-cyclohexyl-5-[4-(1-dimethylamino-3-phenylpropyl)-cyclohexylmethyl]-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexylmethyl}-4-(2-methoxycarbonylethyl)-1-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexylmethyl}-4-methylsulfanylmethyl-1-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 5-{4-[dimethylamino-(4-fluorophenyl)-methyl]-cyclohexylmethyl}-4-(2-methoxycarbonylethyl)-1-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 5-{4-[dimethylamino-(4-fluorophenyl)-methyl]-cyclohexylmethyl}-4-methylsulfanylmethyl-1-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 4-benzylsulfanylmethyl-5-{4-[dimethylamino-(4-fluorophenyl)-methyl]-cyclohexylmethyl}-1-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester

Methyl-4-sec-butyl-5-((4-(4-chlorophenyl)(dimethylamino)methyl)cyclohexyl)methyl)-1-cyclohexyl-4,5-dihydro-1H-imidazole-4-carboxylate

5 in the form of the racemate; in the form of the enantiomers, diastereomers, mixtures of the enantiomers or diastereomers or in the form of an individual enantiomer or diastereomer; in the form of the bases and/or salts of physiologically compatible acids.

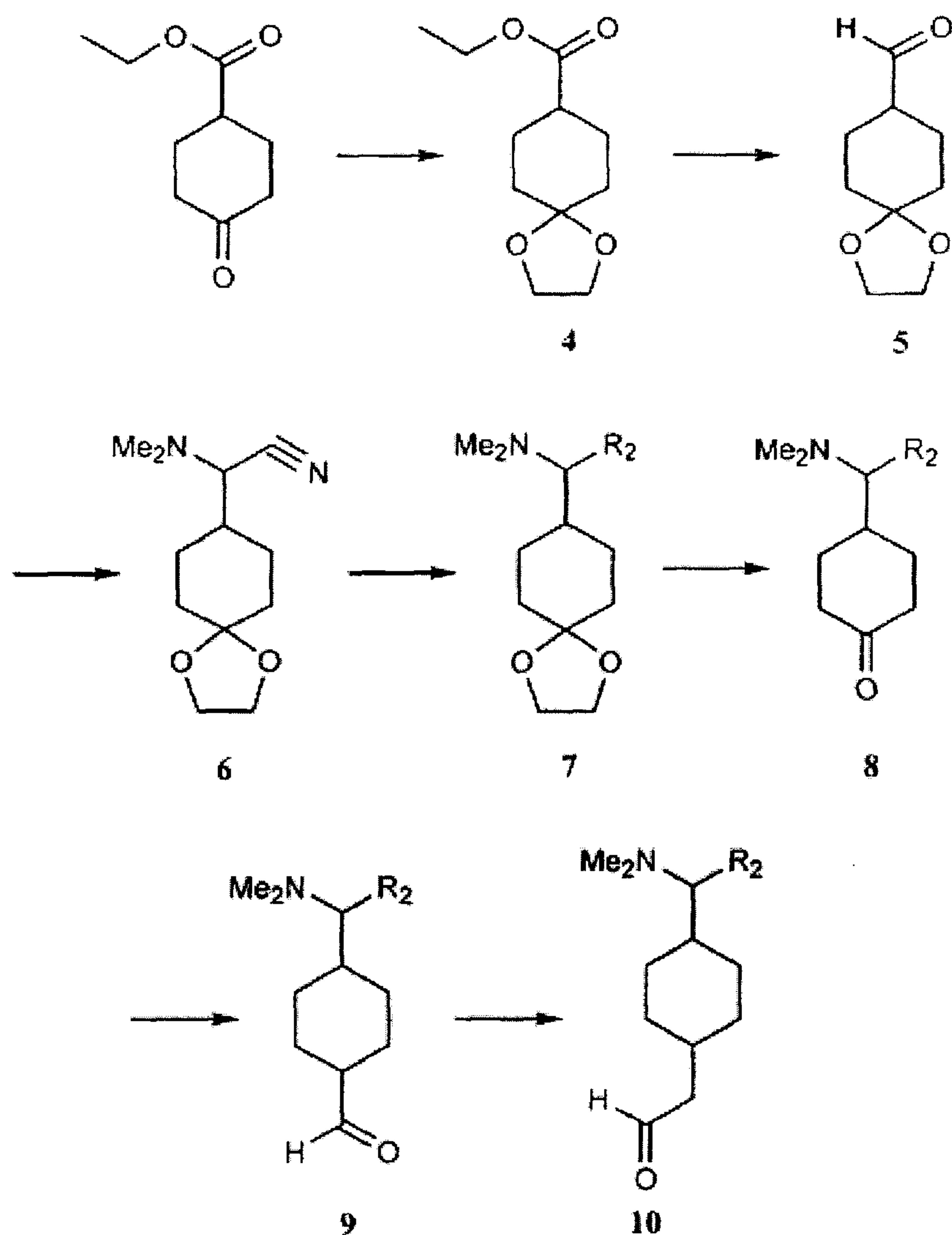
10

#### Examples

General instructions for the synthesis of 4-[dimethylamino-methyl]-cyclohexane-carbaldehydes and 4-[dimethylamino-methyl]-cyclohexyl-acetaldehydes.

15

57

**1st Stage**

Synthesis of the 1,4-dioxaspiro[4.5]decane-8-carboxylic acid ethyl ester 4

4-oxo-cyclohexanecarboxylic acid ethyl ester (52.8 g, 0.31 mole, Merck, Order No. 814249), ethylene glycol (67.4 g, 1.08 mole) and p-toluenesulfonic acid (0.7 g) in toluene (160 ml) were stirred for 20 hours at RT, the reaction solution was poured into diethyl ether (300 ml), and washed with water, sodium hydrogen carbonate solution and sodium chloride solution. The solution was dried (Na<sub>2</sub>SO<sub>4</sub>),

concentrated by evaporation in vacuo, and the remaining colourless liquid was processed further without purification.

## 5 2nd Stage

Synthesis of the 1,4-dioxo-spiro[4.5]decane-8-carbaldehyde  
5

Diisobutyl aluminium hydride (1.5 M solution in toluene,  
10 102 ml, 153 mmole) was added dropwise to a solution of 1,4-dioxo-spiro[4.5]decane-8-carboxylic acid ethyl ester 4 (32.13 g, 150 mmole) in absolute toluene (160 ml) at -70° to -65°C under argon and stirred for 30 minutes. The reaction mixture was then quenched at -70° to -60°C by  
15 adding methanol (80 ml). The reaction solution was heated to RT, saturated sodium chloride solution (100 ml) was added, and the reaction solution was suction filtered through diatomaceous earth. The diatomaceous earth was washed twice with ethyl acetate, and the aqueous solution  
20 was separated and extracted twice with ethyl acetate. The combined organic extracts were washed with saturated sodium chloride solution, dried over sodium sulphate, and concentrated by evaporation in vacuo.

## 25 3rd Stage

Synthesis of the dimethylamino-(1,4-dioxo-spiro[4.5]dec-8-yl)-acetonitrile 6

40% aqueous dimethylamine solution (85 ml, 0.67 mole), 1,4-  
30 dioxo-spiro-[4.5]decane-8-carbaldehyde 5 (240 g, 0.141 mole) and potassium cyanide (22.05 g, 0.338 mole) were added while cooling with ice to a mixture of 4N hydrochloric acid (37 ml) and methanol (22 ml). The

mixture was stirred for four days at room temperature and then extracted, after adding water (80 ml), with diethyl ether (4 x 100 ml). The organic phase was dried over sodium sulphate, concentrated by evaporation in vacuo, and the product was obtained as a white solid.

#### 4th Stage

Synthesis of the [(1,4-dioxo-spiro[4.5]dec-8-yl)-methyl]-dimethylamine **7**

10

A solution of the aminonitrile **6i** (19.89 g 88 mmole) in absolute THF (160 ml) or absolute diethyl ether (160 ml), depending on the solvent of the Grignard reagent, was added dropwise to a 1M solution of the corresponding Grignard reagent in THF or diethyl ether (220 ml, 220 mmole) under argon and cooling with ice, and stirred for 20 hours at RT. To work up the reaction mixture saturated ammonium chloride solution (100 ml) and water (100 ml) were added while cooling with ice, and the mixture was extracted with diethyl ether (3 x 100 ml). The organic phase was washed with water and saturated sodium chloride solution, dried (Na<sub>2</sub>SO<sub>4</sub>) and concentrated by evaporation. The product obtained was used without further purification in the next stage.

25

#### 5th Stage

Synthesis of the 4-[dimethylaminomethyl]-cyclohexanones  
The crude product of the corresponding [(1,4-dioxo-spiro[4.5]dec-8-yl)-methyl]-dimethylamine **7i** (88 mmole) was dissolved in water (40 ml), concentrated hydrochloric acid (59 ml) was added, and the whole was stirred to 20 hours at RT. The reaction mixture was extracted with diethyl ether (2 x 100 ml), the aqueous phase was made alkaline with 5N

30

NaOH while cooling with ice, extracted with dichloromethane (3 x 100 ml), dried, and concentrated by evaporation. The products were obtained as white solids or oils.

#### 5 6th Stage

Synthesis of the 4-[dimethylaminomethyl]-cyclohexane-carbaldehyde **9**

(Methoxymethyl)triphenylphosphonium chloride (25.7 g, 10 75 mmole) was suspended in absolute THF (100 ml) under argon, potassium tert-butyrate (8.42 g, 75 mmole) dissolved in absolute THF (70 ml) was added dropwise, and then stirred for 15 minutes at 0°C.

15 The corresponding 4-[dimethylaminomethyl]-cyclohexanone **8** (50 mmole), dissolved in absolute THF (75 ml), was then added dropwise to the above solution and stirred overnight at RT. The mixture was hydrolysed by adding dropwise water (38 ml) and 6N HCL 112 ml) while cooling with iced water.  
20 After stirring for one hour at RT the mixture was extracted with ether (10 x 50 ml), the aqueous phase was adjusted to pH 11 with 5N NaOH, shaken with ethyl acetate (3 x 50 ml), dried over Na<sub>2</sub>SO<sub>4</sub>, and concentrated by evaporation in vacuo. The crude product was purified by flash chromatography with  
25 ethyl acetate/cyclohexane (1:1). As a rule two diastereomers were obtained in different ratios.

#### 7th Stage

Synthesis of the {4-[dimethylaminomethyl]-cyclohexyl}-  
30 acetaldehydes **10**

(Methoxymethyl)triphenylphosphonium chloride (43.53 g, 127 mmole) was suspended in absolute THF (200 ml) under

argon, potassium tert-butyrate (14.25 g, 127 mmole), dissolved in absolute THF (130 ml) was added dropwise at 0°C, and then stirred for 15 minutes at 0°C.

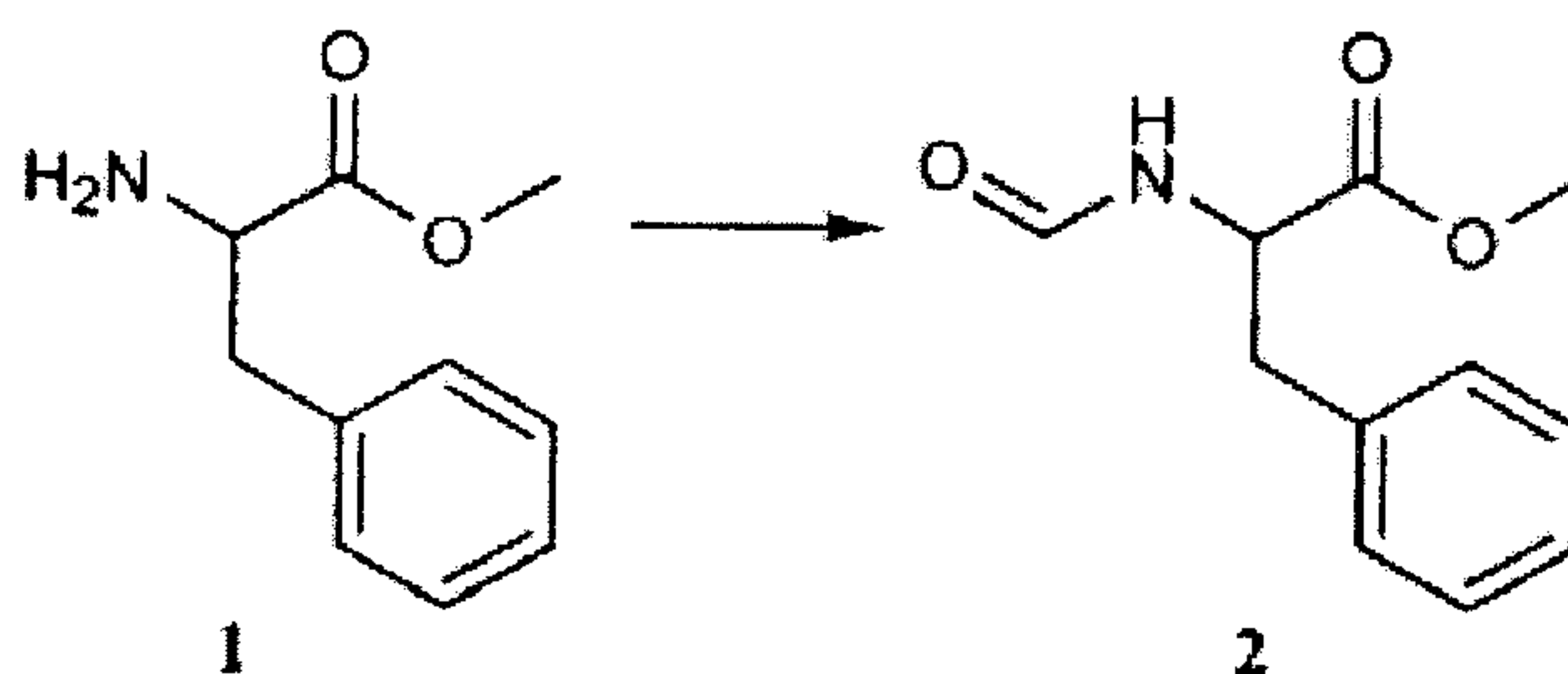
- 5 The corresponding 4-[dimethylaminomethyl]-cyclohexane carbaldehyde **9i** (85 mmole), dissolved in absolute THF (130 ml), was then added dropwise and stirred overnight at RT. The mixture was hydrolysed by adding dropwise water (80 ml) and 6N HCl (200 ml), while cooling with iced water.
- 10 After stirring for one hour at RT the mixture was extracted 10 times with ether (each time 100 ml). The aqueous phase was adjusted to pH 11 with 5N NaOH, shaken three times with ethyl acetate (each time 100 ml), dried over Na<sub>2</sub>SO<sub>4</sub>, and concentrated by evaporation in vacuo. The crude product
- 15 was purified by flash chromatography with ethyl acetate/cyclohexane (1:1 or 1:2). As a rule two diastereomers were obtained in different ratios.

The isonitrile esters (component **C**) were either obtained

20 commercially or were prepared similarly to the method described in R. S. Bon *et al*, Org. Lett. 2003, 5, 20, 3759-3762. In the first stage a formylation was first of all carried out. The isonitrile is obtained therefrom by adding POCl<sub>3</sub>.

25

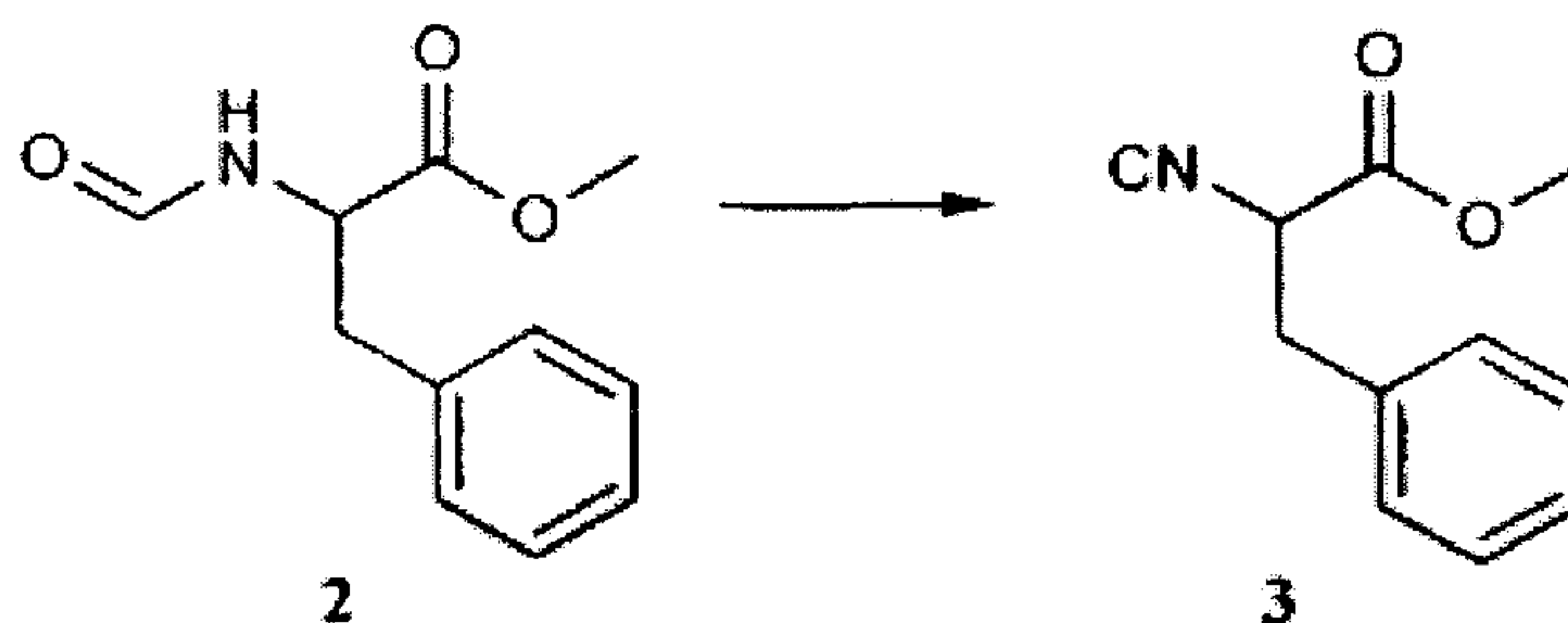
Methyl 2-(formylamino)-3-phenylpropanoate **2**



$^1\text{H-NMR}$  (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 3.07 – 3.22 (m, 2 H); 3.74 (s, 3 H); 4.92 – 5.01 (m, 1 H); 6.20 (bs, 1 H); 7.07 – 7.15 (m, 2 H); 7.23 – 7.34 (m, 3 H); 8.15 (s, 1 H).

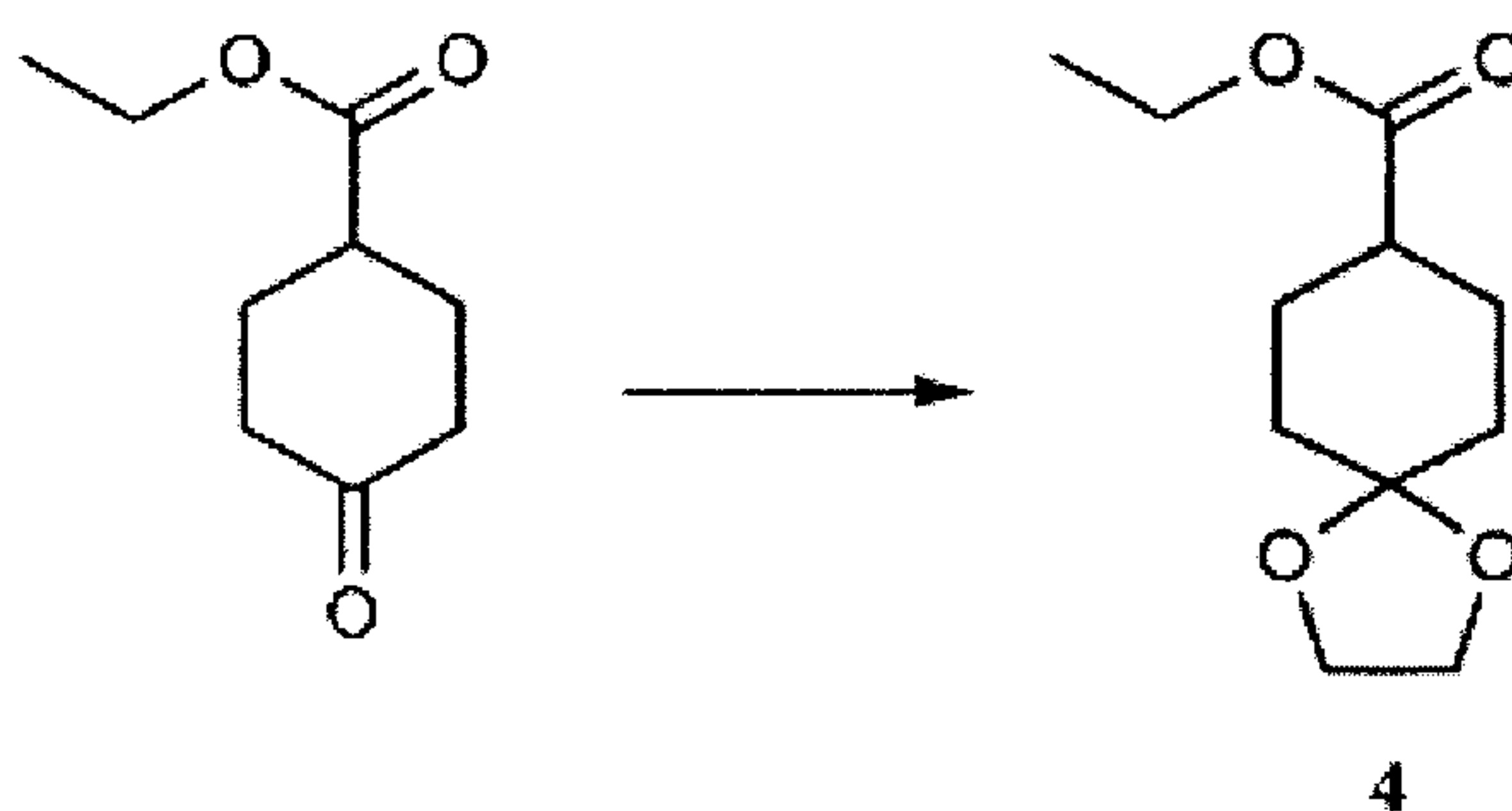
5

2-isocyano-3-phenylpropionic acid methyl ester 3



10  $^1\text{H-NMR}$  (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 3.14 (dd, 1 H,  $J_{\text{AA}'} = 8.66$  Hz,  $J_{\text{AB}} = 8.29$  Hz); 3.23 (dd, 1 H,  $J_{\text{AA}'} = 4.52$  Hz,  $J_{\text{AB}} = 4.90$  Hz); 3.80 (s, 3 H), 4.46 (dd, 1 H,  $J = 8.29$ ;  $J = 4.90$  Hz); 7.22 – 7.39 (m, 5 H).

15 1,4-dioxa-spiro[4.5]decane-8-carboxylic acid ethyl ester 4



4-oxo-cyclohexanecarboxylic acid ethyl ester (52.8 g, 0.31 mole, Merck, Order No. 814249), ethylene glycol (67.4 g, 1.08 mole) and p-toluenesulfonic acid (0.7 g) in toluene (160 ml) were stirred for 20 hours at RT, and the reaction solution was poured into diethyl ether (300 ml) and washed

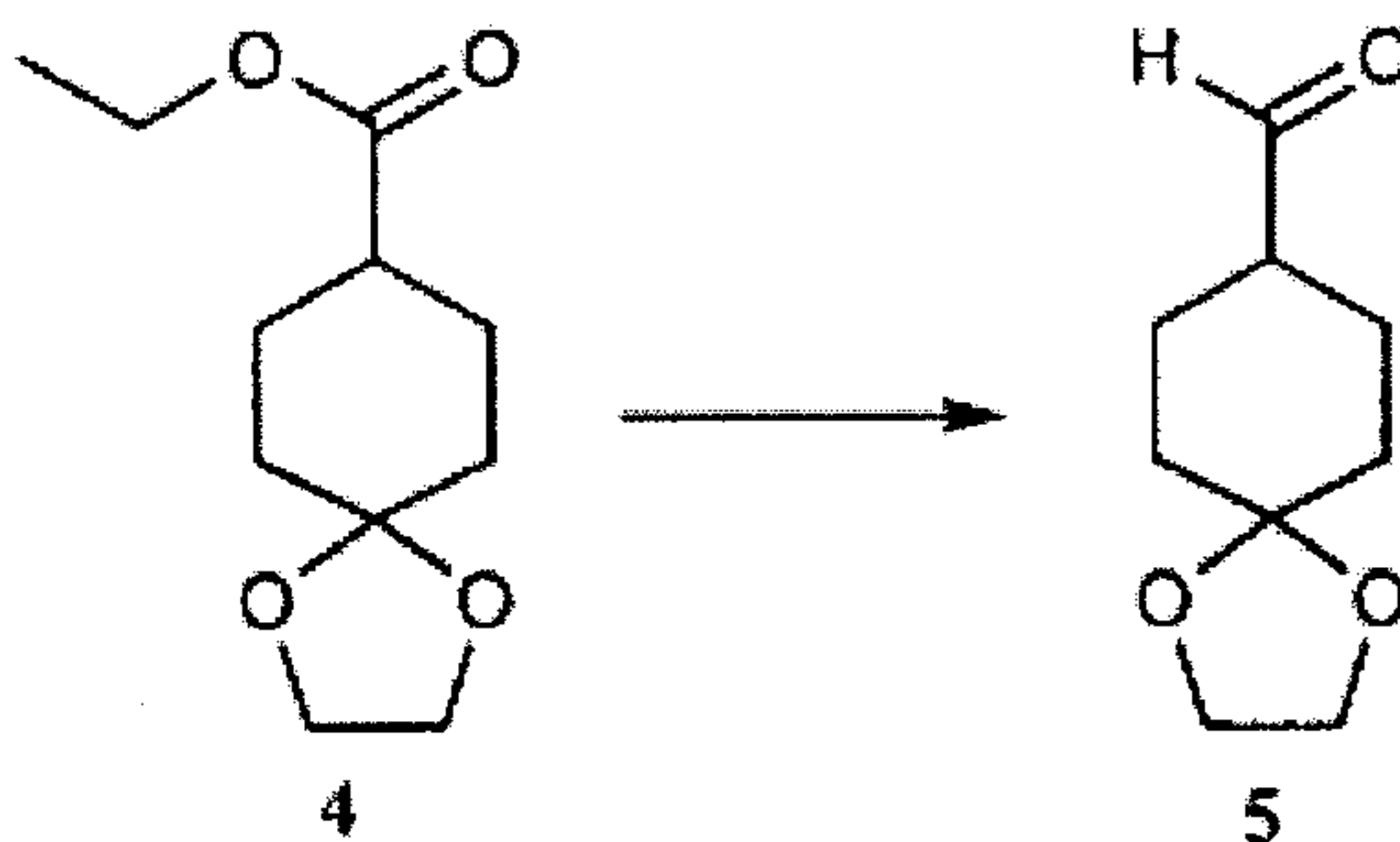
with water, sodium hydrogen carbonate solution and sodium chloride solution. The solution was dried ( $\text{Na}_2\text{SO}_4$ ), concentrated by evaporation in vacuo, and the remaining colourless liquid was processed further without  
5 purification.

Yield 66.5 g (100%)

$^1\text{H}$ -NMR ( $\text{CDCl}_3$ ): 1.24 (t, 3 H); 1.53 (m, 2 H); 1.76 (m, 4 H);  
10 1.92 (m, 2 H); 2.31 (m, 1 H); 3.91 (s, 4 H); 4.11 (q, 2 H).  
 $^{13}\text{C}$ -NMR ( $\text{CDCl}_3$ ): 14.28 (q); 26.32 (t); 33.76 (t); 41.59 (d);  
60.14 (t); 64.21 (t); 107.90 (d); 174.77 (s).

1,4-dioxa-spiro[4.5]decane-8-carbaldehyde **5**

15



Diisobutyl aluminium hydride (1.5 M solution in toluene, 102 ml, 153 mmole) was added dropwise at  $-70^\circ$  to  $-65^\circ\text{C}$   
20 under argon to a solution of 1,4-dioxaspiro[4.5]decane-8-carboxylic acid ethyl ester **4** (32.13 g, 150 mmole) in absolute toluene (160 ml), and stirred for 30 minutes. The reaction mixture was then quenched at  $-70^\circ$  to  $-60^\circ\text{C}$  by adding methanol (80 ml). The reaction solution was heated  
25 to RT, saturated sodium chloride solution (100 ml) was added, and the reaction solution was suction filtered through diatomaceous earth. The diatomaceous earth was

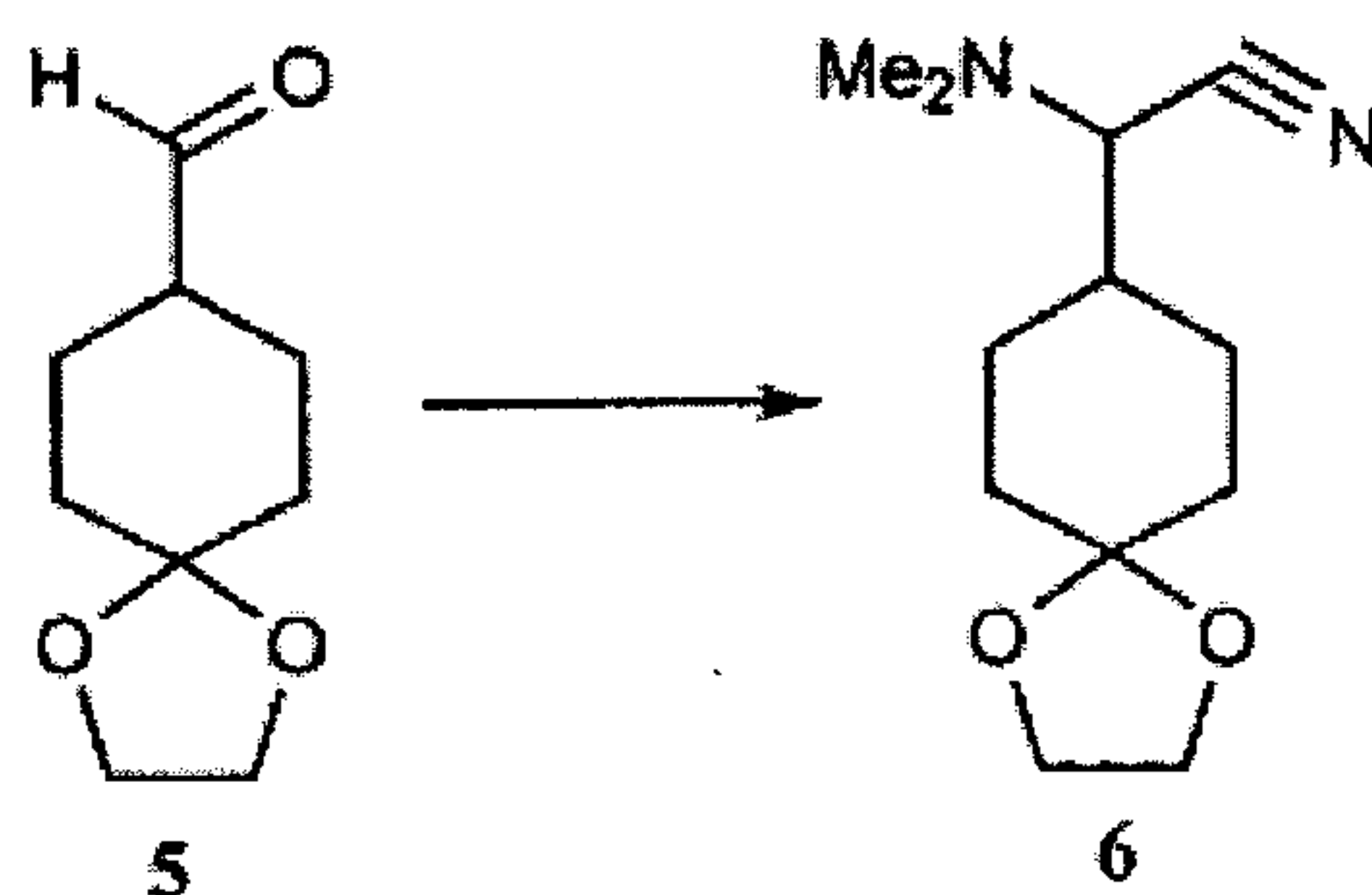
washed twice with ethyl acetate, and the aqueous solution was separated and extracted twice with ethyl acetate. The combined organic extracts were washed with saturated sodium chloride solution, dried over sodium sulphate, and concentrated by evaporation in vacuo.

**Yield: 24.01 g (94%), yellow oil**

$^1\text{H-NMR}$  ( $\text{CDCl}_3$ ): 1.54 (m, 2 H); 1.74 (m, 4 H); 1.91 (m, 2 H); 2.21 (m, 1 H); 3.91 (s, 4 H); 9.60 (s, 1 H).

$^{13}\text{C-NMR}$  ( $\text{CDCl}_3$ ): 23.35 (t); 33.37 (t); 48.18 (d); 64.30 (t); 107.89 (d); 203.51 (s).

15 **Dimethylamino-(1,4-dioxa-spiro[4.5]dec-8-yl)-acetonitrile 6**



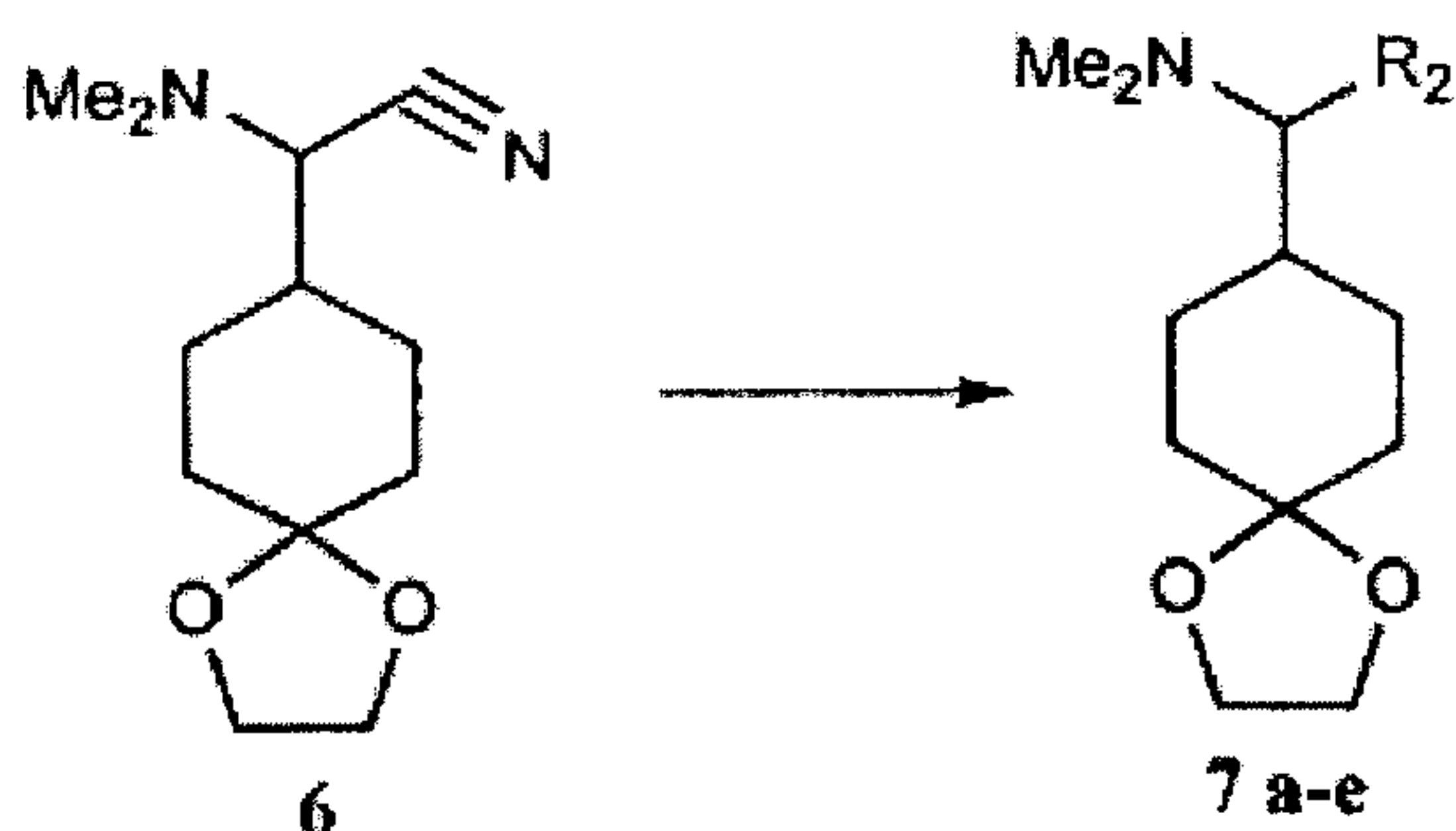
40% aqueous dimethylamine solution (85 ml, 0.67 mole), 1,4-dioxaspiro-[4.5]decane-8-carbaldehyde 5 (240 g, 0.141 mole) and potassium cyanide (22.05 g, 0.338 mole) were added while cooling with ice to a mixture of 4N hydrochloric acid (37 ml) and methanol (22 ml). The mixture was stirred for four days at room temperature and then, after adding water (80 ml), extracted with diethyl ether (4 x 100 ml). The organic phase was dried over sodium sulphate, concentrated by evaporation in vacuo, and the product was obtained as a white solid.

Yield: 25.2 g (81%)

m.p. 48-51°C.

<sup>1</sup>H-NMR (CDCl<sub>3</sub>): 1.23 - 2.03 (m, 9 H); 2.28 (s, 6 H); 3.16  
5 (d, 1 H); 3.93 (m, 4 H).

<sup>13</sup>C-NMR (CDCl<sub>3</sub>): 26.67 (t); 27.93 (t); 33.87 (t); 36.94 (d);  
41.90 (q); 64.30 (t); 64.36 (t); 108.33 (d); 115.94 (s).



[(1,4-dioxaspiro[4.5]dec-8-yl)-4-fluorophenylmethyl]-  
10 dimethylamine **7a** (R<sup>2</sup> = 4-fluorophenyl)

A solution of the aminonitrile **6** (19.89 g 88 mmole) in  
absolute THF (160 ml) was added dropwise under argon and  
cooling with ice to a 1M solution of 4-fluorophenyl  
15 magnesium bromide in THF (220 ml, 220 mmole) and stirred  
for 20 hours at RT. To work up the reaction mixture,  
saturated ammonium chloride solution (100 ml) and water  
(100 ml) were added while cooling with ice, and the mixture  
was extracted with diethyl ether (3 x 100 ml). The organic  
20 phase was washed with water and saturated sodium chloride  
solution, dried (Na<sub>2</sub>SO<sub>4</sub>) and concentrated by evaporation.

Yield: 31 g (>100%)

25 <sup>13</sup>C-NMR (CDCl<sub>3</sub>): 26.68 (t); 28.11 (t); 34.43 (t); 34.55 (t);  
37.37 (d); 41.68 (q); 64.12 (t); 73.65 (d); 108.88 (d)

114.23 (d); 114.44 (d); 130.27; 130.35; 132.43; 160.36 (s);  
162.78 (s).

[(1,4-dioxa-spiro[4.5]dec-8-yl)-3-fluorophenylmethyl]-  
5 dimethylamine **7b** {R<sup>2</sup> = 3-fluorophenyl}

A solution of the aminonitrile **6** (23.45 g, 104 mmole) in  
absolute THF (100 ml) was added to a 1M solution of  
3-fluorophenyl magnesium bromide in THF (208 ml, 208 mmole)  
10 under argon and cooling with ice, and stirred for 20 hours  
at RT. To work up the reaction mixture, saturated ammonium  
chloride solution (100 ml) and water (100 ml) were added  
while cooling with ice, and the mixture was extracted with  
diethyl ether (3 x 100 ml). The organic phase was washed  
15 with water and saturated sodium chloride solution, dried,  
and concentrated by evaporation.

Yield: 33.33 g (99%).

20 <sup>1</sup>H-NMR (CDCl<sub>3</sub>): 1.12 (m, 1 H); 1.26 (m, 1 H); 1.46 - 1.81  
(m, 7 H); 2.10 (s, 6 H); 3.10 (d, 1 H); 3.90 (m, 4 H); 6.85  
(m, 3 H); 7.27 (m, 1 H).

<sup>13</sup>C-NMR (CDCl<sub>3</sub>): 26.80 (t); 28.08 (t); 34.48 (t) 34.45 (t);  
34.59 (t); 37.26 (d); 41.71 (q); 64.19 (t); 74.04 (t);  
25 108.91 (d); 113.51 (d); 113.71 (d); 115.52 (d); 115.72 (d);  
124.83 (d); 128.82 (d); 128.90 (d); 139.66 (s); 161.15 (s);  
163.58 (s).

[(4-chlorophenyl)-(1,4-dioxa-spiro[4.5]dec-8-yl)-  
30 dimethylamine **7c** (R<sup>2</sup> = 4-chlorophenyl)

A solution of the aminonitrile **6** (22.43 g, 100 mmole) in  
absolute ether (100 ml) was added to a 1M solution of 4-

chlorophenyl magnesium bromide in ether (200 ml, 200 mmole) under argon and while cooling with ice, and stirred for 20 hours at RT. To work up the reaction mixture, saturated ammonium chloride solution (100 ml) and water (100 ml) were  
5 added while cooling with ice, and the mixture was extracted with diethyl ether (3 x 100 ml). The organic phase was washed with water and saturated sodium chloride solution, dried, and concentrated by evaporation.

10 Yield: 30.9 g (100%)

$^{13}\text{C}$ -NMR ( $\text{CDCl}_3$ ): 26.65 (t); 28.11 (t); 34.46 (t); 34.60 (t); 37.28 (d); 41.76 (q); 64.17 (t); 73.80 (d); 108.88 (s); 127.72 (d); 129.53 (d); 132.39 (d); 135.33 (d).

15

[(1,4-dioxo-spiro[4.5]dec-8-yl)-thiophen-2-yl-methyl]-dimethylamine (**7d** ( $\text{R}^2 = 2\text{-thienyl}$ ))

A solution of the aminonitrile **6** (2.24 g, 10 mmole) in  
20 absolute THF (10 ml) was added dropwise under argon and while cooling with ice to a 1M solution of thiophen-2-yl-magnesium bromide in THF (20 ml, 20 mmole), and stirred for 20 hours at RT. To work up the reaction mixture, saturated ammonium chloride solution (10 ml) and water (10 ml) were  
25 added while cooling with ice, and the mixture was extracted with diethyl ether (3 x 10 ml). The organic phase was washed with water and saturated sodium chloride solution, dried, and concentrated by evaporation.

30 Yield: 2.8 g (100%)

$^{13}\text{C}$ -NMR ( $\text{CDCl}_3$ ): 27.72 (t); 27.88 (t); 34.27 (t); 39.28 (d); 41.10 (q); 64.11 (t); 68.89 (d); 108.88 (s); 123.55 (d); 125.88 (d); 127.53 (d); 139.50 (s).

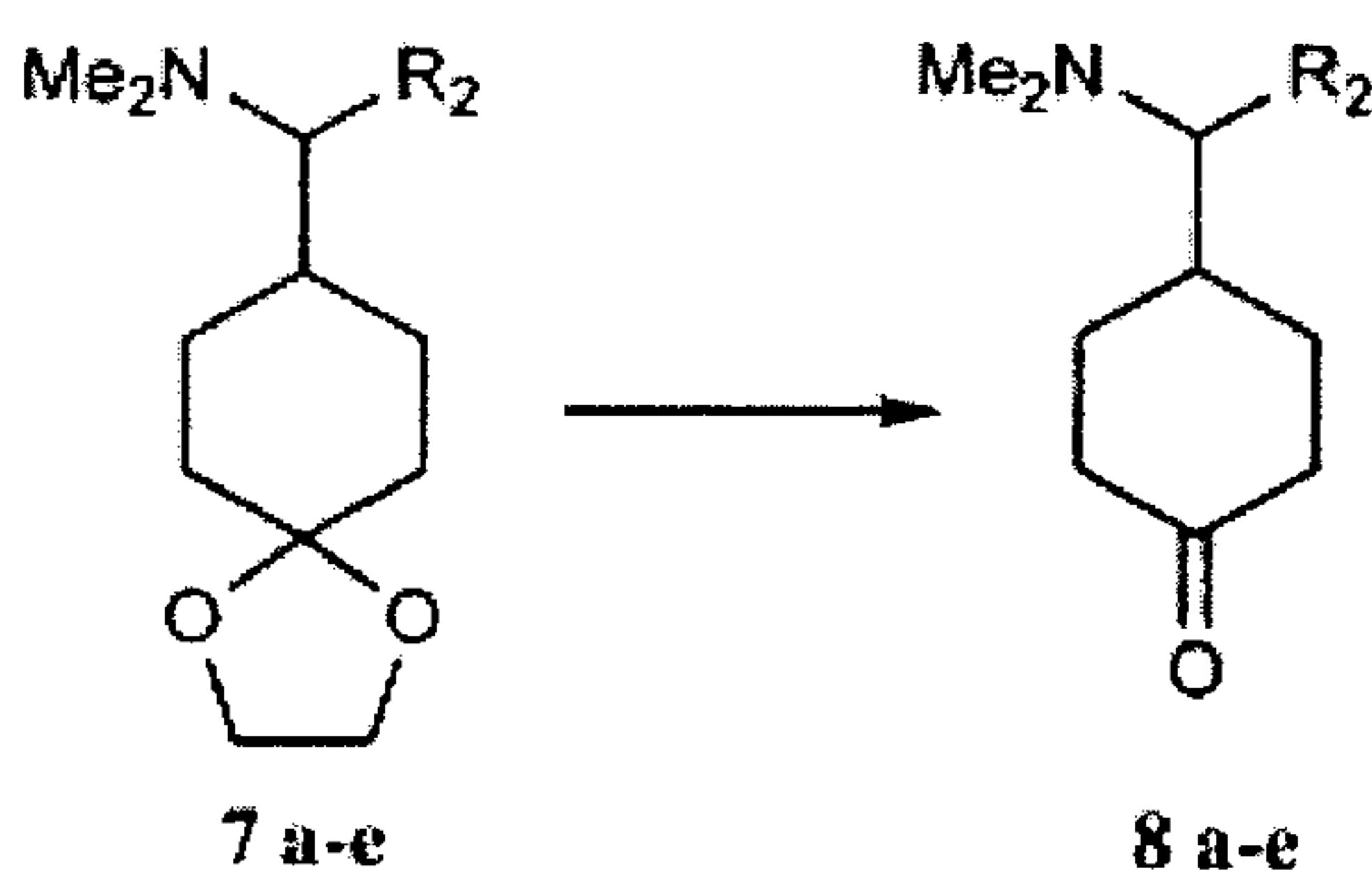
5 [1-(1,4-dioxaspiro[4.5]dec-8-yl)-3-phenylpropyl]-dimethylamine **7e** ( $\text{R}^2$  = phenethyl)

A solution of the aminonitrile **6** (21.93 g, 97 mmole) in absolute THF (180 mmole) was added dropwise under argon and  
 10 while cooling with ice to a 1M solution of phenylethyl magnesium chloride in THF (242 ml, 242 mmole) and stirred for 20 hours at RT. To work up the reaction mixture, saturated ammonium chloride solution (100 ml) and water (100 ml) were added while cooling with ice, and the mixture  
 15 was extracted with diethyl ether (3 x 100 ml). The organic phase was washed with water and saturated sodium chloride solution, dried, and concentrated by evaporation.

Yield: 34 g (>100%)

20

$^{13}\text{C}$ -NMR ( $\text{CDCl}_3$ ): 27.43 (t); 28.95 (t); 29.42 (t); 34.82 (t); 35.40 (t); 38.76 (d); 41.16 (q); 64.17 (t); 67.41 (d); 108.86 (s); 125.41 (d); 127.66 (d); 128.11 (d); 142.69 (s).



25

4-[dimethylamino-(4-fluorophenyl)-methyl]-cyclohexanone **8a** ( $\text{R}^2$  = 4-fluorophenyl)

The crude product of the ketal **7a** (26 g, 88 mmole) was dissolved in water (40 ml), concentrated hydrochloric acid (59 ml) was added, and the whole was stirred for 20 hours at RT. The reaction mixture was extracted with diethyl ether (2 x 100 ml), and the aqueous phase was made alkaline with 5N NaOH while cooling with ice, extracted with dichloromethane (3 x 100 ml) dried, and concentrated by evaporation.

10

Yield: 21.36 g (98%)

<sup>13</sup>C-NMR (CDCl<sub>3</sub>): 28.90 (t); 30.48 (t); 37.00 (t); 40.49 (t); 40.72 (t); 41.79 (q); 72.98 (d); 114.42 (d); 114.62 (d); 130.20 (d); 130.28 (d); 131.88 (s); 160.50 (s); 162.93 (s); 211.44 (s).

15

4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexanone **8b**  
(R<sup>2</sup> = 3-fluorophenyl)

20

The ketal **7b** (30.3 g, 103 mmole) was dissolved in water (44 ml), concentrated hydrochloric acid (64 ml) was added, and the mixture was stirred for 20 hours at RT. The reaction mixture was shaken with diethyl ether (2 x 100 ml), and the aqueous phase was made alkaline with 5N NaOH while cooling with ice, extracted with dichloromethane (3 x 100 ml), dried, and concentrated by evaporation. The ketone was isolated as a colourless solid.

25

Yield: 22.4 g (87%)

30

m.p.: 72-75°C

$^{13}\text{C}$ -NMR ( $\text{CDCl}_3$ ): 28.97 (t); 30.44 (t); 36.90 (t); 40.52 (t); 40.75 (t); 41.82 (q); 73.37 (d); 113.84; 114.06; 115.42; 115.62 124.71; 129.03; 129.11; 139.00; 139.06; 161.16; 163.60; 211.40 (s).

5

4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexanone **8c**  
( $\text{R}^2$  = 4-chlorophenyl)

The ketal **7c** (30.98 g, 100 mmole) was dissolved in water  
10 (44 ml), concentrated hydrochloric acid was added (64 ml),  
and the mixture was stirred for 20 hours at RT. The  
reaction mixture was shaken with diethyl ether (2 x 100  
ml), and the aqueous phase was made alkaline with 5N NaOH  
while cooling with ice, and extracted with dichloromethane  
15 (3 x 100 ml), dried, and concentrated by evaporation. The  
ketone was isolated as an oil.

Yield: 21.9 g (82%)

20  $^{13}\text{C}$ -NMR ( $\text{CDCl}_3$ ): 28.88 (t); 30.45 (t); 36.89 (t); 40.49 (t);  
40.74 (t); 41.83 (q); 73.12 (d); 127.87 (d); 130.16 (d);  
132.75 (d); 134.70 (s); 211.35 (s).

4-(dimethylaminothiophen-2-yl-methyl)-cyclohexanone **8d** ( $\text{R}^2$  =  
25 2-thienyl)

The ketal **7d** (2.80 g, 10 mmole) was dissolved in water  
(4.4 ml), concentrated hydrochloric acid (6.4 ml) was  
added, and the mixture was stirred for 20 hours at RT. The  
30 reaction mixture was shaken with diethyl ether (2 x 10 ml),  
the aqueous phase was made alkaline with 5N NaOH while  
cooling with ice, and was extracted with dichloromethane

(3 x 10 ml), dried, and concentrated by evaporation. The ketone was isolated as an oil.

Yield: 1.79 g (75%)

5

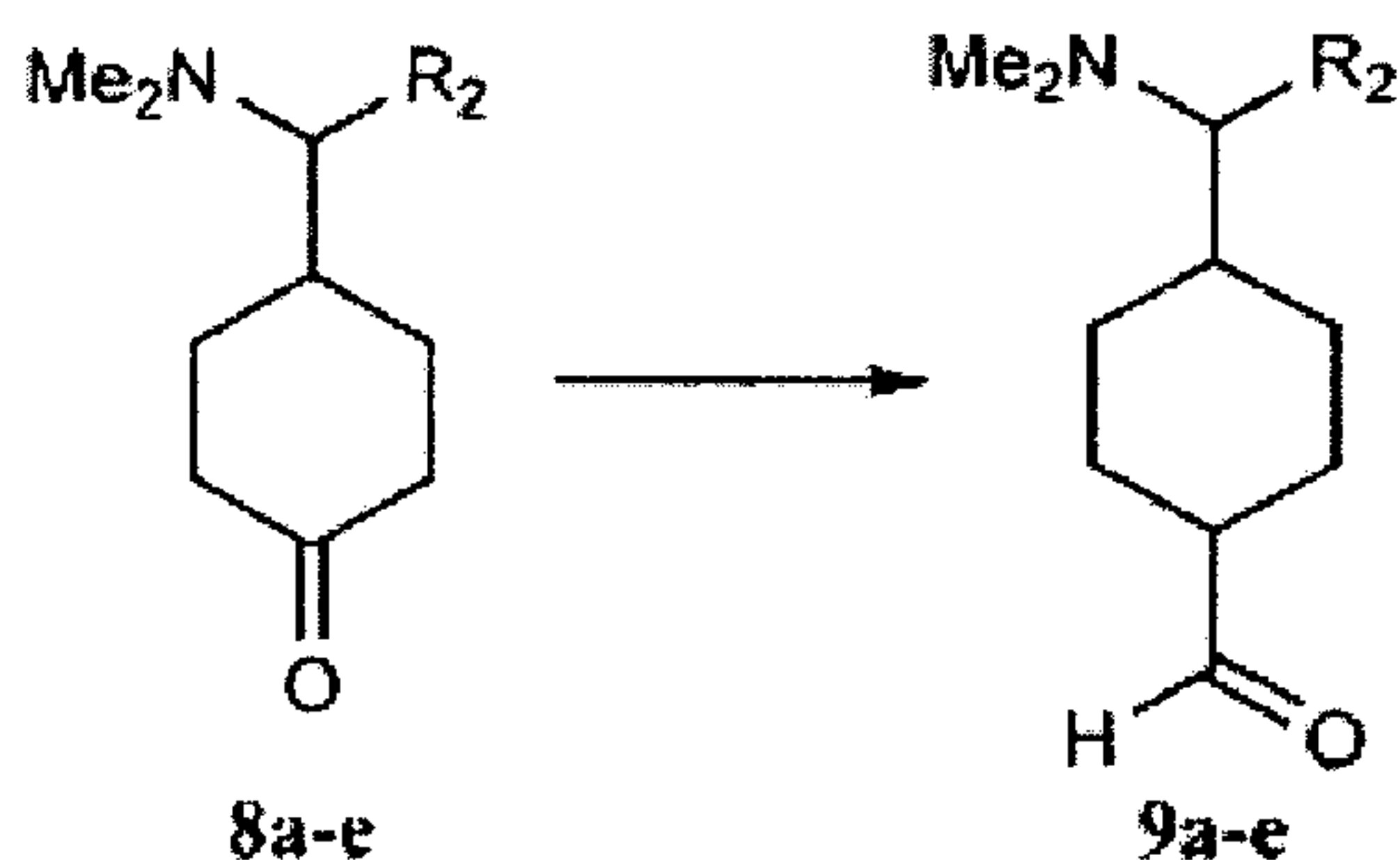
$^{13}\text{C}$ -NMR ( $\text{CDCl}_3$ ): 30.02 (t); 30.18 (t); 38.84 (t); 40.29 (t); 39.28 (d); 41.17 (q); 68.24 (d); 123.88 (d); 126.01 (d); 126.34 (d); 138.77 (d); 211.49 (s).

10 4-(1-dimethylamino-3-phenylpropyl)-cyclohexanone **8e** ( $\text{R}^2$  = phenethyl)

The crude product of the ketal **7e** (29.6 g, 97 mmole) was dissolved in water (44 ml), concentrated hydrochloric acid (64 ml) was added, and the mixture was stirred for 20 hours at RT. The reaction mixture was shaken with diethyl ether (2 x 100 ml), the aqueous phase was made alkaline with 5N NaOH while cooling with ice, and was extracted with dichloromethane (3 x 100 ml), dried, and concentrated by evaporation. The ketone was isolated as a colourless oil.

Yield: 16.9 g (58%)

$^{13}\text{C}$ -NMR ( $\text{CDCl}_3$ ): 29.40 (t); 30.02 (t); 30.97 (t); 35.34 (t); 38.71 (t); 40.79 (t); 41.01 (t); 41.23 (q); 66.65 (d); 125.66 (d); 128.12 (d); 128.19 (d); 142.27 (s); 211.70 (s).



4-[dimethylamino-(4-fluorophenyl)-methyl]-cyclohexane-carbaldehyde **9a** ( $R^2$  = 4-fluorophenyl)

(Methoxymethyl)triphenylphosphonium chloride (25.7 g, 75 mmole) was suspended in absolute THF (100 ml) under argon, potassium tert-butyrate (8.42 g, 75 mmole) dissolved in absolute THF (70 ml) was added dropwise at 0°C, and the mixture was then stirred for 15 minutes at 0°C.

The ketone **8a** (12.44 g, 50 mmole), dissolved in absolute THF (75 mmole), was then added dropwise at RT to the above solution and stirred overnight at RT. The reaction mixture was hydrolysed by adding dropwise water (38 ml) and 6N HCl (112 ml) while cooling with iced water. After stirring for one hour at RT the mixture was extracted with ether (10 x 50 ml), the aqueous phase was adjusted to pH 11 with 5N NaOH, was shaken with ethyl acetate (3 x 50 ml) dried over Na<sub>2</sub>SO<sub>4</sub> and concentrated by evaporation in vacuo. The crude product was purified by flash chromatography with ethyl acetate/cyclohexane (1:1).

Yield: 9.13 g (70%)

<sup>1</sup>H-NMR (DMSO, 600 MHz, selected signals):  $\delta$  = 1.97 (s, 3 H); 1.99 (s, 3 H); 3.08 (d, 1 H,  $J$  = 9.06 Hz); 3.14 (d, 1 H,  $J$  = 9.82 Hz); 9.53 (s, 1 H); 9.56 (s, 1 H).

<sup>13</sup>C-NMR (CDCl<sub>3</sub>, both diastereomers):  $\delta$  = 23.97; 24.21; 25.85; 26.02; 26.17; 27.35; 28.00; 29.90; 37.26; 38.34; 41.50; 41.95; 47.36; 50.55; 72.75; 75.84; 114.25; 114.45; 130.33; 130.40; 132.61; 160.41; 162.83; 204.10; 204.93.

4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexane-carbaldehyde ( $R^2$  = 3-fluorophenyl) **9b**

(Methoxymethyl)triphenylphosphonium chloride (15.42 g, 45 mmole) was suspended in absolute THF (50 ml) under argon, potassium tert-butyrate (5.05 g, 45 mmole), dissolved in absolute THF (50 ml), was added dropwise at 0°C, and the mixture was then stirred for 15 minutes at 0°C.

The ketone **8b** (7.48 g, 0.30 mmole), dissolved in absolute THF (50 ml), was then added dropwise at RT to the above solution and the mixture was stirred overnight at RT. The mixture was hydrolysed by adding dropwise water (25 ml) and 6N HCl (75 ml) while cooling with iced water. After stirring for one hour at RT the mixture was extracted with ether (10 x 50 ml), the aqueous phase was adjusted to pH 11 with 5N NaOH extracted with ethyl acetate (3 x 50 ml) dried over Na<sub>2</sub>SO<sub>4</sub>, and concentrated by evaporation in vacuo. The crude product was purified by flash chromatography with ethyl acetate/cyclohexane (1:1).

Yield: 6.55 g (83%).

m.p.: 40-43°C.

<sup>1</sup>H-NMR (DMSO, 600 MHz, selected signals):  $\delta$  = 1.99 (s, 3 H); 2.01 (s, 3 H); 3.10 (d, 1 H, J = 9.06 Hz); 3.18 (d, 1 H, J = 9.82 Hz); 9.54 (s, 1 H); 9.56 (s, 1 H).

<sup>13</sup>C-NMR (CDCl<sub>3</sub>): 23.93; 24.12; 25.79; 25.95; 26.19; 27.19; 27.99; 29.77; 37.05; 38.16; 41.45; 41.91; 47.30; 50.49; 71.50; 74.78; 113.50; 115.37; 124.78; 128.24; 130.59; 131.24; 131.67; 139.14; 139.76; 160.06; 163.50; 204.01; 204.85.

4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexane-carbaldehyde **9c** ( $R^2$  = 4-chlorophenyl)

(Methoxymethyl)triphenylphosphonium chloride (68.55 g, 200 mmole) was suspended in absolute THF (200 ml) under argon, potassium tert-butyrate (22.44 g, 200 mmole), dissolved in absolute THF (300 ml), was added dropwise at 0°C, and the mixture was then stirred for 15 minutes at 0°C.

The ketone **8c** (38 g, 143 mmol), dissolved in absolute THF (200 ml), was then added at RT to the above solution and the mixture was stirred overnight at RT. The mixture was hydrolysed by adding dropwise water (150 ml) and 6N HCl (450 ml) while cooling with iced water. After stirring for one hour at RT the mixture was extracted with ether (10 x 100 ml), the aqueous phase was adjusted to pH 11 with 5N NaOH, shaken with ethyl acetate (3 x 100 ml) dried over Na<sub>2</sub>SO<sub>4</sub>, and concentrated by evaporation in vacuo. The crude product was purified by passage through two silica gel columns (400 g) with ethyl acetate/cyclohexane (1:1).

Yield: 32.17 g (80%).

<sup>1</sup>H-NMR (DMSO, 600 MHz, selected signals):  $\delta$  = 1.97 (s, 3 H); 1.99 (s, 3 H); 3.07 (d, 1 H,  $J$  = 9.07 Hz); 3.14 (d, 1 H,  $J$  = 9.82 Hz); 9.53 (s, 1 H); 9.55 (s, 1 H).

<sup>13</sup>C-NMR (CDCl<sub>3</sub> both diastereomers):  $\delta$  = 23.92; 24.16; 25.80; 25.97; 26.13; 27.25; 27.90; 29.81; 37.08; 38.19; 41.47; 41.96; 47.29; 50.48; 72.81; 74.54; 127.65; 130.28; 132.40; 134.78; 135.43; 203.98; 204.82.

4-(dimethylaminothiophen-2-yl-methyl)-cyclohexane carbaldehyde **9d** ( $R^2$  = 2-thienyl)

(Methoxymethyl)triphenylphosphonium chloride (20.56 g, 60 mmole) was suspended in absolute THF (70 ml) under argon, potassium tert-butyrate (6.73 g, 60 mmole), dissolved in absolute THF (70 ml), was added dropwise at 0°C, and the mixture was then stirred for 15 minutes at 0°C. The ketone **8d** (9.4 g, 40 mmole), dissolved in absolute THF (70 ml), was then added dropwise at RT to the above solution and the mixture was stirred overnight at RT. The mixture was hydrolysed by adding dropwise water (60 ml) and 6N HCl (180 ml), while cooling with iced water. After stirring for one hour at RT the mixture was extracted with ether (5 x 50 ml), the aqueous phase was adjusted to pH 11 with 5N NaOH, shaken with ethyl acetate (3 x 50 ml), dried over Na<sub>2</sub>SO<sub>4</sub>, and concentrated by evaporation in vacuo. The crude product was purified by flash chromatography with ethyl acetate/cyclohexane (1:1).

Yield: 7.66 g (77%)

20

<sup>1</sup>H-NMR (DMSO, 600 MHz, selected signals): δ = 2.03 (s, 3 H); 2.05 (s, 3 H); 3.44 (d, 1 H, J = 9.82 Hz); 3.52 (d, 1 H, J = 10.58 Hz); 9.54 (s, 1 H); 9.58 (s, 1 H).

<sup>13</sup>C-NMR (CDCl<sub>3</sub>, both diastereomers): δ = 23.74; 23.83; 25.80; 25.84; 26.98; 27.09; 29.15; 29.68; 39.13; 40.20; 40.98; 41.29 (N(CH<sub>3</sub>)<sub>2</sub>); 47.48; 50.49; 67.81; 69.79; 123.61; 123.70; 125.89; 126.20; 126.24; 139.14; 139.48; 204.07; 204.82.

30 4-(1-dimethylamino-3-phenylpropyl)-cyclohexane-carbaldehyde **9e** (R<sup>2</sup> = phenethyl)

(Methoxymethyl)triphenylphosphonium chloride (20.56 g, 60 mmole) was suspended in absolute THF (85 ml) under argon, potassium tert-butyrate (6.73 g, 60 mmole), dissolved in absolute THF (70 ml), was added dropwise at 0°C, and the  
5 mixture was then stirred for 15 minutes at 0°C.

The ketone **8e** (10.2 g, 40 mmole), dissolved in absolute THF (60 ml), was then added dropwise at RT to the above solution, and the mixture was stirred overnight at RT. The  
10 mixture was hydrolysed by dropwise addition of water (35 ml) and 6N HCl (90 ml) while cooling with iced water. After stirring for one hour at RT the mixture was extracted with ether (10 x 50 ml), the aqueous phase was adjusted to pH 11 with 5N NaOH, extracted with ethyl acetate (3 x 50  
15 ml), dried over Na<sub>2</sub>SO<sub>4</sub>, and concentrated by evaporation in vacuo. The crude product was purified by flash chromatography with ethyl acetate/cyclohexane (1:1).

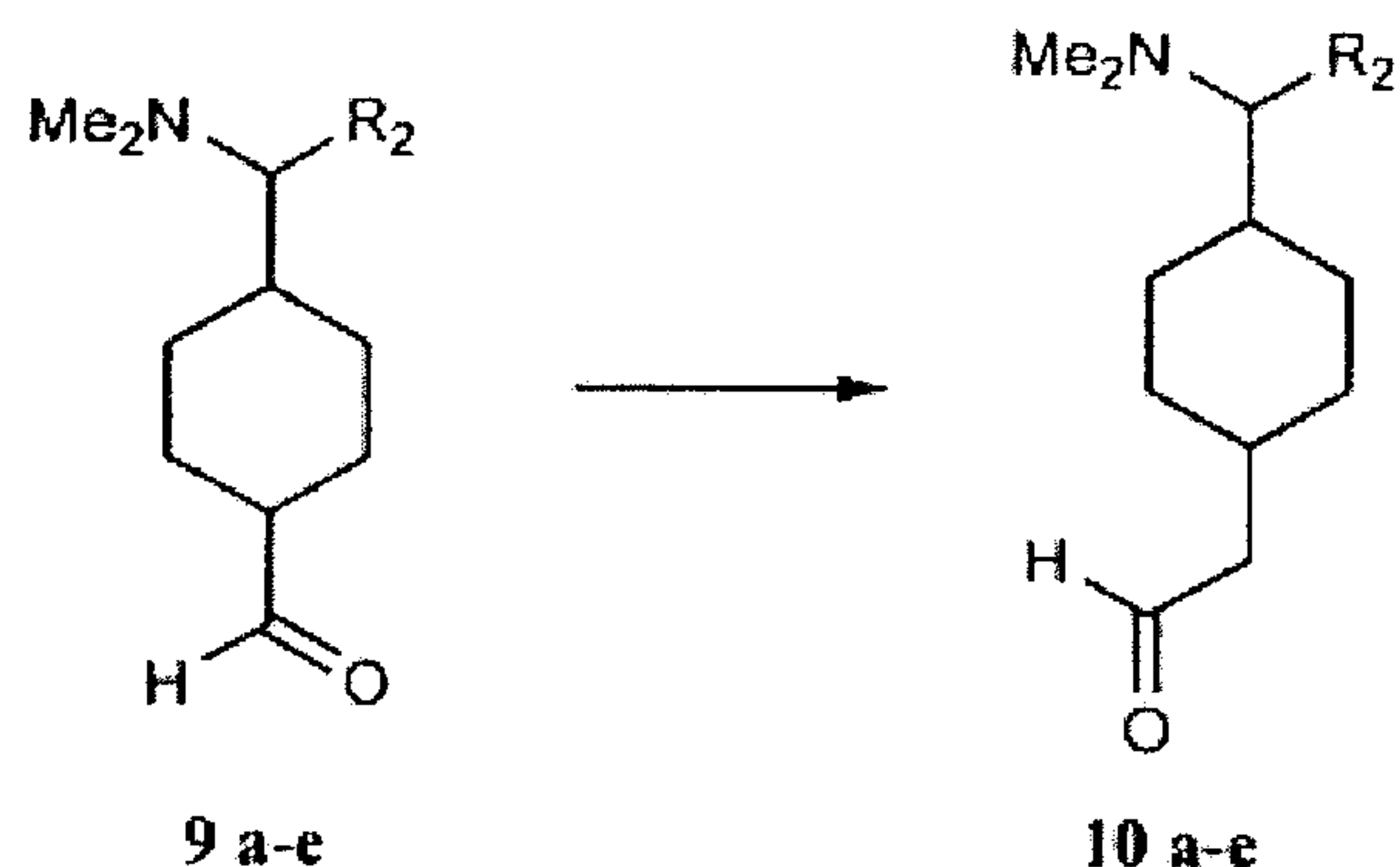
Yield: 6.73 g (63%).

20

<sup>1</sup>H-NMR (DMSO, 600 MHz, selected signals): δ = 2.18 (s, 3 H); 2.20 (s, 3 H dichloromethane); 9.54 (s, 1 H); 9.61 (s, 1 H).

25

<sup>13</sup>C-NMR (CDCl<sub>3</sub>, both diastereomers): δ = 24.35; 24.49; 26.00; 26.09; 26.85; 27.79; 29.07; 29.13; 35.27; 39.02; 40.98; 41.19; 46.99; 50.33; 66.85; 67.85; 70.54; 71.42; 125.40; 125.44; 128.02; 128.13; 131.15; 131.17; 142.45; 204.10; 205.01.



{4-[dimethylamino-(4-fluorophenyl)-methyl]-cyclohexyl}-acetaldehyde **10a** ( $\text{R}^2 = 4\text{-fluorophenyl}$ )

5 (Methoxymethyl)triphenylphosphonium chloride (43.53 g, 127 mmole) was suspended in absolute THF (200 ml) under argon, potassium tert-butyrate (14.25 g, 127 mmole), dissolved in absolute THF (130 ml), was added dropwise at 0°C, and the mixture was then stirred for 15 minutes at 0°C.

10

The aldehyde **9a** (22.3 g, 85 mmole), dissolved in absolute THF (130 ml), was then added dropwise at RT and the mixture was stirred overnight at RT. The mixture was hydrolysed by dropwise addition of water (80 ml) and 6N HCl (200 ml),  
 15 while cooling with iced water. After stirring for one hour at RT the mixture was extracted 10 times with ether (each time 100 ml). The aqueous phase was adjusted to pH 11 with 5N NaOH, shaken three times with ethyl acetate (each time 100 ml), dried over  $\text{Na}_2\text{SO}_4$ , and concentrated by evaporation  
 20 in vacuo. The crude product was purified by flash chromatography with ethyl acetate/cyclohexane (1:1).

Yield: 15.8 g (67%)

25  $^{13}\text{C}$ -NMR ( $\text{CDCl}_3$ , both diastereomers):  $\delta = 25.08; 25.87; 28.80; 29.10; 29.13; 29.62; 30.82; 32.90; 33.08; 36.19;$

38.43; 41.36; 42.01; 47.94; 51.17; 71.11; 74.69; 114.11;  
114.20; 114.32; 130.32; 130.40; 132.00; 132.92; 160.31;  
162.74; 202.15; 202.23.

- 5 {4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexyl}-  
acetaldehyde **10b** ( $R^2$  = 3- fluorophenyl)

(Methoxymethyl)triphenylphosphonium chloride (26.73 g, 78  
mmole) was suspended in absolute THF (90 ml) under argon,  
10 potassium tert-butyrate (8.75 g, 78 mmole), dissolved in  
absolute THF (90 ml), was added dropwise at 0°C, and the  
mixture was then stirred for 15 minutes at 0°C.

The aldehyde **9b** (13.69 g, 52 mmole), dissolved in absolute  
15 THF (90 ml), was then added dropwise at RT and the mixture  
was stirred overnight at RT. The mixture was hydrolysed by  
dropwise addition of water (50 ml) and 6N HCl (150 ml),  
while cooling with iced water. After stirring for one hour  
at RT the mixture was extracted 10 times with ether (each  
20 time 50 ml). The aqueous phase was adjusted to pH 11 with  
5N NaOH, shaken three times with ethyl acetate (each time  
100 ml), dried over Na<sub>2</sub> SO<sub>4</sub> and concentrated by evaporation  
in vacuo. The crude product was purified by flash  
chromatography with ethyl acetate/cyclohexane (1:1).

25

Yield: 12.61 g (87%)

<sup>13</sup>C-NMR (CDCl<sub>3</sub>, both diastereomers):  $\delta$  = 25.19; 25.83;  
28.90; 29.06; 29.14; 29.68; 30.77; 32.92; 32.98; 33.10;  
30 36.05; 38.36; 41.39; 42.04; 48.02; 51.20; 71.48; 75.07;  
113.43; 113.49; 113.64; 113.69; 115.55; 115.76; 124.89;  
128.70; 128.78; 128.88; 139.24; 140.08; 140.14; 161.09;  
163.52; 202.19; 202.27.

{4-[(4-Chlorophenyl)-dimethylaminomethyl]-cyclohexyl}-  
acetaldehyde **10c** ( $R^2$  = 4-chlorophenyl)

5 (Methoxymethyl)triphenylphosphonium chloride (25.02 g, 73 mmole) was suspended in absolute THF (90 ml) under argon, potassium tert-butyrate (8.19 g, 73 mmole), dissolved in absolute THF (90 ml), was added dropwise at 0°C, and the mixture was then stirred for 15 minutes at 0°C.

10

The aldehyde **9c** (13.86 g, 49 mmole), dissolved in absolute THF (90 ml), was then added dropwise at RT and the mixture was stirred overnight at RT. The mixture was hydrolysed by dropwise addition of water (50 ml) and 6N HCl (150 ml),  
15 while cooling with iced water. After stirring for one hour at RT the mixture was extracted 10 times with ether (each time 50 ml). The aqueous phase was adjusted to pH 11 with 5N NaOH, shaken three times with ethyl acetate (each time 100 ml), dried over Na<sub>2</sub>SO<sub>4</sub> and concentrated by evaporation  
20 in vacuo. The crude product was purified by flash chromatography with ethyl acetate/cyclohexane (1:1).

Yield: 12.07 g (84%).

25 <sup>13</sup>C-NMR (CDCl<sub>3</sub>, both diastereomers):  $\delta$  = 25.06; 25.82; 28.74; 29.00; 29.13; 29.60; 30.77; 32.87; 32.94; 33.07; 36.06; 38.32; 41.38; 42.05; 47.95; 51.17; 71.23; 74.80; 127.58; 127.66; 130.31; 132.28; 132.34; 134.81; 135.77; 202.12; 202.20.

30

{4-[dimethylamino-thiophen-2-yl-methyl]-cyclohexyl}-  
acetaldehyde **10d** ( $R^2$  = 2-thienyl)

(Methoxymethyl)triphenylphosphonium chloride (28.79 g, 84 mmole) was suspended in absolute THF (100 ml) under argon, potassium tert-butyrate (9.42 g, 84 mmole), dissolved in absolute THF (100 ml), was added dropwise at 0°C, and the  
5 mixture was then stirred for 15 minutes at 0°C.

The aldehyde **9d** (14.08 g, 56 mmole), dissolved in absolute THF (100 ml), was then added dropwise at RT and the mixture was stirred overnight at RT. The mixture was hydrolysed by  
10 dropwise addition of water (50 ml) and 6N HCl (150 ml), while cooling with iced water. After stirring for one hour at RT the mixture was extracted 10 times with ether (each time 50 ml). The aqueous phase was adjusted to pH 11 with 5N NaOH, shaken three times with ethyl acetate (each time  
15 100 ml), dried over Na<sub>2</sub>SO<sub>4</sub>, and concentrated by evaporation in vacuo. The crude product was purified by flash chromatography with ethyl acetate/cyclohexane (1:2).  
Yield: 11.48 g (77%).

20 <sup>13</sup>C-NMR (CDCl<sub>3</sub>, both diastereomers): δ = 25.80; 25.88; 28.73; 29.95; 30.49, 32.23; 32.76; 37.89; 40.21; 40.88; 41.23; 48.36; 51.09; 66.02; 69.97; 123.19; 123.72; 125.95; 126.31; 139.42; 139.91; 202.61.

25 [4-(1-dimethylamino-3-phenylpropyl)-cyclohexyl]-acetaldehyde **10e** (R<sup>2</sup> = phenethyl)

(Methoxymethyl)triphenylphosphonium chloride (50.3 g, 147 mmole) was suspended in absolute THF (150 ml) under argon, potassium tert-butyrate (16.5 g, 147 mmole), dissolved in  
30 absolute THF (140 ml), was added dropwise at 0°C, and the mixture was then stirred for 15 minutes at 0°C.

The aldehyde **9e** (27.0 g, 98 mmole), dissolved in absolute THF (150 ml), was then added dropwise at RT and the mixture was stirred overnight at RT. The mixture was hydrolysed by dropwise addition of water (102 ml) and 6N HCl (240 ml),  
5 while cooling with iced water. After stirring for one hour at RT the mixture was extracted five times with ether (each time 200 ml). The aqueous phase was adjusted to pH 11 with 5N NaOH while cooling with ice, shaken three times with ethyl acetate (each time 200 ml), dried over Na<sub>2</sub>SO<sub>4</sub> and  
10 concentrated by evaporation in vacuo. The crude product was purified by flash chromatography with ethyl acetate/cyclohexane (1:1).

Yield: 18.1 g (64%)

15

<sup>13</sup>C-NMR (CDCl<sub>3</sub>, both diastereomers):  $\delta$  = 25.55; 26.19; 29.04; 29.15; 29.35; 29.85; 31.00; 32.87; 32.68; 33.04; 35.33; 38.49; 40.86; 41.13; 47.51; 51.15; 65.48; 68.09.

20

#### Examples:

- 9a 4-[dimethylamino-(4-fluorophenyl)-methyl]-cyclohexane  
carbaldehyde
- 9b 4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexane  
carbaldehyde
- 9c 4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexane  
carbaldehyde
- 9d 4-(dimethylamino-thiophen-2-yl-methyl)-cyclohexane  
carbaldehyde
- 9e 4-(1-dimethylamino-3-phenylpropyl)-cyclohexane  
carbaldehyde

- 10a {4-[dimethylamino-(4-fluorophenyl)-methyl]-cyclohexyl}-  
acetaldehyde
- 10b {4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexyl}-  
acetaldehyde
- 10c {4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexyl}-  
acetaldehyde
- 10d [4-(dimethylamino-thiophen-2-yl-methyl)-cyclohexyl]-  
acetaldehyde
- 10e [4-(1-dimethylamino-3-phenylpropyl)-cyclohexyl]-  
acetaldehyde

The synthesis of the imidazoline derivatives according to the invention was carried out with the aid of the SLT106 accelerator from the company Chemspeed Ltd.

5

**Synthesis protocol for the automated synthesis**

220  $\mu$ mole of amine derivative (solution II, 1.1 ml, 0.2 M in methanol) were placed at room temperature in a dry 13 ml double jacket glass reactor (Chemspeed), followed by

10 addition of 220  $\mu$ mole of aldehyde derivative (solution I, 1.1 ml, 0.2 M in methanol) and 110  $\mu$ mole of isonitrile derivative (solution III, 1 ml, 0.1 M in methanol). The reaction mixture was then refluxed for 10 hours. After completion of the reaction the solvent was removed. The

15 compound was purified by means of HPLC. The purification was carried out via HPLC-MS. In all the specified cases the exact mass was found as M+1.

## Examples:

| No. | Name                                                                                                                                                  | Mol.<br>wt. |
|-----|-------------------------------------------------------------------------------------------------------------------------------------------------------|-------------|
| 11. | 1-cyclohexyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexyl}-4-isobutyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester              | 499.36      |
| 12. | 4-(4-chlorobenzyl)-1-cyclohexyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexyl}-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester      | 567.30      |
| 13. | 4-butyl-1-cyclohexyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexyl}-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester                 | 499.36      |
| 14. | 5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexyl}-1-cyclohexyl-4-isobutyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester               | 515.33      |
| 15. | 4-(4-chlorobenzyl)-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexyl}-1-cyclohexyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester       | 583.27      |
| 16. | 4-butyl-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexyl}-1-cyclohexyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester                  | 515.33      |
| 17. | 5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexylmethyl}-1-cyclohexyl-4-isobutyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester         | 529.34      |
| 18. | 4-(4-chlorobenzyl)-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexylmethyl}-1-cyclohexyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester | 597.29      |
| 19. | 4-butyl-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexylmethyl}-1-cyclohexyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester            | 529.34      |
| 20. | 4-(4-chlorobenzyl)-1-cyclohexyl-5-[4-(dimethylamino-thiophen-2-yl-methyl)-cyclohexylmethyl]-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester   | 569.28      |

|     |                                                                                                                                                   |        |
|-----|---------------------------------------------------------------------------------------------------------------------------------------------------|--------|
| 21. | 5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexyl}-4-isobutyl-1-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester              | 459.33 |
| 22. | 4-(4-chlorobenzyl)-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexyl}-1-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester      | 527.27 |
| 23. | 4-butyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexyl}-1-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester                 | 459.33 |
| 24. | 5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexyl}-4-isobutyl-1-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester               | 475.30 |
| 25. | 4-(4-chlorobenzyl)-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexyl}-1-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester       | 543.24 |
| 26. | 5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexylmethyl}-4-isobutyl-1-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester         | 489.31 |
| 27. | 4-(4-chlorobenzyl)-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexylmethyl}-1-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester | 557.26 |
| 28. | 4-butyl-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexylmethyl}-1-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester            | 489.31 |
| 29. | 1-butyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexyl}-4-isobutyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester               | 473.34 |
| 30. | 1-butyl-4-(4-chlorobenzyl)-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexyl}-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester       | 541.29 |
| 31. | 1-butyl-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexyl}-4-isobutyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester                | 489.31 |

|     |                                                                                                                                                  |        |
|-----|--------------------------------------------------------------------------------------------------------------------------------------------------|--------|
| 32. | 1-butyl-4-(4-chlorobenzyl)-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexyl}-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester       | 557.26 |
| 33. | 1,4-dibutyl-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexyl}-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester                      | 489.31 |
| 34. | 1-butyl-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexylmethyl}-4-isobutyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester         | 503.33 |
| 35. | 1-butyl-4-(4-chlorobenzyl)-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexylmethyl}-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester | 571.27 |
| 36. | 1,4-dibutyl-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexylmethyl}-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester                | 503.33 |
| 37. | 5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexyl}-4-isobutyl-1-phenethyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester          | 521.34 |
| 38. | 4-(4-chlorobenzyl)-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexyl}-1-phenethyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester  | 589.29 |
| 39. | 4-butyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexyl}-1-phenethyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester             | 521.34 |
| 40. | 5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexyl}-4-isobutyl-1-phenethyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester           | 537.31 |
| 41. | 4-(4-chlorobenzyl)-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexyl}-1-phenethyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester   | 605.26 |
| 42. | 4-butyl-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexyl}-1-phenethyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester              | 537.31 |

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|-----|----------------------------------------------------------------------------------------------------------------------------------------------------------|--------|
| 43. | 5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexylmethyl}-4-isobutyl-1-phenethyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester             | 551.33 |
| 44. | 4-(4-chlorobenzyl)-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexylmethyl}-1-phenethyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester     | 619.27 |
| 45. | 4-butyl-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexylmethyl}-1-phenethyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester                | 551.33 |
| 46. | 1-benzyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexyl}-4-isobutyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester                     | 507.33 |
| 47. | 1-benzyl-4-(4-chlorobenzyl)-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexyl}-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester             | 575.27 |
| 48. | 1-benzyl-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexyl}-4-isobutyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester                      | 523.30 |
| 49. | 1-benzyl-4-(4-chlorobenzyl)-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexyl}-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester              | 591.24 |
| 50. | 1-benzyl-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexylmethyl}-4-isobutyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester                | 537.31 |
| 51. | 5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexyl}-1-cyclohexyl-4-(2-methoxycarbonyl-ethyl)-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester | 545.30 |
| 52. | 4-benzylsulfanylmethyl-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexyl}-1-cyclohexyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester      | 595.30 |

|     |                                                                                                                                                               |        |
|-----|---------------------------------------------------------------------------------------------------------------------------------------------------------------|--------|
| 53. | 5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexylmethyl}-1-cyclohexyl-4-(2-methoxycarbonylethyl)-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester | 559.32 |
| 54. | Methyl-4-sec-butyl-5-((4-(4-chlorophenyl)(dimethylamino)methyl)cyclohexyl)methyl)-1-cyclohexyl-4,5-dihydro-1H-imidazole-4-carboxylate                         | 529.34 |
| 55. | 5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexylmethyl}-1-cyclohexyl-4-methylsulfanylmethyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester     | 533.28 |
| 56. | 4-benzylsulfanylmethyl-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexylmethyl}-1-cyclohexyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester     | 609.32 |
| 57. | 5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexyl}-4-methylsulfanylmethyl-1-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester              | 463.27 |
| 58. | 4-benzylsulfanylmethyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexyl}-1-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester              | 539.30 |
| 59. | 5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexyl}-4-(2-methoxycarbonylethyl)-1-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester           | 505.27 |
| 60. | 4-benzylsulfanylmethyl-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexyl}-1-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester               | 555.27 |
| 61. | 5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexylmethyl}-4-(2-methoxycarbonylethyl)-1-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester     | 519.29 |
| 62. | 4-sec-butyl-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexylmethyl}-1-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester                    | 489.31 |

|     |                                                                                                                                                           |        |
|-----|-----------------------------------------------------------------------------------------------------------------------------------------------------------|--------|
| 63. | 5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexylmethyl}-4-methylsulfanylmethyl-1-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester     | 493.25 |
| 64. | 4-benzylsulfanylmethyl-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexylmethyl}-1-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester     | 569.28 |
| 65. | 1-butyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexyl}-4-(2-methoxycarbonylethyl)-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester       | 503.32 |
| 66. | 1-butyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexyl}-4-methylsulfanylmethyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester           | 477.28 |
| 67. | 4-benzylsulfanylmethyl-1-butyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexyl}-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester           | 553.31 |
| 68. | 1-butyl-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexyl}-4-(2-methoxycarbonylethyl)-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester        | 519.29 |
| 69. | 4-benzylsulfanylmethyl-1-butyl-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexyl}-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester            | 569.28 |
| 70. | 1-butyl-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexylmethyl}-4-(2-methoxycarbonylethyl)-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester  | 533.30 |
| 71. | 5-[4-(1-dimethylamino-3-phenylpropyl)-cyclohexylmethyl]-4-(2-methoxycarbonylethyl)-1-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester       | 513.36 |
| 72. | 1-butyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexylmethyl}-4-(2-methoxycarbonylethyl)-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester | 517.33 |
| 73. | 1-butyl-4-sec-butyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexylmethyl}-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester                | 487.36 |

|     |                                                                                                                                                               |        |
|-----|---------------------------------------------------------------------------------------------------------------------------------------------------------------|--------|
| 74. | 1-butyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexylmethyl}-4-methylsulfanylmethyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester         | 491.30 |
| 75. | 4-benzylsulfanylmethyl-1-butyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexylmethyl}-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester         | 567.33 |
| 76. | 1-butyl-5-{4-[dimethylamino-(4-fluorophenyl)-methyl]-cyclohexylmethyl}-4-(2-methoxycarbonylethyl)-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester     | 517.33 |
| 77. | 1-butyl-5-{4-[dimethylamino-(4-fluorophenyl)-methyl]-cyclohexylmethyl}-4-methylsulfanylmethyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester         | 491.30 |
| 78. | 1-butyl-5-[4-(1-dimethylamino-3-phenylpropyl)-cyclohexylmethyl]-4-(2-methoxycarbonylethyl)-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester            | 527.37 |
| 79. | 4-benzylsulfanylmethyl-1-butyl-5-[4-(1-dimethylamino-3-phenylpropyl)-cyclohexylmethyl]-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester                | 577.37 |
| 80. | 5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexylmethyl}-4-(2-methoxycarbonylethyl)-1-phenethyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester | 565.33 |
| 81. | 4-sec-butyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexylmethyl}-1-phenethyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester                | 535.36 |
| 82. | 4-benzylsulfanylmethyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexylmethyl}-1-phenethyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester     | 615.33 |
| 83. | 5-{4-[dimethylamino-(4-fluorophenyl)-methyl]-cyclohexylmethyl}-4-(2-methoxycarbonylethyl)-1-phenethyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester | 565.33 |

|     |                                                                                                                                                            |        |
|-----|------------------------------------------------------------------------------------------------------------------------------------------------------------|--------|
| 84. | 5-[4-(1-dimethylamino-3-phenylpropyl)-cyclohexylmethyl]-4-(2-methoxycarbonylethyl)-1-phenethyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester     | 575.37 |
| 85. | 1-benzyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexylmethyl}-4-(2-methoxycarbonylethyl)-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester | 551.32 |
| 86. | 1-benzyl-4-benzylsulfanylmethyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexylmethyl}-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester     | 601.31 |
| 87. | 1-benzyl-5-{4-[dimethylamino-(4-fluorophenyl)-methyl]-cyclohexylmethyl}-4-(2-methoxycarbonylethyl)-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester | 551.32 |
| 88. | 1-butyl-4-sec-butyl-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexylmethyl}-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester                  | 503.33 |
| 89. | 1-butyl-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexylmethyl}-4-methylsulfanylmethyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester       | 507.27 |
| 90. | 4-benzylsulfanylmethyl-1-butyl-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexylmethyl}-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester       | 583.30 |
| 91. | 5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexyl}-4-(2-methoxycarbonylethyl)-1-phenethyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester    | 551.32 |
| 92. | 4-benzylsulfanylmethyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexyl}-1-phenethyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester        | 601.31 |
| 93. | 4-benzylsulfanylmethyl-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexyl}-1-phenethyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester         | 617.28 |

|      |                                                                                                                                                                |        |
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| 94.  | 5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexylmethyl}-4-(2-methoxycarbonylethyl)-1-phenethyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester   | 581.30 |
| 95.  | 1-benzyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexyl}-4-(2-methoxycarbonylethyl)-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester           | 537.30 |
| 96.  | 1-benzyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexyl}-4-methylsulfanylmethyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester               | 511.27 |
| 97.  | 1-benzyl-4-benzylsulfanylmethyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexyl}-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester               | 587.30 |
| 98.  | 1-benzyl-4-benzylsulfanylmethyl-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexyl}-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester                | 603.27 |
| 99.  | 1-benzyl-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexylmethyl}-4-(2-methoxycarbonylethyl)-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester      | 567.29 |
| 100. | 1-benzyl-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexylmethyl}-4-methylsulfanylmethyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester          | 541.25 |
| 101. | 1-benzyl-4-benzylsulfanylmethyl-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexylmethyl}-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester          | 617.28 |
| 102. | 1-cyclohexyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexylmethyl}-4-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester                   | 499.36 |
| 103. | 1-cyclohexyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexylmethyl}-4-(2-methylsulfanyl-ethyl)-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester | 531.33 |

|      |                                                                                                                                                                |        |
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| 104. | 1-cyclohexyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexylmethyl}-4-methyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester                   | 471.33 |
| 105. | 1-cyclohexyl-5-{4-[dimethylamino-(4-fluorophenyl)-methyl]-cyclohexylmethyl}-4-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester                   | 499.36 |
| 106. | 1-cyclohexyl-5-{4-[dimethylamino-(4-fluorophenyl)-methyl]-cyclohexylmethyl}-4-(2-methylsulfanyl-ethyl)-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester | 531.33 |
| 107. | 1-cyclohexyl-5-{4-[dimethylamino-(4-fluorophenyl)-methyl]-cyclohexylmethyl}-4-methyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester                   | 471.33 |
| 108. | 1-cyclohexyl-5-[4-(1-dimethylamino-3-phenylpropyl)-cyclohexylmethyl]-4-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester                          | 509.40 |
| 109. | 1-cyclohexyl-5-[4-(1-dimethylamino-3-phenylpropyl)-cyclohexylmethyl]-4-(2-methylsulfanyl-ethyl)-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester        | 541.37 |
| 110. | 1-cyclohexyl-5-[4-(1-dimethylamino-3-phenylpropyl)-cyclohexylmethyl]-4-methyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester                          | 481.37 |
| 111. | 5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexylmethyl}-1,4-dipropyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester                            | 459.33 |
| 112. | 5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexylmethyl}-4-(2-methylsulfanyl-ethyl)-1-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester     | 491.30 |
| 113. | 1-benzyl-4-(4-chlorobenzyl)-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexylmethyl}-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester              | 605.26 |

|      |                                                                                                                                                           |        |
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| 114. | 1-benzyl-4-butyl-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexylmethyl}-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester                    | 537.31 |
| 115. | 1-cyclohexyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexyl}-4-(2-methoxycarbonylethyl)-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester  | 529.33 |
| 116. | 4-benzylsulfanylmethyl-1-cyclohexyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexyl}-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester      | 579.33 |
| 117. | 5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexylmethyl}-4-methyl-1-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester                  | 431.29 |
| 118. | 5-{4-[dimethylamino-(4-fluorophenyl)-methyl]-cyclohexylmethyl}-1,4-dipropyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester                       | 459.33 |
| 119. | 5-{4-[dimethylamino-(4-fluorophenyl)-methyl]-cyclohexylmethyl}-4-(2-methylsulfanylethyl)-1-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester | 491.30 |
| 120. | 5-[4-(1-dimethylamino-3-phenylpropyl)-cyclohexylmethyl]-1,4-dipropyl-4,5-dihydro-1H-imidazole-imidazole-4-carboxylic acid methyl ester                    | 469.37 |
| 121. | 5-[4-(1-dimethylamino-3-phenylpropyl)-cyclohexylmethyl]-4-(2-methylsulfanylethyl)-1-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester        | 501.34 |
| 122. | 1-butyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexylmethyl}-4-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester                   | 473.34 |
| 123. | 1-butyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexylmethyl}-4-(2-methylsulfanylethyl)-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester  | 505.31 |

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| 124. | 1-butyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexylmethyl}-4-methyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester                      | 445.31 |
| 125. | 1-butyl-5-{4-[dimethylamino-(4-fluorophenyl)-methyl]-cyclohexylmethyl}-4-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester                      | 473.34 |
| 126. | 1-butyl-5-{4-[dimethylamino-(4-fluorophenyl)-methyl]-cyclohexylmethyl}-4-(2-methylsulfanyl-ethyl)-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester    | 505.31 |
| 127. | 1-butyl-5-[4-(1-dimethylamino-3-phenylpropyl)-cyclohexylmethyl]-4-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester                             | 483.38 |
| 128. | 1-butyl-5-[4-(1-dimethylamino-3-phenylpropyl)-cyclohexylmethyl]-4-(2-methylsulfanylethyl)-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester            | 515.35 |
| 129. | 5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexylmethyl}-1-phenethyl-4-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester                  | 521.34 |
| 130. | 5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexylmethyl}-4-(2-methylsulfanylethyl)-1-phenethyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester | 553.31 |
| 131. | 5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexylmethyl}-4-methyl-1-phenethyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester                  | 493.31 |
| 132. | 5-{4-[dimethylamino-(4-fluorophenyl)-methyl]-cyclohexylmethyl}-1-phenethyl-4-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester                  | 521.34 |
| 133. | 5-{4-[dimethylamino-(4-fluorophenyl)-methyl]-cyclohexylmethyl}-4-(2-methylsulfanylethyl)-1-phenethyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester | 553.31 |

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| 134. | 5-{4-[dimethylamino-(4-fluorophenyl)-methyl]-cyclohexylmethyl}-4-methyl-1-phenethyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester                | 493.31 |
| 135. | 5-[4-(1-dimethylamino-3-phenylpropyl)-cyclohexylmethyl]-1-phenethyl-4-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester                       | 531.38 |
| 136. | 5-[4-(1-dimethylamino-3-phenylpropyl)-cyclohexylmethyl]-4-(2-methylsulfanylethyl)-1-phenethyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester      | 563.35 |
| 137. | 5-[4-(1-dimethylamino-3-phenylpropyl)-cyclohexylmethyl]-4-methyl-1-phenethyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester                       | 503.35 |
| 138. | 1-benzyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexylmethyl}-4-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester                   | 507.33 |
| 139. | 1-benzyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexylmethyl}-4-(2-methylsulfanyl-ethyl)-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester | 539.30 |
| 140. | 1-benzyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexylmethyl}-4-methyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester                   | 479.29 |
| 141. | 1-benzyl-5-{4-[dimethylamino-(4-fluorophenyl)-methyl]-cyclohexylmethyl}-4-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester                   | 507.33 |
| 142. | 1-benzyl-5-{4-[dimethylamino-(4-fluorophenyl)-methyl]-cyclohexylmethyl}-4-(2-methylsulfanyl-ethyl)-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester | 539.30 |
| 143. | 1-benzyl-5-{4-[dimethylamino-(4-fluorophenyl)-methyl]-cyclohexylmethyl}-4-methyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester                   | 479.29 |
| 144. | 1-benzyl-5-[4-(1-dimethylamino-3-phenylpropyl)-cyclohexylmethyl]-4-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester                          | 517.37 |

|      |                                                                                                                                                                 |        |
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| 145. | 1-benzyl-5-[4-(1-dimethylamino-3-phenylpropyl)-cyclohexylmethyl]-4-(2-methylsulfanyl-ethyl)-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester             | 549.34 |
| 146. | 1-benzyl-5-[4-(1-dimethylamino-3-phenylpropyl)-cyclohexylmethyl]-4-methyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester                               | 489.34 |
| 147. | 1-cyclohexyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexylmethyl}-4-(2-methoxycarbonyl-ethyl)-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester | 543.35 |
| 148. | 4-sec-butyl-1-cyclohexyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexylmethyl}-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester                 | 513.37 |
| 149. | 1-cyclohexyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexylmethyl}-4-methylsulfanylmethyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester      | 517.31 |
| 150. | 4-benzylsulfanylmethyl-1-cyclohexyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexylmethyl}-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester      | 593.35 |
| 151. | 1-cyclohexyl-5-{4-[dimethylamino-(4-fluorophenyl)-methyl]-cyclohexylmethyl}-4-(2-methoxycarbonyl-ethyl)-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester | 543.35 |
| 152. | 4-sec-butyl-1-cyclohexyl-5-{4-[dimethylamino-(4-fluorophenyl)-methyl]-cyclohexylmethyl}-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester                 | 513.37 |
| 153. | 1-cyclohexyl-5-{4-[dimethylamino-(4-fluorophenyl)-methyl]-cyclohexylmethyl}-4-methylsulfanylmethyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester      | 517.31 |
| 154. | 1-cyclohexyl-5-[4-(1-dimethylamino-3-phenylpropyl)-cyclohexylmethyl]-4-(2-methoxycarbonyl-ethyl)-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester        | 553.39 |

|      |                                                                                                                                                            |        |
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| 155. | 1-cyclohexyl-5-[4-(1-dimethylamino-3-phenylpropyl)-cyclohexylmethyl]-4-methylsulfanylmethyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester        | 527.35 |
| 156. | 4-benzylsulfanylmethyl-1-cyclohexyl-5-[4-(1-dimethylamino-3-phenylpropyl)-cyclohexylmethyl]-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester        | 603.39 |
| 157. | 5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexylmethyl}-4-(2-methoxycarbonylethyl)-1-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester | 503.32 |
| 158. | 5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexylmethyl}-4-methylsulfanylmethyl-1-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester     | 477.28 |
| 159. | 5-{4-[dimethylamino-(4-fluorophenyl)-methyl]-cyclohexylmethyl}-4-(2-methoxycarbonylethyl)-1-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester | 503.32 |
| 160. | 5-{4-[dimethylamino-(4-fluorophenyl)-methyl]-cyclohexylmethyl}-4-methylsulfanylmethyl-1-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester     | 477.28 |
| 161. | 4-benzylsulfanylmethyl-5-{4-[dimethylamino-(4-fluorophenyl)-methyl]-cyclohexylmethyl}-1-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester     | 553.31 |

### Investigations on the efficacy of the compounds according to the invention

5

#### Method for determining the affinity for the human $\mu$ -opiate receptor

The receptor affinity for the human  $\mu$ -opiate receptor is determined in a homogeneous batch in microtiter plates. For this purpose dilution series of the substances to be

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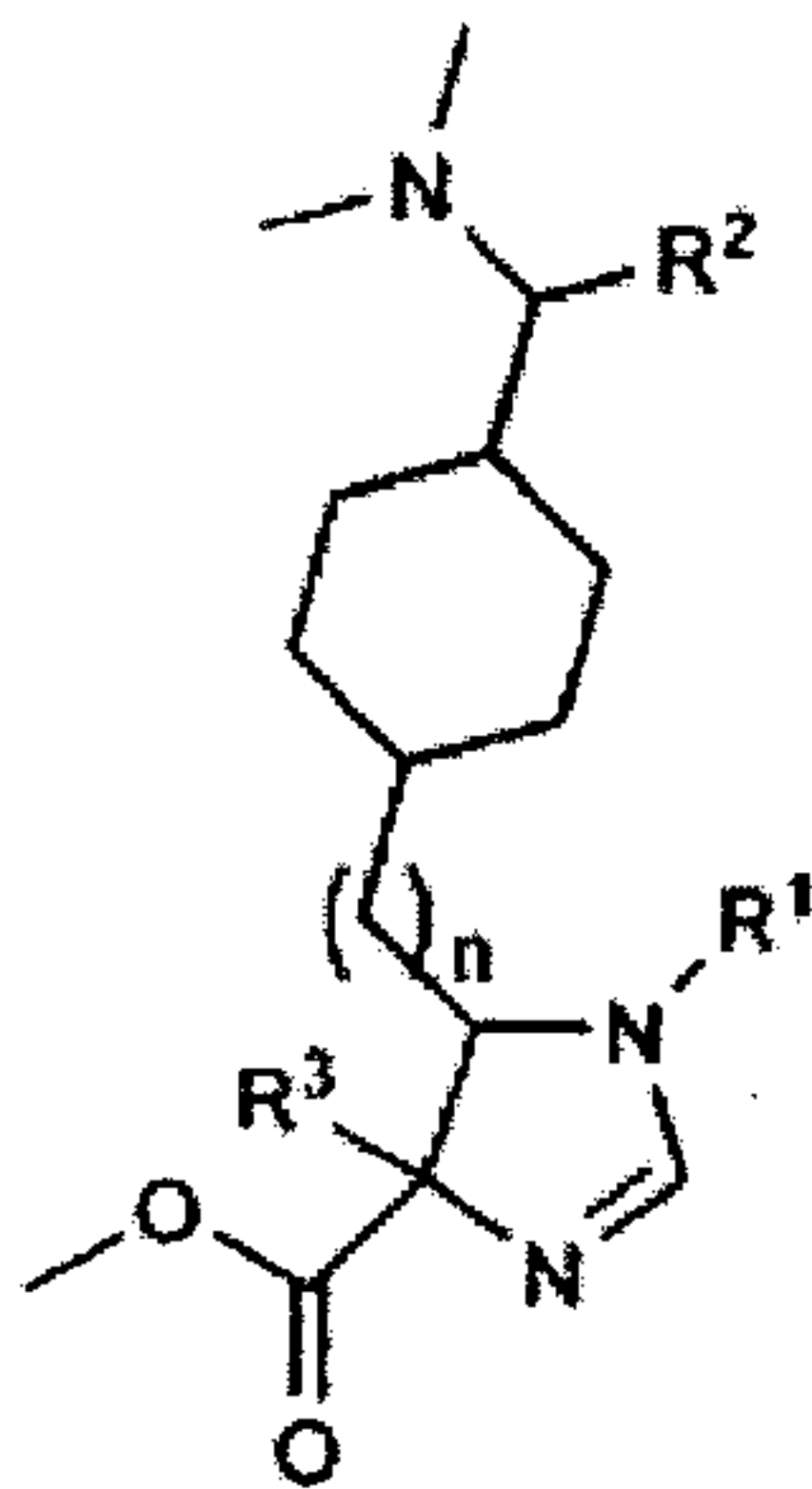
tested are incubated with a receptor membrane preparation (15-40  $\mu$ g protein/250  $\mu$ l incubation batch) of CHO-K1 cells, which express the human  $\mu$ -opiate receptor (RB-HOM receptor membrane preparation from PerkinElmer Life Sciences, 5 Zaventem, Belgium), in the presence of 1 nmole/l of the radioactive ligand [ $^3$ H]-naloxone (NET719, PerkinElmer Life Sciences company, Zaventem, Belgium) and 1 mg WGA-SPA beads (wheat germ agglutinin SPA beads from Amersham/ Pharmacia, Freiburg, Germany) in a total volume of 250  $\mu$ l for 90 10 minutes at room temperature. 50 mmole/l of Tris-HCl supplemented with 0.06% bovine serum albumin is used as incubation buffer. In order to determine the non-specific binding, 100  $\mu$ mole/l of naloxone is additionally added. After the end of the 90 minutes' incubation time the 15 microtiter plates are centrifuged for 20 minutes at 1000 g and the radioactivity is measured in a beta counter (Microbeta-Trilux, PerkinElmer Wallac, Freiburg, Germany). The percentage displacement of the radioactive ligand from its binding to the human  $\mu$ -opiate receptor at a 20 concentration of the test substances of 1  $\mu$ mole/l is determined and is given as percentage inhibition of the specific binding.

Table 1:  $\mu$  Affinities of selected aldehydes

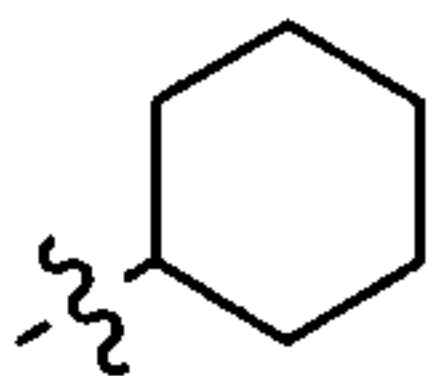
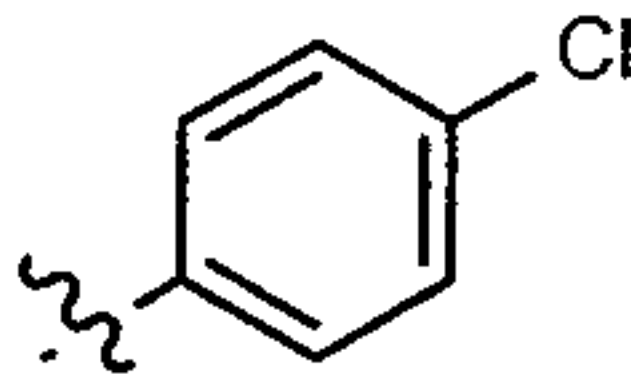
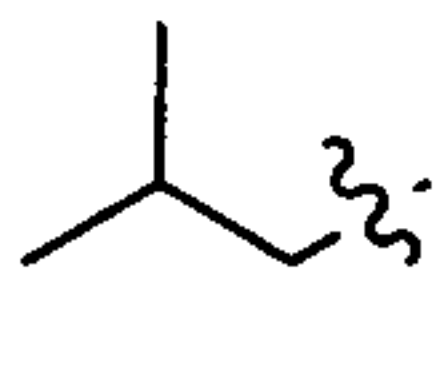
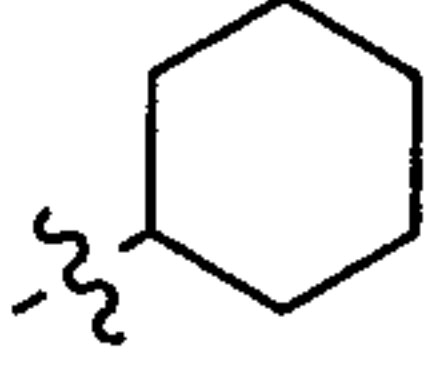
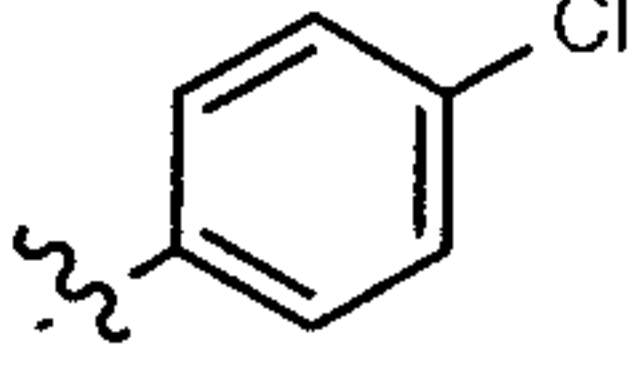
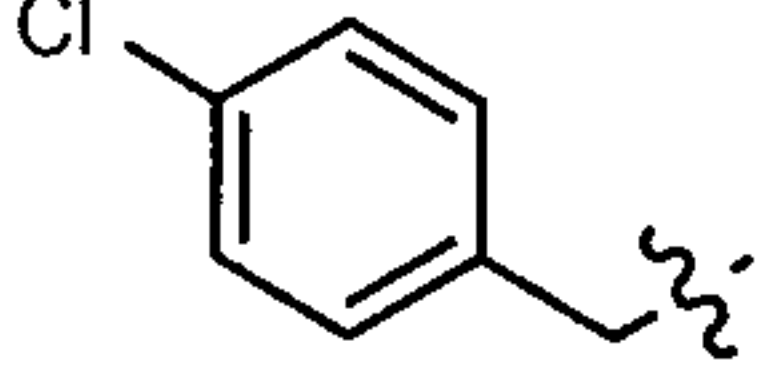
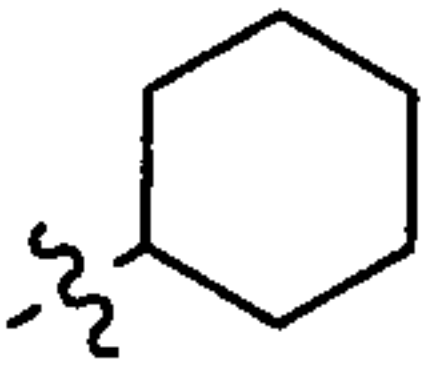
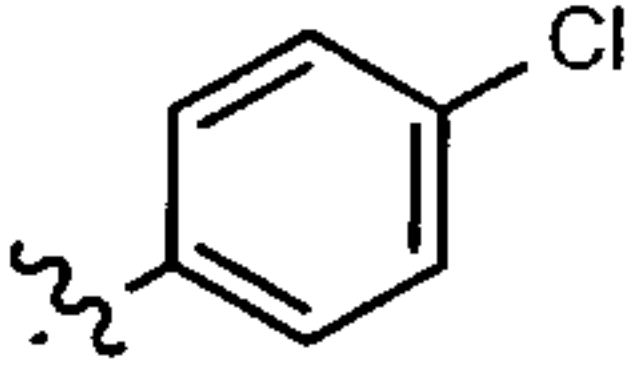
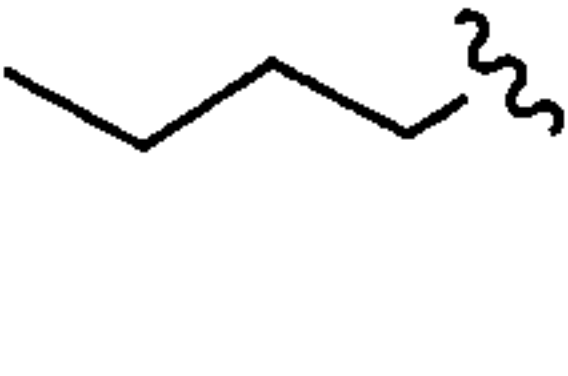
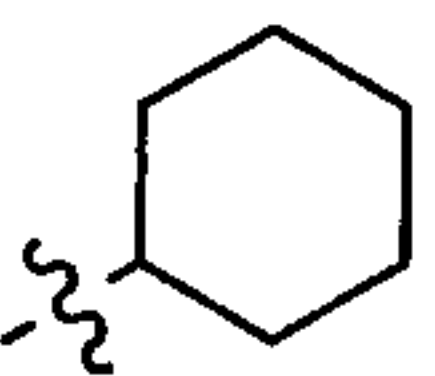
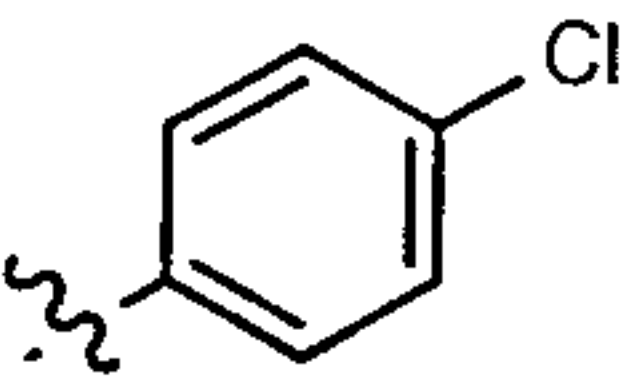
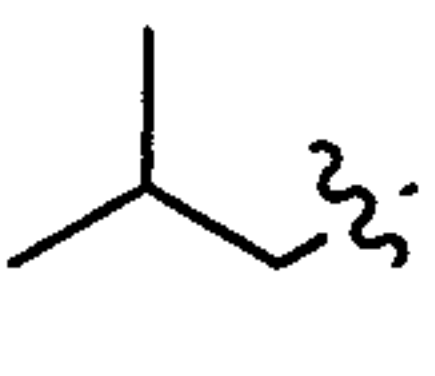
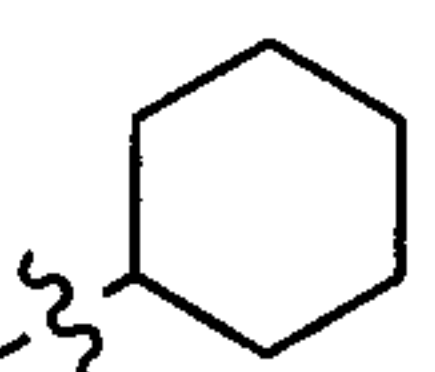
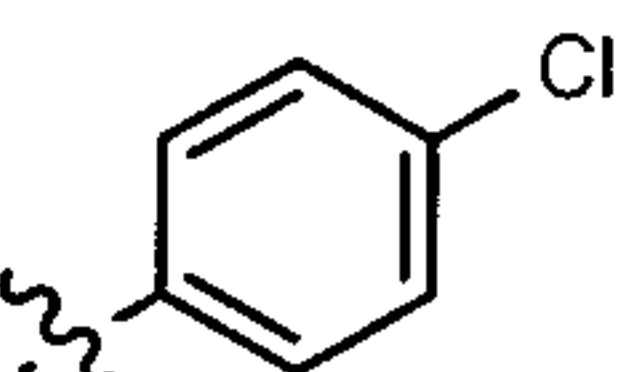
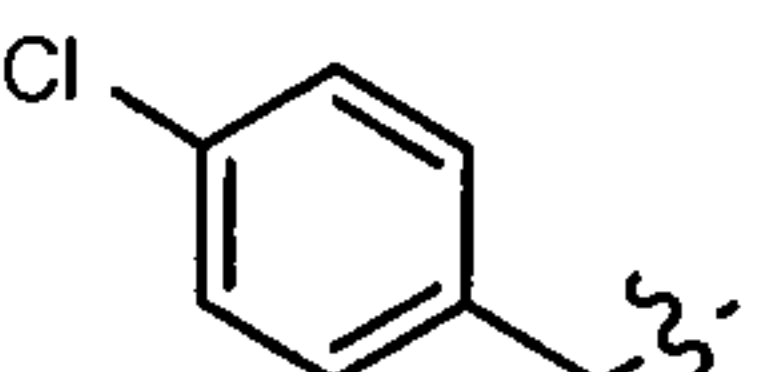
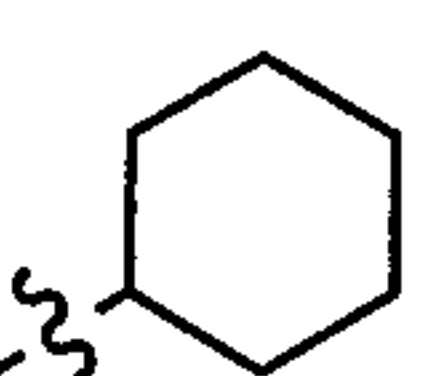
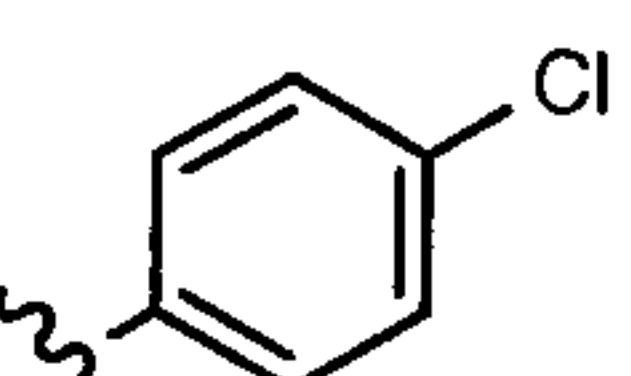
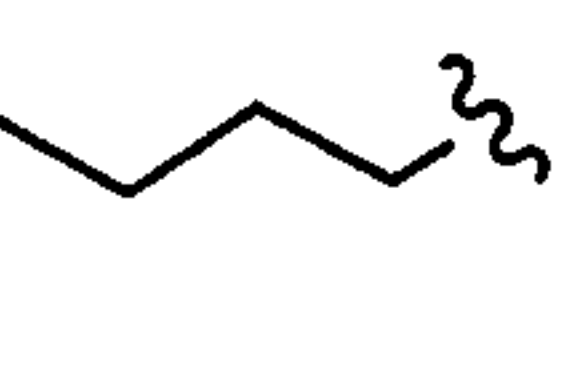
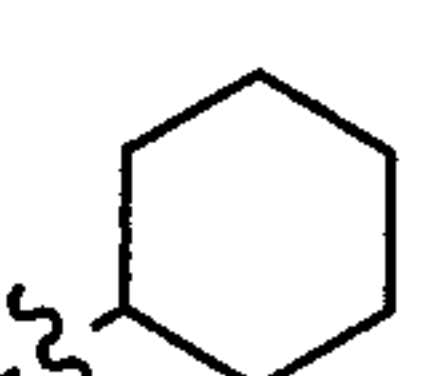
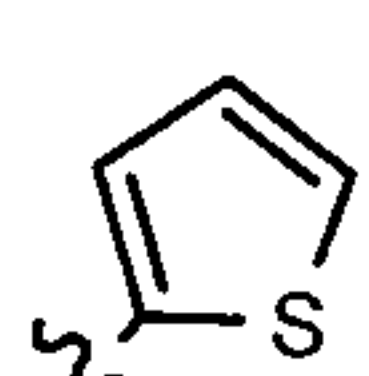
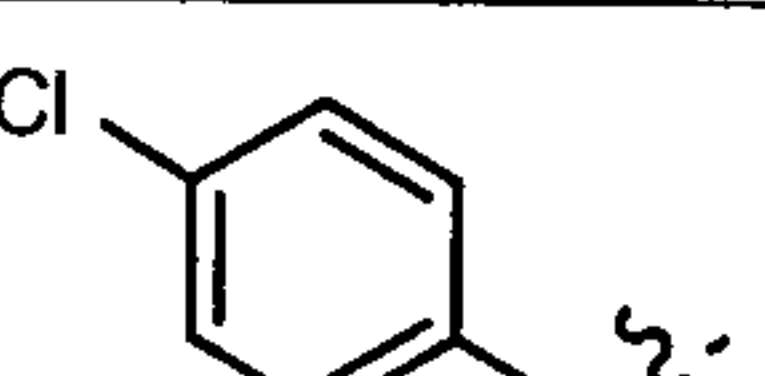
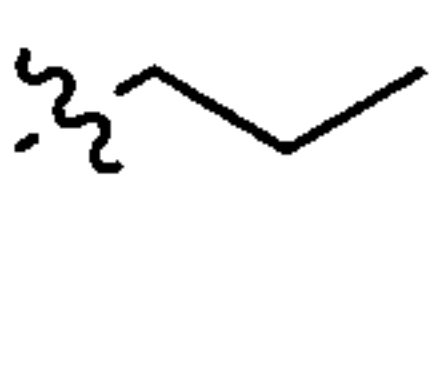
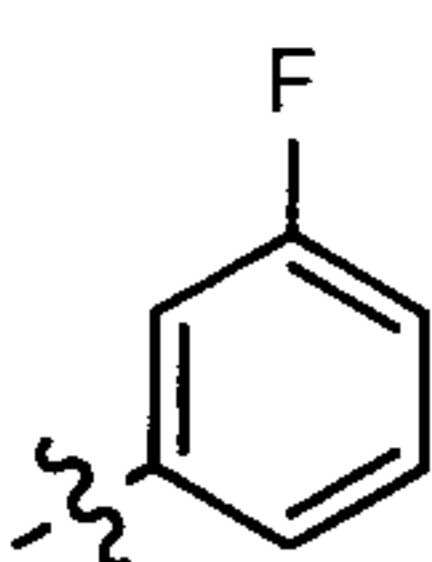
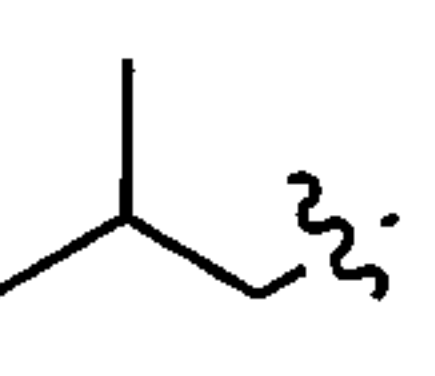
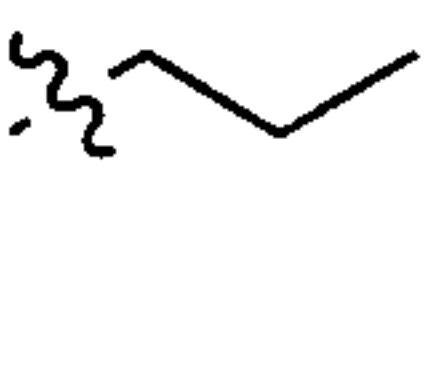
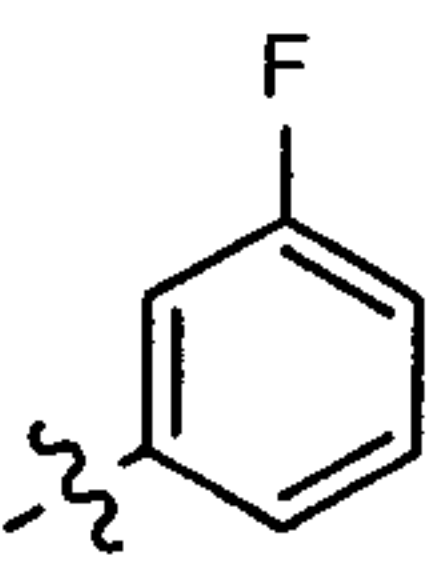
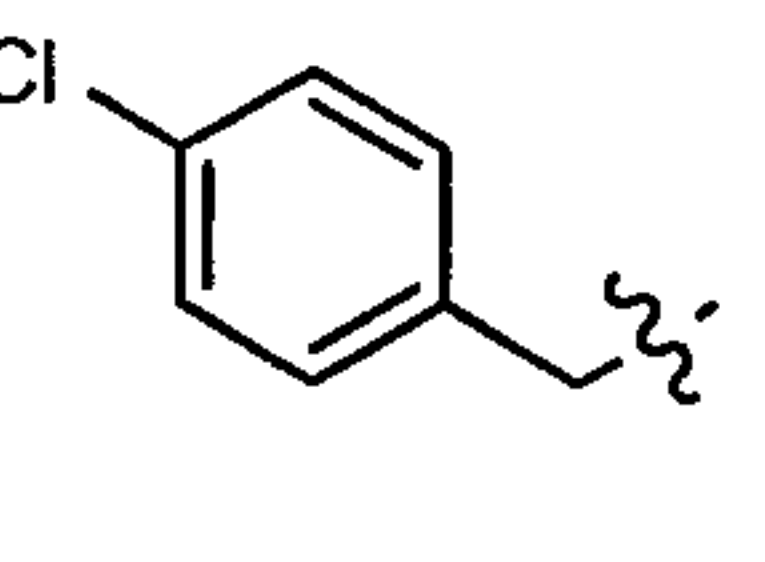
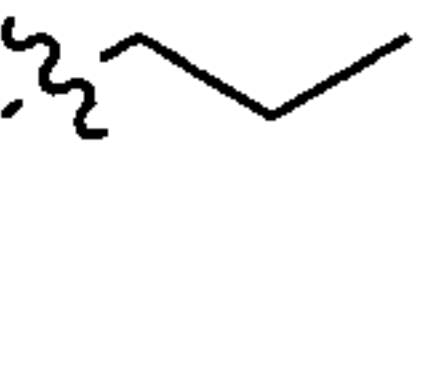
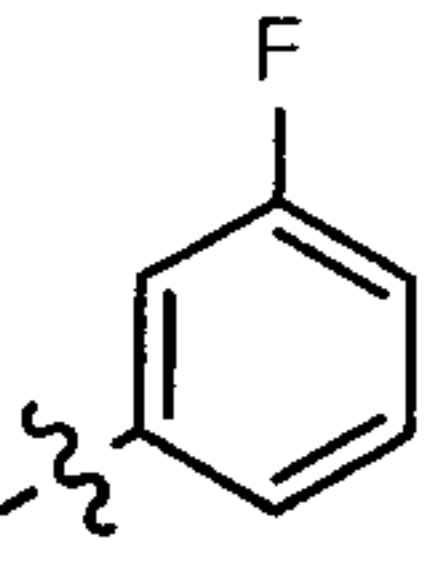
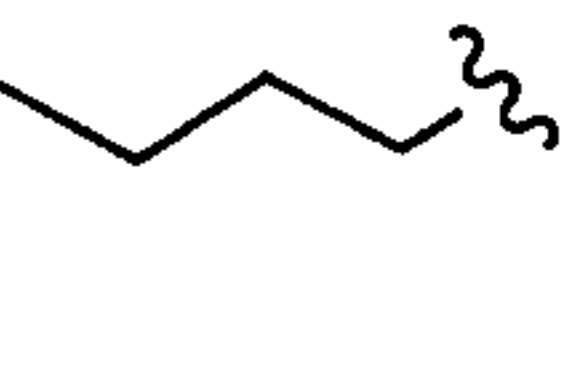
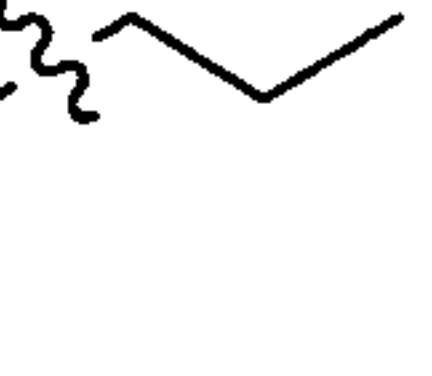
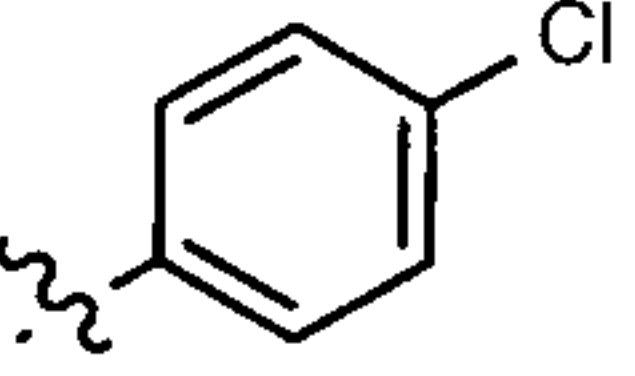
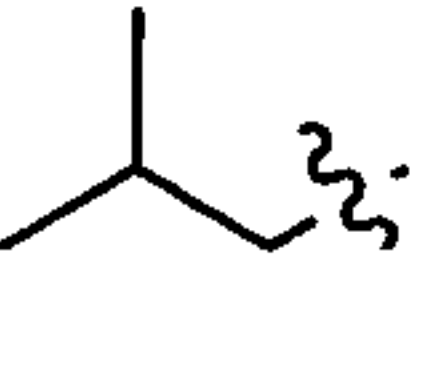
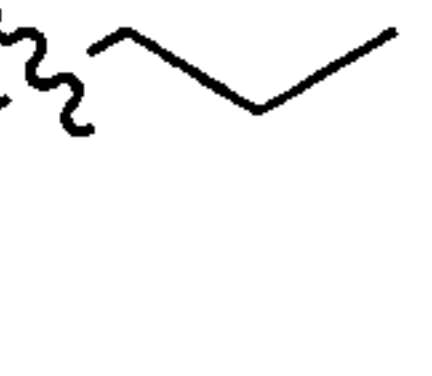
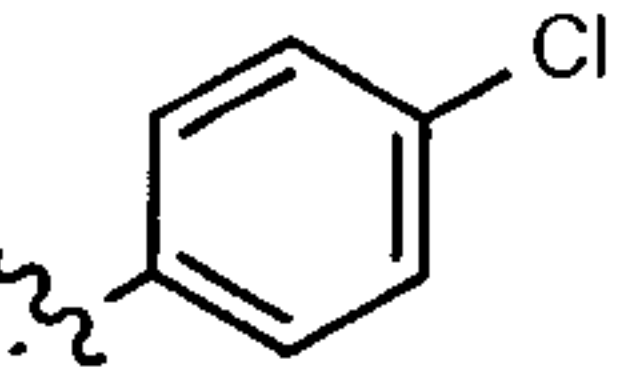
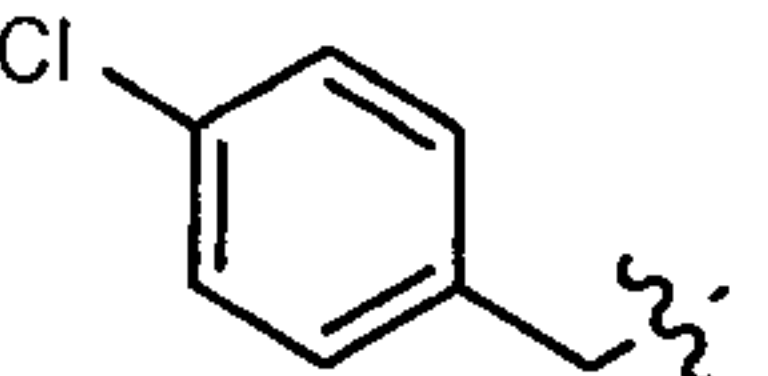
| No. | $\mu$ -Opioid receptor,<br>% inhibition [1 $\mu$ M] |
|-----|-----------------------------------------------------|
| 9c  | 45                                                  |
| 10c | 50                                                  |
| 10b | 67                                                  |
| 9d  | 69                                                  |
| 10d | 79                                                  |

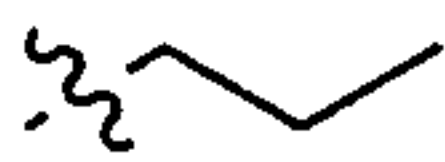
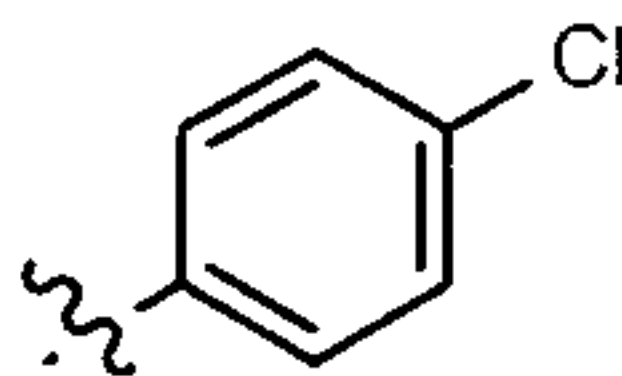
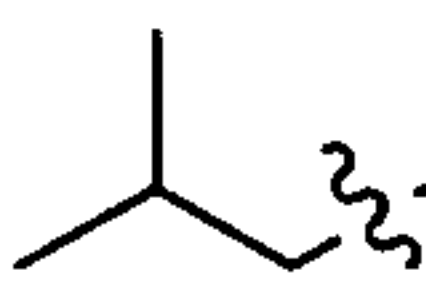
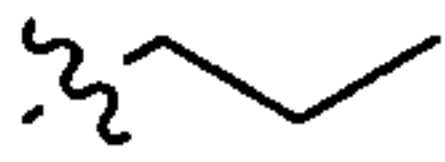
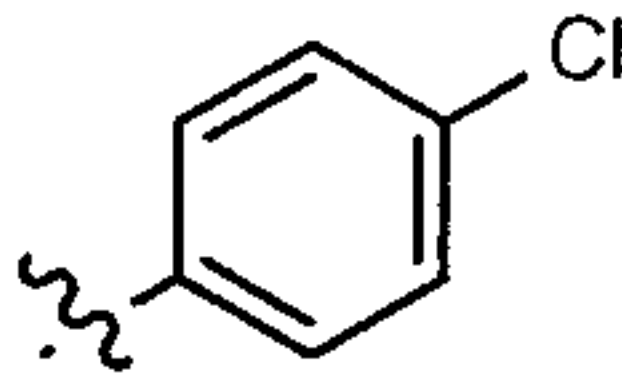
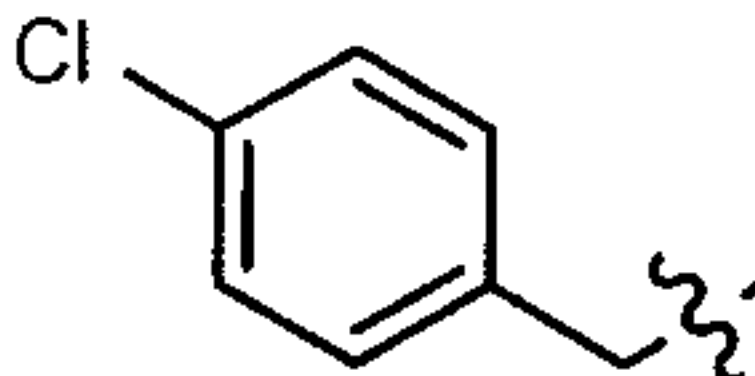
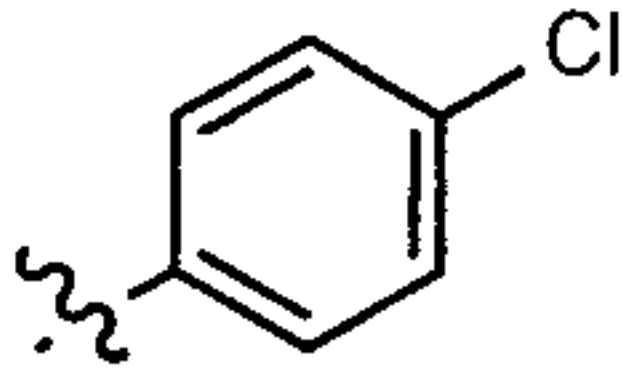
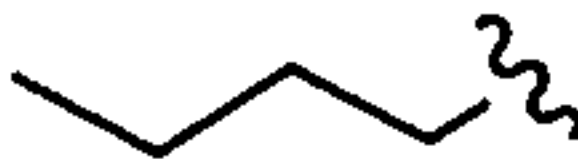
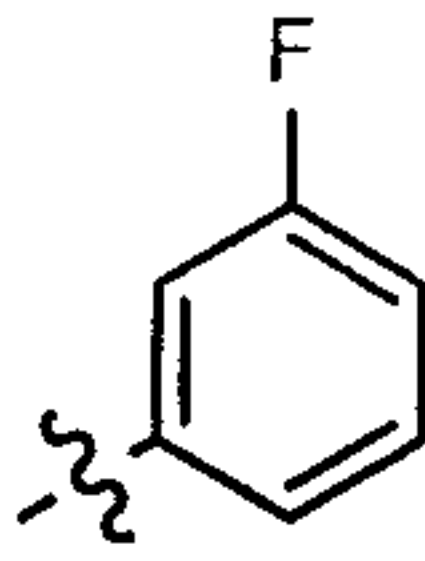
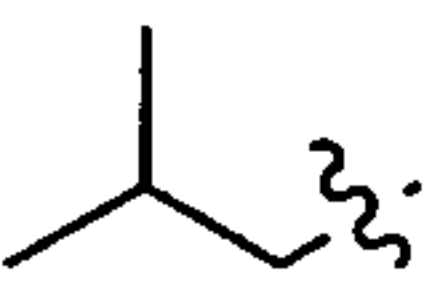
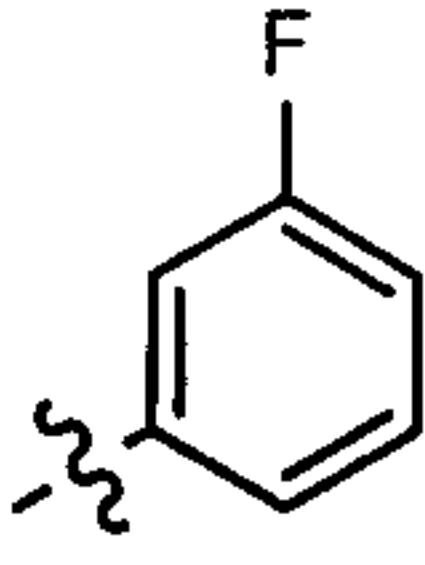
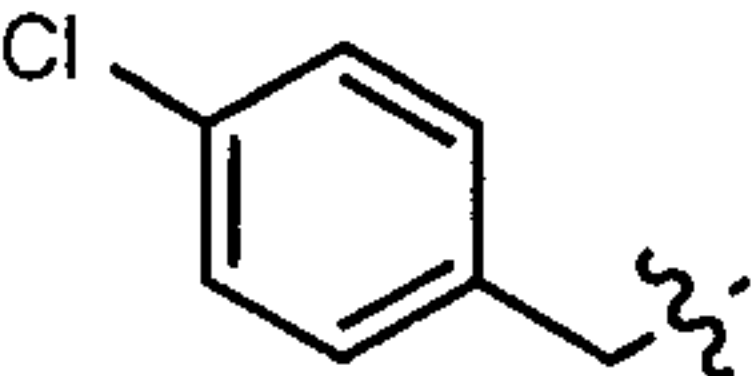
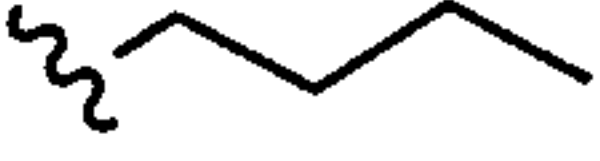
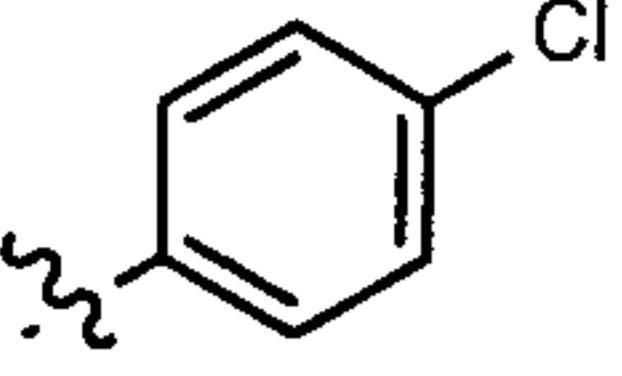
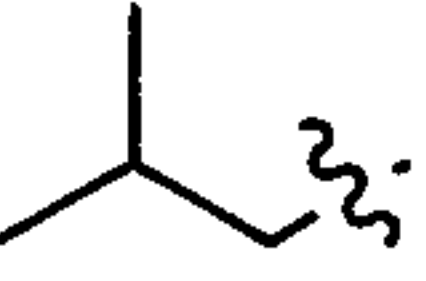
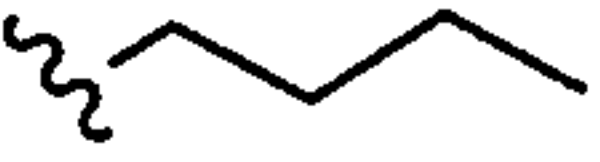
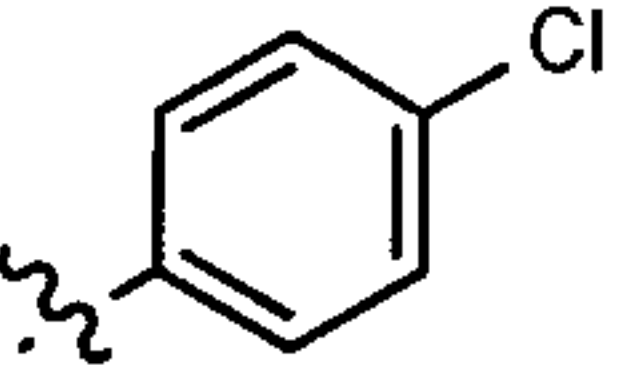
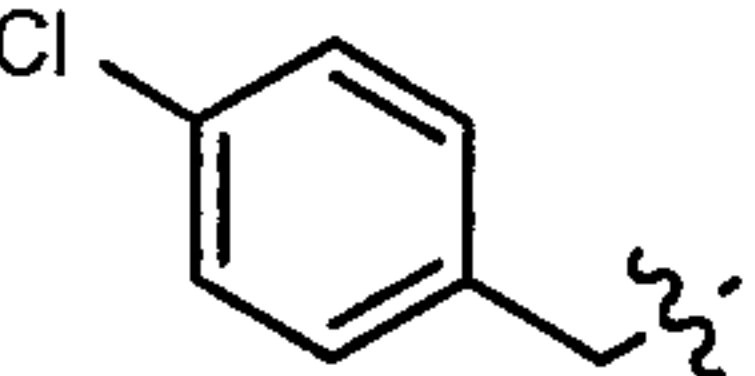
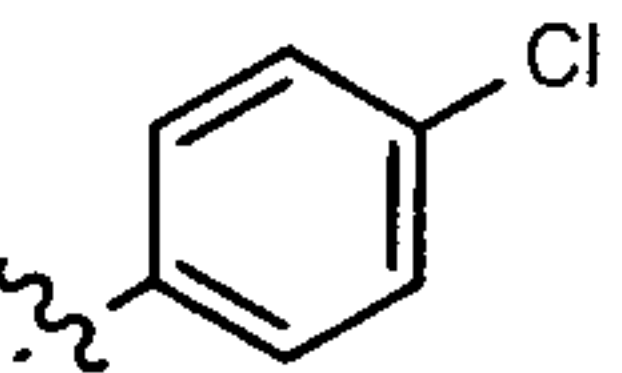
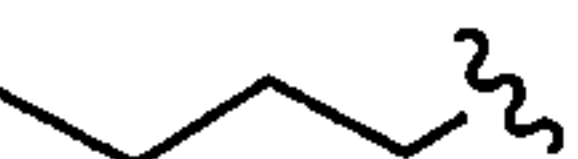
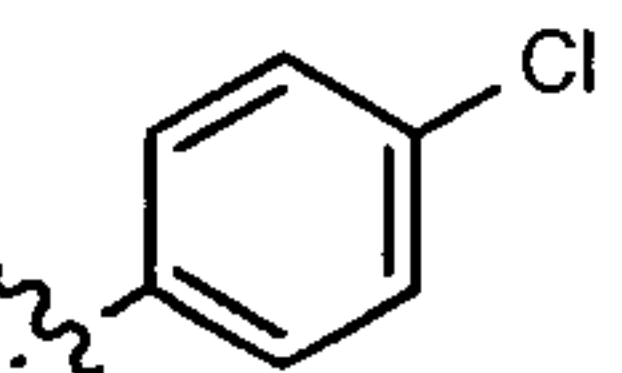
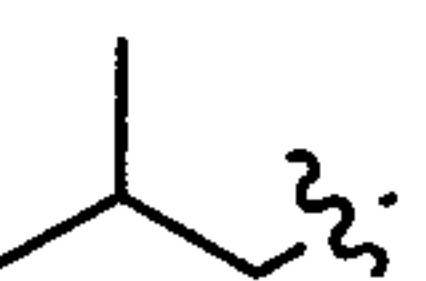
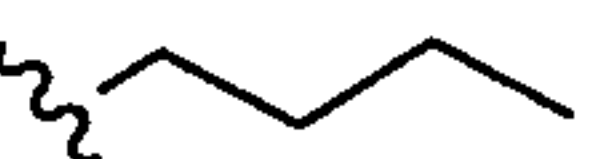
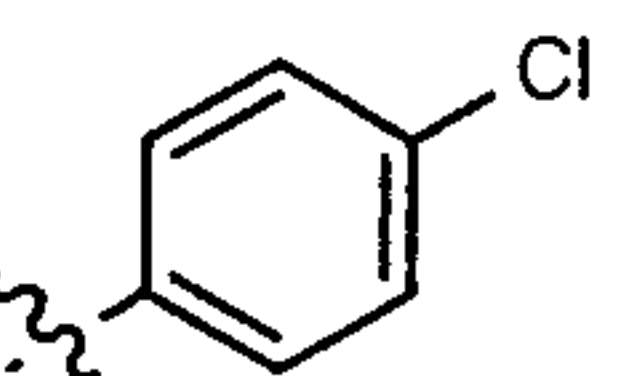
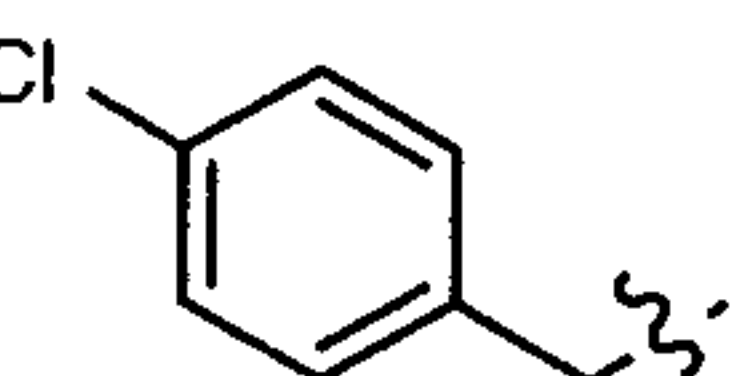
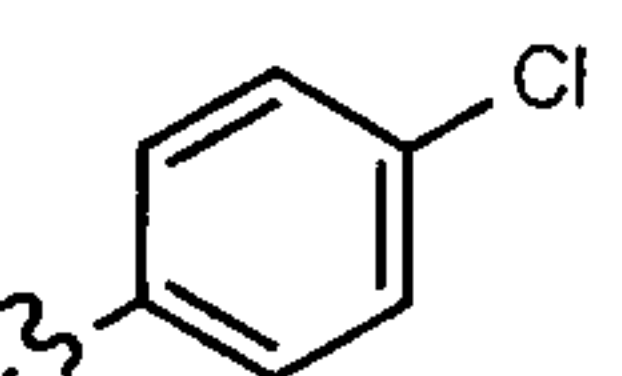
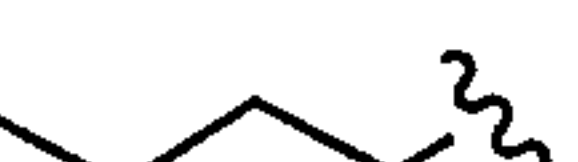
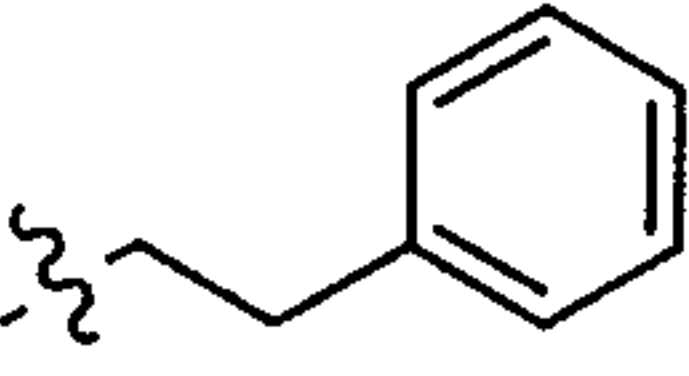
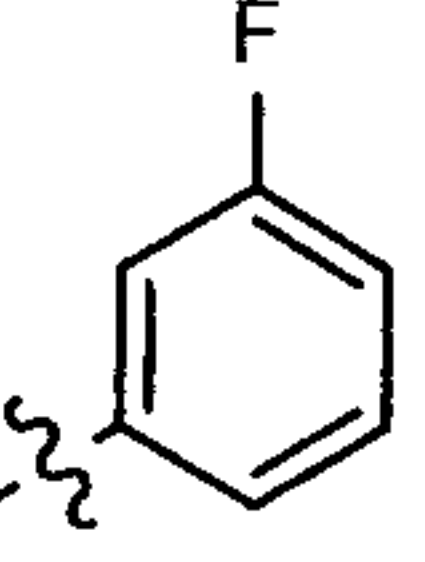
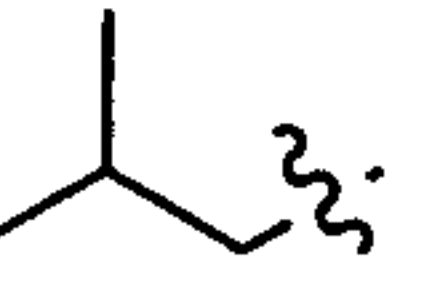
Table 2:  $\mu$  Affinities of Examples 11-161:

5

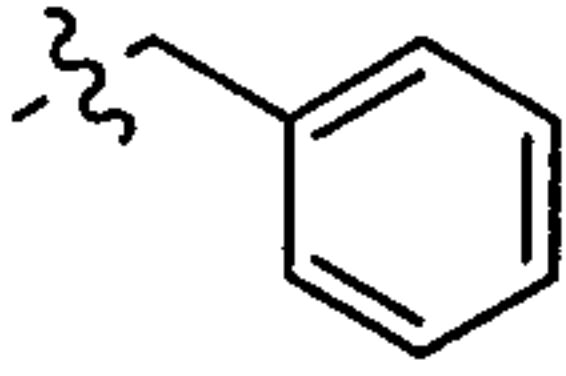
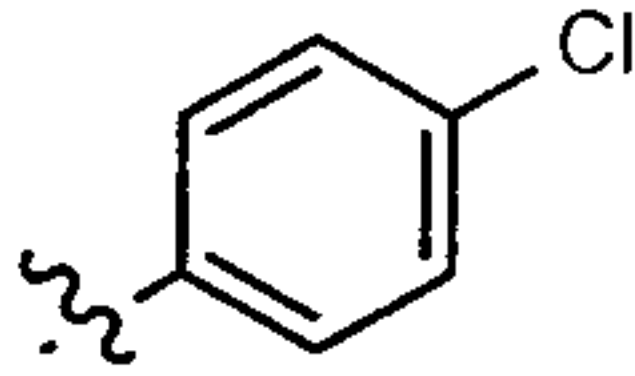
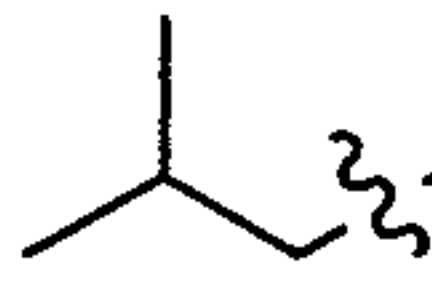
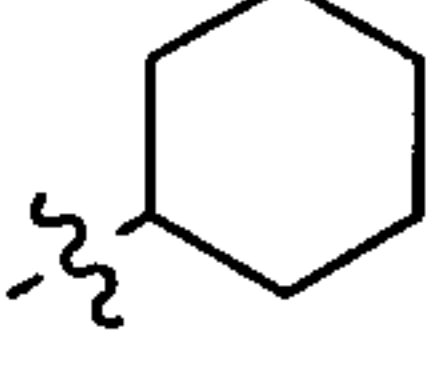
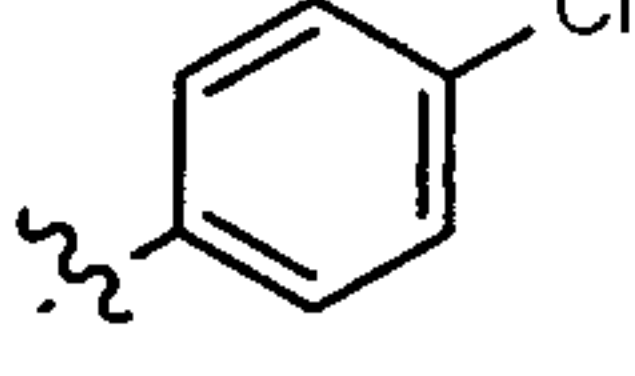
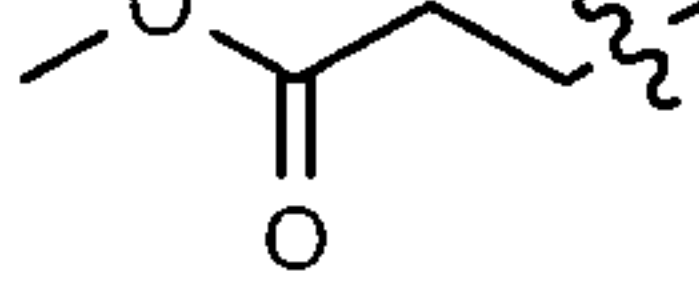
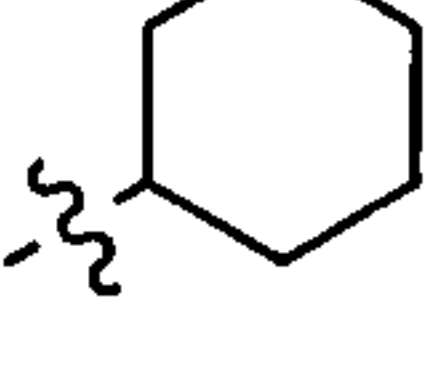
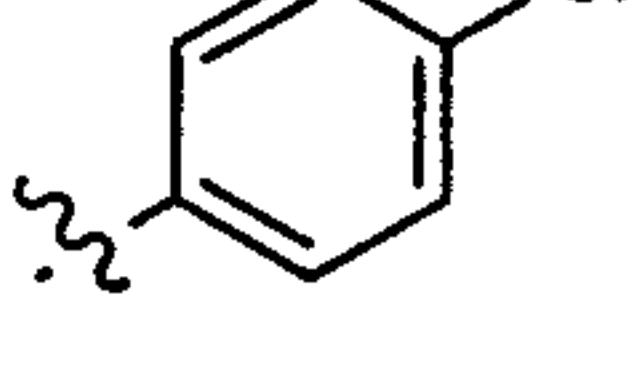
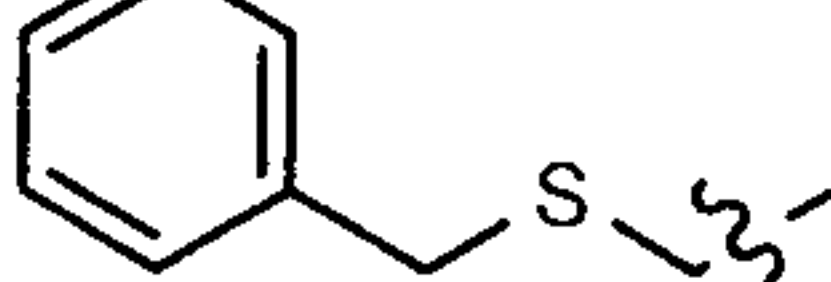
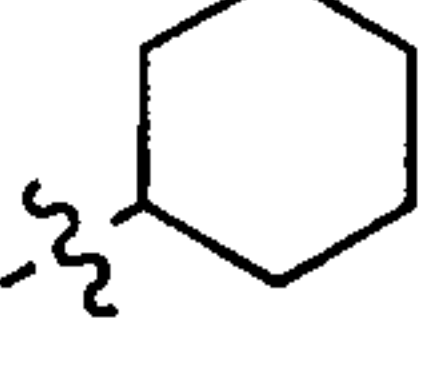
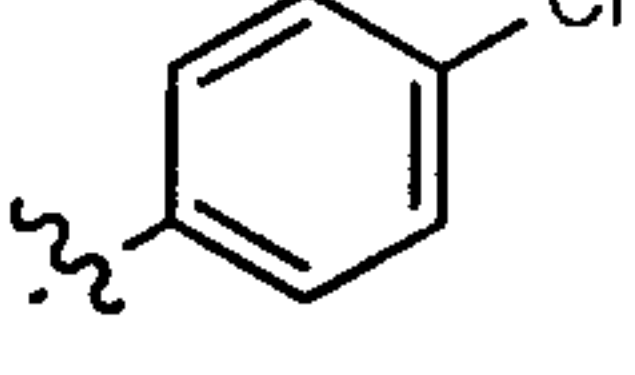
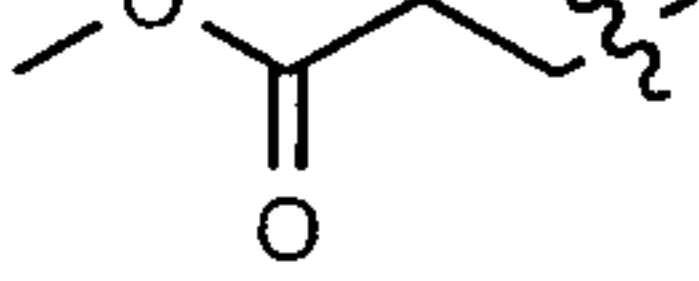
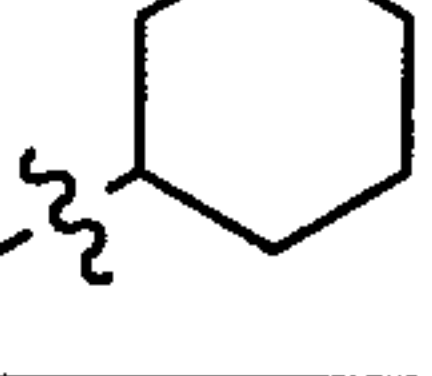
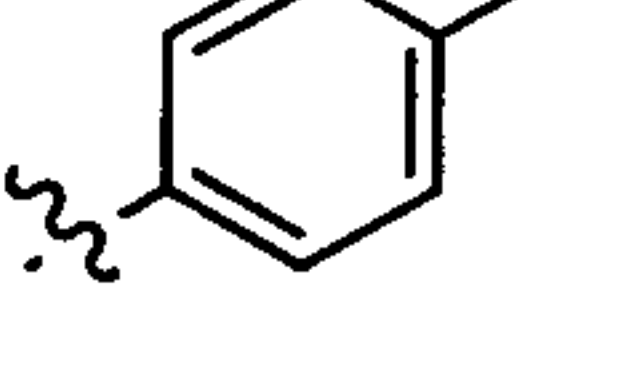
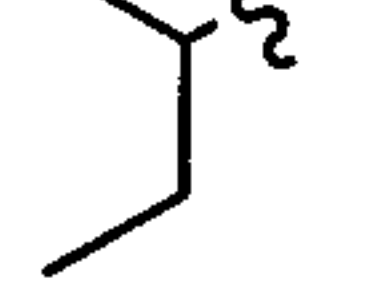
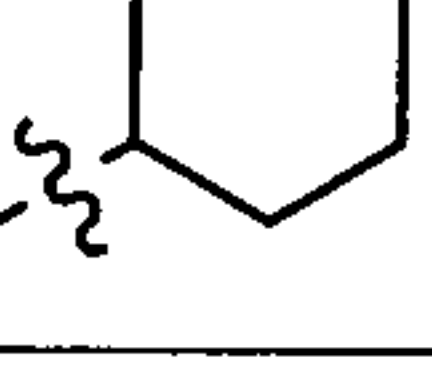
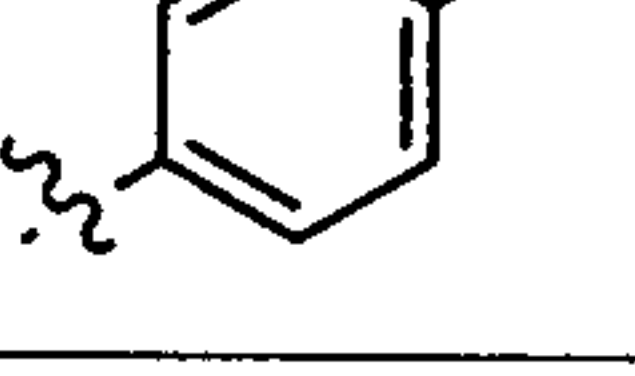
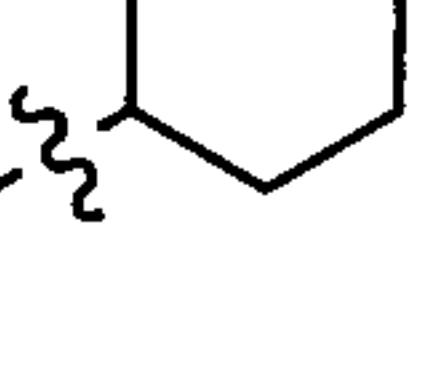
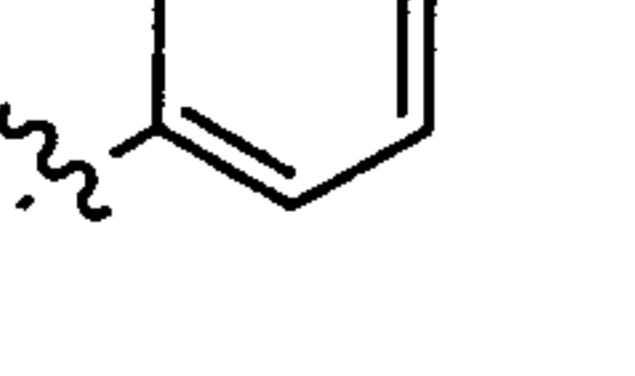
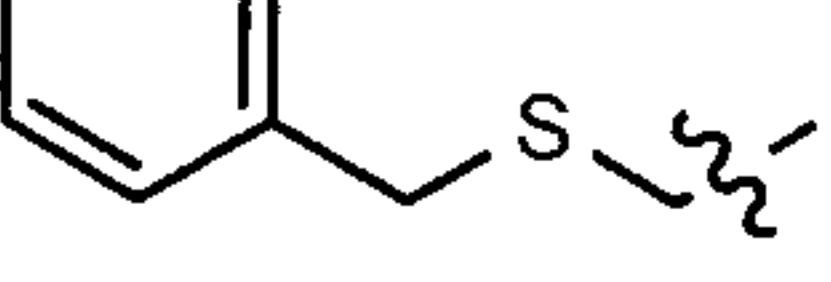
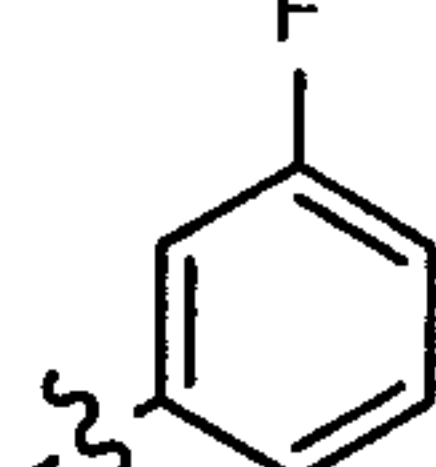
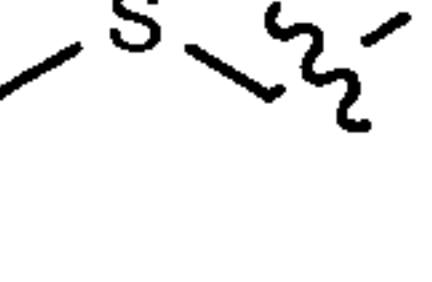
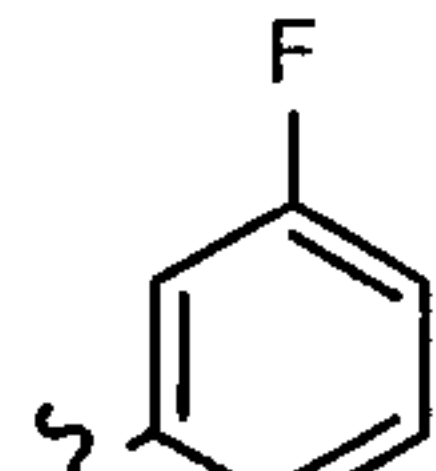
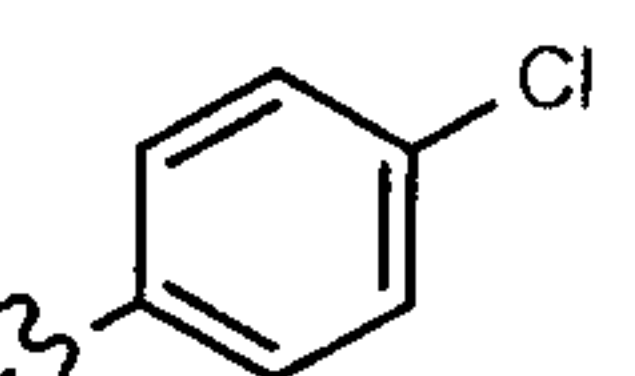
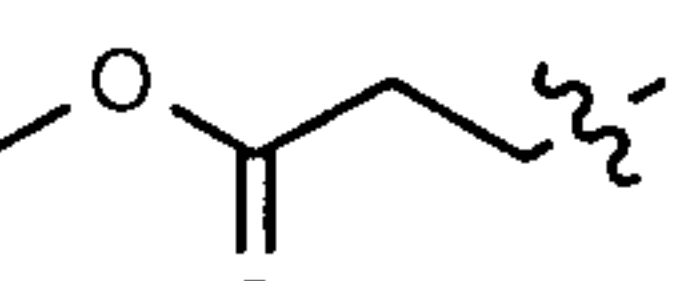
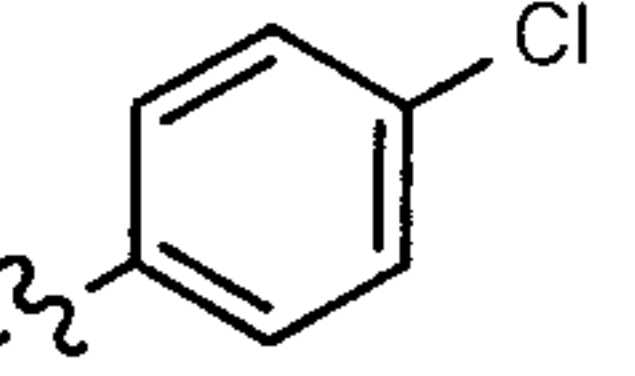


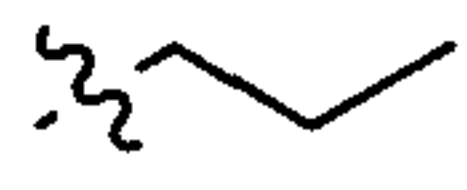
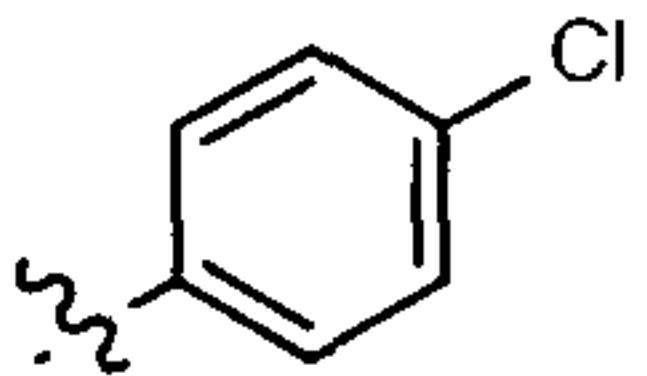
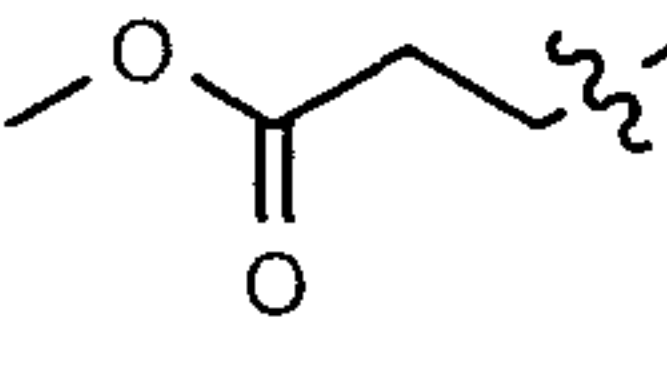
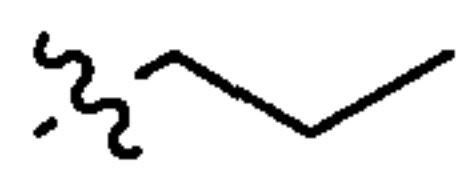
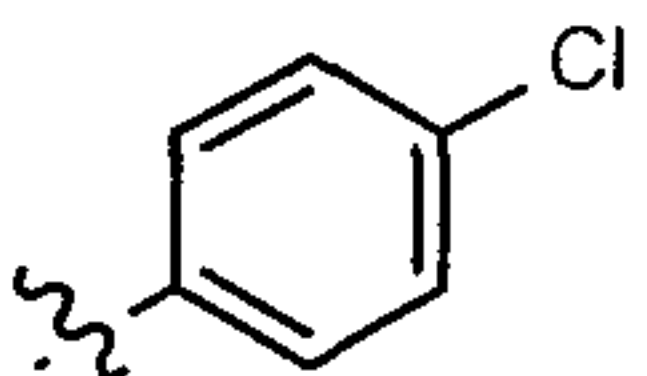
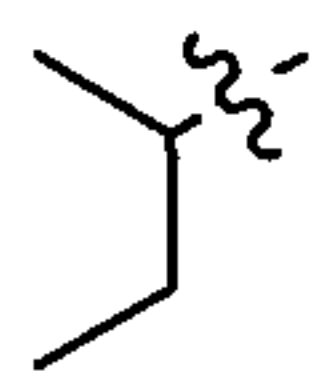
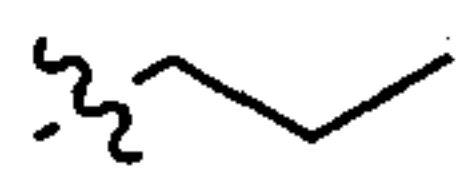
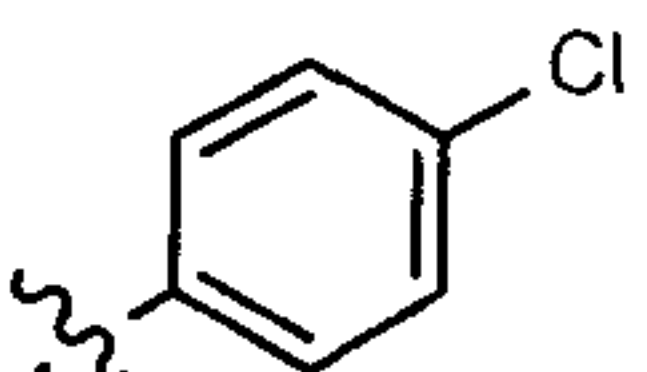
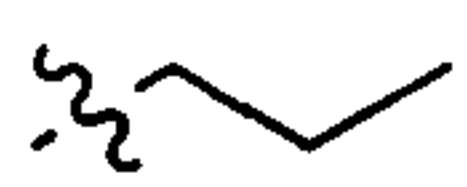
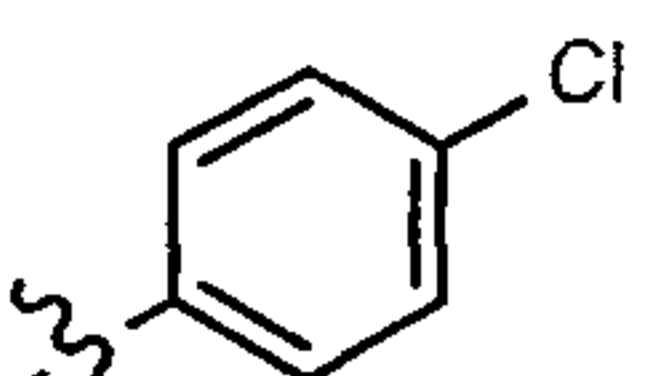
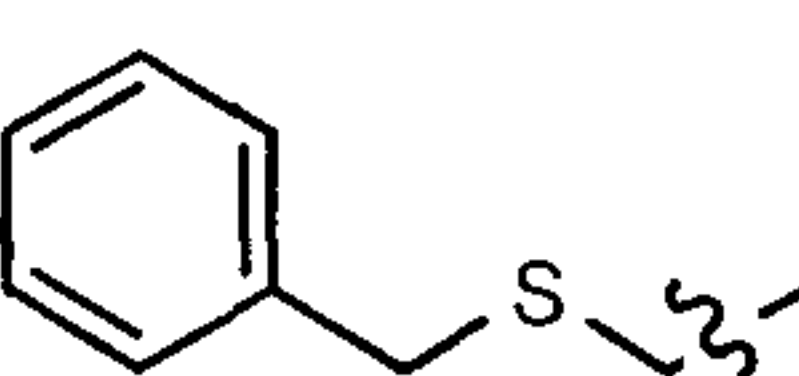
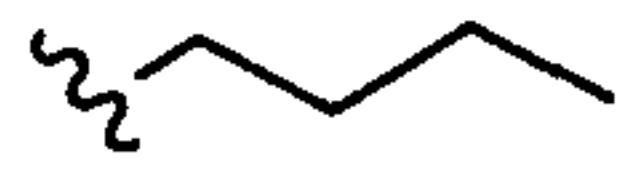
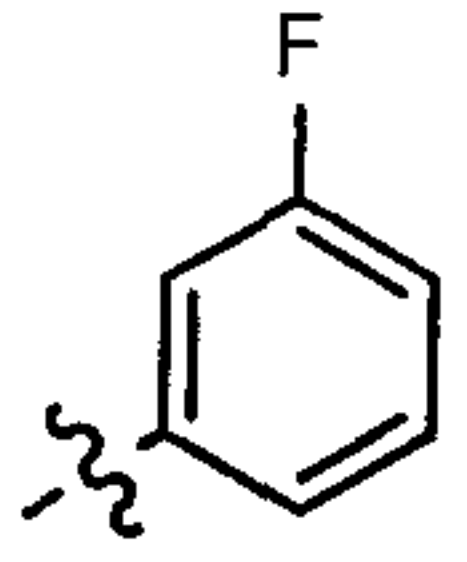
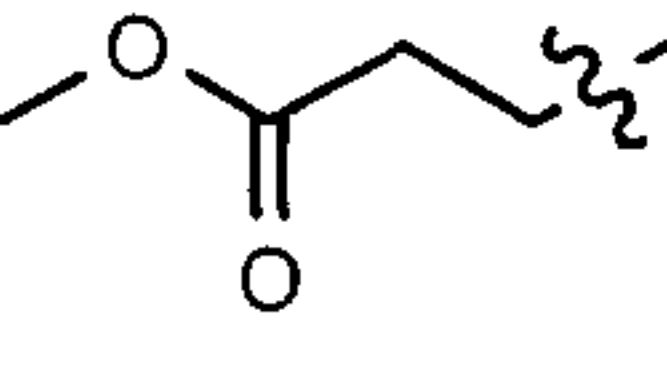
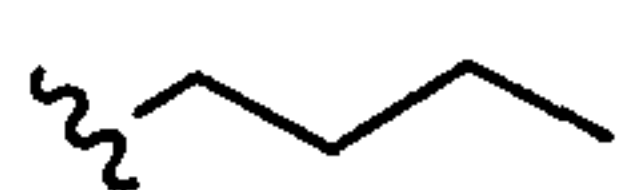
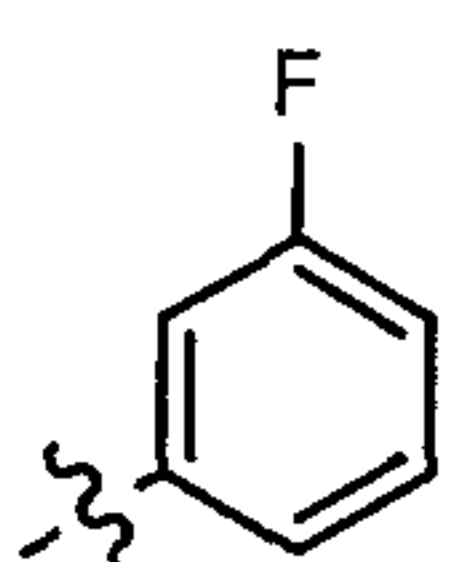
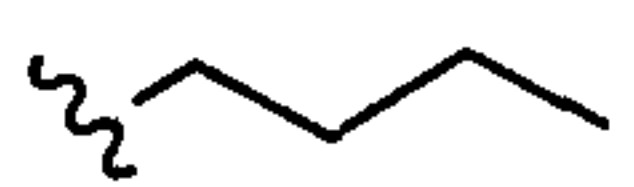
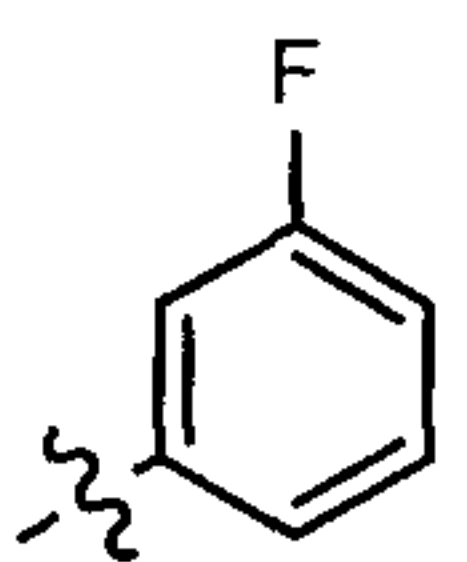
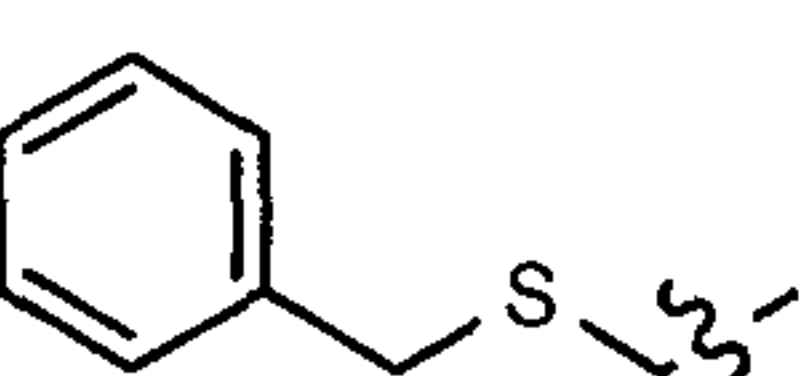
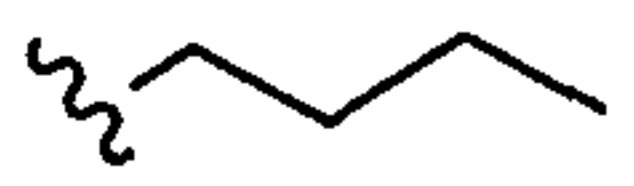
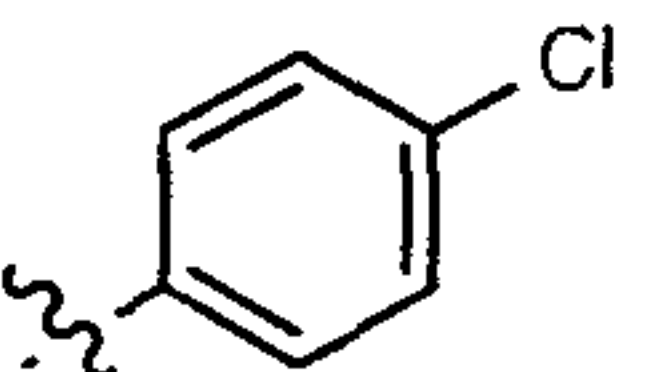
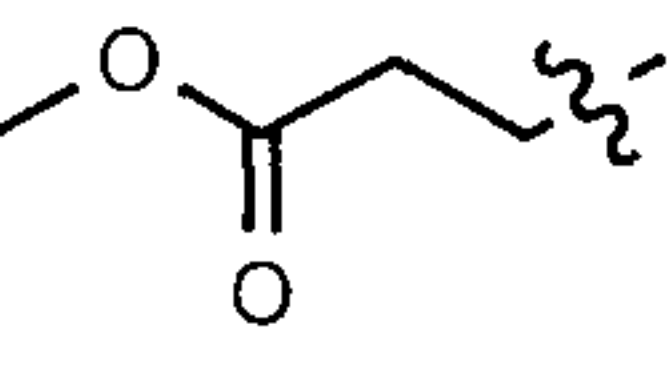
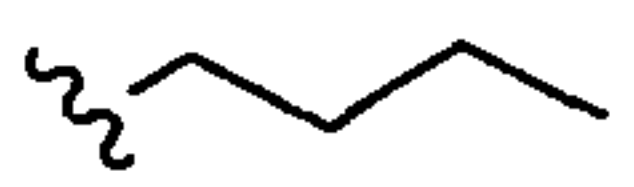
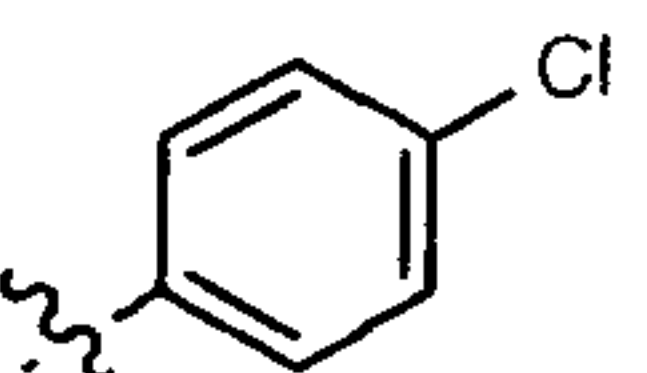
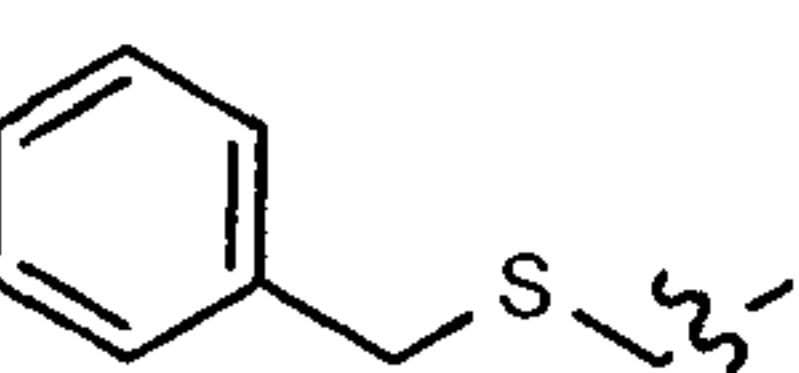
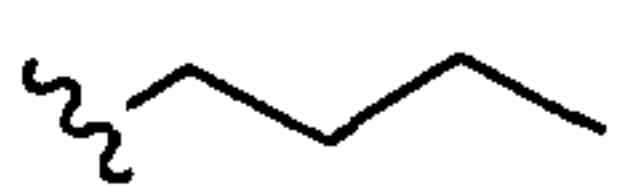
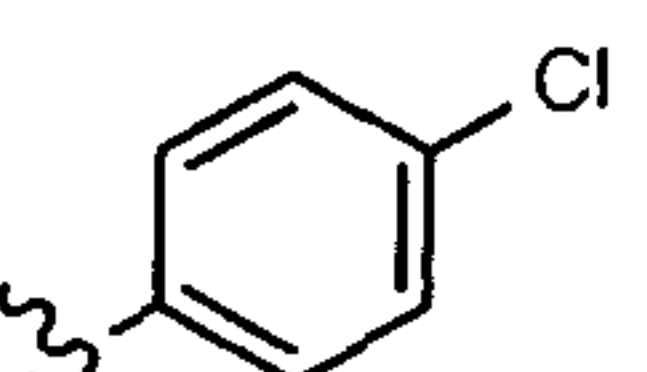
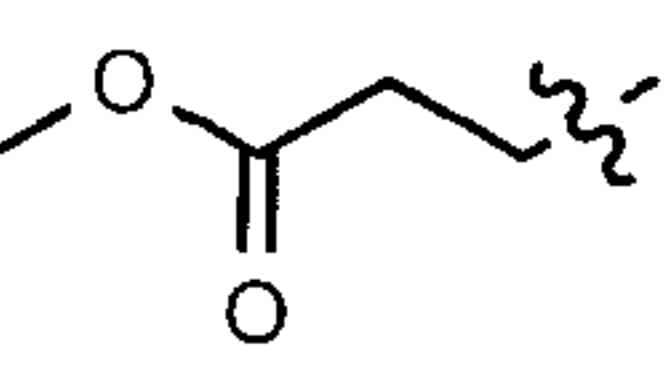
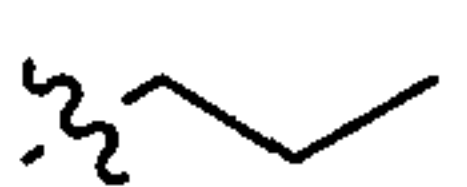
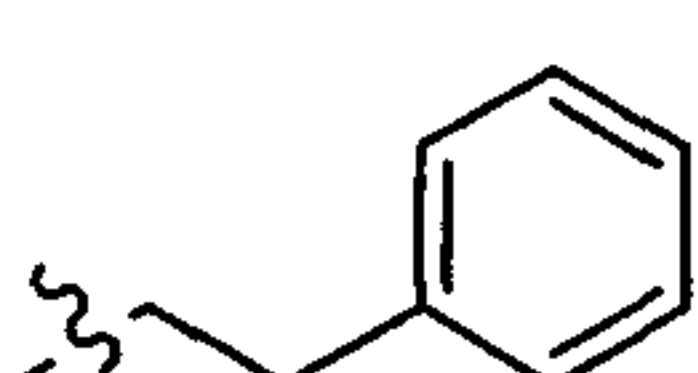
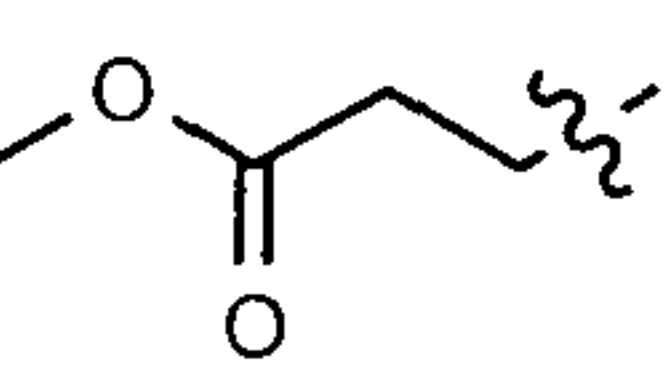
| No. | n | R <sup>1</sup> | R <sup>2</sup> | R <sup>3</sup> | $\mu$ -Opioid receptor,<br>%inhibition [1 $\mu$ M] |
|-----|---|----------------|----------------|----------------|----------------------------------------------------|
| 11  | 0 |                |                |                | 84                                                 |
| 12  | 0 |                |                |                | 73                                                 |
| 13  | 0 |                |                |                | 94                                                 |

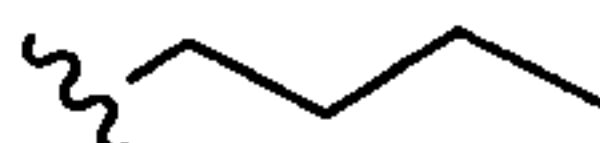
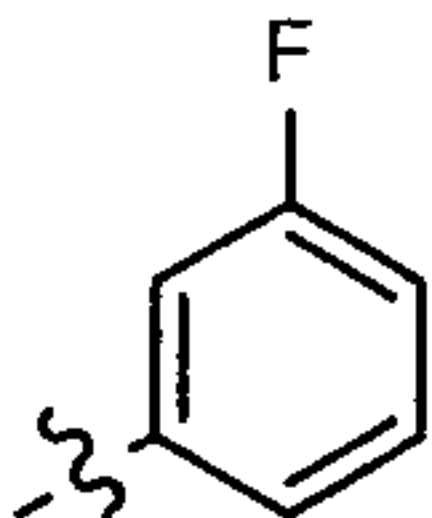
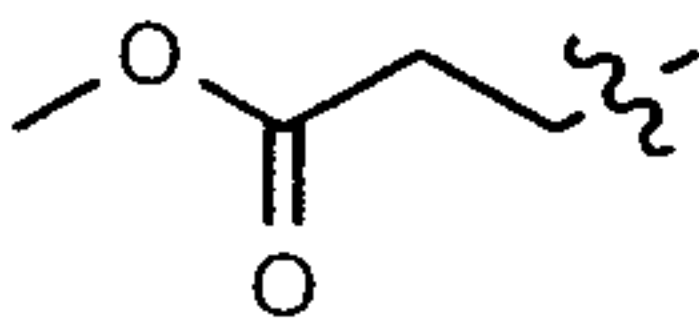
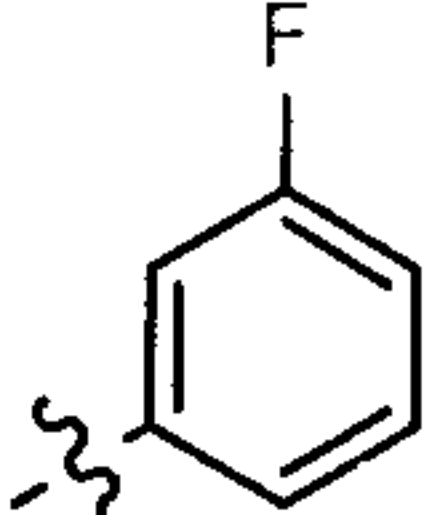
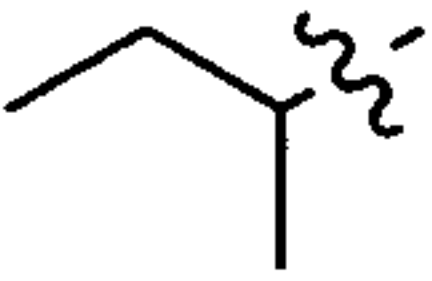
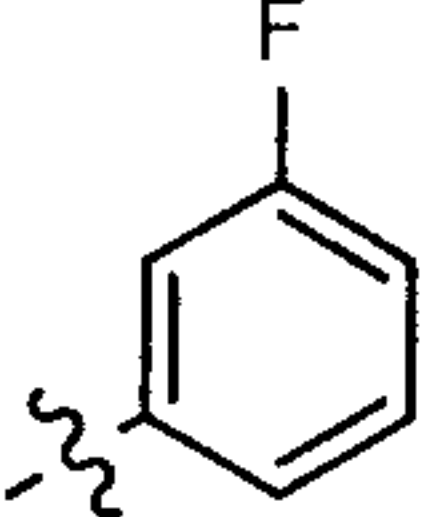
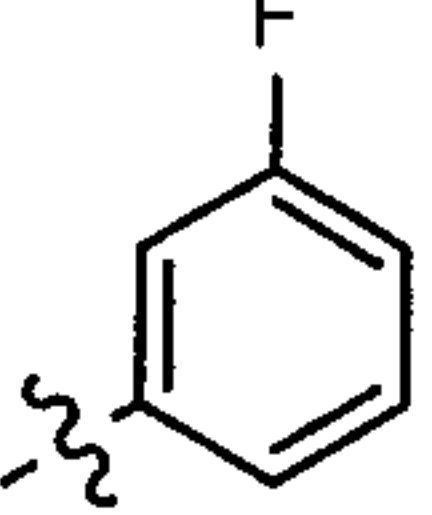
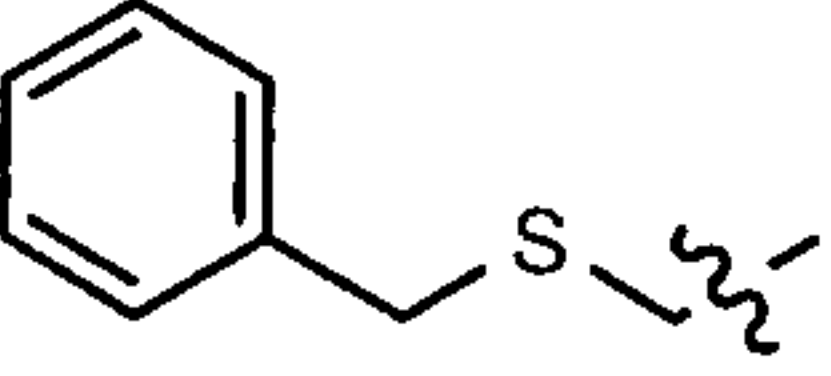
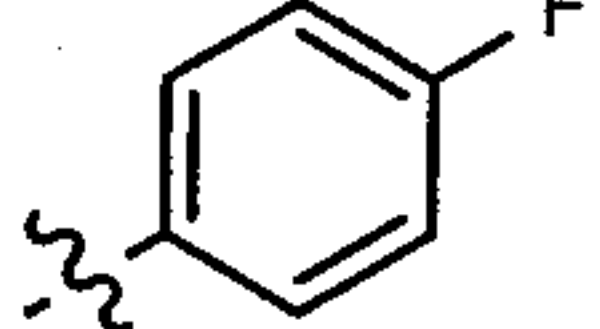
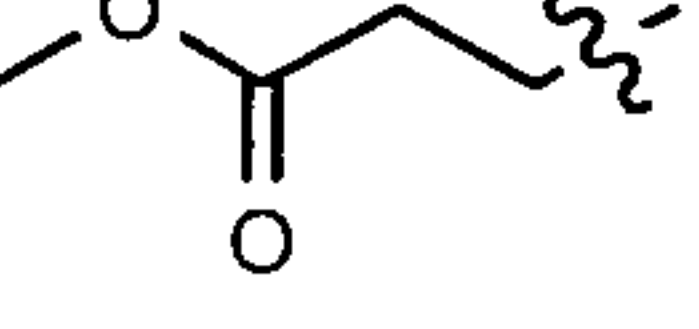
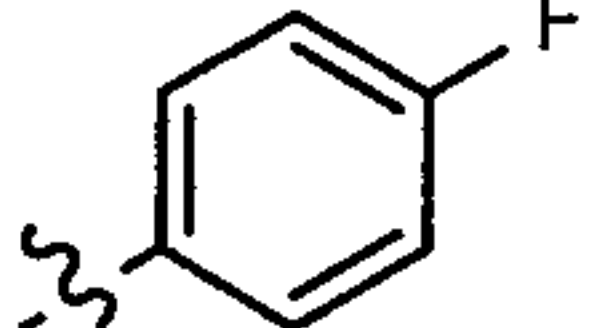
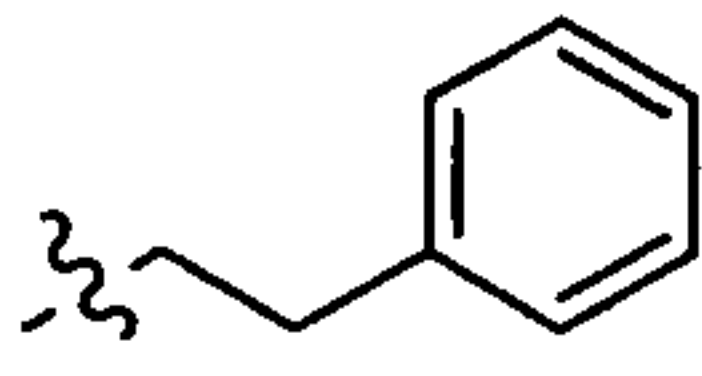
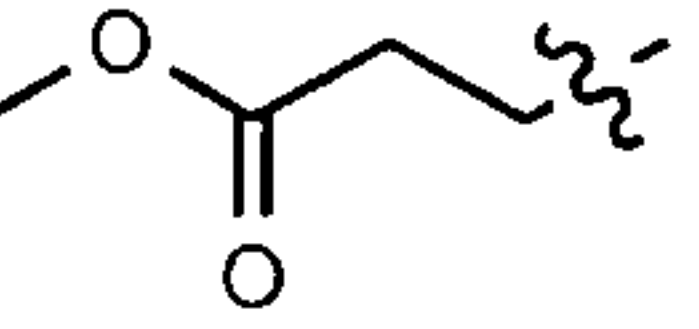
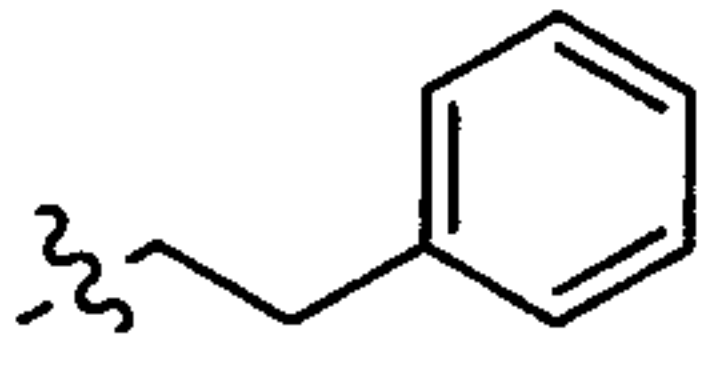
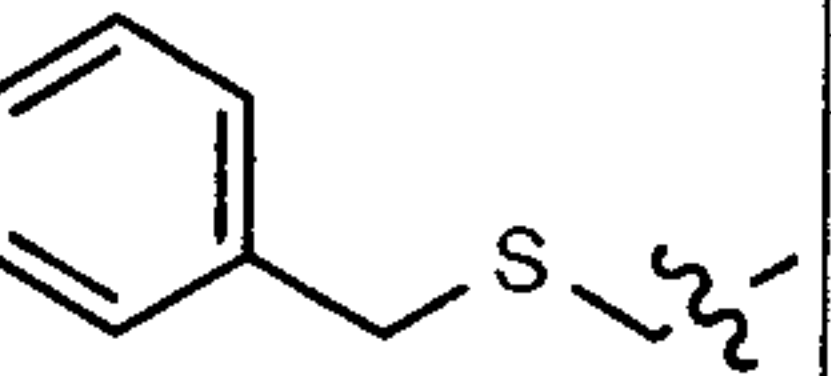
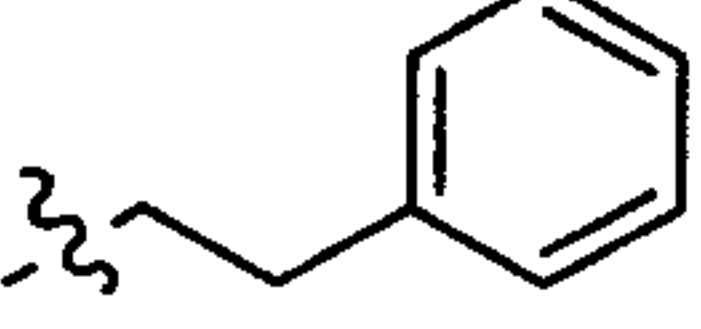
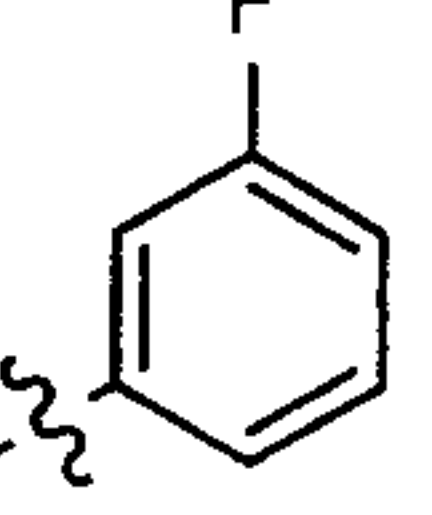
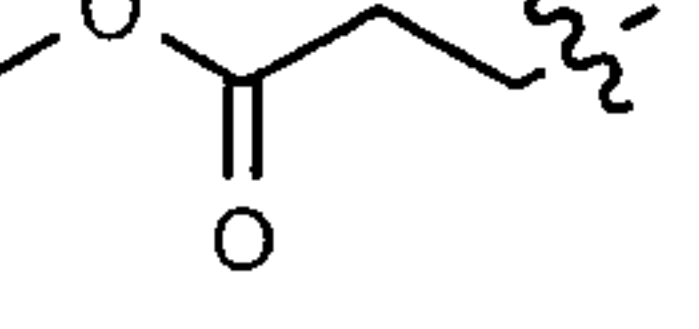
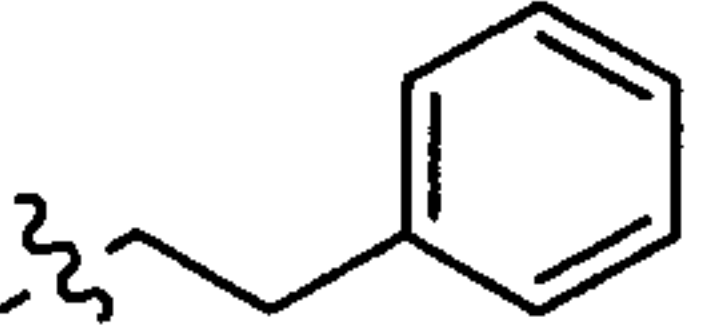
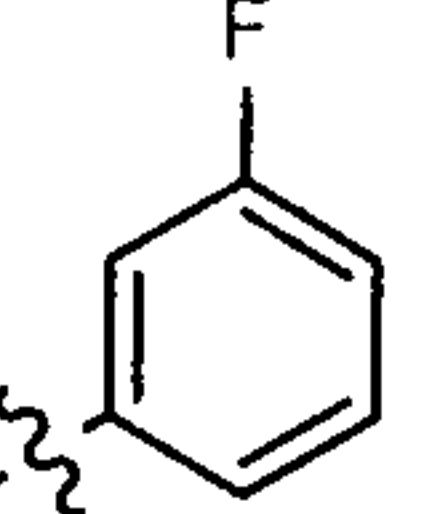
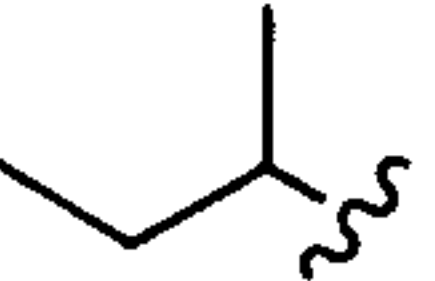
| No. | n | R <sup>1</sup>                                                                      | R <sup>2</sup>                                                                       | R <sup>3</sup>                                                                        | $\mu$ -Opioid receptor,<br>%inhibition [1 $\mu$ M] |
|-----|---|-------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------|----------------------------------------------------|
| 14  | 0 |    |    |    | 92                                                 |
| 15  | 0 |    |    |    | 76                                                 |
| 16  | 0 |    |    |    | 92                                                 |
| 17  | 1 |  |  |  | 96                                                 |
| 18  | 1 |  |  |  | 90                                                 |
| 19  | 1 |  |  |  | 96                                                 |
| 20  | 1 |  |  |  | 95                                                 |
| 21  | 0 |  |  |  | 83                                                 |
| 22  | 0 |  |  |  | 88                                                 |
| 23  | 0 |  |  |  | 76                                                 |
| 24  | 0 |  |  |  | 89                                                 |
| 25  | 0 |  |  |  | 83                                                 |

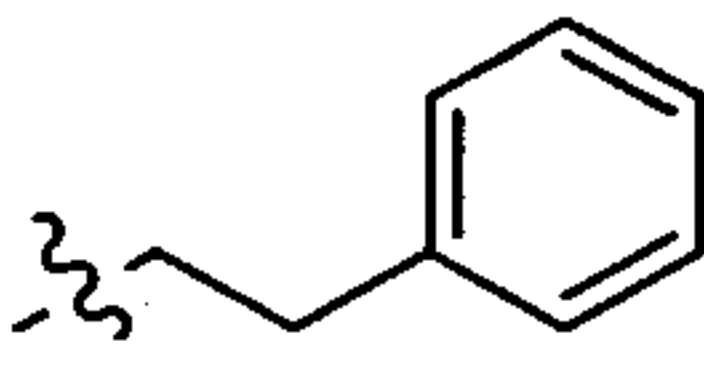
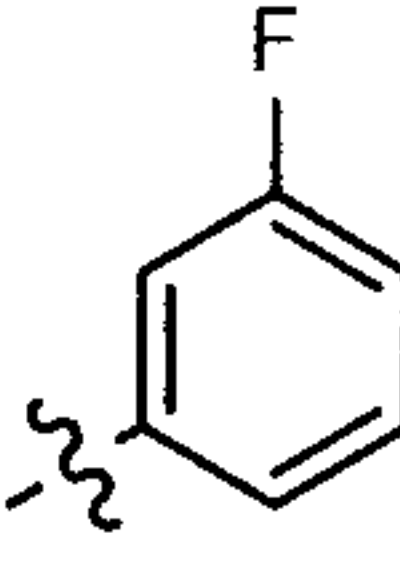
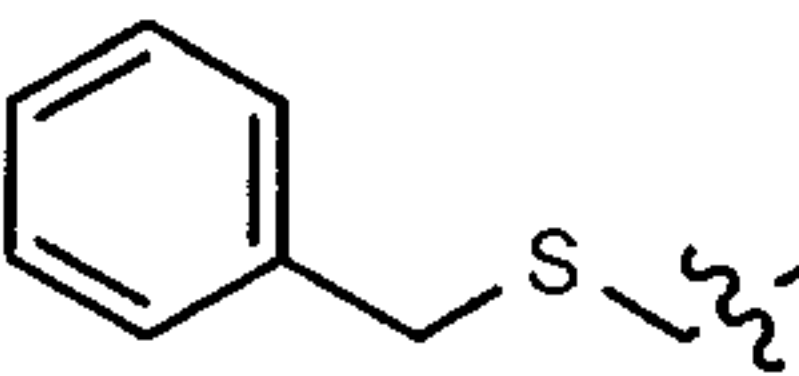
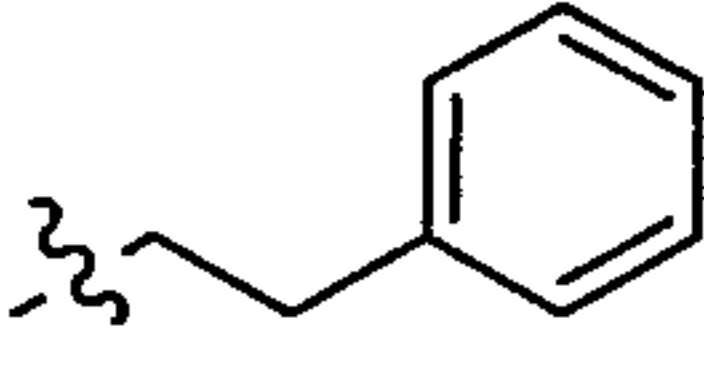
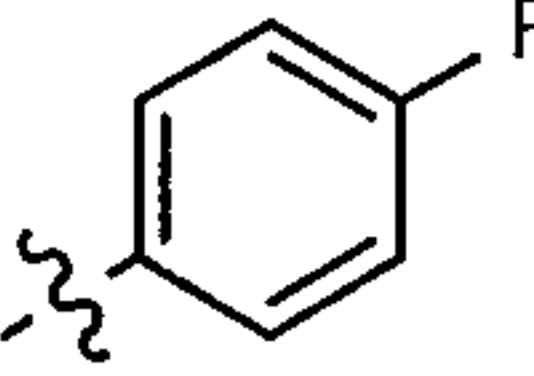
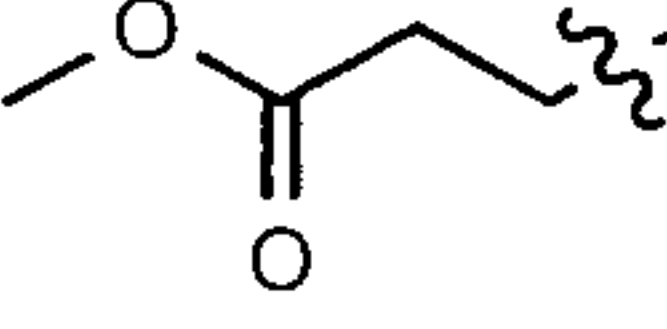
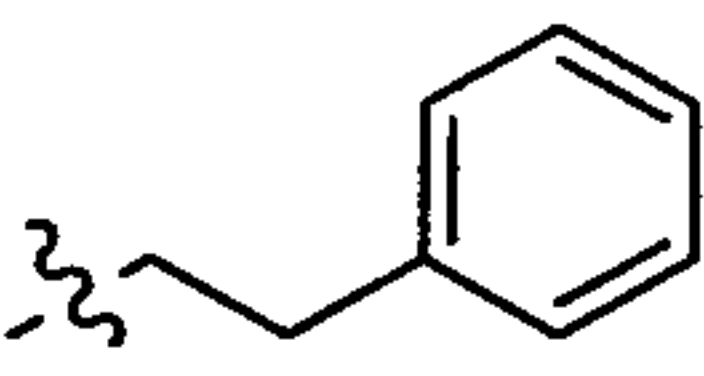
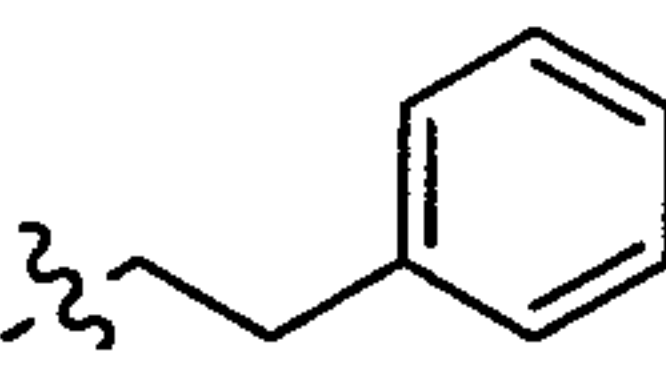
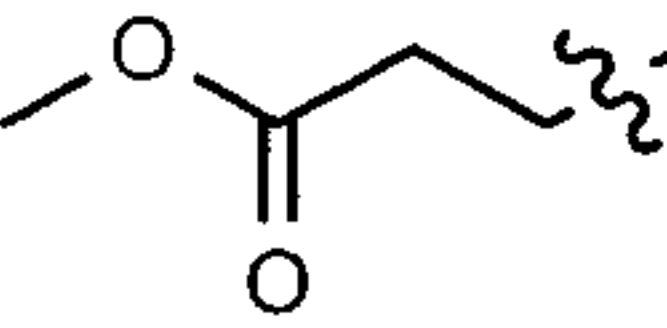
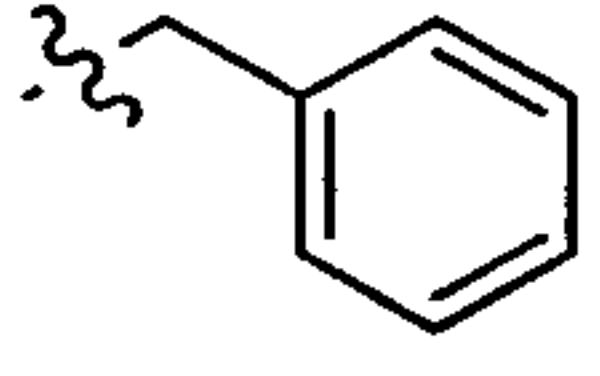
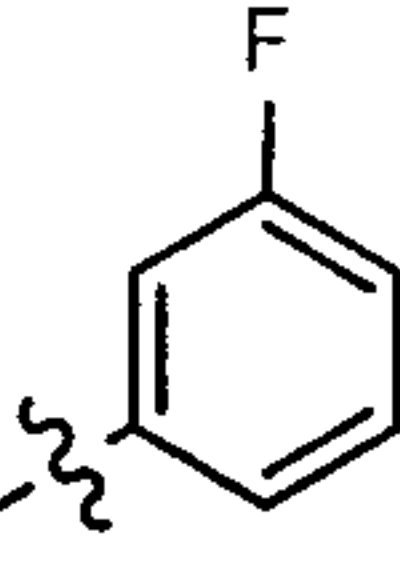
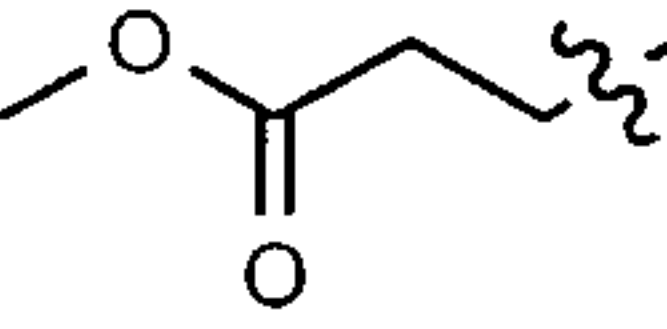
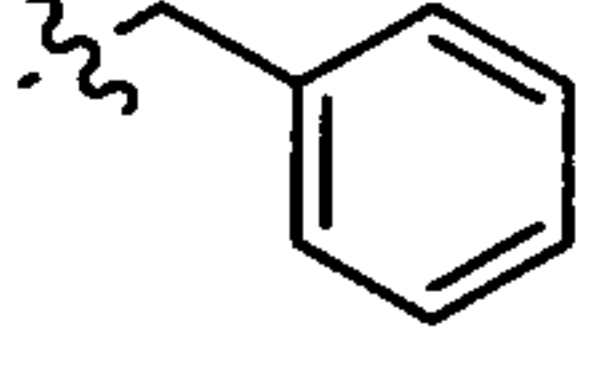
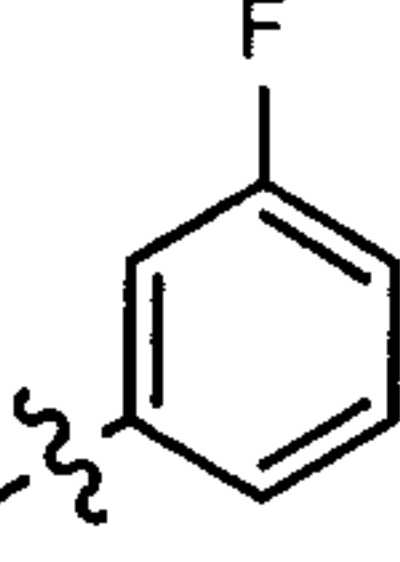
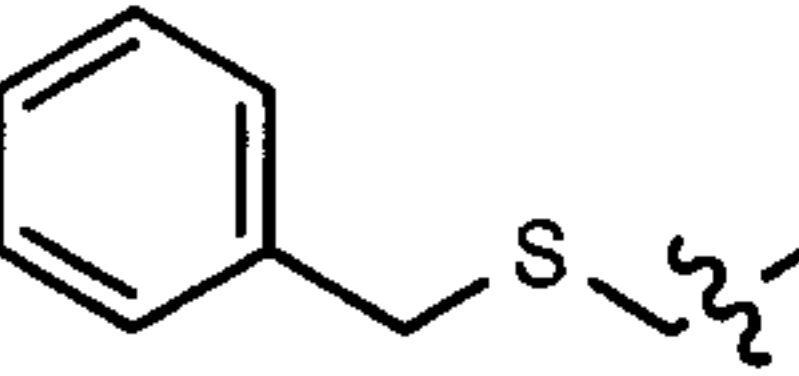
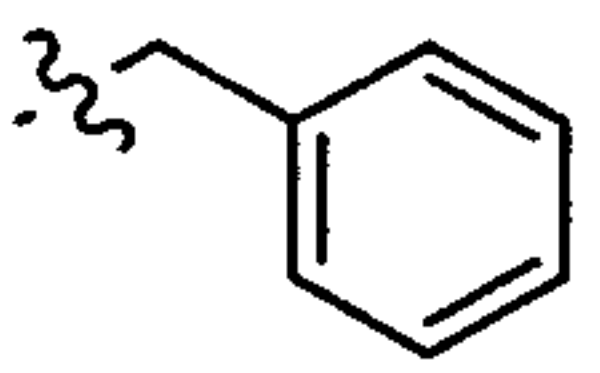
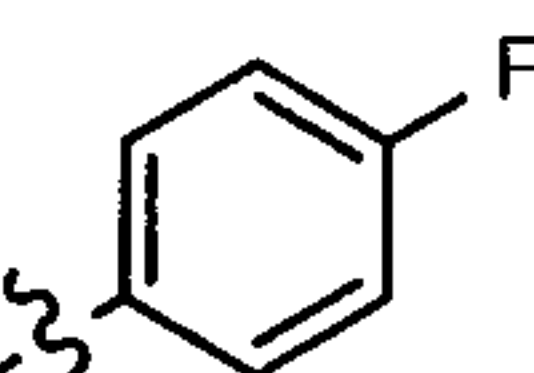
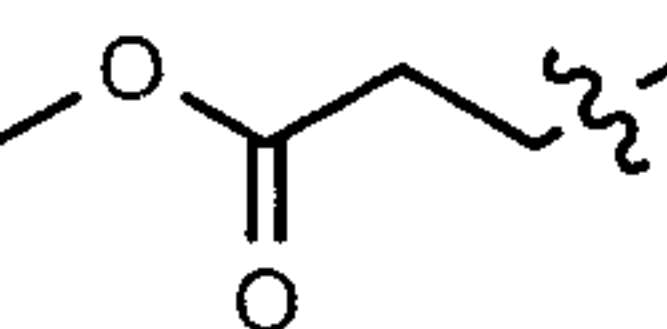
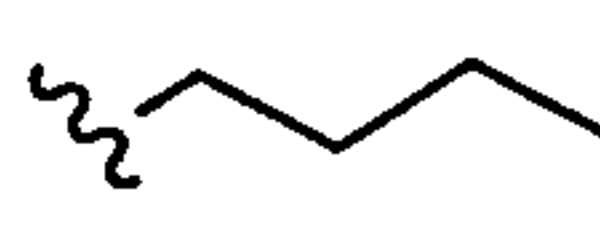
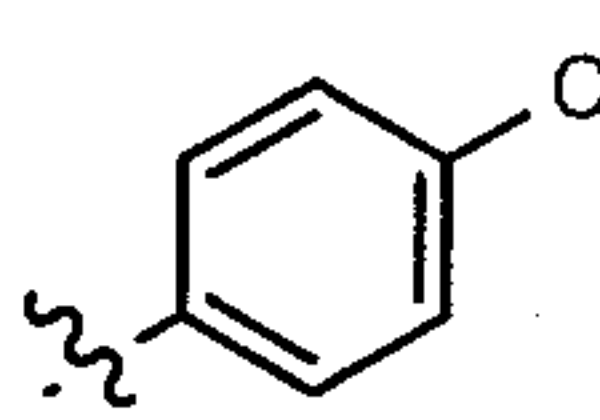
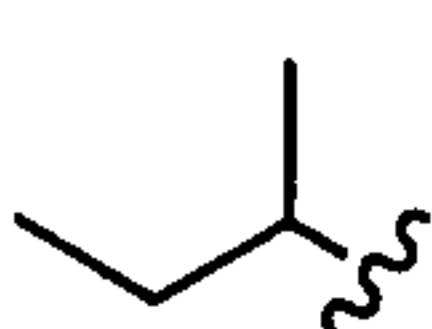
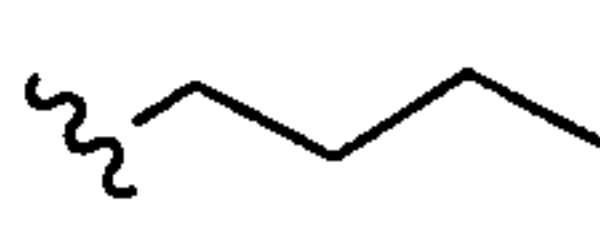
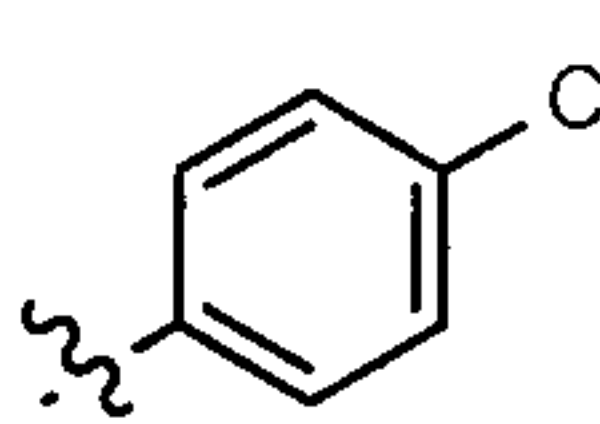
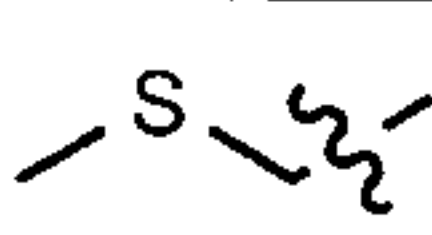
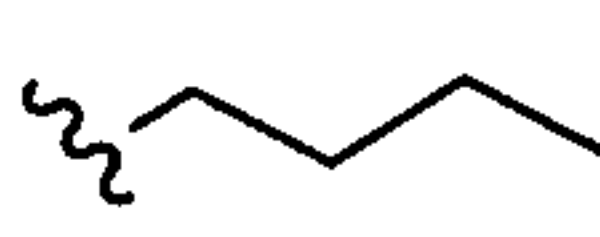
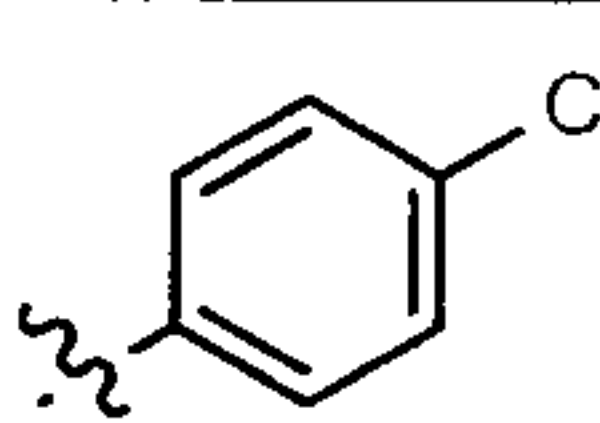
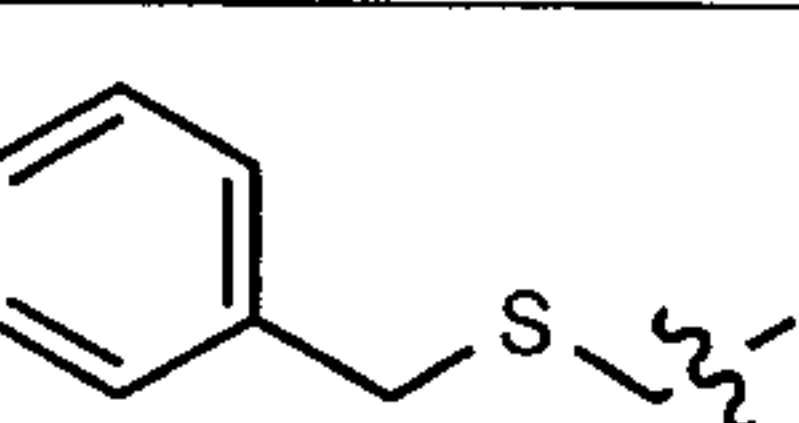
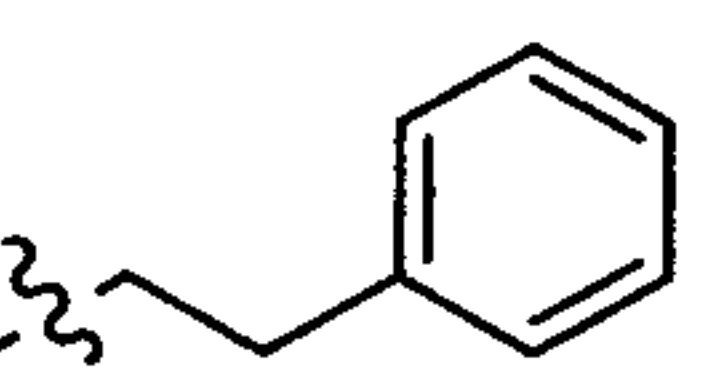
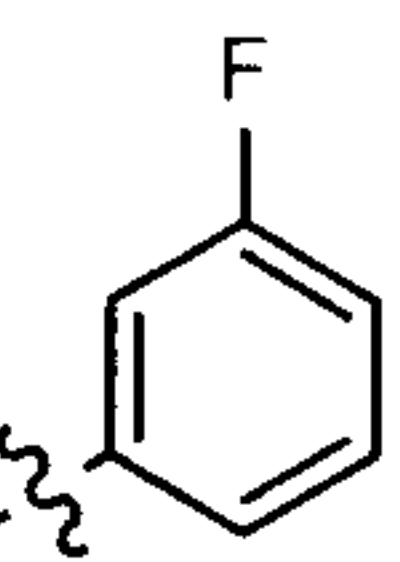
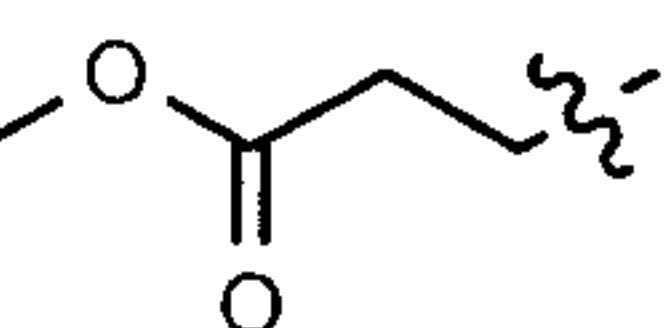
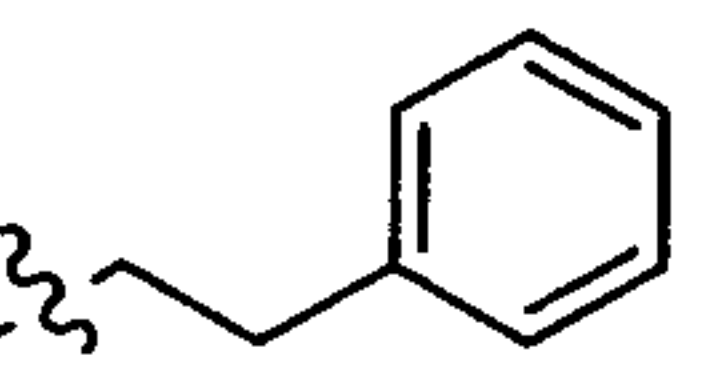
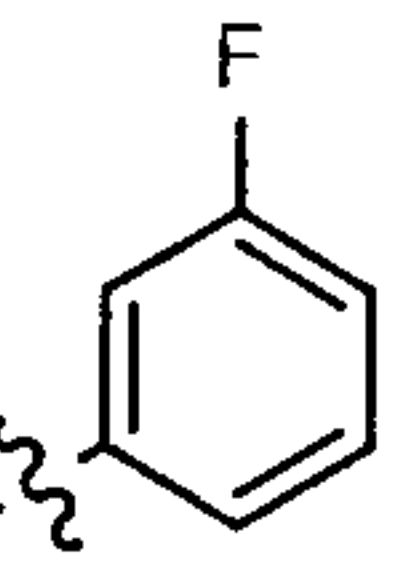
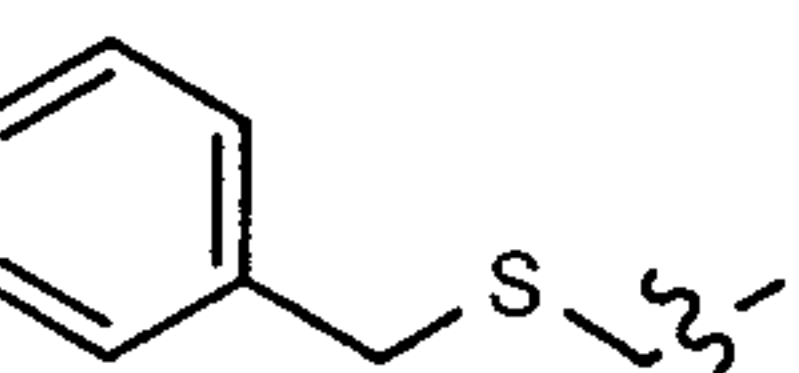
| No. | n | R <sup>1</sup>                                                                      | R <sup>2</sup>                                                                       | R <sup>3</sup>                                                                        | $\mu$ -Opioid receptor,<br>%inhibition [1 $\mu$ M] |
|-----|---|-------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------|----------------------------------------------------|
| 26  | 1 |    |    |    | 96                                                 |
| 27  | 1 |    |    |    | 96                                                 |
| 28  | 1 |    |    |    | 97                                                 |
| 29  | 0 |   |   |   | 89                                                 |
| 30  | 0 |  |  |  | 89                                                 |
| 31  | 0 |  |  |  | 91                                                 |
| 32  | 0 |  |  |  | 74                                                 |
| 33  | 0 |  |  |  | 85                                                 |
| 34  | 1 |  |  |  | 98                                                 |
| 35  | 1 |  |  |  | 92                                                 |
| 36  | 1 |  |  |  | 97                                                 |
| 37  | 0 |  |  |  | 93                                                 |

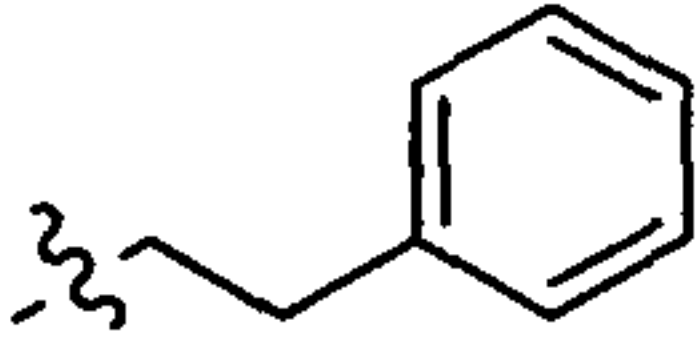
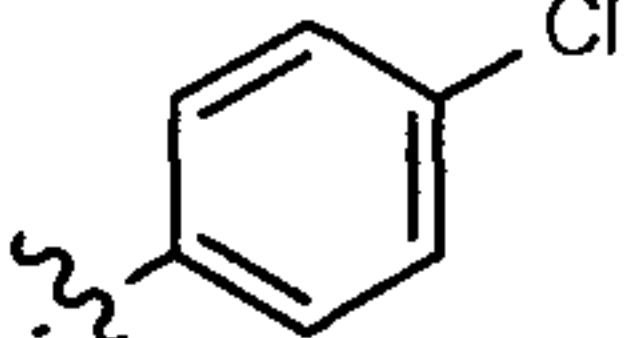
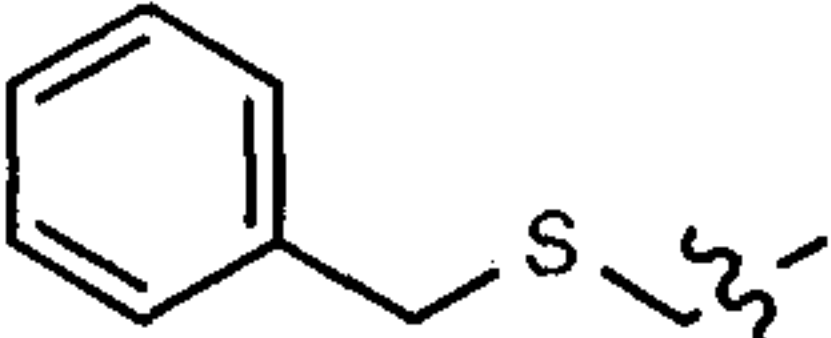
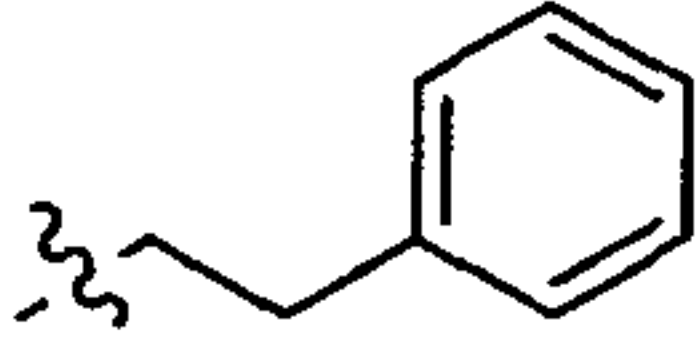
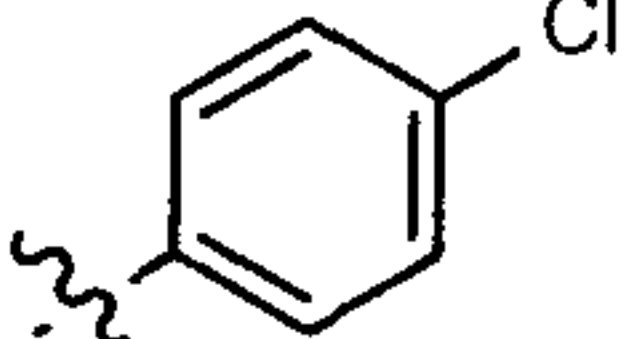
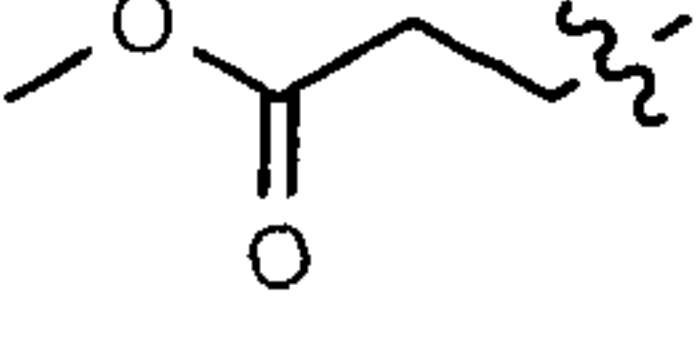
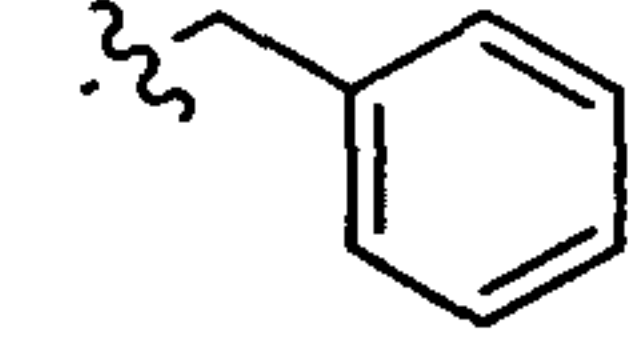
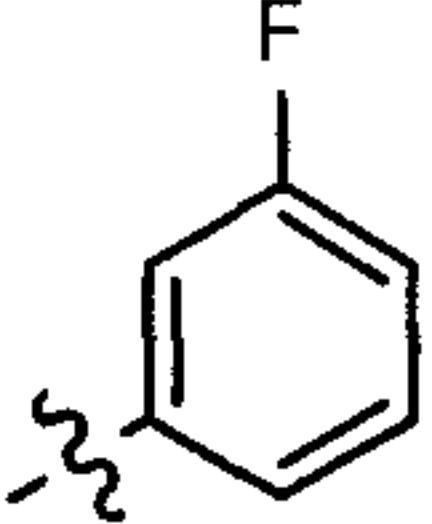
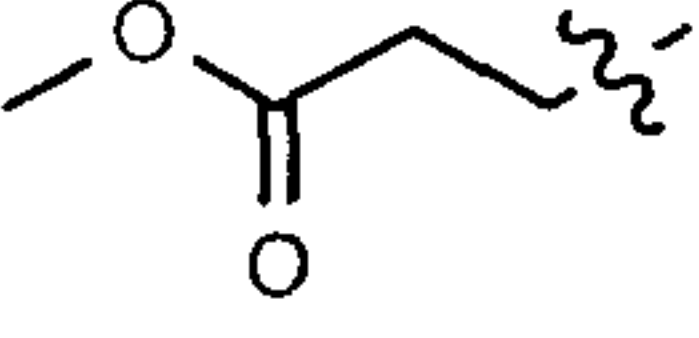
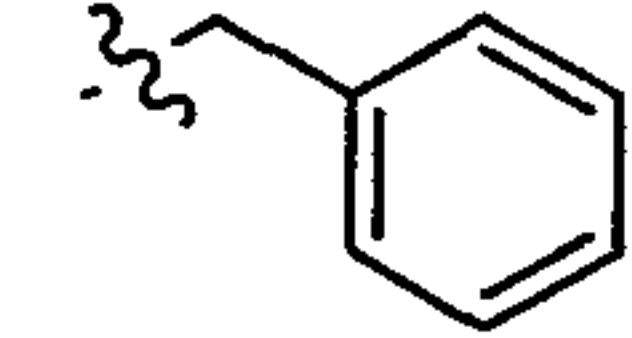
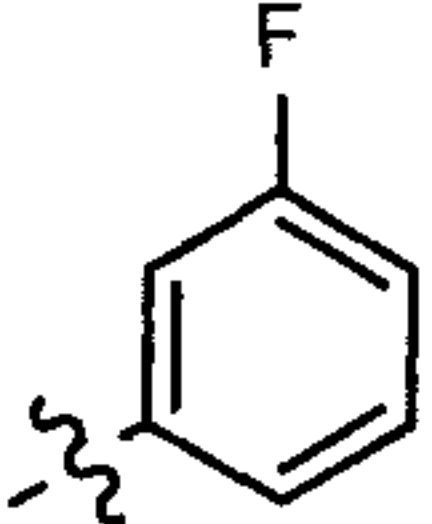
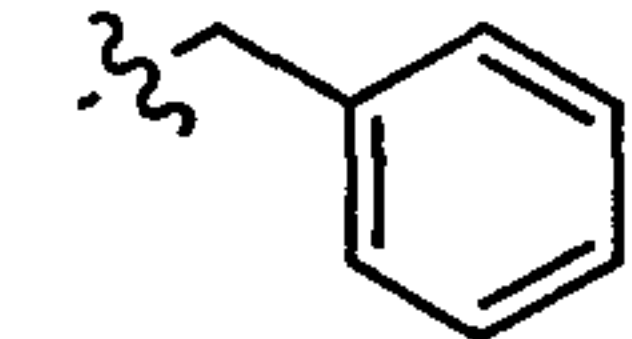
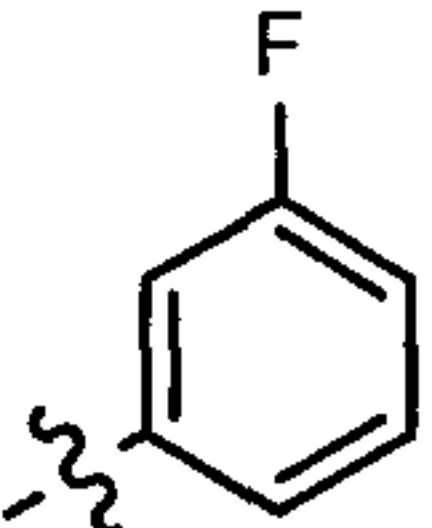
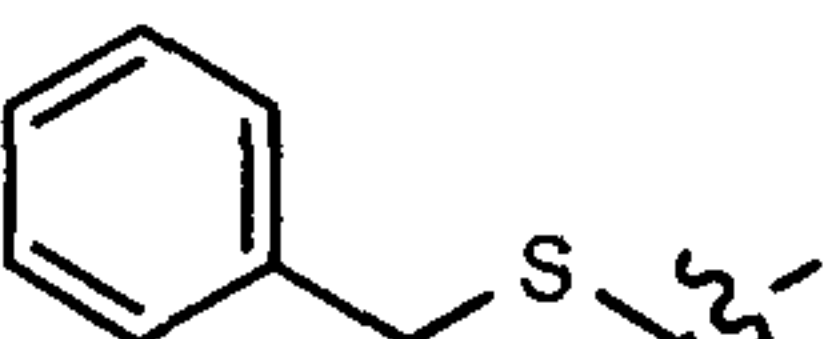
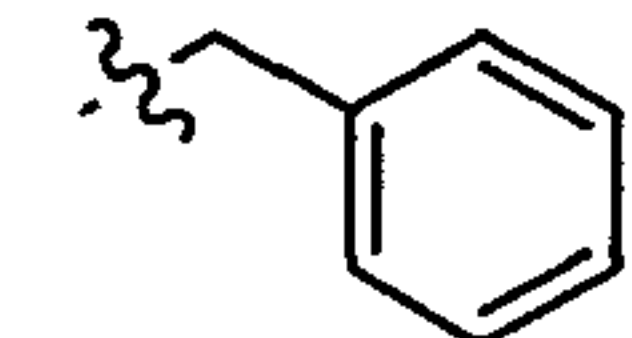
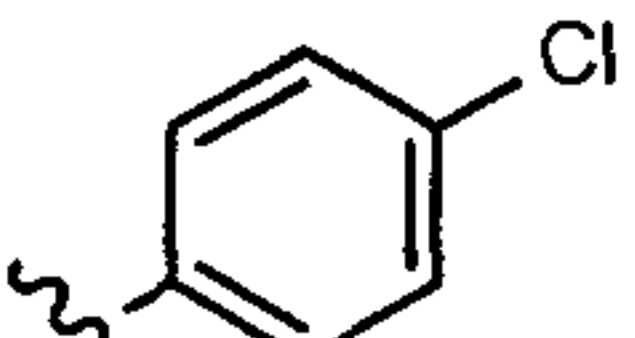
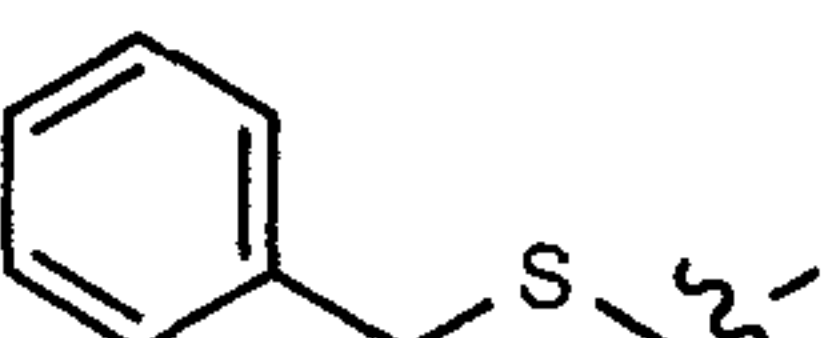
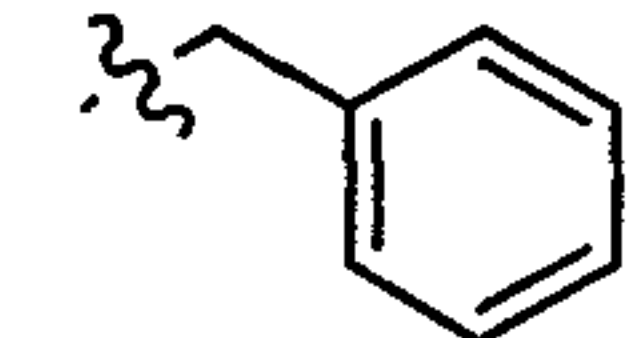
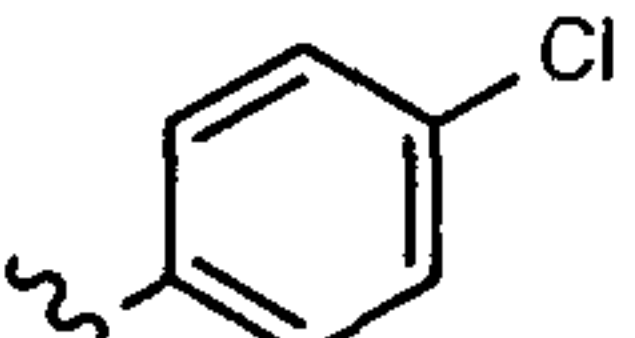
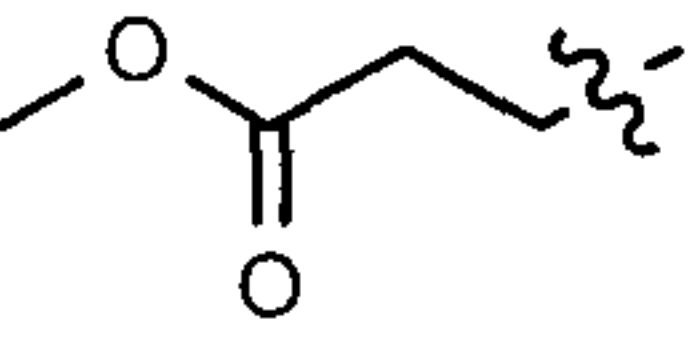
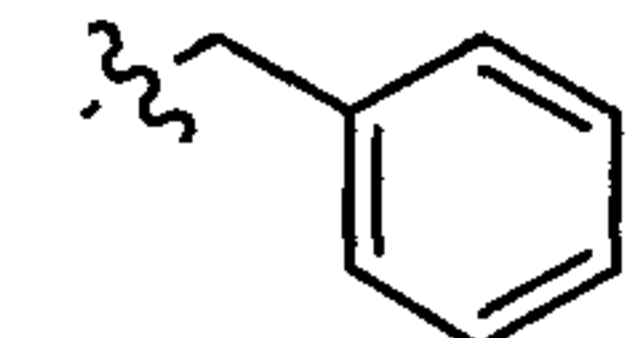
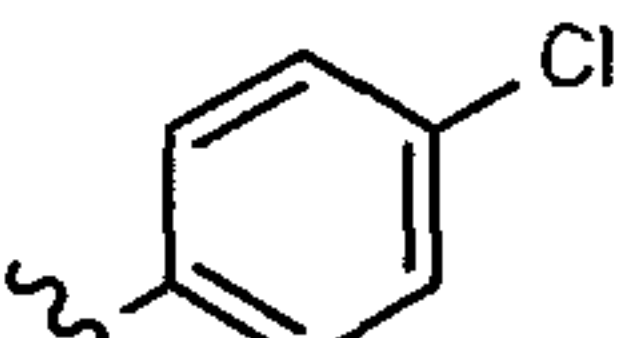
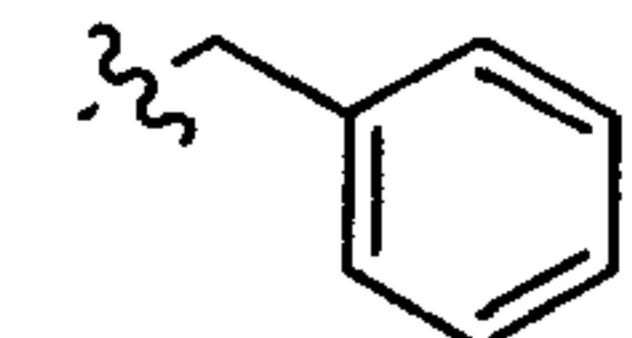
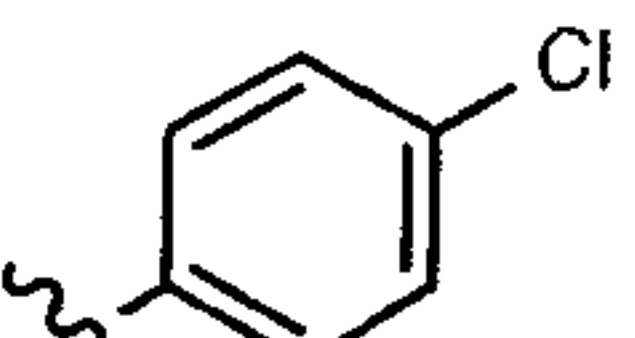
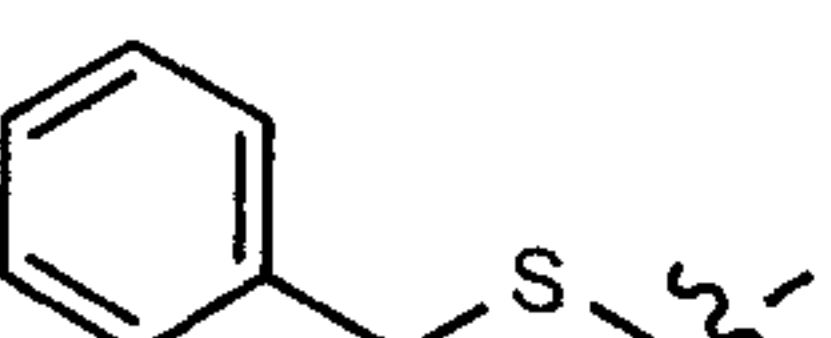
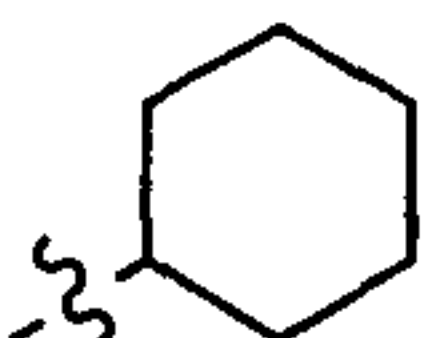
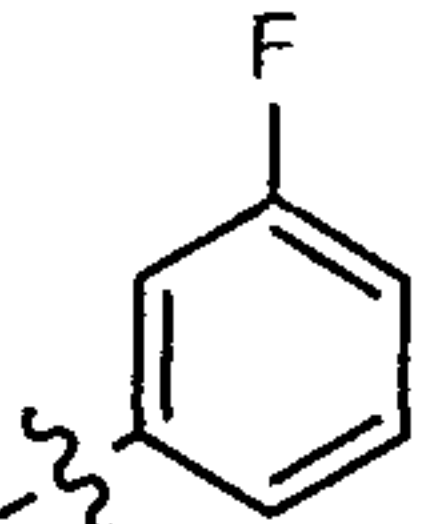
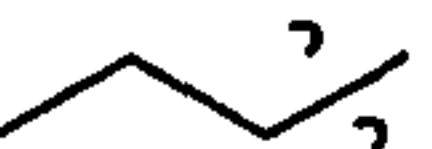
| No. | n | R <sup>1</sup> | R <sup>2</sup> | R <sup>3</sup> | $\mu$ -Opioid receptor,<br>%inhibition [1 $\mu$ M] |
|-----|---|----------------|----------------|----------------|----------------------------------------------------|
| 38  | 0 |                |                |                | 84                                                 |
| 39  | 0 |                |                |                | 88                                                 |
| 40  | 0 |                |                |                | 95                                                 |
| 41  | 0 |                |                |                | 79                                                 |
| 42  | 0 |                |                |                | 94                                                 |
| 43  | 1 |                |                |                | 97                                                 |
| 44  | 1 |                |                |                | 91                                                 |
| 45  | 1 |                |                |                | 97                                                 |
| 46  | 0 |                |                |                | 92                                                 |
| 47  | 0 |                |                |                | 74                                                 |
| 48  | 0 |                |                |                | 93                                                 |
| 49  | 0 |                |                |                | 84                                                 |

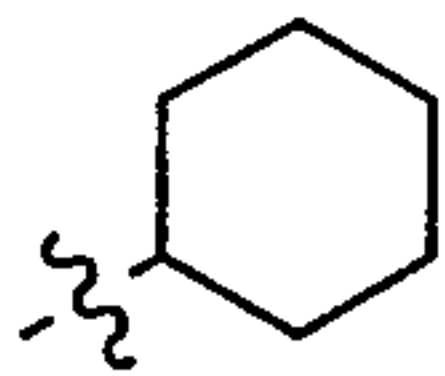
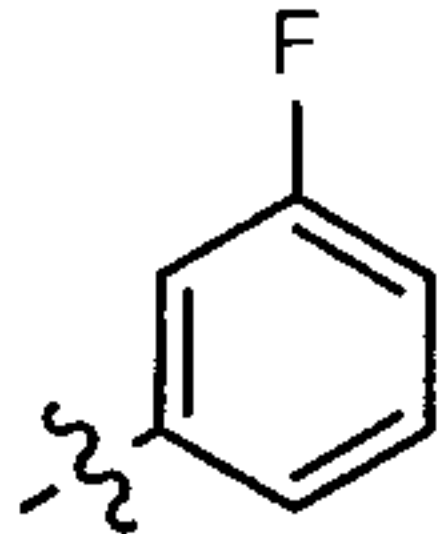
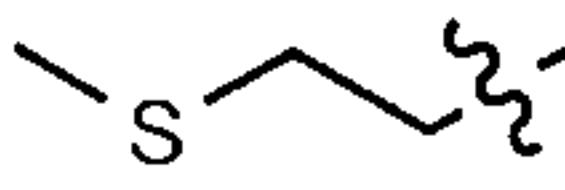
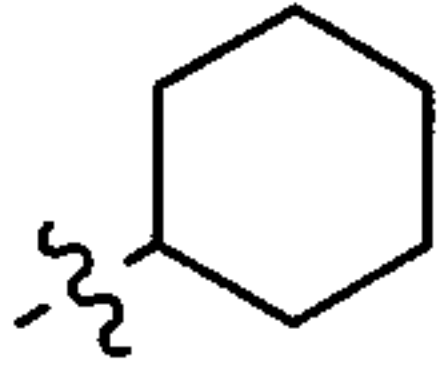
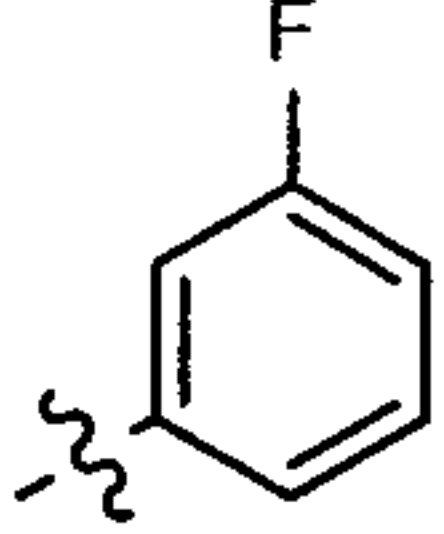
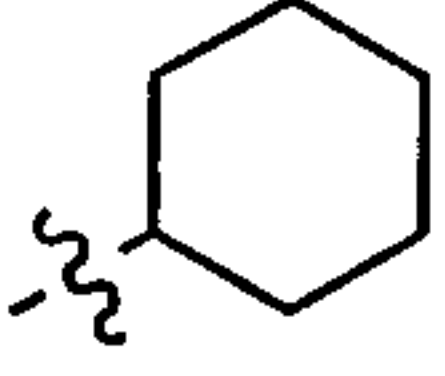
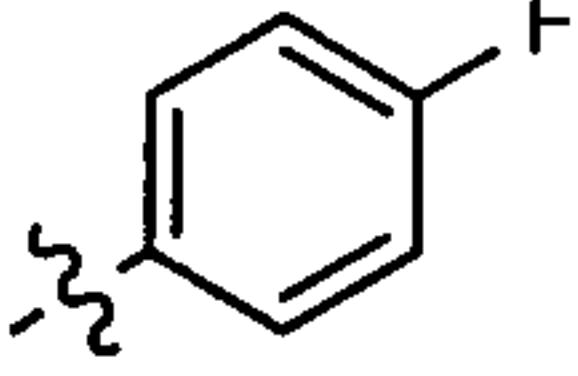
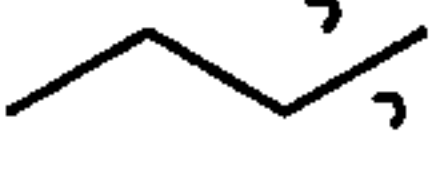
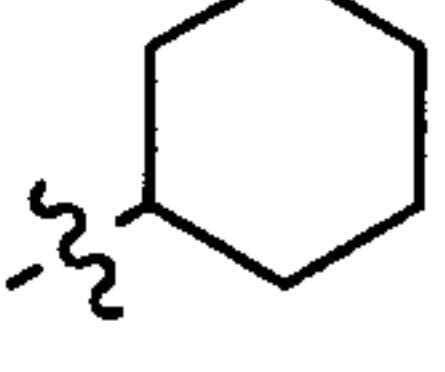
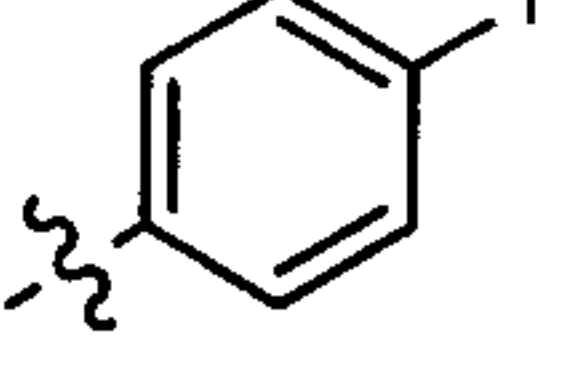
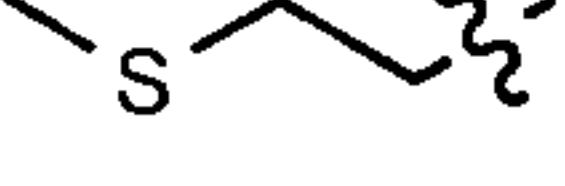
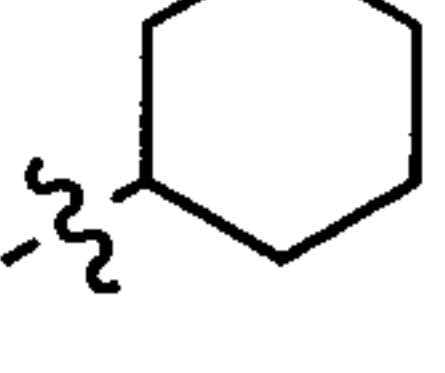
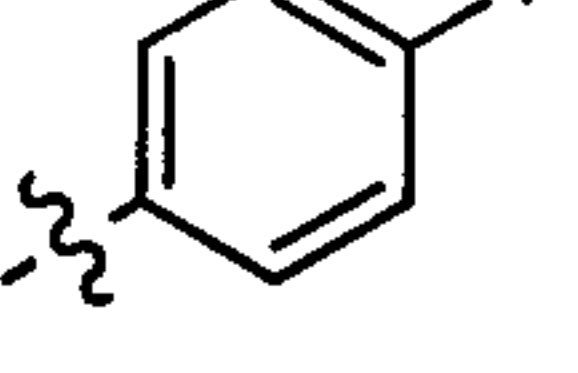
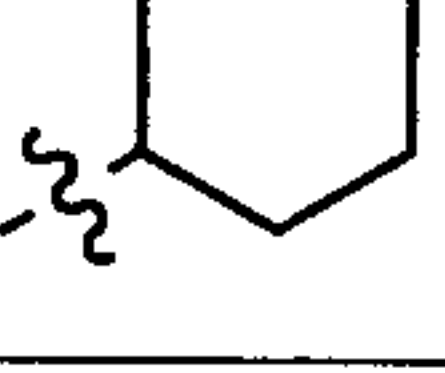
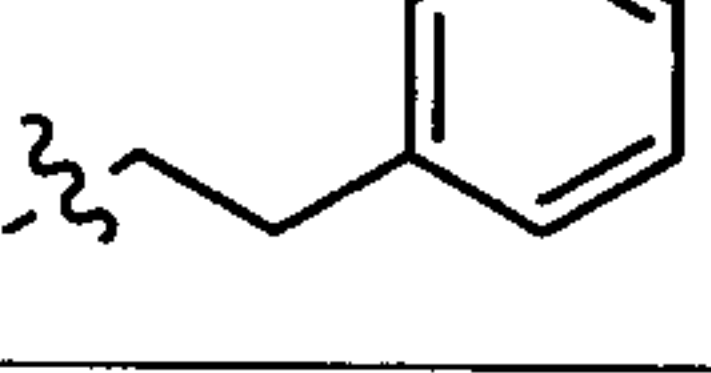
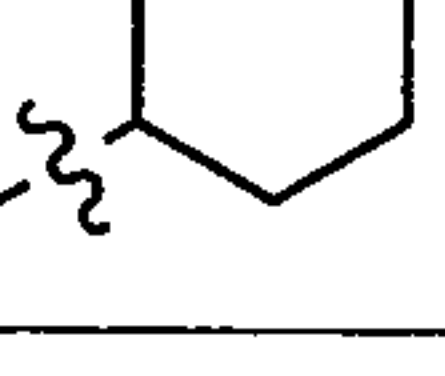
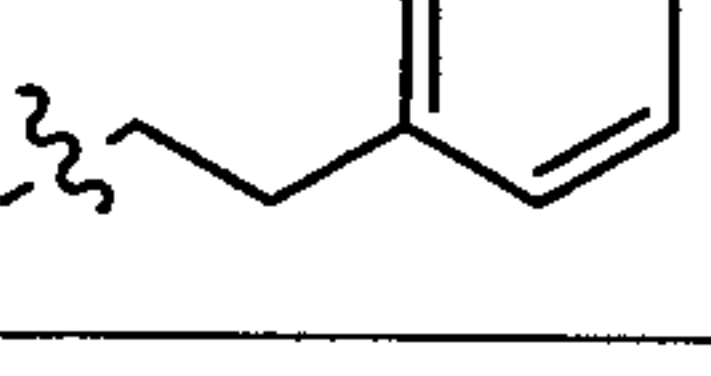
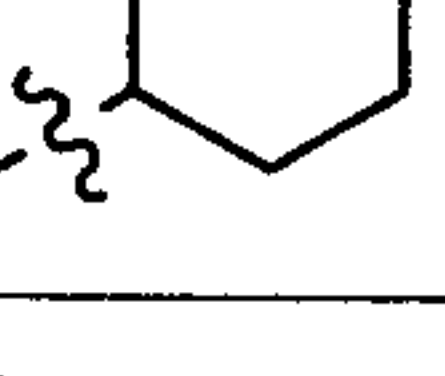
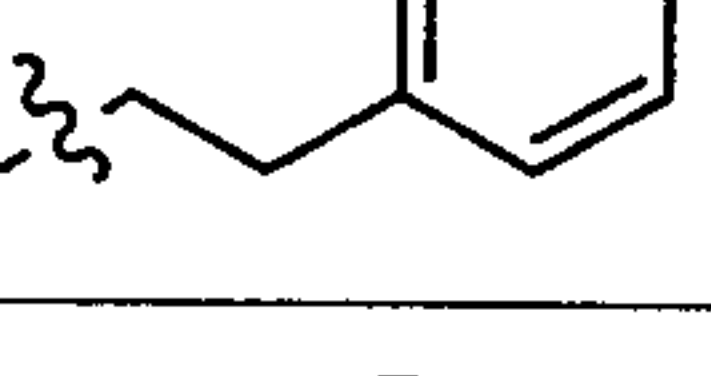
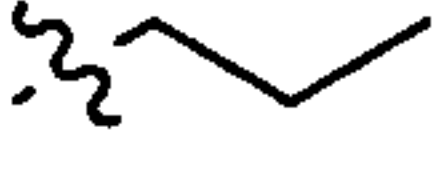
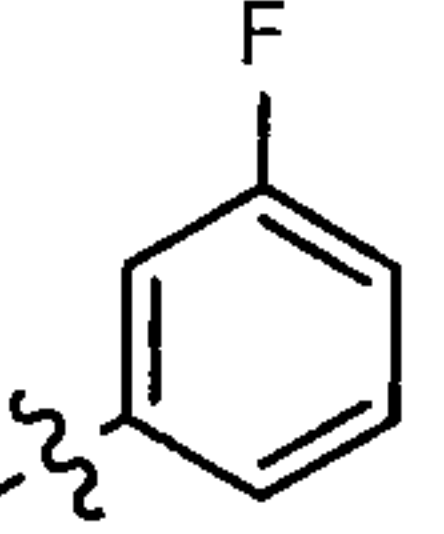
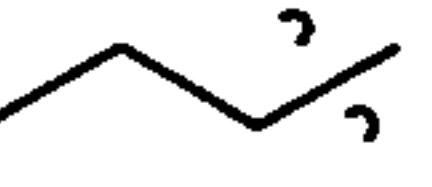
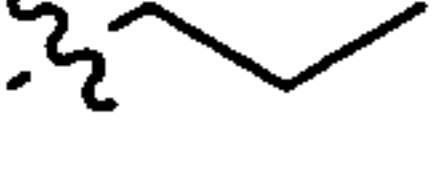
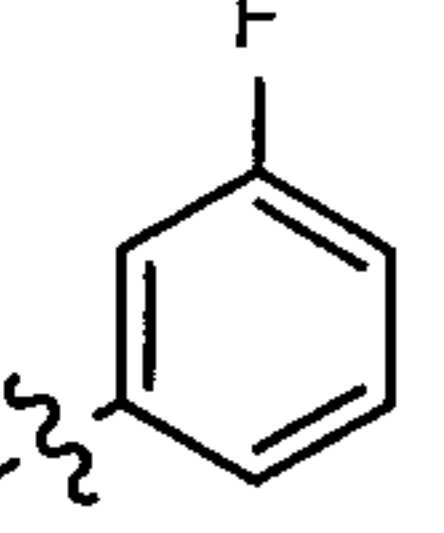
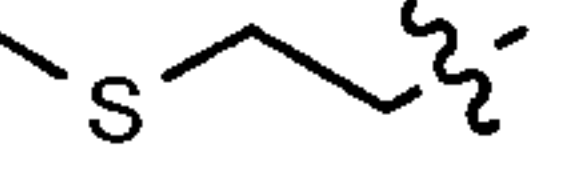
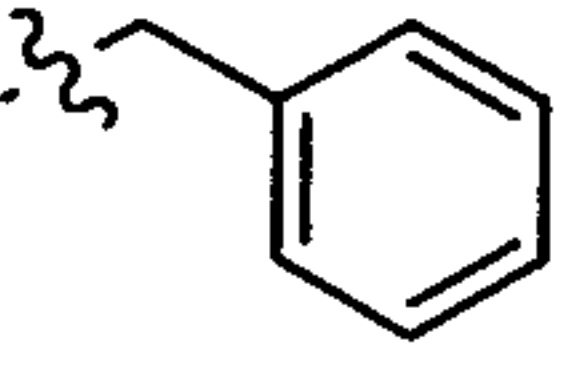
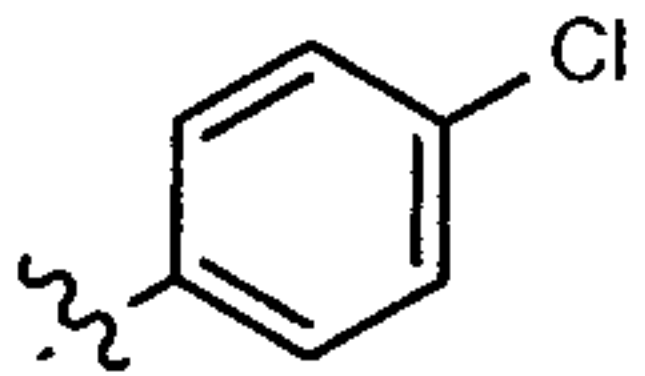
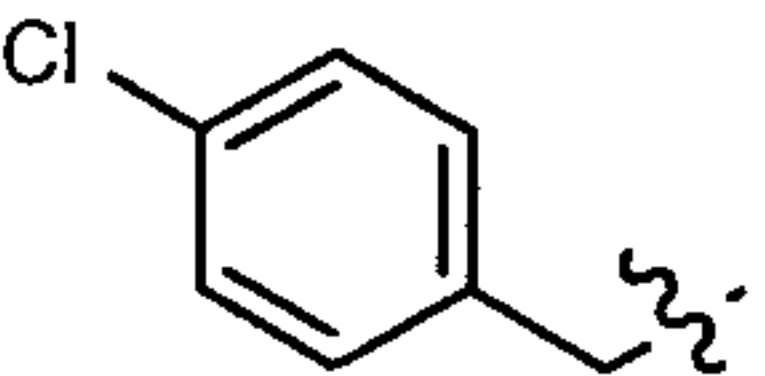
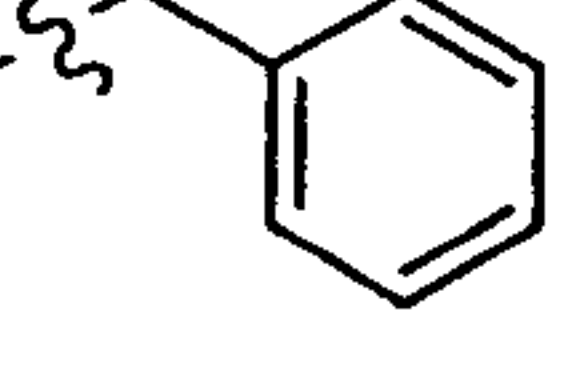
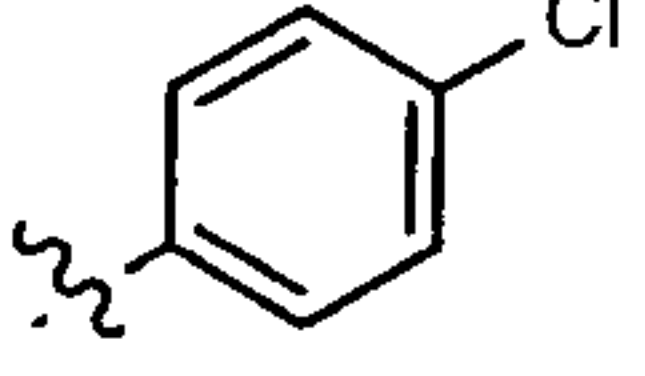
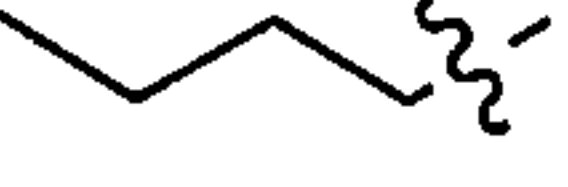
| No. | n | R <sup>1</sup>                                                                      | R <sup>2</sup>                                                                       | R <sup>3</sup>                                                                        | $\mu$ -Opioid receptor,<br>%inhibition [1 $\mu$ M] |
|-----|---|-------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------|----------------------------------------------------|
| 50  | 1 |    |    |    | 94                                                 |
| 51  | 0 |    |    |    | 96                                                 |
| 52  | 0 |    |    |    | 99                                                 |
| 53  | 1 |  |  |  | 96                                                 |
| 54  | 1 |  |  |  | 100                                                |
| 55  | 1 |  |  |  | 91                                                 |
| 56  | 1 |  |  |  | 97                                                 |
| 57  | 0 |  |  |  | 86                                                 |
| 58  | 0 |  |  |  | 81                                                 |
| 59  | 0 |  |  |  | 84                                                 |
| 60  | 0 |  |  |  | 95                                                 |

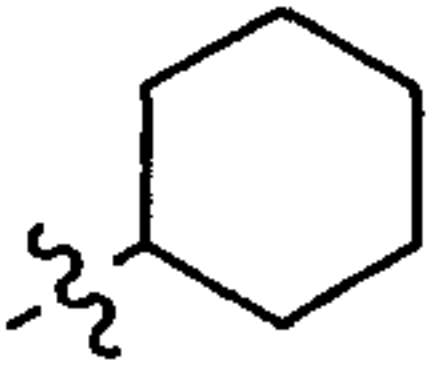
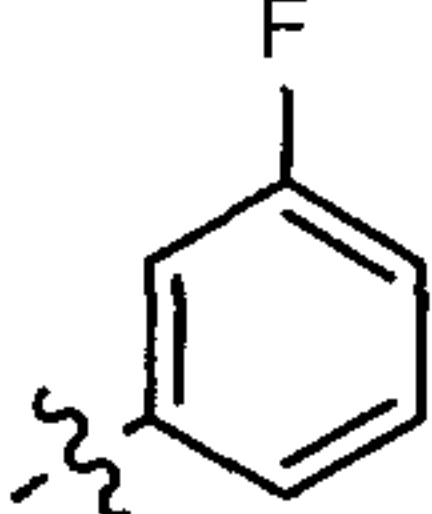
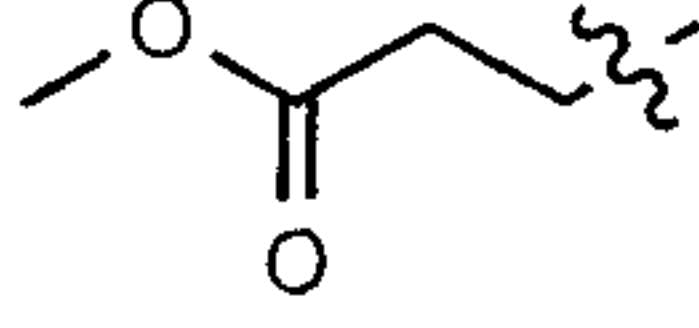
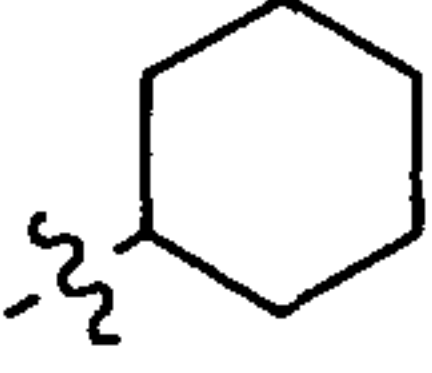
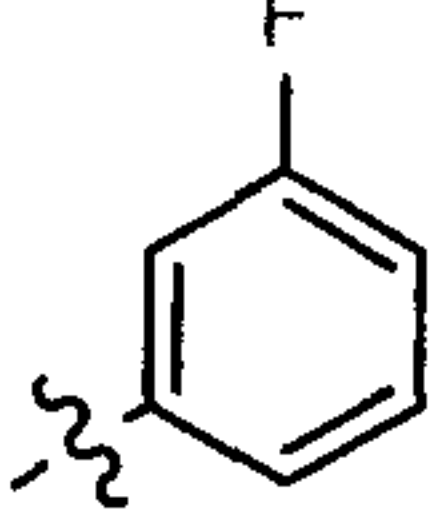
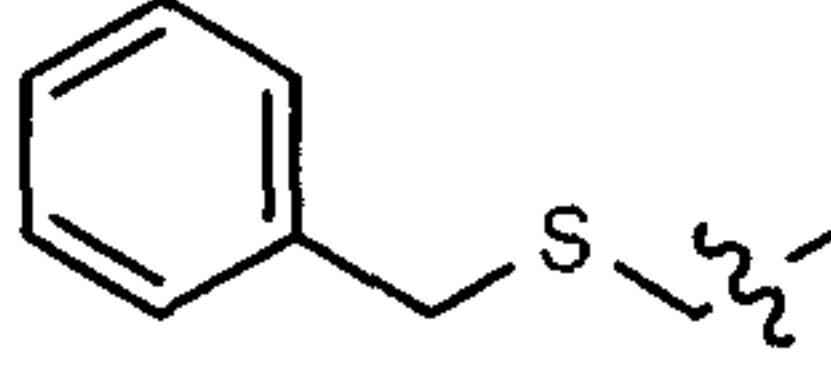
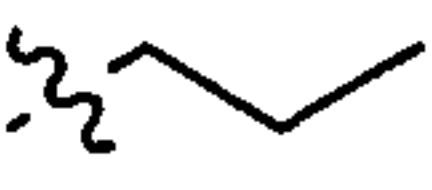
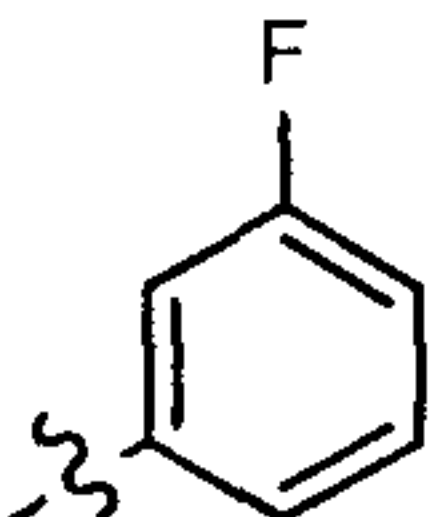
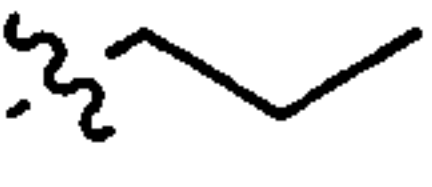
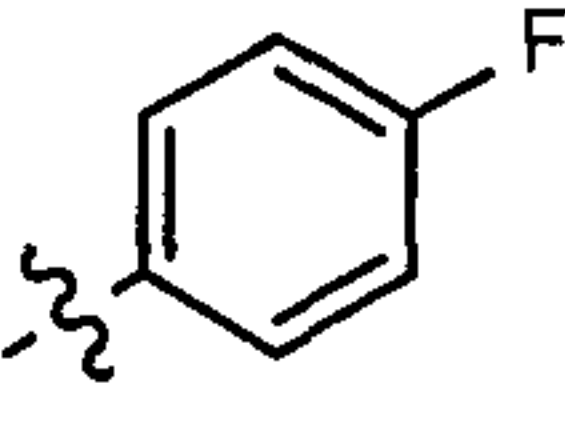
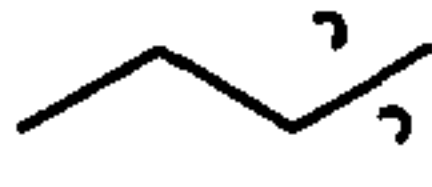
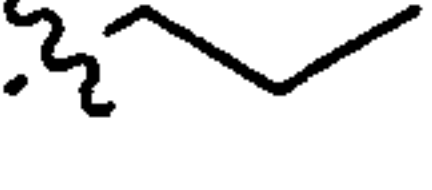
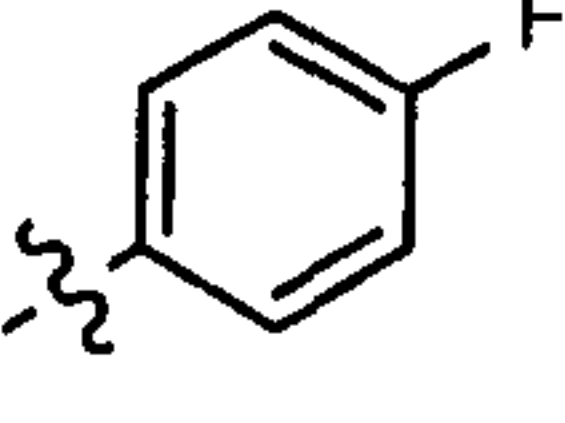
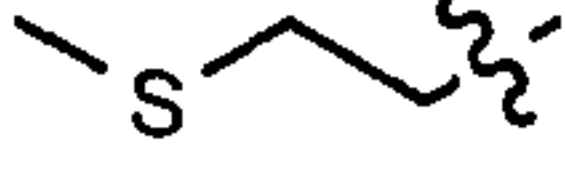
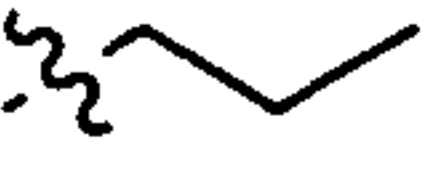
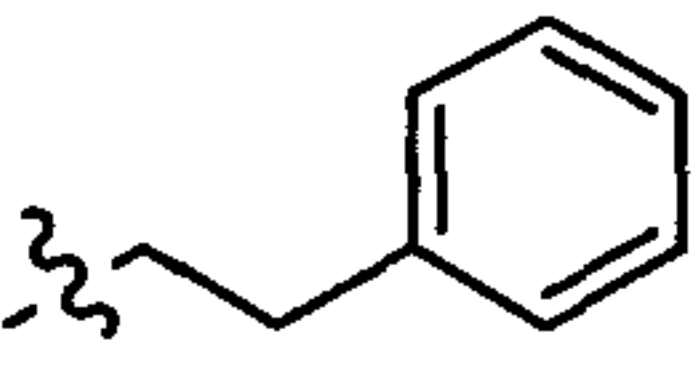
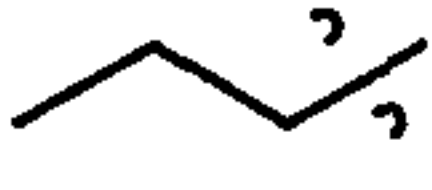
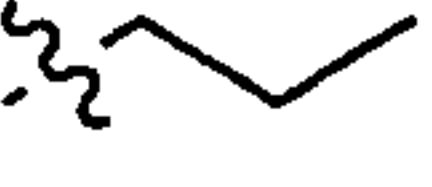
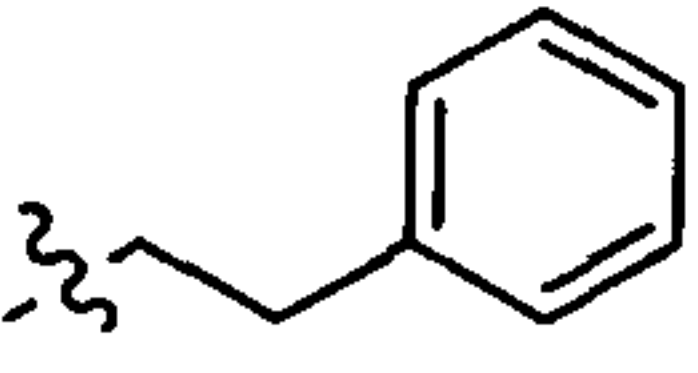
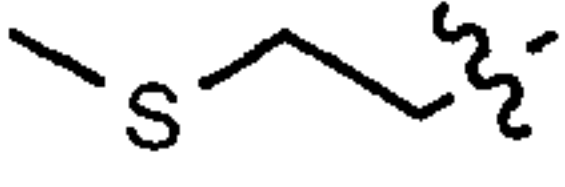
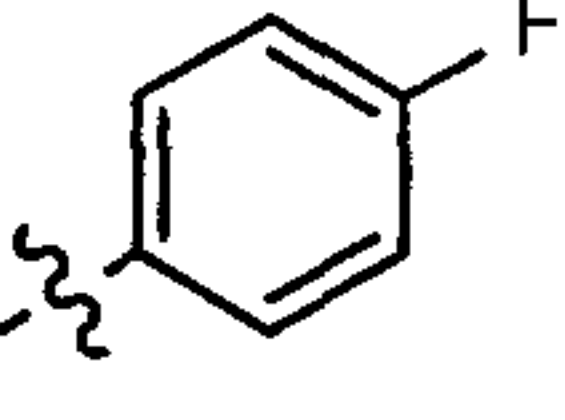
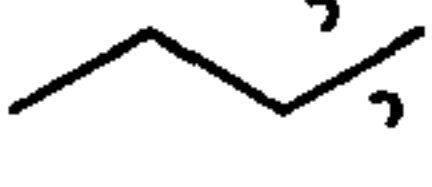
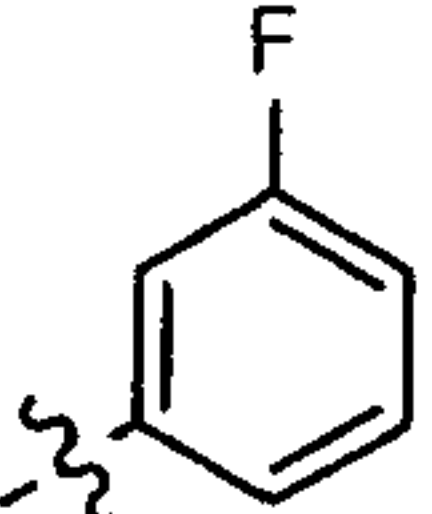
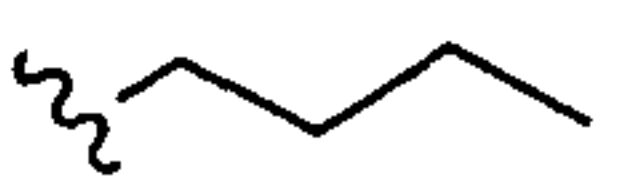
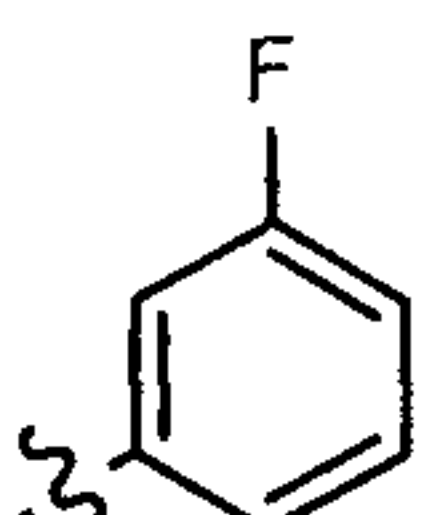
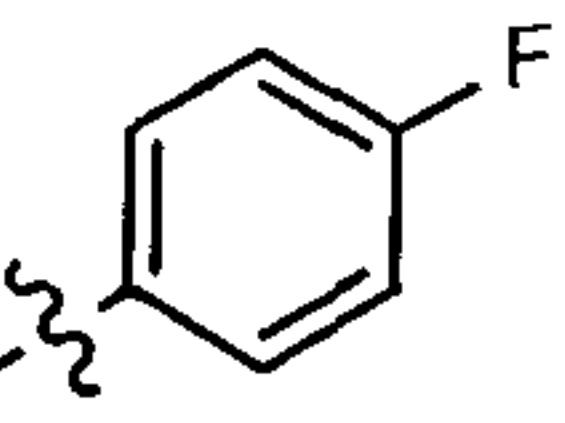
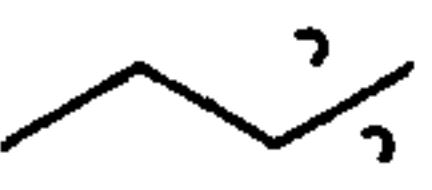
| No. | n | R <sup>1</sup>                                                                      | R <sup>2</sup>                                                                       | R <sup>3</sup>                                                                        | $\mu$ -Opioid receptor,<br>%inhibition [1 $\mu$ M] |
|-----|---|-------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------|----------------------------------------------------|
| 61  | 1 |    |    |    | 93                                                 |
| 62  | 1 |    |    |    | 98                                                 |
| 63  | 1 |    |    |    | 97                                                 |
| 64  | 1 |   |   |   | 98                                                 |
| 65  | 0 |  |  |  | 78                                                 |
| 66  | 0 |  |  |  | 89                                                 |
| 67  | 0 |  |  |  | 88                                                 |
| 68  | 0 |  |  |  | 90                                                 |
| 69  | 0 |  |  |  | 95                                                 |
| 70  | 1 |  |  |  | 96                                                 |
| 71  | 1 |  |  |  | 78                                                 |

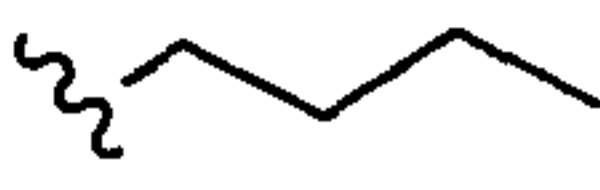
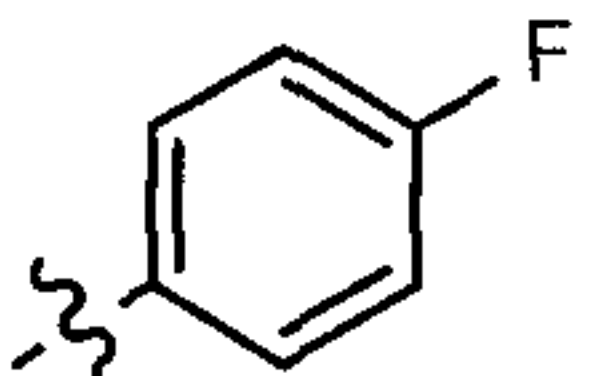
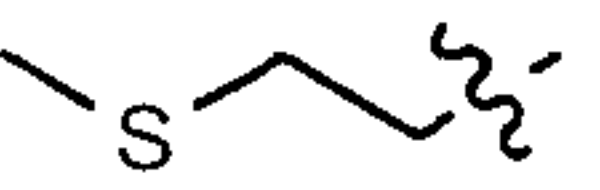
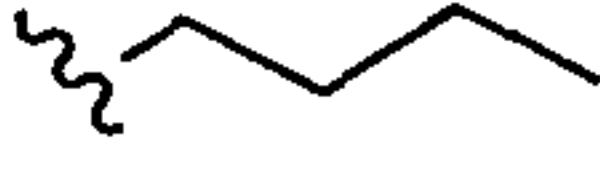
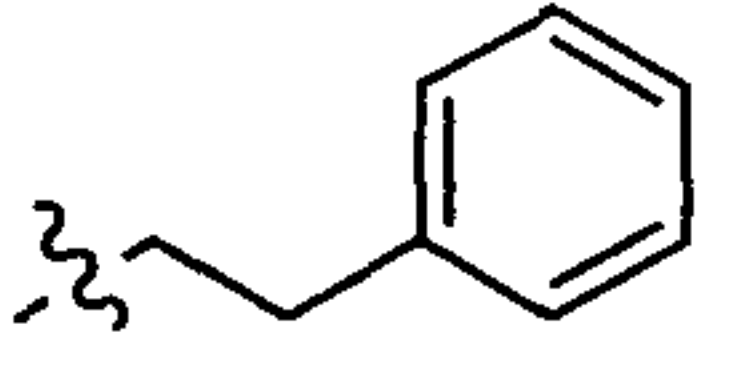
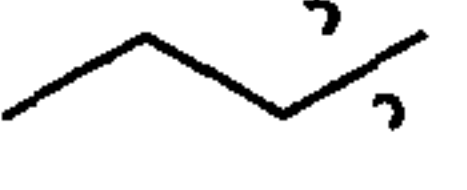
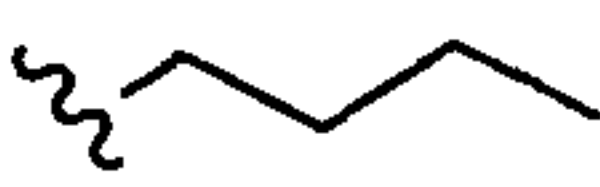
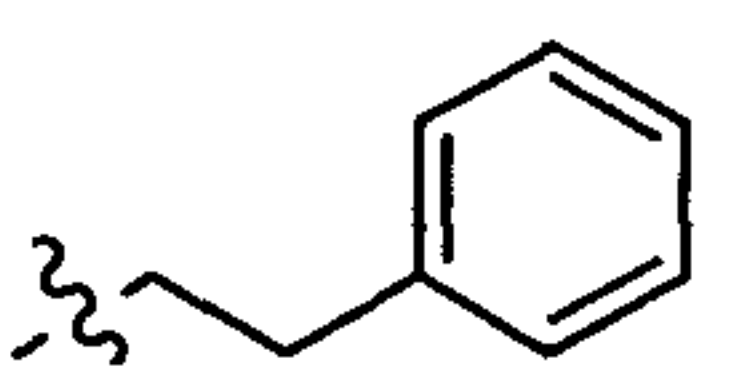
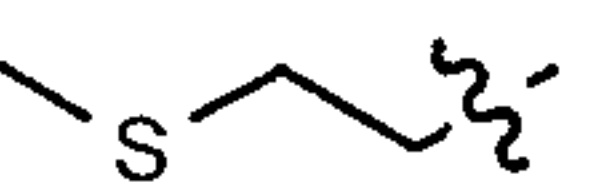
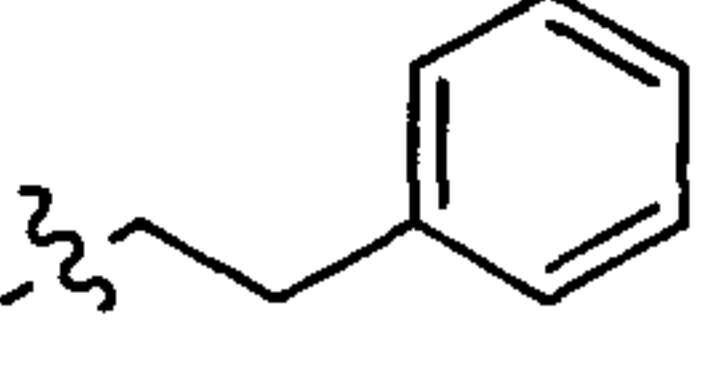
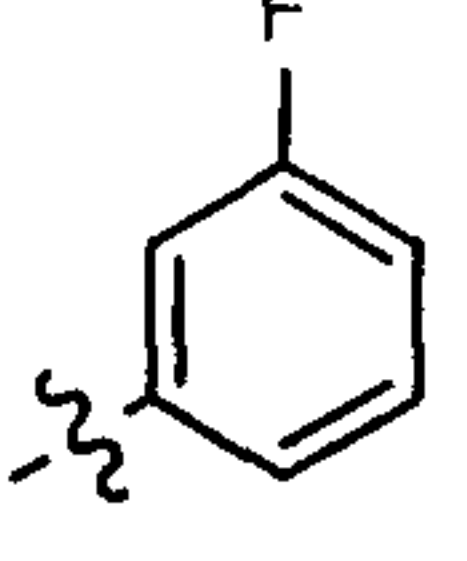
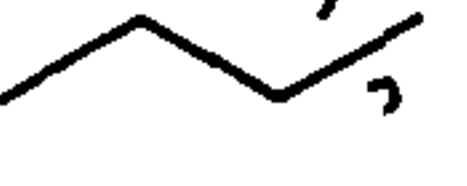
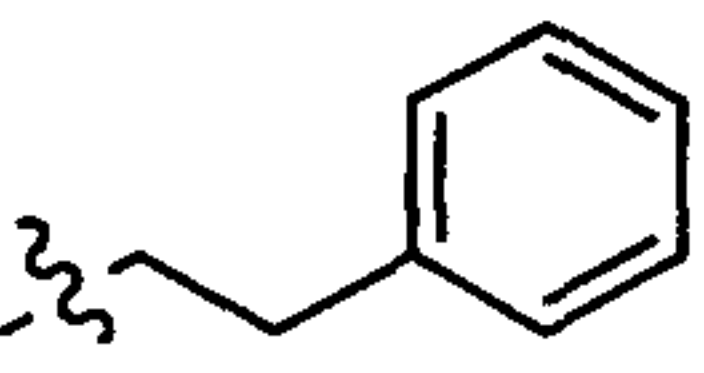
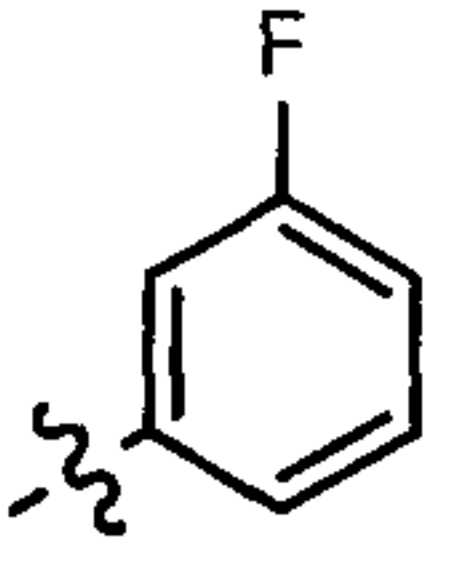
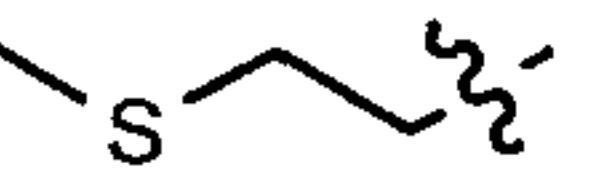
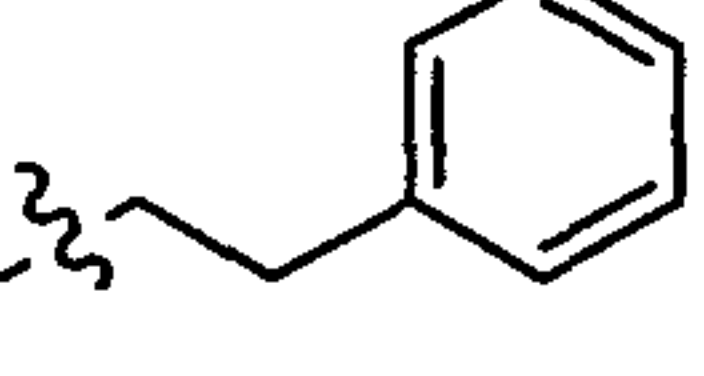
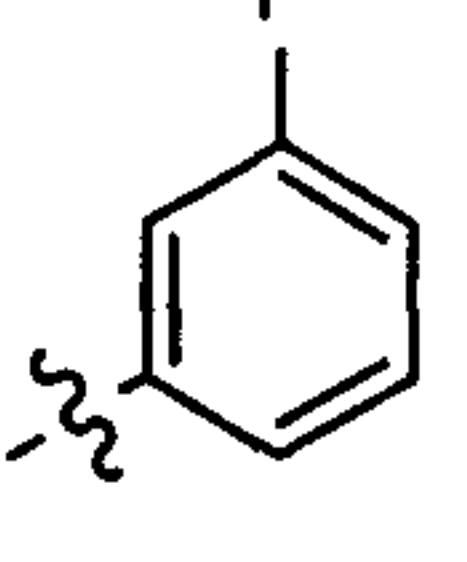
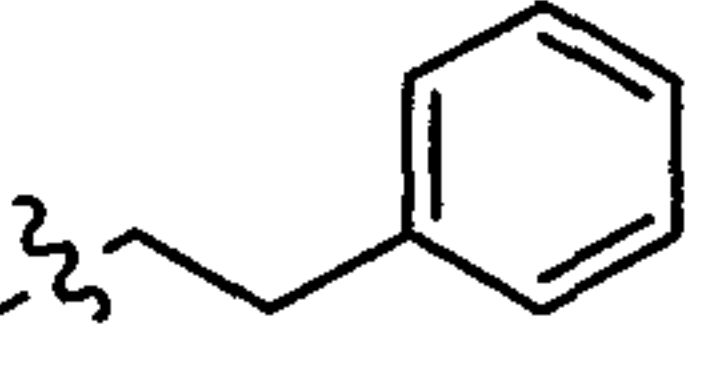
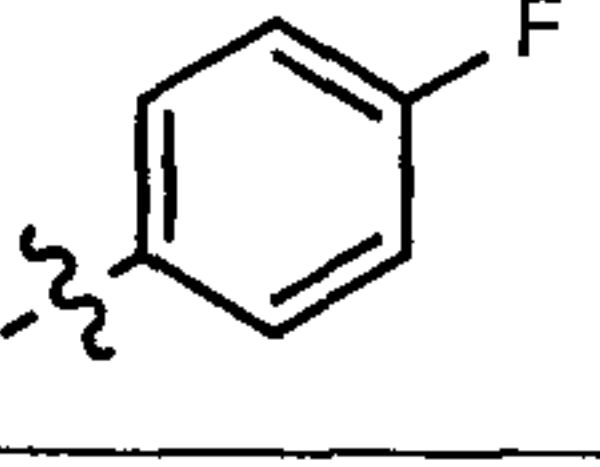
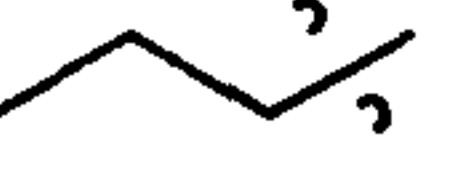
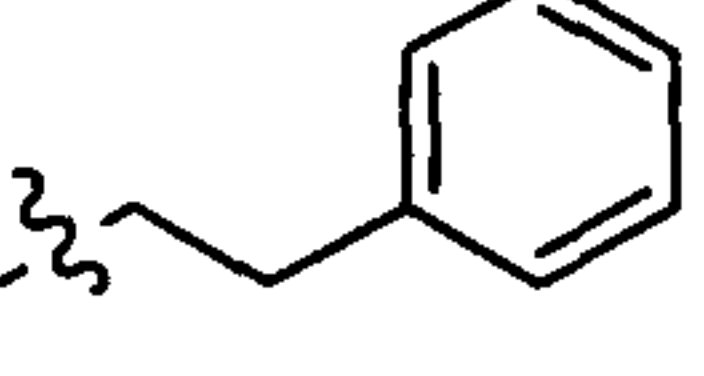
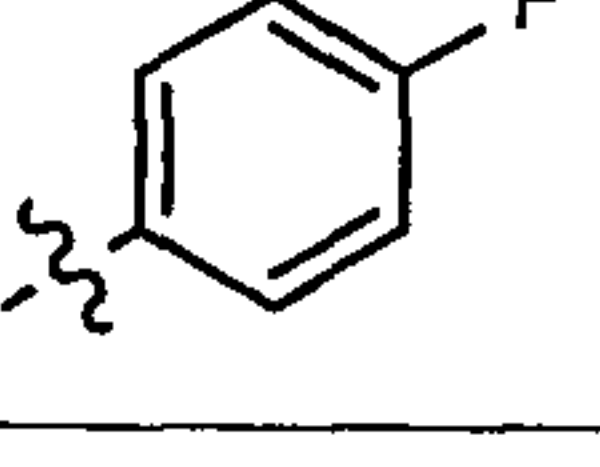
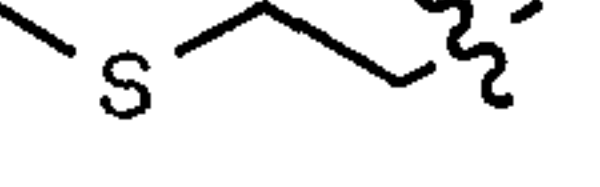
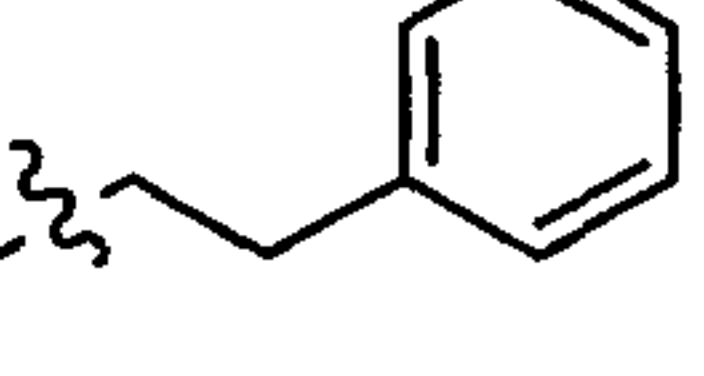
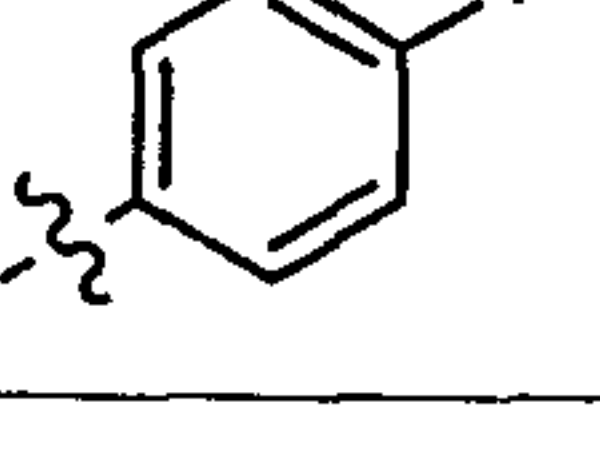
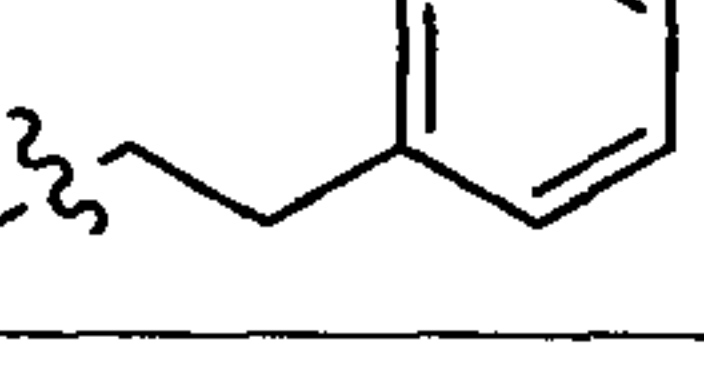
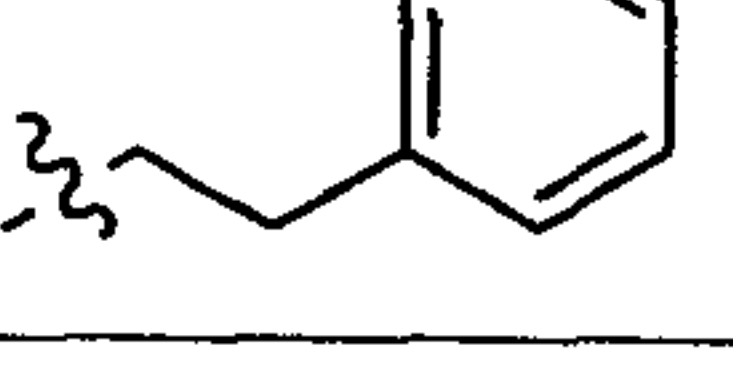
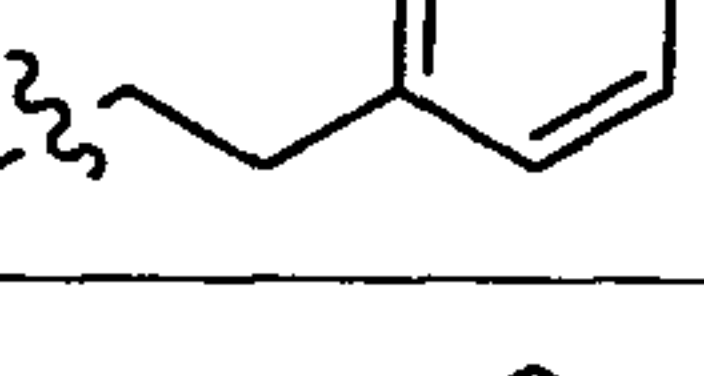
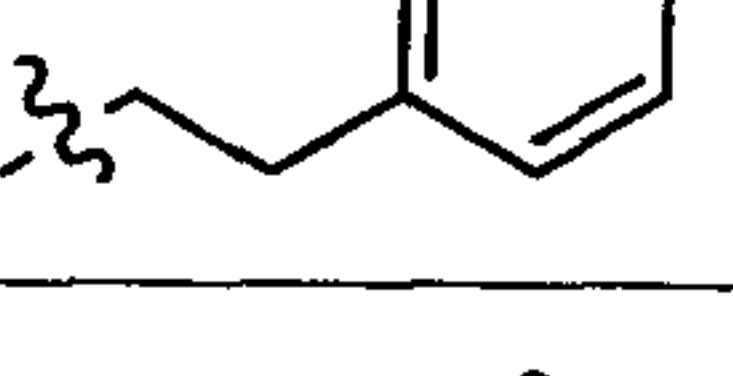
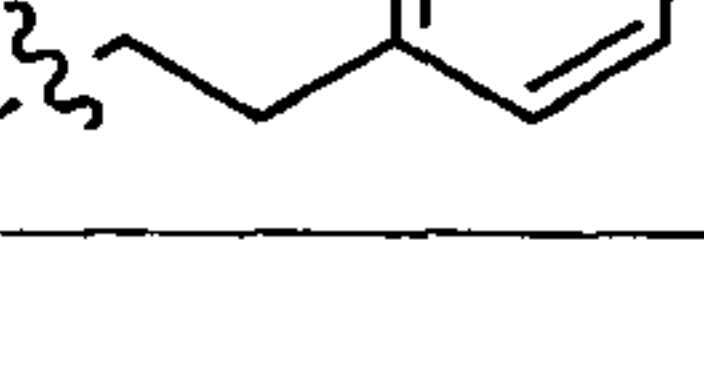
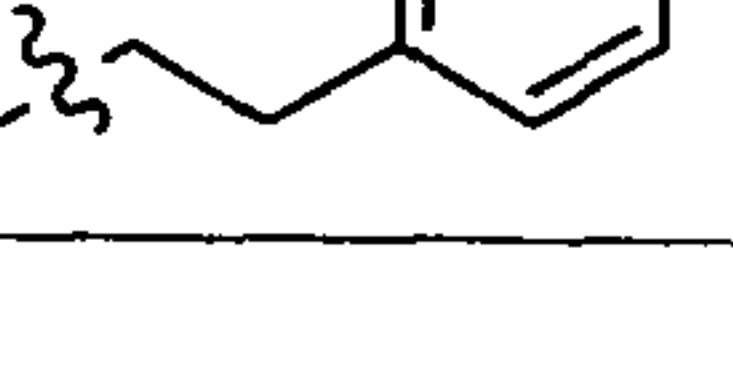
| No. | n | R <sup>1</sup>                                                                      | R <sup>2</sup>                                                                       | R <sup>3</sup>                                                                        | μ-Opioid receptor,<br>%inhibition [1 μM] |
|-----|---|-------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------|------------------------------------------|
| 72  | 1 |    |    |    | 95                                       |
| 73  | 1 |    |    |    | 92                                       |
| 74  | 1 |    |   |    | 95                                       |
| 75  | 1 |  |  |  | 98                                       |
| 76  | 1 |  |  |  | 93                                       |
| 77  | 1 |  |  |  | 88                                       |
| 78  | 1 |  |  |  | 67                                       |
| 79  | 1 |  |  |  | 79                                       |
| 80  | 1 |  |  |  | 90                                       |
| 81  | 1 |  |  |  | 76                                       |

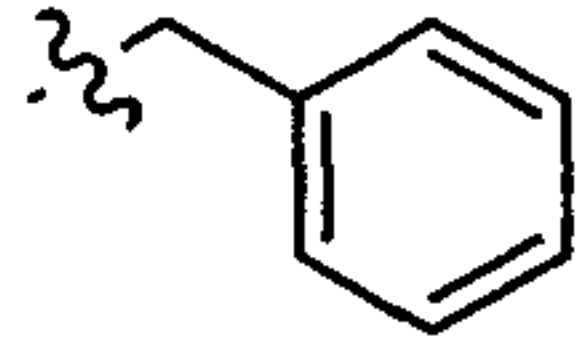
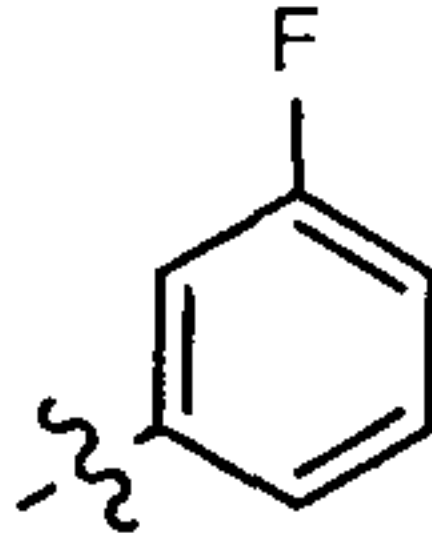
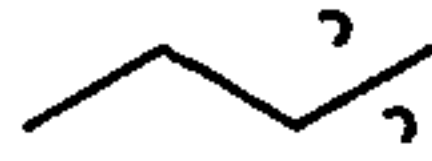
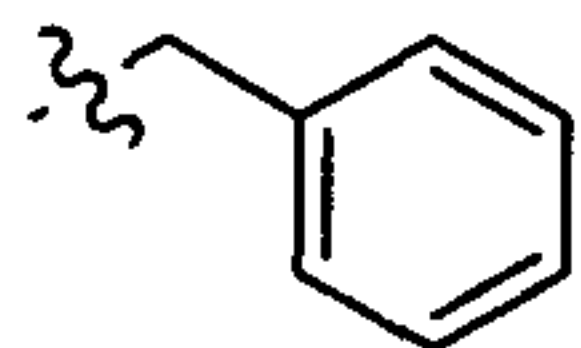
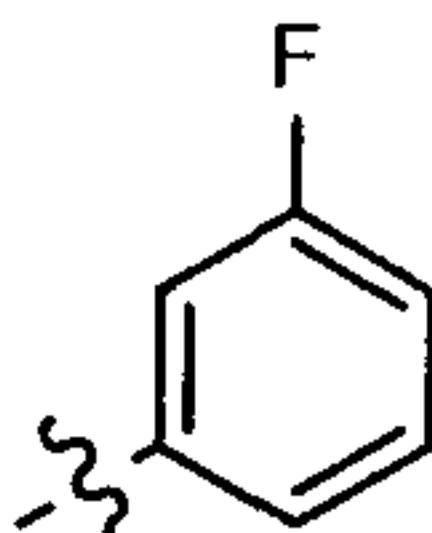
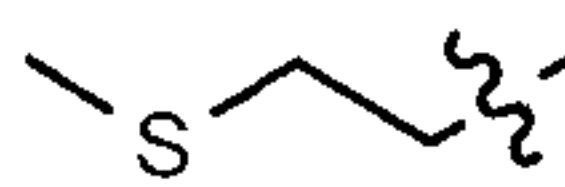
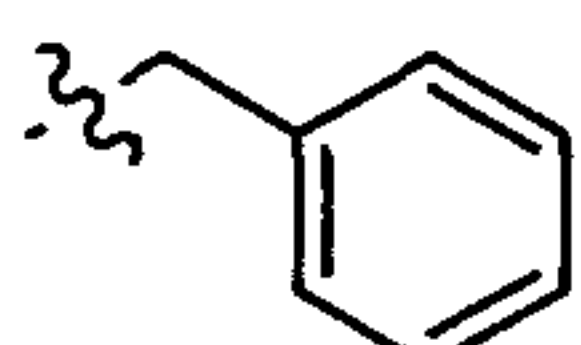
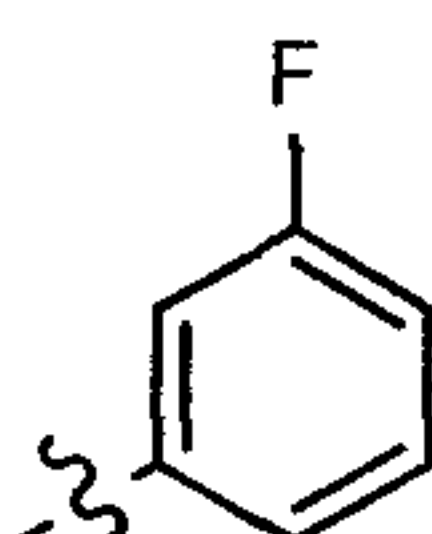
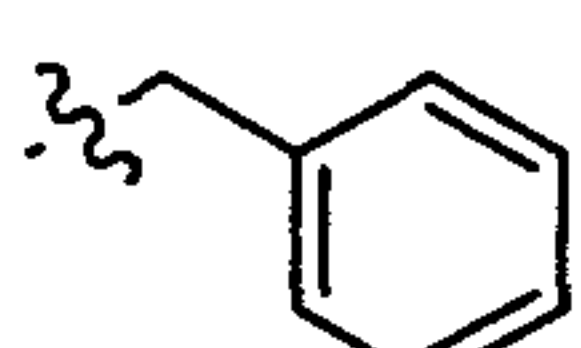
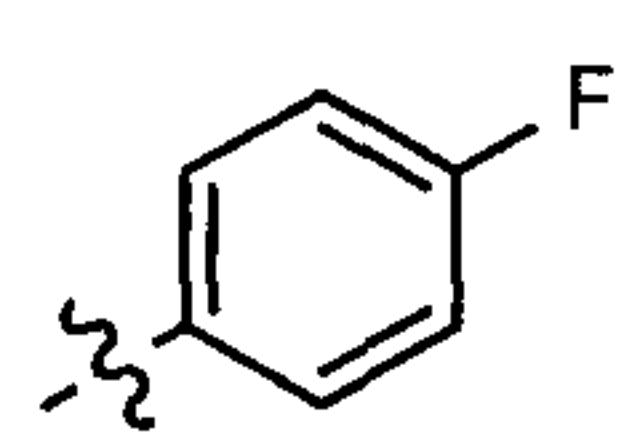
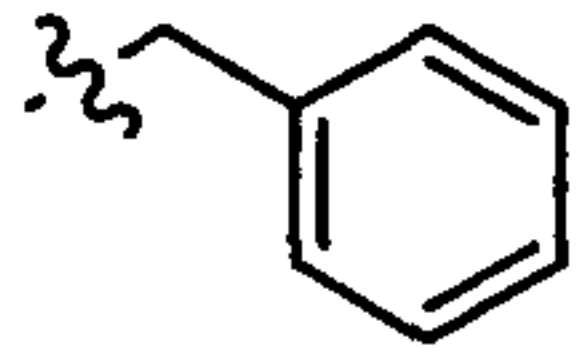
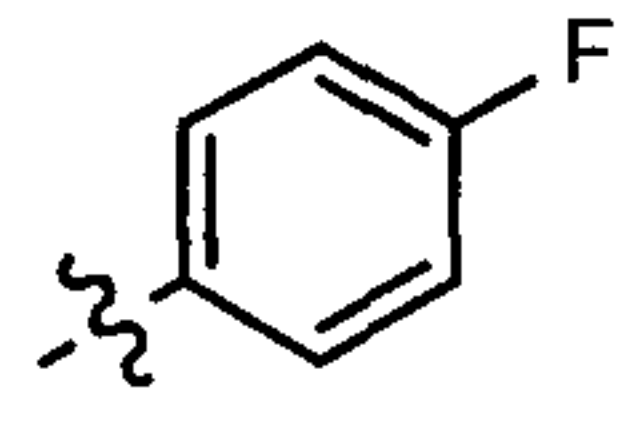
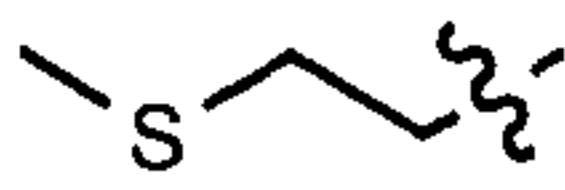
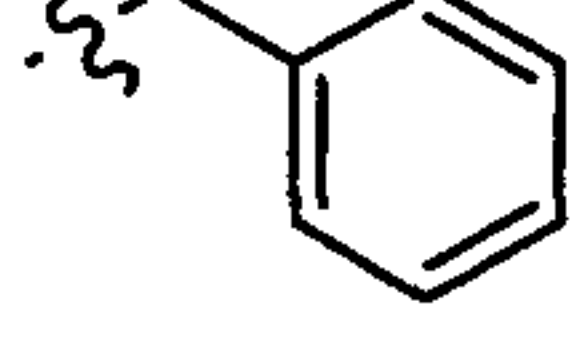
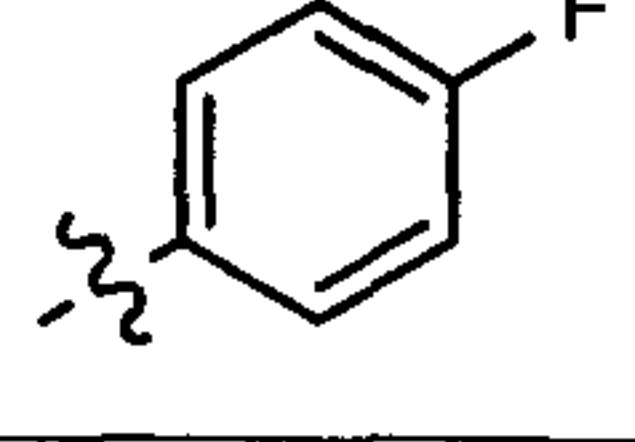
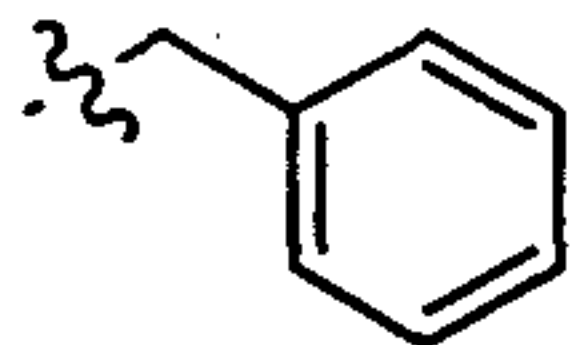
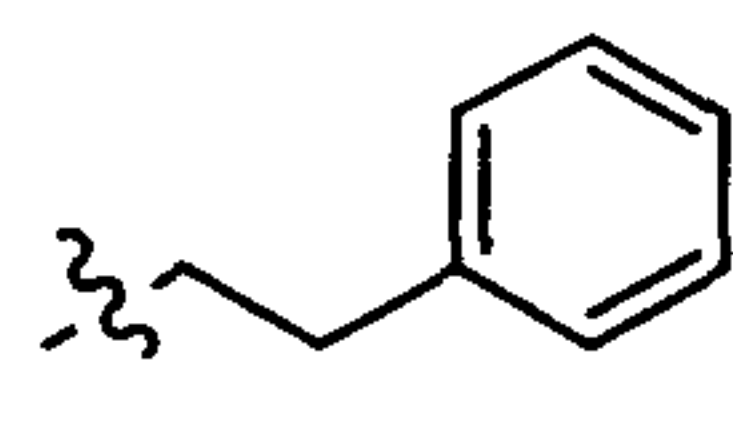
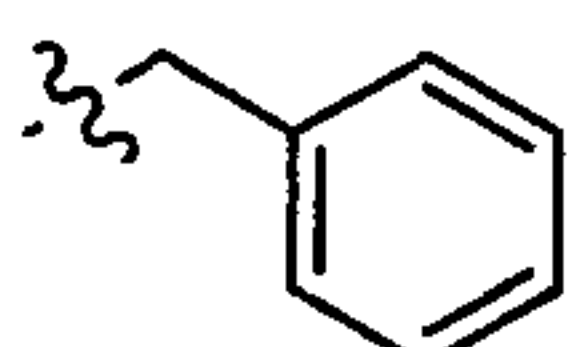
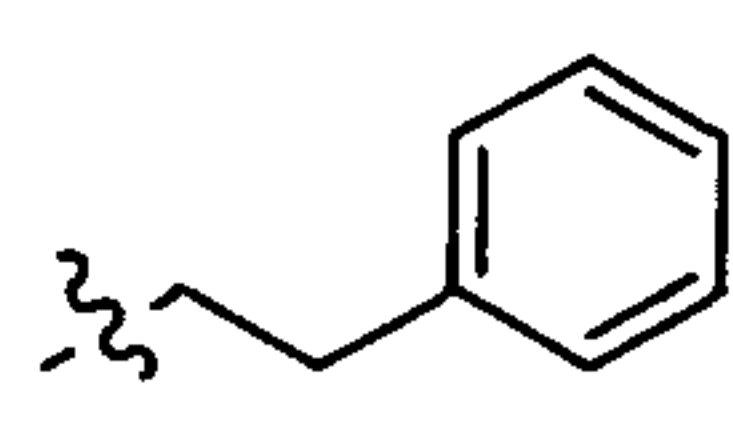
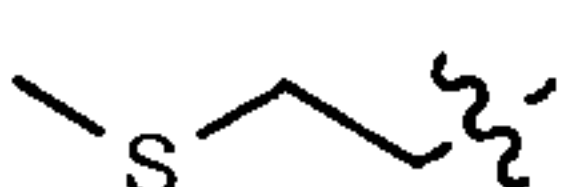
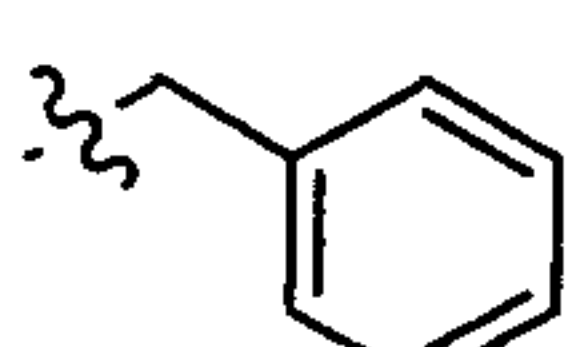
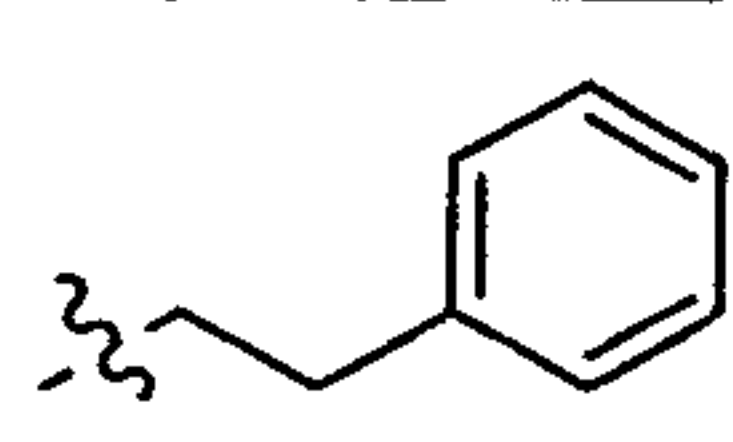
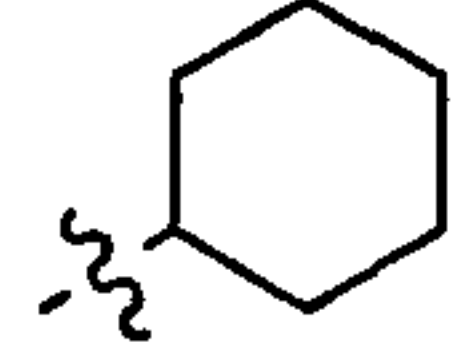
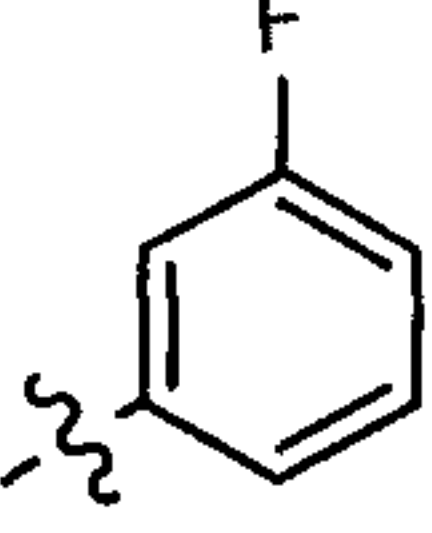
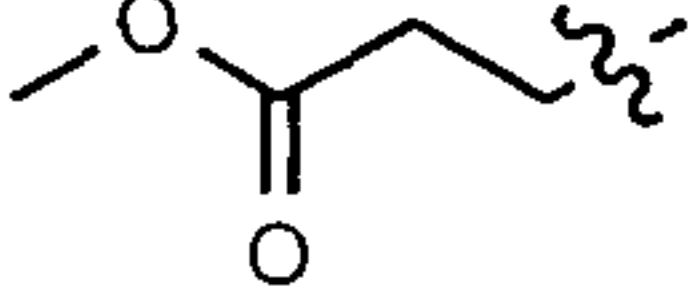
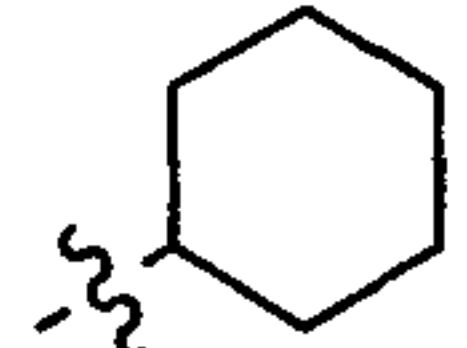
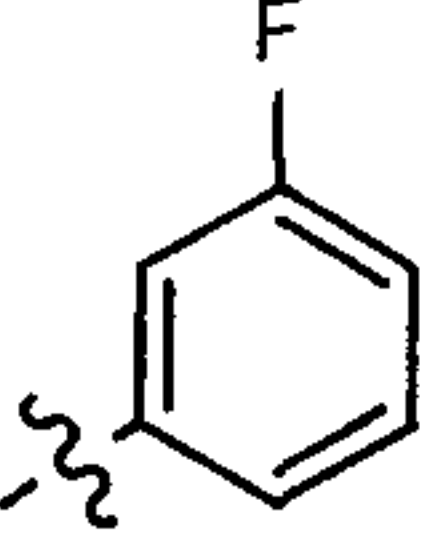
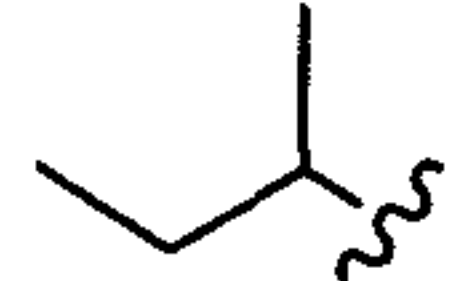
| No. | n | R <sup>1</sup>                                                                      | R <sup>2</sup>                                                                       | R <sup>3</sup>                                                                        | $\mu$ -Opioid receptor,<br>%inhibition [1 $\mu$ M] |
|-----|---|-------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------|----------------------------------------------------|
| 82  | 1 |    |    |    | 95                                                 |
| 83  | 1 |    |    |    | 77                                                 |
| 84  | 1 |    |    |    | 75                                                 |
| 85  | 1 |  |  |  | 95                                                 |
| 86  | 1 |  |  |  | 71                                                 |
| 87  | 1 |  |  |  | 95                                                 |
| 88  | 1 |  |  |  | 98                                                 |
| 89  | 1 |  |  |  | 96                                                 |
| 90  | 1 |  |  |  | 99                                                 |
| 91  | 0 |  |  |  | 85                                                 |
| 92  | 0 |  |  |  | 95                                                 |

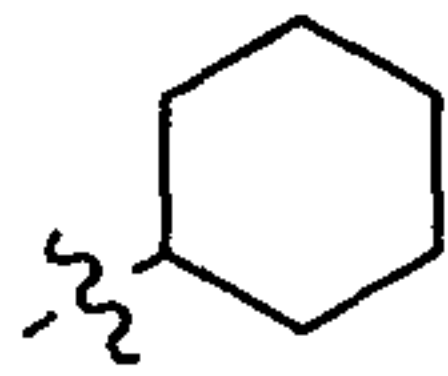
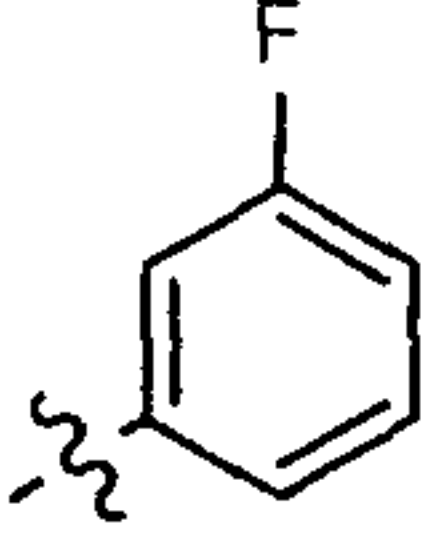
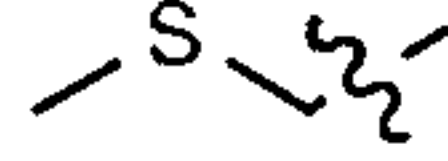
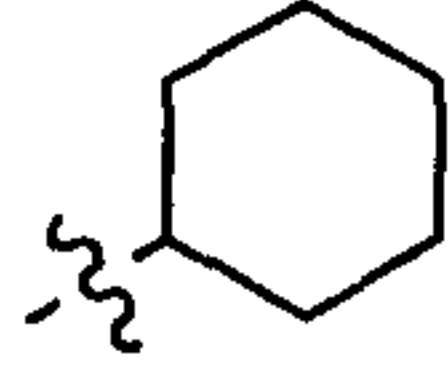
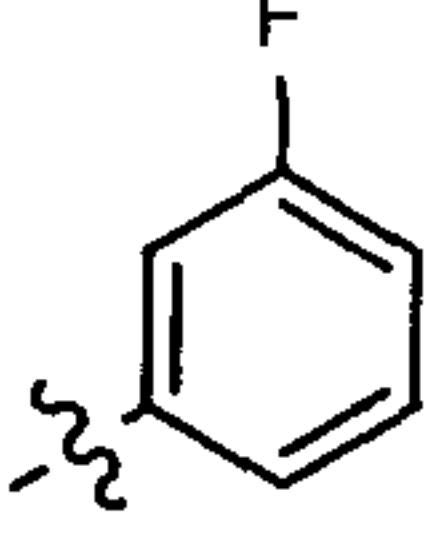
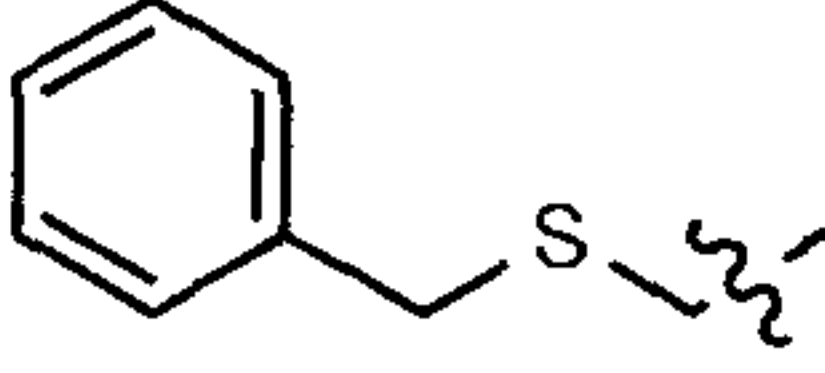
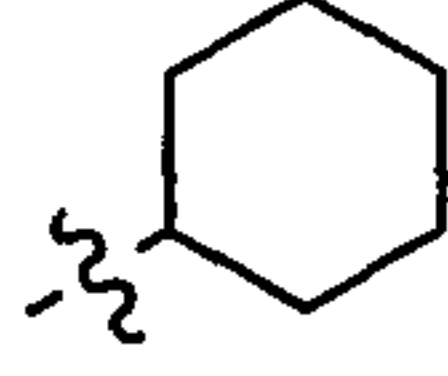
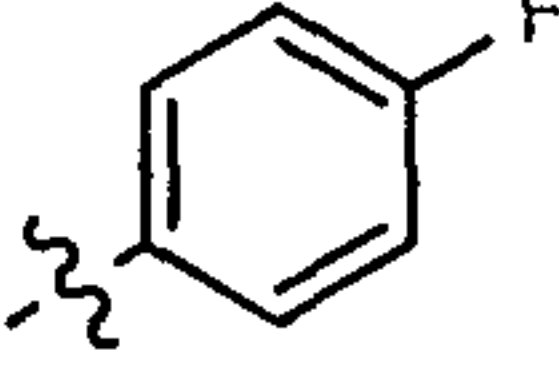
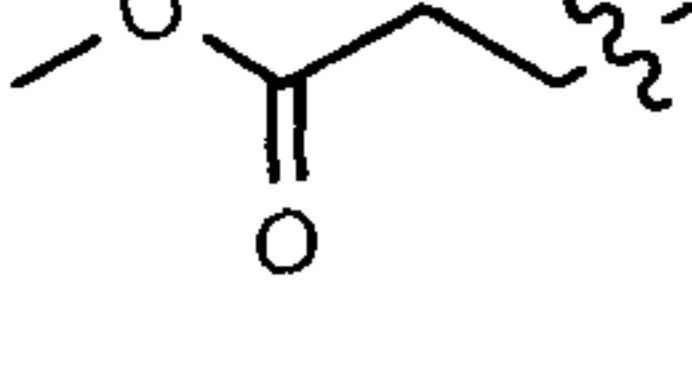
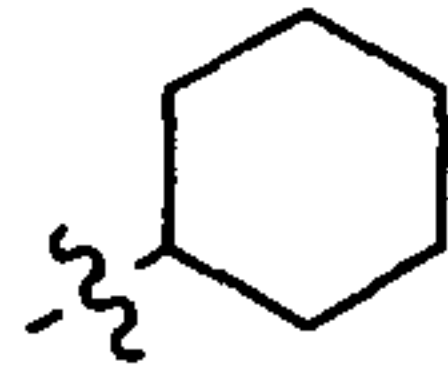
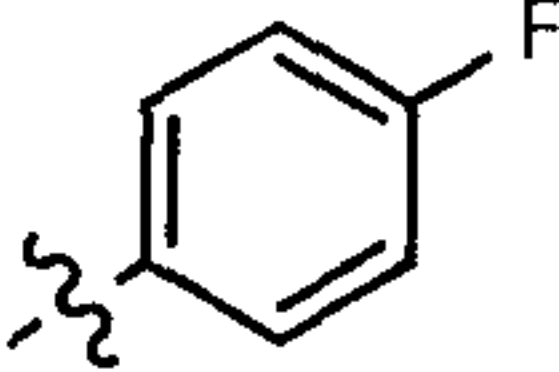
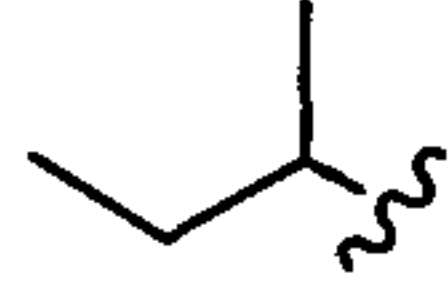
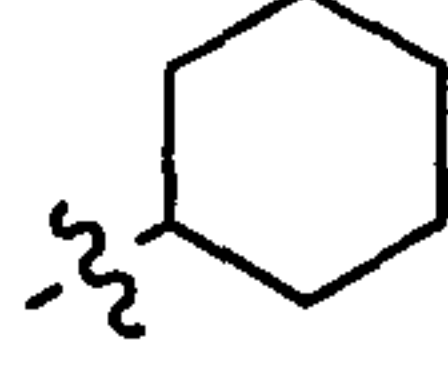
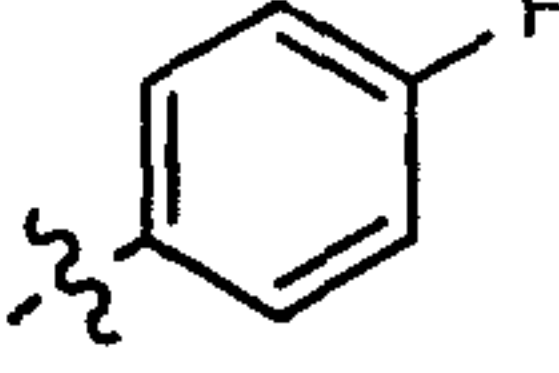
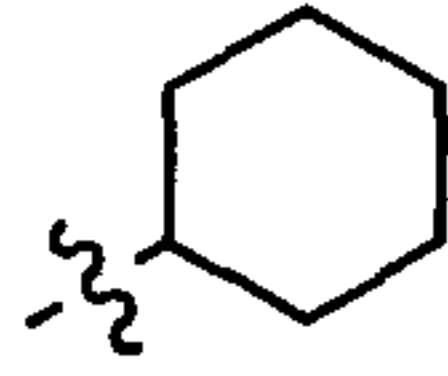
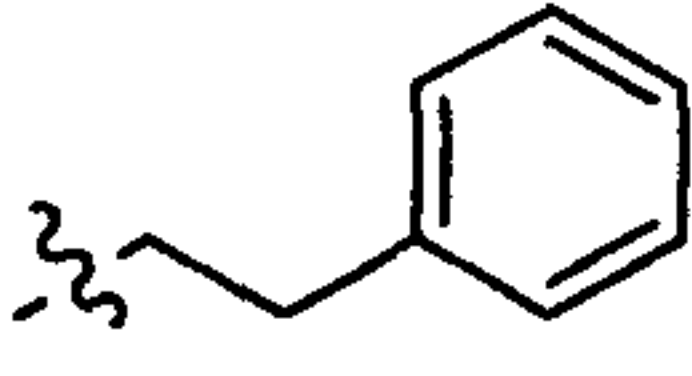
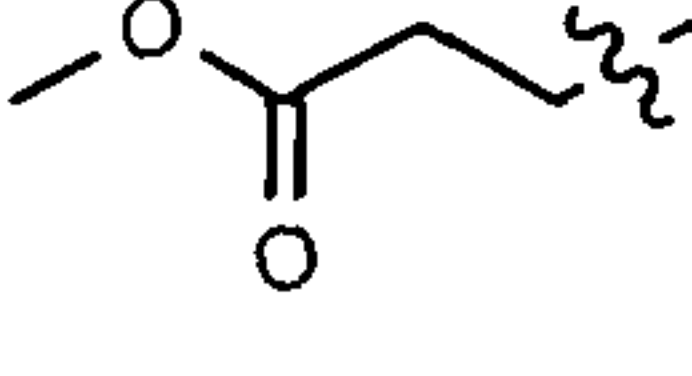
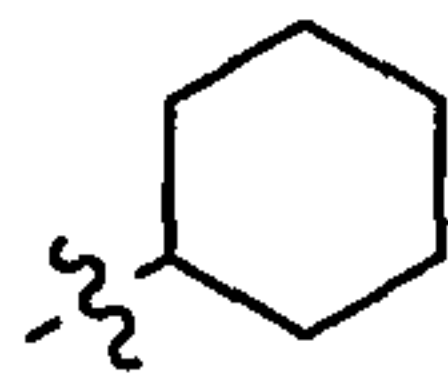
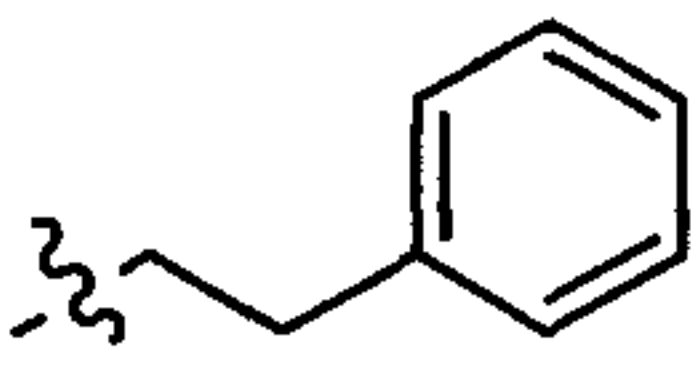
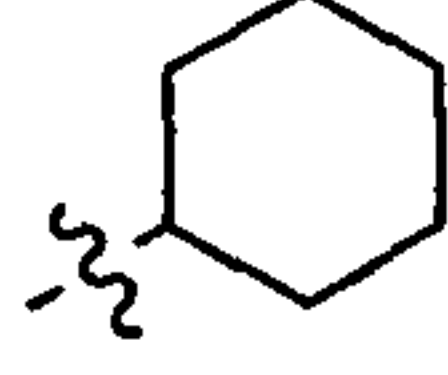
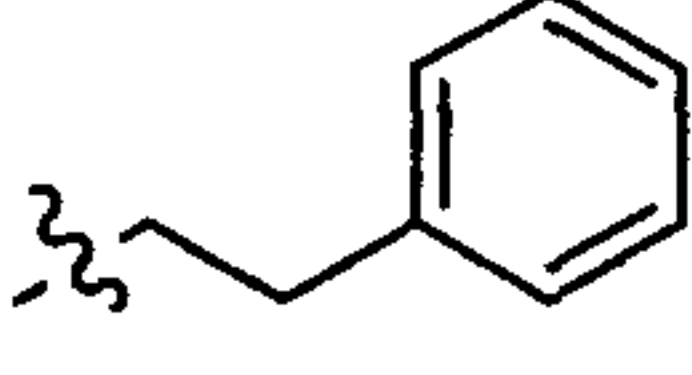
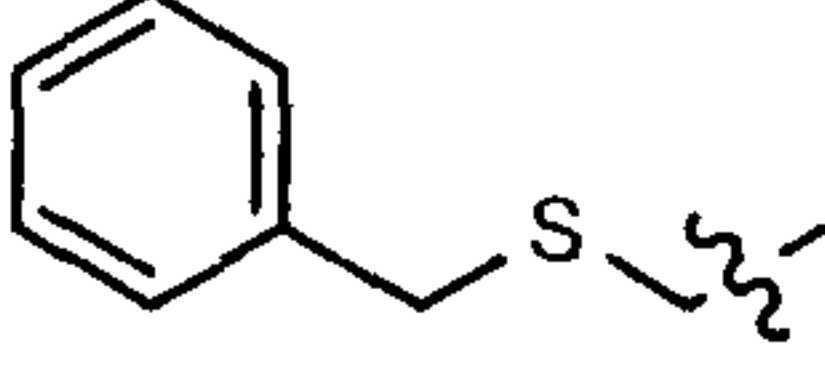
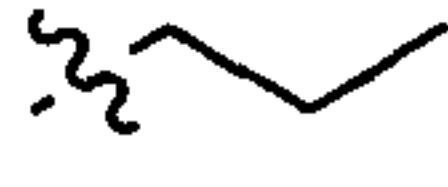
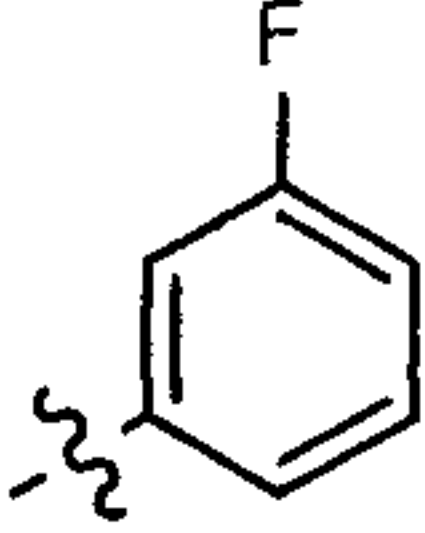
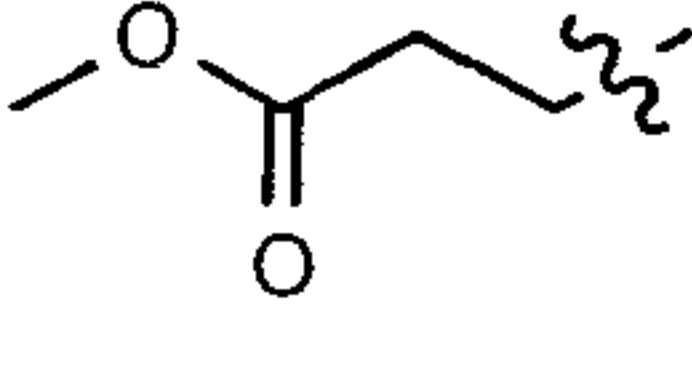
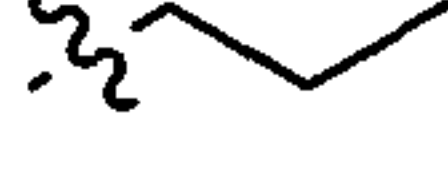
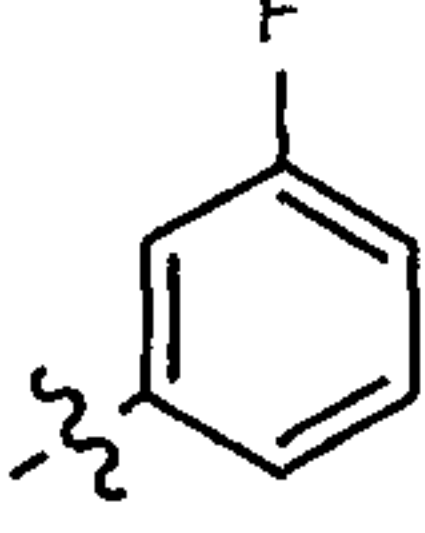
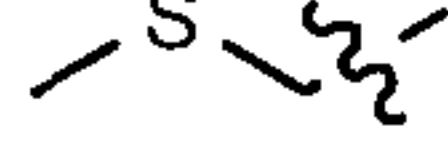
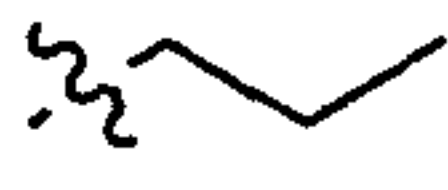
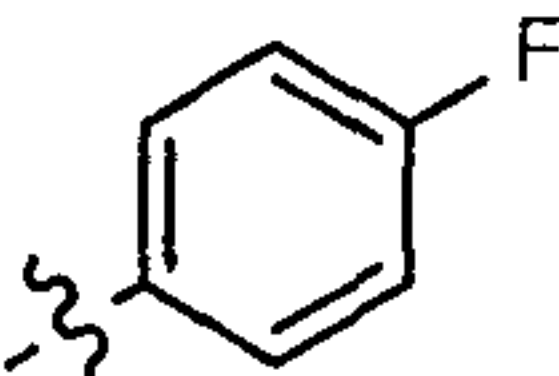
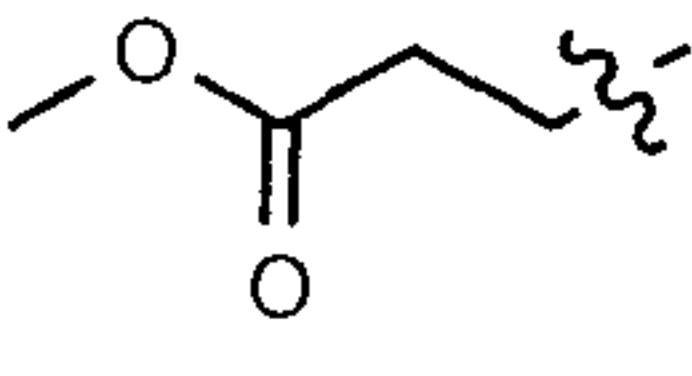
| No. | n | R <sup>1</sup>                                                                      | R <sup>2</sup>                                                                       | R <sup>3</sup>                                                                        | $\mu$ -Opioid receptor,<br>%inhibition [1 $\mu$ M] |
|-----|---|-------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------|----------------------------------------------------|
| 93  | 0 |    |    |    | 92                                                 |
| 94  | 1 |    |    |    | 97                                                 |
| 95  | 0 |    |   |    | 94                                                 |
| 96  | 0 |  |  |  | 97                                                 |
| 97  | 0 |  |  |  | 97                                                 |
| 98  | 0 |  |  |  | 95                                                 |
| 99  | 1 |  |  |  | 100                                                |
| 100 | 1 |  |  |  | 97                                                 |
| 101 | 1 |  |  |  | 96                                                 |
| 102 | 1 |  |  |  | 91                                                 |

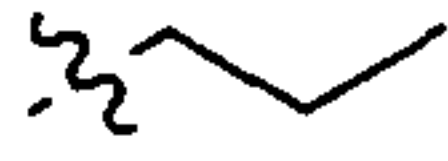
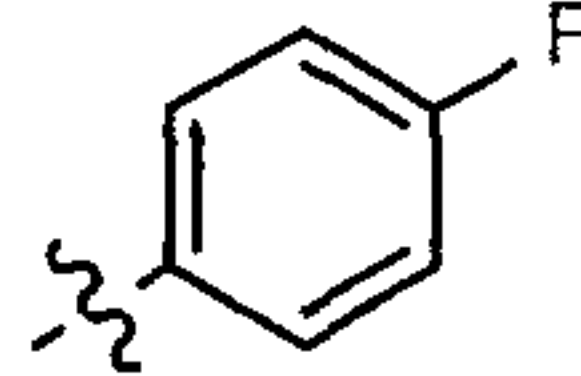
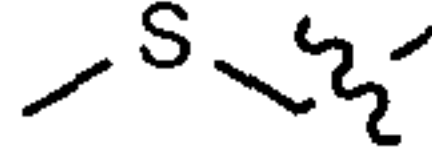
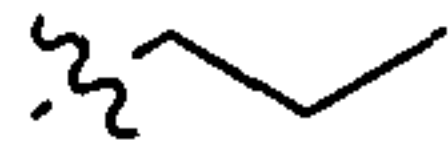
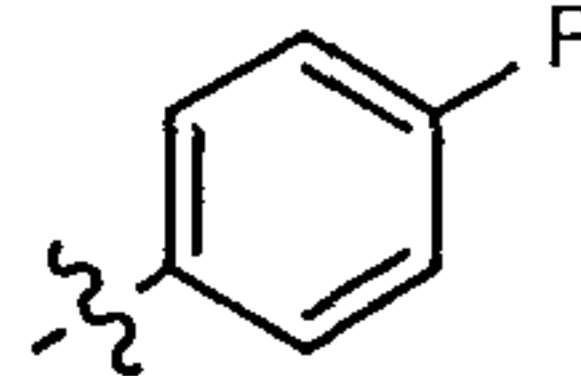
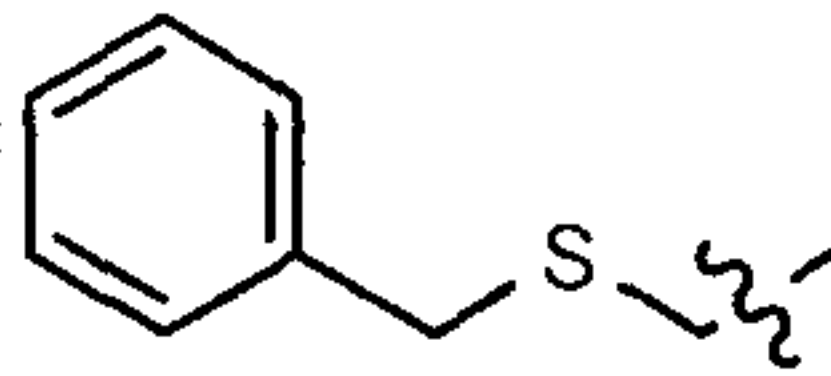
| No. | n | R <sup>1</sup>                                                                      | R <sup>2</sup>                                                                       | R <sup>3</sup>                                                                        | μ-Opioid receptor,<br>%inhibition [1 μM] |
|-----|---|-------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------|------------------------------------------|
| 103 | 1 |    |    |    | 99                                       |
| 104 | 1 |    |    | Me                                                                                    | 93                                       |
| 105 | 1 |   |   |    | 95                                       |
| 106 | 1 |  |  |  | 92                                       |
| 107 | 1 |  |  | Me                                                                                    | 87                                       |
| 108 | 1 |  |  |  | 86                                       |
| 109 | 1 |  |  |  | 87                                       |
| 110 | 1 |  |  | Me                                                                                    | 67                                       |
| 111 | 1 |  |  |  | 90                                       |
| 112 | 1 |  |  |  | 95                                       |
| 113 | 1 |  |  |  | 92                                       |
| 114 | 1 |  |  |  | 86                                       |

| No. | n | R <sup>1</sup>                                                                      | R <sup>2</sup>                                                                       | R <sup>3</sup>                                                                        | $\mu$ -Opioid receptor,<br>%inhibition [1 $\mu$ M] |
|-----|---|-------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------|----------------------------------------------------|
| 115 | 0 |    |    |    | 98                                                 |
| 116 | 0 |    |    |    | 101                                                |
| 117 | 1 |    |   | Me                                                                                    | 88                                                 |
| 118 | 1 |  |  |  | 87                                                 |
| 119 | 1 |  |  |  | 90                                                 |
| 120 | 1 |  |  |  | 62                                                 |
| 121 | 1 |  |  |  | 77                                                 |
| 122 | 1 |  |  |  | 95                                                 |
| 123 | 1 |  |  |  | 98                                                 |
| 124 | 1 |  |  | Me                                                                                    | 95                                                 |
| 125 | 1 |  |  |  | 91                                                 |

| No. | n | R <sup>1</sup>                                                                      | R <sup>2</sup>                                                                       | R <sup>3</sup>                                                                        | μ-Opioid receptor,<br>%inhibition [1 μM] |
|-----|---|-------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------|------------------------------------------|
| 126 | 1 |    |    |    | 98                                       |
| 127 | 1 |    |    |    | 74                                       |
| 128 | 1 |    |    |    | 83                                       |
| 129 | 1 |   |   |   | 93                                       |
| 130 | 1 |  |  |  | 97                                       |
| 131 | 1 |  |  | Me                                                                                    | 100                                      |
| 132 | 1 |  |  |  | 98                                       |
| 133 | 1 |  |  |  | 84                                       |
| 134 | 1 |  |  | Me                                                                                    | 92                                       |
| 135 | 1 |  |  |  | 85                                       |
| 136 | 1 |  |  |  | 76                                       |
| 137 | 1 |  |  | Me                                                                                    | 61                                       |

| No. | n | R <sup>1</sup>                                                                      | R <sup>2</sup>                                                                       | R <sup>3</sup>                                                                        | $\mu$ -Opioid receptor,<br>%inhibition [1 $\mu$ M] |
|-----|---|-------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------|----------------------------------------------------|
| 138 | 1 |    |    |    | 101                                                |
| 139 | 1 |    |    |    | 100                                                |
| 140 | 1 |   |   | Me                                                                                    | 98                                                 |
| 141 | 1 |  |  |  | 98                                                 |
| 142 | 1 |  |  |  | 97                                                 |
| 143 | 1 |  |  | Me                                                                                    | 100                                                |
| 144 | 1 |  |  |  | 90                                                 |
| 145 | 1 |  |  |  | 79                                                 |
| 146 | 1 |  |  | Me                                                                                    | 79                                                 |
| 147 | 1 |  |  |  | 98                                                 |
| 148 | 1 |  |  |  | 95                                                 |

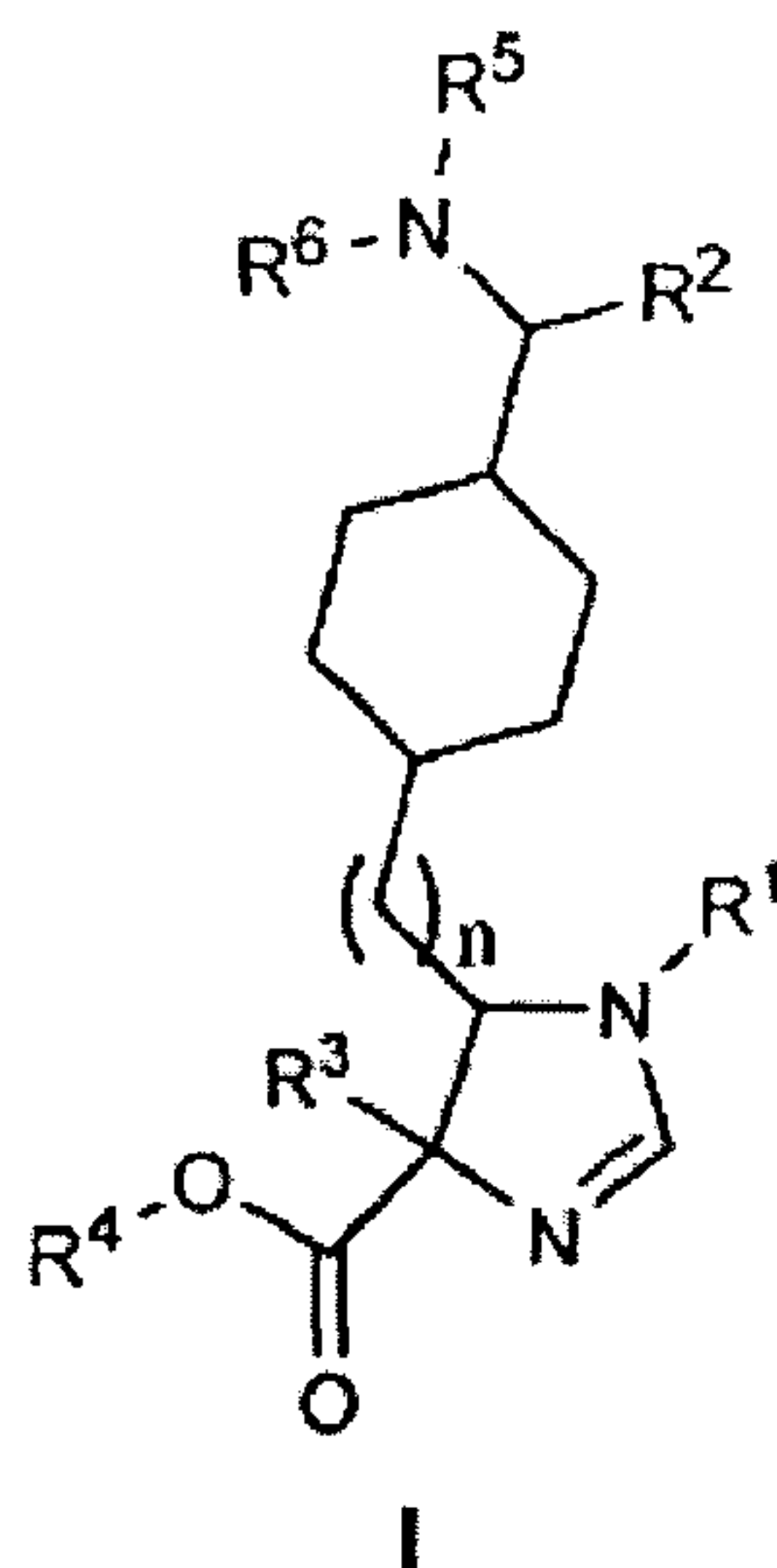
| No. | n | R <sup>1</sup>                                                                      | R <sup>2</sup>                                                                       | R <sup>3</sup>                                                                        | $\mu$ -Opioid receptor,<br>%inhibition [1 $\mu$ M] |
|-----|---|-------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------|----------------------------------------------------|
| 149 | 1 |    |    |    | 99                                                 |
| 150 | 1 |    |    |    | 98                                                 |
| 151 | 1 |   |   |   | 95                                                 |
| 152 | 1 |  |  |  | 93                                                 |
| 153 | 1 |  |  |  | 93                                                 |
| 154 | 1 |  |  |  | 82                                                 |
| 155 | 1 |  |  |  | 86                                                 |
| 156 | 1 |  |  |  | 92                                                 |
| 157 | 1 |  |  |  | 91                                                 |
| 158 | 1 |  |  |  | 95                                                 |
| 159 | 1 |  |  |  | 79                                                 |

| No. | n | R <sup>1</sup>                                                                    | R <sup>2</sup>                                                                     | R <sup>3</sup>                                                                      | $\mu$ -Opioid receptor,<br>%inhibition [1 $\mu$ M] |
|-----|---|-----------------------------------------------------------------------------------|------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------|----------------------------------------------------|
| 160 | 1 |  |  |  | 74                                                 |
| 161 | 1 |  |  |  | 91                                                 |

Claims

1. Substituted imidazoline derivatives of the general Formula I,

5



, wherein

n is 0, 1 or 2;

10

R<sup>1</sup> denotes C<sub>1-8</sub>-alkyl, saturated or unsaturated, branched or unbranched, unsubstituted or monosubstituted or polysubstituted; C<sub>3-8</sub>-cycloalkyl, saturated or unsaturated, unsubstituted or monosubstituted or polysubstituted; an aryl or heteroaryl radical bonded via a C<sub>1-3</sub>-alkyl chain, in each case unsubstituted or monosubstituted or polysubstituted;

15

20

R<sup>2</sup> denotes aryl or heteroaryl, in each case unsubstituted or monosubstituted or polysubstituted; an aryl radical bonded via a C<sub>1-3</sub>-alkyl chain, in each

case unsubstituted or monosubstituted or polysubstituted;

5  $R^3$  denotes  $C_{1-8}$ -alkyl, saturated or unsaturated, branched or unbranched, unsubstituted or monosubstituted or polysubstituted; an aryl radical bonded via a  $C_{1-3}$ -alkyl chain, in each case unsubstituted or monosubstituted or polysubstituted;

10  $R^4$  denotes H,  $C_{1-4}$ -alkyl, or an aryl radical bonded via a  $C_{1-3}$ -alkyl chain;

$R^5$  and  $R^6$  independently of one another denote H;  $C_{1-6}$ -alkyl, in each case saturated or unsaturated, branched or unbranched, wherein  $R^5$  and  $R^6$  do not simultaneously denote H,

or the two radicals  $R^5$  and  $R^6$  together denote  $CH_2CH_2OCH_2CH_2$ , or  $(CH_2)_{3-6}$ ,

20 in the form of the racemate, in the form of the enantiomers, diastereomers, mixtures of the enantiomers or diastereomers or in the form of an individual enantiomer or diastereomer; in the form of the bases and/or salts of physiological compatible acids.

2. Substituted imidazoline derivatives according to claim 1, wherein  $R^1$  denotes  $C_{1-8}$ -alkyl, branched or unbranched, unsubstituted or monosubstituted or polysubstituted with F, Cl, -CN, SH, S- $C_{1-6}$ -alkyl, S-benzyl, OH, O-benzyl, O- $C_{1-6}$ -alkyl,  $CO_2H$ ,  $CO_2$ - $C_{1-6}$ -alkyl;  $C_{3-8}$ -cycloalkyl, in each case unsubstituted or

- monosubstituted or polysubstituted with F, Cl, -CN, SH, S-C<sub>1-6</sub>-alkyl, S-benzyl, OH, O-benzyl, O-C<sub>1-6</sub>-alkyl, CO<sub>2</sub>H, CO<sub>2</sub>-C<sub>1-6</sub>-alkyl; a phenyl radical bonded via a C<sub>1-3</sub>-alkyl chain, in each case unsubstituted or monosubstituted
- 5 or polysubstituted with F, Cl, CN, NO<sub>2</sub>, SH, S-C<sub>1-6</sub>-alkyl, OH, O-C<sub>1-6</sub>-alkyl, CO<sub>2</sub>H, CO<sub>2</sub>-C<sub>1-6</sub>-alkyl, CF<sub>3</sub>, C<sub>1-6</sub>-alkyl.
3. Substituted imidazoline derivatives according to claim
- 10 1, wherein R<sup>1</sup> denotes cyclohexyl, n-propyl, n-butyl, phenethyl or benzyl.
4. Substituted imidazoline derivatives according to one
- 15 of claims 1 to 3, wherein R<sup>2</sup> denotes phenyl or thienyl, in each case unsubstituted or monosubstituted or polysubstituted with F, Cl, CN, NO<sub>2</sub>, SH, S-C<sub>1-6</sub>-alkyl, OH, O-C<sub>1-6</sub>-alkyl, CO<sub>2</sub>H, CO<sub>2</sub>-C<sub>1-6</sub>-alkyl, CF<sub>3</sub>, C<sub>1-6</sub>-alkyl; a phenyl radical bonded via a C<sub>1-3</sub>-alkyl chain, in each case unsubstituted or monosubstituted or
- 20 polysubstituted with F, Cl, CN, NO<sub>2</sub>, SH, S-C<sub>1-6</sub>-alkyl, OH, O-C<sub>1-6</sub>-alkyl, CO<sub>2</sub>H, CO<sub>2</sub>-C<sub>1-6</sub>-alkyl, CF<sub>3</sub>, C<sub>1-6</sub>-alkyl.
5. Substituted imidazoline derivatives according to one
- 25 of claims 1 to 3, wherein R<sup>2</sup> denotes phenyl, unsubstituted or monosubstituted with Cl or F, or thienyl or phenethyl.
6. Substituted imidazoline derivatives according to one
- 30 of claims 1 to 5, wherein R<sup>3</sup> denotes C<sub>1-8</sub>-alkyl, branched or unbranched, unsubstituted or monosubstituted or polysubstituted with F, Cl, -CN, SH, S-C<sub>1-6</sub>-alkyl, S-benzyl, OH, O-benzyl, O-C<sub>1-6</sub>-alkyl, CO<sub>2</sub>H, CO<sub>2</sub>-C<sub>1-6</sub>-alkyl; a phenyl radical bonded via a C<sub>1-3</sub>-

alkyl chain, in each case unsubstituted or monosubstituted or polysubstituted with F, Cl, CN, NO<sub>2</sub>, SH, S-C<sub>1-6</sub>-alkyl, OH, O-C<sub>1-6</sub>-alkyl, CO<sub>2</sub>H, CO<sub>2</sub>-C<sub>1-6</sub>-alkyl, CF<sub>3</sub>, C<sub>1-6</sub>-alkyl.

5

7. Substituted imidazoline derivatives according to one of claims 1 to 5, wherein R<sup>3</sup> denotes sec-butyl, iso-butyl, n-butyl, n-propyl, CH<sub>3</sub>, CH<sub>2</sub>CH<sub>2</sub>COOCH<sub>3</sub>, CH<sub>2</sub>-S-benzyl, CH<sub>2</sub>CH<sub>2</sub>-S-CH<sub>3</sub>, CH<sub>2</sub>-S-CH<sub>3</sub> or 4-Cl-benzyl.

10

8. Substituted imidazoline derivatives according to one of claims 1 to 7, wherein R<sup>4</sup> denotes CH<sub>3</sub>.

9. Substituted imidazoline derivatives according to one of claims 1 to 8, wherein R<sup>5</sup> and R<sup>6</sup> denotes CH<sub>3</sub>.

15

10. Substituted imidazoline derivatives according to one of claims 1 to 9, from the group:

20 1-cyclohexyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexyl}-4-isobutyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester

4-(4-chlorobenzyl)-1-cyclohexyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexyl}-4,5-dihydro-1H-imidazole-  
25 4-carboxylic acid methyl ester

4-butyl-1-cyclohexyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexyl}-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester

5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexyl}-1-cyclohexyl-4-isobutyl-4,5-dihydro-1H-imidazole-4-carboxylic  
30 acid methyl ester

- 4-(4-chlorobenzyl)-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexyl}-1-cyclohexyl-4,5-dihydro-1H-imidazole-carboxylic acid methyl ester
- 4-butyl-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexyl}-1-cyclohexyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexylmethyl}-1-cyclohexyl-4-isobutyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 10 4-(4-chlorobenzyl)-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexylmethyl}-1-cyclohexyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 4-butyl-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexylmethyl}-1-cyclohexyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 15 4-(4-chlorobenzyl)-1-cyclohexyl-5-[4-(dimethylamino-thiophen-2-yl-methyl)-cyclohexylmethyl]-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexyl}-4-isobutyl-1-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 20 4-(4-chlorobenzyl)-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexyl}-1-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 25 4-butyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexyl}-1-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester

- 5- {4- [(4-chlorophenyl)-dimethylaminomethyl]-cyclohexyl}-4-isobutyl-1-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 4-(4-chlorobenzyl)-5- {4- [(4-chlorophenyl)-dimethylamino-methyl]-cyclohexyl}-1-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 5-(4- [(4-chlorophenyl)-dimethylaminomethyl]-cyclohexylmethyl)-4-isobutyl-1-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 10 4-(4-chlorobenzyl)-5- {4- [(4-chlorophenyl)-dimethylaminomethyl]-cyclohexylmethyl}-1-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 4-butyl-5- {4- [(4-chlorophenyl)-dimethylaminomethyl]-cyclohexylmethyl}-1-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 15 1-butyl-5- {4- [dimethylamino-(3-fluorophenyl)-methyl]-cyclohexyl}-4-isobutyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 1-butyl-4-(4-chlorobenzyl)-5- {4- [dimethylamino-(3-fluorophenyl)-methyl]-cyclohexyl}-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 20 1-butyl-5- {4- [(chlorophenyl)-dimethylaminomethyl]-cyclohexyl}-4-isobutyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 25 1-butyl-4-(4-chlorobenzyl)-5- {4- [(4-chlorophenyl)-dimethylaminomethyl]-cyclohexyl}-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester

1,4-dibutyl-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexyl}-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester

1-butyl-5-{4-[(chlorophenyl)-dimethylaminomethyl]-cyclohexylmethyl}-4-isobutyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester

1-butyl-4-(4-chlorobenzyl)-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexylmethyl}-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester

10 1,4-dibutyl-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexylmethyl}-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester

5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexyl}-4-isobutyl-1-phenethyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester

4-(4-chlorobenzyl)-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexyl}-1-phenethyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester

4-butyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexyl}-1-phenethyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester

5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexyl}-4-isobutyl-1-phenethyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester

25 4-(4-chlorobenzyl)-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexyl}-1-phenethyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester

- 4-butyl-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexyl}-1-phenethyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 5- {4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexylmethyl}-4-isobutyl-1-phenethyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 4-(4-chlorobenzyl)-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexylmethyl}-1-phenethyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 10 4-butyl-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexylmethyl}-1-phenethyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 1-benzyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexyl}-4-isobutyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 15 1-benzyl-4-(4-chlorobenzyl)-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexyl}-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 1-benzyl-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexyl}-4-isobutyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 20 1-benzyl-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexyl}-4-isobutyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 1-benzyl-4-(4-chlorobenzyl)-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexyl}-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 25 1-benzyl-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexylmethyl}-4-isobutyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester

- 5- {4- [(4-chlorophenyl)-dimethylaminomethyl]-cyclohexyl}-1-cyclohexyl-4-(2-methoxycarbonylethyl)-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 4-benzylsulfanylmethyl-5- {4- [(4-chlorophenyl)-dimethylaminomethyl]-cyclohexyl}-1-cyclohexyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 5- {4- [(4-chlorophenyl)-dimethylaminomethyl]-cyclohexylmethyl}-1-cyclohexyl-4-(2-methoxycarbonylethyl)-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 10 1-benzyl-5- {4- [dimethylamino-(3-fluorophenyl)-methyl]-cyclohexylmethyl}-4-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 5- {4- [(4-chlorophenyl)-dimethylaminomethyl]-cyclohexylmethyl}-1-cyclohexyl-4-methylsulfanylmethyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 15 4-benzylsulfanylmethyl-5- {4- [(4-chlorophenyl)-dimethylaminomethyl]-cyclohexylmethyl}-1-cyclohexyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 5- {4- [dimethylamino-(3-fluorophenyl)-methyl]-cyclohexyl}-4-methylsulfanylmethyl-1-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 20 4-benzylsulfanylmethyl-5- {4- [dimethylamino-(3-fluorophenyl)-methyl]-cyclohexyl}-1-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 25 5- {4- [(4-chlorophenyl)-dimethylaminomethyl]-cyclohexyl}-4-(2-methoxycarbonylethyl)-1-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester

- 4-benzylsulfanylmethyl-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexyl}-1-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 5-4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexylmethyl}-4-(2-methoxycarbonylethyl)-1-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 4-sec-butyl-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexylmethyl}-1-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 10 5-4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexylmethyl}-4-methylsulfanylmethyl-1-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 4-benzylsulfanylmethyl-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexylmethyl}-1-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 15 1-butyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexyl}-4-(2-methoxycarbonylethyl)-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 1-butyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexyl}-4-methylsulfanylmethyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 20 4-benzylsulfanylmethyl-1-butyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexyl}-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 25 1-butyl-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexyl}-4-(2-methoxycarbonylethyl)-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester

- 4-benzylsulfanylmethyl-1-butyl-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexyl}-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 1-butyl-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexylmethyl}-4-(2-methoxycarbonylethyl)-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 5 1-butyl-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexylmethyl}-4-(2-methoxycarbonylethyl)-1-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 10 1-butyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexylmethyl}-4-(2-methoxycarbonylethyl)-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 1-butyl-4-sec-butyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexylmethyl}-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 15 1-butyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexylmethyl}-4-methylsulfanylmethyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 4-benzylsulfanylmethyl-1-butyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexylmethyl}-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 20 1-butyl-5-{4-[dimethylamino-(4-fluorophenyl)-methyl]-cyclohexylmethyl}-4-(2-methoxycarbonylethyl)-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 1-butyl-5-{4-[dimethylamino-(4-fluorophenyl)-methyl]-cyclohexylmethyl}-4-methylsulfanylmethyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 25 1-butyl-5-{4-[dimethylamino-(4-fluorophenyl)-methyl]-cyclohexylmethyl}-4-methylsulfanylmethyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester

1-butyl-5-[4-(1-dimethylamino-3-phenylpropyl)-cyclohexylmethyl]-4-(2-methoxycarbonylethyl)-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester

4-benzylsulfanylmethyl-1-butyl-5-[4-(1-dimethylamino-3-phenylpropyl)-cyclohexylmethyl]-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester

5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexylmethyl}-4-(2-methoxycarbonylethyl)-1-phenethyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester

10 4-sec-butyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexylmethyl}-1-phenethyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester

4-benzylsulfanylmethyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexylmethyl}-1-phenethyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester

5-{4-[dimethylamino-(4-fluorophenyl)-methyl]-cyclohexylmethyl}-4-(2-methoxycarbonylethyl)-1-phenethyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester

5-[4-(1-dimethylamino-3-phenylpropyl)-cyclohexylmethyl]-4-(2-methoxycarbonylethyl)-1-phenethyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester

1-benzyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexylmethyl}-4-(2-methoxycarbonylethyl)-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester

25 1-benzyl-4-benzylsulfanylmethyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexylmethyl}-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester

1-benzyl-5-{4-[dimethylamino-(4-fluorophenyl)-methyl]-cyclohexylmethyl}-4-(2-methoxycarbonylethyl)-4,5-dihydro-1H-imidazole-carboxylic acid methyl ester

1-butyl-4-sec-butyl-5-{4-[(4-chlorophenyl)-dimethylamino-methyl]-cyclohexylmethyl}-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester

1-butyl-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexylmethyl}-4-methylsulfanylmethyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester

10 4-benzylsulfanylmethyl-1-butyl-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexylmethyl}-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester

5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexyl}-4-(2-methoxycarbonylethyl)-1-phenethyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester

4-benzylsulfanylmethyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexyl}-1-phenethyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester

4-benzylsulfanylmethyl-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexyl}-1-phenethyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester

5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexylmethyl}-4-(2-methoxycarbonylethyl)-1-phenethyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester

25 1-benzyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexyl}-4-(2-methoxycarbonylethyl)-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester

1-benzyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-  
cyclohexyl-4-methylsulfanylmethyl-4,5-dihydro-1H-imidazole-  
4-carboxylic acid methyl ester

1-benzyl-4-benzylsulfanylmethyl-5-{4-[dimethylamino-(3-  
5 fluorophenyl)-methyl]-cyclohexyl}-4,5-dihydro-1H-imidazole-  
4-carboxylic acid methyl ester

1-benzyl-4-benzylsulfanylmethyl-5-{4-[(4-chlorophenyl)-  
dimethylaminomethyl]-cyclohexyl}-4,5-dihydro-1H-imidazole-  
4-carboxylic acid methyl ester

10 1-benzyl-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-  
cyclohexylmethyl}-4-(2-methoxycarbonylethyl)-4,5-dihydro-  
1H-imidazole-4-carboxylic acid methyl ester

1-benzyl-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-  
cyclohexylmethyl}-4-methylsulfanylmethyl-4,5-dihydro-1H-  
15 imidazole-4-carboxylic acid methyl ester

1-benzyl-4-benzylsulfanylmethyl-5-{4-[(4-chlorophenyl)-  
dimethylaminomethyl]-cyclohexylmethyl}-4,5-dihydro-1H-  
imidazole-4-carboxylic acid methyl ester

1-cyclohexyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-  
20 cyclohexylmethyl}-4-propyl-4,5-dihydro-1H-imidazole-4-  
carboxylic acid methyl ester

1-cyclohexyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-  
cyclohexylmethyl}-4-(2-methylsulfanylethyl)-4,5-dihydro-1H-  
imidazole-4-carboxylic acid methyl ester

25 1-cyclohexyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-  
cyclohexylmethyl}-4-methyl-4,5-dihydro-1H-imidazole-4-  
carboxylic acid methyl ester

1-cyclohexyl-5-{4-[dimethylamino-(4-fluorophenyl)-methyl]-cyclohexylmethyl}-4-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester

1-cyclohexyl-5-{4-[dimethylamino-(4-fluorophenyl)-methyl]-cyclohexylmethyl}-4-(2-methylsulfanylethyl)-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester

1-cyclohexyl-5-{4-[dimethylamino-(4-fluorophenyl)-methyl]-cyclohexylmethyl}-4-methyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester

10 1-cyclohexyl-5-[4-(1-dimethylamino-3-phenylpropyl)-cyclohexylmethyl]-4-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester

1-cyclohexyl-5-[4-(1-dimethylamino-3-phenylpropyl)-cyclohexylmethyl]-4-(2-methylsulfanylethyl)-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester

1-cyclohexyl-5-[4-(1-dimethylamino-3-phenylpropyl)-cyclohexylmethyl]-4-methyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester

5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexylmethyl}-1,4-dipropyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester

5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexylmethyl}-4-(2-methylsulfanylethyl)-1-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester

25 1-benzyl-4-(4-chlorobenzyl)-5-{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexylmethyl}-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester

1-benzyl-4-butyl-5-{4-[(chlorophenyl)-dimethylaminomethyl]-cyclohexylmethyl}-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester

1-cyclohexyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexyl}-4-(2-methoxycarbonyl ethyl)-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester

4-benzylsulfanylmethyl-1-cyclohexyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexyl}-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester

10 5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexylmethyl}-4-methyl-1-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester

5-{4-[dimethylamino-(4-fluorophenyl)-methyl]-cyclohexylmethyl}-1,4-dipropyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester

5-{4-[dimethylamino-(4-fluorophenyl)-methyl]-cyclohexylmethyl}-4-(2-methylsulfanylethyl)-1-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester

20 5-[4-(1-dimethylamino-3-phenylpropyl)-cyclohexylmethyl]-1,4-dipropyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester

5-[4-(1-dimethylamino-3-phenylpropyl)-cyclohexylmethyl]-4-(2-methylsulfanylethyl)-1-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester

25 1-butyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexylmethyl}-4-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester

1-butyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-  
cyclohexylmethyl}-4-(2-methylsulfanylethyl)-4,5-dihydro-1H-  
imidazole-4-carboxylic acid methyl ester

1-butyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-  
5 cyclohexylmethyl}-4-methyl-4,5-dihydro-1H-imidazole-4-  
carboxylic acid methyl ester

1-butyl-5-{4-[dimethylamino-(4-fluorophenyl)-methyl]-  
cyclohexylmethyl}-4-propyl-4,5-dihydro-1H-imidazole-4-  
carboxylic acid methyl ester

10 1-butyl-5-{4-[dimethylamino-(4-fluorophenyl)-methyl]-  
cyclohexylmethyl}-4-(2-methylsulfanylethyl)-4,5-dihydro-1H-  
imidazole-4-carboxylic acid methyl ester

1-butyl-5-[4-(1-dimethylamino-3-phenylpropyl)-  
cyclohexylmethyl]-4-propyl-4,5-dihydro-1H-imidazole-4-  
15 carboxylic acid methyl ester

1-butyl-5-[4-(1-dimethylamino-3-phenylpropyl)-  
cyclohexylmethyl]-4-(2-methylsulfanylethyl)-4,5-dihydro-1H-  
imidazole-4-carboxylic acid methyl ester

5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-  
20 cyclohexylmethyl}-1-phenethyl-4-propyl-4,5-dihydro-1H-  
imidazole-4-carboxylic acid methyl ester

5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-  
cyclohexylmethyl}-4-(2-methylsulfanylethyl)-1-phenethyl-  
4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester

25 5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-  
cyclohexylmethyl}-4-methyl-1-phenethyl-4,5-dihydro-1H-  
imidazole-4-carboxylic acid methyl ester

5-{4-[dimethylamino-(4-fluorophenyl)-methyl]-  
cyclohexylmethyl}-1-phenethyl-4-propyl-4,5-dihydro-1H-  
imidazole-4-carboxylic acid methyl ester

5-{4-[dimethylamino-(4-fluorophenyl)-methyl]-  
5 cyclohexylmethyl}-4-(2-methylsulfanylethyl)-1-phenethyl-  
4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester

5-{4-[dimethylamino-(4-fluorophenyl)-methyl]-  
cyclohexylmethyl}-4-methyl-1-phenethyl-4,5-dihydro-1H-  
imidazole-4-carboxylic acid methyl ester

10 5-[4-(1-dimethylamino-3-phenylpropyl)-cyclohexylmethyl]-1-  
phenethyl-4-propyl-4,5-dihydro-1H-imidazole-4-carboxylic  
acid methyl ester

5-[4-(1-dimethylamino-3-phenylpropyl)-cyclohexylmethyl]-4-  
(2-methylsulfanylethyl)-1-phenethyl-4,5-dihydro-1H-  
15 imidazole-4-carboxylic acid methyl ester

5-[4-(1-dimethylamino-3-phenylpropyl)-cyclohexylmethyl]-4-  
methyl-1-phenethyl-4,5-dihydro-1H-imidazole-4-carboxylic  
acid methyl ester

1-benzyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-  
20 cyclohexylmethyl}-4-propyl-4,5-dihydro-1H-imidazole-4-  
carboxylic acid methyl ester

1-benzyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-  
cyclohexylmethyl}-4-(2-methylsulfanylethyl)-4,5-dihydro-1H-  
imidazole-4-carboxylic acid methyl ester

25 1-benzyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-  
cyclohexylmethyl}-4-methyl-4,5-dihydro-1H-imidazole-4-  
carboxylic acid methyl ester

1-benzyl-5-{4-[dimethylamino-(4-fluorophenyl)-methyl]-cyclohexylmethyl}-4-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester

1-benzyl-5-{4-[dimethylamino-(4-fluorophenyl)-methyl]-cyclohexylmethyl}-4-(2-methylsulfanylethyl)-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester

1-benzyl-5-{4-[dimethylamino-(4-fluorophenyl)-methyl]-cyclohexylmethyl}-4-methyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester

10 1-benzyl-5-[4-(1-dimethylamino-3-phenylpropyl)-cyclohexylmethyl]-4-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester

1-benzyl-5-[4-(1-dimethylamino-3-phenylpropyl)-cyclohexylmethyl]-4-(2-methylsulfanylethyl)-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester

1-benzyl-5-[4-(1-dimethylamino-3-phenylpropyl)-cyclohexylmethyl]-4-methyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester

1-cyclohexyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexylmethyl}-4-(2-methoxycarbonylethyl)-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester

4-sec-butyl-1-cyclohexyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexylmethyl}-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester

25 1-cyclohexyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexylmethyl}-4-methylsulfanylmethyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester

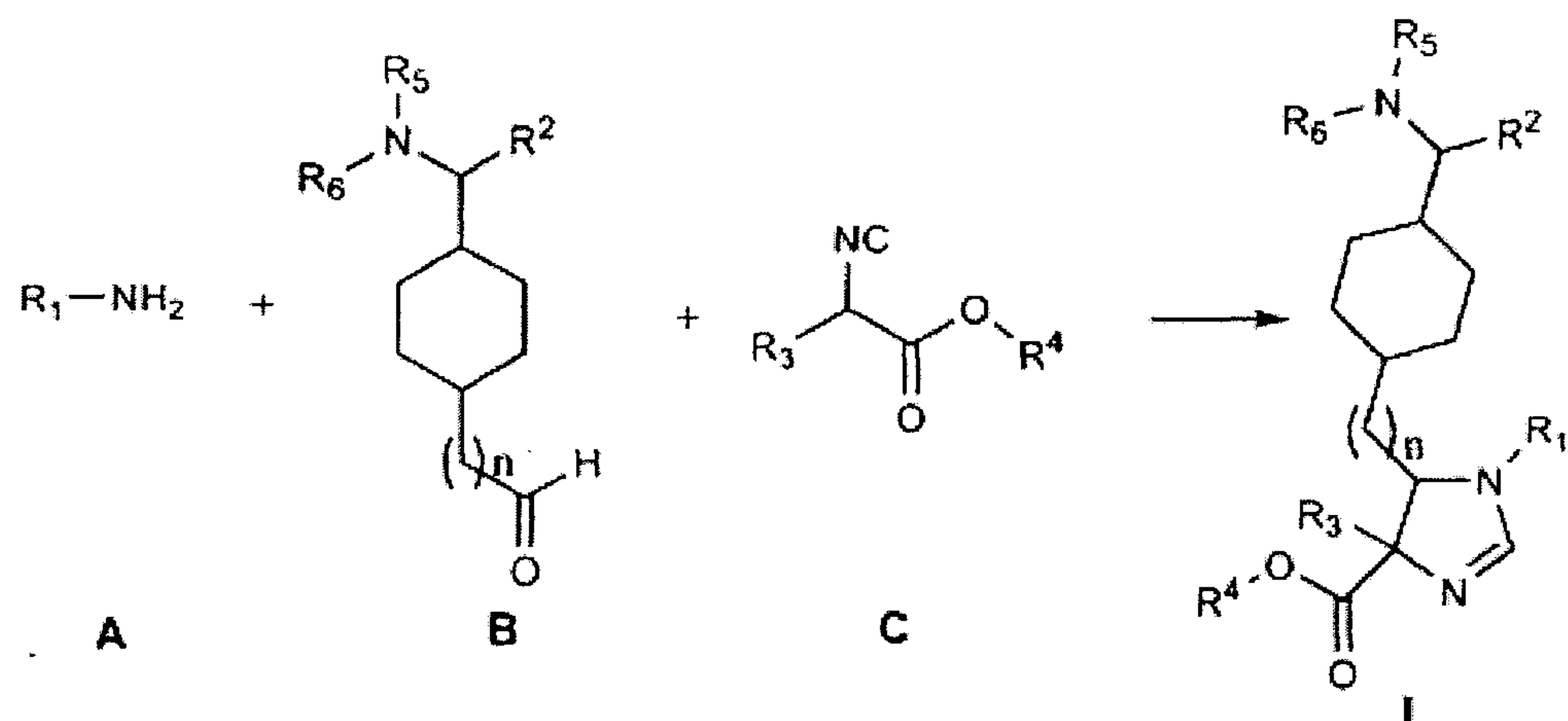
- 4-benzylsulfanylmethyl-1-cyclohexyl-5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexylmethyl}-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 1-cyclohexyl-5-{4-[dimethylamino-(4-fluorophenyl)-methyl]-cyclohexylmethyl}-4-(2-methoxycarbonylethyl)-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 4-sec-butyl-1-cyclohexyl-5-{4-[dimethylamino-(4-fluorophenyl)-methyl]-cyclohexylmethyl}-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 10 1-cyclohexyl-5-{4-[dimethylamino-(4-fluorophenyl)-methyl]-cyclohexylmethyl}-4-methylsulfanylmethyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 1-cyclohexyl-5-[4-(1-dimethylamino-3-phenylpropyl)-cyclohexylmethyl]-4-(2-methoxycarbonylethyl)-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 15 1H-imidazole-4-carboxylic acid methyl ester
- 1-cyclohexyl-5-[4-(1-dimethylamino-3-phenylpropyl)-cyclohexylmethyl]-4-methylsulfanylmethyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 4-benzylsulfanylmethyl-1-cyclohexyl-5-[4-(1-dimethylamino-3-phenylpropyl)-cyclohexylmethyl]-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 20 4-carboxylic acid methyl ester
- 5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexylmethyl}-4-(2-methoxycarbonylethyl)-1-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 25 5-{4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexylmethyl}-4-methylsulfanylmethyl-1-propyl-4,5-dihydro-1H-imidazole-4-carboxylic acid methyl ester

- 5- {4- [dimethylamino- (4-fluorophenyl) -methyl] -  
cyclohexylmethyl} -4- (2-methoxycarbonylethyl) -1-propyl-4,5-  
dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 5- {4- [dimethylamino- (4-fluorophenyl) -methyl] -  
5 cyclohexylmethyl} -4-methylsulfanylmethyl-1-propyl-4,5-  
dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 4-benzylsulfanylmethyl-5- {4- [dimethylamino- (4-  
fluorophenyl) -methyl] -cyclohexylmethyl} -1-propyl-4,5-  
dihydro-1H-imidazole-4-carboxylic acid methyl ester
- 10 methyl-4-sec-butyl-5- ((4- (4-  
chlorophenyl) (dimethylamino)methyl)cyclohexyl)methyl) -1-  
cyclohexyl-4,5-dihydro-1H-imidazole-4-carboxylate

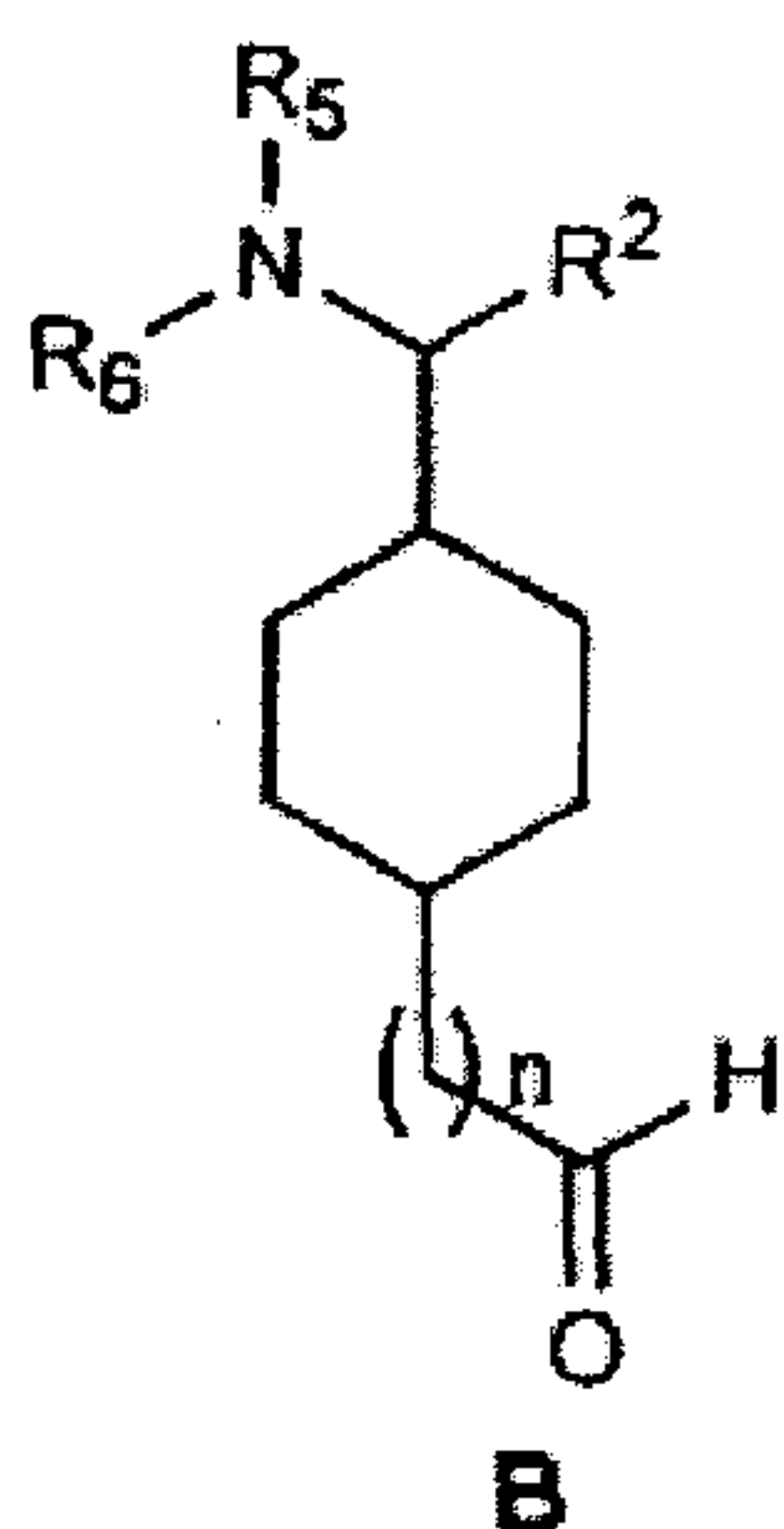
15 in the form of the racemate; in the form of the  
enantiomers, diastereomers, mixtures of the  
enantiomers or diastereomers or in the form of an  
individual enantiomer or diastereomer; in the form of  
the bases and/or salts of physiologically compatible  
acids.

20

11. Process for the preparation of an imidazoline  
derivative according to the invention, wherein amines  
of the general Formula A are reacted with aldehydes of  
the general Formula B and isonitrile esters of the  
25 general Formula C in an organic solvent, for example  
ethanol or methanol, at a temperature of 20°-100°C  
according to the following synthesis reaction scheme,  
to form substituted imidazoline derivatives of the  
general Formula I



12. Substituted aldehyde of the general Formula B



5

wherein the radicals  $R^2$ ,  $R^5$ ,  $R^6$  as well as  $n$  have the meanings given in claims 1, 4, 5 and 9.

13. Substituted aldehydes according to claim 12, from the group

- 4-[dimethylamino-(4-fluorophenyl)-methyl]-cyclohexanecarbaldehyde
- 4-(1-dimethylamino-3-phenylpropyl)-cyclohexanecarbaldehyde
- 4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexanecarbaldehyde

4-[(4-chlorophenyl)-dimethylaminomethyl]-  
cyclohexanecarbaldehyde

{4-[(4-chlorophenyl)-dimethylaminomethyl]-cyclohexyl}-  
acetaldehyde

5 {4-[dimethylamino-(3-fluorophenyl)-methyl]-cyclohexyl}-  
acetaldehyde

4-(dimethylamino-thiophen-2-yl-methyl)-  
cyclohexanecarbaldehyde

{4-[dimethylamino-(4-fluorophenyl)-methyl]-cyclohexyl}-  
10 acetaldehyde

[4-(dimethylamino-thiophen-2-yl-methyl)-cyclohexyl]-  
acetaldehyde

[4-(1-dimethylamino-3-phenylpropyl)-cyclohexyl]-  
acetaldehyde

15

in the form of the racemate; in the form of the  
enantiomers, diastereomers, mixtures of enantiomers or  
diastereomers or in the form of an individual  
enantiomer or diastereomer; in the form of the bases  
20 and/or salts of physiologically compatible acids.

20

14. Medicament containing at least one substituted  
imidazoline derivative according to claim 1 or a  
substituted aldehyde according to claim 12, optionally  
25 in the form of the racemate; in the form of the  
enantiomers, diastereomers, mixtures of the  
enantiomers or diastereomers or in the form of an  
individual enantiomer or diastereomer; in the form of  
the bases and/or salts of physiologically compatible  
30 acids and optionally containing suitable additives  
and/or auxiliary substances and/or optionally further  
active substances.

15. Use of a substituted imidazoline derivative according to claim 1 or a substituted aldehyde according to claim 12, optionally in the form of the racemate; in the form of the enantiomers, diastereomers, mixtures  
5 of the enantiomers or diastereomers or in the form of an individual enantiomer or diastereomer; in the form of the bases and/or salts of physiological compatible acids, for the preparation of a medicament for the treatment of pain, in particular acute, neuropathic or  
10 chronic pain.
16. Use of a substituted imidazoline derivative according to claim 1 or a substituted aldehyde according to claim 12, optionally in the form of the racemate; in  
15 the form of the enantiomers, diastereomers, mixtures of the enantiomers or diastereomers or in the form of an individual enantiomer or diastereomer; in the form of the bases and/or salts of physiological compatible acids, for the preparation of a medicament for the  
20 treatment of depression, urinary incontinence, diarrhea, pruritus, alcohol and drug misuse, drug dependency, loss of drive and/or anxiety.

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