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(54) Titre : BETA-AMINOALCOOLS SUBSTITUES UTILISES EN TANT QUE MEDICAMENTS
(54) Title: SUBSTITUTED BETA-AMINOALCOHOLS USED AS MEDICAMENTS

(57) **Abrégé/Abstract:**

The invention relates to medicaments containing substituted aminoalcohols and the use of substituted aminoalcohols in the production of medicaments. The invention also relates to substituted 2-(aminomethyl)cycloalkane-1-ol-compounds and a method for the production thereof.



ABSTRACT

The invention relates to medicaments containing substituted aminoalcohols and the use of substituted aminoalcohols in the production of medicaments. The invention also relates to substituted 2-(aminomethyl)cycloalkane-1-ol-compounds and a method for the production thereof.

SUBSTITUTED BETA-AMINOALCOHOLS AS PHARMACEUTICAL
PREPARATIONS

The present invention relates to pharmaceutical
5 preparations containing substituted aminoalcohols and to
the use of substituted aminoalcohols for the production of
pharmaceutical preparations and to substituted 2-
(aminomethyl)cycloalkan-1-ol compounds and processes for
the production thereof.

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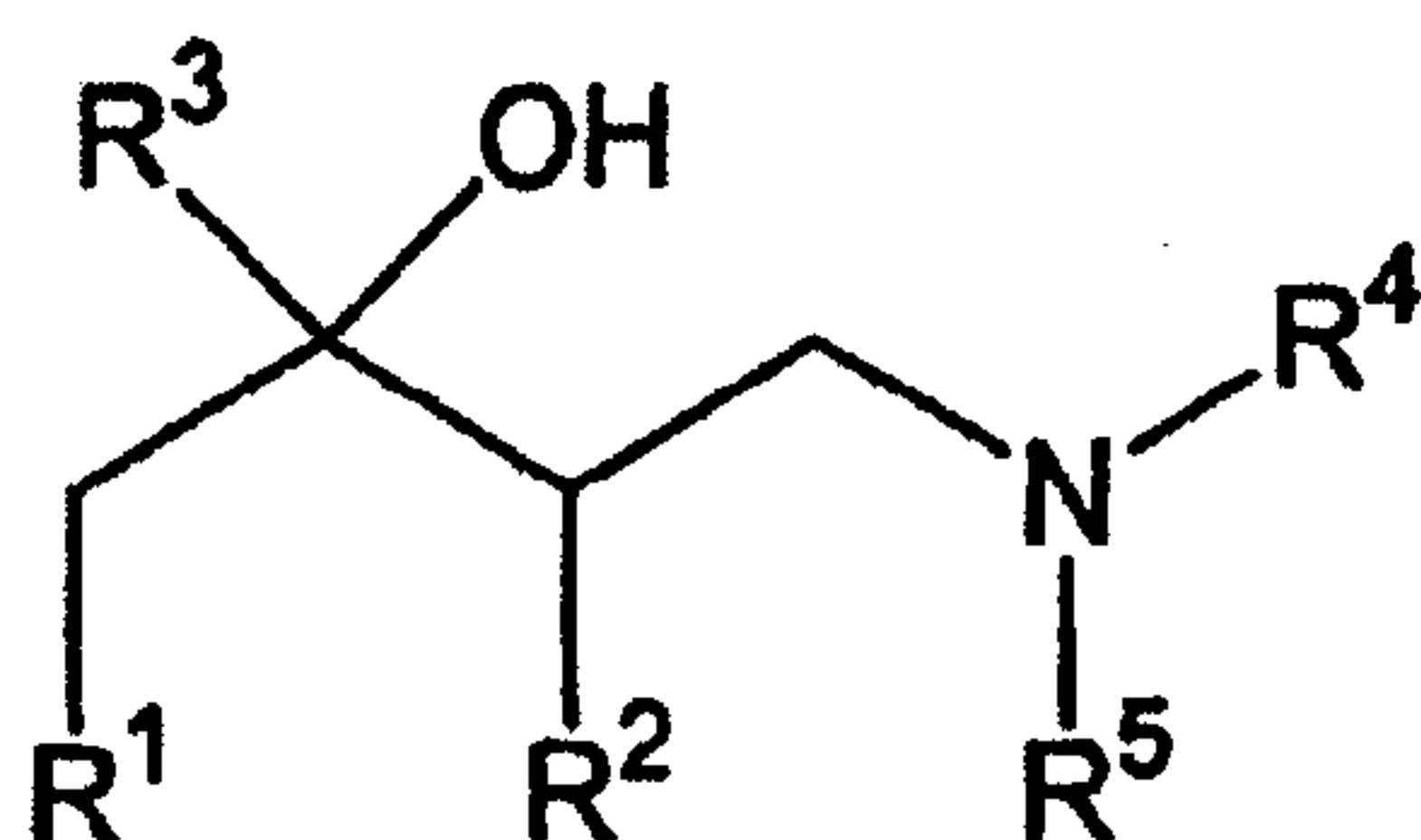
The treatment of pain is of great medical significance.
There is a worldwide need for effective pain treatments.
The urgency of the requirement for effective therapeutic
methods for providing tailored and targeted treatment of
15 chronic and non-chronic pain, this being taken to mean pain
treatment which is effective and satisfactory from the
patient's standpoint, is evident from the large number of
scientific papers relating to applied analgesia and to
basic nociception research which have appeared in recent
20 times.

The object of the invention was therefore to provide novel
pharmaceutical preparations for the treatment of pain.

25 According to the invention, this object is achieved by the
provision of pharmaceutical preparations containing
aminoalcohols of the formula I stated hereinafter, since
these pharmaceutical preparations exhibit in particular an
excellent analgesic action and may be used for the
30 treatment of pain, as an antiemetic and/or a nootropic
(neurotropic), for the treatment of cardiovascular
diseases, urinary incontinence, diarrhoea, pruritus,
dependency on alcohol and/or drugs and/or medicines, and/or

inflammation, for the treatment of depression, to increase vigilance and/or libido.

The invention therefore provides pharmaceutical
5 preparations containing aminoalcohols of the general formula I,



in which

- 10 R^1 and R^2 , identical or different, in each case denote a linear or branched, saturated or unsaturated aliphatic residue, or together form a $(CH_2)_n$ chain, wherein n denotes an integer,
- 15 R^3 denotes a linear or branched, saturated or unsaturated aliphatic residue, a saturated or unsaturated cycloaliphatic residue, an aryl residue or a heteroaryl residue, wherein the respective ring system may be optionally mono- or polysubstituted and/or attached via a
- 20 linear or branched, saturated or unsaturated aliphatic bridge and/or the aryl or heteroaryl residue may be part of a polycyclic system,

R^4 and R^5 together form a $(CH_2)_m$ chain, wherein m denotes an
25 integer and optionally one or more CH_2 groups may be replaced by oxygen,

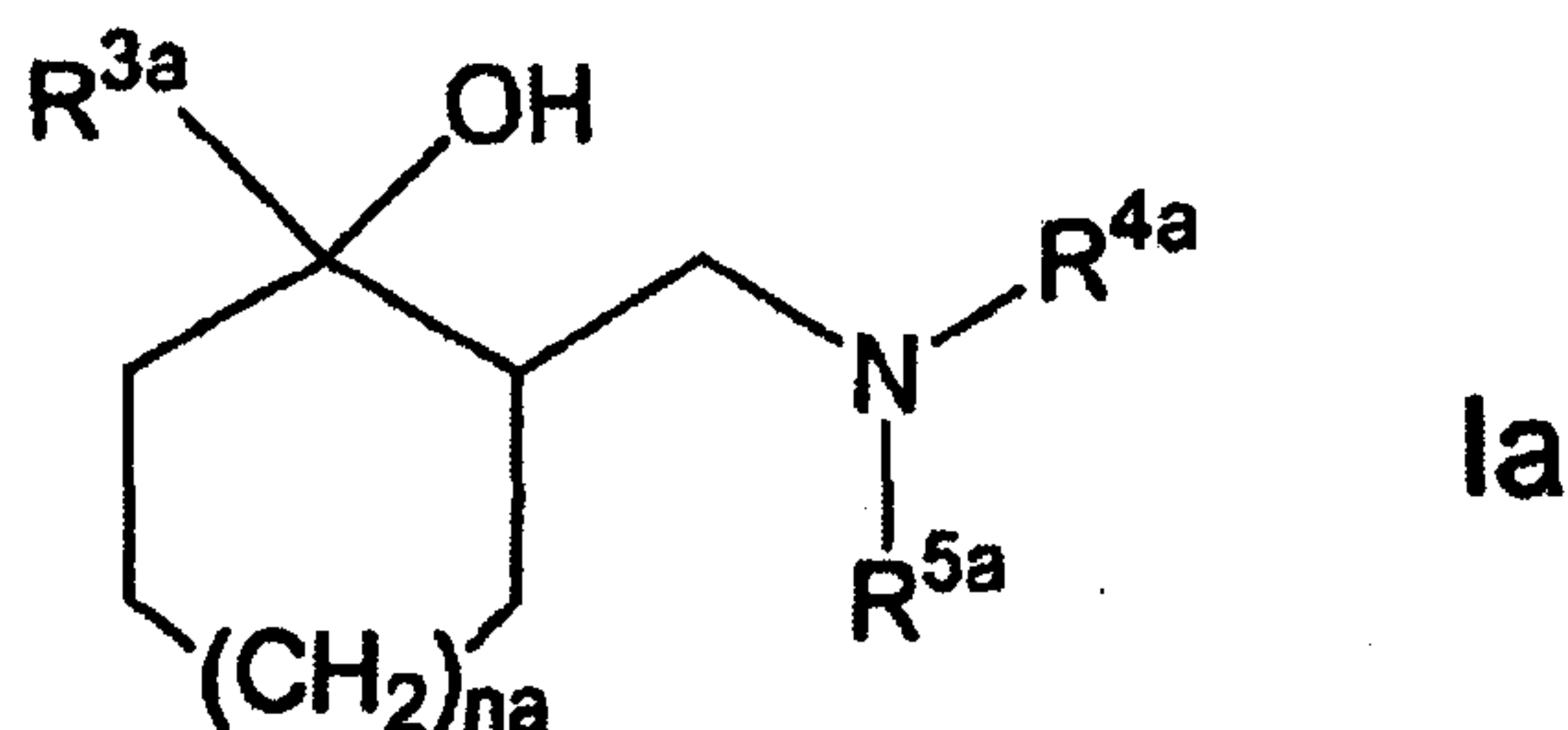
in the form of the diastereomers thereof, the enantiomers thereof and mixtures thereof - including the racemates

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thereof - and in the form of corresponding bases, salts and solvates as active ingredient

with the exception of compounds of the general formula Ia,

5

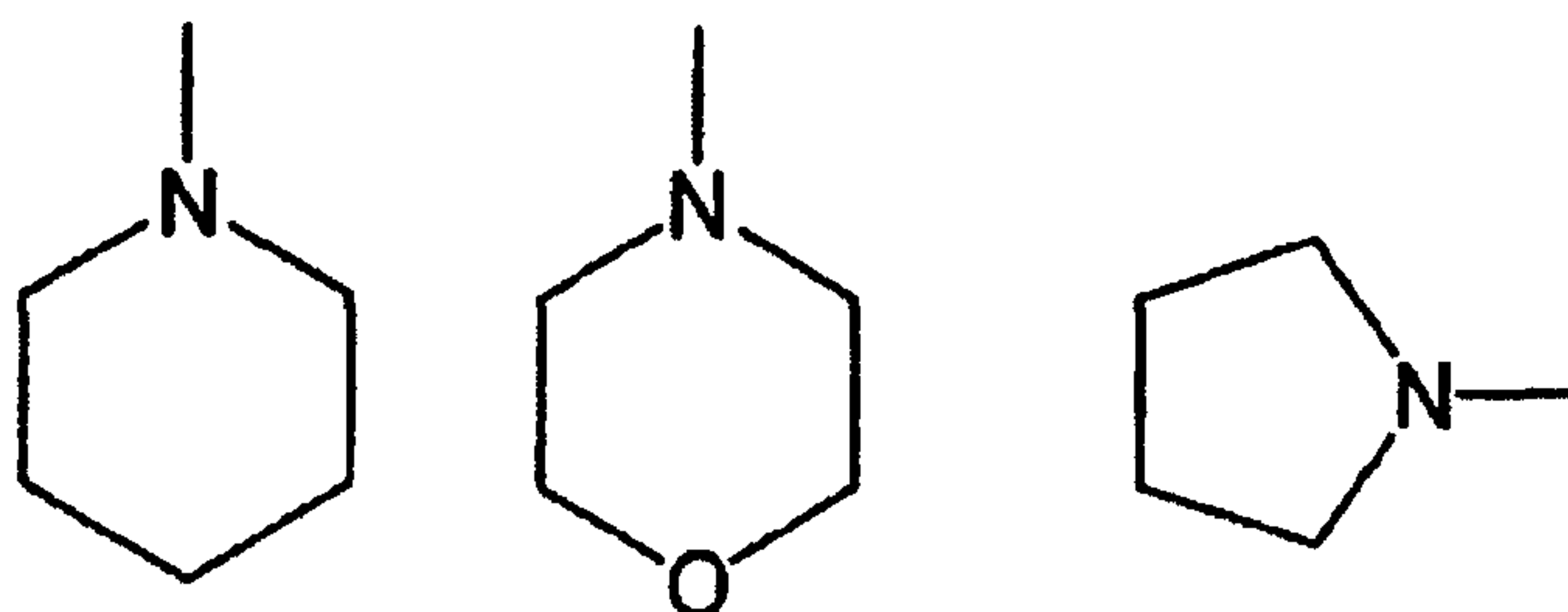


in which

na denotes 0, 1 or 2,

- 10 R^{3a} denotes a phenyl residue, which is substituted in the meta position with an alkoxy group with 1-3 carbons or an aralkoxy group and

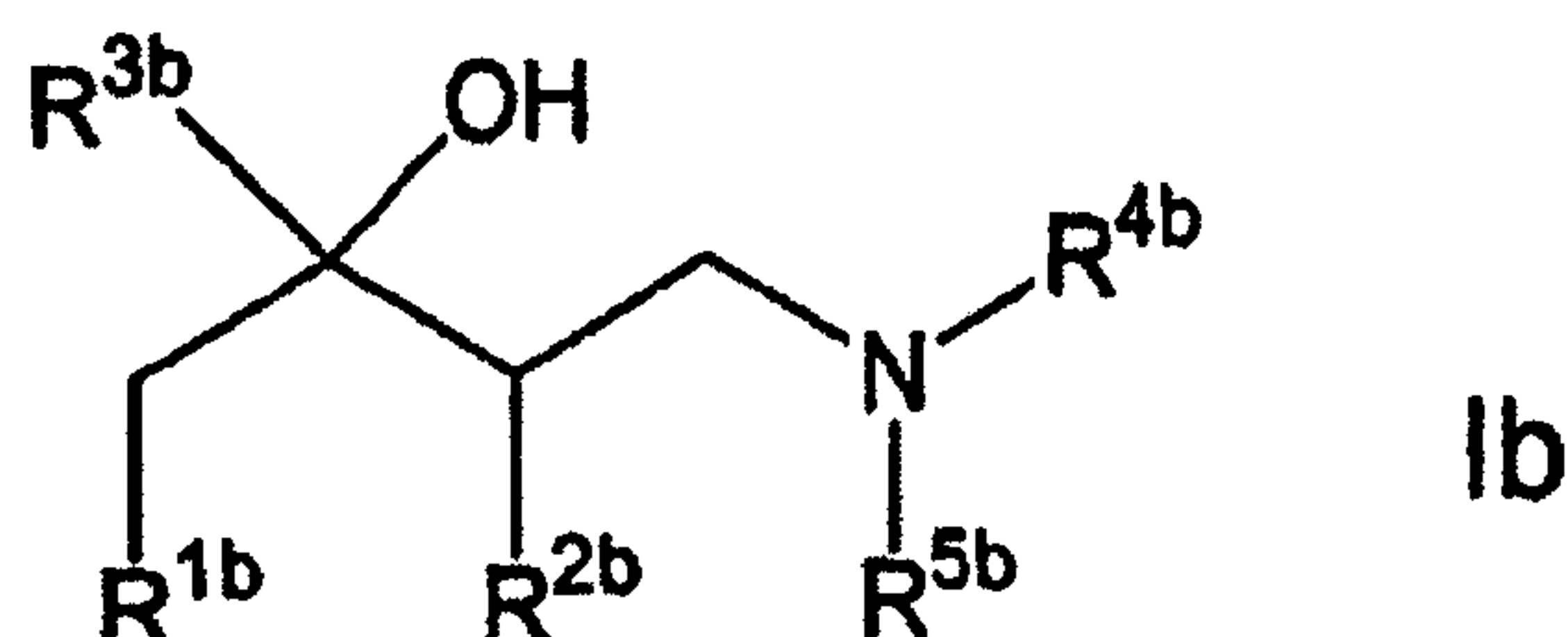
R^{4a} and R^{5a} together form, including the nitrogen atom, one
15 of the rings listed hereinafter,



with the exception of compounds of the general formula Ib,

20

4



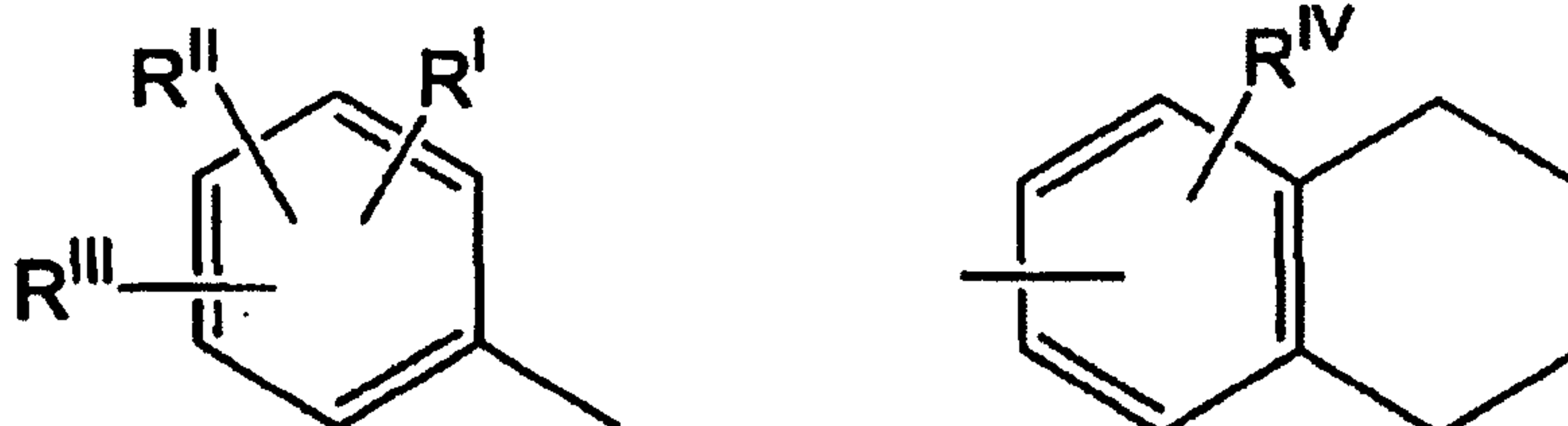
in which

R^{1b} denotes a lower alkyl residue or a phenyl residue,

R^{2b} denotes a lower alkyl residue,

R^{4b} and R^{5b} together form a pyrrolidine or a piperidine ring and

R^{3b} denotes one of the following residues,



in which

R^I denotes hydrogen, a lower alkyl residue or a lower alkoxy residue,

R^{II} denotes hydrogen or a lower alkyl residue,

R^{III} denotes hydrogen, halogen, a trihalomethyl residue, a lower alkyl residue or a lower alkoxy residue and

R^{IV} denotes a lower alkoxy residue,

and with the exception of 1-benzyl-2-(piperidin-1-yl-methyl)-cyclohexan-1-ol, 1-phenyl-2-(piperidin-1-ylmethyl)-

cyclohexan-1-ol, 3-(4-methylphenyl)-2-n-propyl-1-pyrrolidin-1-ylpentan-3-ol and 3-(phenyl)-2-n-propyl-1-pyrrolidin-1-ylpentan-3-ol

5 and optionally physiologically acceptable auxiliary substances.

Pharmaceutical preparations are preferred which contain at least one compound of the general formula I, in which

10

R^1 and R^2 , identical or different, in each case denote a linear or branched, saturated or unsaturated aliphatic C_{1-6} residue, or together form a $(CH_2)_n$ chain, wherein n denotes an integer from 2-9,

15

R^3 denotes a linear or branched, saturated or unsaturated aliphatic C_{1-6} residue, a saturated or unsaturated cycloaliphatic C_{3-7} residue, a phenyl residue or a five- or six-membered heteroaryl residue, wherein the respective
20 ring system may optionally be mono- or polysubstituted and/or attached via a linear or branched, saturated or unsaturated aliphatic C_{1-5} bridge,

R^4 and R^5 together form a $(CH_2)_m$ chain, wherein m denotes an
25 integer from 4-6 and optionally one or more CH_2 groups may be replaced by oxygen

with the exception of the above-excepted compounds.

30 Pharmaceutical preparations are additionally preferred which contain at least one compound of the general formula I, in which

R^1 and R^2 , identical or different, in each case denote a linear or branched, saturated or unsaturated aliphatic C_{1-3} residue, or together form a $(CH_2)_n$ chain, wherein n denotes an integer from 2-9,

5

R^3 denotes a linear or branched, saturated or unsaturated aliphatic C_{1-3} residue, a saturated or unsaturated cycloaliphatic C_{5-6} residue, a phenyl residue or a five- or six-membered heteroaryl residue, wherein the respective ring system may optionally be mono- or polysubstituted with halogen, an alkyl group, an alkoxy group and/or a trihalogenated alkyl group and/or may be attached via a linear or branched, saturated or unsaturated aliphatic C_{1-3} bridge,

15

R^4 and R^5 together form a $(CH_2)_m$ chain, wherein m denotes an integer from 4-6 and optionally one or more CH_2 groups may be replaced by oxygen

20 with the exception of the above-excepted compounds.

Pharmaceutical preparations are additionally preferred which contain at least one compound of the general formula I, in which

25

R^1 and R^2 in each case denote a methyl group, or together form a $(CH_2)_n$ chain, wherein n denotes 2, 3, 4, 5 or 9,

R^3 denotes a vinyl residue, a cyclopentyl residue, a cyclohexyl residue, a thiophenyl residue or a phenyl residue, wherein the cyclohexyl residue may optionally be attached via a methylene bridge or the phenyl residue may optionally be mono- or polysubstituted with fluorine,

30

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chlorine, a methyl group, an isopropyl group, a methoxy group and/or a trifluoromethyl group and/or may optionally be attached via a linear saturated aliphatic C₁₋₃ bridge or an ethynyl bridge,

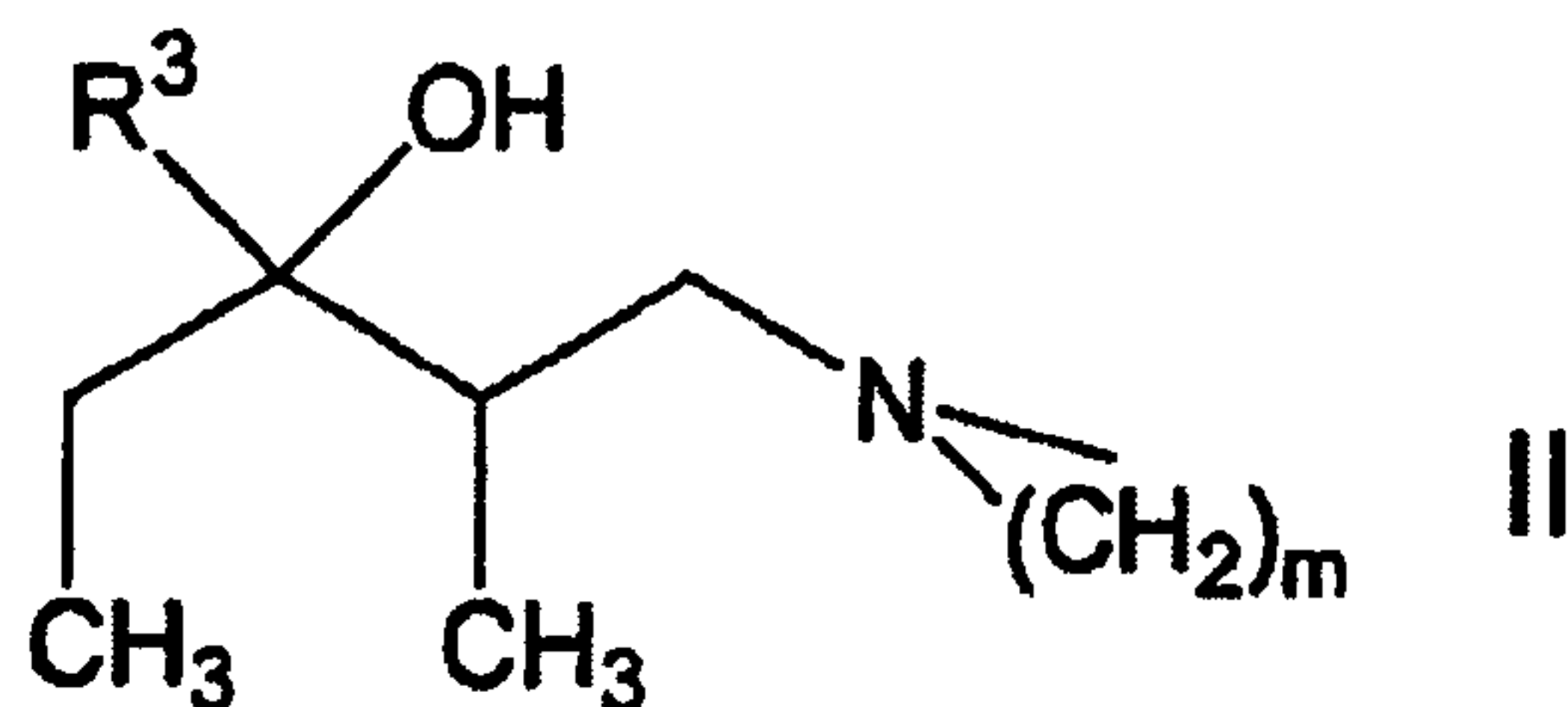
5

R⁴ and R⁵ together form a (CH₂)_m chain, wherein m denotes 4, 5 or 6

with the exception of the above-excepted compounds.

10

Pharmaceutical preparations are particularly preferred which contain at least one compound of the general formula II,



15

in which

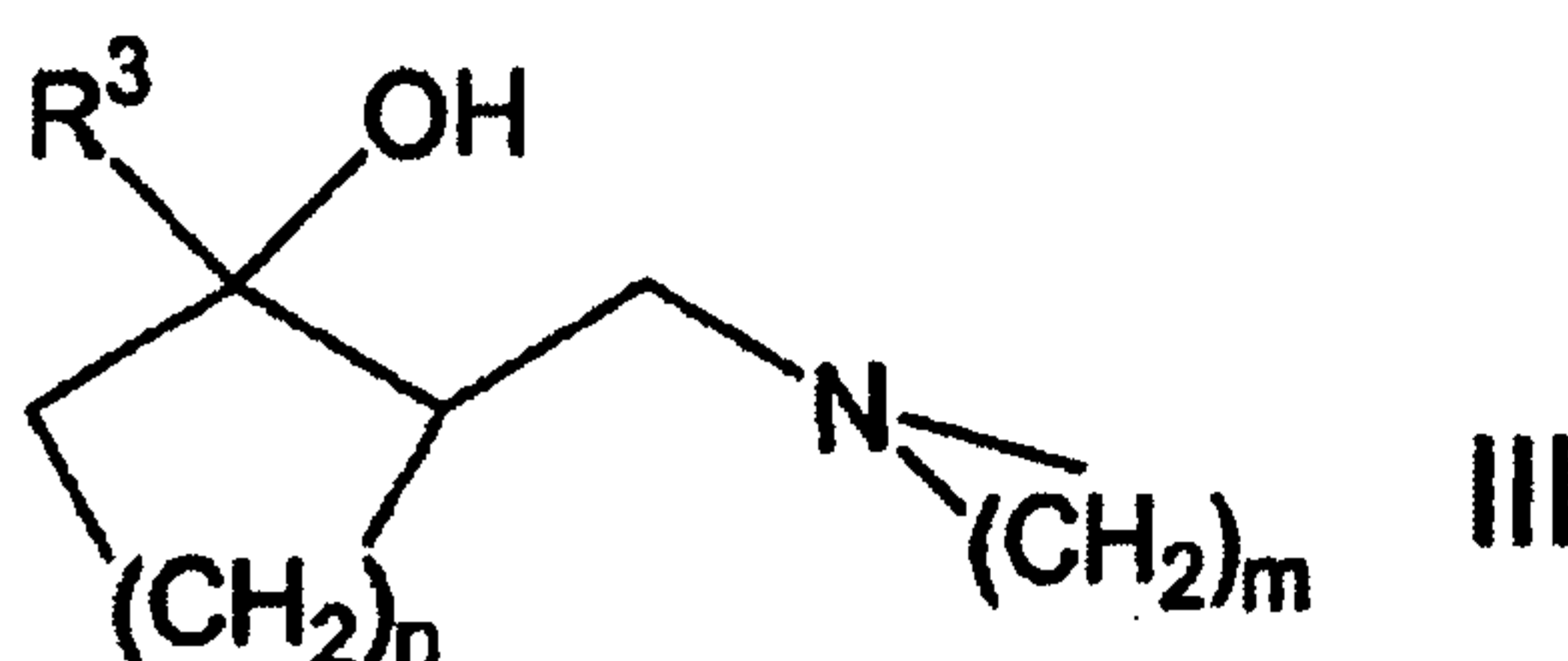
m denotes an integer from 4-6,

20 R³ denotes a linear or branched, saturated or unsaturated aliphatic residue, a saturated or unsaturated cycloaliphatic residue, an aryl residue or a heteroaryl residue, wherein the respective ring system may be optionally mono- or polysubstituted and/or attached via a
 25 linear or branched, saturated or unsaturated aliphatic bridge and/or the aryl or heteroaryl residue may be part of a polycyclic system

with the exception of the above-excepted compounds.

Pharmaceutical preparations are particularly preferred which contain at least one compound of the general formula III,

5



in which

n denotes an integer from 2-9 and m denotes an integer from 4-6 and

10

R³ denotes a linear or branched, saturated or unsaturated aliphatic residue, a saturated or unsaturated cycloaliphatic residue, an aryl residue or a heteroaryl residue, wherein the respective ring system may be

15 optionally mono- or polysubstituted and/or attached via a linear or branched, saturated or unsaturated aliphatic bridge and/or the aryl or heteroaryl residue may be part of a polycyclic system

20 with the exception of the above-excepted compounds.

Pharmaceutical preparations are additionally preferred which contain at least one compound of the general formula II or III, in which

25

R³ denotes a linear or branched, saturated or unsaturated aliphatic C₁₋₆ residue, a saturated or unsaturated cycloaliphatic C₃₋₇ residue, a phenyl residue or a five- or six-membered heteroaryl residue, wherein the respective

ring system may optionally be mono- or polysubstituted and/or attached via a linear or branched, saturated or unsaturated aliphatic C₁₋₅ bridge

5 and the other symbols have the above-stated meaning

with the exception of the above-excepted compounds.

Pharmaceutical preparations are additionally preferred
10 which contain at least one compound of the general formula II or III, in which

R³ denotes a linear or branched, saturated or unsaturated aliphatic C₁₋₃ residue, a saturated or unsaturated
15 cycloaliphatic C₅₋₆ residue, a phenyl residue or a five- or six-membered heteroaryl residue, wherein the respective ring system may optionally be mono- or polysubstituted with halogen, an alkyl group, an alkoxy group and/or a trihalogenated alkyl group and/or may be attached via a
20 linear or branched, saturated or unsaturated aliphatic C₁₋₃ bridge

and the other symbols have the above-stated meaning

25 with the exception of the above-excepted compounds.

Pharmaceutical preparations are additionally preferred which contain at least one compound of the general formula II or III, in which

30

R³ denotes a vinyl residue, a cyclopentyl residue, a cyclohexyl residue, a thiophenyl residue or a phenyl residue, wherein the cyclohexyl residue may optionally be

attached via a methylene bridge or the phenyl residue may optionally be mono- or polysubstituted with fluorine, chlorine, a methyl group, an isopropyl group, a methoxy group and/or a trifluoromethyl group and/or may optionally
5 be attached via a linear saturated aliphatic C₁₋₃ bridge or an ethynyl bridge

and the other symbols have the above-stated meaning

10 with the exception of the above-excepted compounds.

A heteroaryl residue is understood to be an optionally mono- or polysubstituted, five- to seven-membered aromatic residue with at least one, optionally 2, 3, 4 or 5
15 heteroatoms, which may be identical or different, which residue may be part of a polycyclic system. Preferred heteroatoms are nitrogen, oxygen and sulfur. Heteroaryl residues are particularly preferably selected from the group comprising pyrrolyl, indolyl, furyl (furanyl),
20 benzofuranyl, thienyl (thiophenyl), benzothienyl, pyrazolyl, imidazolyl, thiazolyl, oxazolyl, isoxazolyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, pyranyl, indazolyl, purinyl, indolizinyl, quinolinyl, isoquinolinyl, quinazolinyl, carbazolyl, phenazinyl and phenothiazinyl
25 residues. Attachment may be effected via any desired bondable ring atom. The optionally present substituents may be identical or different and attached to any desired, bondable ring atom.

30 An aryl residue is understood to mean an optionally mono- or polysubstituted aromatic residue, which may be part of a polycyclic system. A phenyl residue is particularly preferred. Attachment may be effected via any desired

bondable ring atom. The optionally present substituents may be identical or different and attached to any desired, bondable ring atom.

- 5 Very particularly preferred are pharmaceutical preparations containing at least one compound selected from the group comprising

- 1- (2,3-Dichloro-phenyl) -2-pyrrolidin-1-ylmethyl-
10 cyclohexanol
2-Pyrrolidin-1-ylmethyl-1-p-tolyl-cyclohexanol
1- (4-Methoxy-phenyl) -2-pyrrolidin-1-ylmethyl-cyclohexanol
1-Phenyl-2-pyrrolidin-1-ylmethyl-cyclopentanol
1- (4-Chloro-phenyl) -2-pyrrolidin-1-ylmethyl-cyclopentanol
15 1-Benzyl-2-pyrrolidin-1-ylmethyl-cyclopentanol
1- (4-Fluoro-3-methyl-phenyl) -2-pyrrolidin-1-ylmethyl-
cyclopentanol
2-Pyrrolidin-1-ylmethyl-1-o-tolyl-cyclopentanol
2-Pyrrolidin-1-ylmethyl-1-vinyl-cyclopentanol
20 1- (4-tert-Butyl-phenyl) -2-pyrrolidin-1-ylmethyl-
cyclopentanol
2-Pyrrolidin-1-ylmethyl-bicyclopentyl-1-ol
2-Pyrrolidin-1-ylmethyl-1-m-tolyl-cyclopentanol
1-Cyclohexyl-2-pyrrolidin-1-ylmethyl-cyclopentanol
25 1- (4-Fluoro-phenyl) -2-pyrrolidin-1-ylmethyl-cyclopentanol
1-Phenethyl-2-pyrrolidin-1-ylmethyl-cyclopentanol
1-Phenylethynyl-2-pyrrolidin-1-ylmethyl-cyclopentanol
2-Pyrrolidin-1-ylmethyl-1-thiophen-2-yl-cyclopentanol
1- (2,4-Dichloro-phenyl) -2-pyrrolidin-1-ylmethyl-
30 cyclopentanol
1- (3-Phenyl-propyl) -2-pyrrolidin-1-ylmethyl-cyclopentanol
1- (2,3-Dichloro-phenyl) -2-pyrrolidin-1-ylmethyl-
cyclopentanol

- 2-Pyrrolidin-1-ylmethyl-1-p-tolyl-cyclopentanol
1-(4-Methoxy-phenyl)-2-pyrrolidin-1-ylmethyl-cyclopentanol
1-Phenyl-2-pyrrolidin-1-ylmethyl-cycloheptanol
1-(4-Chloro-phenyl)-2-pyrrolidin-1-ylmethyl-cycloheptanol
5 1-Benzyl-2-pyrrolidin-1-ylmethyl-cycloheptanol
1-(4-Fluoro-3-methyl-phenyl)-2-pyrrolidin-1-ylmethyl-
cycloheptanol
2-Pyrrolidin-1-ylmethyl-1-o-tolyl-cycloheptanol
2-Pyrrolidin-1-ylmethyl-1-vinyl-cycloheptanol
10 1-(4-tert-Butyl-phenyl)-2-pyrrolidin-1-ylmethyl-
cycloheptanol
1-Cyclopentyl-2-pyrrolidin-1-ylmethyl-cycloheptanol
2-Pyrrolidin-1-ylmethyl-1-m-tolyl-cycloheptanol
1-Cyclohexyl-2-pyrrolidin-1-ylmethyl-cycloheptanol
15 1-(4-Fluoro-phenyl)-2-pyrrolidin-1-ylmethyl-cycloheptanol
1-Phenethyl-2-pyrrolidin-1-ylmethyl-cycloheptanol
1-Phenylethynyl-2-pyrrolidin-1-ylmethyl-cycloheptanol
2-Pyrrolidin-1-ylmethyl-1-thiophen-2-yl-cycloheptanol
1-(2,4-Dichloro-phenyl)-2-pyrrolidin-1-ylmethyl-
20 cycloheptanol
1-(3-Phenyl-propyl)-2-pyrrolidin-1-ylmethyl-cycloheptanol
1-(2,3-Dichloro-phenyl)-2-pyrrolidin-1-ylmethyl-
cycloheptanol
2-Pyrrolidin-1-ylmethyl-1-p-tolyl-cycloheptanol
25 1-(4-Methoxy-phenyl)-2-pyrrolidin-1-ylmethyl-cycloheptanol
2-Azepan-1-ylmethyl-1-phenyl-cyclohexanol
2-Azepan-1-ylmethyl-1-benzyl-cyclohexanol
2-Azepan-1-ylmethyl-1-(4-fluoro-3-methyl-phenyl)-
cyclohexanol
30 2-Azepan-1-ylmethyl-1-o-tolyl-cyclohexanol
2-Azepan-1-ylmethyl-1-vinyl-cyclohexanol
2-Azepan-1-ylmethyl-1-(4-tert-butyl-phenyl)-cyclohexanol
2-Azepan-1-ylmethyl-1-cyclopentyl-cyclohexanol

- 2-Azepan-1-ylmethyl-1-m-tolyl-cyclohexanol
2-Azepan-1-ylmethyl-bicyclohexyl-1-ol
2-Azepan-1-ylmethyl-1-(4-fluoro-phenyl)-cyclohexanol
2-Azepan-1-ylmethyl-1-phenethyl-cyclohexanol
5 2-Azepan-1-ylmethyl-1-thiophen-2-yl-cyclohexanol
2-Azepan-1-ylmethyl-1-(2,4-dichloro-phenyl)-cyclohexanol
2-Azepan-1-ylmethyl-1-(3-methoxy-phenyl)-cyclohexanol
2-Azepan-1-ylmethyl-1-(3-phenyl-propyl)-cyclohexanol
2-Azepan-1-ylmethyl-1-p-tolyl-cyclohexanol
10 2-Azepan-1-ylmethyl-1-(4-methoxy-phenyl)-cyclohexanol
2-Azepan-1-ylmethyl-1-phenyl-cyclopentanol
2-Azepan-1-ylmethyl-1-(4-chloro-phenyl)-cyclopentanol
2-Azepan-1-ylmethyl-1-benzyl-cyclopentanol
2-Azepan-1-ylmethyl-1-(4-fluoro-3-methyl-phenyl)-
15 cyclopentanol
2-Azepan-1-ylmethyl-1-o-tolyl-cyclopentanol
2-Azepan-1-ylmethyl-1-vinyl-cyclopentanol
2-Azepan-1-ylmethyl-1-(4-tert-butyl-phenyl)-cyclopentanol
2-Azepan-1-ylmethyl-bicyclopentyl-1-ol
20 2-Azepan-1-ylmethyl-1-m-tolyl-cyclopentanol
2-Azepan-1-ylmethyl-1-cyclohexyl-cyclopentanol
2-Azepan-1-ylmethyl-1-(4-fluoro-phenyl)-cyclopentanol
2-Azepan-1-ylmethyl-1-phenethyl-cyclopentanol
2-Azepan-1-ylmethyl-1-phenylethynyl-cyclopentanol
25 2-Azepan-1-ylmethyl-1-thiophen-2-yl-cyclopentanol
2-Azepan-1-ylmethyl-1-(3-methoxy-phenyl)-cyclopentanol
2-Azepan-1-ylmethyl-1-(3-phenyl-propyl)-cyclopentanol
2-Azepan-1-ylmethyl-1-p-tolyl-cyclopentanol
2-Azepan-1-ylmethyl-1-(4-methoxy-phenyl)-cyclopentanol
30 2-Azepan-1-ylmethyl-1-phenyl-cycloheptanol
2-Azepan-1-ylmethyl-1-benzyl-cycloheptanol
2-Azepan-1-ylmethyl-1-(4-fluoro-3-methyl-phenyl)-
cycloheptanol

- 2-Azepan-1-ylmethyl-1-o-tolyl-cycloheptanol
2-Azepan-1-ylmethyl-1-vinyl-cycloheptanol
2-Azepan-1-ylmethyl-1-(4-tert-butyl-phenyl)-cycloheptanol
2-Azepan-1-ylmethyl-1-cyclopentyl-cycloheptanol
5 2-Azepan-1-ylmethyl-1-m-tolyl-cycloheptanol
2-Azepan-1-ylmethyl-1-cyclohexyl-cycloheptanol
2-Azepan-1-ylmethyl-1-(4-fluoro-phenyl)-cycloheptanol
2-Azepan-1-ylmethyl-1-phenethyl-cycloheptanol
2-Azepan-1-ylmethyl-1-phenylethynyl-cycloheptanol
10 2-Azepan-1-ylmethyl-1-thiophen-2-yl-cycloheptanol
2-Azepan-1-ylmethyl-1-(2,4-dichloro-phenyl)-cycloheptanol
2-Azepan-1-ylmethyl-1-(3-methoxy-phenyl)-cycloheptanol
2-Azepan-1-ylmethyl-1-(3-phenyl-propyl)-cycloheptanol
2-Azepan-1-ylmethyl-1-p-tolyl-cycloheptanol
15 2-Azepan-1-ylmethyl-1-(4-methoxy-phenyl)-cycloheptanol
3-Ethyl-4-methyl-1-phenyl-5-pyrrolidin-1-yl-pent-1-yn-3-ol
3-Benzyl-2-methyl-1-piperidin-1-yl-pentan-3-ol
3-(4-tert-Butyl-phenyl)-2-methyl-1-piperidin-1-yl-pentan-3-ol
20 3-Cyclopentyl-2-methyl-1-piperidin-1-yl-pentan-3-ol
2-Methyl-1-piperidin-1-yl-3-m-tolyl-pentan-3-ol
3-Cyclohexyl-2-methyl-1-piperidin-1-yl-pentan-3-ol
3-(4-Fluoro-phenyl)-2-methyl-1-piperidin-1-yl-pentan-3-ol
3-Ethyl-2-methyl-5-phenyl-1-piperidin-1-yl-pentan-3-ol
25 3-Ethyl-4-methyl-1-phenyl-5-piperidin-1-yl-pent-1-yn-3-ol
2-Azepan-1-ylmethyl-1-(3-phenyl-propyl)-cyclopentanol
2-Azepan-1-ylmethyl-1-(2,3-dichloro-phenyl)-cyclopentanol
1-Benzyl-2-piperidin-1-ylmethyl-cyclododecanol
1-(4-tert-Butyl-phenyl)-2-piperidin-1-ylmethyl-
30 cyclododecanol
1-Cyclopentyl-2-piperidin-1-ylmethyl-cyclododecanol
1-Cyclohexyl-2-piperidin-1-ylmethyl-cyclododecanol
1-Phenethyl-2-piperidin-1-ylmethyl-cyclododecanol

- 1-Phenylethynyl-2-piperidin-1-ylmethyl-cyclododecanol
2-Piperidin-1-ylmethyl-1-thiophen-2-yl-cyclododecanol
1-(3-Phenyl-propyl)-2-piperidin-1-ylmethyl-cyclododecanol
1-(4-Methoxy-phenyl)-2-piperidin-1-ylmethyl-cyclododecanol
5 2-Azepan-1-ylmethyl-1-benzyl-cyclododecanol
2-Azepan-1-ylmethyl-1-vinyl-cyclododecanol
2-Azepan-1-ylmethyl-1-(4-tert-butyl-phenyl)-cyclododecanol
2-Azepan-1-ylmethyl-1-phenethyl-cyclododecanol
2-Azepan-1-ylmethyl-1-(3-phenyl-propyl)-cyclododecanol
10 1-Phenyl-2-pyrrolidin-1-ylmethyl-cyclododecanol
1-(4-Chloro-phenyl)-2-pyrrolidin-1-ylmethyl-cyclododecanol
1-(4-tert-Butyl-phenyl)-2-pyrrolidin-1-ylmethyl-
cyclododecanol
1-Cyclopentyl-2-pyrrolidin-1-ylmethyl-cyclododecanol
15 1-(4-Fluoro-3-methyl-phenyl)-2-pyrrolidin-1-ylmethyl-
cyclooctanol
2-Pyrrolidin-1-ylmethyl-1-o-tolyl-cyclooctanol
2-Pyrrolidin-1-ylmethyl-1-vinyl-cyclooctanol
2-Piperidin-1-ylmethyl-1-p-tolyl-cyclooctanol
20 1-Cyclohexylmethyl-2-pyrrolidin-1-ylmethyl-cyclohexanol
1-(4-Chloro-3-trifluormethyl-phenyl)-2-pyrrolidin-1-
ylmethyl-cycloheptanol
1-(3-Fluoro-benzyl)-2-pyrrolidin-1-ylmethyl-cycloheptanol
2-Azepan-1-ylmethyl-1-(3-fluoro-phenyl)-cyclohexanol
25 2-Azepan-1-ylmethyl-1-(3-chloro-phenyl)-cyclohexanol
2-Azepan-1-ylmethyl-1-cyclohexylmethyl-cyclopentanol
2-Azepan-1-ylmethyl-1-(2-chloro-6-fluoro-benzyl)-
cyclopentanol
2-Azepan-1-ylmethyl-1-(2,5-dimethyl-benzyl)-cyclopentanol
30 2-Azepan-1-ylmethyl-1-(4-fluoro-benzyl)-cycloheptanol
2-Azepan-1-ylmethyl-1-(3-methoxy-benzyl)-cycloheptanol
2-Azepan-1-ylmethyl-1-(3-methoxy-benzyl)-cycloheptanol
1-Azepan-1-yl-3-cyclohexylmethyl-2-methyl-pentan-3-ol

1-Azepan-1-yl-3-(5-fluoro-2-methoxy-phenyl)-2-methyl-pentan-3-ol

2-Azepan-1-ylmethyl-1-(3-fluoro-benzyl)-cyclopentanol

1-(4-Fluoro-benzyl)-2-piperidin-1-ylmethyl-cyclododecanol

5 1-(3-Fluoro-benzyl)-2-piperidin-1-ylmethyl-cyclododecanol

1-(2-Chloro-benzyl)-2-pyrrolidin-1-ylmethyl-cyclododecanol

1-(3-Chloro-phenyl)-2-pyrrolidin-1-ylmethyl-cyclooctanol

2-Azepan-1-ylmethyl-1-(3-phenyl-propyl)-cyclooctanol

- 10 The pharmaceutical preparations according to the invention may contain the compounds of formula I, preferably of the general formula II or III, in the form of the enantiomers thereof or the diastereomers thereof or in the form of a mixture of at least two of the above-stated stereoisomers, including the racemates thereof.

The pharmaceutical preparations according to the invention are preferably suitable for the treatment of pain, as an antiemetic and/or a nootropic (neurotropic), for the treatment of cardiovascular diseases, urinary incontinence, diarrhoea, pruritus, dependency on alcohol and/or drugs and/or medicines, and/or inflammation, for the treatment of depression, to increase vigilance and/or libido.

- 25 The invention also provides the use of substituted aminoalcohols of the general formula I, preferably of the general formula II or III, with the exception of compounds of the formula Ia, to produce pharmaceutical preparations for the treatment of pain as well as the use of substituted aminoalcohols of the general formula I, preferably of the general formula II or III, for the treatment of emesis, cardiovascular diseases, urinary incontinence, diarrhoea, pruritus, dependency on alcohol and/or drugs and/or

medicines, and/or inflammation, for the treatment of depression, to increase drive, vigilance and/or libido.

The pharmaceutical preparations according to the invention
5 may be formulated as liquid, semisolid or solid dosage forms, for example in the form of solutions for injection, drops, succi, syrups, sprays, suspensions, tablets, patches, capsules, dressings, suppositories, ointments, creams, lotions, gels, emulsions, aerosols or in
10 multiparticulate form, for example in the form of pellets or granules, and also be administered as such.

In addition to at least one compound of the general formula I, preferably of the general formula II or III, the
15 pharmaceutical preparations according to the invention conventionally contain further physiologically acceptable pharmaceutical auxiliary substances, which are preferably selected from the group consisting of matrix materials, fillers, solvents, diluents, surface-active substances,
20 dyes, preservatives, suspending agents, slip agents, lubricants, aromas and binders.

Selection of the physiologically acceptable auxiliary substances and the quantities thereof which are to be used
25 depends upon whether the pharmaceutical preparation is to be administered orally, subcutaneously, parenterally, intravenously, intraperitoneally, intradermally, intramuscularly, intranasally, buccally, rectally or topically, for example onto infections of the skin, mucous
30 membranes and eyes. Preparations in the form of tablets, coated tablets, capsules, granules, pellets, drops, succi and syrups are preferred for oral administration, while solutions, suspensions, readily reconstitutible dried

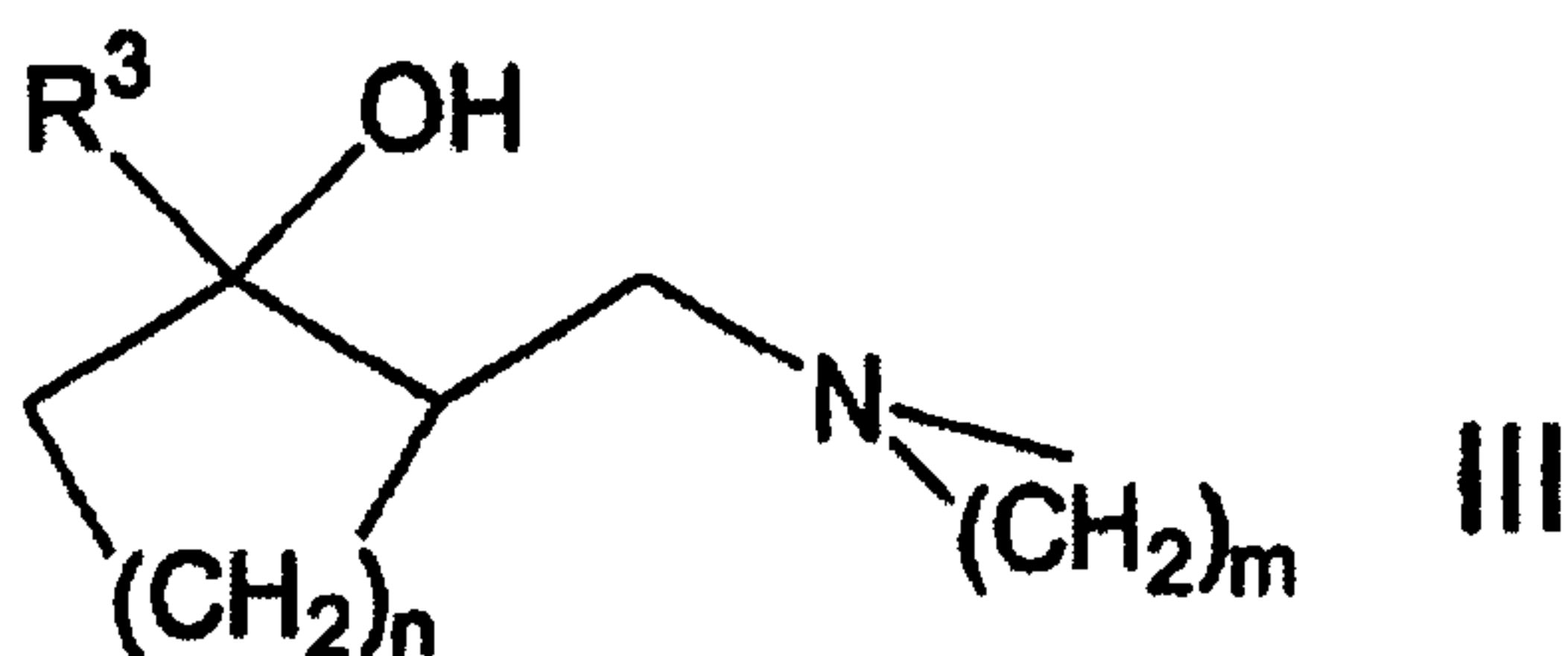
preparations and sprays are preferred for parenteral, topical and inhalatory administration. Compounds of the general formula I, preferably of the general formula II or III, in a depot in dissolved form or in a dressing, optionally with the addition of skin penetration promoters, are suitable percutaneous administration preparations.

Production of the pharmaceutical preparations according to the invention proceeds with the assistance of conventional means, devices, methods and processes known to the person skilled in the art, such as are described for example in "Remington's Pharmaceutical Sciences", ed. A.R. Gennaro, 17th ed., Mack Publishing Company, Easton, Pa. (1985), in particular in part 8, chapters 76 to 93. The corresponding literature description is hereby introduced as a reference and is deemed to be part of the disclosure.

The quantity of the respective compound of the general formula I, preferably of the general formula II or III, to be administered to the patient may vary and is for example dependent on the weight or age of the patient and on the mode of administration, the indication and the severity of the complaint. Conventionally, at least one compound of the general formula I, preferably of the general formula II or III, is administered in a quantity of 0.005 to 500 mg/kg, preferably of 0.05 to 5 mg/kg, of patient body weight.

The invention further provides 2-(aminomethyl)-cycloalkan-1-ol compounds of the general formula III,

19



in which

n denotes an integer from 2-9 and m denotes an integer from 4-6 in the following combinations,

5

n	m
2	4
2	6
3	6
4	4
4	6
5	4
5	5
5	6
9	4
9	5
9	6

wherein optionally one or more CH₂ groups of the (CH₂)_m chain may be replaced by oxygen,

- 10 R³ denotes a linear or branched, saturated or unsaturated aliphatic residue, a saturated or unsaturated cycloaliphatic residue, an aryl residue or a heteroaryl residue, wherein the respective ring system may be optionally mono- or polysubstituted and/or attached via a
- 15 linear or branched, saturated or unsaturated aliphatic

bridge and/or the aryl or heteroaryl residue may be part of a polycyclic system

in the form of the pure diastereomers thereof, the pure
5 enantiomers thereof and mixtures thereof - including the racemates thereof - and in the form of corresponding bases, salts and solvates.

Compounds of the general formula III are preferred, in
10 which

R^3 denotes a linear or branched, saturated or unsaturated aliphatic C_{1-6} residue, a saturated or unsaturated cycloaliphatic C_{3-7} residue, a phenyl residue or a five- or
15 six-membered heteroaryl residue, wherein the respective ring system may optionally be mono- or polysubstituted and/or attached via a linear or branched, saturated or unsaturated aliphatic C_{1-5} bridge,

20 and the other symbols have the above-stated meaning.

Compounds of the general formula III are additionally preferred, in which

25 R^3 denotes a linear or branched, saturated or unsaturated aliphatic C_{1-3} residue, a saturated or unsaturated cycloaliphatic C_{5-6} residue, a phenyl residue or a five- or six-membered heteroaryl residue, wherein the respective ring system may optionally be mono- or polysubstituted with
30 halogen, an alkyl group, an alkoxy group and/or a trihalogenated alkyl group and/or may be attached via a linear or branched, saturated or unsaturated aliphatic C_{1-3} bridge

and the other symbols have the above-stated meaning.

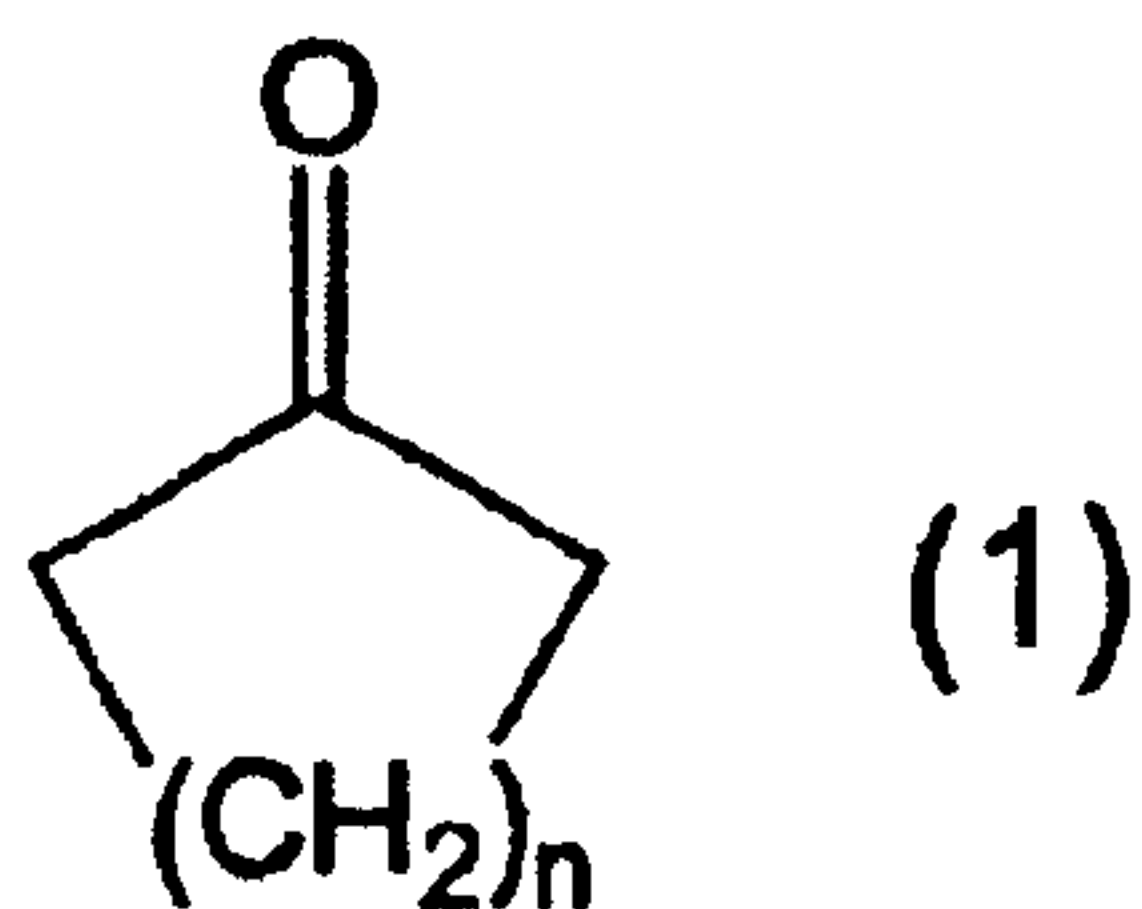
Compounds of the general formula III are additionally
5 preferred, in which

R^3 denotes a vinyl residue, a cyclopentyl residue, a
cyclohexyl residue, a thiophenyl residue or a phenyl
residue, wherein the cyclohexyl residue may optionally be
10 attached via a methylene bridge or the phenyl residue may
optionally be mono- or polysubstituted with fluorine,
chlorine, a methyl group, an isopropyl group, a methoxy
group and/or a trifluoromethyl group and/or may optionally
be attached via a linear saturated aliphatic C_{1-3} bridge or
15 an ethynyl bridge

and the other symbols have the above-stated meaning.

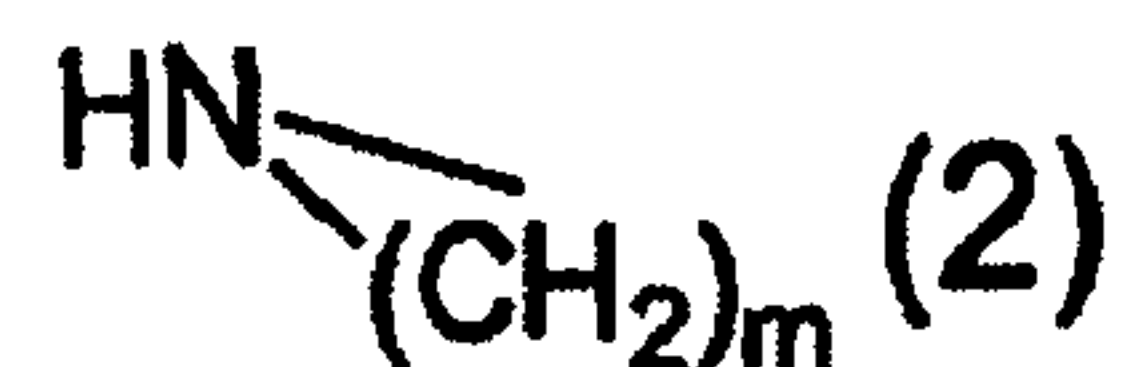
The invention also provides a process for the production of
20 compounds according to any one of claims 25-28,
characterised in that

A) a ketone of the formula (1), in which n has the
meaning stated in claim 25,

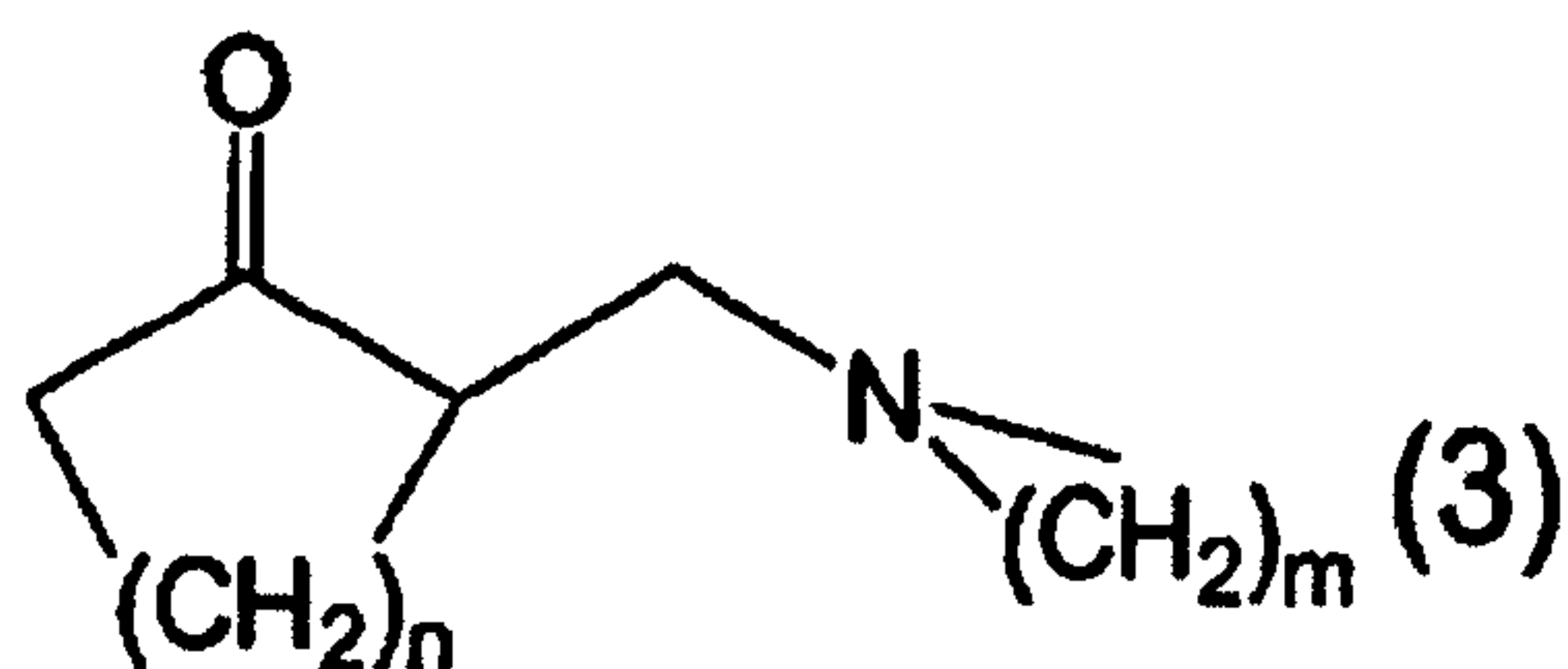


25

is reacted with paraformaldehyde and a cyclic amine of
the formula (2), in which m has the meaning stated in
claim 25,



according to a Mannich reaction in a suitable solvent,
preferably in ethanol with the addition of
5 hydrochloric acid or in acetic acid, with heating,
then the reaction mixture is worked up and the product
of the formula (3) is isolated and optionally purified
or



10

B) a compound of the formula (3) is reacted with a
Grignard compound or an organolithium compound of the
formulae R^3MgCl , R^3MgBr , R^3MgI , MgR^3_2 or LiR^3 , in which
 R^3 has the meaning stated in claim 25, in a suitable
15 solvent, preferably diethyl ether or tetrahydrofuran,
then the reaction mixture is worked up and the
compound of the general formula I is isolated and
optionally purified.

20 The starting compounds used are commercially obtainable or
may be obtained using conventional methods known to the
person skilled in the art.

The reactions are known to the person skilled in the art
25 from the literature.

The solvents and reaction conditions used for the
respective process step correspond to the solvents and

reaction conditions conventional for these types of reactions.

The free bases of the respective compounds according to the invention of the general formula III may be converted into the corresponding physiologically acceptable salts by reaction with an inorganic or organic acid, preferably with hydrochloric acid, hydrobromic acid, sulfuric acid, phosphoric acid, methanesulfonic acid, p-toluenesulfonic acid, carbonic acid, formic acid, acetic acid, oxalic acid, succinic acid, tartaric acid, mandelic acid, fumaric acid, lactic acid, citric acid, glutamic acid or aspartic acid. The salts formed comprise, inter alia, hydrochlorides, hydrobromides, phosphates, carbonates, hydrogencarbonates, formates, acetates, oxalates, succinates, tartrates, fumarates, citrates and glutamates.

The free bases of the respective compounds according to the invention of the general formula III may be converted into the corresponding hydrochlorides by combining the compounds according to the invention of the general formula I as free bases dissolved in a suitable organic solvent, such as for example butan-2-one (methyl ethyl ketone), with trimethylsilyl chloride (TMSCl). They may also be converted into the hydrobromides in a corresponding manner.

The hydrates may be formed by crystallisation from an aqueous solution.

If the compounds according to the invention of the general formula III are obtained by the production process according to the invention in the form of the racemates thereof or other mixtures of their various enantiomers

and/or diastereomers, these may be separated and optionally isolated by conventional processes known to the person skilled in the art. Examples are chromatographic separation processes, in particular liquid chromatography processes at
5 standard pressure or at elevated pressure, preferably MPLC and HPLC processes, and fractional crystallisation processes. Individual enantiomers, e.g. diastereomeric salts formed by means of HPLC on a chiral phase or by means of crystallisation with chiral acids, such as (+)-tartaric
10 acid, (-)-tartaric acid or (+)-10-camphorsulfonic acid, may here in particular be separated from one another.

The compounds of the general formula III according to the invention are toxicologically safe and are therefore
15 suitable as pharmaceutical active ingredients in pharmaceutical preparations.

Examples

Preparation

5 Mannich reaction

One equivalent of the amine hydrochloride, 1-1.5 equivalents of the ketone and 1-1.2 equivalents of paraformaldehyde in 8-10 equivalents of acetic acid were heated with stirring for 15-20 minutes to 95-98°C. Then the
10 acetic acid was removed by vacuum-distillation under mild conditions and the reaction mixture combined with acetone or successively with acetone and diisopropyl ether. The Mannich compound precipitated out in crystalline form as the hydrochloride.

15 It was possible, in some cases, advantageously to perform the Mannich reaction in ethanol, combined with a few drops of concentrated hydrochloric acid, with refluxing for several hours (at most 5 to 7 hours).

Further purification of the Mannich compound was effected,
20 where necessary, by silica gel chromatography with ethyl acetate as eluent.

Grignard reaction

The Mannich compound dissolved in THF (400 μ l, 0.5 M) was
25 initially introduced into a heat-treated reaction vessel cooled to -10°C under inert gas. 2 equivalents of the prepared Grignard or organolithium reagent in THF or diethyl ether (800 μ l, 0.5 M) were then added with stirring. The reaction mixture was stirred at room
30 temperature. After three hours it was re-cooled to -10°C and hydrolysed with ammonium chloride solution.

The reaction mixture was extracted twice with ethyl acetate and vacuum-evaporated at 40°C.

To characterise the product, an ESI-MS spectrograph was recorded.

Biological data

5

Investigations relating to noradrenaline reuptake inhibition (NA uptake inhibition)

The compounds according to the invention are NA uptake
10 inhibitors.

In order to be able to carry out these in vitro studies, synaptosomes were freshly isolated from rat brain regions. A so-called "P₂" fraction was used, which was prepared
15 according to the instructions given by Gray and Whittaker (E.G. Gray and V.P. Whittaker (1962) J. Anat. 76, 79-88). For NA uptake, these vesicular particles were isolated from the hypothalamus of male rat brains.

20 The following characteristics were determined for the NA transporter:

NA uptake: $K_m = 0.32 \pm 0.11 \mu M$

25 (In each case $N = 4$, i.e. means $\pm$ SEM from 4 independent series of tests, which were performed as parallel tests in triplicate).

A detailed description of the method may be found in the
30 literature (M.Ch. Frink, H.-H. Hennies, W. Englberger, M. Haurand and B. Wilffert (1996) *Arzneim.-Forsch./Drug Res.* 46 (III), 11, 1029-1036).

The NA uptake inhibition of selected compounds was determined. The values were determined at a test concentration of 10^{-5} M.

Example	NA Uptake (% inhibition)
1-(2,3-Dichloro-phenyl)-2-pyrrolidin-1-ylmethyl-cyclohexanol	60
2-Pyrrolidin-1-ylmethyl-1-p-tolyl-cyclohexanol	59
1-(4-Chloro-phenyl)-2-pyrrolidin-1-ylmethyl-cyclopentanol	68
1-(4-Fluoro-3-methyl-phenyl)-2-pyrrolidin-1-ylmethyl-cyclopentanol	59
2-Pyrrolidin-1-ylmethyl-1-m-tolyl-cyclopentanol	52
1-Phenethyl-2-pyrrolidin-1-ylmethyl-cyclopentanol	59
1-Phenylethynyl-2-pyrrolidin-1-ylmethyl-cyclopentanol	92
1-(3-Phenyl-propyl)-2-pyrrolidin-1-ylmethyl-cyclopentanol	65
1-(2,3-Dichloro-phenyl)-2-pyrrolidin-1-ylmethyl-cyclopentanol	53
2-Pyrrolidin-1-ylmethyl-1-p-tolyl-cyclopentanol	78
1-Phenyl-2-pyrrolidin-1-ylmethyl-cycloheptanol	56
1-(4-Chloro-phenyl)-2-pyrrolidin-1-ylmethyl-cycloheptanol	75
1-(4-Fluoro-3-methyl-phenyl)-2-pyrrolidin-1-ylmethyl-cycloheptanol	83
2-Pyrrolidin-1-ylmethyl-1-m-tolyl-cycloheptanol	67
1-(4-Fluoro-phenyl)-2-pyrrolidin-1-ylmethyl-cycloheptanol	57
1-Phenethyl-2-pyrrolidin-1-ylmethyl-cycloheptanol	82
1-Phenylethynyl-2-pyrrolidin-1-ylmethyl-cycloheptanol	66
1-(2,4-Dichloro-phenyl)-2-pyrrolidin-1-ylmethyl-cycloheptanol	55
1-(3-Phenyl-propyl)-2-pyrrolidin-1-ylmethyl-cycloheptanol	63
1-(2,3-Dichloro-phenyl)-2-pyrrolidin-1-ylmethyl-cycloheptanol	63
2-Pyrrolidin-1-ylmethyl-1-p-tolyl-cycloheptanol	76
1-(4-Methoxy-phenyl)-2-pyrrolidin-1-ylmethyl-cycloheptanol	69
2-Azepan-1-ylmethyl-1-(4-fluoro-3-methyl-phenyl)-cyclohexanol	54
2-Azepan-1-ylmethyl-1-(4-fluoro-phenyl)-cyclohexanol	52
2-Azepan-1-ylmethyl-1-phenethyl-cyclohexanol	70
2-Azepan-1-ylmethyl-1-(3-phenyl-propyl)-cyclohexanol	77
2-Azepan-1-ylmethyl-1-p-tolyl-cyclohexanol	64
2-Azepan-1-ylmethyl-1-(4-methoxy-phenyl)-cyclohexanol	58
2-Azepan-1-ylmethyl-1-(4-chloro-phenyl)-cyclopentanol	80
2-Azepan-1-ylmethyl-1-(4-fluoro-3-methyl-phenyl)-cyclopentanol	73
2-Azepan-1-ylmethyl-1-m-tolyl-cyclopentanol	59
2-Azepan-1-ylmethyl-1-phenethyl-cyclopentanol	92
2-Azepan-1-ylmethyl-1-phenylethynyl-cyclopentanol	99
2-Azepan-1-ylmethyl-1-thiophen-2-yl-cyclopentanol	51
2-Azepan-1-ylmethyl-1-(3-phenyl-propyl)-cyclopentanol	59
2-Azepan-1-ylmethyl-1-p-tolyl-cyclopentanol	70
2-Azepan-1-ylmethyl-1-(4-methoxy-phenyl)-cyclopentanol	58
2-Azepan-1-ylmethyl-1-phenyl-cycloheptanol	52
2-Azepan-1-ylmethyl-1-benzyl-cycloheptanol	55

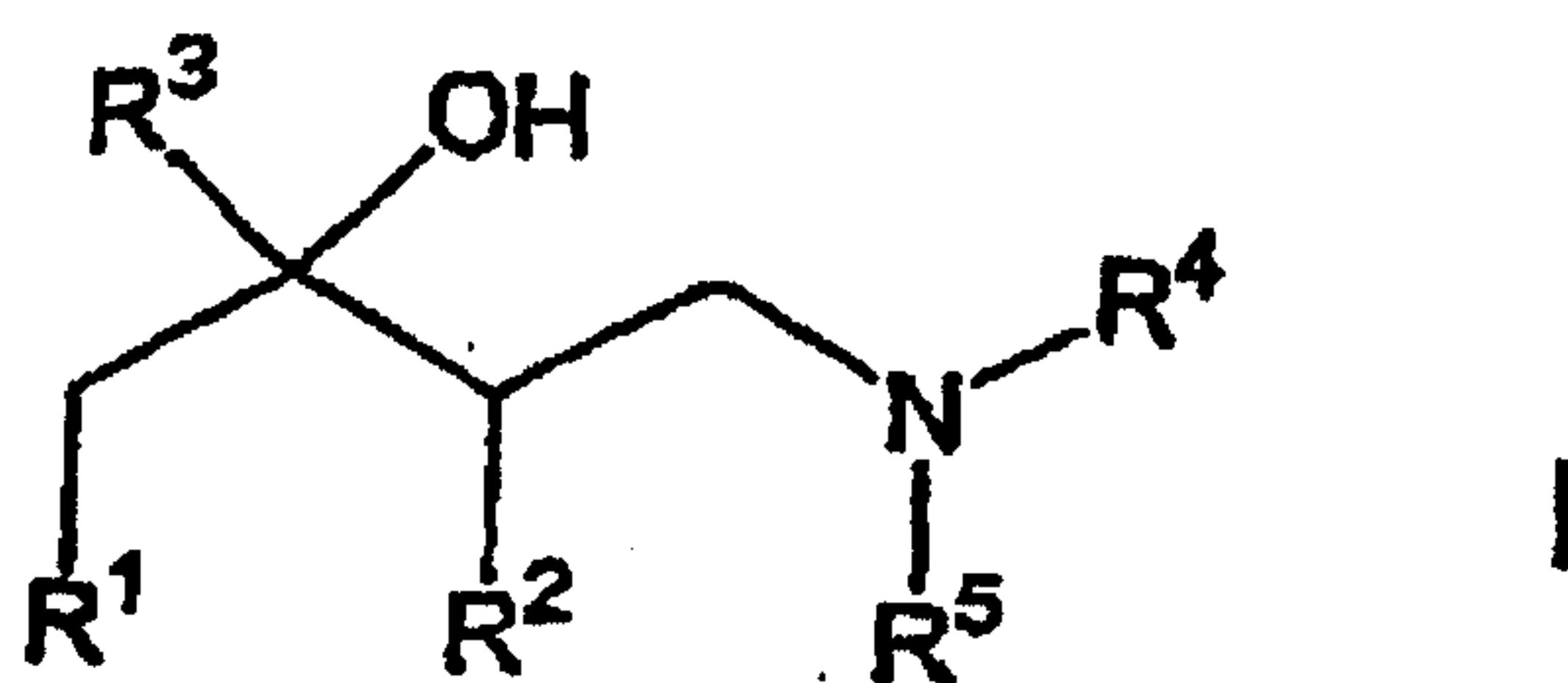
Example	NA Uptake (% inhibition)
2-Azepan-1-ylmethyl-1-(4-fluoro-3-methyl-phenyl)- cycloheptanol	63
2-Azepan-1-ylmethyl-1-phenethyl-cycloheptanol	87
2-Azepan-1-ylmethyl-1-p-tolyl-cycloheptanol	58
2-Azepan-1-ylmethyl-1-(4-methoxy-phenyl)-cycloheptanol	58
3-Ethyl-4-methyl-1-phenyl-5-pyrrolidin-1-yl-pent-1-yn-3-ol	76

29

Claims

1. A pharmaceutical preparation containing at least one substituted aminoalcohol of the general formula I,

5



in which

10 R^1 and R^2 , identical or different, in each case denote a linear or branched, saturated or unsaturated aliphatic residue,

15 R^3 denotes a linear or branched, saturated or unsaturated aliphatic residue, a saturated or unsaturated cycloaliphatic residue or a heteroaryl residue, wherein the respective ring system may be optionally mono- or polysubstituted and/or attached via a linear or branched, saturated or unsaturated aliphatic bridge and/or the heteroaryl residue may be
20 part of a polycyclic system or denote an aryl residue, wherein the ring system may be optionally mono- or polysubstituted and/or attached via a linear or branched, unsaturated aliphatic bridge and/or the aryl residue may be part of a polycyclic system,

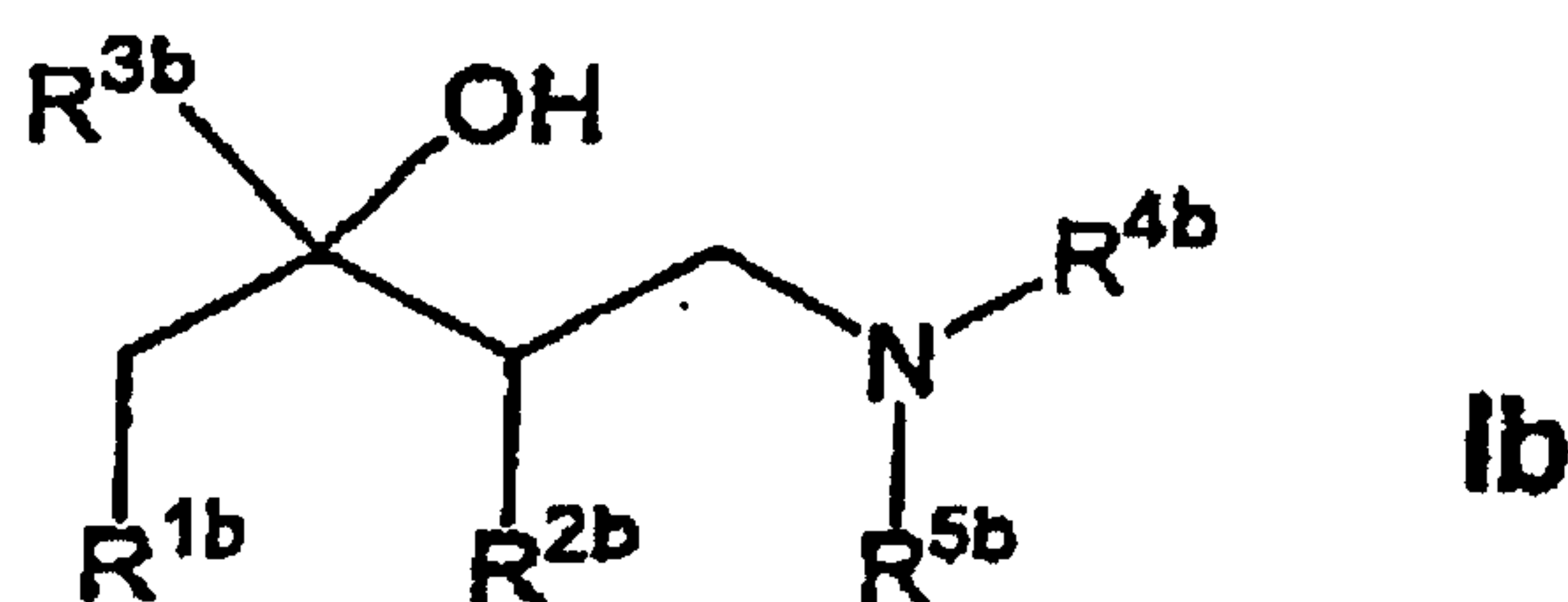
25

R^4 and R^5 together form a $(CH_2)_m$ chain, wherein m denotes an integer and optionally one or more CH_2 groups may be replaced by oxygen,

30

in the form of the diastereomers thereof, the
enantiomers thereof and mixtures thereof - including
the racemates thereof - and in the form of
corresponding bases, salts and solvates as active
ingredient

with the exception of compounds of the general
formula Ib,



in which

R^{1b} denotes a lower alkyl residue,

R^{2b} denotes a lower alkyl residue,

R^{4b} and R^{5b} together form a pyrrolidine or a piperidine
ring and

R^{3b} denotes one of the following residues,



in which

3\

R^I denotes hydrogen, a lower alkyl residue or a lower alkoxy residue,

R^{II} denotes hydrogen or a lower alkyl residue,

5

R^{III} denotes hydrogen, halogen, a trihalomethyl residue, a lower alkyl residue or a lower alkoxy residue and

10

R^{IV} denotes a lower alkoxy residue,

and with the exception of 3-(4-methylphenol)-2-n-propyl-1-pyrrolidin-1-ylpentan-3-ol and 3-(phenyl)-2-n-propyl-1-pyrrolidin-1-ylpentan-3-ol

15

and optionally physiologically acceptable auxiliary substances.

2. A pharmaceutical preparation containing at least one compound according to claim 1, characterised in that

20

R^1 and R^2 , identical or different, in each case denote a linear or branched, saturated or unsaturated aliphatic C_{1-6} residue,

25

R^3 denotes a linear or branched, saturated or unsaturated aliphatic C_{1-6} residue, a saturated or unsaturated cycloaliphatic C_{3-7} residue or a five- or six-membered heteroaryl residue, wherein the

30

respective ring system may optionally be mono- or polysubstituted and/or may be attached via a linear or branched, saturated or unsaturated aliphatic C_{1-5} bridge, or denotes a phenyl residue, wherein the ring

32

system may optionally be mono- or polysubstituted and/or may be attached via a linear or branched, unsaturated aliphatic C₁₋₅ bridge,

5 R⁴ and R⁵ together form a (CH₂)_m chain, wherein m denotes an integer from 4-6 and optionally one or more CH₂ groups may be replaced by oxygen.

10 3. A pharmaceutical preparation containing at least one compound according to claim 1, characterised in that

R¹ and R², identical or different, in each case denote a linear or branched, saturated or unsaturated aliphatic C₁₋₃ residue,

15

R³ denotes a linear or branched, saturated or unsaturated aliphatic C₁₋₃ residue, a saturated or unsaturated cycloaliphatic C₅₋₆ residue or a five- or six-membered heteroaryl residue, wherein the

20

respective ring system may optionally be mono- or polysubstituted with halogen, an alkyl group, an alkoxy group and/or a trihalogenated alkyl group and/or may be attached via a linear or branched,

saturated or unsaturated aliphatic C₁₋₃ bridge, or

25

denotes a phenyl residue, wherein the ring system may optionally be mono- or polysubstituted with halogen, an alkyl group, an alkoxy group and/or a

trihalogenated alkyl group and/or may be attached via a linear or branched, unsaturated aliphatic C₁₋₃

30

bridge,

33

R^4 and R^5 together form a $(CH_2)_m$ chain, wherein m denotes an integer from 4-6 and optionally one or more CH_2 groups may be replaced by oxygen.

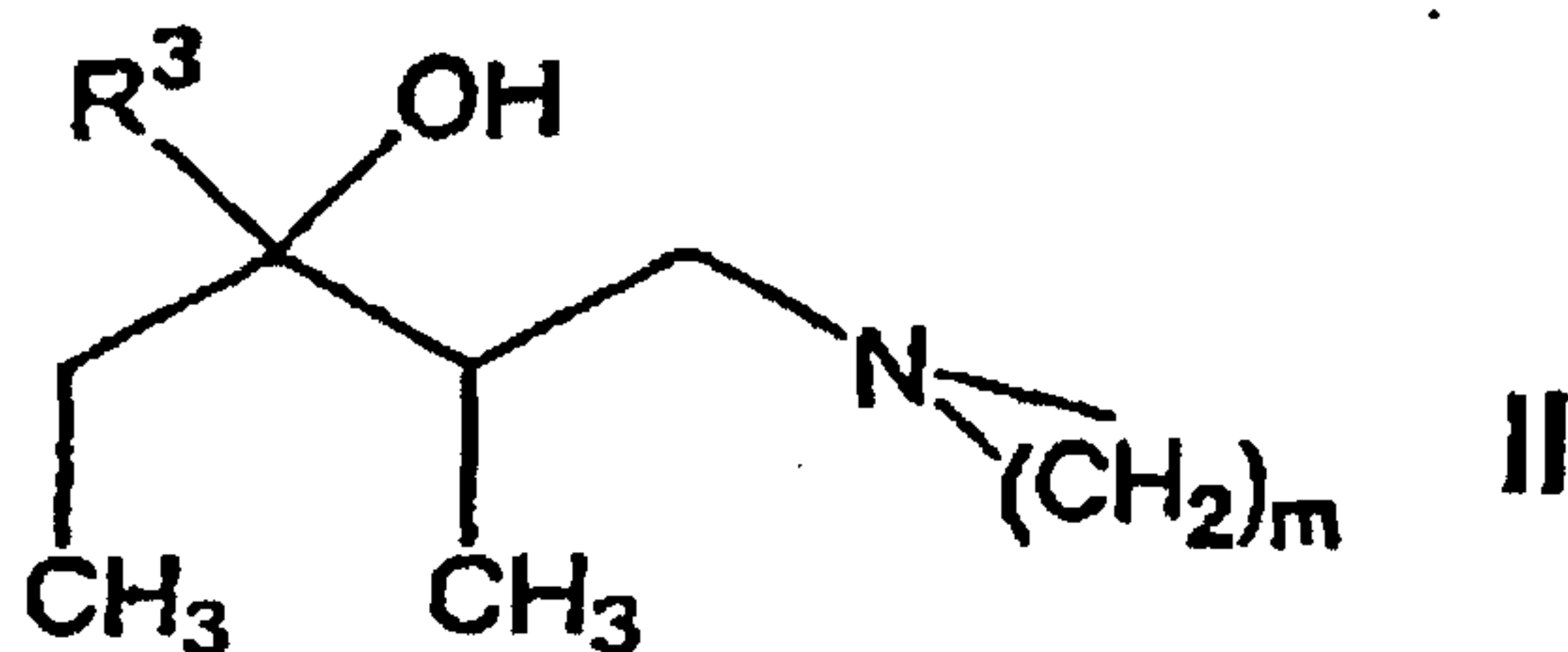
- 5 4. A pharmaceutical preparation containing at least one compound according to claim 1, characterised in that

R^1 and R^2 in each case denote a methyl group,

- 10 R^3 denotes a vinyl residue, a cyclopentyl residue, a cyclohexyl residue, a thiophenyl residue or a phenyl residue, wherein the cyclohexyl residue may optionally be attached via a methylene bridge or the phenyl residue may optionally be mono- or polysubstituted
15 with fluorine, chlorine, a methyl group, an isopropyl group, a methoxy group and/or a trifluoromethyl group and/or attached via a ethynyl bridge,

- 20 R^4 and R^5 together form a $(CH_2)_m$ chain, wherein m denotes 4, 5 or 6.

5. A pharmaceutical preparation containing at least one compound according to claim 1 corresponding to the general formula II,



25

in which

m denotes an integer from 4-6.

34

6. A pharmaceutical preparation containing at least one compound according to claim 5, characterised in that

5 R³ denotes a linear or branched, saturated or unsaturated aliphatic C₁₋₆ residue, a saturated or unsaturated cycloaliphatic C₃₋₇ residue or a five- or six-membered heteroaryl residue, wherein the respective ring system may optionally be mono- or polysubstituted and/or may be attached via a linear or
10 branched, saturated or unsaturated aliphatic C₁₋₅ bridge, or denotes a phenyl residue, wherein the ring system may optionally be mono- or polysubstituted and/or may be attached via a linear or branched, unsaturated C₁₋₅ bridge.

15

7. A pharmaceutical preparation containing at least one compound according to claim 5, characterised in that

20 R³ denotes a linear or branched, saturated or unsaturated aliphatic C₁₋₃ residue, a saturated or unsaturated cycloaliphatic C₅₋₆ residue or a five- or six-membered heteroaryl residue, wherein the respective ring system may optionally be mono- or polysubstituted with halogen, an alkyl group, an
25 alkoxy group and/or a trihalogenated alkyl group and/or may be attached via a linear or branched, saturated or unsaturated aliphatic C₁₋₃ bridge, or denotes a phenyl residue, the ring system of which may optionally be mono- or polysubstituted with halogen,
30 an alkyl group, an alkoxy group and/or a trihalogenated alkyl group and/or may be attached via a linear or branched, unsaturated aliphatic C₁₋₃ bridge.

8. A pharmaceutical preparation containing at least one compound according to claim 5, characterised in that
- 5 R^3 denotes a vinyl residue, a cyclopentyl residue, a cyclohexyl residue, a thiophenyl residue or a phenyl residue, wherein the cyclohexyl residue may optionally be attached via a methylene bridge or the phenyl residue may optionally be mono- or polysubstituted
- 10 with fluorine, chlorine, a methyl group, an isopropyl group, a methoxy group and/or a trifluoromethyl group and/or attached via a ethynyl bridge.
9. A pharmaceutical preparation containing at least one
- 15 substituted aminoalcohol according to claim 1 selected from among the group comprising
- 3-Ethyl-4-methyl-1-phenyl-5-pyrrolidin-1-yl-pent-1-yn-3-ol
- 20 3-(4-tert-Butyl-phenyl)-2-methyl-1-piperidin-1-yl-pentan-3-ol,
- 3-Cyclopentyl-2-methyl-1-piperidin-1-yl-pentan-3-ol
- 2-Methyl-1-piperidin-1-yl-3-m-tolyl-pentan-3-ol
- 3-Cyclohexyl-2-methyl-1-piperidin-1-yl-pentan-3-ol
- 25 3-(4-Fluoro-phenyl)-2-methyl-1-piperidin-1-yl-pentan-3-ol
- 3-Ethyl-4-methyl-1-phenyl-5-piperidin-1-yl-pent-1-yn-3-ol
- 1-Azepan-1-yl-3-cyclohexylmethyl-2-methyl-pentan-3-ol
- 30 1-Azepan-1-yl-3-(5-fluoro-2-methoxy-phenyl)-2-methyl-pentan-3-ol

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in the form of the diastereomers thereof, the enantiomers thereof and mixtures thereof - including the racemates thereof - and in the form of corresponding bases, salts and solvates

5

and optionally physiologically acceptable auxiliary substances.

10. A pharmaceutical preparation according to any one of
10 claims 1-9 for the treatment of pain.
11. A pharmaceutical preparation according to any one of claims 1-9 as an antiemetic.
- 15 12. A pharmaceutical preparation according to any one of claims 1-9 as a nootropic (neurotropic).
13. A pharmaceutical preparation according to any one of claims 1-9 for the treatment of cardiovascular
20 diseases.
14. A pharmaceutical preparation according to any one of claims 1-9 for the treatment of urinary incontinence.
- 25 15. A pharmaceutical preparation according to any one of claims 1-9 for the treatment of diarrhoea.
16. A pharmaceutical preparation according to any one of claims 1-9 for the treatment of pruritus.
- 30 17. A pharmaceutical preparation according to any one of claims 1-9 for the treatment of dependency on alcohol and/or drugs and/or medicines.

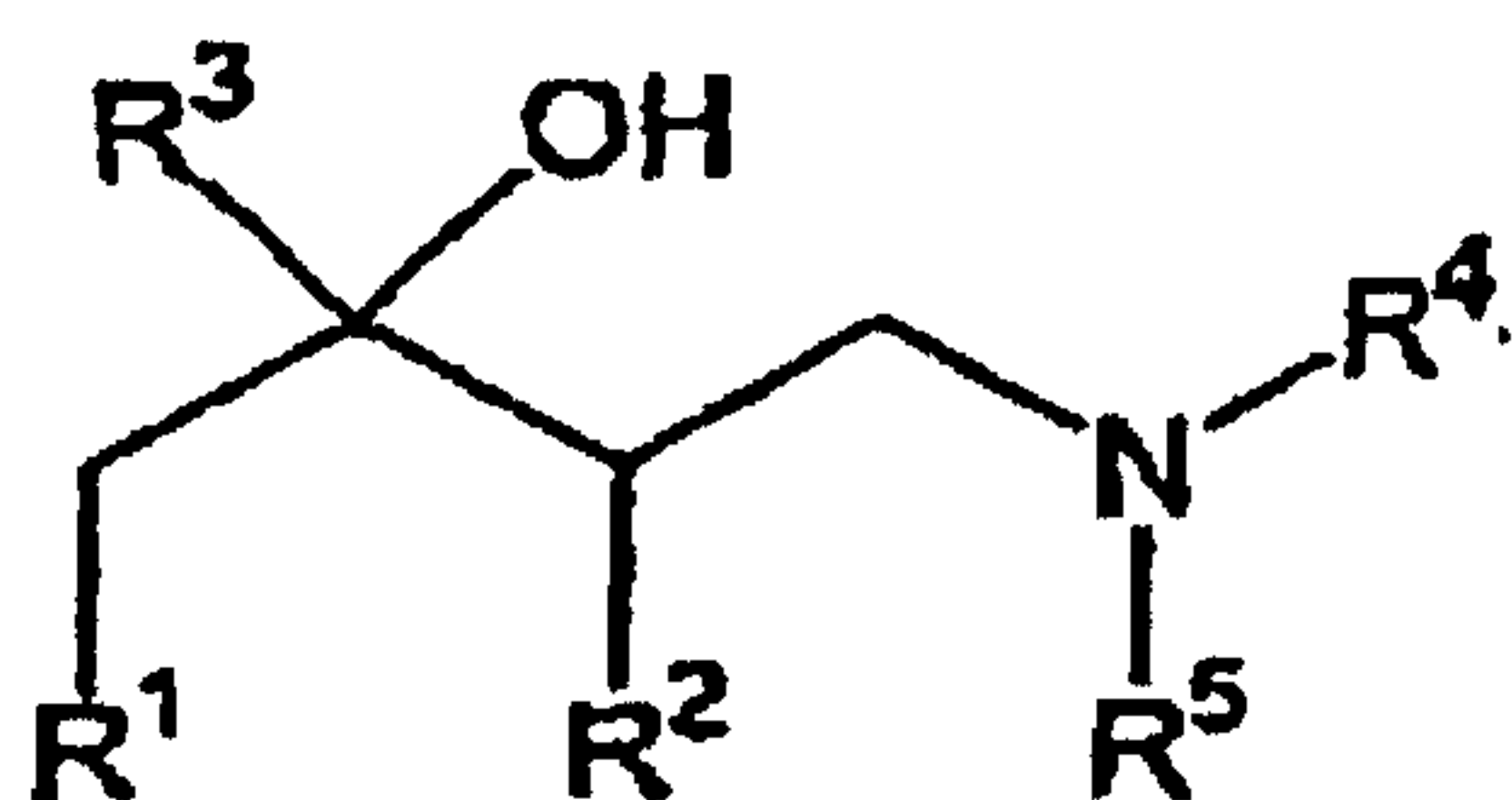
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18. A pharmaceutical preparation according to any one of claims 1-9 for the treatment of inflammation.
- 5 19. A pharmaceutical preparation according to any one of claims 1-9 for the treatment of depression.
20. A pharmaceutical preparation according to any one of claims 1-9 for increasing vigilance.
- 10 21. A pharmaceutical preparation according to any one of claims 1-9 for increasing libido.
- 15 22. Use of at least one compound according to any one of claims 1-9 with the exception of 3-(4-methylphenyl)-2-n-propyl-1-pyrrolidin-1-ylpentan-3-ol and 3-(phenyl)-2-n-propyl-1-pyrrolidin-1-ylpentan-3-ol for the production of a pharmaceutical preparation for the treatment of pain.
- 20 23. Use of at least one compound according to any one of claims 1-9 not excepting compounds for the production of a pharmaceutical preparation for the treatment of emesis, cardiovascular diseases, urinary incontinence, diarrhoea, pruritus, dependency on alcohol and/or drugs and/or medicines and/or inflammation, for the treatment of depression, to increase drive, vigilance and/or libido.
- 25 24. A pharmaceutical preparation containing at least one substituted aminoalcohol of the general formula I,
- 30

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20



I

in which

5 R^1 and R^2 together form a $(CH_2)_n$ chain, wherein n denotes an integer,

10 R^3 denotes a linear or branched, saturated or unsaturated aliphatic residue, a saturated or unsaturated cycloaliphatic residue, an aryl residue or a heteroaryl residue, wherein the respective ring system may be optionally mono- or polysubstituted and/or attached via a linear or branched, saturated or unsaturated aliphatic bridge and/or the aryl or
15 heteroaryl residue may be part of a polycyclic system,

R^4 and R^5 together form a $(CH_2)_m$ chain, wherein m denotes an integer and optionally one or more CH_2 groups may be replaced by oxygen,

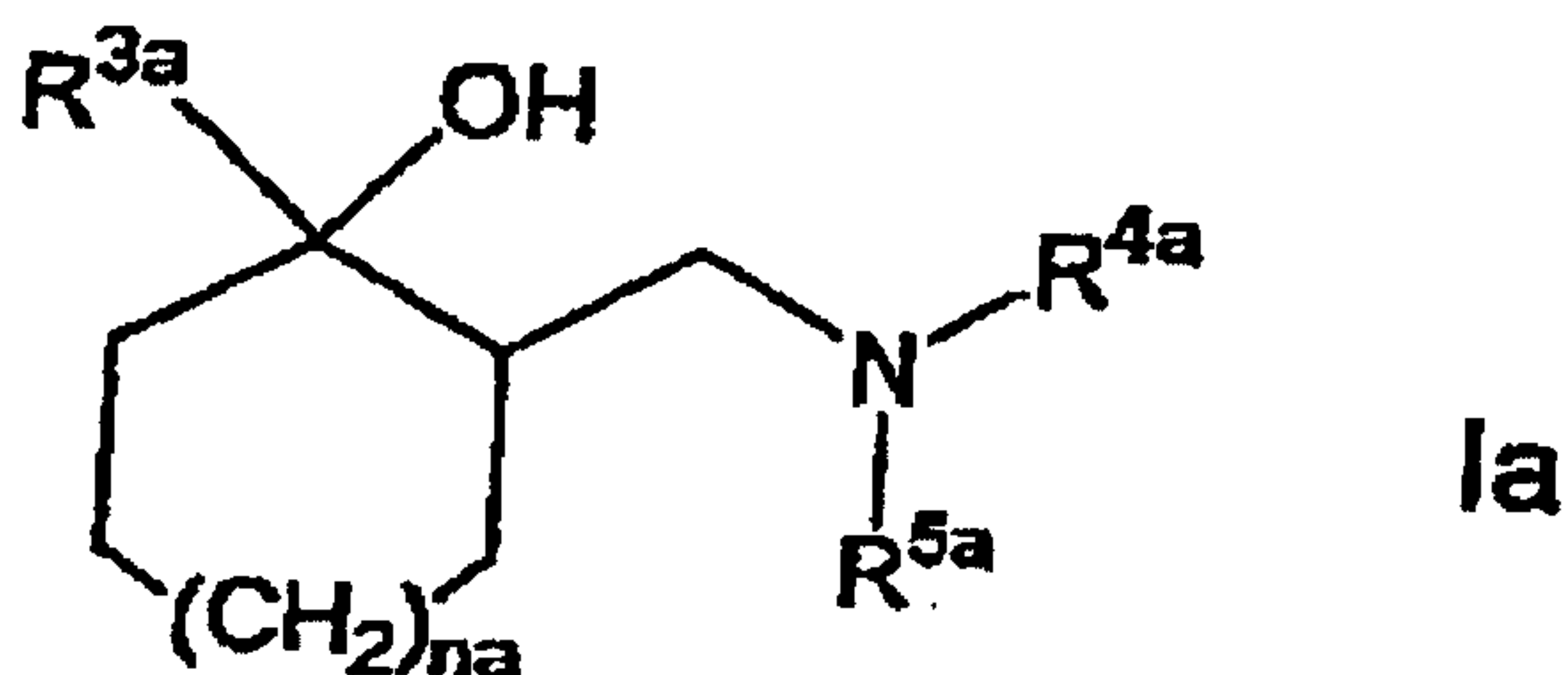
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in the form of the diastereomers thereof, the enantiomers thereof and mixtures thereof - including the racemates thereof - and in the form of corresponding bases, salts and solvates as active
25 ingredient

with the exception of compounds of the general formula Ia,

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in which

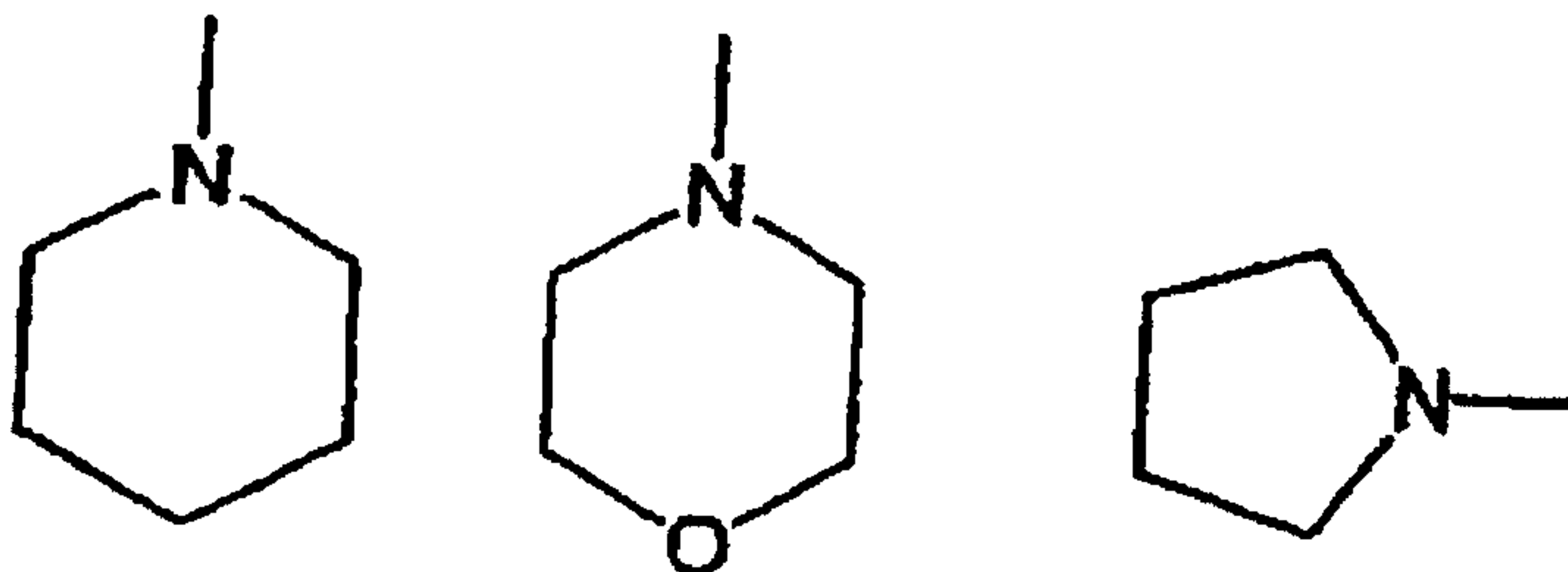
na denotes 0, 1 or 2,

5

R^{3a} denotes a phenyl residue, which is substituted in the meta position with an alkoxy group with 1-3 carbons or an aralkoxy group and

10

R^{4a} and R^{5a} together form, including the nitrogen atom, one of the rings listed hereinafter,



15

and with the exception of 1-benzyl-2-(piperidin-1-ylmethyl)-cyclohexan-1-ol and 1-phenyl-2-(piperidin-1-ylmethyl)-cyclohexan-1-ol

and optionally physiologically acceptable auxiliary substances.

20

25. A pharmaceutical preparation containing at least one compound according to claim 24, characterised in that

40

R^1 and R^2 together form a $(CH_2)_n$ chain, wherein n denotes an integer from 2-9,

5 R^3 denotes a linear or branched, saturated or unsaturated aliphatic C_{1-6} residue, a saturated or unsaturated cycloaliphatic C_{3-7} residue, a phenyl residue or a five- or six-membered heteroaryl residue, wherein the respective ring system may optionally be
10 mono- or polysubstituted and/or attached via a linear or branched, saturated or unsaturated aliphatic C_{1-5} bridge,

R^4 and R^5 together form a $(CH_2)_m$ chain, wherein m denotes an integer from 4-6 and optionally one or more
15 CH_2 groups may be replaced by oxygen.

26. A pharmaceutical preparation containing at least one compound according to claim 24, characterised in that

20 R^1 and R^2 together form a $(CH_2)_n$ chain, wherein n denotes an integer from 2-9,

R^3 denotes a linear or branched, saturated or unsaturated aliphatic C_{1-3} residue, a saturated or
25 unsaturated cycloaliphatic C_{5-6} residue, a phenyl residue or a five- or six-membered heteroaryl residue, wherein the respective ring system may optionally be mono- or polysubstituted with halogen, an alkyl group, an alkoxy group and/or a trihalogenated alkyl group
30 and/or may be attached via a linear or branched, saturated or unsaturated aliphatic C_{1-3} bridge.

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R^4 and R^5 together form a $(CH_2)_m$ chain, wherein m denotes an integer from 4-6 and optionally one or more CH_2 groups may be replaced by oxygen.

- 5 27. A pharmaceutical preparation containing at least one compound according to claim 24, characterised in that

R^1 and R^2 together form a $(CH_2)_n$ chain, wherein n denotes 2, 3, 4, 5 or 9,

10

R^3 denotes a vinyl residue, a cyclopentyl residue, a cyclohexyl residue, a thiophenyl residue or a phenyl residue, wherein the cyclohexyl residue may optionally be attached via a methylene bridge or the phenyl residue may optionally be mono- or polysubstituted with fluorine, chlorine, a methyl group, an isopropyl group, a methoxy group and/or a trifluoromethyl group and/or may optionally be attached via a linear saturated aliphatic C_{1-3} bridge or an ethynyl bridge,

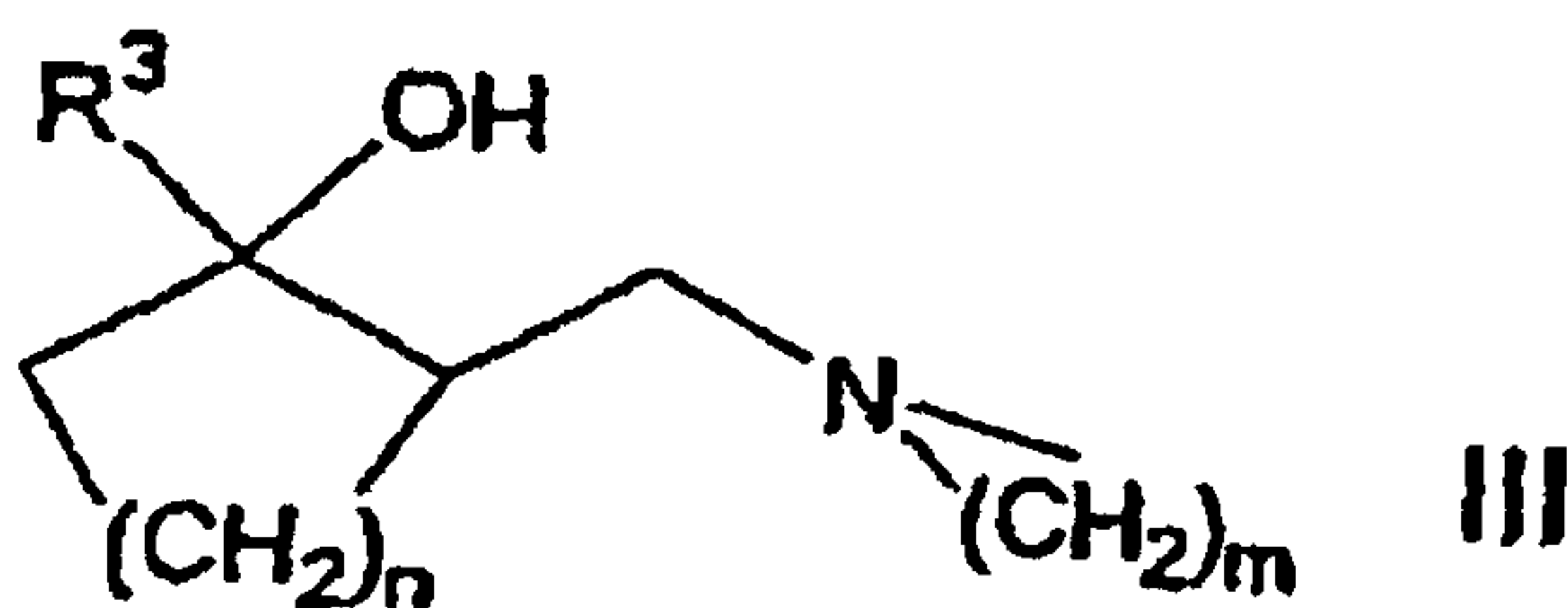
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20

R^4 and R^5 together form a $(CH_2)_m$ chain, wherein m denotes 4, 5 or 6.

28. A pharmaceutical preparation containing at least one compound according to claim 24 corresponding to the general formula III,

25



in which

n denotes an integer from 2-9 and m denotes an integer from 4-6.

29. A pharmaceutical preparation containing at least one
5 compound according to claim 28, characterised in that

10 R^3 denotes a linear or branched, saturated or unsaturated aliphatic C_{1-6} residue, a saturated or unsaturated cycloaliphatic C_{3-7} residue, a phenyl residue or a five- or six-membered heteroaryl residue, wherein the respective ring system may optionally be mono- or polysubstituted and/or attached via a linear or branched, saturated or unsaturated aliphatic C_{1-5} bridge.

15

30. A pharmaceutical preparation containing at least one
compound according to claim 28, characterised in that

20 R^3 denotes a linear or branched, saturated or unsaturated aliphatic C_{1-3} residue, a saturated or unsaturated cycloaliphatic C_{5-6} residue, a phenyl residue or a five- or six-membered heteroaryl residue, wherein the respective ring system may optionally be mono- or polysubstituted with halogen, an alkyl group,
25 an alkoxy group and/or a trihalogenated alkyl group and/or may be attached via a linear or branched, saturated or unsaturated aliphatic C_{1-3} bridge.

31. A pharmaceutical preparation containing at least one
30 compound according to claim 28, characterised in that

R^3 denotes a vinyl residue, a cyclopentyl residue, a cyclohexyl residue, a thiophenyl residue or a phenyl

residue, wherein the cyclohexyl residue may optionally be attached via a methylene bridge or the phenyl residue may optionally be mono- or polysubstituted with fluorine, chlorine, a methyl group, an isopropyl group, a methoxy group and/or a trifluoromethyl group and/or may optionally be attached via a linear saturated aliphatic C₁₋₃ bridge or an ethynyl bridge.

32. A pharmaceutical preparation containing at least one substituted aminoalcohol according to claim 24 selected from among the group comprising

1-(2,3-Dichloro-phenyl)-2-pyrrolidin-1-ylmethyl-cyclohexanol

2-Pyrrolidin-1-ylmethyl-1-p-tolyl-cyclohexanol

1-(4-Methoxy-phenyl)-2-pyrrolidin-1-ylmethyl-cyclohexanol

1-Phenyl-2-pyrrolidin-1-ylmethyl-cyclopentanol

1-(4-Chloro-phenyl)-2-pyrrolidin-1-ylmethyl-cyclopentanol

1-Benzyl-2-pyrrolidin-1-ylmethyl-cyclopentanol

1-(4-Fluoro-3-methyl-phenyl)-2-pyrrolidin-1-ylmethyl-cyclopentanol

2-Pyrrolidin-1-ylmethyl-1-o-tolyl-cyclopentanol

2-Pyrrolidin-1-ylmethyl-1-vinyl-cyclopentanol

1-(4-tert-Butyl-phenyl)-2-pyrrolidin-1-ylmethyl-cyclopentanol

2-Pyrrolidin-1-ylmethyl-bicyclopentyl-1-ol

2-Pyrrolidin-1-ylmethyl-1-m-tolyl-cyclopentanol

1-Cyclohexyl-2-pyrrolidin-1-ylmethyl-cyclopentanol

1-(4-Fluoro-phenyl)-2-pyrrolidin-1-ylmethyl-cyclopentanol

1-Phenethyl-2-pyrrolidin-1-ylmethyl-cyclopentanol

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- 1-Phenylethynyl-2-pyrrolidin-1-ylmethyl-cyclopentanol
2-Pyrrolidin-1-ylmethyl-1-thiophen-2-yl-cyclopentanol
1-(2,4-Dichloro-phenyl)-2-pyrrolidin-1-ylmethyl-
cyclopentanol
5 1-(3-Phenyl-propyl)-2-pyrrolidin-1-ylmethyl-
cyclopentanol
1-(2,3-Dichloro-phenyl)-2-pyrrolidin-1-ylmethyl-
cyclopentanol
2-Pyrrolidin-1-ylmethyl-1-p-tolyl-cyclopentanol
10 1-(4-Methoxy-phenyl)-2-pyrrolidin-1-ylmethyl-
cyclopentanol
1-Phenyl-2-pyrrolidin-1-ylmethyl-cycloheptanol
1-(4-Chloro-phenyl)-2-pyrrolidin-1-ylmethyl-
cycloheptanol
15 1-Benzyl-2-pyrrolidin-1-ylmethyl-cycloheptanol
1-(4-Fluoro-3-methyl-phenyl)-2-pyrrolidin-1-ylmethyl-
cycloheptanol
2-Pyrrolidin-1-ylmethyl-1-o-tolyl-cycloheptanol
2-Pyrrolidin-1-ylmethyl-1-vinyl-cycloheptanol
20 1-(4-tert-Butyl-phenyl)-2-pyrrolidin-1-ylmethyl-
cycloheptanol
1-Cyclopentyl-2-pyrrolidin-1-ylmethyl-cycloheptanol
2-Pyrrolidin-1-ylmethyl-1-m-tolyl-cycloheptanol
1-Cyclohexyl-2-pyrrolidin-1-ylmethyl-cycloheptanol
25 1-(4-Fluoro-phenyl)-2-pyrrolidin-1-ylmethyl-
cycloheptanol
1-Phenethyl-2-pyrrolidin-1-ylmethyl-cycloheptanol
1-Phenylethynyl-2-pyrrolidin-1-ylmethyl-cycloheptanol
2-Pyrrolidin-1-ylmethyl-1-thiophen-2-yl-cycloheptanol
30 1-(2,4-Dichloro-phenyl)-2-pyrrolidin-1-ylmethyl-
cycloheptanol
1-(3-Phenyl-propyl)-2-pyrrolidin-1-ylmethyl-
cycloheptanol

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- 1- (2,3-Dichloro-phenyl) -2-pyrrolidin-1-ylmethyl-
cycloheptanol
- 2-Pyrrolidin-1-ylmethyl-1-p-tolyl-cycloheptanol
- 1- (4-Methoxy-phenyl) -2-pyrrolidin-1-ylmethyl-
cycloheptanol
- 2-Azepan-1-ylmethyl-1-phenyl-cyclohexanol
- 2-Azepan-1-ylmethyl-1-benzyl-cyclohexanol
- 2-Azepan-1-ylmethyl-1- (4-fluoro-3-methyl-phenyl) -
cyclohexanol
- 2-Azepan-1-ylmethyl-1-o-tolyl-cyclohexanol
- 2-Azepan-1-ylmethyl-1-vinyl-cyclohexanol
- 2-Azepan-1-ylmethyl-1- (4-tert-butyl-phenyl) -
cyclohexanol
- 2-Azepan-1-ylmethyl-1-cyclopentyl-cyclohexanol
- 2-Azepan-1-ylmethyl-1-m-tolyl-cyclohexanol
- 2-Azepan-1-ylmethyl-bicyclohexyl-1-ol
- 2-Azepan-1-ylmethyl-1- (4-fluoro-phenyl) -cyclohexanol
- 2-Azepan-1-ylmethyl-1-phenethyl-cyclohexanol
- 2-Azepan-1-ylmethyl-1-thiophen-2-yl-cyclohexanol
- 2-Azepan-1-ylmethyl-1- (2,4-dichloro-phenyl) -
cyclohexanol
- 2-Azepan-1-ylmethyl-1- (3-methoxy-phenyl) -cyclohexanol
- 2-Azepan-1-ylmethyl-1- (3-phenyl-propyl) -cyclohexanol
- 2-Azepan-1-ylmethyl-1-p-tolyl-cyclohexanol
- 2-Azepan-1-ylmethyl-1- (4-methoxy-phenyl) -cyclohexanol
- 2-Azepan-1-ylmethyl-1-phenyl-cyclopentanol
- 2-Azepan-1-ylmethyl-1- (4-chloro-phenyl) -cyclopentanol
- 2-Azepan-1-ylmethyl-1-benzyl-cyclopentanol
- 2-Azepan-1-ylmethyl-1- (4-fluoro-3-methyl-phenyl) -
cyclopentanol
- 2-Azepan-1-ylmethyl-1-o-tolyl-cyclopentanol
- 2-Azepan-1-ylmethyl-1-vinyl-cyclopentanol

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- 2-Azepan-1-ylmethyl-1-(4-tert-butyl-phenyl)-
cyclopentanol
- 2-Azepan-1-ylmethyl-bicyclopentyl-1-ol
- 2-Azepan-1-ylmethyl-1-m-tolyl-cyclopentanol
- 5 2-Azepan-1-ylmethyl-1-cyclohexyl-cyclopentanol
- 2-Azepan-1-ylmethyl-1-(4-fluoro-phenyl)-cyclopentanol
- 2-Azepan-1-ylmethyl-1-phenethyl-cyclopentanol
- 2-Azepan-1-ylmethyl-1-phenylethynyl-cyclopentanol
- 2-Azepan-1-ylmethyl-1-thiophen-2-yl-cyclopentanol
- 10 2-Azepan-1-ylmethyl-1-(3-methoxy-phenyl)-cyclopentanol
- 2-Azepan-1-ylmethyl-1-(3-phenyl-propyl)-cyclopentanol
- 2-Azepan-1-ylmethyl-1-p-tolyl-cyclopentanol
- 2-Azepan-1-ylmethyl-1-(4-methoxy-phenyl)-cyclopentanol
- 2-Azepan-1-ylmethyl-1-phenyl-cycloheptanol
- 15 2-Azepan-1-ylmethyl-1-benzyl-cycloheptanol
- 2-Azepan-1-ylmethyl-1-(4-fluoro-3-methyl-phenyl)-
cycloheptanol
- 2-Azepan-1-ylmethyl-1-o-tolyl-cycloheptanol
- 2-Azepan-1-ylmethyl-1-vinyl-cycloheptanol
- 20 2-Azepan-1-ylmethyl-1-(4-tert-butyl-phenyl)-
cycloheptanol
- 2-Azepan-1-ylmethyl-1-cyclopentyl-cycloheptanol
- 2-Azepan-1-ylmethyl-1-m-tolyl-cycloheptanol
- 2-Azepan-1-ylmethyl-1-cyclohexyl-cycloheptanol
- 25 2-Azepan-1-ylmethyl-1-(4-fluoro-phenyl)-cycloheptanol
- 2-Azepan-1-ylmethyl-1-phenethyl-cycloheptanol
- 2-Azepan-1-ylmethyl-1-phenylethynyl-cycloheptanol
- 2-Azepan-1-ylmethyl-1-thiophen-2-yl-cycloheptanol
- 2-Azepan-1-ylmethyl-1-(2,4-dichloro-phenyl)-
cycloheptanol
- 30 2-Azepan-1-ylmethyl-1-(3-methoxy-phenyl)-cycloheptanol
- 2-Azepan-1-ylmethyl-1-(3-phenyl-propyl)-cycloheptanol
- 2-Azepan-1-ylmethyl-1-p-tolyl-cycloheptanol

- 2-Azepan-1-ylmethyl-1-(4-methoxy-phenyl)-cycloheptanol
2-Azepan-1-ylmethyl-1-(3-phenyl-propyl)-cyclopentanol
2-Azepan-1-ylmethyl-1-(2,3-dichloro-phenyl)-
cyclopentanol
- 5 1-Benzyl-2-piperidin-1-ylmethyl-cyclododecanol
1-(4-tert-Butyl-phenyl)-2-piperidin-1-ylmethyl-
cyclododecanol
1-Cyclopentyl-2-piperidin-1-ylmethyl-cyclododecanol
1-Cyclohexyl-2-piperidin-1-ylmethyl-cyclododecanol
- 10 1-Phenethyl-2-piperidin-1-ylmethyl-cyclododecanol
1-Phenylethynyl-2-piperidin-1-ylmethyl-cyclododecanol
2-Piperidin-1-ylmethyl-1-thiophen-2-yl-cyclododecanol
1-(3-Phenyl-propyl)-2-piperidin-1-ylmethyl-
cyclododecanol
- 15 1-(4-Methoxy-phenyl)-2-piperidin-1-ylmethyl-
cyclododecanol
2-Azepan-1-ylmethyl-1-benzyl-cyclododecanol
2-Azepan-1-ylmethyl-1-vinyl-cyclododecanol
2-Azepan-1-ylmethyl-1-(4-tert-butyl-phenyl)-
cyclododecanol
- 20 2-Azepan-1-ylmethyl-1-phenethyl-cyclododecanol
2-Azepan-1-ylmethyl-1-(3-phenyl-propyl)-cyclododecanol
1-Phenyl-2-pyrrolidin-1-ylmethyl-cyclododecanol
1-(4-Chloro-phenyl)-2-pyrrolidin-1-ylmethyl-
cyclododecanol
- 25 1-(4-tert-Butyl-phenyl)-2-pyrrolidin-1-ylmethyl-
cyclododecanol
1-Cyclopentyl-2-pyrrolidin-1-ylmethyl-cyclododecanol
1-(4-Fluoro-3-methyl-phenyl)-2-pyrrolidin-1-ylmethyl-
cyclooctanol
- 30 2-Pyrrolidin-1-ylmethyl-1-o-tolyl-cyclooctanol
2-Pyrrolidin-1-ylmethyl-1-vinyl-cyclooctanol
2-Piperidin-1-ylmethyl-1-p-tolyl-cyclooctanol

- 1-Cyclohexylmethyl-2-pyrrolidin-1-ylmethyl-
cyclohexanol
- 1-(4-Chloro-3-trifluormethyl-phenyl)-2-pyrrolidin-1-
ylmethyl-cycloheptanol
- 5 1-(3-Fluoro-benzyl)-2-pyrrolidin-1-ylmethyl-
cycloheptanol
- 2-Azepan-1-ylmethyl-1-(3-fluoro-phenyl)-cyclohexanol
- 2-Azepan-1-ylmethyl-1-(3-chloro-phenyl)-cyclohexanol
- 2-Azepan-1-ylmethyl-1-cyclohexylmethyl-cyclopentanol
- 10 2-Azepan-1-ylmethyl-1-(2-chloro-6-fluoro-benzyl)-
cyclopentanol
- 2-Azepan-1-ylmethyl-1-(2,5-dimethyl-benzyl)-
cyclopentanol
- 2-Azepan-1-ylmethyl-1-(4-fluoro-benzyl)-cycloheptanol
- 15 2-Azepan-1-ylmethyl-1-(3-methoxy-benzyl)-cycloheptanol
- 2-Azepan-1-ylmethyl-1-(3-methoxy-benzyl)-cycloheptanol
- 2-Azepan-1-ylmethyl-1-(3-fluoro-benzyl)-cyclopentanol
- 1-(4-Fluoro-benzyl)-2-piperidin-1-ylmethyl-
cyclododecanol
- 20 1-(3-Fluoro-benzyl)-2-piperidin-1-ylmethyl-
cyclododecanol
- 1-(2-Chloro-benzyl)-2-pyrrolidin-1-ylmethyl-
cyclododecanol
- 1-(3-Chloro-phenyl)-2-pyrrolidin-1-ylmethyl-
25 cyclooctanol
- 2-Azepan-1-ylmethyl-1-(3-phenyl-propyl)-cyclooctanol

in the form of the diastereomers thereof, the
enantiomers thereof and mixtures thereof - including
30 the racemates thereof - and in the form of
corresponding bases, salts and solvates

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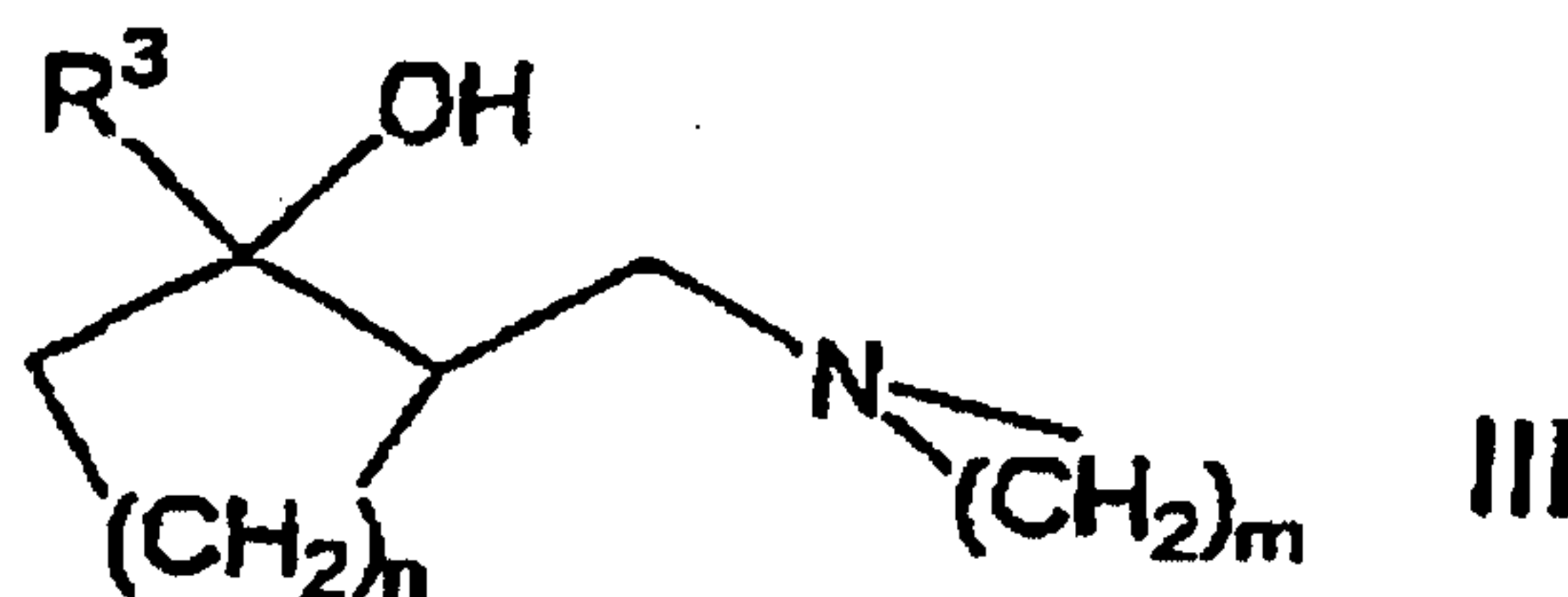
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and optionally physiologically acceptable auxiliary substances.

- 5 33. A pharmaceutical preparation according to any one of claims 24-32 for the treatment of pain.
34. A pharmaceutical preparation according to any one of claims 24-32 as an antiemetic.
- 10 35. A pharmaceutical preparation according to any one of claims 24-32 as a nootropic (neurotropic).
36. A pharmaceutical preparation according to any one of claims 24-32 for the treatment of cardiovascular
15 diseases.
37. A pharmaceutical preparation according to any one of claims 24-32 for the treatment of urinary
incontinence.
- 20 38. A pharmaceutical preparation according to any one of claims 24-32 for the treatment of diarrhoea.
39. A pharmaceutical preparation according to any one of
25 claims 24-32 for the treatment of pruritus.
40. A pharmaceutical preparation according to claims 24-32 for the treatment of dependency on alcohol and/or drugs and/or medicines.
- 30 41. A pharmaceutical preparation according to any one of claims 24-32 for the treatment of inflammation.

50

42. A pharmaceutical preparation according to any one of claims 24-32 for the treatment of depression.
43. A pharmaceutical preparation according to any one of claims 24-32 for increasing vigilance.
44. A pharmaceutical preparation according to any one of claims 24-32 for increasing libido.
45. Use of at least one compound according to any one of claims 24-32 with the exception of compounds of the formula Ia for the production of a pharmaceutical preparation for the treatment of pain.
46. Use of at least one compound according to any one of claims 24-32 not excepting compounds for the production of a pharmaceutical preparation for the treatment of emesis, cardiovascular diseases, urinary incontinence, diarrhoea, pruritus, dependency on alcohol and/or drugs and/or medicines, and/or inflammation, for the treatment of depression, to increase drive, vigilance and/or libido.
47. 2-(Aminomethyl)-cycloalkan-1-ol compounds of the general formula III,



in which

51

n denotes an integer from 2-9 and m denotes an integer from 4-6 in the following combinations,

n	m
2	4
2	6
3	6
4	4
4	5
4	6
5	4
5	5
5	6
9	4
9	5
9	6

5 wherein optionally one or more CH_2 groups of the $(\text{CH}_2)_m$ chain may be replaced by oxygen,

10 R^3 denotes a linear or branched, saturated or unsaturated aliphatic residue, a saturated or unsaturated cycloaliphatic residue, an aryl residue or a heteroaryl residue, wherein the respective ring system may be optionally mono- or polysubstituted and/or attached via a linear or branched, saturated or unsaturated aliphatic bridge and/or the aryl or
15 heteroaryl residue may be part of a polycyclic system

in the form of the pure diastereomers thereof, the pure enantiomers thereof and mixtures thereof -

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including the racemates thereof - and in the form of corresponding bases, salts and solvates.

48. Compounds according to claim 47, characterised in that

5

R³ denotes a linear or branched, saturated or unsaturated aliphatic C₁₋₆ residue, a saturated or unsaturated cycloaliphatic C₃₋₇ residue, a phenyl residue or a five- or six-membered heteroaryl residue, wherein the respective ring system may optionally be mono- or polysubstituted and/or attached via a linear or branched, saturated or unsaturated aliphatic C₁₋₅ bridge.

10

15 49. Compounds according to claim 47, characterised in that

R³ denotes a linear or branched, saturated or unsaturated aliphatic C₁₋₃ residue, a saturated or unsaturated cycloaliphatic C₅₋₆ residue, a phenyl residue or a five- or six-membered heteroaryl residue, wherein the respective ring system may optionally be mono- or polysubstituted with halogen, an alkyl group, an alkoxy group and/or a trihalogenated alkyl group and/or may be attached via a linear or branched, saturated or unsaturated aliphatic C₁₋₃ bridge.

20

25

50. Compounds according to claim 47, characterised in that

R³ denotes a vinyl residue, a cyclopentyl residue, a cyclohexyl residue, a thiophenyl residue or a phenyl residue, wherein the cyclohexyl residue may optionally be attached via a methylene bridge or the phenyl residue may optionally be mono- or polysubstituted

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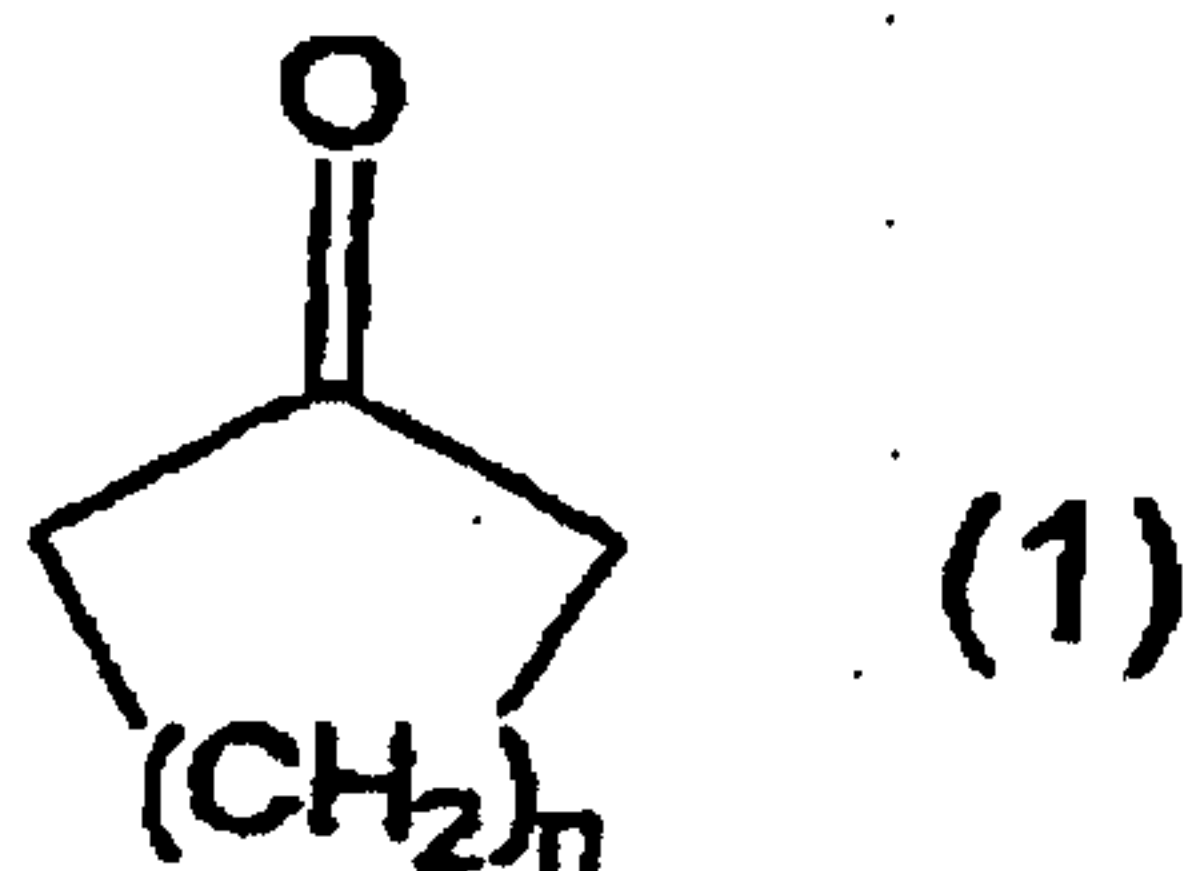
with fluorine, chlorine, a methyl group, an isopropyl group, a methoxy group and/or a trifluoromethyl group and/or may optionally be attached via a linear saturated aliphatic C₁₋₃ bridge or an ethynyl bridge.

5

51. A process for the production of compounds according to any one of claims 47-50, characterised in that

10

A) a ketone of the formula (1), in which n has the meaning stated in claim 47,



15

is reacted with paraformaldehyde and a cyclic amine of the formula (2), in which m has the meaning stated in claim 47,

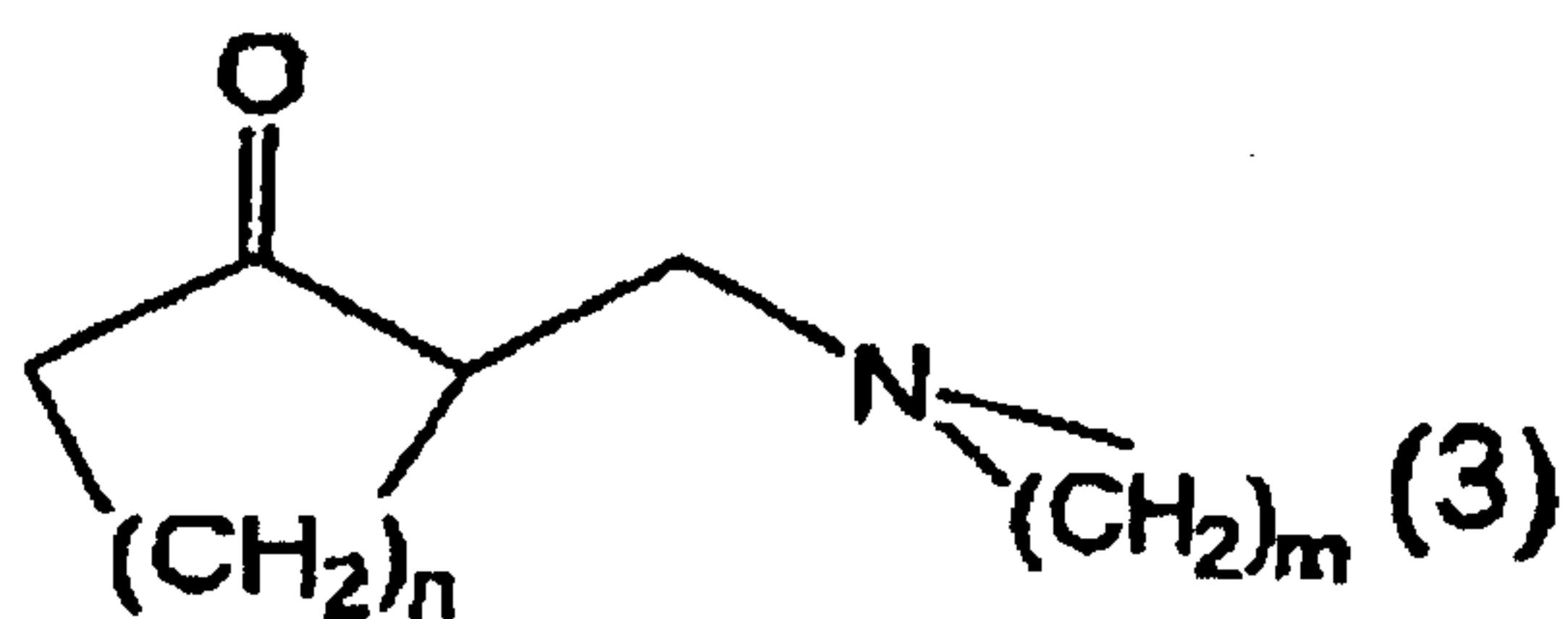


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according to a Mannich reaction in a suitable solvent, preferably in ethanol with the addition of hydrochloric acid or in acetic acid, with heating, then the reaction mixture is worked up and the product of the formula (3) is isolated and optionally purified or

25

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B) a compound of the formula (3) is reacted with a Grignard compound or an organolithium compound of the formulae R^3MgCl , R^3MgBr , R^3MgI , MgR^3_2 or LiR^3 , in which R^3 has the meaning stated in claim 47, in a suitable solvent, preferably diethyl ether or tetrahydrofuran, then the reaction mixture is worked up and the compound of the general formula I is isolated and optionally purified.

Patent Agents
H. H. H. H. H. Co.