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(54) Titre : DERIVES D'AMINOMETHYLE-PHENYLE-CYCLOHEXANE
(54) Title: AMINOMETHYL-PHENYL-CYCLOHEXANONE DERIVATIVES

(57) **Abrégé/Abstract:**

The invention relates to aminomethyl-phenyl-cyclohexanone derivatives, to methods for the production thereof, to the use of aminomethyl-phenyl-cyclohexanone derivatives for producing medicaments, and to medicaments containing aminomethyl-phenyl-cyclohexanone derivatives.

Abstract

The invention relates to aminomethyl-phenyl-cyclohexanone derivatives, to methods for the production thereof, to the use of aminomethyl-phenyl-cyclohexanone derivatives for producing medicaments, and to medicaments containing aminomethyl-phenyl-cyclohexanone derivatives.

Patent application by Grünenthal GmbH, D-52078 Aachen
(our reference G 2933)

Aminomethyl-phenyl-cyclohexanone derivatives

5

The present invention relates to aminomethyl-phenyl-cyclohexanone derivatives and processes for their preparation, the use of aminomethyl-phenyl-cyclohexanone derivatives for the preparation of medicaments and
10 medicaments comprising aminomethyl-phenyl-cyclohexanone derivatives.

Treatment of chronic and non-chronic states of pain is of great importance in medicine. There is a worldwide need
15 for pain treatments with a good action for target-orientated treatment of chronic and non-chronic states of pain appropriate for the patient, by which is to be understood successful and satisfactory pain treatment for the patient. This manifests itself in the large number of
20 scientific works which have been published in the field of applied analgesia and basic research in nociception in recent years.

Conventional opioids, such as e.g. morphine, have a good
25 action in the treatment of severe to very severe pain. However, their use is limited by the known side effects, e.g. respiratory depression, vomiting, sedation, constipation, addiction, dependency and development of tolerance. They can therefore be administered over a
30 relatively long period of time or in relatively high dosages only if particular safety precautions are taken, such as e.g. specific prescription instructions (Goodman, Gilman, The Pharmacological Basis of Therapeutics, Pergamon Press, New York 1990). They furthermore show a lower
35 activity with some states of pain, in particular neuropathic pain.

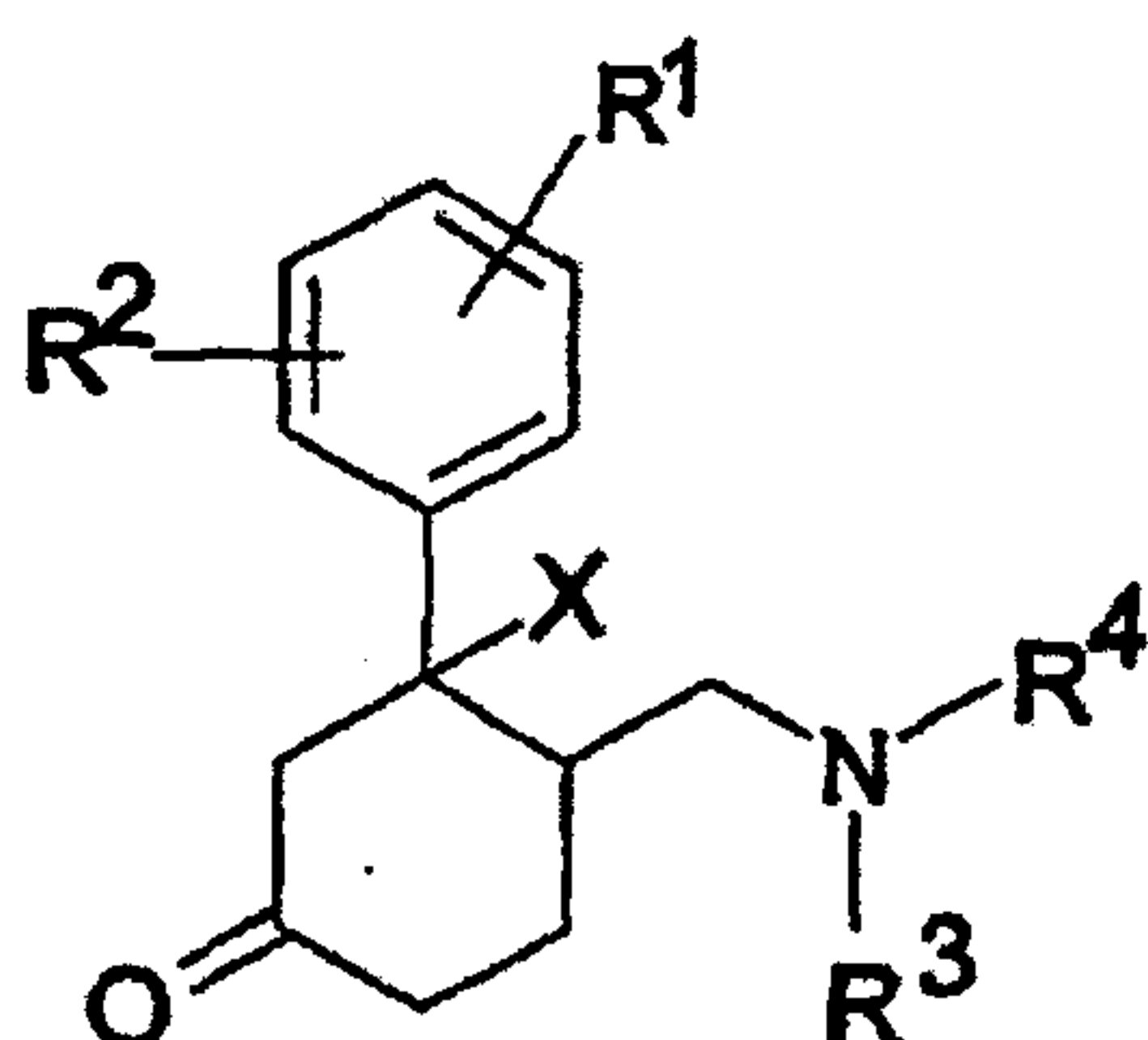
Tramadol hydrochloride - (1RS,2RS)-2-
[(dimethylamino)methyl]-1-(3-methoxyphenyl)cyclohexanol
hydrochloride - is another known therapeutic for treatment
5 of severe pain. It occupies a special position among
analgesics having an action on the central nervous system,
inasmuch as this active compound brings about potent
inhibition of pain without the side effects known of
opioids (J. Pharmacol. Exptl. Ther. 267, 331 (1993)), both
10 the enantiomers of tramadol and the enantiomers of tramadol
metabolites participating in the analgesic action (J.
Pharmacol. Exp. Ther. 260, 275 (1992)). Needless to say,
tramadol is also not without side effects.

15 Substituted aminomethyl-phenyl-cyclohexanone derivatives
are already described in DE 195 25 137 A1 (Grünenthal
GmbH), as in German Patent Application 198 30 105.7-44
(Grünenthal GmbH). However, these are always synthesis
precursors which are not described themselves as active
20 compounds in medicaments or as having an analgesic action.

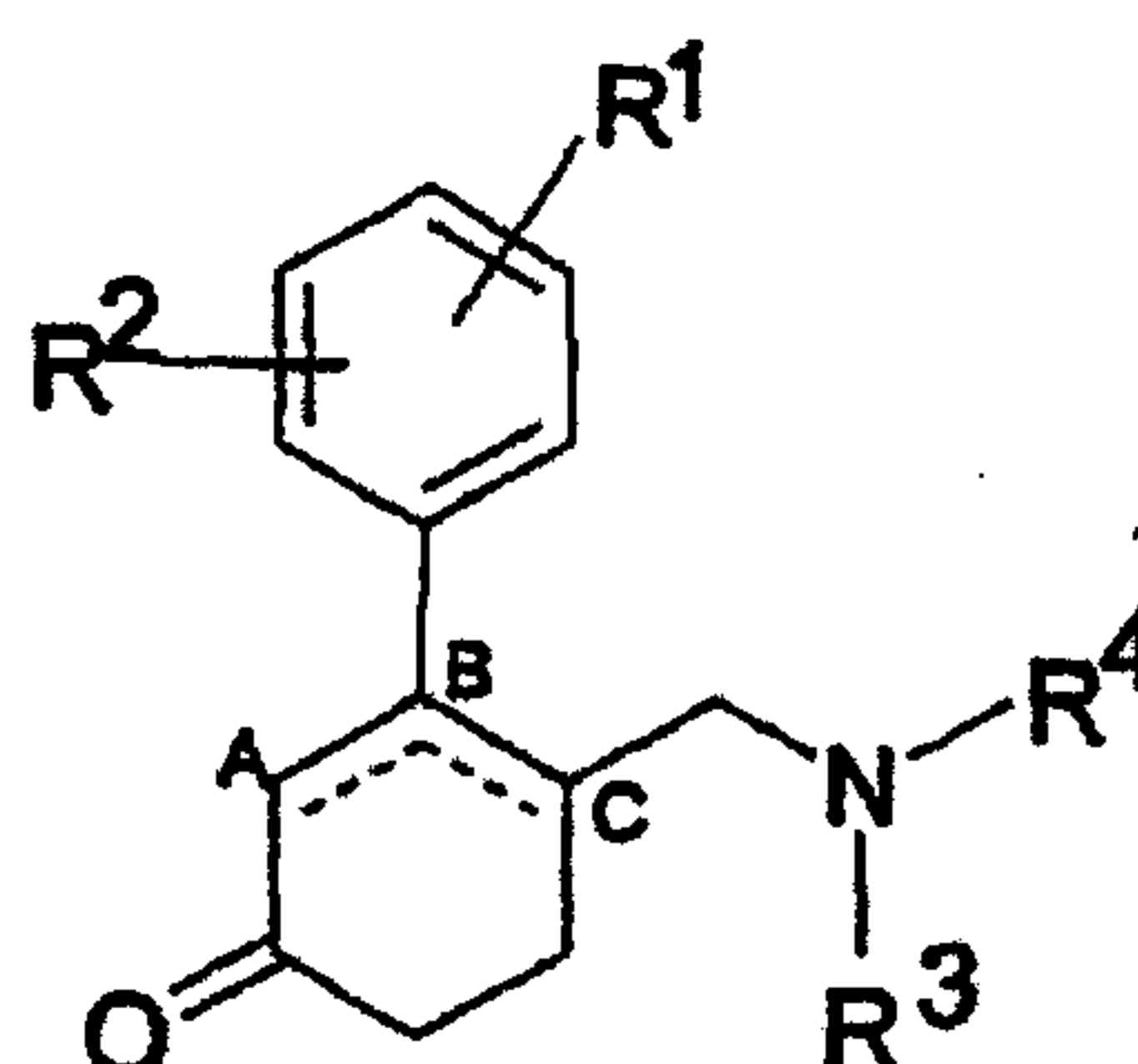
An object on which the invention was based was to provide
substances which have an analgesic action and are suitable
for treatment of pain. These substances should furthermore
25 have as few side effects as possible, such as e.g. nausea,
vomiting, dependency, respiratory depression or
constipation.

This object is achieved by the aminomethyl-phenyl-
30 cyclohexanone derivatives according to the invention. The
invention therefore provides aminomethyl-phenyl-
cyclohexanone derivatives of the general formula I or Ia,
also in the form of their diastereomers or enantiomers and
of their free bases or of a salt formed with a

physiologically tolerated acid, in particular the hydrochloride salt,



I



Ia

wherein

R^1 and R^2 independently of one another are chosen from R^5 or YR^5 , where $Y = C_1-C_{10}$ -alkyl, C_2-C_{10} -alkenyl or C_2-C_{10} -alkinyl, branched or unbranched and mono- or polysubstituted or unsubstituted, wherein R^5 is chosen from

H, F, Cl, Br, I, CN, NO_2 ; C_1-C_8 -alkyl, C_2-C_8 -alkenyl or C_2-C_8 -alkinyl, in each case branched or unbranched and mono- or polysubstituted or unsubstituted; C_3-C_7 -cycloalkyl, saturated or unsaturated and mono- or polysubstituted or unsubstituted, or a corresponding heterocyclic radical, in which one C atom in the ring is replaced by S, O or NR^6 , where R^6 is chosen from

H, C_1-C_{10} -alkyl, C_2-C_{10} -alkenyl or C_2-C_{10} -alkinyl, in each case branched or unbranched and mono- or polysubstituted or unsubstituted;

aryl or heteroaryl, in each case mono- or polysubstituted or unsubstituted;

5 OR⁷, OC(O)R⁷, OC(O)OR⁷, OC(S)R⁷, C(O)R⁷, C(O)OR⁷, C(S)R⁷, C(S)OR⁷, SR⁷, S(O)R⁷ or S(O₂)R⁷, wherein R⁷ is chosen from

10 H, C₁-C₁₈-alkyl, C₂-C₁₈-alkenyl or C₂-C₁₈-alkinyl, in each case branched or unbranched and mono- or polysubstituted or unsubstituted; C₃-C₇-cycloalkyl, saturated or unsaturated and mono- or polysubstituted or unsubstituted, or a corresponding heterocyclic radical, in which one C atom in the ring is replaced by S, O or NR⁸, where R⁸ is chosen from

15 H, C₁-C₁₀-alkyl, C₂-C₁₀-alkenyl or C₂-C₁₀-alkinyl, in each case branched or unbranched and mono- or polysubstituted or unsubstituted; alkylaryl, saturated or unsaturated and mono- or polysubstituted or unsubstituted; aryl or heteroaryl, in each case mono- or polysubstituted or unsubstituted; or

25 NR⁹R¹⁰, C(O)NR⁹R¹⁰ or S(O₂)NR⁹R¹⁰, wherein R⁹ and R¹⁰ independently of one another are chosen from

30 H, C₁-C₁₈-alkyl, C₂-C₁₈-alkenyl or C₂-C₁₈-alkinyl, in each case branched or unbranched and mono- or polysubstituted or unsubstituted; C₃-C₇-cycloalkyl, saturated or unsaturated and mono- or polysubstituted or unsubstituted, or a corresponding heterocyclic radical, in which one C atom in

the ring is replaced by S, O or NR^{11} , where R^{11} is chosen from

5 H, $\text{C}_1\text{-C}_{10}$ -alkyl, $\text{C}_2\text{-C}_{10}$ -alkenyl or $\text{C}_2\text{-C}_{10}$ -alkinyl, in each case branched or unbranched and mono- or polysubstituted or unsubstituted;

10 alkylaryl, saturated or unsaturated and mono- or polysubstituted or unsubstituted; aryl or heteroaryl, in each case mono- or polysubstituted or unsubstituted;

or

15 R^9 and R^{10} together form a $\text{C}_3\text{-C}_7$ -cycloalkyl, saturated or unsaturated and mono- or polysubstituted or unsubstituted, or a corresponding heterocyclic radical, in which one C atom in the ring is replaced by S, O or NR^{12} , where R^{12} is chosen from

20 H, $\text{C}_1\text{-C}_{10}$ -alkyl, $\text{C}_2\text{-C}_{10}$ -alkenyl or $\text{C}_2\text{-C}_{10}$ -alkinyl, in each case branched or unbranched and mono- or polysubstituted or unsubstituted;

25 or

R^1 and R^2 together form $-\text{CH}=\text{CH}-\text{CH}=\text{CH}-$, wherein the naphthyl system formed can be mono- or polysubstituted,

30

X is chosen from

H, F, Cl, Br, I, CF_3 , $\text{O-S(O}_2\text{)-C}_6\text{H}_4\text{-pCH}_3$, OR^{13} or OC(O)R^{13} , wherein R^{13} is chosen from

5 H; C₁-C₁₀-alkyl, C₂-C₁₀-alkenyl or C₂-C₁₀-alkynyl, in each case branched or unbranched and mono- or polysubstituted or unsubstituted; C₃-C₇-cycloalkyl, saturated or unsaturated and mono- or polysubstituted or unsubstituted, or a corresponding heterocyclic radical, in which one C atom in the ring is replaced by N, S or O; alkylaryl, saturated or unsaturated and
10 mono- or polysubstituted or unsubstituted; aryl or heteroaryl, in each case mono- or polysubstituted or unsubstituted;

or

15

if the compound contains no X, according to formula Ia a double bond is formed between C atom A and C atom B or C atom B and C atom C;

20

and

R³, R⁴ independently of one another are chosen from
H, C₁-C₁₀-alkyl, C₂-C₁₀-alkenyl or C₂-C₁₀-alkynyl, in each case branched or unbranched and mono- or
25 polysubstituted or unsubstituted; C₃-C₇-cycloalkyl, saturated or unsaturated and mono- or polysubstituted or unsubstituted, or a corresponding heterocyclic radical, in which one C atom in the ring is replaced by N, S or O;
30 alkylaryl, saturated or unsaturated and mono- or polysubstituted or unsubstituted; aryl or heteroaryl, in each case mono- or polysubstituted or unsubstituted;

or

R^3 and R^4 together form a C_3 - C_7 -cycloalkyl, saturated or unsaturated and mono- or polysubstituted or unsubstituted, or a corresponding heterocyclic radical, in which one C atom in the ring is replaced by S, O or NR^{14} , where R^{14} is chosen from

H, C_1 - C_{10} -alkyl, C_2 - C_{10} -alkenyl or C_2 - C_{10} -alkynyl, in each case branched or unbranched and mono- or polysubstituted or unsubstituted.

On the other hand, the invention does not provide

- 15 • compounds such as those in which $X = OH$, $R^2 = H$, R^3 and $R^4 = CH_3$, and R^1 at the same time is R^5 , where $R^5 = OR^7$, where $R^7 = H$, CH_3 or an unsubstituted or substituted pyridyl, thienyl, thiazoyl or phenyl group, or $R^5 = OC(O)OR^7$, where
20 $R^7 = C_1$ - C_5 -alkyl, or $R^5 = OC(O)R^7$, where $R^7 = C_1$ - C_5 -alkyl, $NH-C_6H_4-C_1$ - C_3 -alkyl, $C_6H_4-OC(O)C_1$ - C_3 -alkyl, $C_6H_4-CH_2-N(C_1$ - C_4 -alkyl) $_2$, $C_6H_4-CH_2-(N$ -4-morpholino) or $CHZ'-NHZ''$, where Z' and Z'' are identical or different and are chosen from H or C_1 - C_6 -alkyl,
25 • or compounds such as those in which $X = H$ or according to formula Ia a double bond is formed between C atom A and C atom B, $R^2 = H$, R^3 and $R^4 = C_1$ - C_6 -alkyl, aryl or C_3 - C_7 -cycloalkyl and R^1 at the
30 same time is H, C_1 - C_6 -alkoxy, O- C_3 - C_7 -cycloalkyl, O-aryl or O-heterocyclyl.

In connection with alkyl, alkenyl, alkynyl and cycloalkyl and the "corresponding heterocyclic radical", the term

substituted here in the context of this invention is understood as meaning the replacement of a hydrogen radical by F, Cl, Br, I, NH₂, SH or OH, polysubstituted radicals being understood as meaning radicals which are substituted
5 more than once both on different and on the same atoms, for example three times on the same C atom, as in the case of CF₃, or at different places, as in the case of -CH(OH)-CH=CH-CHCl₂.

10 Furthermore, -C(O)- denotes

8

which also applies to -C(S)- or -S(O)- and -S(O₂)-.

The term "C₁-C₈-alkyl" or "C₁-C₁₀-alkyl" in the context of
15 this invention denotes hydrocarbons having 1 to 8 or 10 carbon atoms respectively. Examples which may be mentioned are methyl, ethyl, propyl, isopropyl, n-butane, sec-butyl, tert-butyl, n-pentane, neopentyl, n-hexane, n-heptane, n-octane, n-nonane or n-decane.

20

The term "C₁-C₁₈-alkyl" in the context of this invention denotes hydrocarbons having 1 to 18 carbon atoms. Examples which may be mentioned are methyl, ethyl, propyl, isopropyl, n-butane, sec-butyl, tert-butyl, n-pentane,
25 neopentyl, n-butane, sec-butyl, n-hexane, n-heptane, n-octane, n-nonane, n-decane, n-undecane, n-dodecane, n-tridecane, n-tetradecane, n-pentadecane, n-hexadecane, n-heptadecane or n-octadecane, unsubstituted or mono or polysubstituted.

30

The term "C₂-C₁₀-alkenyl" or "C₂-C₁₀-alkinyl" or "C₂-C₁₈-alkenyl" or "C₂-C₁₈-alkinyl" in the context of this

invention denotes hydrocarbons having 2 to 8 or 2 to 18 carbon atoms respectively. Examples which may be mentioned are propenyl, butenyl, pentenyl, hexenyl, heptenyl or octenyl, unsubstituted or mono or polysubstituted, or
5 propinyl, butinyl, pentinyl, hexinyl, heptinyl or octinyl, unsubstituted or mono- or polysubstituted.

The term C₃-C₇-cycloalkyl in the context of this invention denotes cyclic hydrocarbons having 3 to 7 carbon atoms.
10 Examples which may be mentioned are cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, cyclohexenyl or cycloheptenyl, saturated or unsaturated and unsubstituted or mono or polysubstituted. In the context of the invention a "corresponding heterocyclic radical" is
15 understood as meaning a C₃-C₇-cycloalkyl in which one C atom in the ring is replaced by S, O or N. Examples which may be mentioned for this are pyrrolidine, pyran, thiolane, piperidine or tetrahydrofuran.

20 The term "aryl" in the context of this invention denotes phenyls or naphthyls.

The term "alkylaryl" in the context of this invention denotes aryls substituted by at least C₁-C₁₀-alkylene, the
25 terms aryl and alkyl having the same meaning as above. In this group benzaryl may be mentioned in particular.

The term "heteroaryl" in the context of this invention denotes 5- or 6-membered aromatic compounds which are
30 optionally provided with a fused-on ring system and contain one or two heteroatoms from the groups consisting of nitrogen, oxygen and/or sulfur. Examples which may be mentioned in this group are furan, thiophene, pyrrole,

pyridine, pyrimidine, quinoline, isoquinoline, phthalazine or quinazoline.

In respect of aryl, alkylaryl or heteroaryl, mono- or
5 polysubstituted in the context of this invention is understood as meaning substitution of the ring system by F, Cl, Br, I, NH₂, SH, OH, CF₃; mono- or polysubstituted or unsubstituted C₁-C₆-alkyl, C₁-C₆-alkoxy, C₂-C₈-alkenyl, C₂-C₈-alkinyl; or aryl, in particular phenyl; on one or various
10 atoms.

The expression salt formed with a physiologically tolerated acid in the context of this invention is understood as meaning salts of the particular active compound with
15 inorganic or organic acids which are physiologically tolerated - in particular when used in humans and/or mammals. The hydrochloride is particularly preferred.

In preferred aminomethyl-phenyl-cyclohexanone derivatives
20 according to formula I or Ia according to the invention, R¹ = R⁵, where R⁵ is chosen from

H, F, Cl, Br, I, CHF₂, CF₃, NO₂, NH₂; C₁-C₄-alkyl or C₂-C₄-alkenyl, branched or unbranched and mono- or polysubstituted or unsubstituted; aryl,
25 substituted or unsubstituted, OR⁷, C(O)OR⁷ or SR⁷, wherein R⁷ is chosen from

H; C₁-C₄-alkyl, branched or unbranched and mono- or polysubstituted or unsubstituted; preferably H, CF₃ or CH₃,
30 or S(O₂)NR⁹R¹⁰, wherein R⁹ and R¹⁰ independently of one another are chosen from

H; C₁-C₄-alkyl, branched or unbranched and mono- or polysubstituted or unsubstituted;

wherein particularly preferably $R^1 = R^5$, where R^5 is chosen from

5 H, F, Cl, OH, CH₃, C₂H₅, C₂H₃, CHF₂, CF₃, SCH₃, OCF₃, OCH₃, OC₂H₅, C(O)OCH₃, C(O)OC₂H₅ or phenyl,

while R^2 , X, R^3 and R^4 have one of the meanings already mentioned.

10 In further preferred aminomethyl-phenyl-cyclohexanone derivatives according to formula I or Ia according to the invention, $R^2 = R^5$, wherein R^5 is chosen from

15 H, F, Cl, Br, I, SCH₃; C₁-C₄-alkyl, C₂-C₄-alkenyl, branched or unbranched and mono- or polysubstituted or unsubstituted, preferably CF₃; OR⁷, where R^7 is chosen from C₁-C₄-alkyl, branched or unbranched and mono- or polysubstituted or unsubstituted, preferably CH₃;

20 while R^1 , X, R^3 and R^4 have one of the meanings already mentioned.

In further preferred aminomethyl-phenyl-cyclohexanone derivatives according to formula I or Ia according to the invention, R^1 and R^2 have different meanings or R^1 and R^2 together form -CH=CH-CH=CH-, wherein the naphthyl system formed can be mono- or polysubstituted, preferably by halogen, OC₁₋₃-alkyl or C₁₋₃-alkyl, unsubstituted or mono or 30 polysubstituted, in particular by OCH₃.

In aminomethyl-phenyl-cyclohexanone derivatives according to formula I or Ia according to the invention which are also preferred, X is chosen from

H, F, Cl, OH, CF₃, O-S(O₂)-C₆H₄-pCH₃ or OC(O)R⁷,
where R⁷ = H; C₁-C₄-alkyl or C₂-C₄-alkenyl,
branched or unbranched and mono- or
polysubstituted or unsubstituted,
5 preferably H, F, Cl, OH, O-S(O₂)-C₆H₄-pCH₃ or
OC(O)R⁷, where R⁷ = C₁-C₄-alkyl, preferably CH₃, in
particular H or OH;

or

10

if the compound contains no X, according to formula Ia
a double bond is formed between C atom A and C atom B
or C atom B and C atom C,

15 while R¹, R², R³ and R⁴ have one of the meanings already
mentioned.

In further aminomethyl-phenyl-cyclohexanone derivatives
according to formula I or Ia according to the invention

20

R³ and R⁴ independently of one another are chosen from
C₁-C₄-alkyl, branched or unbranched and mono- or
polysubstituted or unsubstituted, preferably CH₃,

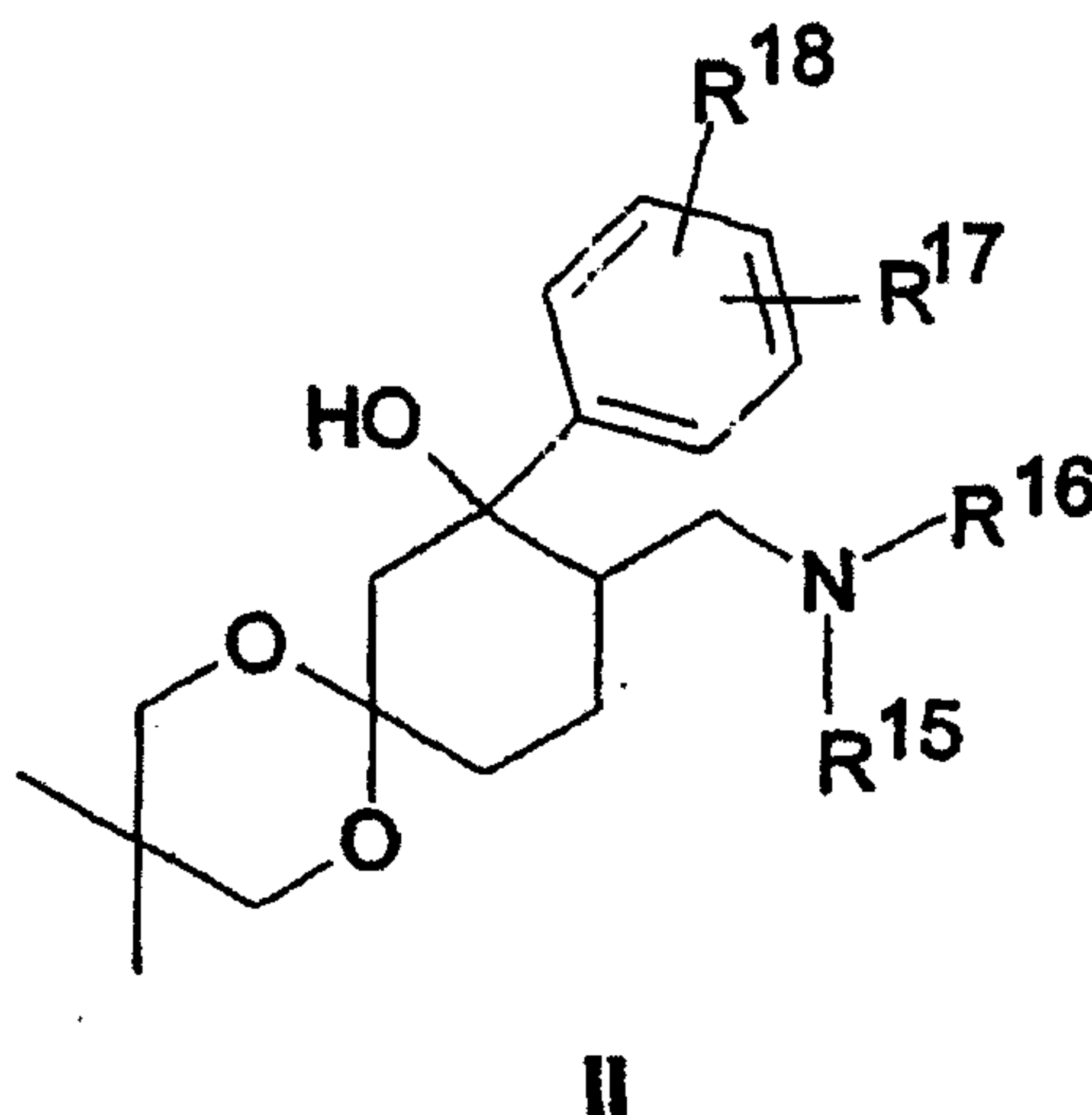
25 or

R³ and R⁴ together form a C₃-C₇-cycloalkyl, saturated
or unsaturated and mono- or polysubstituted or
unsubstituted,

30

while R¹, R² and X have one of the meanings already
mentioned.

The invention also provides a process for the preparation of the aminomethyl-phenyl-cyclohexanone derivatives, which are already described as such as being provided by the invention, according to formula Ia or according to formula I where X = H, in which compounds of the formula II



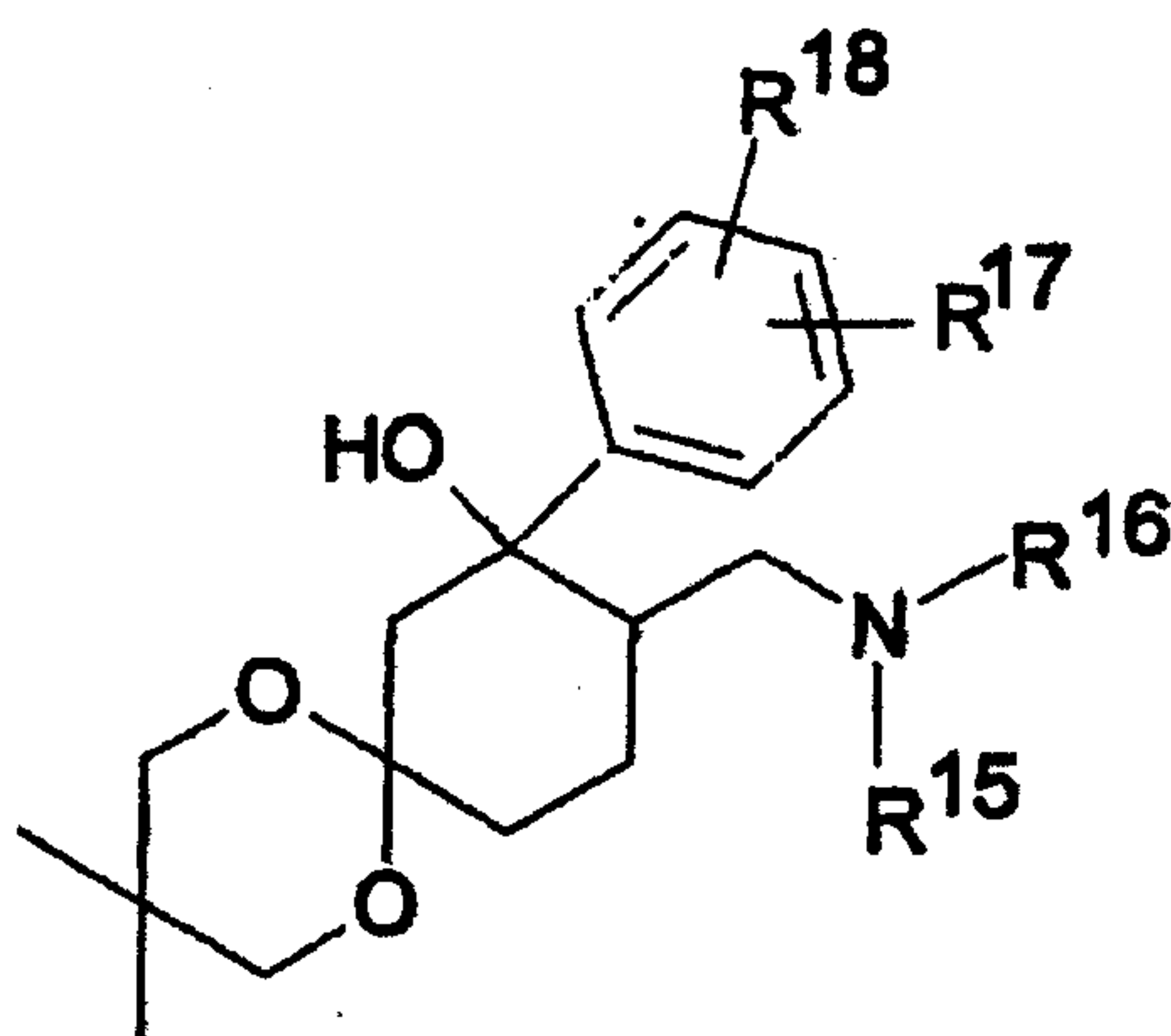
in which R¹⁵ has a meaning corresponding to R³, R¹⁶ to R⁴, R¹⁷ to R¹ and R¹⁸ to R² as already described, are reacted with acids, preferably hydrochloric acid, formic acid or acetic acid, at room temperature. The product according to formula Ia is then either purified as the end product or the product is hydrogenated with catalytically activated hydrogen to give a product according to formula I where X = H, which is then purified. The hydrogenation is preferably carried out with platinum or palladium as the catalyst absorbed on to a support material, such as active charcoal, in ethyl acetate or a C₁ - C₄-alkyl alcohol, under pressures of 0.1 to 10 bar and/or at temperatures of 20°C to 80°C.

20

The invention also provides a process for the preparation of the aminomethyl-phenyl-cyclohexanone derivatives, which are already described as such as being provided by the invention, according to formula I where X ≠ H, in which compounds of the formula II

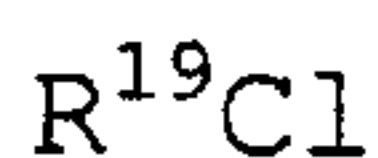
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II

in which R^{15} has a meaning corresponding to R^3 , R^{16} to R^4 , R^{17} to R^1 and R^{18} to R^2 as already described, are reacted with
 5 acids, preferably hydrochloric acid, formic acid or acetic acid, at temperatures of between 0°C and 5°C . The product according to formula 1 where $X = \text{OH}$ and R^{15} to R^{18} are unchanged is then either purified as the end product or further processed. If the product is to be converted into
 10 a compound where X is F , Cl , Br , I or CF_3 , the OH group representing X is exchanged for F or Cl or Br or I or CF_3 by known processes. If the product is to be converted into a compound where X is OR^{13} , wherein R^{13} has one of the meanings already described, the OH group representing X is
 15 etherified with a halide of the formula III



III

20 wherein R^{19} has a meaning analogous to R^{13} . If the product is to be converted into a compound where X is $\text{O-S(O}_2\text{)-C}_6\text{H}_4\text{-CH}_3$ or OC(O)R^{13} , wherein R^{13} has one of the meanings already described, the OH group representing X is esterified with an acid chloride of the formula IV

25

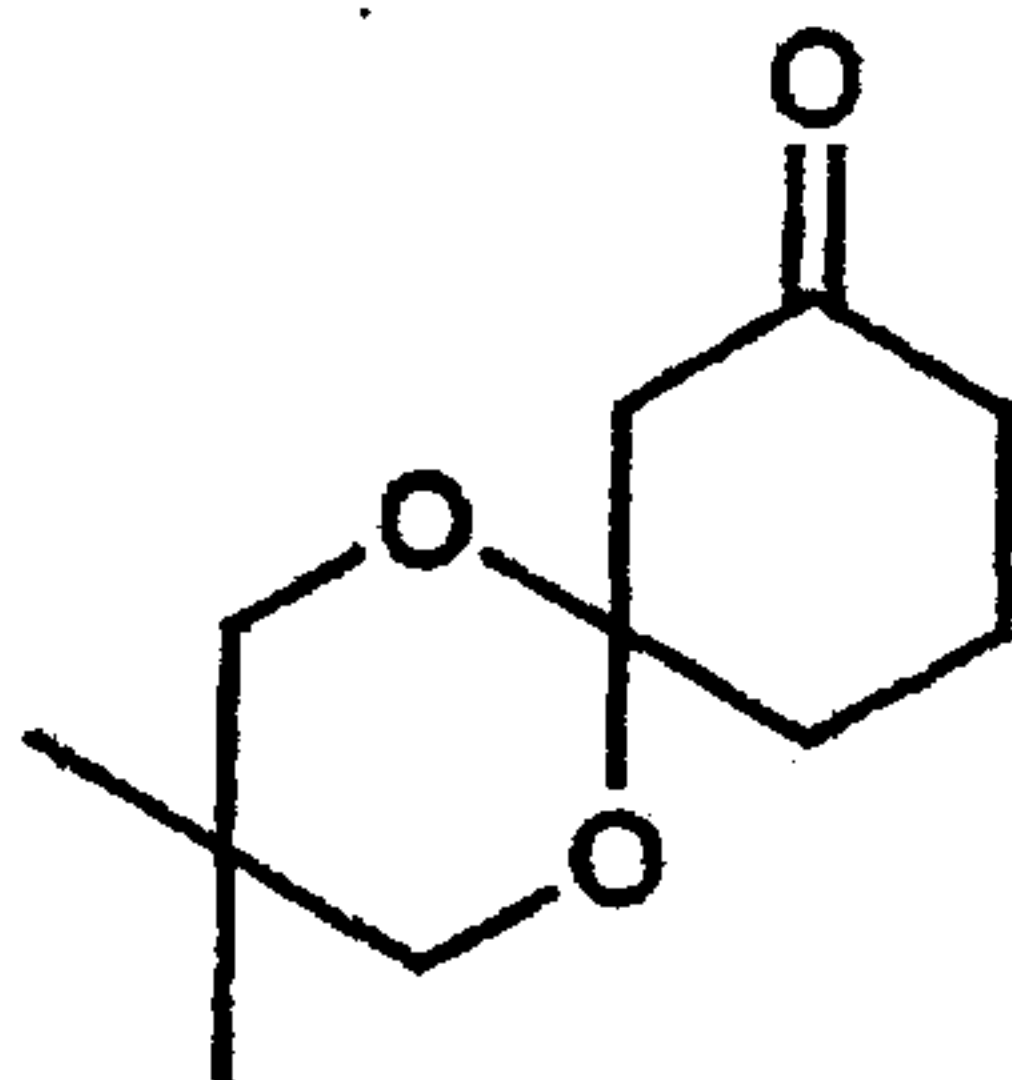
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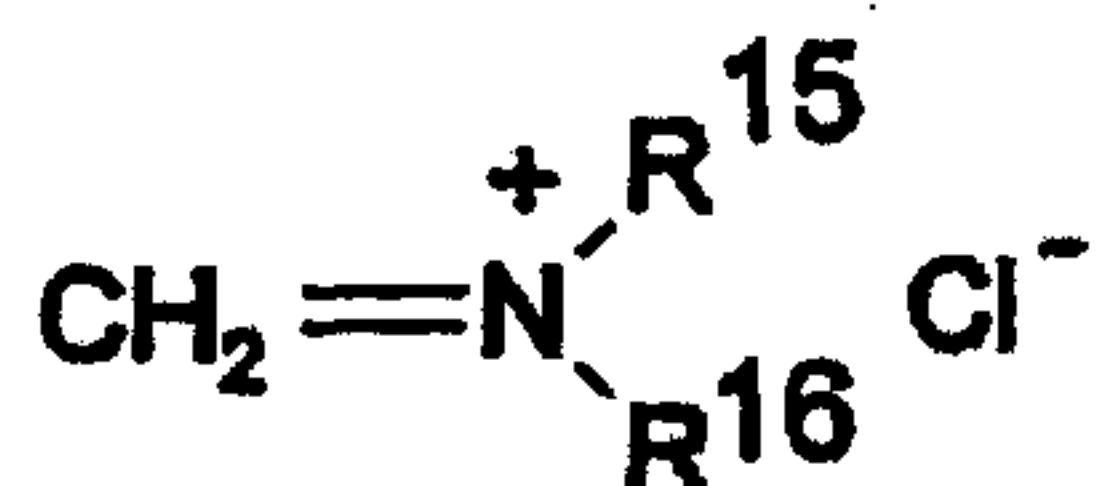
IV

or $Cl-S(O_2)-C_6H_4-CH_3$, wherein R^{20} has a meaning analogous to
 5 R^{13} . Finally, the end product is purified.

The invention also provides a preparation process for the
 starting substance according to formula II of the processes
 described above. In this, 3,3-dimethyl-1,5-dioxaspiro[5.5]
 10 undecan-8-one



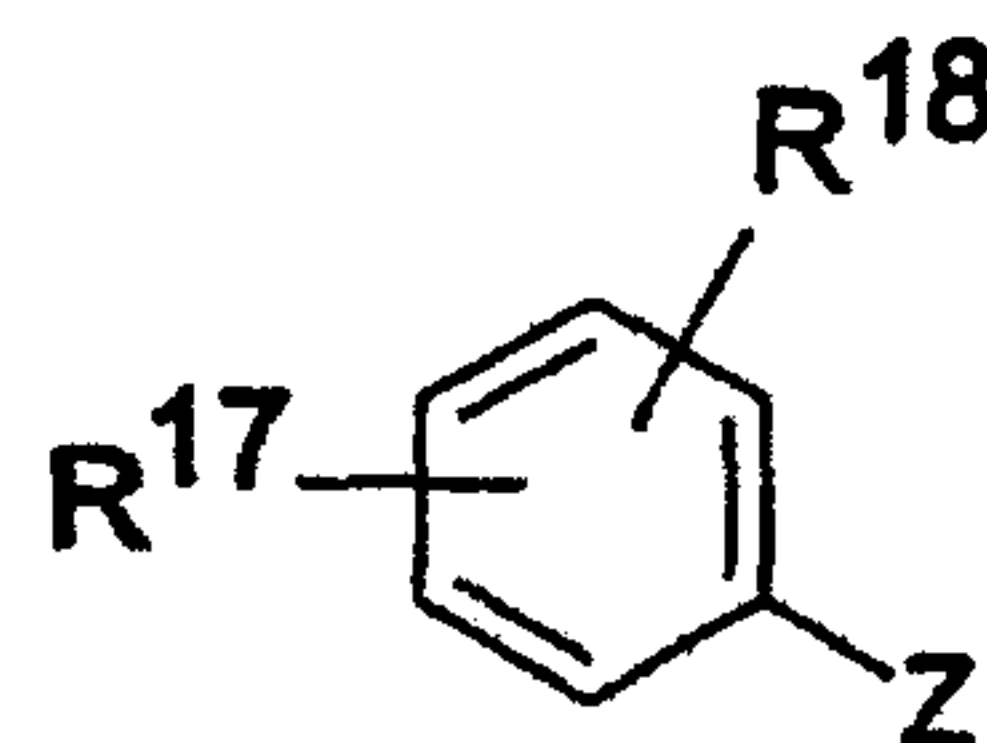
is first reacted with immonium salts of the formula V or
 with formaldehyde and an amine of the formula VI, wherein
 15 R^{15} has a meaning corresponding to R^3 and R^{16} to R^4 as
 already described.



V



VI



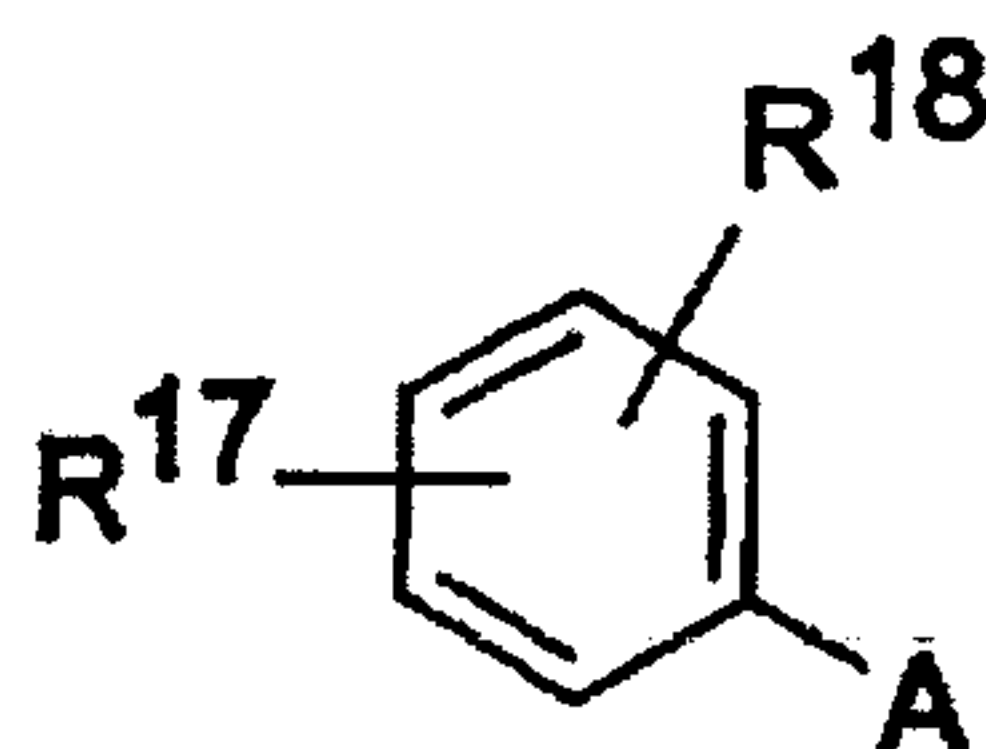
VII

The Mannich bases obtained in this way are then reacted
 20 with an organometallic compound of the formula VII, in
 which Z denotes $MgCl$, $MgBr$, MgI or lithium and R^{17} has a
 meaning corresponding to R^1 and R^{18} to R^2 as already
 described, at temperatures of between $-70^\circ C$ and $60^\circ C$.
 Preferred solvents in this reaction are diethyl ether or

tetrahydrofuran. The reaction with a Grignard compound of the formula **VII** can be carried out with or without the addition of an entraining reagent. If an entraining reagent is employed, 1,2-dibromoethane is preferred.

5

Grignard compounds of the formula **VII**, in which Z denotes MgCl, MgBr or MgI, are predominantly commercially obtainable, but can also be prepared by reaction of halogen compounds of the formula **VIII**, in which A denotes Cl, Br or I and R¹⁷ has a meaning corresponding to R¹ and R¹⁸ to R² as already described, with magnesium. Organolithium compounds of the formula **VII**, in which Z denotes Li, can be obtained by halogen-lithium exchange by reaction of halogen compounds of the formula **VIII**, in which A denotes Cl, Br or I, with, for example, n-butyllithium/hexane solution.

**VIII**

OH, SH and NH₂ groups can undergo undesirable side reactions under the reaction conditions mentioned. It is therefore preferable to provide these with protective groups, or in the case of NH₂ to replace this by NO₂, and to split off the protective group or reduce the NO₂ group in the last reaction step before the purification. The Application therefore also provides a modification of the processes described above, in which in R¹⁵ to R²⁰ according to formulae II to VII, and optionally also VIII, at least one OH group has been replaced by an OSi(Ph)₂tert-but group, at least one SH group has been replaced by an S-p-methoxybenzyl group and/or at least one NH₂ group has been replaced by an NO₂

group and, after conclusion of the entire reaction sequence, before purification of the end product, an OSi(Ph)₂tert-but group is split off with tetrabutylammonium fluoride in tetrahydrofuran and/or at least one p-methoxybenzyl group is split off with a metal amine, preferably sodium amine, and/or at least one NO₂ group is reduced to NH₂.

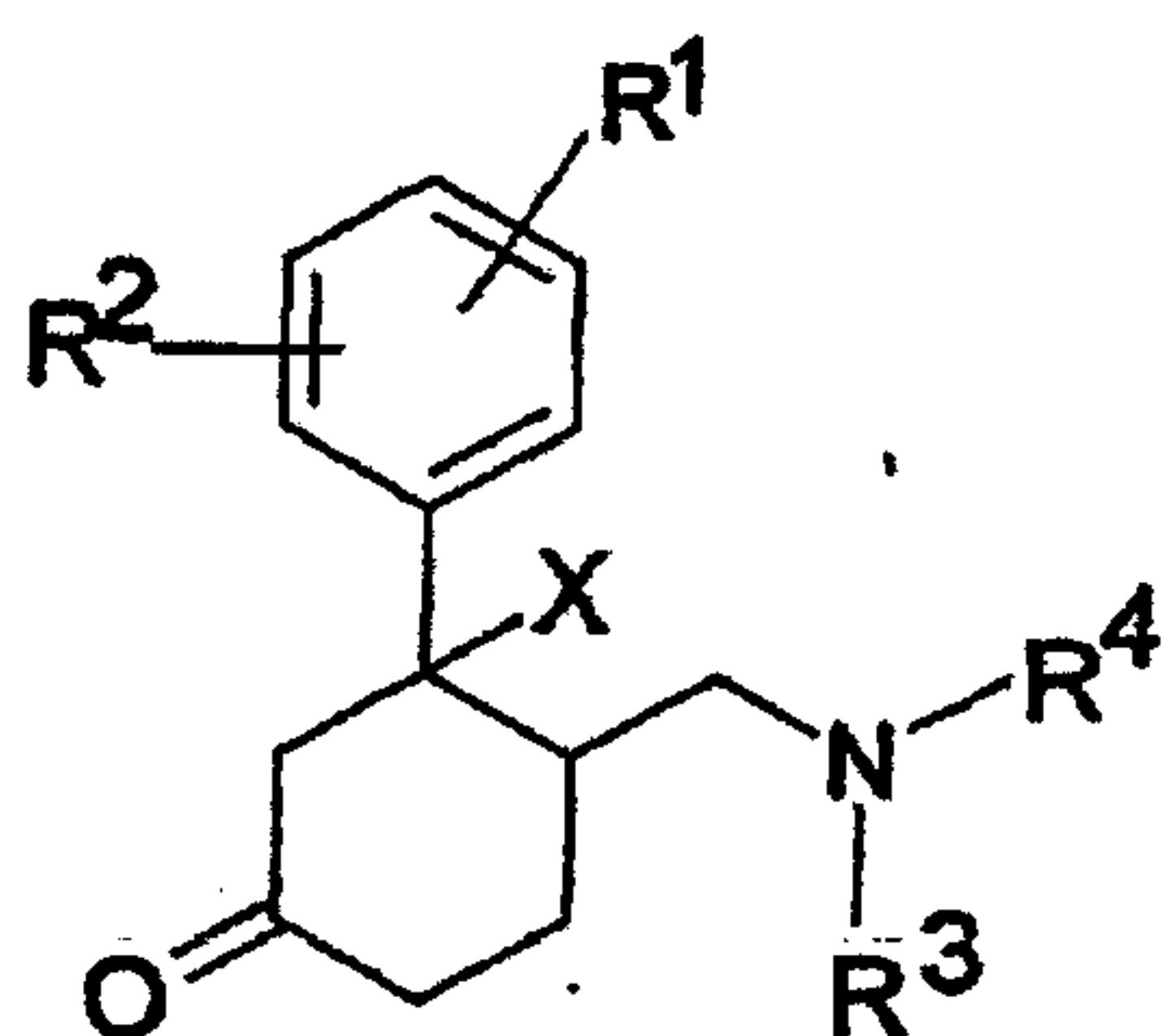
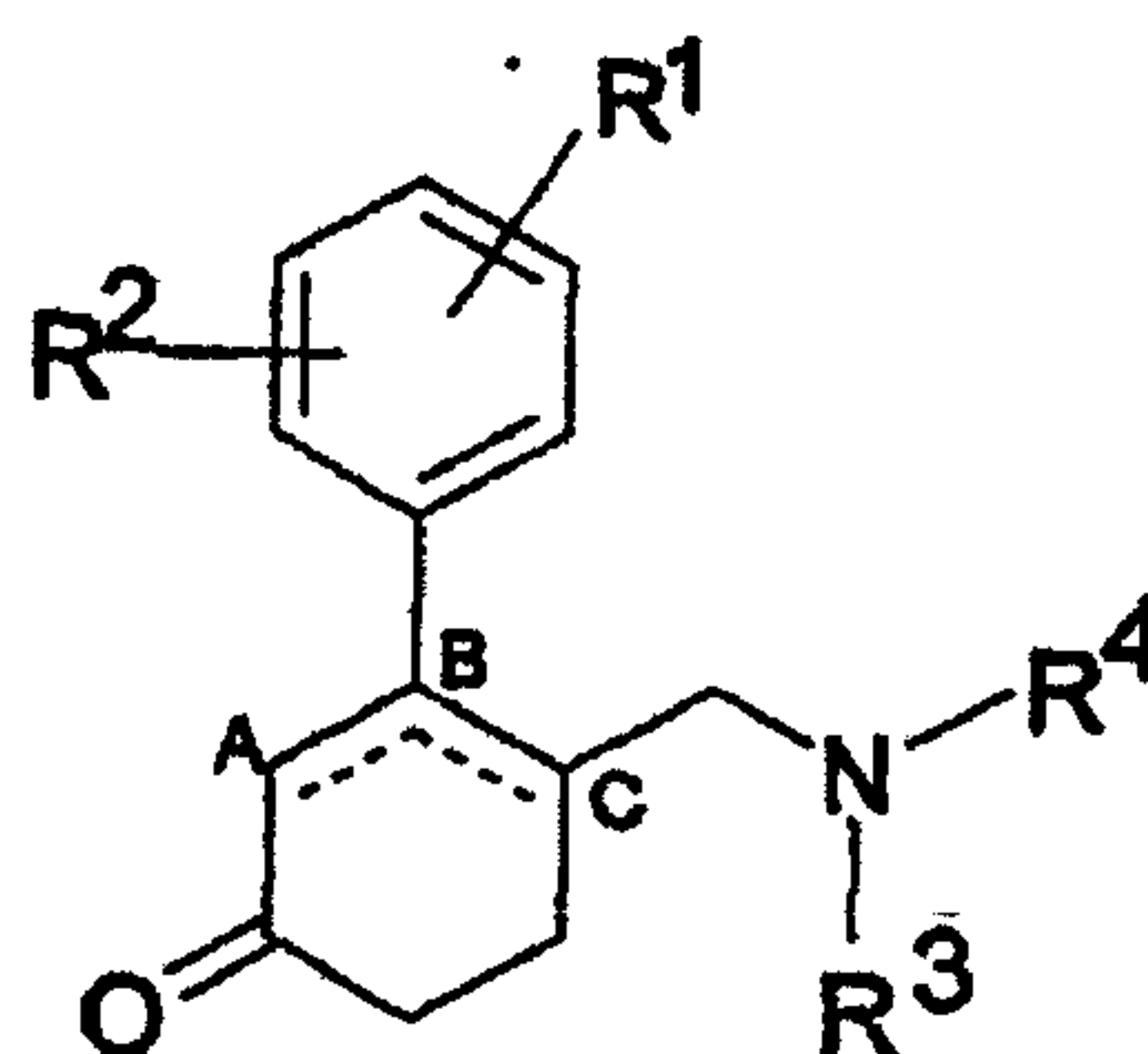
Furthermore, carboxylic acid or thiocarboxylic acid groups are not stable under certain circumstances under the reaction conditions mentioned, so that it is preferable to react methyl esters thereof and to hydrolyse the process product with KOH solution or NaOH solution in methanol at 40°C - 60°C after conclusion of the entire reaction sequence, before the purification. The invention therefore also provides a modification of the processes described above in which, after conclusion of the entire reaction sequence, before purification as the end product, a process product with at least one C(O)OCH₃, OC(O)OCH₃ and/or C(S)OCH₃ group is hydrolysed with KOH solution or NaOH solution in methanol at 40°C - 60°C.

The purification of the compounds obtained in the individual reaction sequences is carried out by crystallization or column chromatography.

The compounds of the formula **I** or **Ia** can be converted into their salts in a manner known per se with physiologically tolerated acids, such as hydrochloric acid, hydrobromic acid, sulfuric acid, methanesulfonic acid, formic acid, acetic acid, oxalic acid, succinic acid, tartaric acid, mandelic acid, fumaric acid, lactic acid, citric acid, glutamic acid and/or aspartic acid. The salt formation is preferably carried out in a solvent, such as diisopropyl

ether, acetic acid alkyl esters, acetone and/or 2-butanone. Trimethylchlorosilane in aqueous solution is particularly suitable for preparation of the hydrochlorides.

- 5 The aminomethyl-phenyl-cyclohexanone derivatives according to the invention are toxicologically acceptable, so that they are suitable as the pharmaceutical active compound in medicaments.
- 10 The invention therefore also provides medicaments which comprise, as the active compound, at least one aminomethyl-phenyl-cyclohexanone derivative of the general formula I or Ia

**I****Ia**

15

wherein

20 R^1 and R^2 independently of one another are chosen from R^5 or YR^5 , where $Y = C_1-C_{10}$ -alkyl, C_2-C_{10} -alkenyl or C_2-C_{10} -alkynyl, branched or unbranched and mono- or polysubstituted or unsubstituted, wherein R^5 is chosen from

25 H, F, Cl, Br, I, CN, NO_2 ; C_1-C_8 -alkyl, C_2-C_8 -alkenyl or C_2-C_8 -alkynyl, in each case branched or

- unbranched and mono- or polysubstituted or unsubstituted; C₃-C₇-cycloalkyl, saturated or unsaturated and mono- or polysubstituted or unsubstituted, or a corresponding heterocyclic radical, in which one C atom in the ring is replaced by S, O or NR⁶, where R⁶ is chosen from H, C₁-C₁₀-alkyl, C₂-C₁₀-alkenyl or C₂-C₁₀-alkynyl, in each case branched or unbranched and mono- or polysubstituted or unsubstituted;
- aryl or heteroaryl, in each case mono- or polysubstituted or unsubstituted;
- OR⁷, OC(O)R⁷, OC(O)OR⁷, OC(S)R⁷, C(O)R⁷, C(O)OR⁷, C(S)R⁷, C(S)OR⁷, SR⁷, S(O)R⁷ or S(O₂)R⁷, wherein R⁷ is chosen from H, C₁-C₁₈-alkyl, C₂-C₁₈-alkenyl or C₂-C₁₈-alkynyl, in each case branched or unbranched and mono- or polysubstituted or unsubstituted; C₃-C₇-cycloalkyl, saturated or unsaturated and mono- or polysubstituted or unsubstituted, or a corresponding heterocyclic radical, in which one C atom in the ring is replaced by S, O or NR⁸, where R⁸ is chosen from H, C₁-C₁₀-alkyl, C₂-C₁₀-alkenyl or C₂-C₁₀-alkynyl, in each case branched or unbranched and mono- or polysubstituted or unsubstituted;
- alkylaryl, saturated or unsaturated and mono- or polysubstituted or unsubstituted; aryl or heteroaryl, in each case mono- or polysubstituted or unsubstituted; or

NR^9R^{10} , $\text{C}(\text{O})\text{NR}^9\text{R}^{10}$ or $\text{S}(\text{O}_2)\text{NR}^9\text{R}^{10}$, wherein R^9 and R^{10} independently of one another are chosen from

5 H, $\text{C}_1\text{-C}_{18}$ -alkyl, $\text{C}_2\text{-C}_{18}$ -alkenyl or $\text{C}_2\text{-C}_{18}$ -alkynyl, in each case branched or unbranched and mono- or polysubstituted or unsubstituted; $\text{C}_3\text{-C}_7$ -cycloalkyl, saturated or unsaturated and mono- or polysubstituted or unsubstituted, or a corresponding
10 heterocyclic radical, in which one C atom in the ring is replaced by S, O or NR^{11} , where R^{11} is chosen from

H, $\text{C}_1\text{-C}_{10}$ -alkyl, $\text{C}_2\text{-C}_{10}$ -alkenyl or $\text{C}_2\text{-C}_{10}$ -alkynyl, in each case branched or
15 unbranched and mono- or polysubstituted or unsubstituted;
alkylaryl, saturated or unsaturated and mono- or polysubstituted or unsubstituted;
aryl or heteroaryl, in each case mono- or
20 polysubstituted or unsubstituted;

or

R^9 and R^{10} together form a $\text{C}_3\text{-C}_7$ -cycloalkyl, saturated or unsaturated and mono- or
25 polysubstituted or unsubstituted, or a corresponding heterocyclic radical, in which one C atom in the ring is replaced by S, O or NR^{12} , where R^{12} is chosen from

30 H, $\text{C}_1\text{-C}_{10}$ -alkyl, $\text{C}_2\text{-C}_{10}$ -alkenyl or $\text{C}_2\text{-C}_{10}$ -alkynyl, in each case branched or unbranched and mono- or polysubstituted or unsubstituted;

or

R^1 and R^2 together form $-\text{CH}=\text{CH}-\text{CH}=\text{CH}-$, wherein the naphthyl system formed can be mono- or polysubstituted,

X is chosen from

H, F, Cl, Br, I, CF_3 , $\text{O}-\text{S}(\text{O}_2)-\text{C}_6\text{H}_4-\text{pCH}_3$, OR^{13} or $\text{OC}(\text{O})\text{R}^{13}$, wherein R^{13} is chosen from

H; C_1-C_{10} -alkyl, C_2-C_{10} -alkenyl or C_2-C_{10} -alkynyl, in each case branched or unbranched and mono- or polysubstituted or unsubstituted; C_3-C_7 -cycloalkyl, saturated or unsaturated and mono- or polysubstituted or unsubstituted, or a corresponding heterocyclic radical, in which one C atom in the ring is replaced by N, S or O; alkylaryl, saturated or unsaturated and mono- or polysubstituted or unsubstituted; aryl or heteroaryl, in each case mono- or polysubstituted or unsubstituted;

or

if the compound contains no X, according to formula Ia a double bond is formed between C atom A and C atom B or C atom B and C atom C;

and

R^3 , R^4 independently of one another are chosen from H, C_1-C_{10} -alkyl, C_2-C_{10} -alkenyl or C_2-C_{10} -alkynyl, in each case branched or unbranched and mono- or polysubstituted or unsubstituted; C_3-C_7 -

cycloalkyl, saturated or unsaturated and mono- or polysubstituted or unsubstituted, or a corresponding heterocyclic radical, in which one C atom in the ring is replaced by N, S or O; alkylaryl, saturated or unsaturated and mono- or polysubstituted or unsubstituted; aryl or heteroaryl, in each case mono- or polysubstituted or unsubstituted;

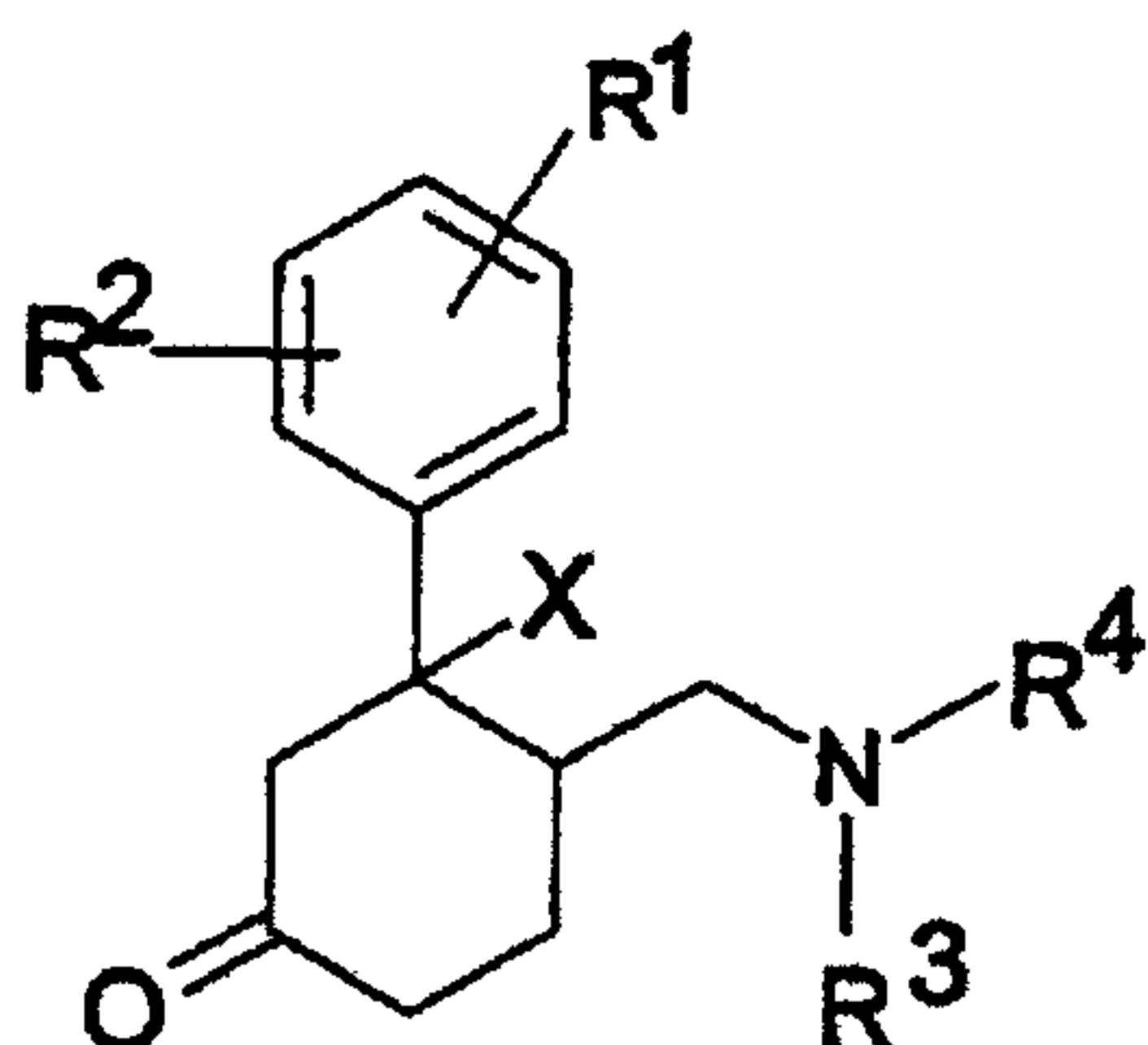
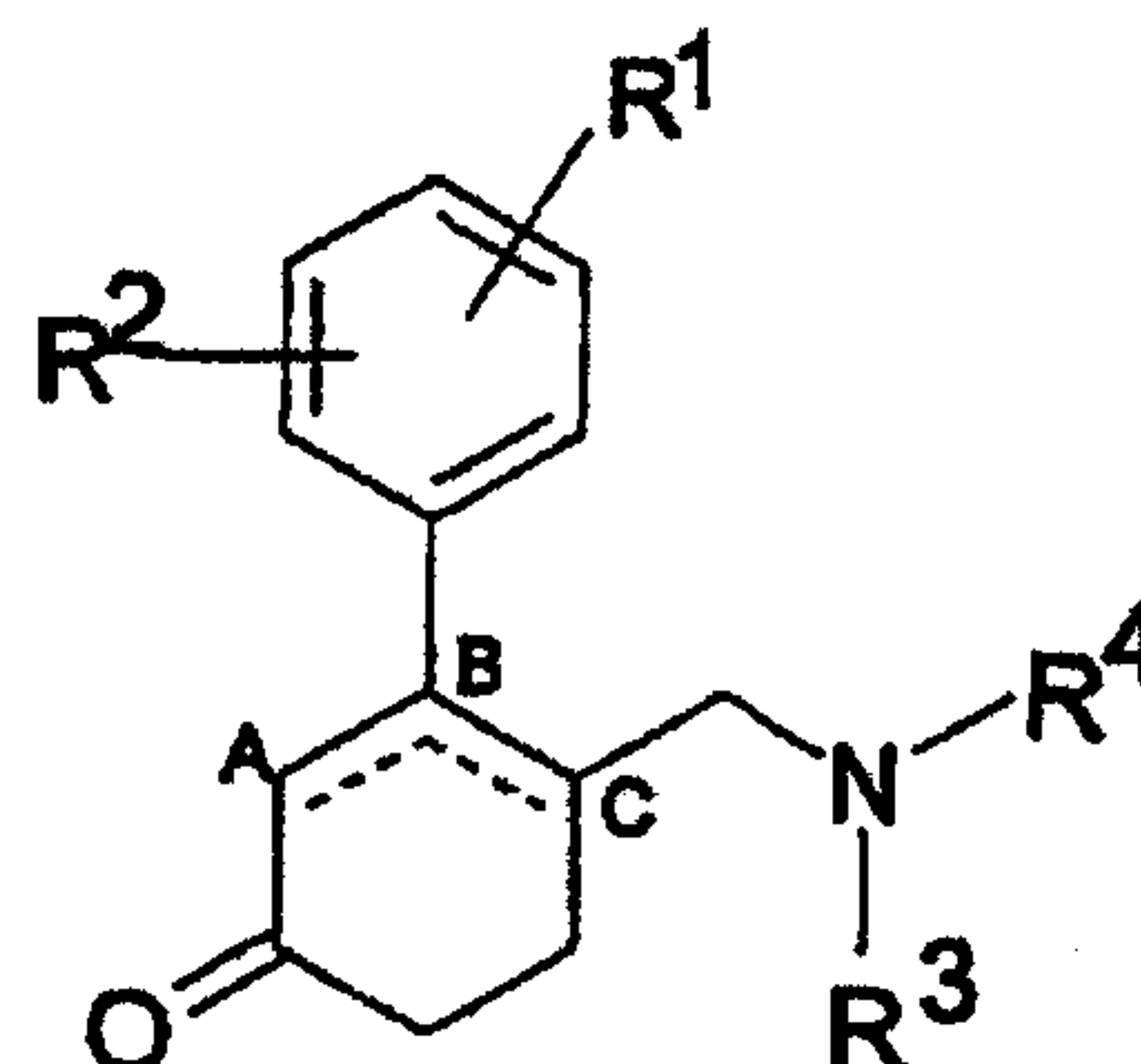
10 or

R^3 and R^4 together form a C_3 - C_7 -cycloalkyl, saturated or unsaturated and mono- or polysubstituted or unsubstituted, or a corresponding heterocyclic radical, in which one C atom in the ring is replaced by S, O or NR^{14} , where R^{14} is chosen from H, C_1 - C_{10} -alkyl, C_2 - C_{10} -alkenyl or C_2 - C_{10} -alkinyl, in each case branched or unbranched and mono- or polysubstituted or unsubstituted;

in the form of its diastereomers or enantiomers and of its free base or of a salt formed with a physiologically tolerated acid, in particular the hydrochloride salt.

25

Preferred medicaments are those comprising at least one aminomethyl-phenyl-cyclohexanone derivative of the general formula I or Ia

**I****Ia**

in which, independently of one another

- 5 $R^1 = R^5$, wherein R^5 is chosen from
H, F, Cl, Br, I, CHF_2 , CF_3 , NO_2 , NH_2 ; C_1 - C_4 -alkyl
or C_2 - C_4 -alkenyl, branched or unbranched and mono-
or polysubstituted or unsubstituted; aryl,
substituted or unsubstituted; OR^7 , $\text{C}(\text{O})\text{OR}^7$ or SR^7 ,
10 wherein R^7 is chosen from

- H; C_1 - C_4 -alkyl, branched or unbranched and
mono- or polysubstituted or unsubstituted;
preferably H, CF_3 or CH_3 ,
or $\text{S}(\text{O}_2)\text{NR}^9\text{R}^{10}$, wherein R^9 and R^{10} independently of
15 one another are chosen from

- H; C_1 - C_4 -alkyl, branched or unbranched and
mono- or polysubstituted or unsubstituted;
wherein particularly preferably $R^1 = R^5$, where R^5 is
chosen from
20 H, F, Cl, OH, CH_3 , C_2H_5 , C_2H_3 , CHF_2 , CF_3 , SCH_3 ,
 OCF_3 , OCH_3 , OC_2H_5 , $\text{C}(\text{O})\text{OCH}_3$ or $\text{C}(\text{O})\text{OC}_2\text{H}_5$, or
phenyl

and/or $R^2 = R^5$, wherein R^5 is chosen from

H, F, Cl, Br, I, SCH₃; C₁-C₄-alkyl, C₂-C₄-alkenyl, branched or unbranched and mono- or polysubstituted or unsubstituted, preferably CF₃; OR⁷, where R⁷ is chosen from C₁-C₄-alkyl, branched or unbranched and mono- or polysubstituted or unsubstituted, preferably CH₃;

and/or R¹ and R² have different meanings or R¹ and R² together form -CH=CH-CH=CH-, wherein the naphthyl system formed can be mono- or polysubstituted, preferably by halogen, OC₁₋₃-alkyl or C₁₋₃-alkyl, unsubstituted or mono or polysubstituted, in particular by OCH₃;

and/or X is chosen from

H, F, Cl, OH, CF₃, O-S(O₂)-C₆H₄-pCH₃ or OC(O)R⁷, where R⁷ = H; C₁-C₄-alkyl or C₂-C₄-alkenyl, branched or unbranched and mono- or polysubstituted or unsubstituted, preferably H, F, Cl, OH, O-S(O₂)-C₆H₄-pCH₃ or OC(O)R⁷, where R⁷ = C₁-C₄-alkyl, preferably CH₃, in particular H or OH;

or

if the compound contains no X, according to formula Ia a double bond is formed between C atom A and C atom B or C atom B and C atom C,

and/or R³ and R⁴ independently of one another are chosen from

C₁-C₄-alkyl, branched or unbranched and mono- or polysubstituted or unsubstituted, preferably CH₃;

or

5 R³ and R⁴ together form a C₃-C₇-cycloalkyl,
saturated or unsaturated and mono- or
polysubstituted or unsubstituted,

and/or R¹, R², X, R³ and/or R⁴ have one of the meanings
already mentioned.

10 Particularly preferred medicaments here are those which
comprise as the active compound at least one aminomethyl-
phenyl-cyclohexanone derivative chosen from the following
group:

- 15 • *rac-cis*-[4-dimethylaminomethyl-3-hydroxy-3-(3-methoxy-
phenyl)-cyclohexanone],
- *rac-cis*-[4-dimethylaminomethyl-3-(3-methoxy-phenyl)-
cyclohexanone],
- *rac-trans*-[4-dimethylaminomethyl-3-(3-methoxy-phenyl)-
20 cyclohexanone],
- *rac-cis*-[4-dimethylaminomethyl-3-(3-hydroxy-phenyl)-
cyclohexanone],
- *rac-trans*-[4-dimethylaminomethyl-3-(3-hydroxy-phenyl)-
cyclohexanone] or
- 25 • 4-dimethylaminomethyl-3-(3-methoxy-phenyl)-cyclohex-2-
enone
- 4-dimethylaminomethyl-3-phenyl-cyclohex-2-enone;
- 4-dimethylaminomethyl-3-(3-hydroxy-phenyl)-cyclohex-2-
30 enone;

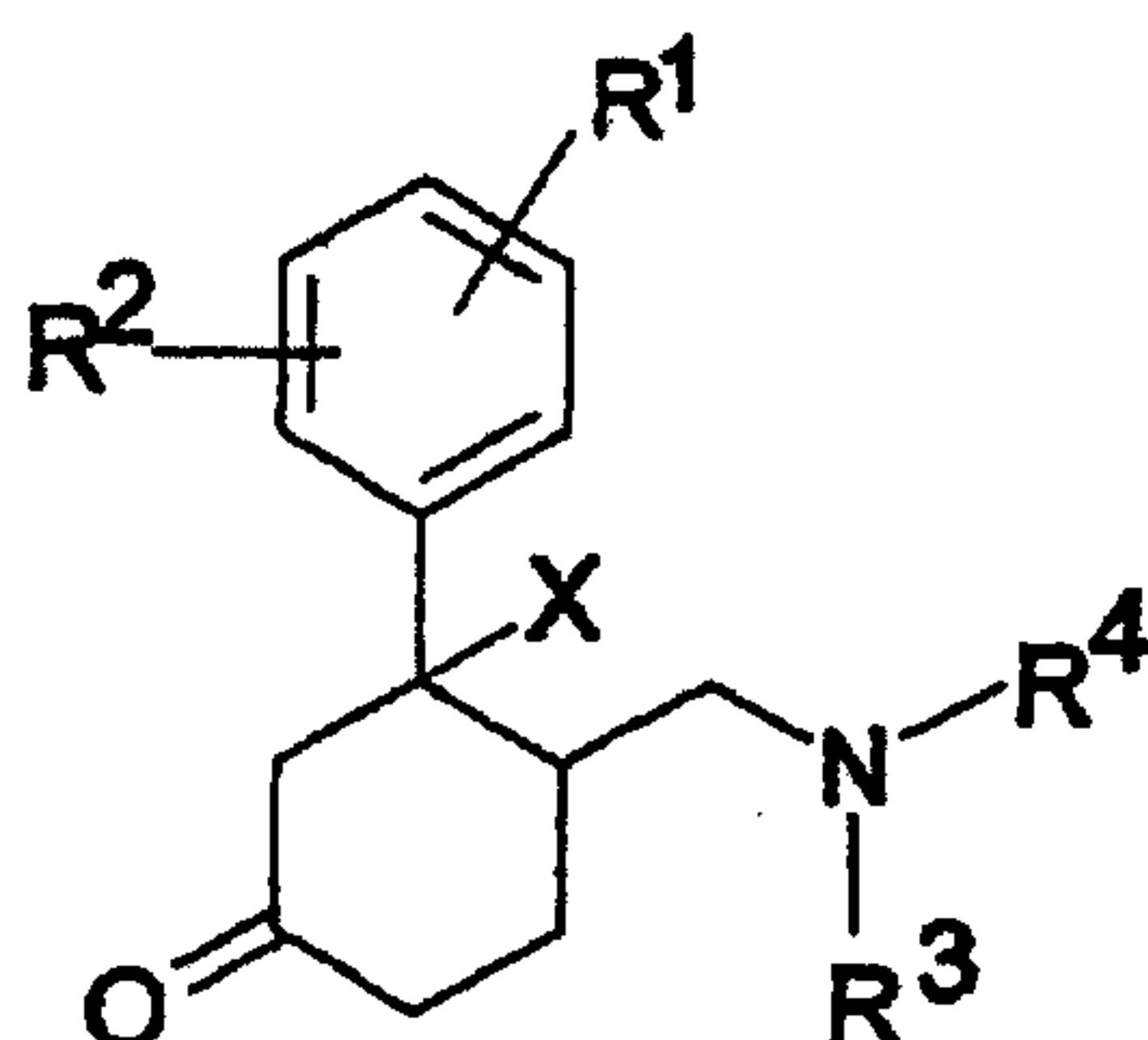
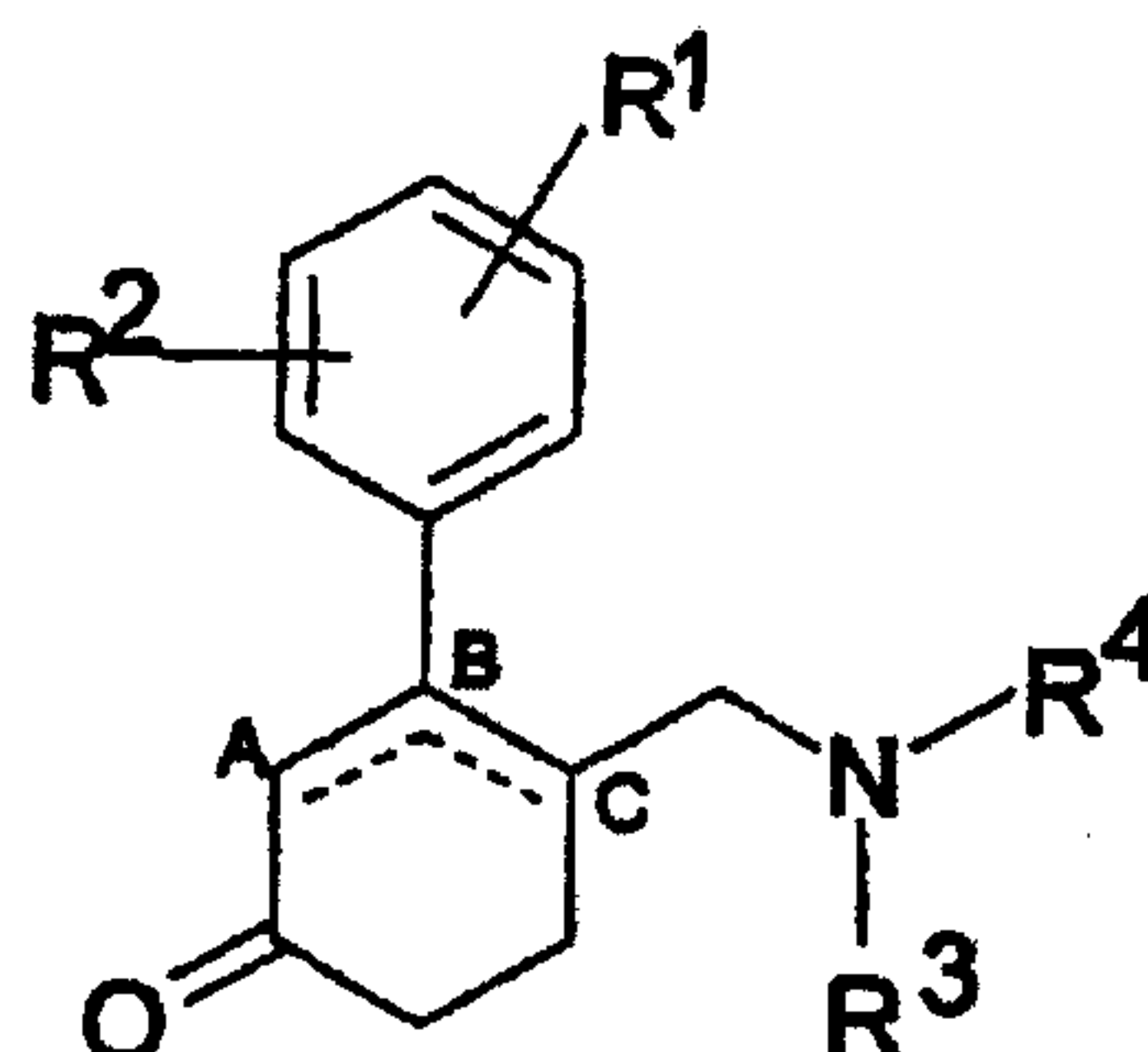
- rac-trans-4-dimethylaminomethyl-3-phenyl-cyclohexanone;
- rac-cis-4-dimethylaminomethyl-3-phenyl-cyclohexanone;
- 5 • 4-dimethylaminomethyl-3-(4-methoxy-phenyl)-cyclohex-2-enone;
- 4-dimethylaminomethyl-3-naphthalen-2-yl-cyclohex-2-
- 10 enone;
- rac-trans-4-dimethylaminomethyl-3-hydroxy-3-naphthalen-2-yl-cyclohexanone;
- 15 • rac-trans-4-dimethylaminomethyl-3-(3-fluoro-phenyl)-cyclohexanone;
- rac-cis-4-dimethylaminomethyl-3-(3-fluoro-phenyl)-cyclohexanone;
- 20 • rac-cis-4-dimethylaminomethyl-3-hydroxy-3-(2-methoxy-phenyl)-cyclohexanone
- rac-cis-4-dimethylaminomethyl-3-hydroxy-3-(6-methoxy-
- 25 naphthalen-2-yl)-cyclohexanone;
- 4-dimethylaminomethyl-3-(6-methoxy-naphthalen-2-yl)-cyclohex-2-enone;
- 30 • rac-cis-3-biphenyl-4-yl-4-dimethylaminomethyl-3-hydroxy-cyclohexanone

- 3-(3-difluoromethyl-phenyl)-4-dimethylaminomethyl-cyclohex-2-enone;
 - 5 • 4-dimethylaminomethyl-3-(3-fluoro-phenyl)-cyclohex-2-enone;
 - 3-(3,4-difluoro-phenyl)-4-dimethylaminomethyl-cyclohex-2-enone;
 - 10 • 4-dimethylaminomethyl-3-(4-fluoro-phenyl)-cyclohex-2-enone;
 - 4-dimethylaminomethyl-3-(4-trifluoromethyl-phenyl)-cyclohex-2-enone;
 - 15 • 3-(3,5-dichloro-phenyl)-4-dimethylaminomethyl-cyclohex-2-enone;
 - 3-(3,5-difluoro-phenyl)-4-dimethylaminomethyl-cyclohex-2-enone;
 - 20 • rac-cis-3-(3,5-difluoro-phenyl)-4-dimethylaminomethyl-3-hydroxy-cyclohexanone
- 25 as the free base or in the form of a salt formed with a physiologically tolerated acid, in particular the hydrochloride salt.

The medicaments according to the invention comprise, in
30 addition to at least one aminomethyl-phenyl-cyclohexanone derivative, carrier materials, fillers, solvents, diluents, dyestuffs and/or binders and can be administered as liquid medicament forms in the form of injection solutions, drops

or juices, or as semi-solid medicament forms in the form of granules, tablets, pellets, patches, capsules, plasters or aerosols. The choice of auxiliary substances and the amounts thereof to be employed depends on whether the medicament is to be administered orally, perorally, parenterally, intravenously, intraperitoneally, intradermally, intramuscularly, intranasally, buccally, rectally or locally, for example on infections of the skin, the mucous membranes and the eyes. Formulations in the form of tablets, coated tablets, capsules, granules, drops, juices and syrups are suitable for oral administration, and solutions, suspensions, easily reconstitutable dry formulations and sprays are suitable for parenteral, topical and inhalatory administration. Aminomethyl-phenyl-cyclohexanone derivatives according to the invention in a depot in dissolved form or in a patch, optionally with the addition of agents which promote penetration through the skin, are suitable formulations for percutaneous administration. Formulation forms which can be used orally or percutaneously can release the aminomethyl-phenyl-cyclohexanone derivatives in a delayed manner. The amount of active compound to be administered to the patient varies according to the weight of the patient, the mode of administration, the indication and the severity of the disease. 50 to 500 mg/kg of at least one aminomethyl-phenyl-cyclohexanone derivative are usually administered.

The aminomethyl-phenyl-cyclohexanone derivatives are preferably employed for treatment of pain, so that the invention also provides the use of at least one aminomethyl-phenyl-cyclohexanone derivative of the general formula I or Ia

**I****Ia**

wherein

5 R^1 and R^2 independently of one another are chosen from R^5 or YR^5 , where $Y = C_1-C_{10}$ -alkyl, C_2-C_{10} -alkenyl or C_2-C_{10} -alkinyl, branched or unbranched and mono- or polysubstituted or unsubstituted, wherein R^5 is chosen from

10

H, F, Cl, Br, I, CN, NO_2 ; C_1-C_8 -alkyl, C_2-C_8 -alkenyl or C_2-C_8 -alkinyl, in each case branched or unbranched and mono- or polysubstituted or unsubstituted; C_3-C_7 -cycloalkyl, saturated or

15 unsaturated and mono- or polysubstituted or unsubstituted, or a corresponding heterocyclic radical, in which one C atom in the ring is replaced by S, O or NR^6 , where R^6 is chosen from

15

20

H, C_1-C_{10} -alkyl, C_2-C_{10} -alkenyl or C_2-C_{10} -alkinyl, in each case branched or unbranched and mono- or polysubstituted or unsubstituted;

25

aryl or heteroaryl, in each case mono- or polysubstituted or unsubstituted;

OR⁷, OC(O)R⁷, OC(O)OR⁷, OC(S)R⁷, C(O)R⁷, C(O)OR⁷, C(S)R⁷, C(S)OR⁷, SR⁷, S(O)R⁷ or S(O₂)R⁷, wherein R⁷ is chosen from

5 H, C₁-C₁₈-alkyl, C₂-C₁₈-alkenyl or C₂-C₁₈-alkinyl, in each case branched or unbranched and mono- or polysubstituted or unsubstituted; C₃-C₇-cycloalkyl, saturated or unsaturated and mono- or polysubstituted or
10 unsubstituted, or a corresponding heterocyclic radical, in which one C atom in the ring is replaced by S, O or NR⁸, where R⁸ is chosen from

15 H, C₁-C₁₀-alkyl, C₂-C₁₀-alkenyl or C₂-C₁₀-alkinyl, in each case branched or unbranched and mono- or polysubstituted or unsubstituted;
 alkylaryl, saturated or unsaturated and mono- or polysubstituted or unsubstituted;
20 aryl or heteroaryl, in each case mono- or polysubstituted or unsubstituted; or

NR⁹R¹⁰, C(O)NR⁹R¹⁰ or S(O₂)NR⁹R¹⁰, wherein R⁹ and R¹⁰ independently of one another are chosen from

25 H, C₁-C₁₈-alkyl, C₂-C₁₈-alkenyl or C₂-C₁₈-alkinyl, in each case branched or unbranched and mono- or polysubstituted or unsubstituted; C₃-C₇-cycloalkyl, saturated or unsaturated and mono- or polysubstituted or
30 unsubstituted, or a corresponding heterocyclic radical, in which one C atom in the ring is replaced by S, O or NR¹¹, where R¹¹ is chosen from

H, C₁-C₁₀-alkyl, C₂-C₁₀-alkenyl or C₂-C₁₀-alkynyl, in each case branched or unbranched and mono- or polysubstituted or unsubstituted;

5 alkylaryl, saturated or unsaturated and mono- or polysubstituted or unsubstituted; aryl or heteroaryl, in each case mono- or polysubstituted or unsubstituted;

10 or

R⁹ and R¹⁰ together form a C₃-C₇-cycloalkyl, saturated or unsaturated and mono- or polysubstituted or unsubstituted, or a
15 corresponding heterocyclic radical, in which one C atom in the ring is replaced by S, O or NR¹², where R¹² is chosen from

H, C₁-C₁₀-alkyl, C₂-C₁₀-alkenyl or C₂-C₁₀-alkynyl, in each case branched or
20 unbranched and mono- or polysubstituted or unsubstituted;

or

25 R¹ and R² together form -CH=CH-CH=CH-, wherein the naphthyl system formed can be mono- or polysubstituted,

X is chosen from

30 H, F, Cl, Br, I, CF₃, O-S(O₂)-C₆H₄-pCH₃, OR¹³ or OC(O)R¹³, wherein R¹³ is chosen from

H; C₁-C₁₀-alkyl, C₂-C₁₀-alkenyl or C₂-C₁₀-alkynyl, in each case branched or unbranched and mono- or polysubstituted or

5 unsubstituted; C₃-C₇-cycloalkyl, saturated or
unsaturated and mono- or polysubstituted or
unsubstituted, or a corresponding
heterocyclic radical, in which one C atom in
the ring is replaced by N, S or O;
alkylaryl, saturated or unsaturated and
mono- or polysubstituted or unsubstituted;
aryl or heteroaryl, in each case mono- or
polysubstituted or unsubstituted;

10

or

15

if the compound contains no X, according to
formula Ia a double bond is formed between C atom
A and C atom B or C atom B and C atom C;

and

20 R³, R⁴ independently of one another are chosen from
H, C₁-C₁₀-alkyl, C₂-C₁₀-alkenyl or C₂-C₁₀-alkinyl,
in each case branched or unbranched and mono- or
polysubstituted or unsubstituted; C₃-C₇-
cycloalkyl, saturated or unsaturated and mono- or
polysubstituted or unsubstituted, or a
25 corresponding heterocyclic radical, in which one
C atom in the ring is replaced by N, S or O;
alkylaryl, saturated or unsaturated and mono- or
polysubstituted or unsubstituted; aryl or
heteroaryl, in each case mono- or polysubstituted
30 or unsubstituted;

or

R^3 and R^4 together form a C_3 - C_7 -cycloalkyl, saturated or unsaturated and mono- or polysubstituted or unsubstituted, or a corresponding heterocyclic radical, in which one C atom in the ring is replaced

5

by S, O or NR^{14} , where R^{14} is chosen from H, C_1 - C_{10} -alkyl, C_2 - C_{10} -alkenyl or C_2 - C_{10} -alkynyl, in each case branched or unbranched and mono- or polysubstituted or unsubstituted;

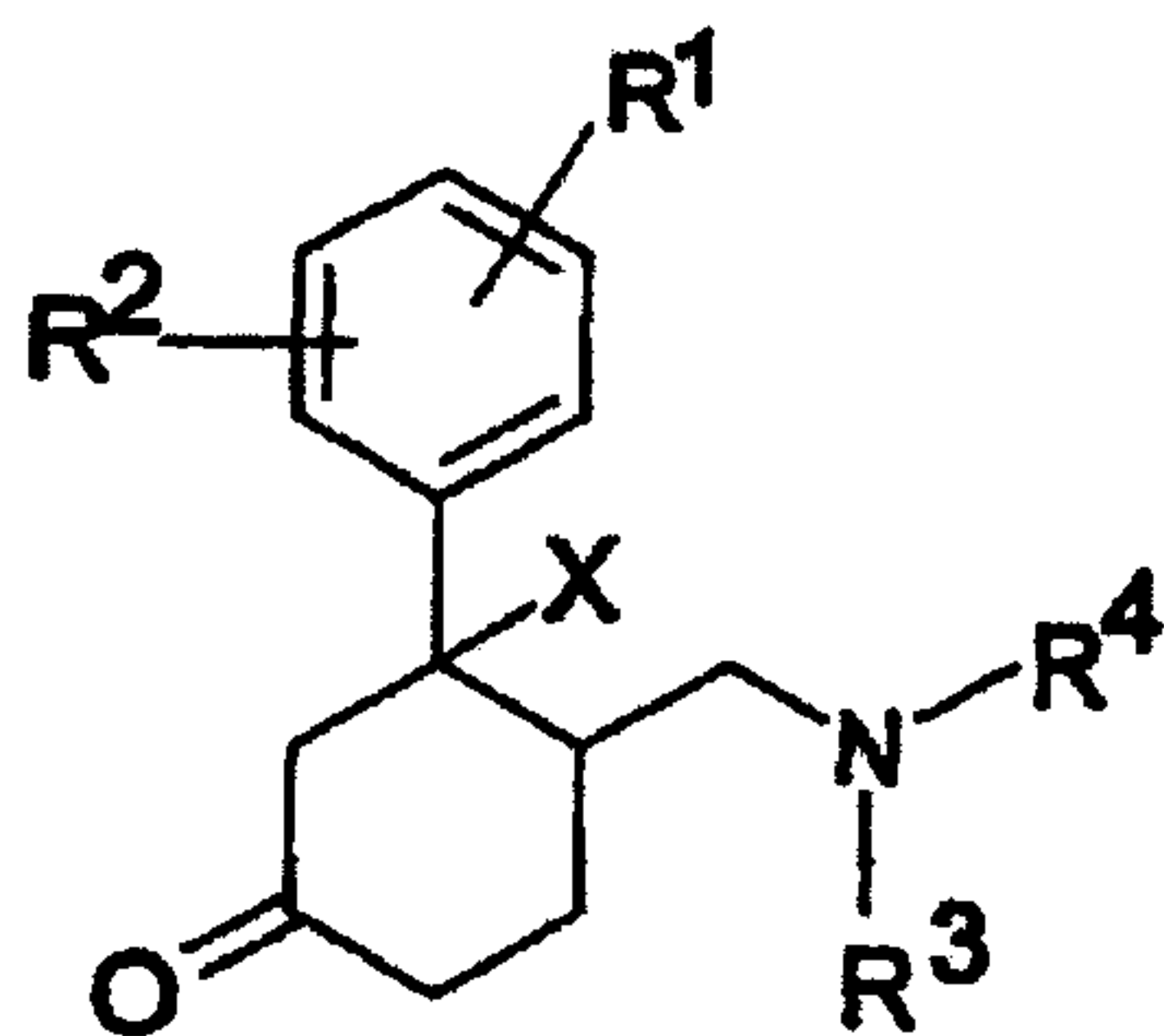
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in the form of its diastereomers or enantiomers and of its free base or of a salt formed with a physiologically tolerated acid, in particular the hydrochloride salt, for the preparation of a medicament for treatment of pain.

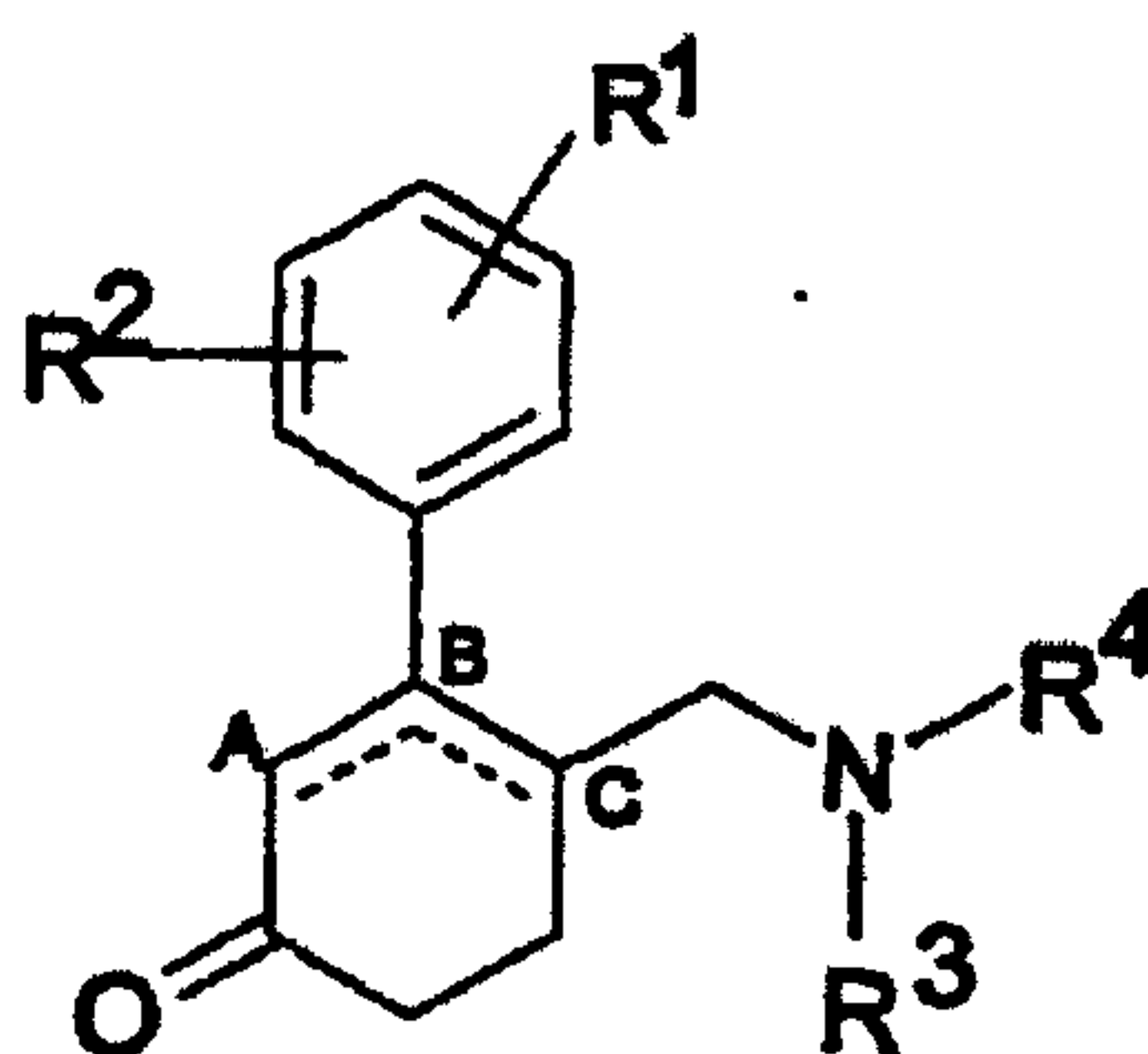
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It has been found, surprisingly, that the aminomethyl-phenyl-cyclohexanone derivatives according to the invention are very suitable for further indications, in particular for treatment of urinary incontinence, itching and/or diarrhoea, and also in other indications. The Application therefore also provides the use of at least one aminomethyl-phenyl-cyclohexanone derivative of the general formula I or Ia

20



I



Ia

25

wherein

5 R^1 and R^2 independently of one another are chosen from R^5 or YR^5 , where $Y = C_1-C_{10}$ -alkyl, C_2-C_{10} -alkenyl or C_2-C_{10} -alkinyl, branched or unbranched and mono- or polysubstituted or unsubstituted, wherein R^5 is chosen from

10 H, F, Cl, Br, I, CN, NO_2 ; C_1-C_8 -alkyl, C_2-C_8 -alkenyl or C_2-C_8 -alkinyl, in each case branched or unbranched and mono- or polysubstituted or unsubstituted; C_3-C_7 -cycloalkyl, saturated or unsaturated and mono- or polysubstituted or unsubstituted, or a corresponding heterocyclic
15 radical, in which one C atom in the ring is replaced by S, O or NR^6 , where R^6 is chosen from
H, C_1-C_{10} -alkyl, C_2-C_{10} -alkenyl or C_2-C_{10} -alkinyl, in each case branched or unbranched and mono- or polysubstituted or
20 unsubstituted;

aryl or heteroaryl, in each case mono- or polysubstituted or unsubstituted;

25 OR^7 , $OC(O)R^7$, $OC(O)OR^7$, $OC(S)R^7$, $C(O)R^7$, $C(O)OR^7$, $C(S)R^7$, $C(S)OR^7$, SR^7 , $S(O)R^7$ or $S(O_2)R^7$, wherein R^7 is chosen from

30 H, C_1-C_{18} -alkyl, C_2-C_{18} -alkenyl or C_2-C_{18} -alkinyl, in each case branched or unbranched and mono- or polysubstituted or unsubstituted; C_3-C_7 -cycloalkyl, saturated or unsaturated and mono- or polysubstituted or unsubstituted, or a corresponding heterocyclic radical, in which one C atom in

the ring is replaced by S, O or NR^8 , where R^8 is chosen from

5 H, $\text{C}_1\text{-C}_{10}$ -alkyl, $\text{C}_2\text{-C}_{10}$ -alkenyl or $\text{C}_2\text{-C}_{10}$ -alkynyl, in each case branched or unbranched and mono- or polysubstituted or unsubstituted;

10 alkylaryl, saturated or unsaturated and mono- or polysubstituted or unsubstituted; aryl or heteroaryl, in each case mono- or polysubstituted or unsubstituted; or

NR^9R^{10} , $\text{C}(\text{O})\text{NR}^9\text{R}^{10}$ or $\text{S}(\text{O}_2)\text{NR}^9\text{R}^{10}$, wherein R^9 and R^{10} independently of one another are chosen from

15 H, $\text{C}_1\text{-C}_{18}$ -alkyl, $\text{C}_2\text{-C}_{18}$ -alkenyl or $\text{C}_2\text{-C}_{18}$ -alkynyl, in each case branched or unbranched and mono- or polysubstituted or unsubstituted; $\text{C}_3\text{-C}_7$ -cycloalkyl, saturated or unsaturated and mono- or polysubstituted or unsubstituted, or a corresponding
20 heterocyclic radical, in which one C atom in the ring is replaced by S, O or NR^{11} , where R^{11} is chosen from

25 H, $\text{C}_1\text{-C}_{10}$ -alkyl, $\text{C}_2\text{-C}_{10}$ -alkenyl or $\text{C}_2\text{-C}_{10}$ -alkynyl, in each case branched or unbranched and mono- or polysubstituted or unsubstituted;

30 alkylaryl, saturated or unsaturated and mono- or polysubstituted or unsubstituted; aryl or heteroaryl, in each case mono- or polysubstituted or unsubstituted;

or

5 R⁹ and R¹⁰ together form a C₃-C₇-cycloalkyl, saturated or unsaturated and mono- or polysubstituted or unsubstituted, or a corresponding heterocyclic radical, in which one C atom in the ring is replaced by S, O or NR¹², where R¹² is chosen from

10 H, C₁-C₁₀-alkyl, C₂-C₁₀-alkenyl or C₂-C₁₀-alkynyl, in each case branched or unbranched and mono- or polysubstituted or unsubstituted;

or

15 R¹ and R² together form -CH=CH-CH=CH-, wherein the naphthyl system formed can be mono- or polysubstituted,

X is chosen from

20 H, F, Cl, Br, I, CF₃, O-S(O₂)-C₆H₄-pCH₃, OR¹³ or OC(O)R¹³, wherein R¹³ is chosen from

25 H; C₁-C₁₀-alkyl, C₂-C₁₀-alkenyl or C₂-C₁₀-alkynyl, in each case branched or unbranched and mono- or polysubstituted or unsubstituted; C₃-C₇-cycloalkyl, saturated or unsaturated and mono- or polysubstituted or unsubstituted, or a corresponding heterocyclic radical, in which one C atom in the ring is replaced by N, S or O; alkylaryl, saturated or unsaturated and
30 mono- or polysubstituted or unsubstituted; aryl or heteroaryl, in each case mono- or polysubstituted or unsubstituted;

or

if the compound contains no X, according to
formula Ia a double bond is formed between C atom
A and C atom B or C atom B and C atom C;

5

and

R^3 , R^4 independently of one another are chosen from
H, C_1 - C_{10} -alkyl, C_2 - C_{10} -alkenyl or C_2 - C_{10} -alkinyl,
10 in each case branched or unbranched and mono- or
polysubstituted or unsubstituted; C_3 - C_7 -
cycloalkyl, saturated or unsaturated and mono- or
polysubstituted or unsubstituted, or a
corresponding heterocyclic radical, in which one
15 C atom in the ring is replaced by N, S or O;
alkylaryl, saturated or unsaturated and mono- or
polysubstituted or unsubstituted; aryl or
heteroaryl, in each case mono- or polysubstituted
or unsubstituted;

20

or

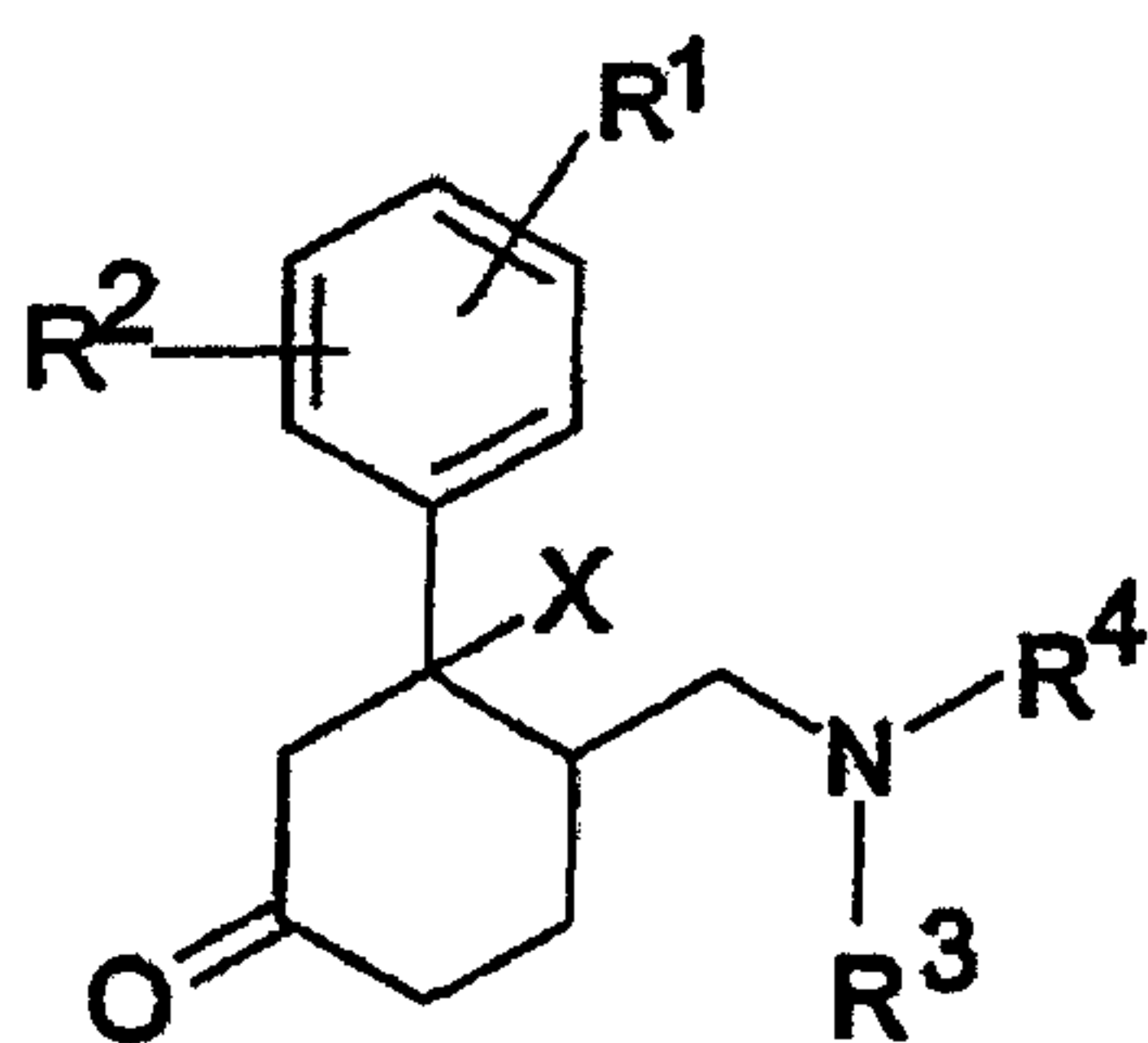
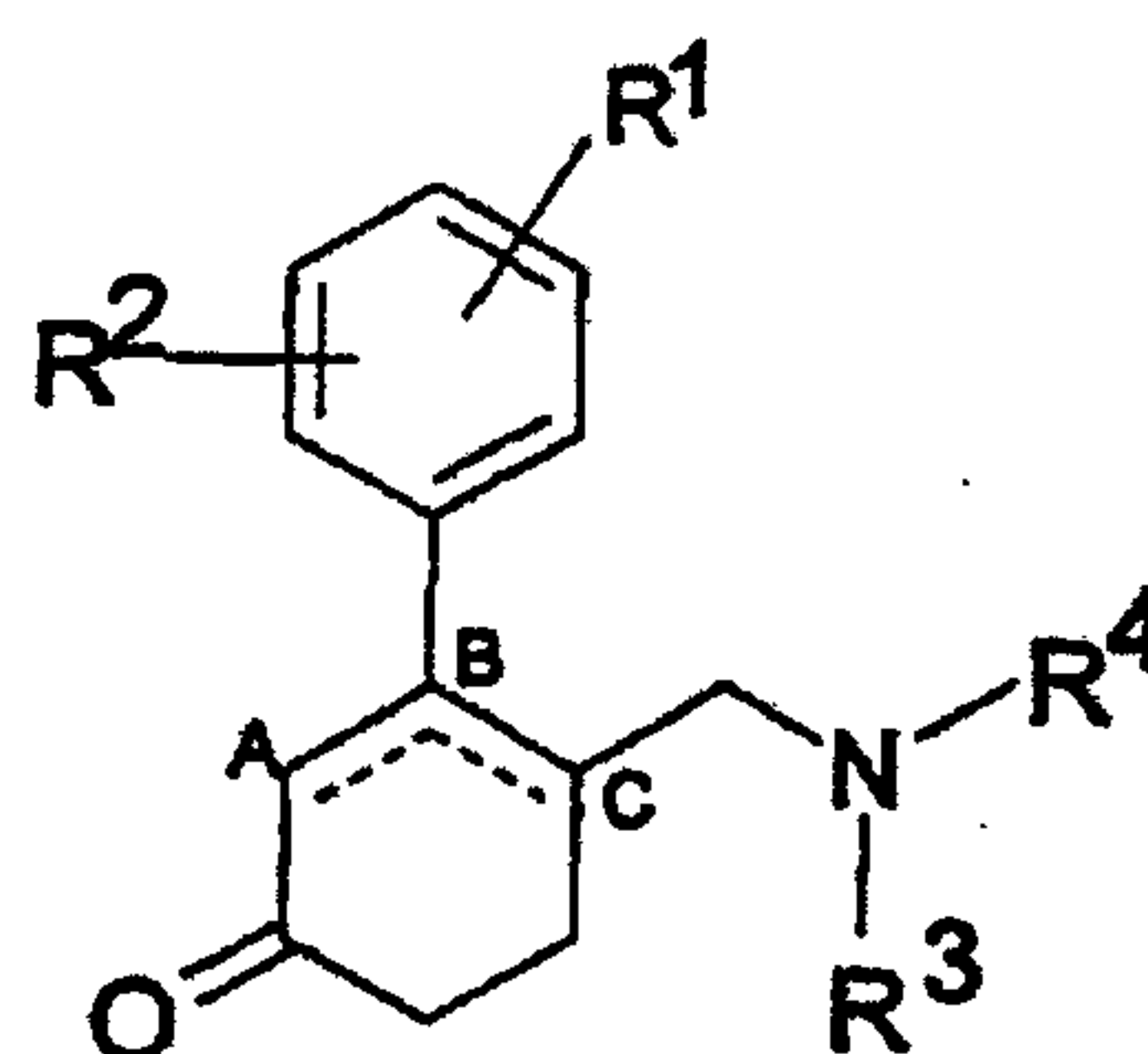
R^3 and R^4 together form a C_3 - C_7 -cycloalkyl, saturated or
unsaturated and mono- or polysubstituted or
25 unsubstituted, or a corresponding heterocyclic
radical, in which one C atom in the ring is replaced
by S, O or NR^{14} , where R^{14} is chosen from

H, C_1 - C_{10} -alkyl, C_2 - C_{10} -alkenyl or C_2 - C_{10} -
alkinyl, in each case branched or unbranched
30 and mono- or polysubstituted or
unsubstituted;

in the form of its diastereomers or enantiomers and of its
free base or of a salt formed with a physiologically

tolerated acid, in particular the hydrochloride salt, for the preparation of a medicament for treatment of inflammatory and allergic reactions, depressions, drug and/or alcohol abuse, gastritis, cardiovascular diseases, respiratory tract diseases, coughing, mental illnesses and/or epilepsy, and in particular urinary incontinence, itching and/or diarrhoea.

The use of at least one aminomethyl-phenyl-cyclohexanone derivative according to formula I or Ia

**I****Ia**

in which, independently of one another

- 15 $R^1 = R^5$, wherein R^5 is chosen from
H, F, Cl, Br, I, CHF_2 , CF_3 , NO_2 , NH_2 ; C_1 - C_4 -alkyl
or C_2 - C_4 -alkenyl, branched or unbranched and mono-
or polysubstituted or unsubstituted; aryl,
substituted or unsubstituted; OR^7 , $\text{C}(\text{O})\text{OR}^7$ or SR^7 ,
20 wherein R^7 is chosen from
H; C_1 - C_4 -alkyl, branched or unbranched and
mono- or polysubstituted or unsubstituted;
preferably H, CF_3 or CH_3 ,
or $\text{S}(\text{O}_2)\text{NR}^9\text{R}^{10}$, wherein R^9 and R^{10} independently of
25 one another are chosen from

H; C₁-C₄-alkyl, branched or unbranched and mono- or polysubstituted or unsubstituted; wherein particularly preferably R¹ = R⁵, where R⁵ is chosen from

5 H, F, Cl, OH, CH₃, C₂H₅, C₂H₃, CHF₂, CF₃, SCH₃, OCF₃, OCH₃, OC₂H₅, C(O)OCH₃, C(O)OC₂H₅ or phenyl,

and/or R² = R⁵, wherein R⁵ is chosen from

10 H, F, Cl, Br, I, SCH₃; C₁-C₄-alkyl, C₂-C₄-alkenyl, branched or unbranched and mono- or polysubstituted or unsubstituted, preferably CF₃; OR⁷, where R⁷ is chosen from C₁-C₄-alkyl, branched or unbranched and mono- or polysubstituted or unsubstituted, preferably CH₃;

15

and/or R¹ and R² have different meanings, or

R¹ and R² together form -CH=CH-CH=CH-, wherein the naphthyl system formed can be mono- or polysubstituted, preferably by halogen, OC₁₋₃-alkyl or C₁₋₃-alkyl, unsubstituted or mono or polysubstituted, in particular by OCH₃,

20

25 **and/or** X is chosen from

H, F, Cl, OH, CF₃, O-S(O₂)-C₆H₄-pCH₃ or OC(O)R⁷, where R⁷ = H; C₁-C₄-alkyl or C₂-C₄-alkenyl, branched or unbranched and mono- or polysubstituted or unsubstituted; preferably H, F, Cl, OH, O-S(O₂)-C₆H₄-pCH₃ or OC(O)R⁷, where R⁷ = C₁-C₄-alkyl, preferably CH₃, in particular H or OH;

30

or

if the compound contains no X, according to formula Ia a double bond is formed between C atom A and C atom B or C atom B and C atom C,

5

and/or R³ and R⁴ independently of one another are chosen from

C₁-C₄-alkyl, branched or unbranched and mono- or polysubstituted or unsubstituted, preferably CH₃;

10

or

R³ and R⁴ together form a C₃-C₇-cycloalkyl, saturated or unsaturated and mono- or polysubstituted or unsubstituted,

15

and/or R¹, R², X, R³ and/or R⁴ have one of the meanings already given,

20 is preferred here.

The use of at least one aminomethyl-phenyl-cyclohexanone derivative chosen from the group consisting of

- 25
- *rac-cis*-[4-dimethylaminomethyl-3-hydroxy-3-(3-methoxy-phenyl)-cyclohexanone],
 - *rac-cis*-[4-dimethylaminomethyl-3-(3-methoxy-phenyl)-cyclohexanone],
 - *rac-trans*-[4-dimethylaminomethyl-3-(3-methoxy-phenyl)-cyclohexanone],
 - *rac-cis*-[4-dimethylaminomethyl-3-(3-hydroxy-phenyl)-cyclohexanone],
- 30

- *rac-trans*-[4-dimethylaminomethyl-3-(3-hydroxy-phenyl)-cyclohexanone] or
- 4-dimethylaminomethyl-3-(3-methoxy-phenyl)-cyclohex-2-enone
- 5 • 4-dimethylaminomethyl-3-phenyl-cyclohex-2-enone;
- 4-dimethylaminomethyl-3-(3-hydroxy-phenyl)-cyclohex-2-enone;
- 10 • *rac-trans*-4-dimethylaminomethyl-3-phenyl-cyclohexanone;
- *rac-cis*-4-dimethylaminomethyl-3-phenyl-cyclohexanone;
- 15 • 4-dimethylaminomethyl-3-(4-methoxy-phenyl)-cyclohex-2-enone;
- 4-dimethylaminomethyl-3-naphthalen-2-yl-cyclohex-2-enone;
- 20 • *rac-trans*-4-dimethylaminomethyl-3-hydroxy-3-naphthalen-2-yl-cyclohexanone;
- *rac-trans*-4-dimethylaminomethyl-3-(3-fluoro-phenyl)-cyclohexanone;
- 25 • *rac-cis*-4-dimethylaminomethyl-3-(3-fluoro-phenyl)-cyclohexanone;
- 30 • *rac-cis*-4-dimethylaminomethyl-3-hydroxy-3-(2-methoxy-phenyl)-cyclohexanone

- rac-cis-4-dimethylaminomethyl-3-hydroxy-3-(6-methoxy-naphthalen-2-yl)-cyclohexanone;
- 5 • 4-dimethylaminomethyl-3-(6-methoxy-naphthalen-2-yl)-cyclohex-2-enone;
- rac-cis-3-biphenyl-4-yl-4-dimethylaminomethyl-3-hydroxy-cyclohexanone
- 10 • 3-(3-difluoromethyl-phenyl)-4-dimethylaminomethyl-cyclohex-2-enone;
- 4-dimethylaminomethyl-3-(3-fluoro-phenyl)-cyclohex-2-enone;
- 15 • 3-(3,4-difluoro-phenyl)-4-dimethylaminomethyl-cyclohex-2-enone;
- 4-dimethylaminomethyl-3-(4-fluoro-phenyl)-cyclohex-2-enone;
- 20 • 4-dimethylaminomethyl-3-(4-trifluoromethyl-phenyl)-cyclohex-2-enone;
- 25 • 3-(3,5-dichloro-phenyl)-4-dimethylaminomethyl-cyclohex-2-enone;
- 3-(3,5-difluoro-phenyl)-4-dimethylaminomethyl-cyclohex-2-enone;
- 30 • rac-cis-3-(3,5-difluoro-phenyl)-4-dimethylaminomethyl-3-hydroxy-cyclohexanone

as the free base or in the form of a salt formed with a physiologically tolerated acid, in particular the hydrochloride salt,

5

is particularly preferred.

The invention is explained further by examples in the following, without limiting it thereto.

10

Examples

The following examples show compounds according to the invention and the preparation thereof, and activity studies carried out with these.

15

The following information generally applies:

The yields of the compounds prepared are not optimized.

20

All temperatures are uncorrected.

Silica gel 60 (0.040 - 0.063 mm) from E. Merck, Darmstadt was employed as the stationary phase for the column chromatography.

25

The thin layer chromatography studies were carried out with HPTLC precoated plates, silica gel 60 F 254 from E. Merck, Darmstadt.

30

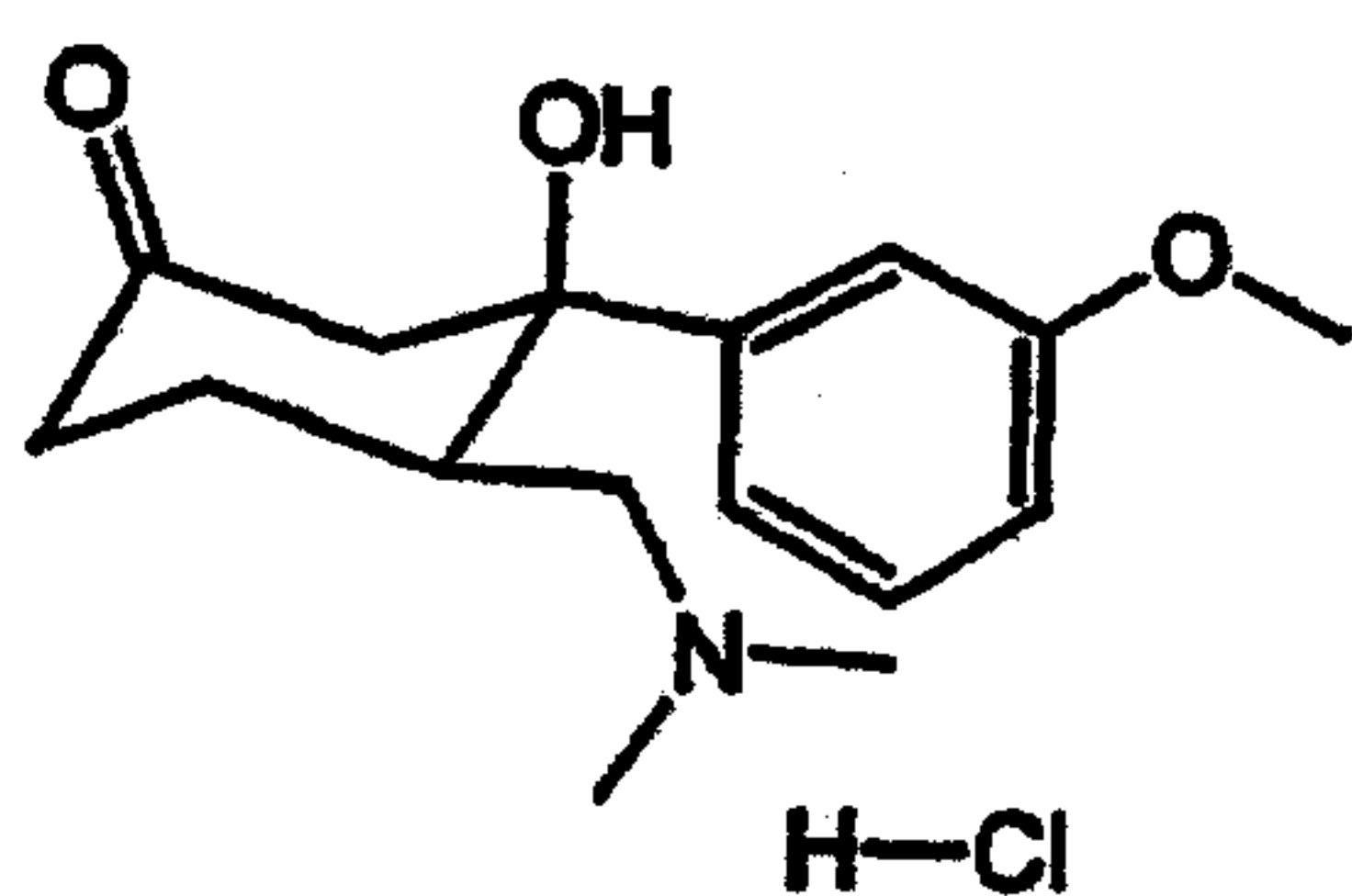
The mixing ratios of the mobile phases for all the chromatographic studies are always stated in volume/volume.

The term ether means diethyl ether.

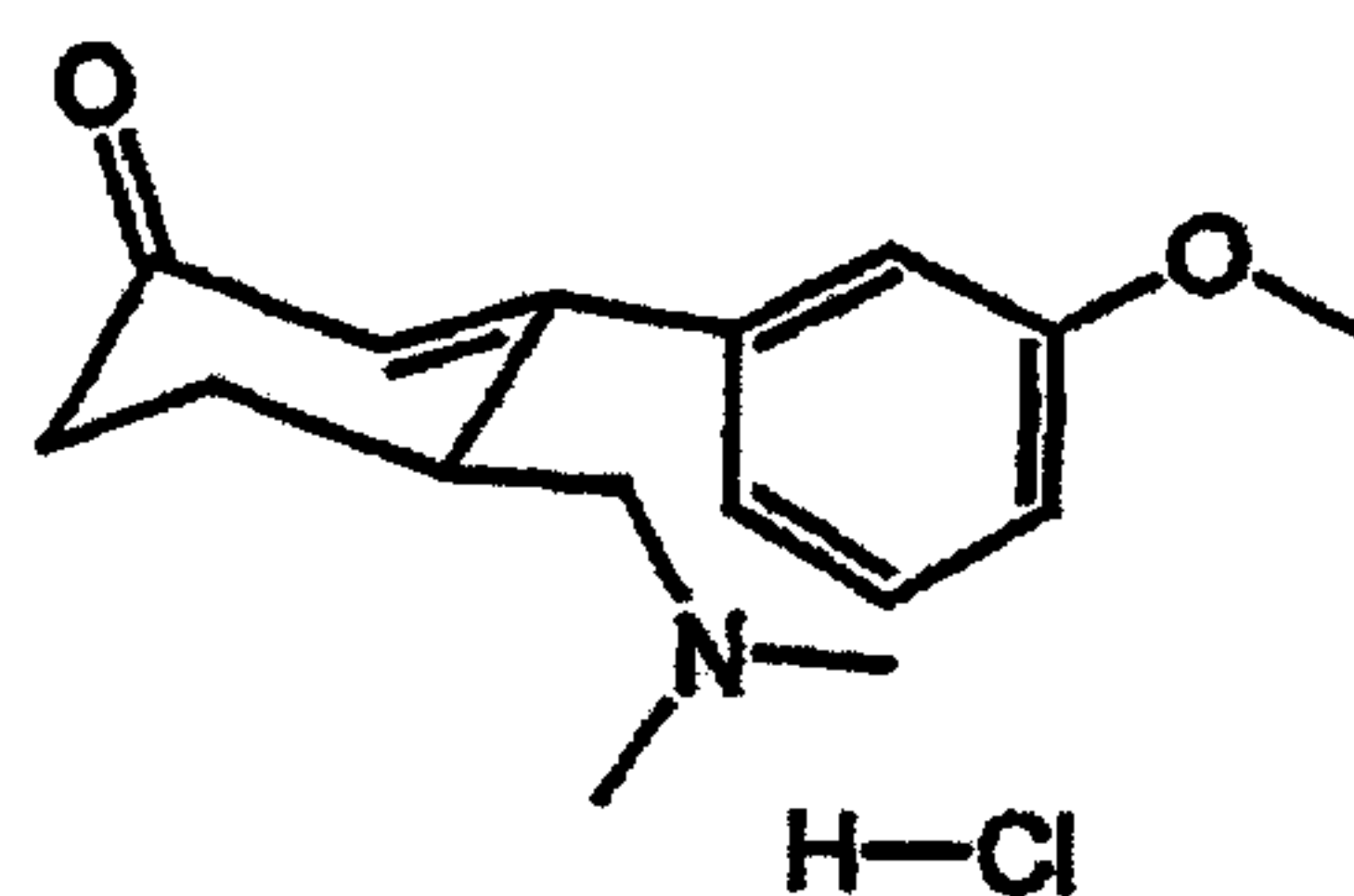
Unless stated otherwise, petroleum ether with the
boiling range of 50°C-70°C was used.

Example 1

rac-cis-[4-Dimethylaminomethyl-3-hydroxy-3-(3-methoxy-phenyl)-cyclohexanone] (compound 1) and 4-dimethylaminomethyl-3-(3-methoxy-phenyl)-cyclohex-2-enone (compound 6)



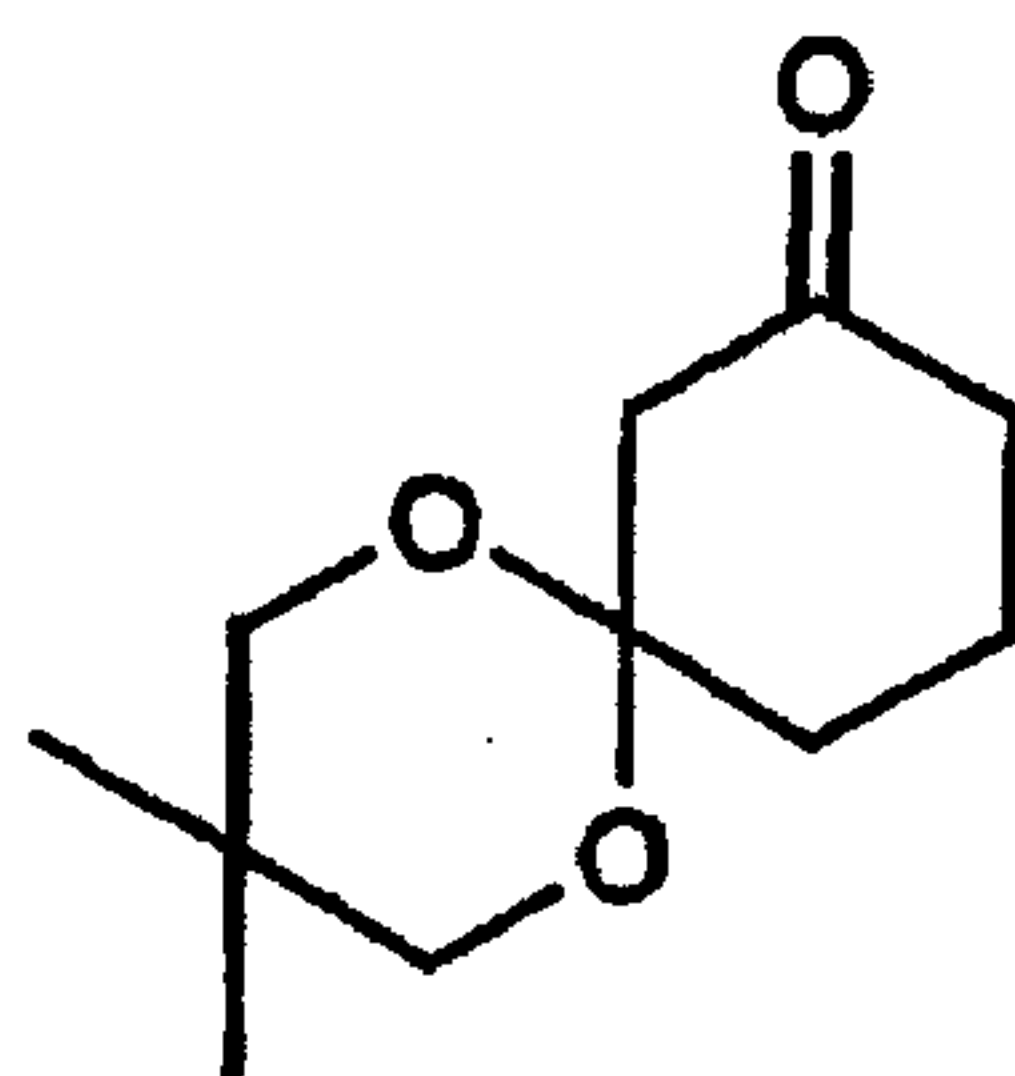
(1)



(6)

Stage 1:

3,3-Dimethyl-1,5-dioxaspiro[5.5]undecan-8-one

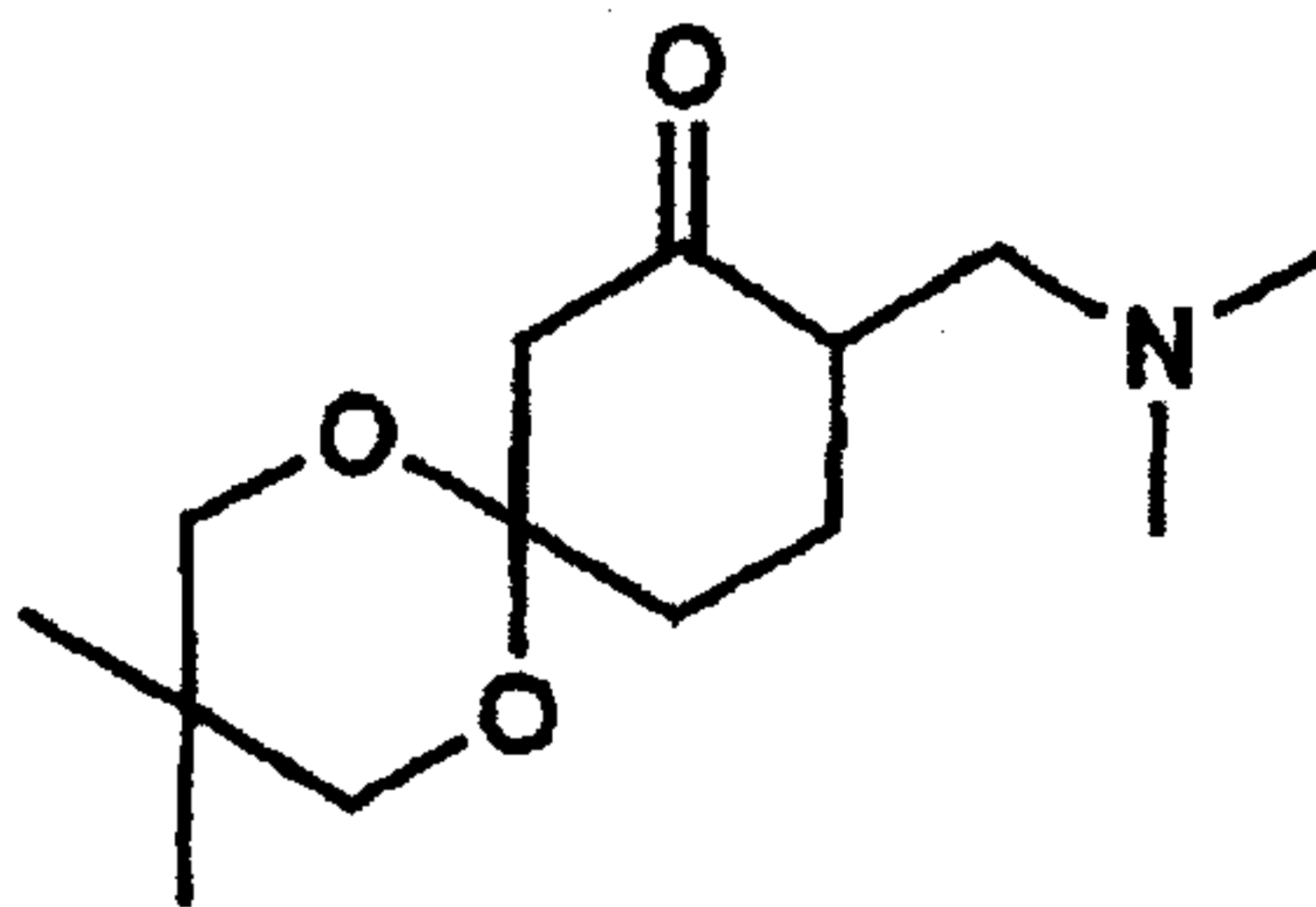


448.5 g 1,3-cyclohexanedione, 416 g 2,2-dimethyl-1,3-propanediol and 12 g p-toluenesulfonic acid were introduced into 3,000 ml methylene chloride and the mixture was heated under reflux for 24 hours using a water separator. When the reaction had ended the

mixture was cooled to room temperature and 2,000 ml 32% sodium hydroxide solution were added. The phases were separated and the organic phase was washed first with sodium bicarbonate solution (44.4 g sodium bicarbonate solution/850 ml water) and then with 350 ml water. The organic phase was dried over sodium sulfate and the solvent was then evaporated in vacuo. 345 g (50% of theory) 3,3-dimethyl-1,5-dioxaspiro[5.5]undecan-8-one were obtained in this way.

Stage 2:

9-Dimethylaminomethyl-1,5-dioxaspiro[5.5]undecan-8-one

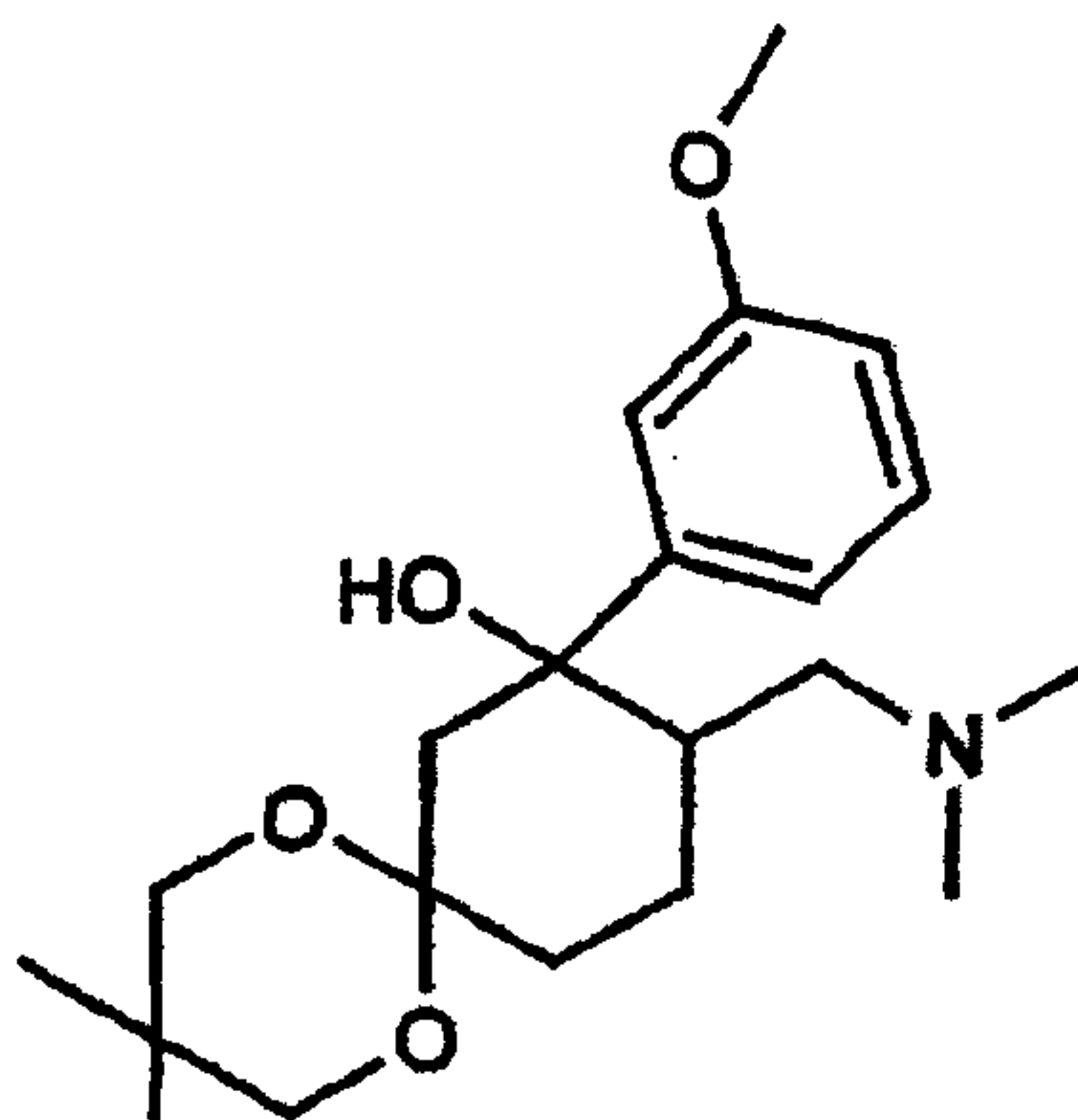


345 g 3,3-dimethyl-1,5-dioxaspiro[5.5]undecan-8-one were dissolved in 1,900 ml analytical grade acetonitrile. The mixture was cooled to 0°C and 140 g N,N-dimethylmethyle-immonium chloride and one drop of acetyl chloride were then added. The mixture was stirred at 0°C for 6 hours. The reaction mixture was left overnight at room temperature. The white solid which had precipitated out was filtered off with suction, washed with acetone and dried in vacuo. 310 g 9-dimethylaminomethyl-1,5-dioxaspiro[5.5]undecan-8-one hydrochloride were obtained in this way as a white solid. To liberate the base, the solid was dissolved in water, and an equimolar amount of saturated sodium carbonate solution was added. The

mixture was stirred for one hour. The mixture was extracted 3 times with 500 ml ethyl acetate. The combined organic phases were dried over sodium sulfate and the solvent was evaporated in vacuo. 300 g (68% of theory) 9-dimethylaminomethyl-1,5-dioxaspiro[5.5]undecan-8-one were obtained in this way.

Stage 3:

9-Dimethylaminomethyl-8-(3-methoxy-phenyl)-3,3-dimethyl-1,5-dioxaspiro[5.5]undecan-8-ol

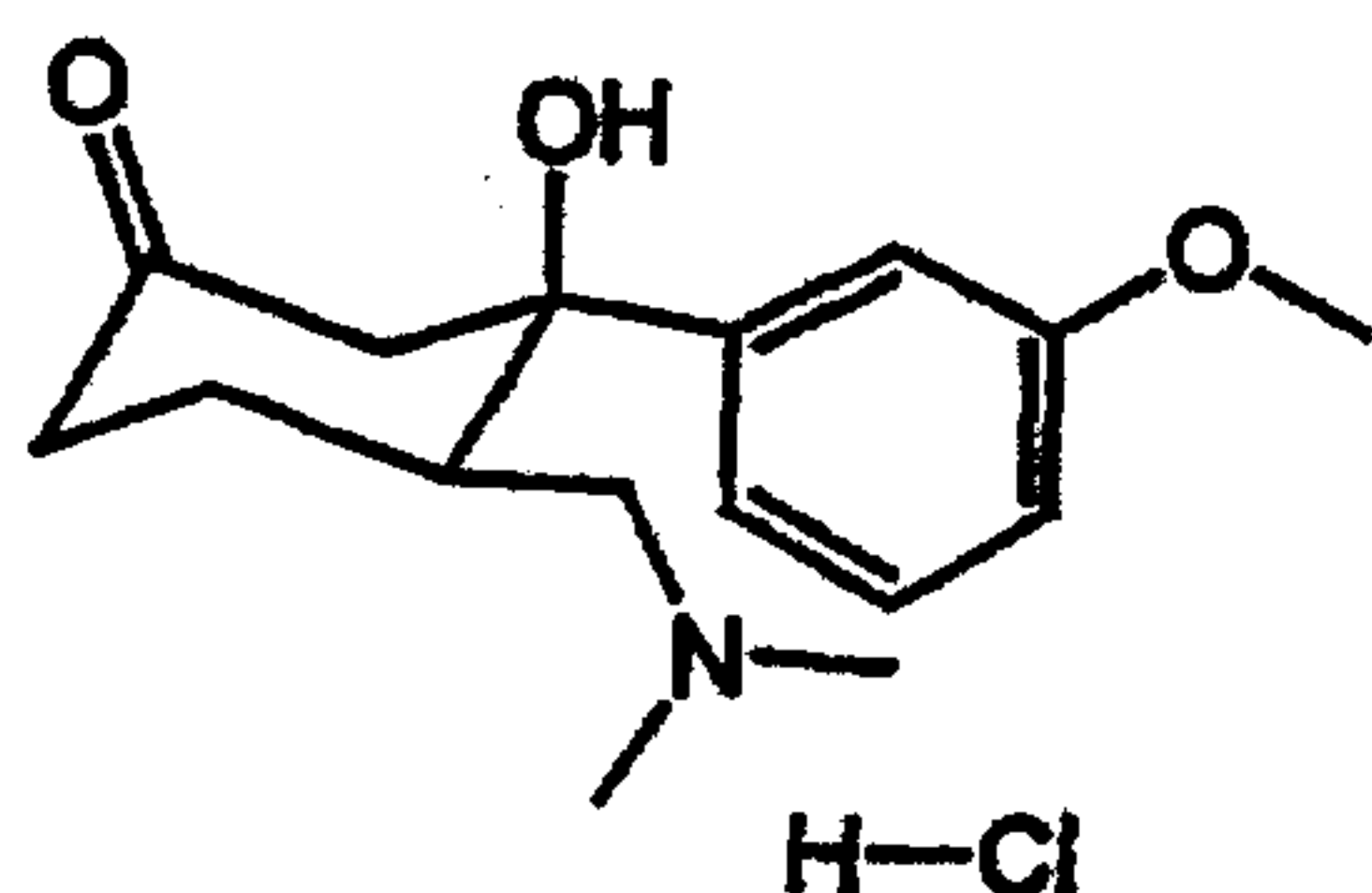


36 g magnesium were initially introduced into 150 ml analytical grade tetrahydrofuran. 280.5 g 3-bromoanisole in 300 ml analytical grade tetrahydrofuran were then added dropwise. The reaction mixture was allowed to after-react for 1 hour and was then cooled to 20°C. 290 g 9-dimethylaminomethyl-1,5-dioxaspiro[5.5]undecan-8-one in 700 ml analytical grade tetrahydrofuran were added dropwise at this temperature. The mixture was allowed to after-react overnight at room temperature. First 200 ml of a 20% ammonium chloride solution, then 300 ml water and then 100 ml of a 32% hydrochloric acid solution were then added dropwise at a temperature of 10 - 15°C. The phases were separated and the aqueous phase was extracted twice with 400 ml ethyl acetate

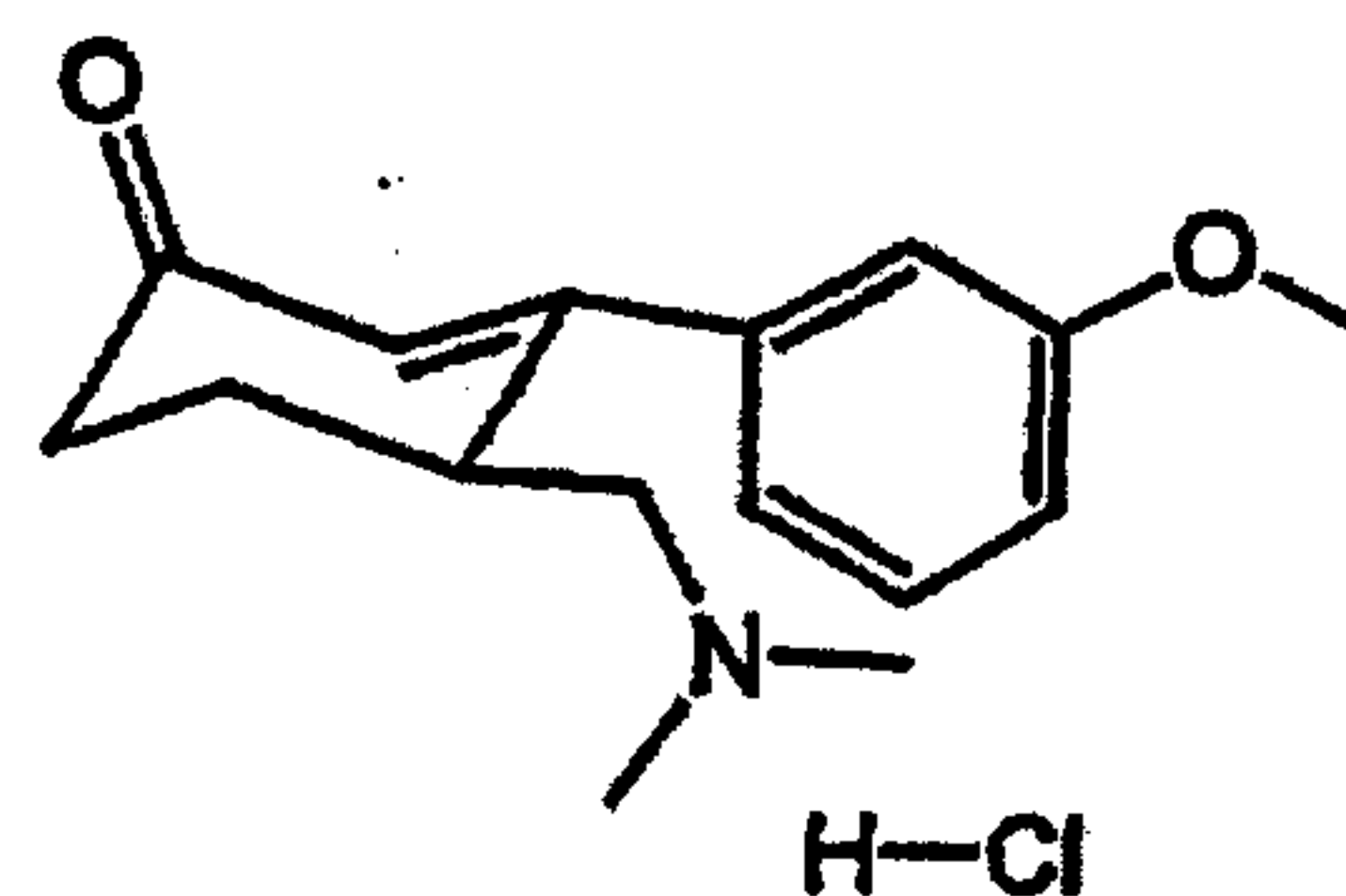
each time. The organic phase was dried over magnesium sulfate and the solvent was then evaporated in vacuo. 1,000 ml petroleum ether were added to the crude base obtained in this way. The title compound started to crystallize out after a short time. To complete the crystallization, 2,100 ml diisopropyl ether were added and the mixture was subsequently stirred at 5°C for 2 hours. The solid was filtered off with suction, washed with diisopropyl ether and then dried in vacuo. 156 g (41.2% of theory) were obtained in this way in the form of a white solid.

Stage 4

rac-cis-[4-Dimethylaminomethyl-3-hydroxy-3-(3-methoxy-phenyl)-cyclohexanone] hydrochloride (1) and 4-dimethylaminomethyl-3-(3-methoxy-phenyl)-cyclohex-2-enone hydrochloride (6)



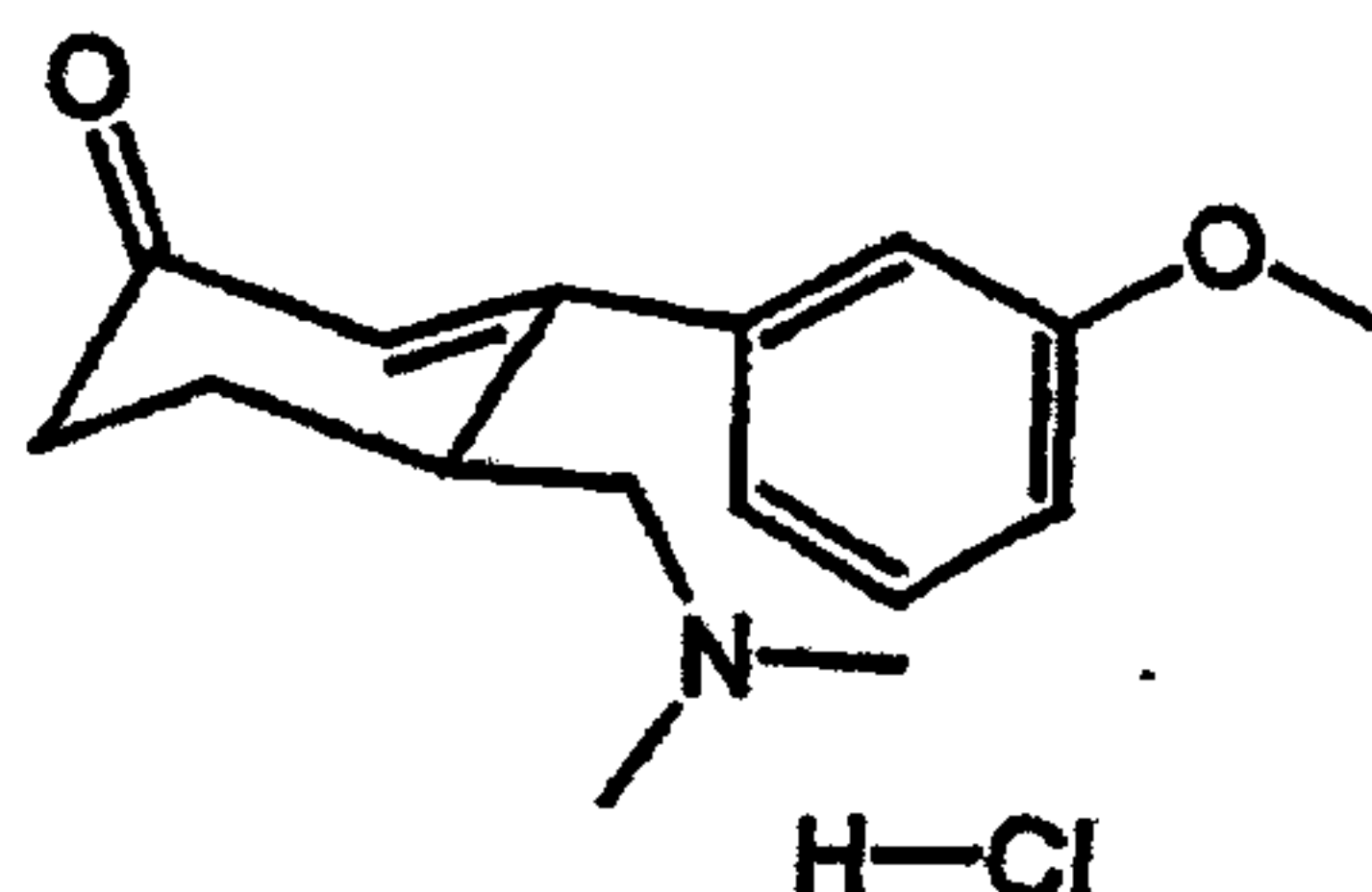
(1)



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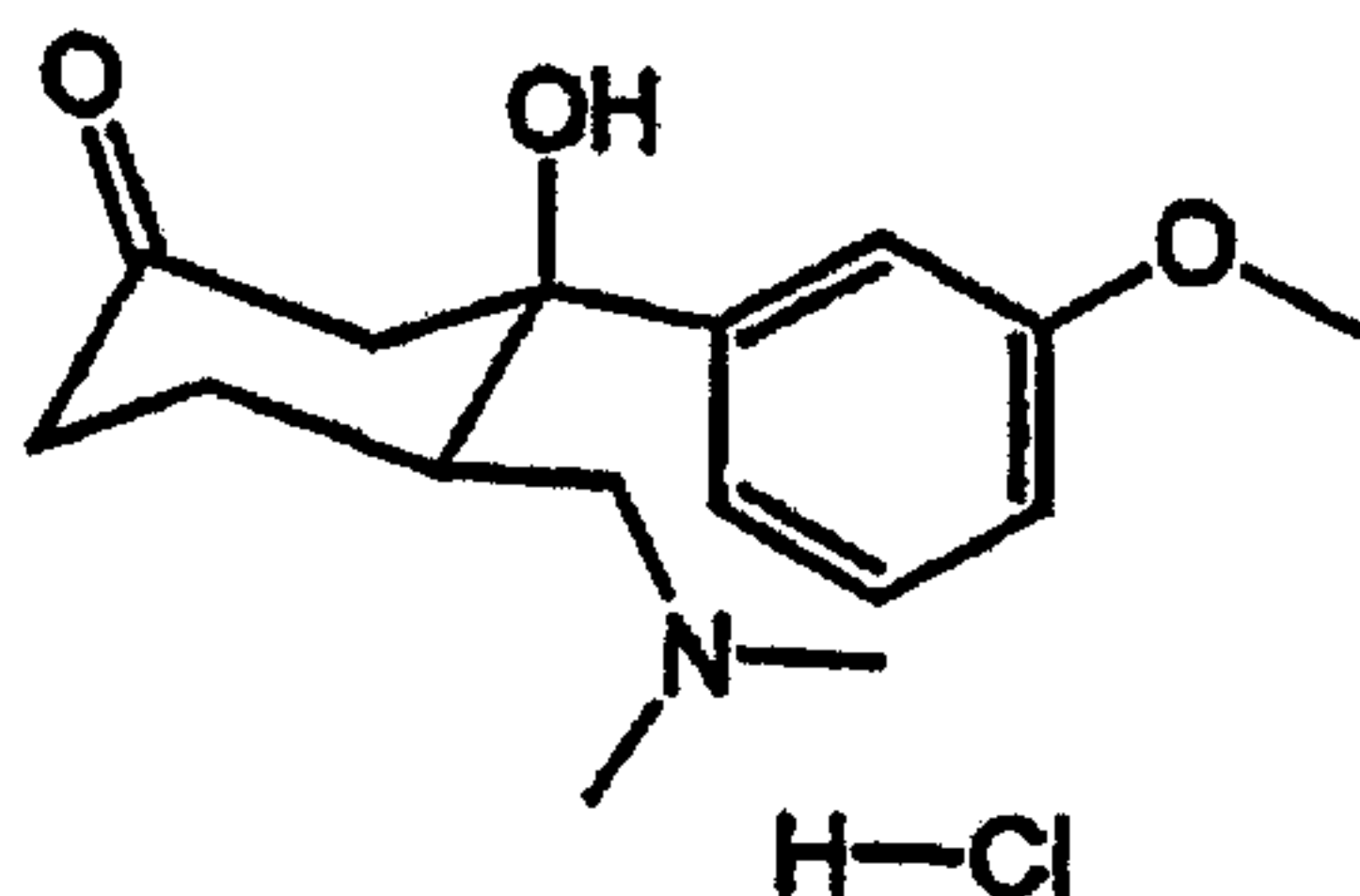
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a) 4-Dimethylaminomethyl-3-(3-methoxy-phenyl)-cyclohex-2-enone hydrochloride (compound 6)



182 g 9-dimethylaminomethyl-8-(3-methoxy-phenyl)-3,3-dimethyl-1,5-dioxaspiro[5.5]undecan-8-ol were dissolved in 1,200 ml tetrahydrofuran and the reaction mixture was cooled to 5°C. A mixture of 600 ml 32% hydrochloric acid solution and 600 ml water was added at this temperature. The mixture was stirred at room temperature for 72 hours. When the reaction had ended 500 ml ethyl acetate were added at 5°C and the reaction mixture was then brought to pH 12 with 32% sodium hydroxide solution. The phases were separated and the aqueous phase was washed three times with 300 ml ethyl acetate each time. The combined organic phases were then washed twice with 100 ml saturated sodium chloride solution each time, dried over magnesium sulfate and then freed from the solvent. Purification was carried out via hydrochloride formation. For this, 4-dimethylaminomethyl-3-(3-methoxy-phenyl)-cyclohex-2-enone base was dissolved in 500 ml acetone and an equimolar amount of water and trimethylchlorosilane was added. The hydrochloride which had precipitated out was filtered off with suction and dried in vacuo. 63.6 g (78.9% of theory) 4-dimethylaminomethyl-3-(3-methoxy-phenyl)-cyclohex-2-enone hydrochloride were obtained in this way.

b) *rac-cis*-[4-Dimethylaminomethyl-3-hydroxy-3-(3-methoxy-phenyl)-cyclohexanone] hydrochloride (compound 1)



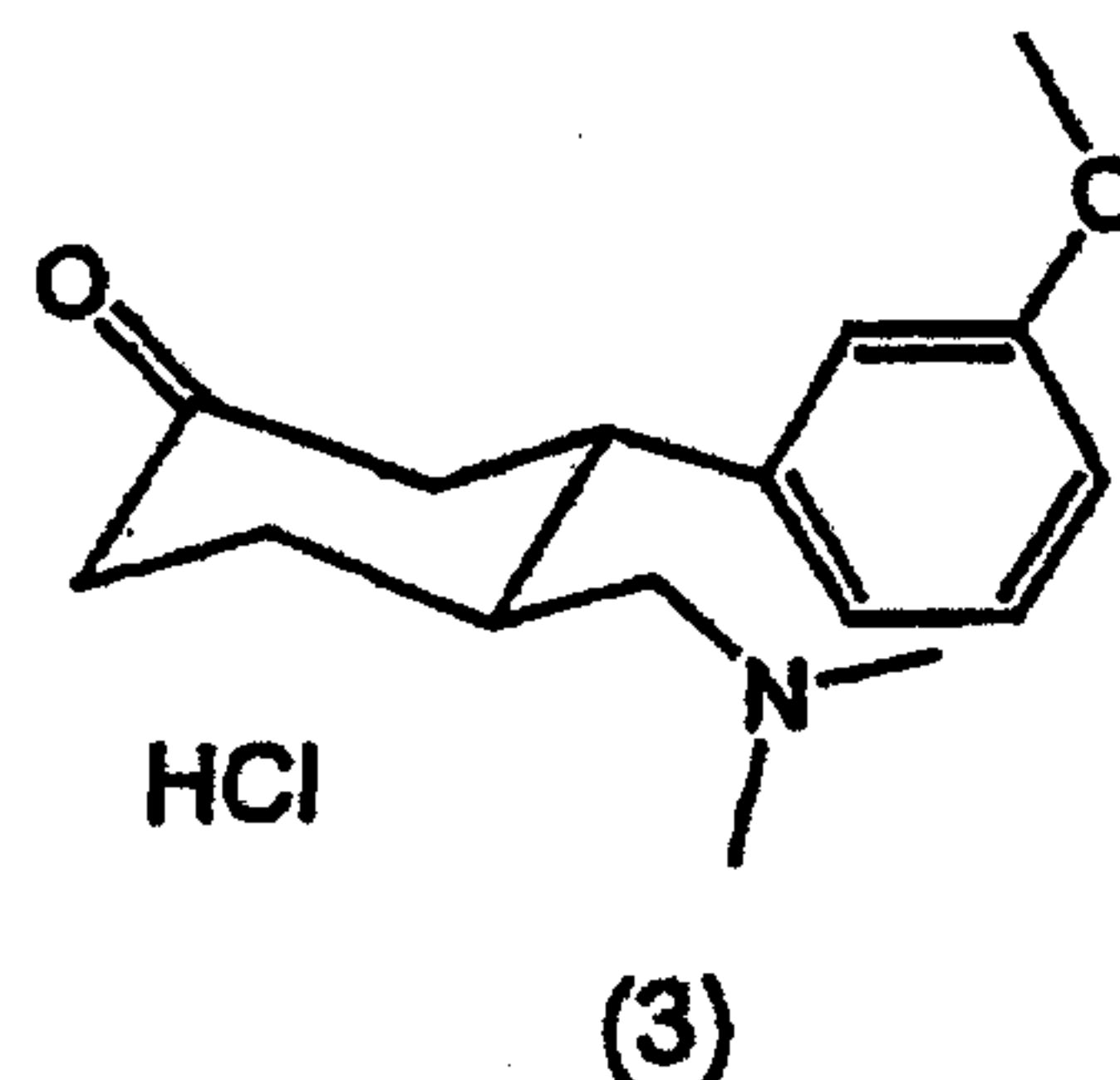
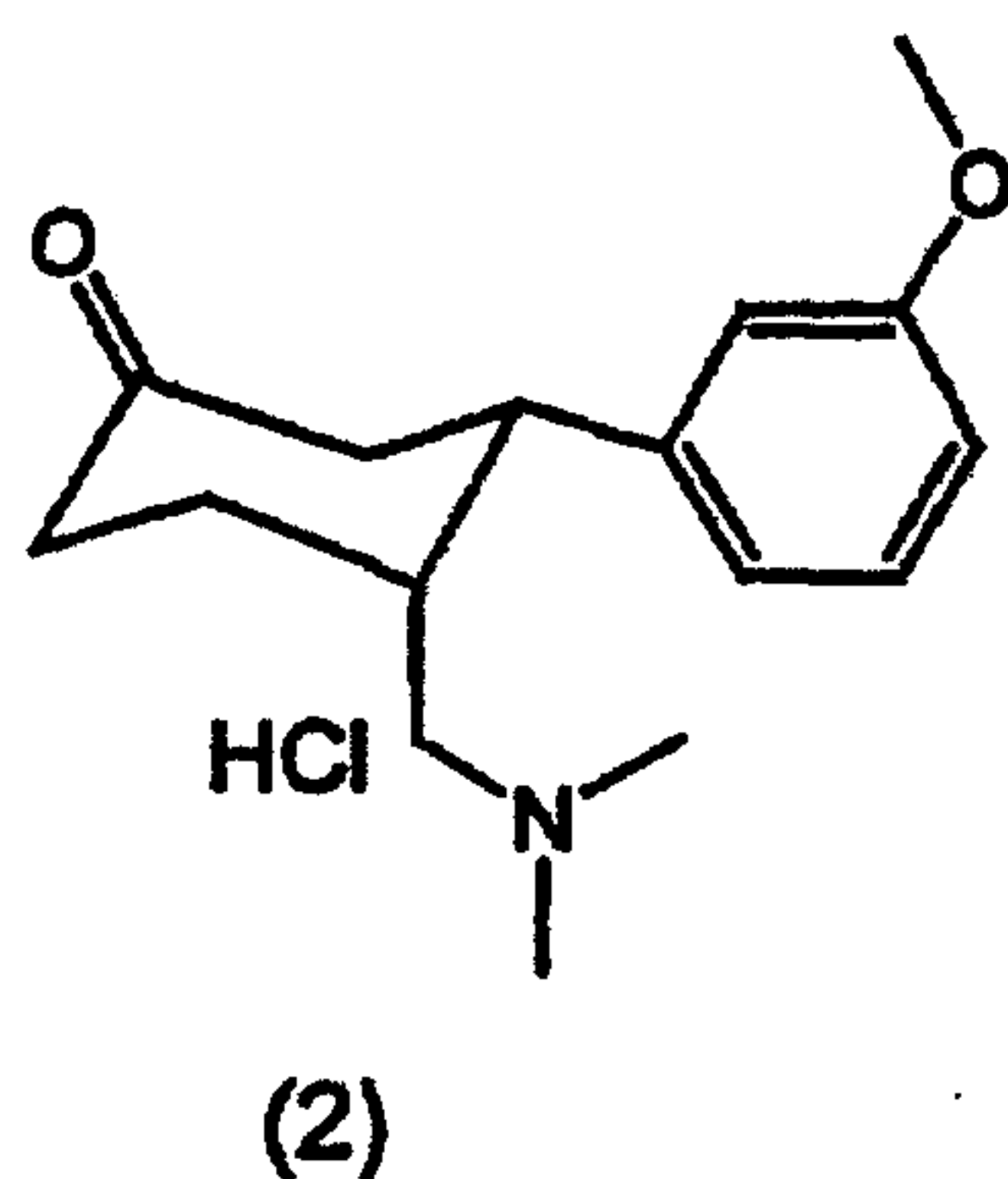
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150 g 9-dimethylaminomethyl-8-(3-methoxy-phenyl)-3,3-dimethyl-1,5-dioxaspiro[5.5]undecan-8-ol were dissolved in tetrahydrofuran and the solution was cooled to -10°C. 1,000 ml of a mixture of water and 32% hydrochloric acid (5 : 1) were then added dropwise. The mixture was left overnight at 5°C. 750 ml diethyl ether were then added and the pH was then brought to 12 with 200 ml 32% sodium hydroxide solution. The phases were separated and the aqueous phase was extracted twice with 200 ml diethyl ether each time. The combined organic phases were washed with 200 ml saturated sodium chloride solution and dried over sodium sulfate and the solvent was then evaporated in vacuo. *rac-cis*-[4-Dimethylaminomethyl-3-hydroxy-3-(3-methoxy-phenyl)-cyclohexanone] base was dissolved in acetone, and an equimolar amount of water and trimethylchlorosilane was added. The hydrochloride which had precipitated out was filtered off with suction and dried in vacuo. 67 g (59% of theory) *rac-cis*-[4-dimethylaminomethyl-3-hydroxy-3-(3-methoxy-phenyl)-cyclohexanone] hydrochloride were obtained in this way.

25

Example 2

rac-cis-[4-Dimethylaminomethyl-3-(3-methoxy-phenyl)-cyclohexanone] hydrochloride (compound 2) and *rac-trans*-[4-dimethylaminomethyl-3-(3-methoxy-phenyl)-cyclohexanone] hydrochloride (compound 3)

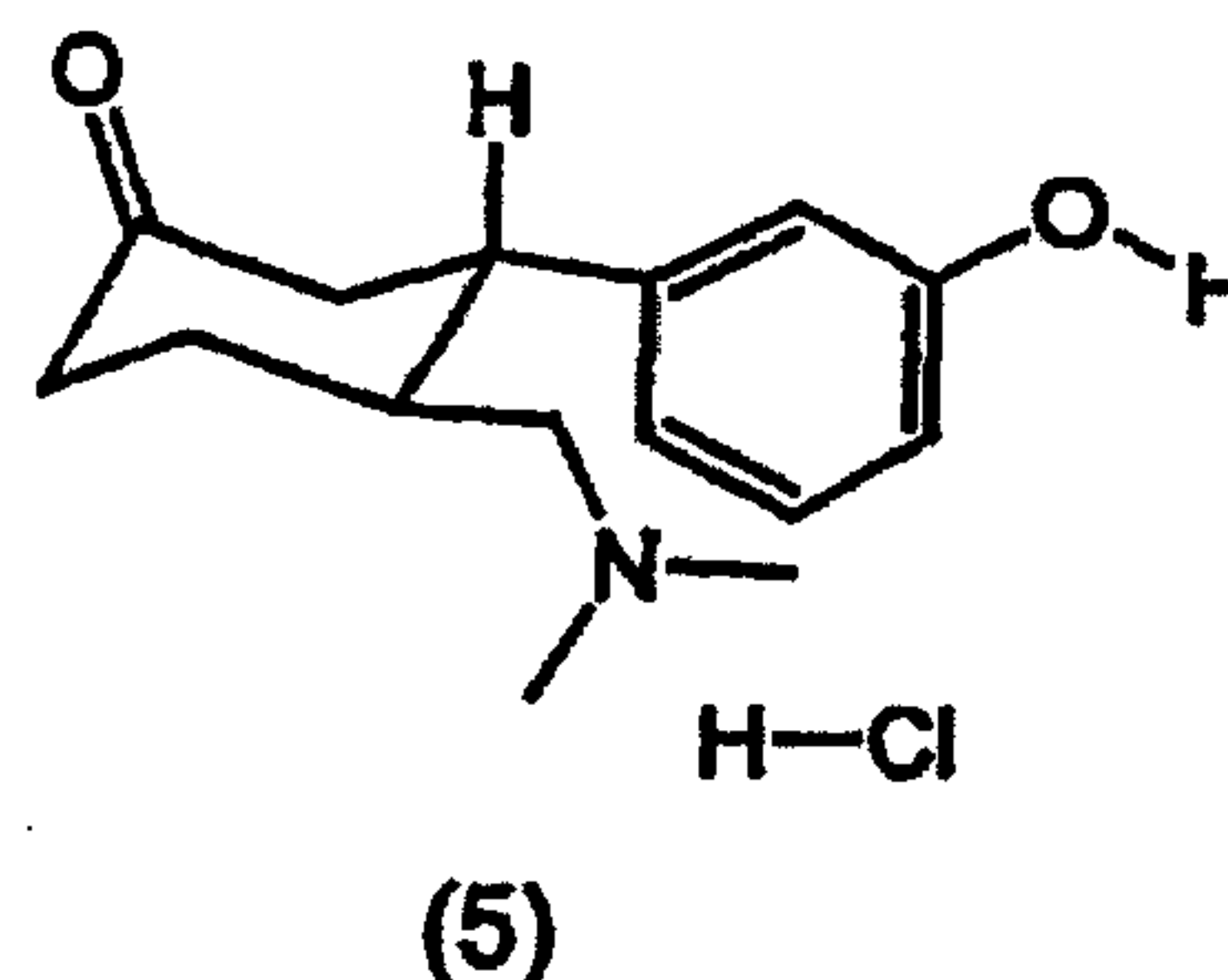
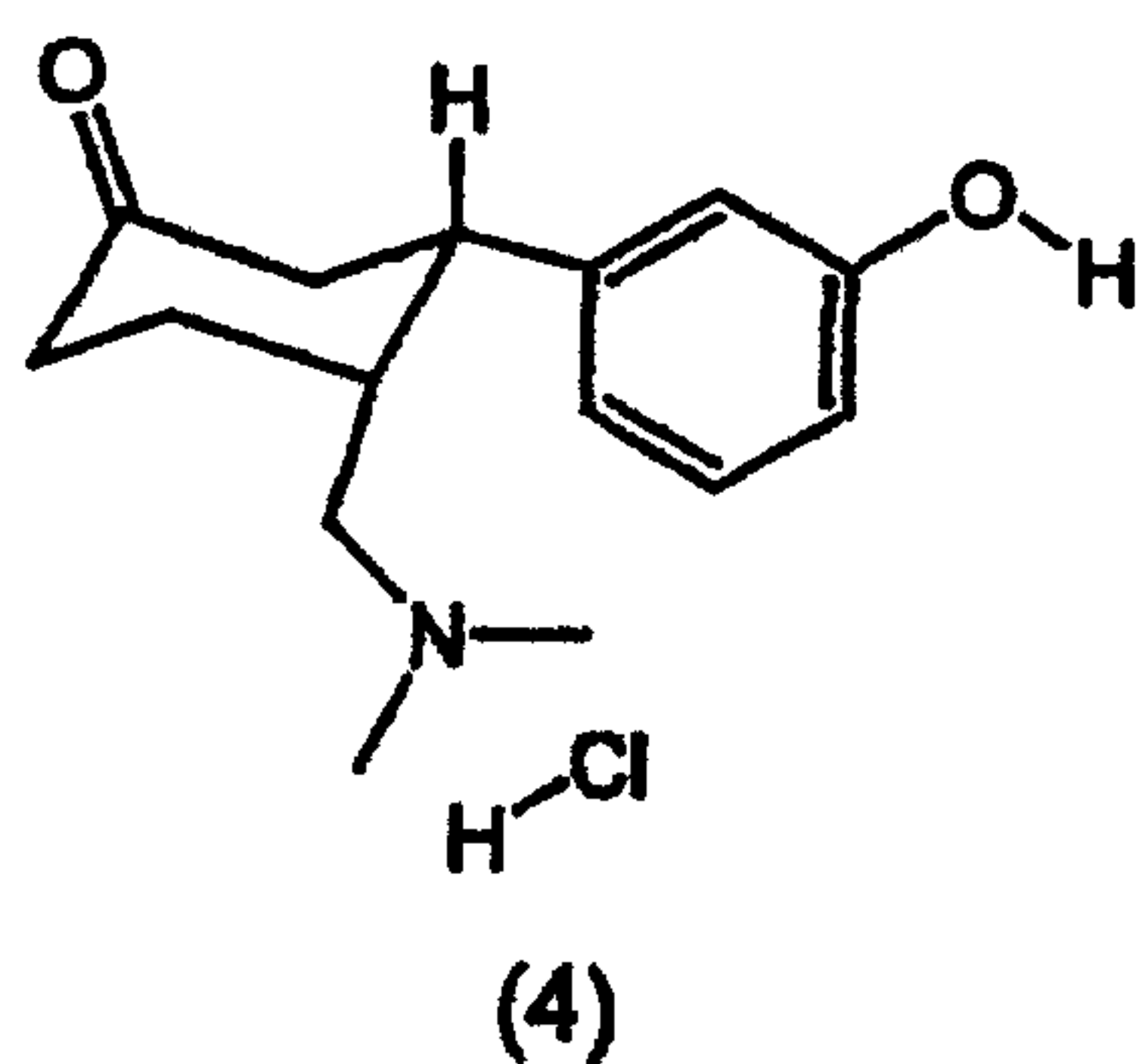


28.5 g 4-dimethylaminomethyl-3-(3-methoxy-phenyl)-cyclohex-2-enone, which was prepared according to example 1 stage 4a), were dissolved in 250 ml absolute methanol. 2.8 g palladium-on-charcoal (10%) were added as a catalyst, while stirring and passing dry nitrogen over. Hydrogenation was then carried out for five hours under a pressure of 0.2 bar and at a temperature of 20°C. After filtration, the solvent was evaporated off in vacuo and the residue was purified by column chromatography on silica gel with ethyl acetate/methanol/diisopropyl ether = 4/1/5 as the eluting agent. 7.5 g *rac-cis*-[4-dimethylaminomethyl-3-(3-methoxy-phenyl)]-cyclohexanone in the form of an oil were obtained as the first product fraction. To prepare the hydrochloride, the base was dissolved in acetone, and an equimolar amount of water and trimethylchlorosilane was added. The hydrochloride which had precipitated out was filtered off with suction and dried in vacuo.

7.2 g (25.4% of theory) *rac-cis*-[4-dimethylaminomethyl-3-(3-methoxy-phenyl)]-cyclohexanone hydrochloride were obtained in this way. The second product fraction gave 7.8 g *rac-trans*-[4-dimethylaminomethyl-3-(3-methoxy-phenyl)]-cyclohexanone, likewise as an oil. To prepare the hydrochloride, the base was dissolved in acetone, and an equimolar amount of water and trimethylchlorosilane was added. The hydrochloride which had precipitated out was filtered off with suction and dried in vacuo. 7.4 g (26.1% of theory) *rac-trans*-[4-dimethylaminomethyl-3-(3-methoxy-phenyl)]-cyclohexanone hydrochloride were obtained in this way.

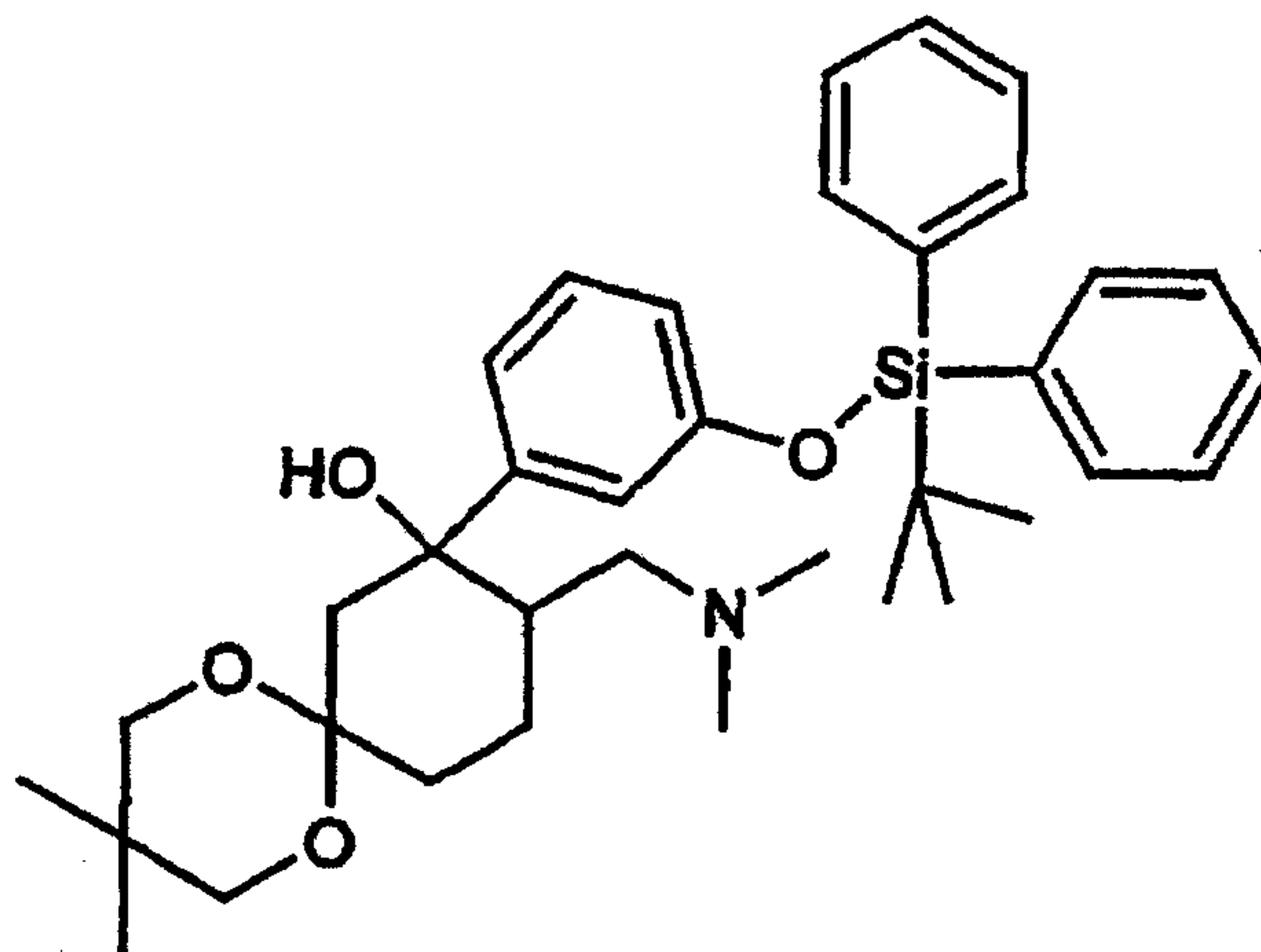
Example 3

rac-cis-[4-Dimethylaminomethyl-3-(3-hydroxy-phenyl)]-cyclohexanone (compound 4) and *rac-trans*-[4-dimethylaminomethyl-3-(3-hydroxy-phenyl)]-cyclohexanone (compound 5)



Stage 1

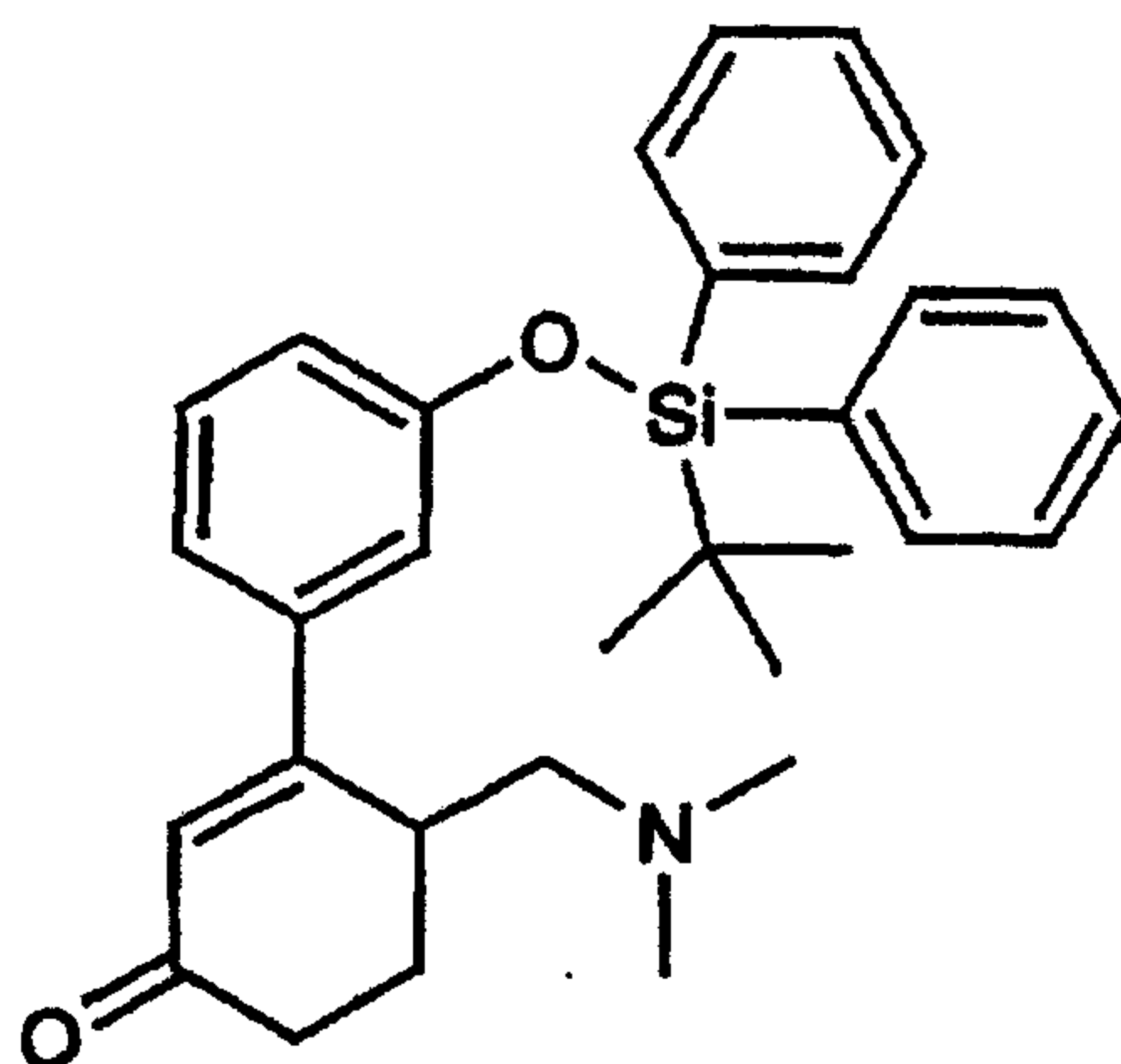
8-[3-(tert-Butyl-diphenyl-silanyloxy)-phenyl]-9-dimethylaminomethyl-3,3-dimethyl-1,5-dioxaspiro-[5.5]undecan-8-ol



17.3 g magnesium filings were initially introduced into tetrahydrofuran. 293 g (3-bromo-phenoxy)-tert-butyl-diphenylsilane in 150 ml tetrahydrofuran were then added dropwise (under gentle reflux). The mixture was allowed to after-react for 1 hour. 142 g 9-dimethylaminomethyl-1,5-dioxa-spiro[5.5]undecan-8-one, which was prepared according to example 1, stage 2, were then added dropwise at 20°C. The mixture was stirred at room temperature for 10 hours. Hydrolysis was then carried out at 10 - 15°C with 200 ml 20% ammonium chloride solution and then with 500 ml water. The aqueous phase was extracted twice with 300 ml ethyl acetate each time. The combined organic phases were dried over magnesium sulfate and the solvent was then evaporated in vacuo. The residue was purified on silica gel with ethyl acetate/methanol = 9/1. 197 g (60% of theory) of the title compound were obtained in this way.

Stage 2

3-[3-(tert-Butyl-diphenyl-silanyloxy)-phenyl]-4-dimethylaminomethyl-cyclohex-2-enone



5

10

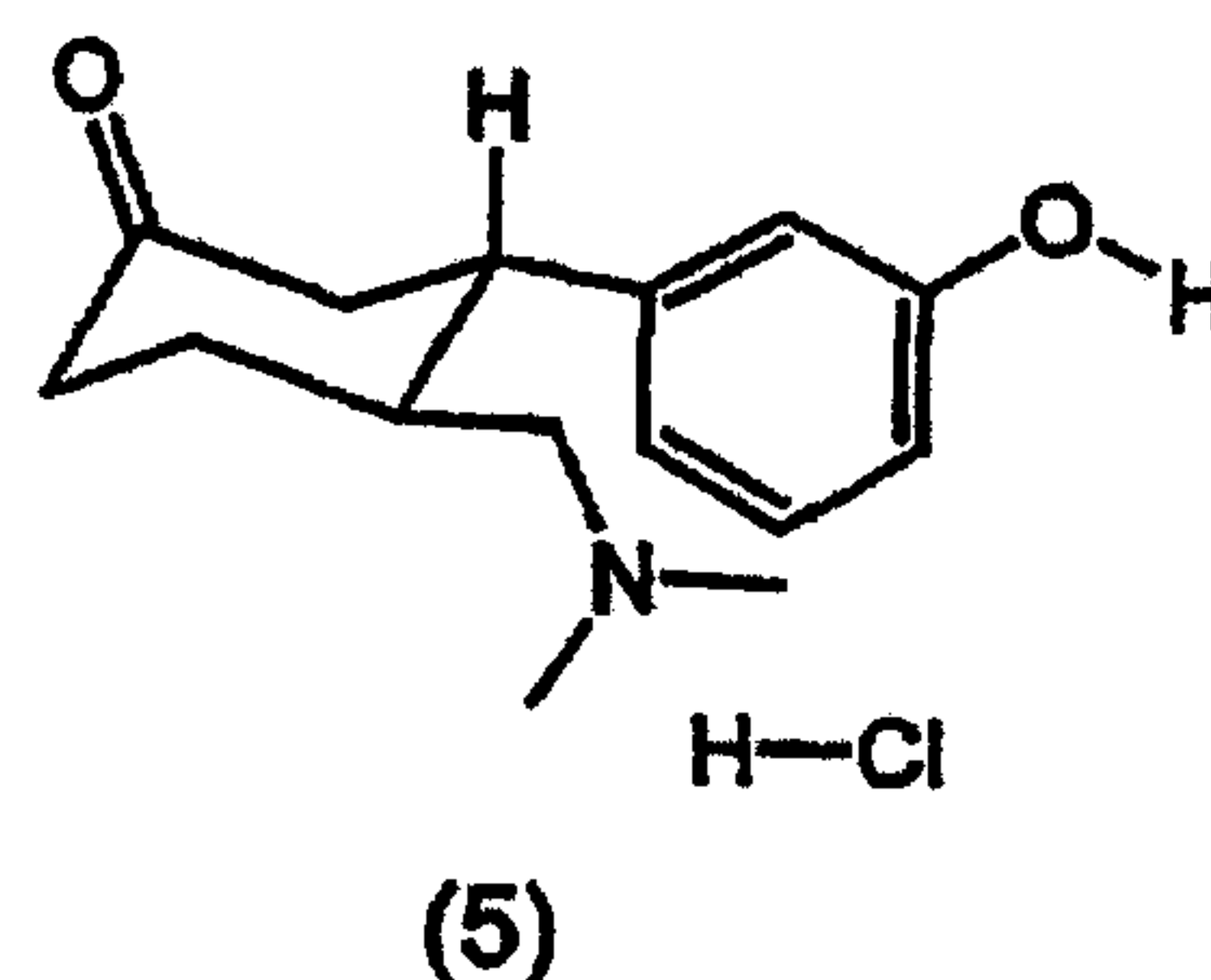
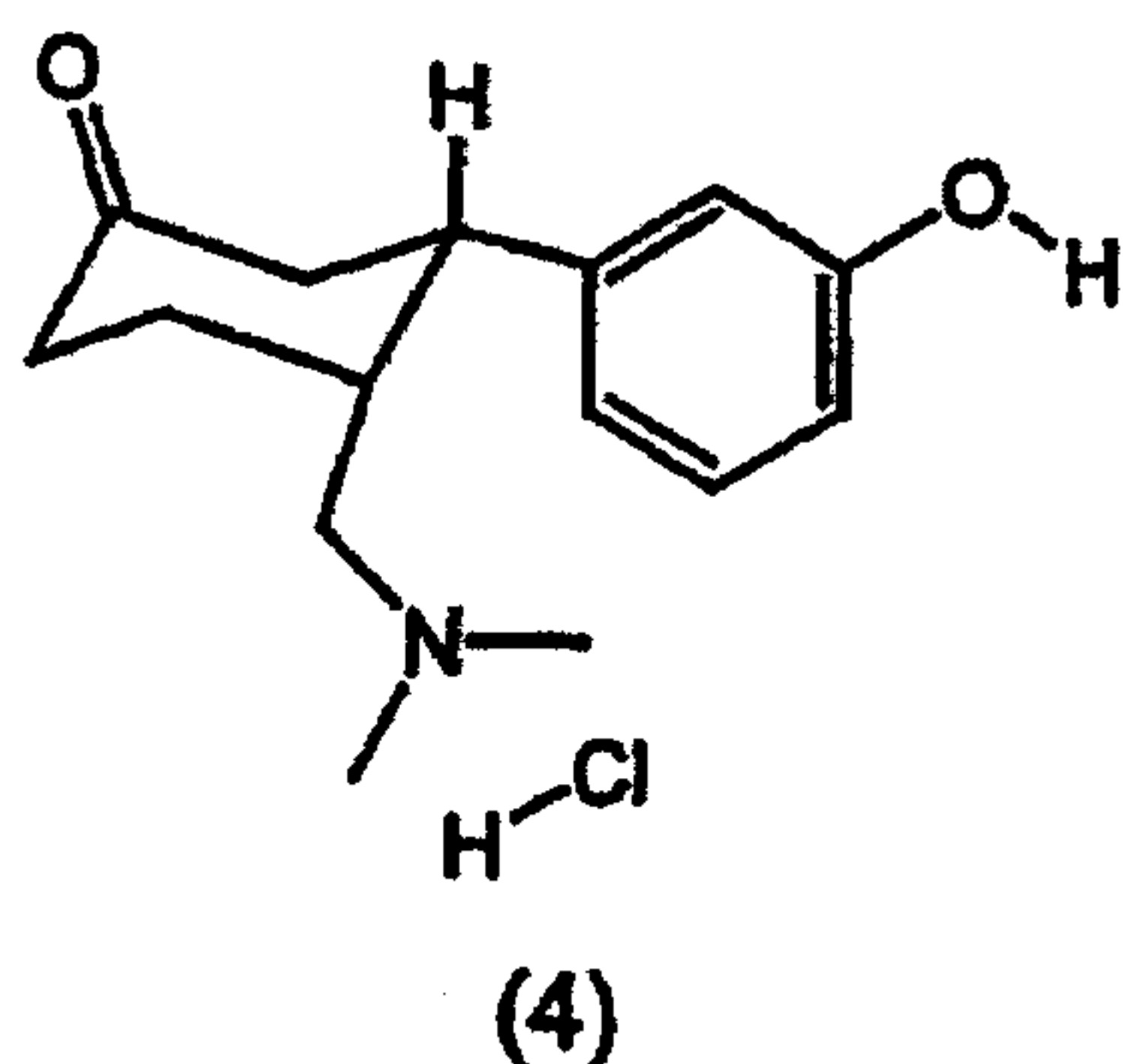
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20

197 g 8-[3-(tert-Butyl-diphenyl-silanyloxy)-phenyl]-9-dimethylaminomethyl-3,3-dimethyl-1,5-dioxaspiro-[5.5]undecan-8-ol were dissolved in tetrahydrofuran and the solution was cooled to 5°C. A mixture of 300 ml concentrated hydrochloric acid and 300 ml water was added dropwise at this temperature. The mixture was then stirred at room temperature for 10 hours. 400 ml ethyl acetate were then added, while cooling with ice, and the pH was then brought to 12 with 32% sodium hydroxide solution. The phases were separated and the aqueous phase was extracted three times with 400 ml ethyl acetate each time. The combined organic phases were washed twice with 100 ml saturated sodium chloride solution each time and dried over magnesium sulfate and the solvent was then evaporated in vacuo. The residue was purified on silica gel with ethyl acetate/methanol = 1/1. 68 g (42% of theory) of the title compound were obtained in this way.

Stage 3

rac-cis-[4-Dimethylaminomethyl-3-(3-hydroxy-phenyl)-cyclohexanone (4) and *rac-trans*-[4-dimethylaminomethyl-3-(3-hydroxy-phenyl)-cyclohexanone (5)



25 g 3-[3-(tert-butyl-diphenyl-silanyloxy)-phenyl]-4-dimethylaminomethyl-cyclohex-2-enone were dissolved in 110 ml absolute methanol. 2,8 g palladium-on-charcoal (10%) were added as a catalyst, while stirring and passing dry nitrogen over. Hydrogenation was then carried out for five hours under a pressure of 0.2 bar and at a temperature of 20°C. After filtration the solvent was evaporated off in vacuo and the residue was dissolved in 60 ml tetrahydrofuran. 15 ml tetrabutylammonium fluoride were then added at room temperature. When the reaction had ended the mixture was quenched with water and then extracted with ethyl acetate. The organic phase was washed with saturated sodium chloride solution. The organic phase was then dried over magnesium sulfate and the solvent was evaporated in vacuo. The residue was purified by column chromatography on silica gel with ethyl acetate/methanol/diisopropyl ether = 4/1/5 as the eluting agent. 5 g *rac-cis*-[4-dimethylaminomethyl-3-(3-hydroxy-phenyl)-cyclohexanone in the form of an oil

were obtained as the first product fraction. To prepare the hydrochloride, the base was dissolved in acetone, and an equimolar amount of water and trimethylchlorosilane was added. The hydrochloride which had precipitated out was filtered off with suction and dried in vacuo. 4.8 g (32.9% of theory) *rac-cis*-[4-dimethylaminomethyl-3-(3-hydroxy-phenyl)-cyclohexanone hydrochloride were obtained in this way. The second product fraction gave 3.5 g *rac-trans*-[4-dimethylaminomethyl-3-(3-hydroxy-phenyl)-cyclohexanone, likewise as an oil. To prepare the hydrochloride, the base was dissolved in acetone, and an equimolar amount of water and trimethylchlorosilane was added. The hydrochloride which had precipitated out was filtered off with suction and dried in vacuo. 3.2 g (21.9% of theory) *rac-trans*-[4-dimethylaminomethyl-3-(3-hydroxy-phenyl)-cyclohexanone hydrochloride were obtained in this way.

20 **Example 4**

The following examples were synthesized according to the instructions given and the structures are demonstrated by NMR analyses.

25

- 4-dimethylaminomethyl-3-phenyl-cyclohex-2-enone;e
- 4-dimethylaminomethyl-3-(3-hydroxy-phenyl)-cyclohex-2-enone;
- 30 ▪ *rac-trans*-4-dimethylaminomethyl-3-phenyl-cyclohexanone;
- *rac-cis*-4-dimethylaminomethyl-3-phenyl-cyclohexanone;

- 4-dimethylaminomethyl-3-(4-methoxy-phenyl)-cyclohex-2-enone;
- 5 ▪ 4-dimethylaminomethyl-3-naphthalen-2-yl-cyclohex-2-enone;
- rac-trans-4-dimethylaminomethyl-3-hydroxy-3-naphthalen-2-yl-cyclohexanone;
- 10 ▪ rac-trans-4-dimethylaminomethyl-3-(3-fluoro-phenyl)-cyclohexanone;
- rac-cis-4-dimethylaminomethyl-3-(3-fluoro-phenyl)-cyclohexanone;
- 15 ▪ rac-cis-4-dimethylaminomethyl-3-hydroxy-3-(2-methoxy-phenyl)-cyclohexanone
- 20 ▪ rac-cis-4-dimethylaminomethyl-3-hydroxy-3-(6-methoxy-naphthalen-2-yl)-cyclohexanone;
- 4-dimethylaminomethyl-3-(6-methoxy-naphthalen-2-yl)-cyclohex-2-enone;
- 25 ▪ rac-cis-3-biphenyl-4-yl-4-dimethylaminomethyl-3-hydroxy-cyclohexanone
- 3-(3-difluoromethyl-phenyl)-4-dimethylaminomethyl-cyclohex-2-enone;
- 30 ▪ 4-dimethylaminomethyl-3-(3-fluoro-phenyl)-cyclohex-2-enone;

- 3-(3,4-difluoro-phenyl)-4-dimethylaminomethyl-cyclohex-2-enone;
- 5 ▪ 4-dimethylaminomethyl-3-(4-fluoro-phenyl)-cyclohex-2-enone;
- 4-dimethylaminomethyl-3-(4-trifluoromethyl-phenyl)-cyclohex-2-enone;
- 10 ▪ 3-(3,5-dichloro-phenyl)-4-dimethylaminomethyl-cyclohex-2-enone;
- 3-(3,5-difluoro-phenyl)-4-dimethylaminomethyl-cyclohex-2-enone;
- 15 ▪ rac-cis-3-(3,5-difluoro-phenyl)-4-dimethylaminomethyl-3-hydroxy-cyclohexanone

Example 5

20

Pharmacological studies

Writhing test

25 The antinociceptive activity of the compounds according to the invention was investigated in mice in the phenylquinone-induced writhing test, modified by I.C. Hendershot, J. Forsaith, J. Pharmacol. Exp. Ther. 125, 237-240 (1959). Male NMRI mice weighing 25 -

30 30.g were used for this. Groups of 10 animals per substance dose received 0.3 ml/mouse of a 0.02% aqueous solution of phenylquinone (phenylbenzoquinone, Sigma, Deisenhofen; preparation of the solution with the addition of 5% ethanol and storage in a water bath

at 45°C) administered intraperitoneally 10 minutes after intravenous administration of a compound according to the invention. The animals were placed individually in observation cages. The number of pain-induced stretching movements (so-called writhing reactions = straightening of the body with stretching of the hind extremities) was counted by means of a push-button counter for 5 - 20 minutes after the administration of phenylquinone. Animals which received physiological saline solution i.v. and phenylquinone i.v. were also run as a control.

All the substances were tested in the standard dose of 10 mg/kg. The percentage inhibition (% inhibition) of the writhing reactions by a substance was calculated according to the following equation:

$$\% \text{ inhibition} = 100 - [\text{WR treated animals} / \text{WR control} \times 100]$$

All the compounds according to the invention investigated showed a moderate to potent analgesic action.

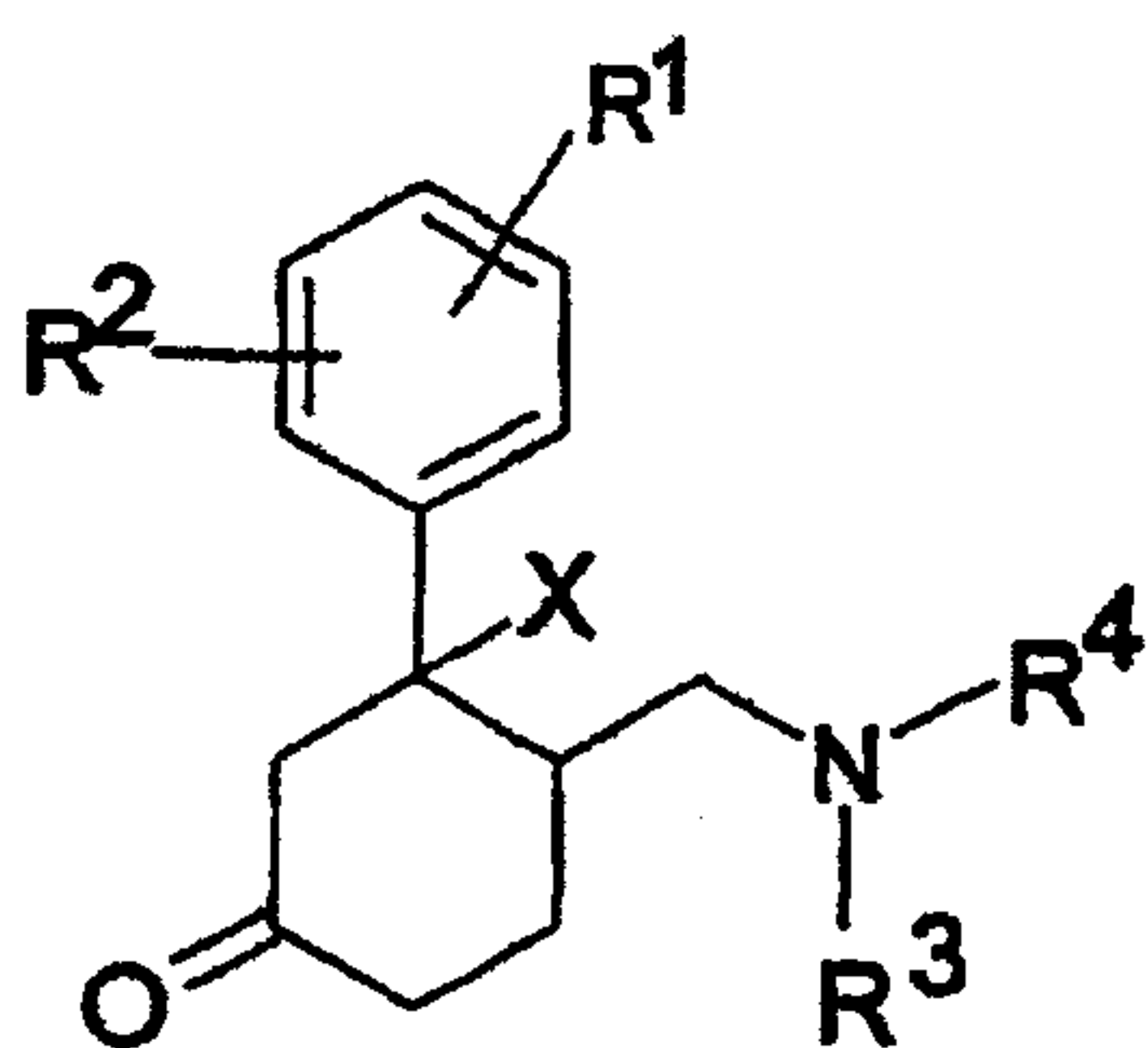
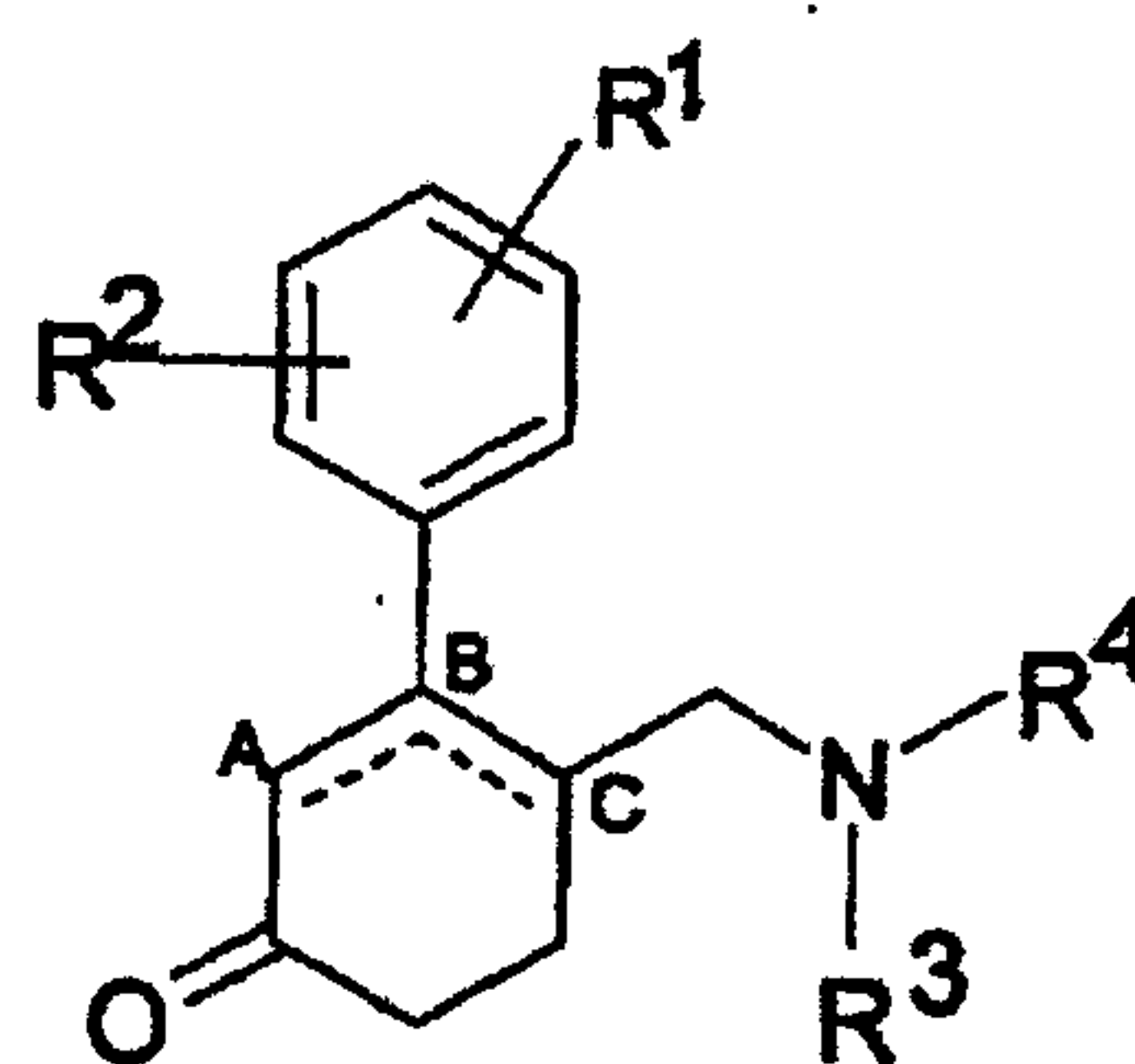
The results of selected writhing investigations are summarized in table 1.

Table 1: Analgesia test in the writhing test in mice

Compound	% inhibition of the writhing reactions 10 mg/kg i.v.
2	96
3	92
4	100

Patent claims:

1. Aminomethyl-phenyl-cyclohexanone derivatives of the general formula I and Ia, also in the form of their diastereomers or enantiomers and of their free base or of a salt formed with a physiologically tolerated acid, in particular the hydrochloride salt

**I****Ia**

wherein

R^1 and R^2 independently of one another are chosen from R^5 or YR^5 , where $Y = C_1-C_{10}$ -alkyl, C_2-C_{10} -alkenyl or C_2-C_{10} -alkinyl, branched or unbranched and mono- or polysubstituted or unsubstituted, wherein R^5 is chosen from

H, F, Cl, Br, I, CN, NO_2 ; C_1-C_8 -alkyl, C_2-C_8 -alkenyl or C_2-C_8 -alkinyl, in each case branched or unbranched and mono- or polysubstituted or unsubstituted; C_3-C_7 -cycloalkyl, saturated or unsaturated and mono- or polysubstituted or unsubstituted, or a corresponding heterocyclic radical, in which one C atom in the ring is replaced by S, O or NR^6 , where R^6 is chosen from

H, C₁-C₁₀-alkyl, C₂-C₁₀-alkenyl or C₂-C₁₀-alkynyl, in each case branched or unbranched and mono- or polysubstituted or unsubstituted;

5

aryl or heteroaryl, in each case mono- or polysubstituted or unsubstituted;

10

OR⁷, OC(O)R⁷, OC(O)OR⁷, OC(S)R⁷, C(O)R⁷, C(O)OR⁷, C(S)R⁷, C(S)OR⁷, SR⁷, S(O)R⁷ or S(O₂)R⁷, wherein R⁷ is chosen from

15

H, C₁-C₁₈-alkyl, C₂-C₁₈-alkenyl or C₂-C₁₈-alkynyl, in each case branched or unbranched and mono- or polysubstituted or unsubstituted; C₃-C₇-cycloalkyl, saturated or unsaturated and mono- or polysubstituted or unsubstituted, or a corresponding heterocyclic radical, in which one C atom in the ring is replaced by S, O or NR⁸, where R⁸ is chosen from

20

H, C₁-C₁₀-alkyl, C₂-C₁₀-alkenyl or C₂-C₁₀-alkynyl, in each case branched or unbranched and mono- or polysubstituted or unsubstituted;

25

alkylaryl, saturated or unsaturated and mono- or polysubstituted or unsubstituted; aryl or heteroaryl, in each case mono- or polysubstituted or unsubstituted; or

30

NR⁹R¹⁰, C(O)NR⁹R¹⁰ or S(O₂)NR⁹R¹⁰, wherein R⁹ and R¹⁰ independently of one another are chosen from H, C₁-C₁₈-alkyl, C₂-C₁₈-alkenyl or C₂-C₁₈-alkynyl, in each case branched or unbranched and mono- or polysubstituted or

5 unsubstituted; C₃-C₇-cycloalkyl, saturated or
unsaturated and mono- or polysubstituted or
unsubstituted, or a corresponding
heterocyclic radical, in which one C atom in
the ring is replaced by S, O or NR¹¹, where
R¹¹ is chosen from

10 H, C₁-C₁₀-alkyl, C₂-C₁₀-alkenyl or C₂-C₁₀-
alkinyl, in each case branched or
unbranched and mono- or polysubstituted
or unsubstituted;

alkylaryl, saturated or unsaturated and
mono- or polysubstituted or unsubstituted;
aryl or heteroaryl, in each case mono- or
polysubstituted or unsubstituted;

15 or

20 R⁹ and R¹⁰ together form a C₃-C₇-cycloalkyl,
saturated or unsaturated and mono- or
polysubstituted or unsubstituted, or a
corresponding heterocyclic radical, in which
one C atom in the ring is replaced by S, O
or NR¹², where R¹² is chosen from

25 H, C₁-C₁₀-alkyl, C₂-C₁₀-alkenyl or C₂-C₁₀-
alkinyl, in each case branched or
unbranched and mono- or polysubstituted
or unsubstituted;

30 or

R¹ and R² together form -CH=CH-CH=CH-, wherein the
naphthyl system formed can be mono- or
polysubstituted,

X is chosen from

H, F, Cl, Br, I, CF₃, O-S(O₂)-C₆H₄-pCH₃, OR¹³ or
OC(O)R¹³, wherein R¹³ is chosen from

5 H; C₁-C₁₀-alkyl, C₂-C₁₀-alkenyl or C₂-C₁₀-
alkinyl, in each case branched or unbranched
and mono- or polysubstituted or
unsubstituted; C₃-C₇-cycloalkyl, saturated or
unsaturated and mono- or polysubstituted or
unsubstituted, or a corresponding
10 heterocyclic radical, in which one C atom in
the ring is replaced by N, S or O;
alkylaryl, saturated or unsaturated and
mono- or polysubstituted or unsubstituted;
aryl or heteroaryl, in each case mono- or
15 polysubstituted or unsubstituted;

or

20 if the compound contains no X, according to
formula Ia a double bond is formed between C atom
A and C atom B or C atom B and C atom C;

and

25 R³, R⁴ independently of one another are chosen from
H, C₁-C₁₀-alkyl, C₂-C₁₀-alkenyl or C₂-C₁₀-alkinyl,
in each case branched or unbranched and mono- or
polysubstituted or unsubstituted; C₃-C₇-
cycloalkyl, saturated or unsaturated and mono- or
30 polysubstituted or unsubstituted, or a
corresponding heterocyclic radical, in which one
C atom in the ring is replaced by N, S or O;
alkylaryl, saturated or unsaturated and mono- or
polysubstituted or unsubstituted; aryl or

heteroaryl, in each case mono- or polysubstituted or unsubstituted;

or

5

R^3 and R^4 together form a C_3 - C_7 -cycloalkyl, saturated or unsaturated and mono- or polysubstituted or unsubstituted, or a corresponding heterocyclic radical, in which one C atom in the ring is replaced
10 by S, O or NR^{14} , where R^{14} is chosen from

H, C_1 - C_{10} -alkyl, C_2 - C_{10} -alkenyl or C_2 - C_{10} -alkinyl, in each case branched or unbranched and mono- or polysubstituted or unsubstituted

15

with the proviso that

if $X = OH$, $R^2 = H$, R^3 and R^4 are each CH_3 , R^1 is not at the same time R^5 , where $R^5 = OR^7$, where $R^7 = H$, CH_3 or
20 an unsubstituted or substituted pyridyl, thienyl, thiazoyl or phenyl group, or $R^5 = OC(O)OR^7$, where $R^7 = C_1$ - C_5 -alkyl, or $R^5 = OC(O)R^7$, where $R^7 = C_1$ - C_5 -alkyl, NH- C_6H_4 - C_1 - C_3 -alkyl, C_6H_4 - $OC(O)$ - C_1 - C_3 -alkyl, C_6H_4 - CH_2 - $N(C_1$ - C_4 -alkyl) $_2$, C_6H_4 - CH_2 -(N-4-morpholino) or $CHZ'-NHZ''$, where
25 Z' and Z'' are identical or different and are chosen from H or C_1 - C_6 -alkyl,

or

30

if $X = H$ or according to formula Ia a double bond is formed between C atom A and C atom B, $R^2 = H$, R^3 and R^4 in each case independently of one another are C_1 - C_6 -alkyl, aryl or C_3 - C_7 -cycloalkyl, R^1 is not at the same

time H, C₁₋₆-alkoxy, O-C₃₋₇-cycloalkyl, O-aryl or O-heterocyclyl.

2. Aminomethyl-phenyl-cyclohexanone derivatives according to claim 1, characterized in that $R^1 = R^5$, where R^5 is chosen from

H, F, Cl, Br, I, CHF₂, CF₃, NO₂, NH₂; C₁₋₄-alkyl or C₂₋₄-alkenyl, branched or unbranched and mono- or polysubstituted or unsubstituted; aryl, substituted or unsubstituted; OR⁷, C(O)OR⁷ or SR⁷, wherein R⁷ is chosen from

H; C₁₋₄-alkyl, branched or unbranched and mono- or polysubstituted or unsubstituted; preferably H, CF₃ or CH₃, or S(O₂)NR⁹R¹⁰, wherein R⁹ and R¹⁰ independently of one another are chosen from

H; C₁₋₄-alkyl, branched or unbranched and mono- or polysubstituted or unsubstituted; wherein particularly preferably R¹ = R⁵, where R⁵ is chosen from

H, F, Cl, OH, CH₃, C₂H₅, C₂H₃, CHF₂, CF₃, SCH₃, OCF₃, OCH₃, OC₂H₅, C(O)OCH₃, C(O)OC₂H₅ or phenyl

while R², X, R³ and R⁴ have one of the meanings mentioned in the preceding claims.

3. Aminomethyl-phenyl-cyclohexanone derivatives according to one of claims 1 or 2, characterized in that $R^2 = R^5$, wherein R⁵ is chosen from

H, F, Cl, Br, I, SCH₃; C₁₋₄-alkyl, C₂₋₄-alkenyl, branched or unbranched and mono- or polysubstituted or unsubstituted, preferably CF₃;

OR⁷, where R⁷ is chosen from C₁-C₄-alkyl, branched or unbranched and mono- or polysubstituted or unsubstituted, preferably CH₃;

5 while R¹, X, R³ and R⁴ have one of the meanings mentioned in the preceding claims.

4. Aminomethyl-phenyl-cyclohexanone derivatives according to one of claims 1 to 3, characterized in that R¹ and
10 R² have different meanings or

R¹ and R² together form -CH=CH-CH=CH-, wherein the naphthyl system formed can be mono- or polysubstituted, preferably by halogen, OC₁₋₃-
15 alkyl or C₁₋₃-alkyl, unsubstituted or mono or polysubstituted, in particular by OCH₃.

5. Aminomethyl-phenyl-cyclohexanone derivatives according to one of claims 1 to 4, characterized in that

20 X is chosen from

H, F, Cl, OH, CF₃, O-S(O₂)-C₆H₄-pCH₃ or OC(O)R⁷,
where R⁷ = H; C₁-C₄-alkyl or C₂-C₄-alkenyl,
25 branched or unbranched and mono- or polysubstituted or unsubstituted,
preferably H, F, Cl, OH, O-S(O₂)-C₆H₄-pCH₃ or OC(O)R⁷, where R⁷ = C₁-C₄-alkyl, preferably CH₃, in particular H or OH,

30

or

if the compound contains no X, according to formula Ia a double bond is formed between C atom A and C atom B or C atom B and C atom C,

5 while R^1 , R^2 , R^3 and R^4 have one of the meanings mentioned in the preceding claims.

6. Aminomethyl-phenyl-cyclohexanone derivatives according to one of claims 1 to 5, characterized in that

10

R^3 and R^4 independently of one another are chosen from C_1 - C_4 -alkyl, branched or unbranched and mono- or polysubstituted or unsubstituted, preferably CH_3 ,

15

or

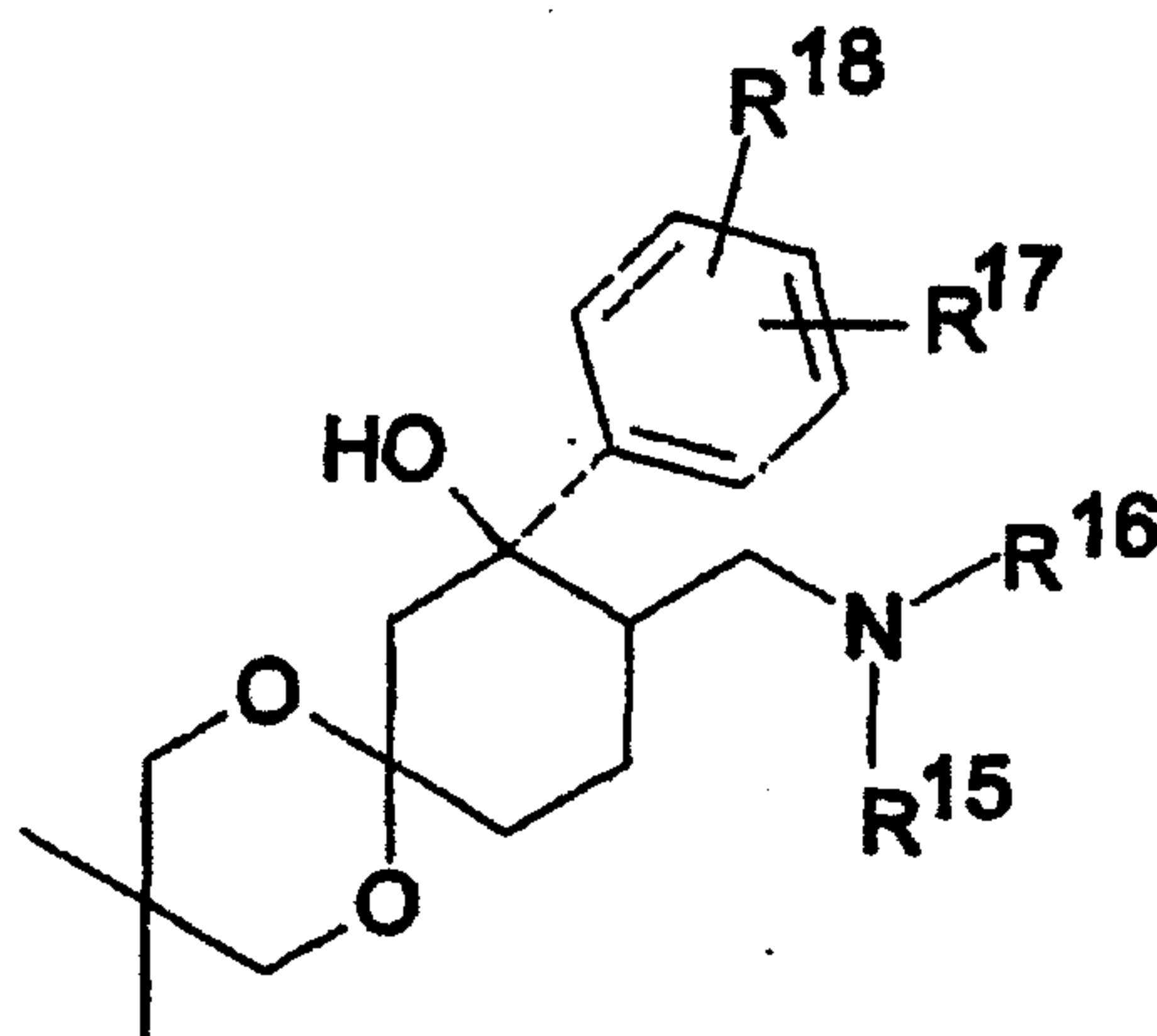
R^3 and R^4 together form a C_3 - C_7 -cycloalkyl, saturated or unsaturated and mono- or polysubstituted or unsubstituted,

20

while R^1 , R^2 and X have one of the meanings mentioned in the preceding claims.

7. Process for the preparation of aminomethyl-phenyl-cyclohexanone derivatives according to claim 1 according to formula Ia or according to formula I where $X = H$, characterized in that compounds of the formula II

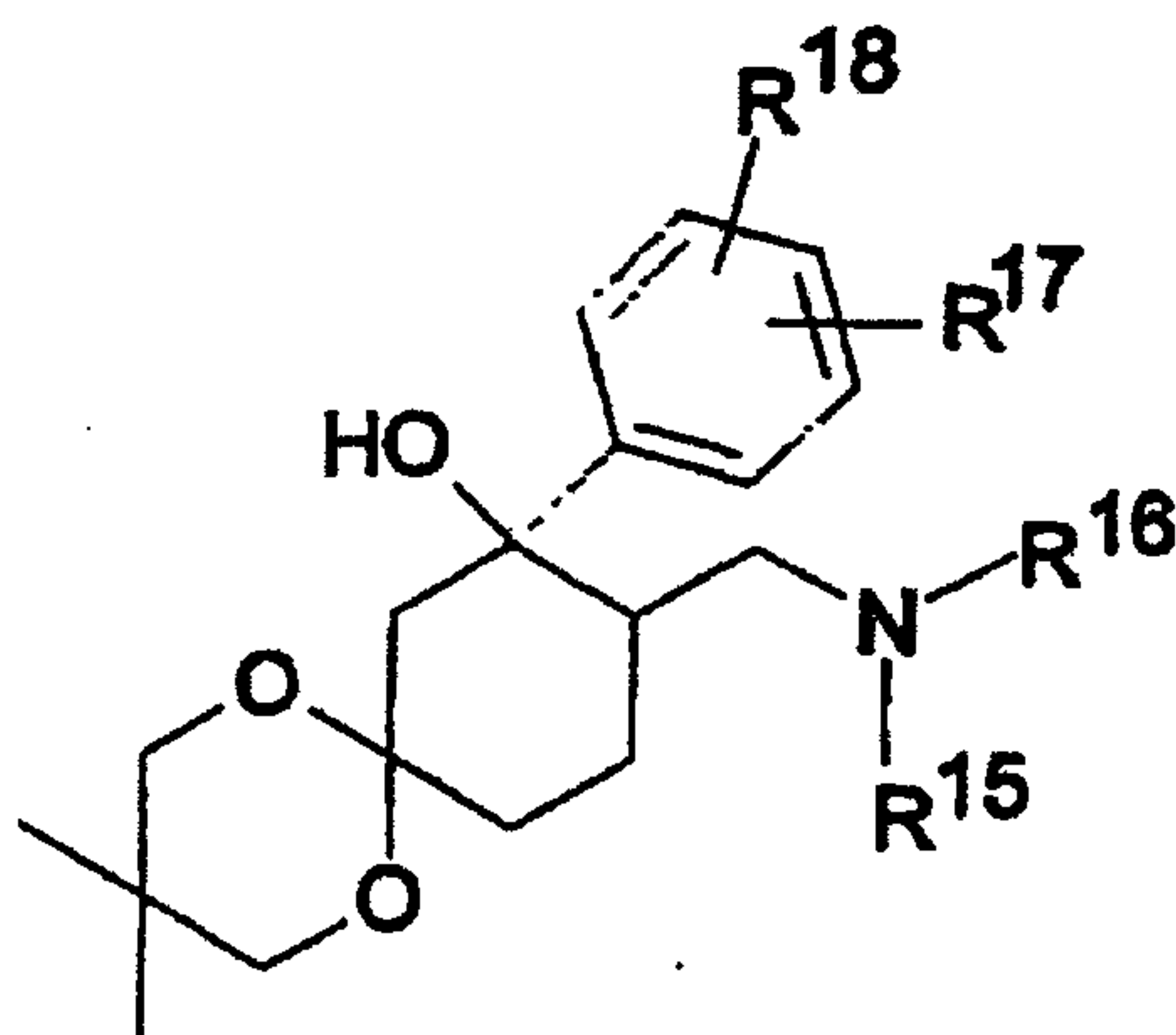
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II

in which R^{15} has a meaning corresponding to R^3 , R^{16} to
 R^4 , R^{17} to R^1 and R^{18} to R^2 according to claim 1, are
 5 reacted with acids, preferably hydrochloric acid,
 formic acid or acetic acid, at room temperature and
 the product according to formula Ia is then either
 purified or hydrogenated with catalytically activated
 hydrogen, preferably with platinum or palladium as a
 10 catalyst absorbed on a support material, such as
 active charcoal, preferably in ethyl acetate or a
 $C_1 - C_4$ -alkyl alcohol, under pressures of 0.1 to 10 bar
 and/or at temperatures of 20°C to 80°C , and the
 product according to formula I where $X = \text{H}$ is then
 15 purified.

8. Process for the preparation of aminomethyl-phenyl-
 cyclohexanone derivatives according to claim 1
 according to formula I where $X \neq \text{H}$, characterized in
 20 that compounds of the formula II



II

in which R^{15} has a meaning corresponding to R^3 , R^{16} to R^4 , R^{17} to R^1 and R^{18} to R^2 according to claim 1, are
 5 reacted with acids, preferably hydrochloric acid, at temperatures of between 0°C and 5°C and the products according to formula I formed in this way, where $X = \text{OH}$ and R^{15} to R^{18} are unchanged, are either purified or further processed, wherein, if X is to be F, Cl, Br, I or CF_3 , the $X = \text{OH}$ group is exchanged for F or Cl or Br or I or CF_3 , and if X is to be OR^{13} , wherein R^{13} has one
 10 of the meanings described in claim 1, the $X = \text{OH}$ group is etherified with a halide of the formula III

15



III

wherein R^{19} has a meaning analogous to R^{13} , or if $X = \text{O-S(O}_2\text{)-C}_6\text{H}_4\text{-CH}_3$ or OC(O)R^{13} , wherein R^{13} has one of the
 20 meanings described in claim 1, the $X = \text{OH}$ group is esterified with an acid chloride of the formula IV

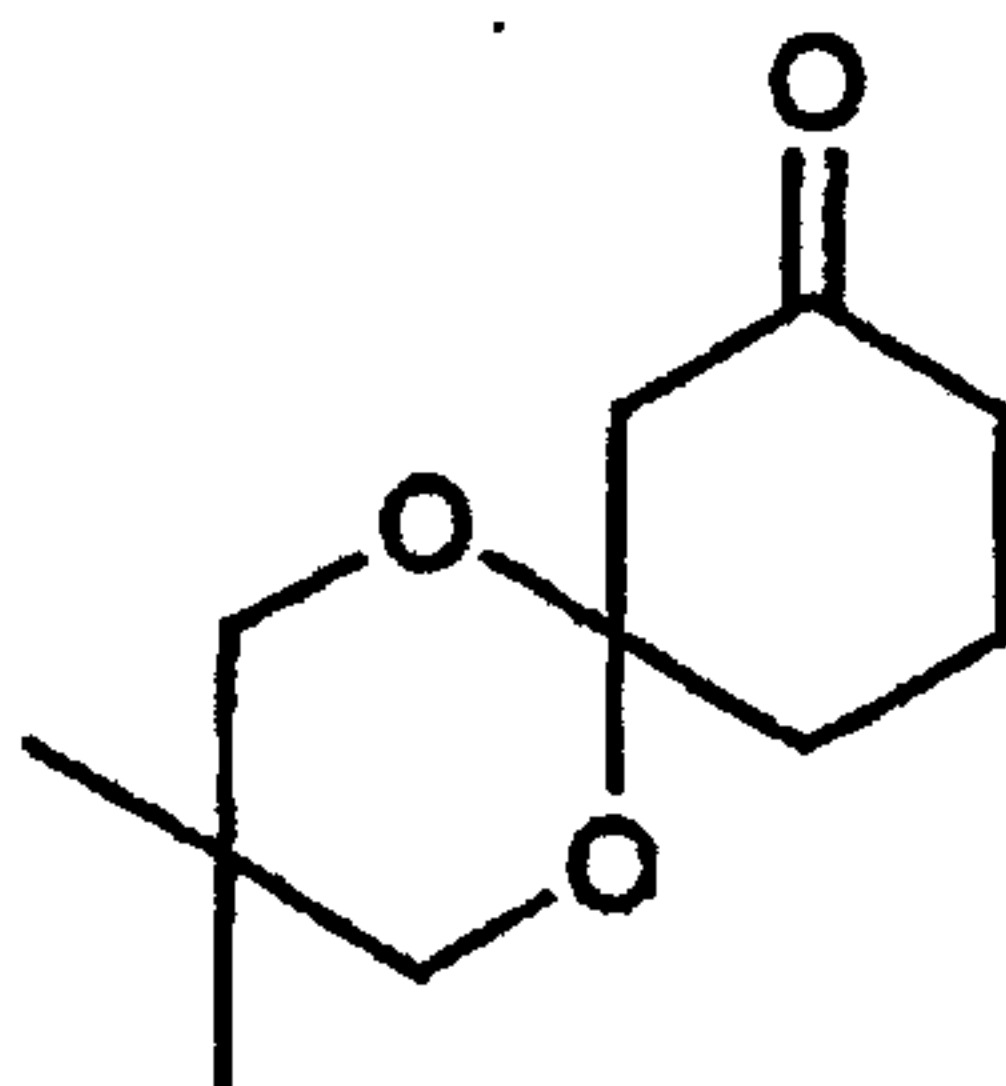


IV

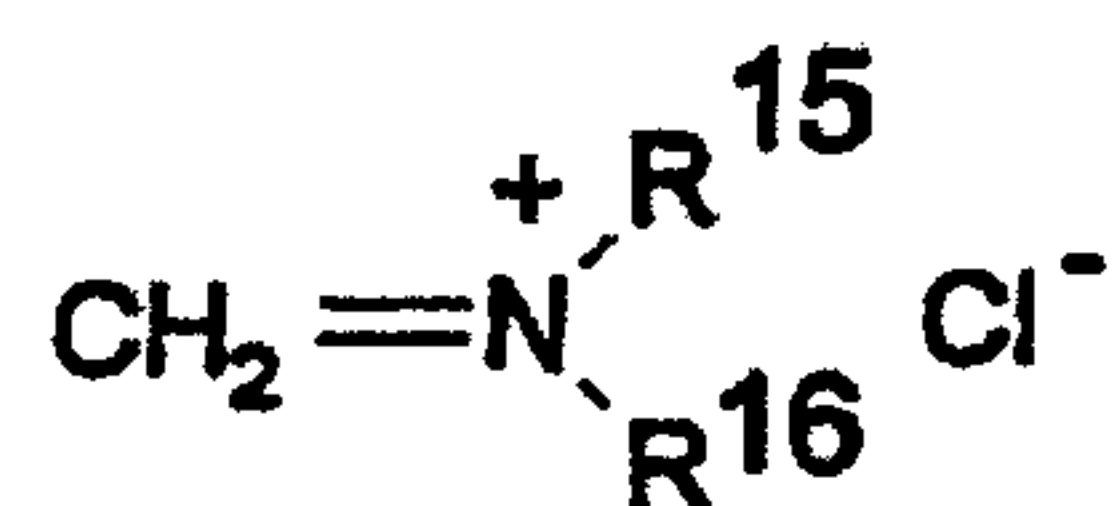
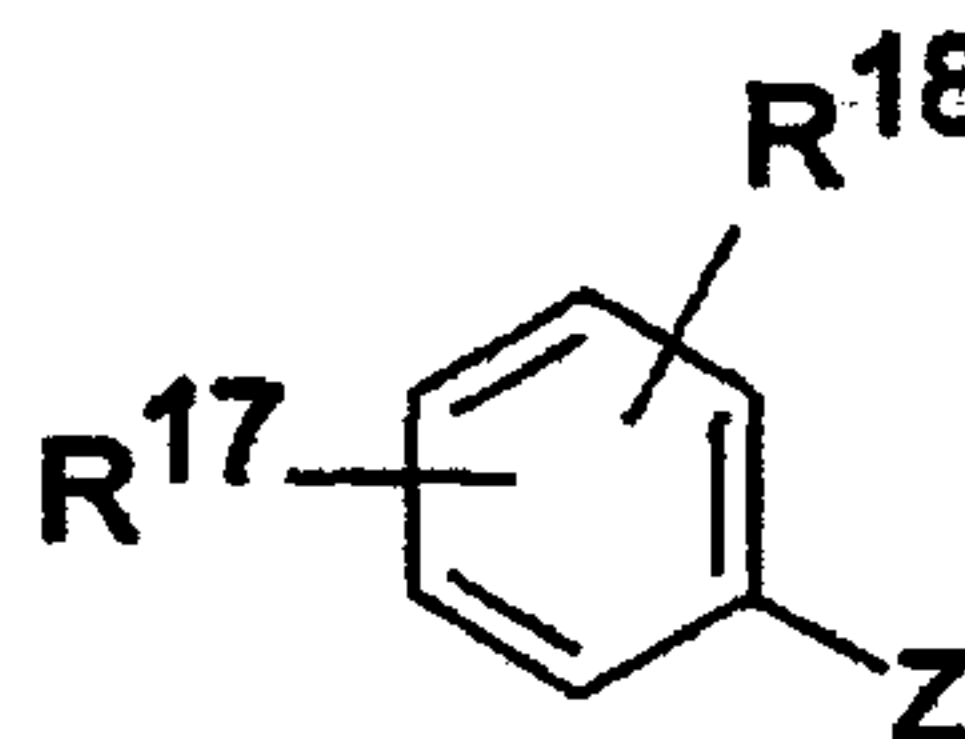
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or $\text{Cl-S(O}_2\text{)-C}_6\text{H}_4\text{-CH}_3$, wherein R^{20} has a meaning analogous to R^{13} , and finally the product is purified.

9. Process according to one of claims 7 or 8,
 5 characterized in that to prepare the starting substance according to formula II, 3,3-dimethyl-1,5-dioxaspiro[5.5]-undecan-8-one



- 10 is first reacted with immonium salts of the formula V or with formaldehyde and an amine of the formula VI, wherein R^{15} has a meaning corresponding to R^3 and R^{16} to R^4 according to claim 1,

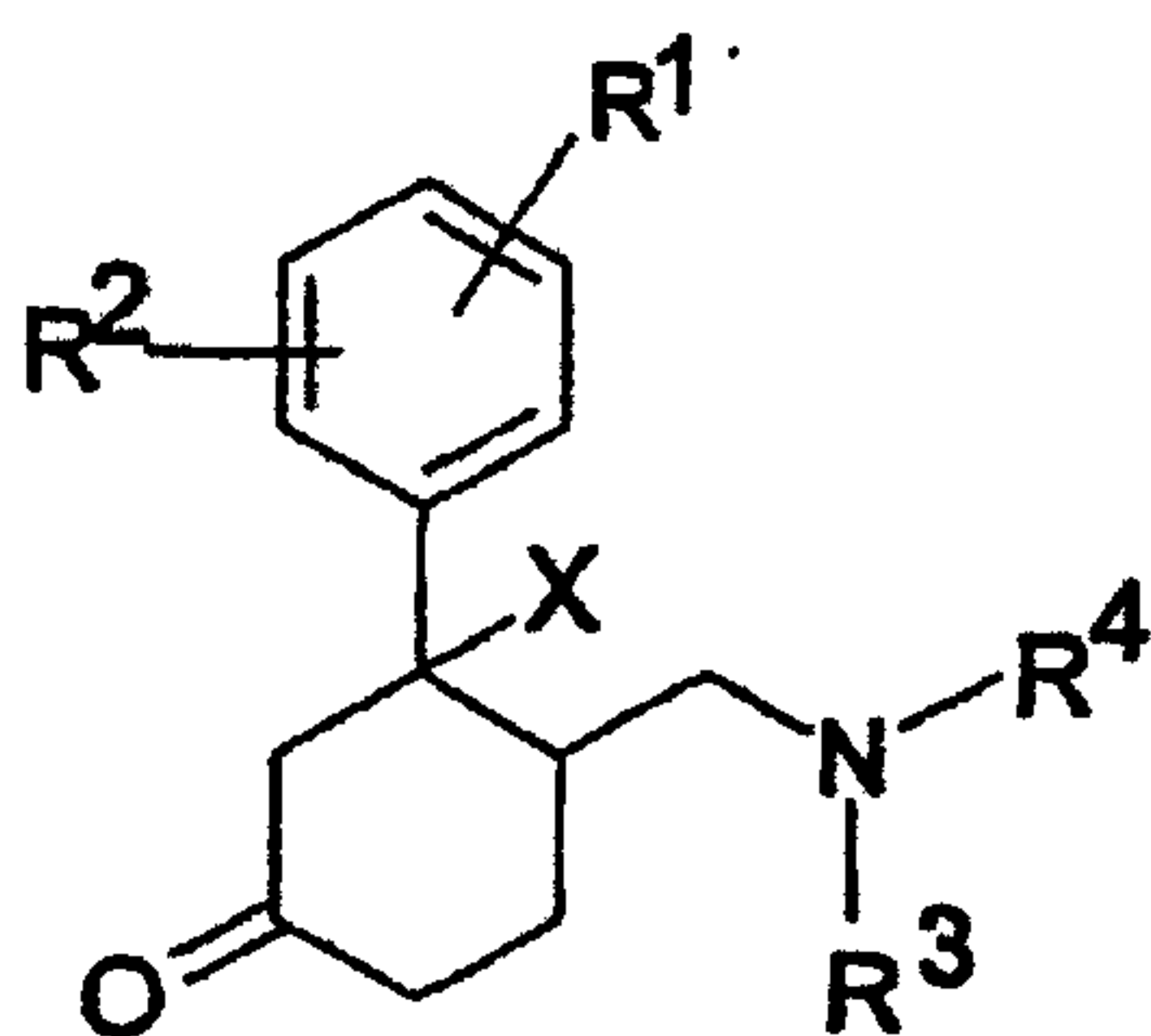
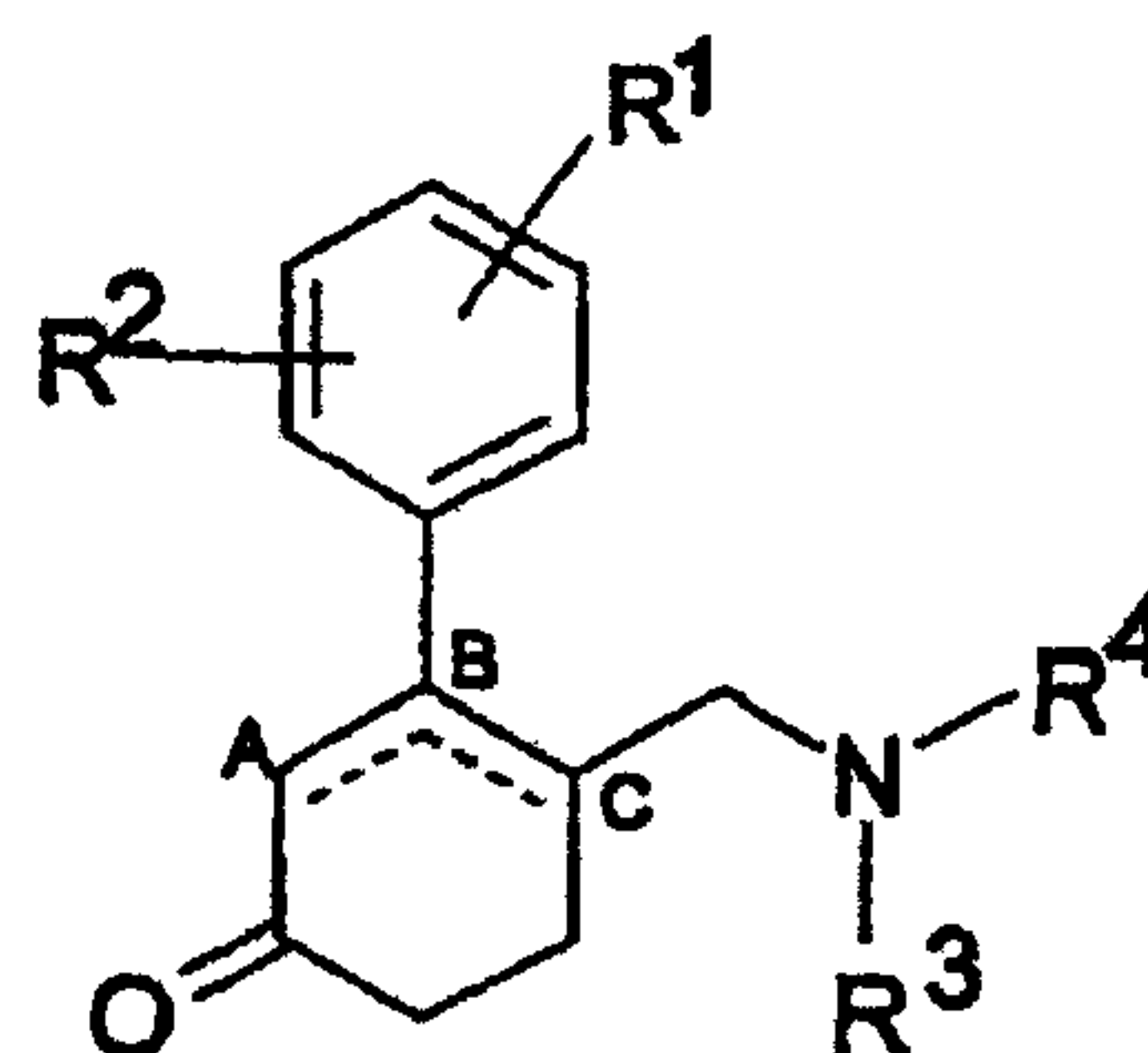
**V****VI****VII**

15

and the Mannich bases obtained in this way are then reacted with an organometallic compound of the formula VII, in which Z denotes MgCl, MgBr, MgI or lithium and R^{17} has a meaning corresponding to R^1 and R^{18} to R^2

- 20 according to claim 1, at temperatures of between -70°C and 60°C , preferably in diethyl ether and/or tetrahydrofuran.

10. Process according to one of claims 7 to 9,
characterized in that before the concluding
purification a process product with at least one
C(O)OCH₃, OC(O)OCH₃ and/or C(S)OCH₃ group is hydrolysed
5 with KOH solution or NaOH solution in methanol at
40°C - 60°C.
11. Process according to one of claims 7 to 10,
characterized in that in R¹⁵ to R²⁰ according to
10 formulae II to VII at least one OH group has been
replaced by an OSi(Ph)₂tert-but group, at least one SH
group has been replaced by an S-p-methoxybenzyl group
and/or at least one NH₂ group has been replaced by an
NO₂ group and, directly before purification of the end
15 product, at least one OSi(Ph)₂tert-but group is split
off with tetrabutylammonium fluoride in
tetrahydrofuran and/or at least one p-methoxybenzyl
group is split off with a metal amine, preferably
sodium amine, and/or at least one NO₂ group is reduced
20 to NH₂.
12. Medicaments comprising as the active compound at least
one aminomethyl-phenyl-cyclohexanone derivative of the
general formula I or Ia

**I****Ia**

wherein

5 R^1 and R^2 independently of one another are chosen from R^5 or YR^5 , where $Y = C_1-C_{10}$ -alkyl, C_2-C_{10} -alkenyl or C_2-C_{10} -alkinyl, branched or unbranched and mono- or polysubstituted or unsubstituted, wherein R^5 is chosen from

10 H, F, Cl, Br, I, CN, NO_2 , C_1-C_8 -alkyl, C_2-C_8 -alkenyl or C_2-C_8 -alkinyl, in each case branched or unbranched and mono- or polysubstituted or unsubstituted; C_3-C_7 -cycloalkyl, saturated or
 15 unsaturated and mono- or polysubstituted or unsubstituted, or a corresponding heterocyclic radical, in which one C atom in the ring is replaced by S, O or NR^6 , where R^6 is chosen from
 H, C_1-C_{10} -alkyl, C_2-C_{10} -alkenyl or C_2-C_{10} -alkinyl, in each case branched or unbranched
 20 and mono- or polysubstituted or unsubstituted;

aryl or heteroaryl, in each case mono- or polysubstituted or unsubstituted;

25

OR^7 , $OC(O)R^7$, $OC(O)OR^7$, $OC(S)R^7$, $C(O)R^7$, $C(O)OR^7$, $C(S)R^7$, $C(S)OR^7$, SR^7 , $S(O)R^7$ or $S(O_2)R^7$, wherein R^7 is chosen from

30 H, C_1-C_{18} -alkyl, C_2-C_{18} -alkenyl or C_2-C_{18} -alkinyl, in each case branched or unbranched and mono- or polysubstituted or unsubstituted; C_3-C_7 -cycloalkyl, saturated or unsaturated and mono- or polysubstituted or unsubstituted, or a corresponding

heterocyclic radical, in which one C atom in the ring is replaced by S, O or NR^8 , where R^8 is chosen from

5 H, $\text{C}_1\text{-C}_{10}$ -alkyl, $\text{C}_2\text{-C}_{10}$ -alkenyl or $\text{C}_2\text{-C}_{10}$ -alkynyl, in each case branched or unbranched and mono- or polysubstituted or unsubstituted;

10 alkylaryl, saturated or unsaturated and mono- or polysubstituted or unsubstituted; aryl or heteroaryl, in each case mono- or polysubstituted or unsubstituted; or

NR^9R^{10} , $\text{C}(\text{O})\text{NR}^9\text{R}^{10}$ or $\text{S}(\text{O}_2)\text{NR}^9\text{R}^{10}$, wherein R^9 and R^{10} independently of one another are chosen from

15 H, $\text{C}_1\text{-C}_{18}$ -alkyl, $\text{C}_2\text{-C}_{18}$ -alkenyl or $\text{C}_2\text{-C}_{18}$ -alkynyl, in each case branched or unbranched and mono- or polysubstituted or unsubstituted; $\text{C}_3\text{-C}_7$ -cycloalkyl, saturated or unsaturated and mono- or polysubstituted or unsubstituted, or a corresponding
20 heterocyclic radical, in which one C atom in the ring is replaced by S, O or NR^{11} , where R^{11} is chosen from

25 H, $\text{C}_1\text{-C}_{10}$ -alkyl, $\text{C}_2\text{-C}_{10}$ -alkenyl or $\text{C}_2\text{-C}_{10}$ -alkynyl, in each case branched or unbranched and mono- or polysubstituted or unsubstituted;

30 alkylaryl, saturated or unsaturated and mono- or polysubstituted or unsubstituted; aryl or heteroaryl, in each case mono- or polysubstituted or unsubstituted;

or

5 R⁹ and R¹⁰ together form a C₃-C₇-cycloalkyl, saturated or unsaturated and mono- or polysubstituted or unsubstituted, or a corresponding heterocyclic radical, in which one C atom in the ring is replaced by S, O or NR¹², where R¹² is chosen from

10 H, C₁-C₁₀-alkyl, C₂-C₁₀-alkenyl or C₂-C₁₀-alkinyl, in each case branched or unbranched and mono- or polysubstituted or unsubstituted;

or

15 R¹ and R² together form -CH=CH-CH=CH-, wherein the naphthyl system formed can be mono- or polysubstituted,

X is chosen from

20 H, F, Cl, Br, I, CF₃, O-S(O₂)-C₆H₄-pCH₃, OR¹³ or OC(O)R¹³, wherein R¹³ is chosen from

25 H; C₁-C₁₀-alkyl, C₂-C₁₀-alkenyl or C₂-C₁₀-alkinyl, in each case branched or unbranched and mono- or polysubstituted or unsubstituted; C₃-C₇-cycloalkyl, saturated or unsaturated and mono- or polysubstituted or unsubstituted, or a corresponding heterocyclic radical, in which one C atom in the ring is replaced by N, S or O; alkylaryl, saturated or unsaturated and
30 mono- or polysubstituted or unsubstituted; aryl or heteroaryl, in each case mono- or polysubstituted or unsubstituted;

or

if the compound contains no X, according to formula Ia a double bond is formed between C atom A and C atom B or C atom B and C atom C;

5

and

R^3 , R^4 independently of one another are chosen from H, C_1 - C_{10} -alkyl, C_2 - C_{10} -alkenyl or C_2 - C_{10} -alkinyl, in each case branched or unbranched and mono- or polysubstituted or unsubstituted; C_3 - C_7 -cycloalkyl, saturated or unsaturated and mono- or polysubstituted or unsubstituted, or a corresponding heterocyclic radical, in which one C atom in the ring is replaced by N, S or O; alkylaryl, saturated or unsaturated and mono- or polysubstituted or unsubstituted; aryl or heteroaryl, in each case mono- or polysubstituted or unsubstituted;

10

15

20

or

R^3 and R^4 together form a C_3 - C_7 -cycloalkyl, saturated or unsaturated and mono- or polysubstituted or unsubstituted, or a corresponding heterocyclic radical, in which one C atom in the ring is replaced by S, O or NR^{14} , where R^{14} is chosen from

25

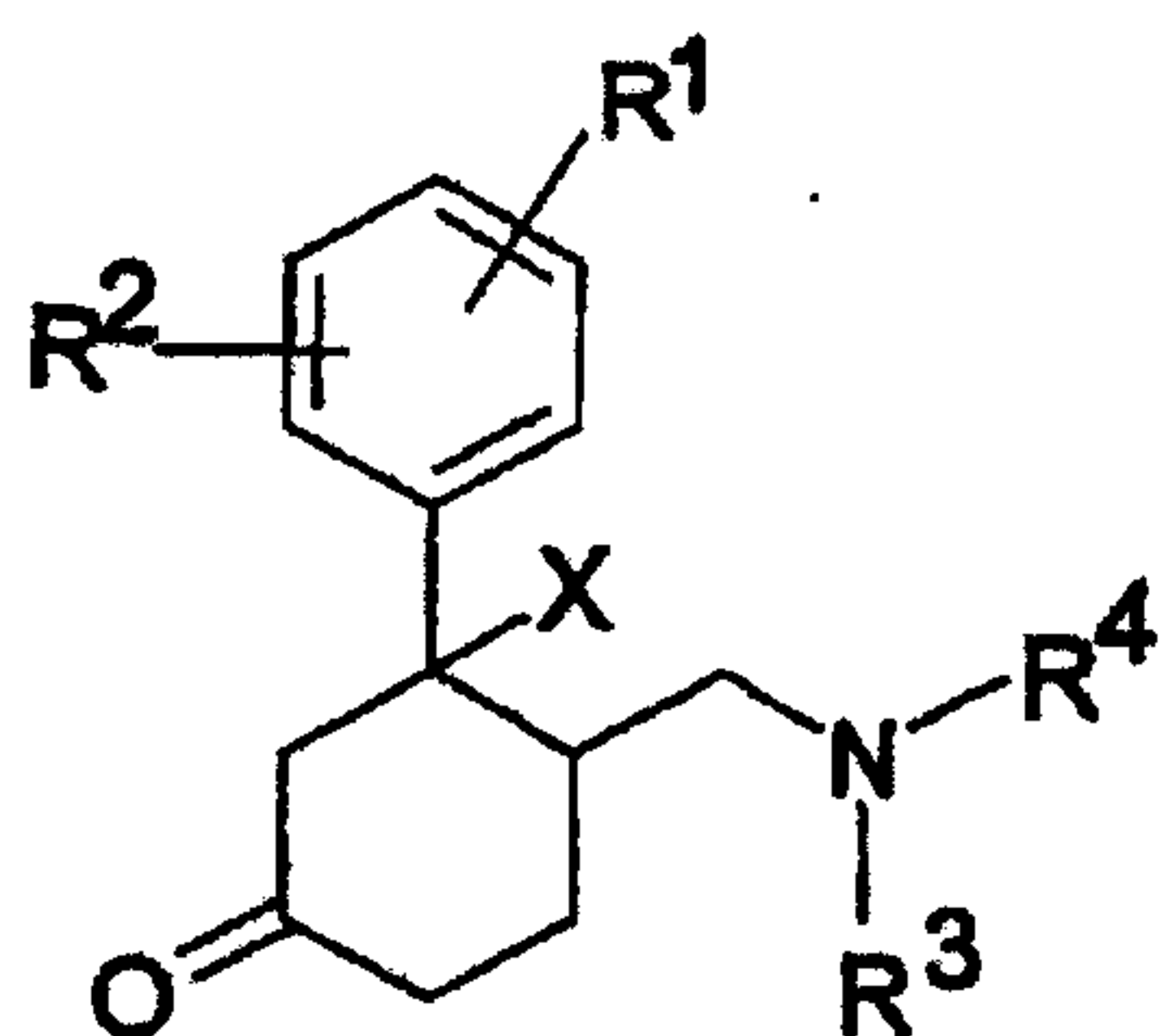
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H, C_1 - C_{10} -alkyl, C_2 - C_{10} -alkenyl or C_2 - C_{10} -alkinyl, in each case branched or unbranched and mono- or polysubstituted or unsubstituted;

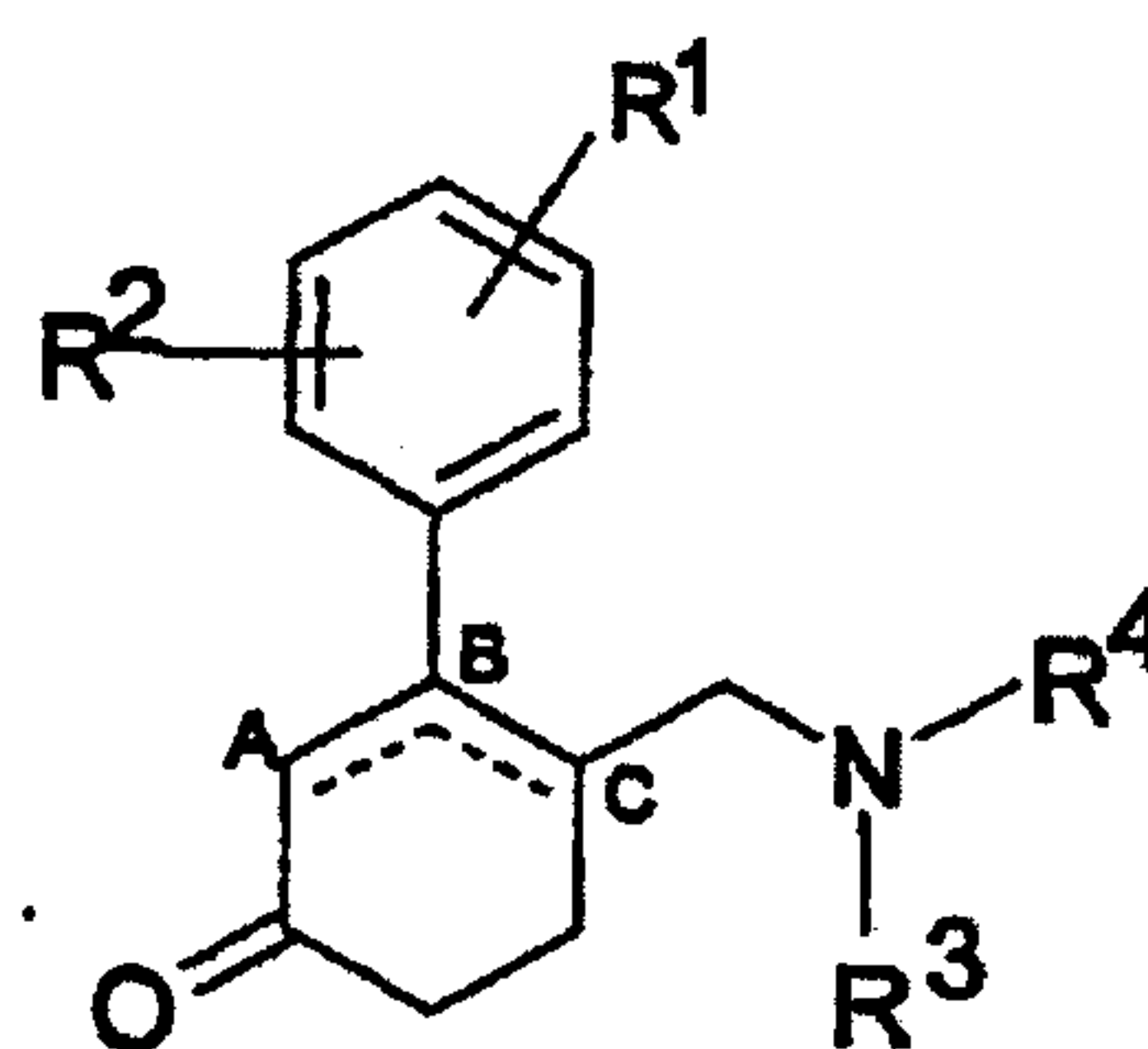
in the form of its diastereomers or enantiomers and of its free base or of a salt formed with a

physiologically tolerated acid, in particular the hydrochloride salt.

13. Medicaments according to claim 12, characterized in that, independently of one another in the general formulae I and Ia



I



Ia

$R^1 = R^5$, wherein R^5 is chosen from

- 10 H, F, Cl, Br, I, CHF_2 , CF_3 , NO_2 , NH_2 ; C_1 - C_4 -alkyl or C_2 - C_4 -alkenyl, branched or unbranched and mono- or polysubstituted or unsubstituted; aryl, substituted or unsubstituted; OR^7 , C(O)OR^7 or SR^7 , wherein R^7 is chosen from

- 15 H; C_1 - C_4 -alkyl, branched or unbranched and mono- or polysubstituted or unsubstituted; preferably H, CF_3 or CH_3 , or $\text{S(O}_2\text{)NR}^9\text{R}^{10}$, wherein R^9 and R^{10} independently of one another are chosen from

- 20 H; C_1 - C_4 -alkyl, branched or unbranched and mono- or polysubstituted or unsubstituted; wherein particularly preferably $R^1 = R^5$, where R^5 is chosen from

- 25 H, F, Cl, OH, CH_3 , C_2H_5 , C_2H_3 , CHF_2 , CF_3 , SCH_3 , OCF_3 , OCH_3 , OC_2H_5 , C(O)OCH_3 , $\text{C(O)OC}_2\text{H}_5$ or phenyl,

and/or $R^2 = R^5$, wherein R^5 is chosen from

H, F, Cl, Br, I, SCH₃; C₁-C₄-alkyl, C₂-C₄-alkenyl,
branched or unbranched and mono- or
5 polysubstituted or unsubstituted, preferably CF₃;
OR⁷, where R⁷ is chosen from C₁-C₄-alkyl, branched
or unbranched and mono- or polysubstituted or
unsubstituted, preferably CH₃;

10 **and/or** R^1 and R^2 have different meanings or R^1 and R^2
together form -CH=CH-CH=CH-, wherein the naphthyl
system formed can be mono- or polysubstituted,
preferably by halogen, OC₁₋₃-alkyl or C₁₋₃-alkyl,
unsubstituted or mono or polysubstituted, in
15 particular by OCH₃,

and/or X is chosen from

H, F, Cl, OH, CF₃, O-S(O₂)-C₆H₄-pCH₃ or OC(O)R⁷,
where R⁷ = H; C₁-C₄-alkyl or C₂-C₄-alkenyl,
20 branched or unbranched and mono- or
polysubstituted or unsubstituted,
preferably H, F, Cl, OH, O-S(O₂)-C₆H₄-pCH₃ or
OC(O)R⁷, where R⁷ = C₁-C₄-alkyl, preferably CH₃, in
particular H or OH,

25

or

if the compound contains no X, according to
formula Ia a double bond is formed between C atom
30 A and C atom B or C atom B and C atom C,

and/or R^3 and R^4 independently of one another are
chosen from

C₁-C₄-alkyl, branched or unbranched and mono- or polysubstituted or unsubstituted, preferably CH₃;

or

5

R³ and R⁴ together form a C₃-C₇-cycloalkyl, saturated or unsaturated and mono- or polysubstituted or unsubstituted,

10 **and/or** R¹, R², X, R³ and/or R⁴ have one of the meanings mentioned in the preceding claims.

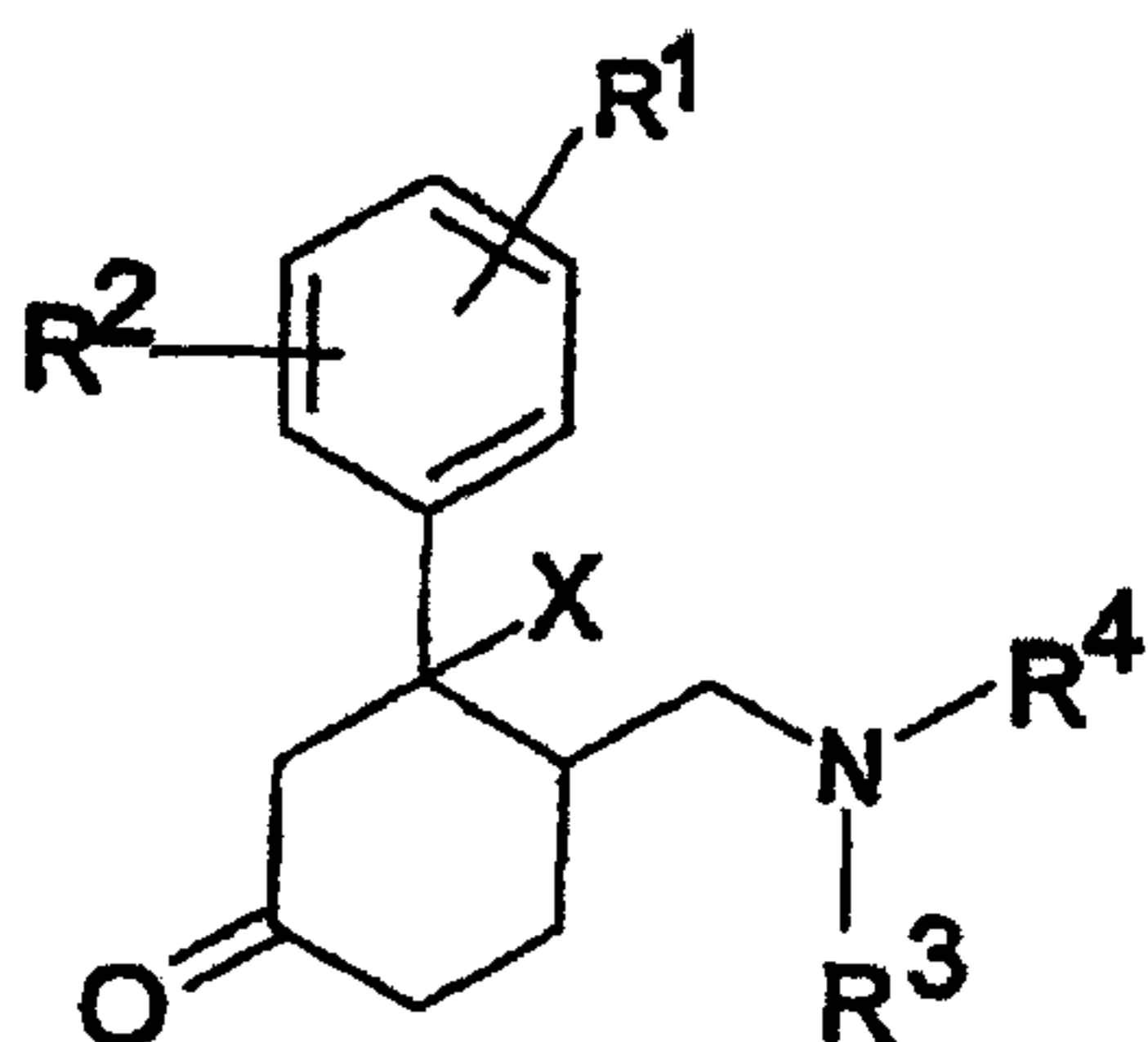
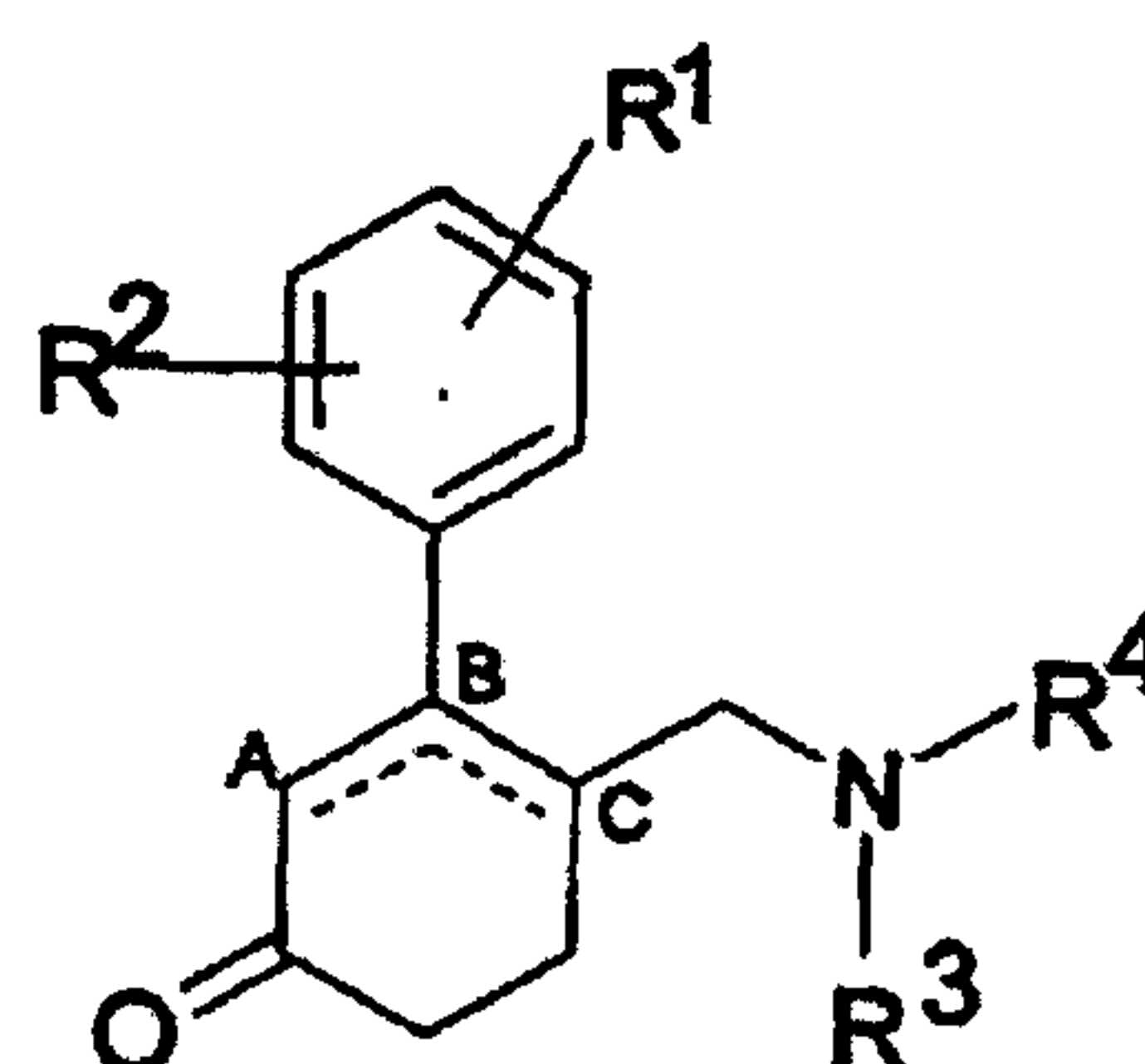
14. Medicaments according to claim 12, comprising as the active compound at least one aminomethyl-phenyl-cyclohexanone derivative chosen from the group consisting of

15

- *rac-cis*-[4-dimethylaminomethyl-3-hydroxy-3-(3-methoxy-phenyl)-cyclohexanone],
- 20 • *rac-cis*-[4-dimethylaminomethyl-3-(3-methoxy-phenyl)-cyclohexanone],
- *rac-trans*-[4-dimethylaminomethyl-3-(3-methoxy-phenyl)-cyclohexanone],
- *rac-cis*-[4-dimethylaminomethyl-3-(3-hydroxy-phenyl)-cyclohexanone],
- 25 • *rac-trans*-[4-dimethylaminomethyl-3-(3-hydroxy-phenyl)-cyclohexanone] or
- 4-dimethylaminomethyl-3-(3-methoxy-phenyl)-cyclohex-2-enone
- 30 • 4-dimethylaminomethyl-3-phenyl-cyclohex-2-enone;
- 4-dimethylaminomethyl-3-(3-hydroxy-phenyl)-cyclohex-2-enone;

- rac-trans-4-dimethylaminomethyl-3-phenyl-cyclohexanone;
- rac-cis-4-dimethylaminomethyl-3-phenyl-cyclohexanone;
- 5 • 4-dimethylaminomethyl-3-(4-methoxy-phenyl)-cyclohex-2-enone;
- 4-dimethylaminomethyl-3-naphthalen-2-yl-cyclohex-2-
- 10 enone;
- rac-trans-4-dimethylaminomethyl-3-hydroxy-3-naphthalen-2-yl-cyclohexanone;
- 15 • rac-trans-4-dimethylaminomethyl-3-(3-fluoro-phenyl)-cyclohexanone;
- rac-cis-4-dimethylaminomethyl-3-(3-fluoro-phenyl)-cyclohexanone;
- 20 • rac-cis-4-dimethylaminomethyl-3-hydroxy-3-(2-methoxy-phenyl)-cyclohexanone
- rac-cis-4-dimethylaminomethyl-3-hydroxy-3-(6-methoxy-
- 25 naphthalen-2-yl)-cyclohexanone;
- 4-dimethylaminomethyl-3-(6-methoxy-naphthalen-2-yl)-cyclohex-2-enone;
- 30 • rac-cis-3-biphenyl-4-yl-4-dimethylaminomethyl-3-hydroxy-cyclohexanone

- 3-(3-difluoromethyl-phenyl)-4-dimethylaminomethyl-cyclohex-2-enone;
- 5 • 4-dimethylaminomethyl-3-(3-fluoro-phenyl)-cyclohex-2-enone;
- 3-(3,4-difluoro-phenyl)-4-dimethylaminomethyl-cyclohex-2-enone;
- 10 • 4-dimethylaminomethyl-3-(4-fluoro-phenyl)-cyclohex-2-enone;
- 4-dimethylaminomethyl-3-(4-trifluoromethyl-phenyl)-cyclohex-2-enone;
- 15 • 3-(3,5-dichloro-phenyl)-4-dimethylaminomethyl-cyclohex-2-enone;
- 3-(3,5-difluoro-phenyl)-4-dimethylaminomethyl-cyclohex-2-enone;
- 20 • rac-cis-3-(3,5-difluoro-phenyl)-4-dimethylaminomethyl-3-hydroxy-cyclohexanone
- 25 as the free base or in the form of a salt formed with a physiologically tolerated acid, in particular the hydrochloride salt.
- 15. Use of at least one aminomethyl-phenyl-cyclohexanone
- 30 derivative of the general formula I or Ia

**I****Ia**

wherein

5 R^1 and R^2 independently of one another are chosen from R^5 or YR^5 , where $Y = C_1-C_{10}$ -alkyl, C_2-C_{10} -alkenyl or C_2-C_{10} -alkynyl, branched or unbranched and mono- or polysubstituted or unsubstituted, wherein R^5 is chosen from

10

H, F, Cl, Br, I, CN, NO_2 , C_1-C_8 -alkyl, C_2-C_8 -alkenyl or C_2-C_8 -alkynyl, in each case branched or unbranched and mono- or polysubstituted or unsubstituted; C_3-C_7 -cycloalkyl, saturated or unsaturated and mono- or polysubstituted or unsubstituted, or a corresponding heterocyclic radical, in which one C atom in the ring is replaced by S, O or NR^6 , where R^6 is chosen from

15

H, C_1-C_{10} -alkyl, C_2-C_{10} -alkenyl or C_2-C_{10} -alkynyl, in each case branched or unbranched and mono- or polysubstituted or unsubstituted;

20

aryl or heteroaryl, in each case mono- or polysubstituted or unsubstituted;

25

OR^7 , $OC(O)R^7$, $OC(O)OR^7$, $OC(S)R^7$, $C(O)R^7$, $C(O)OR^7$, $C(S)R^7$, $C(S)OR^7$, SR^7 , $S(O)R^7$ or $S(O_2)R^7$, wherein R^7 is chosen from

5 H, C_1 - C_{18} -alkyl, C_2 - C_{18} -alkenyl or C_2 - C_{18} -alkynyl, in each case branched or unbranched and mono- or polysubstituted or unsubstituted; C_3 - C_7 -cycloalkyl, saturated or unsaturated and mono- or polysubstituted or unsubstituted, or a corresponding
10 heterocyclic radical, in which one C atom in the ring is replaced by S, O or NR^8 , where R^8 is chosen from

 H, C_1 - C_{10} -alkyl, C_2 - C_{10} -alkenyl or C_2 - C_{10} -alkynyl, in each case branched or
15 unbranched and mono- or polysubstituted or unsubstituted;
 alkylaryl, saturated or unsaturated and mono- or polysubstituted or unsubstituted;
 aryl or heteroaryl, in each case mono- or
20 polysubstituted or unsubstituted; or

NR^9R^{10} , $C(O)NR^9R^{10}$ or $S(O_2)NR^9R^{10}$, wherein R^9 and R^{10} independently of one another are chosen from

 H, C_1 - C_{18} -alkyl, C_2 - C_{18} -alkenyl or C_2 - C_{18} -alkynyl, in each case branched or unbranched
25 and mono- or polysubstituted or unsubstituted; C_3 - C_7 -cycloalkyl, saturated or unsaturated and mono- or polysubstituted or unsubstituted, or a corresponding
 heterocyclic radical, in which one C atom in the ring is replaced by S, O or NR^{11} , where
30 R^{11} is chosen from

 H, C_1 - C_{10} -alkyl, C_2 - C_{10} -alkenyl or C_2 - C_{10} -alkynyl, in each case branched or

- unbranched and mono- or polysubstituted
or unsubstituted;
alkylaryl, saturated or unsaturated and
mono- or polysubstituted or unsubstituted;
5 aryl or heteroaryl, in each case mono- or
polysubstituted or unsubstituted;
- or
- 10 R^9 and R^{10} together form a C_3 - C_7 -cycloalkyl,
saturated or unsaturated and mono- or
polysubstituted or unsubstituted, or a
corresponding heterocyclic radical, in which
one C atom in the ring is replaced by S, O
15 or NR^{12} , where R^{12} is chosen from
H, C_1 - C_{10} -alkyl, C_2 - C_{10} -alkenyl or C_2 - C_{10} -
alkinyl, in each case branched or
unbranched and mono- or polysubstituted
or unsubstituted;
- 20 or
- R^1 and R^2 together form $-CH=CH-CH=CH-$, wherein the
naphthyl system formed can be mono- or
25 polysubstituted,
- X is chosen from
H, F, Cl, Br, I, CF_3 , $O-S(O_2)-C_6H_4-pCH_3$, OR^{13} or
 $OC(O)R^{13}$, wherein R^{13} is chosen from
30 H; C_1 - C_{10} -alkyl, C_2 - C_{10} -alkenyl or C_2 - C_{10} -
alkinyl, in each case branched or unbranched
and mono- or polysubstituted or
unsubstituted; C_3 - C_7 -cycloalkyl, saturated or
unsaturated and mono- or polysubstituted or

unsubstituted, or a corresponding
heterocyclic radical, in which one C atom in
the ring is replaced by N, S or O;
alkylaryl, saturated or unsaturated and
mono- or polysubstituted or unsubstituted;
aryl or heteroaryl, in each case mono- or
polysubstituted or unsubstituted;

or

if the compound contains no X, according to
formula Ia a double bond is formed between C atom
A and C atom B or C atom B and C atom C;

and

R^3 , R^4 independently of one another are chosen from
H, C_1 - C_{10} -alkyl, C_2 - C_{10} -alkenyl or C_2 - C_{10} -alkinyl,
in each case branched or unbranched and mono- or
polysubstituted or unsubstituted; C_3 - C_7 -
cycloalkyl, saturated or unsaturated and mono- or
polysubstituted or unsubstituted, or a
corresponding heterocyclic radical, in which one
C atom in the ring is replaced by N, S or O;
alkylaryl, saturated or unsaturated and mono- or
polysubstituted or unsubstituted; aryl or
heteroaryl, in each case mono- or polysubstituted
or unsubstituted;

or

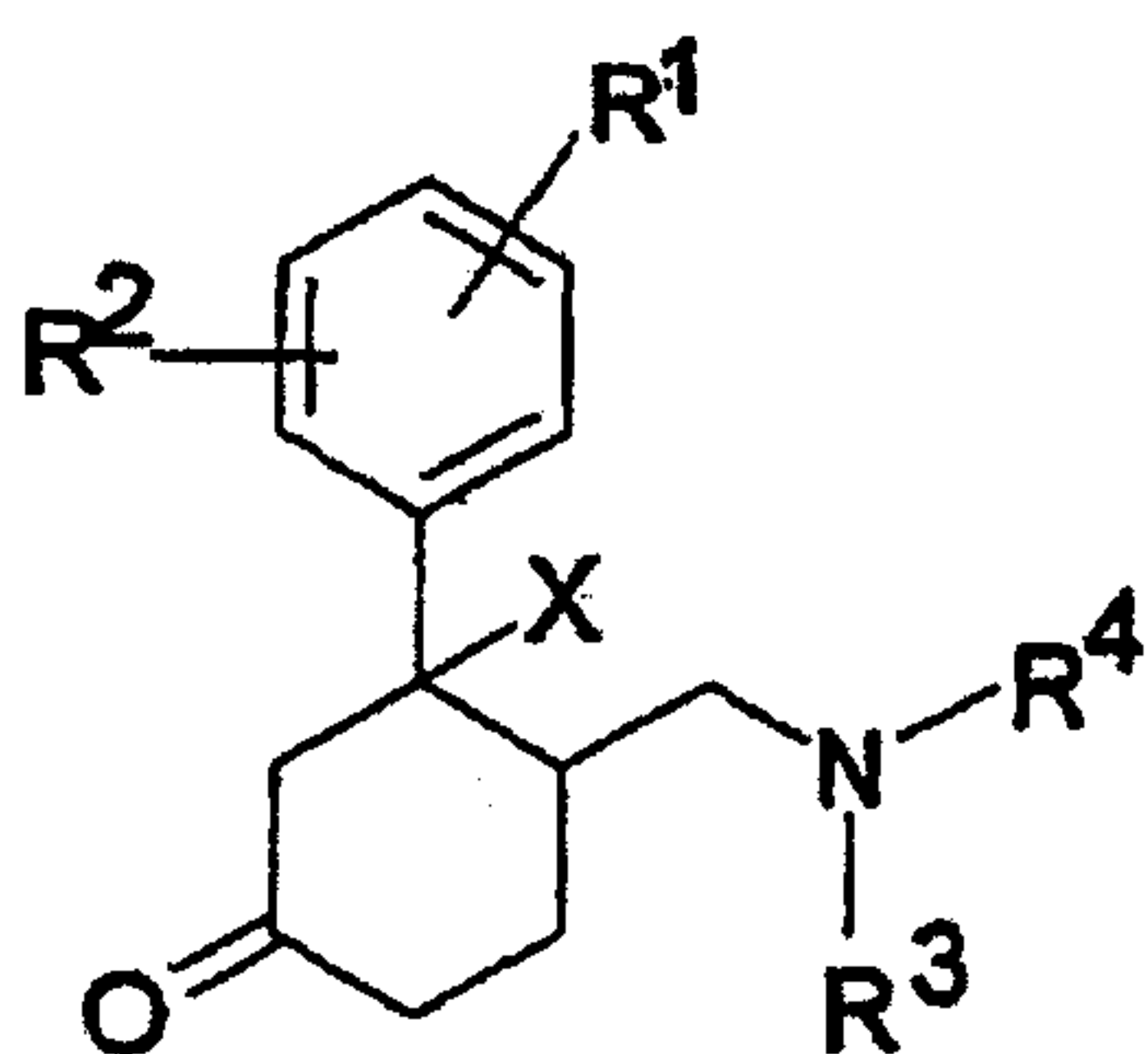
R^3 and R^4 together form a C_3 - C_7 -cycloalkyl, saturated or
unsaturated and mono- or polysubstituted or
unsubstituted, or a corresponding heterocyclic

radical, in which one C atom in the ring is replaced by S, O or NR^{14} , where R^{14} is chosen from

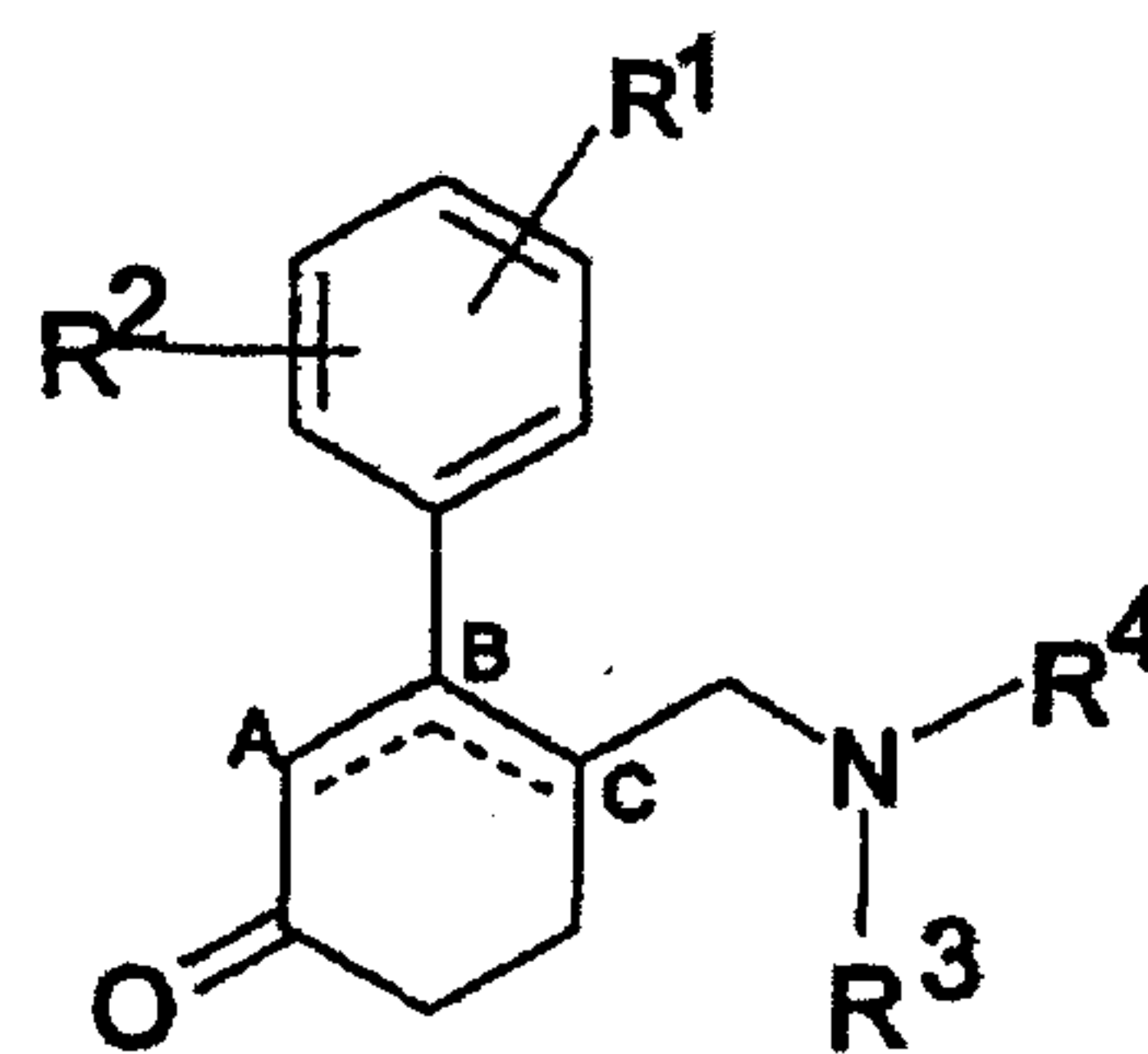
H, $\text{C}_1\text{-C}_{10}$ -alkyl, $\text{C}_2\text{-C}_{10}$ -alkenyl or $\text{C}_2\text{-C}_{10}$ -alkynyl, in each case branched or unbranched and mono- or polysubstituted or unsubstituted;

in the form of its diastereomers or enantiomers and of its free base or of a salt formed with a physiologically tolerated acid, in particular the hydrochloride salt, for the preparation of a medicament for treatment of pain.

16. Use of at least one aminomethyl-phenyl-cyclohexanone derivative of the general formula I or Ia



I



Ia

wherein

R^1 and R^2 independently of one another are chosen from R^5 or YR^5 , where $\text{Y} = \text{C}_1\text{-C}_{10}$ -alkyl, $\text{C}_2\text{-C}_{10}$ -alkenyl or $\text{C}_2\text{-C}_{10}$ -alkynyl, branched or unbranched and mono- or polysubstituted or unsubstituted, wherein R^5 is chosen from

- 5 H, F, Cl, Br, I, CN, NO₂, C₁-C₈-alkyl, C₂-C₈-alkenyl or C₂-C₈-alkinyl, in each case branched or unbranched and mono- or polysubstituted or unsubstituted; C₃-C₇-cycloalkyl, saturated or unsaturated and mono- or polysubstituted or unsubstituted, or a corresponding heterocyclic radical, in which one C atom in the ring is replaced by S, O or NR⁶, where R⁶ is chosen from
- 10 H, C₁-C₁₀-alkyl, C₂-C₁₀-alkenyl or C₂-C₁₀-alkinyl, in each case branched or unbranched and mono- or polysubstituted or unsubstituted;
- 15 aryl or heteroaryl, in each case mono- or polysubstituted or unsubstituted;
- OR⁷, OC(O)R⁷, OC(O)OR⁷, OC(S)R⁷, C(O)R⁷, C(O)OR⁷, C(S)R⁷, C(S)OR⁷, SR⁷, S(O)R⁷ or S(O₂)R⁷, wherein R⁷ is chosen from
- 20 H, C₁-C₁₈-alkyl, C₂-C₁₈-alkenyl or C₂-C₁₈-alkinyl, in each case branched or unbranched and mono- or polysubstituted or unsubstituted; C₃-C₇-cycloalkyl, saturated or unsaturated and mono- or polysubstituted or unsubstituted, or a corresponding
- 25 heterocyclic radical, in which one C atom in the ring is replaced by S, O or NR⁸, where R⁸ is chosen from
- 30 H, C₁-C₁₀-alkyl, C₂-C₁₀-alkenyl or C₂-C₁₀-alkinyl, in each case branched or unbranched and mono- or polysubstituted or unsubstituted;
- alkylaryl, saturated or unsaturated and mono- or polysubstituted or unsubstituted;

aryl or heteroaryl, in each case mono- or polysubstituted or unsubstituted; or

5 NR^9R^{10} , $\text{C}(\text{O})\text{NR}^9\text{R}^{10}$ or $\text{S}(\text{O}_2)\text{NR}^9\text{R}^{10}$, wherein R^9 and R^{10} independently of one another are chosen from

10 H, $\text{C}_1\text{-C}_{18}$ -alkyl, $\text{C}_2\text{-C}_{18}$ -alkenyl or $\text{C}_2\text{-C}_{18}$ -alkynyl, in each case branched or unbranched and mono- or polysubstituted or unsubstituted; $\text{C}_3\text{-C}_7$ -cycloalkyl, saturated or unsaturated and mono- or polysubstituted or unsubstituted, or a corresponding heterocyclic radical, in which one C atom in the ring is replaced by S, O or NR^{11} , where R^{11} is chosen from

15 H, $\text{C}_1\text{-C}_{10}$ -alkyl, $\text{C}_2\text{-C}_{10}$ -alkenyl or $\text{C}_2\text{-C}_{10}$ -alkynyl, in each case branched or unbranched and mono- or polysubstituted or unsubstituted;

20 alkylaryl, saturated or unsaturated and mono- or polysubstituted or unsubstituted; aryl or heteroaryl, in each case mono- or polysubstituted or unsubstituted;

or

25

R^9 and R^{10} together form a $\text{C}_3\text{-C}_7$ -cycloalkyl, saturated or unsaturated and mono- or polysubstituted or unsubstituted, or a corresponding heterocyclic radical, in which one C atom in the ring is replaced by S, O or NR^{12} , where R^{12} is chosen from

30

H, $\text{C}_1\text{-C}_{10}$ -alkyl, $\text{C}_2\text{-C}_{10}$ -alkenyl or $\text{C}_2\text{-C}_{10}$ -alkynyl, in each case branched or

unbranched and mono- or polysubstituted
or unsubstituted;

or

5 R^1 and R^2 together form $-\text{CH}=\text{CH}-\text{CH}=\text{CH}-$, wherein the
naphthyl system formed can be mono- or
polysubstituted,

X is chosen from

10 H, F, Cl, Br, I, CF_3 , $\text{O}-\text{S}(\text{O}_2)-\text{C}_6\text{H}_4-\text{pCH}_3$, OR^{13} or
 $\text{OC}(\text{O})\text{R}^{13}$, wherein R^{13} is chosen from

H; C_1-C_{10} -alkyl, C_2-C_{10} -alkenyl or C_2-C_{10} -
alkynyl, in each case branched or unbranched
and mono- or polysubstituted or
15 unsubstituted; C_3-C_7 -cycloalkyl, saturated or
unsaturated and mono- or polysubstituted or
unsubstituted, or a corresponding
heterocyclic radical, in which one C atom in
the ring is replaced by N, S or O;
20 alkylaryl, saturated or unsaturated and
mono- or polysubstituted or unsubstituted;
aryl or heteroaryl, in each case mono- or
polysubstituted or unsubstituted;

25 or

if the compound contains no X, according to
formula Ia a double bond is formed between C atom
A and C atom B or C atom B and C atom C;

30

and

R^3 , R^4 independently of one another are chosen from

5 H, C₁-C₁₀-alkyl, C₂-C₁₀-alkenyl or C₂-C₁₀-alkinyl,
in each case branched or unbranched and mono- or
polysubstituted or unsubstituted; C₃-C₇-
cycloalkyl, saturated or unsaturated and mono- or
polysubstituted or unsubstituted, or a
corresponding heterocyclic radical, in which one
C atom in the ring is replaced by N, S or O;
alkylaryl, saturated or unsaturated and mono- or
polysubstituted or unsubstituted; aryl or
10 heteroaryl, in each case mono- or polysubstituted
or unsubstituted;

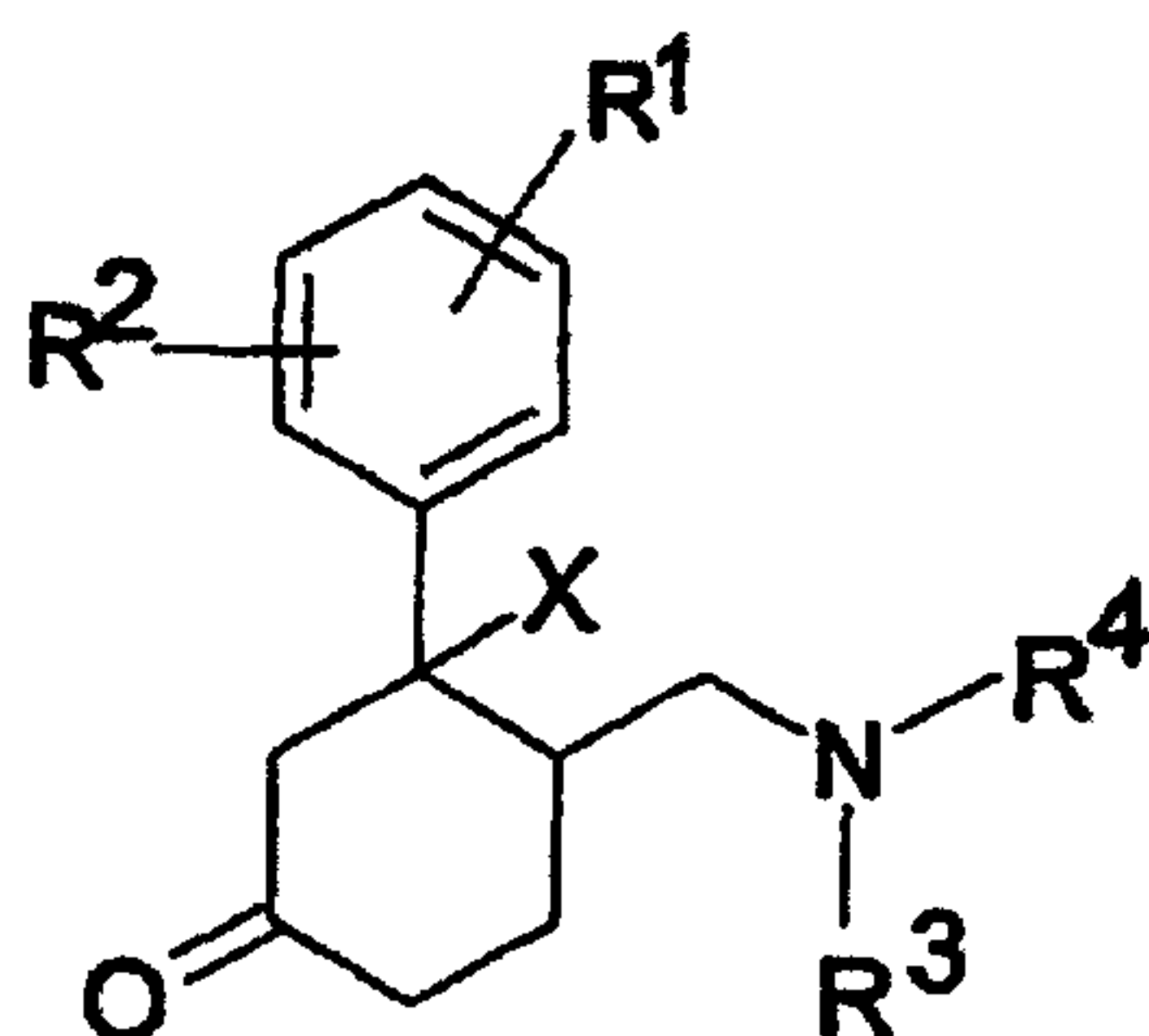
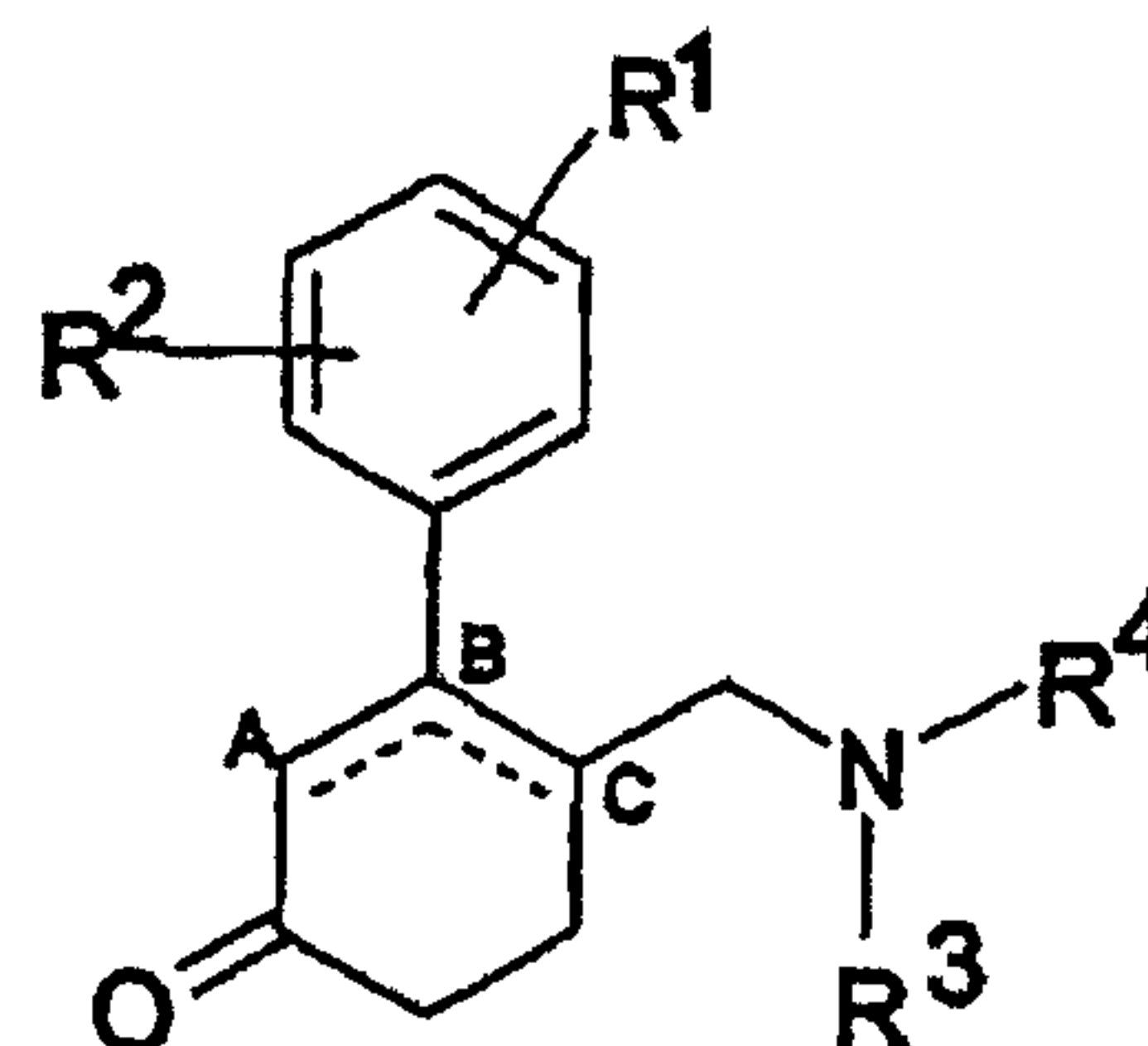
or

15 R³ and R⁴ together form a C₃-C₇-cycloalkyl, saturated or
unsaturated and mono- or polysubstituted or
unsubstituted, or a corresponding heterocyclic
radical, in which one C atom in the ring is replaced
by S, O or NR¹⁴, where R¹⁴ is chosen from

20 H, C₁-C₁₀-alkyl, C₂-C₁₀-alkenyl or C₂-C₁₀-
alkinyl, in each case branched or unbranched
and mono- or polysubstituted or
unsubstituted;

25 in the form of its diastereomers or enantiomers and of
its free base or of a salt formed with a
physiologically tolerated acid, in particular the
hydrochloride salt, for the preparation of a
medicament for treatment of inflammatory and allergic
30 reactions, depressions, drug and/or alcohol abuse,
gastritis, cardiovascular diseases, respiratory tract
diseases, coughing, mental illnesses and/or epilepsy,
and in particular urinary incontinence, itching and/or
diarrhoea.

17. Use according to one of claims 15 or 16, characterized in that, independently of one another, in the general formulae I and Ia

**I****Ia**

5

$R^1 = R^5$, wherein R^5 is chosen from

H, F, Cl, Br, I, CHF_2 , CF_3 , NO_2 , NH_2 ; C_1 - C_4 -alkyl or C_2 - C_4 -alkenyl, branched or unbranched and mono- or polysubstituted or unsubstituted; aryl, substituted or unsubstituted; OR^7 , $\text{C}(\text{O})\text{OR}^7$ or SR^7 , wherein R^7 is chosen from

10

H; C_1 - C_4 -alkyl, branched or unbranched and mono- or polysubstituted or unsubstituted; preferably H, CF_3 or CH_3 ,

15

or $\text{S}(\text{O}_2)\text{NR}^9\text{R}^{10}$, wherein R^9 and R^{10} independently of one another are chosen from

H; C_1 - C_4 -alkyl, branched or unbranched and mono- or polysubstituted or unsubstituted; wherein particularly preferably $R^1 = R^5$, where R^5 is chosen from

20

H, F, Cl, OH, CH_3 , C_2H_5 , C_2H_3 , CHF_2 , CF_3 , SCH_3 , OCF_3 , OCH_3 , OC_2H_5 , $\text{C}(\text{O})\text{OCH}_3$, $\text{C}(\text{O})\text{OC}_2\text{H}_5$ or phenyl,

25

and/or $R^2 = R^5$, wherein R^5 is chosen from

H, F, Cl, Br, I, SCH₃; C₁-C₄-alkyl, C₂-C₄-alkenyl, branched or unbranched and mono- or polysubstituted or unsubstituted, preferably CF₃; OR⁷, where R⁷ is chosen from C₁-C₄-alkyl, branched or unbranched and mono- or polysubstituted or unsubstituted, preferably CH₃;

and/or R¹ and R² have different meanings or R¹ and R² together form -CH=CH-CH=CH-, wherein the naphthyl system formed can be mono- or polysubstituted, preferably by halogen, OC₁₋₃-alkyl or C₁₋₃-alkyl, unsubstituted or mono or polysubstituted, in particular by OCH₃,

and/or X is chosen from

H, F, Cl, OH, CF₃, O-S(O₂)-C₆H₄-pCH₃ or OC(O)R⁷, where R⁷ = H; C₁-C₄-alkyl or C₂-C₄-alkenyl, branched or unbranched and mono- or polysubstituted or unsubstituted, preferably H, F, Cl, OH, O-S(O₂)-C₆H₄-pCH₃ or OC(O)R⁷, where R⁷ = C₁-C₄-alkyl, preferably CH₃, in particular H or OH;

or

if the compound contains no X, according to formula Ia a double bond is formed between C atom A and C atom B or C atom B and C atom C,

and/or R³ and R⁴ independently of one another are chosen from

C₁-C₄-alkyl, branched or unbranched and mono- or polysubstituted or unsubstituted, preferably CH₃;

or

5 R³ and R⁴ together form a C₃-C₇-cycloalkyl,
saturated or unsaturated and mono- or
polysubstituted or unsubstituted,

and/or R¹, R², X, R³ and/or R⁴ have one of the meanings
mentioned in the preceding claims.

10

18. Use according to one of claims 15 or 16, characterized
in that at least one aminomethyl-phenyl-cyclohexanone
derivative chosen from the group consisting of

15

- *rac-cis*-[4-dimethylaminomethyl-3-hydroxy-3-(3-methoxy-phenyl)-cyclohexanone],

- *rac-cis*-[4-dimethylaminomethyl-3-(3-methoxy-phenyl)-cyclohexanone],

20

- *rac-trans*-[4-dimethylaminomethyl-3-(3-methoxy-phenyl)-cyclohexanone],

- *rac-cis*-[4-dimethylaminomethyl-3-(3-hydroxy-phenyl)-cyclohexanone],

- *rac-trans*-[4-dimethylaminomethyl-3-(3-hydroxy-phenyl)-cyclohexanone] or

25

- 4-dimethylaminomethyl-3-(3-methoxy-phenyl)-cyclohex-2-enone

- 4-dimethylaminomethyl-3-phenyl-cyclohex-2-enone;

30

- 4-dimethylaminomethyl-3-(3-hydroxy-phenyl)-cyclohex-2-enone;

- rac-trans-4-dimethylaminomethyl-3-phenyl-cyclohexanone;
- rac-cis-4-dimethylaminomethyl-3-phenyl-cyclohexanone;
- 5 • 4-dimethylaminomethyl-3-(4-methoxy-phenyl)-cyclohex-2-enone;
- 4-dimethylaminomethyl-3-naphthalen-2-yl-cyclohex-2-
- 10 enone;
- rac-trans-4-dimethylaminomethyl-3-hydroxy-3-naphthalen-2-yl-cyclohexanone;
- 15 • rac-trans-4-dimethylaminomethyl-3-(3-fluoro-phenyl)-cyclohexanone;
- rac-cis-4-dimethylaminomethyl-3-(3-fluoro-phenyl)-cyclohexanone;
- 20 • rac-cis-4-dimethylaminomethyl-3-hydroxy-3-(2-methoxy-phenyl)-cyclohexanone
- rac-cis-4-dimethylaminomethyl-3-hydroxy-3-(6-methoxy-
- 25 naphthalen-2-yl)-cyclohexanone;
- 4-dimethylaminomethyl-3-(6-methoxy-naphthalen-2-yl)-cyclohex-2-enone;
- 30 • rac-cis-3-biphenyl-4-yl-4-dimethylaminomethyl-3-hydroxy-cyclohexanone

- 3-(3-difluoromethyl-phenyl)-4-dimethylaminomethyl-cyclohex-2-enone;
- 5 • 4-dimethylaminomethyl-3-(3-fluoro-phenyl)-cyclohex-2-enone;
- 3-(3,4-difluoro-phenyl)-4-dimethylaminomethyl-cyclohex-2-enone;
- 10 • 4-dimethylaminomethyl-3-(4-fluoro-phenyl)-cyclohex-2-enone;
- 4-dimethylaminomethyl-3-(4-trifluoromethyl-phenyl)-cyclohex-2-enone;
- 15 • 3-(3,5-dichloro-phenyl)-4-dimethylaminomethyl-cyclohex-2-enone;
- 3-(3,5-difluoro-phenyl)-4-dimethylaminomethyl-cyclohex-2-enone;
- 20 • rac-cis-3-(3,5-difluoro-phenyl)-4-dimethylaminomethyl-3-hydroxy-cyclohexanone
- 25 as the free base or in the form of a salt formed with a physiologically tolerated acid, in particular the hydrochloride salt, is used as the active compound.