

example, pent-2-en-1-yl) or hexenyl (for example, hex-2-en-1-yl). Alkynyl is preferably straight-chain and, particularly preferably, propargyl, but may also be, for example ethynyl, prop-1-yn-1-yl, butynyl (for example, but-2-yn-1-yl), pentynyl (for example, pent-2-yn-1-yl) or hexynyl (for example, hex-2-yn-1-yl). Alkoxy-alkyl is also preferably straight-chain and is preferably alkoxyethyl (wherein the alkoxy group has 1—4 C atoms), in particular 2-methoxyethyl, 2-ethoxyethyl, 2-propoxyethyl or 2-isopropoxyethyl, and also, for example, alkoxypropyl, for example 2- or 3-methoxypropyl; alkoxybutyl, for example 2-, 3- or 4-methoxybutyl; or alkoxypropyl, for example, 5-methoxypentyl. Alkenyloxyalkyl is preferably 2-alkenyloxyethyl, in particular 2-allyloxyethyl, and also 2-vinyloxyethyl or 2-propenyloxyethyl, and also, for example, alkenyloxypropyl, such as 2- or 3-allyloxypropyl. Cycloalkyl is preferably cyclopentyl or cyclohexyl, but may also be, for example, cyclopropyl, cyclobutyl, 1-, 2- or 3-methylcyclopentyl, 1-, 2-, 3- or 4-methylcyclohexyl, cycloheptyl or cyclooctyl.

If the R^2 radical is alkyl, it is preferably branched alkyl, in particular with 3 or 4 C atoms, such as isopropyl, isobutyl or tert-butyl, but it may also be, for example, methyl, ethyl, n-propyl, n-butyl, sec-butyl, pentyl, such as 1-, 2- or 3-pentyl, isopentyl, neopentyl, tert-pentyl, hexyl, such as 1-, 2- or 3-hexyl, or isohexyl. Hydroxy-alkyl may, for example, be: hydroxymethyl, 1- or 2-hydroxyethyl, 1-, 2- or 3-hydroxypropyl, 1-hydroxy-1-methylethyl, 1-methyl-2-hydroxyethyl, 1-, 2-, 3- or 4-hydroxybutyl, 5-hydroxypentyl or 6-hydroxyhexyl. If R^2 is cycloalkyl, it is preferably one of the cycloalkyl radicals mentioned above. Aralkyl has 7—15, preferably 7—11, C atoms and is preferably 2-phenylethyl, and may also be, for example, benzyl, 1-phenylethyl, 1-methyl-2-phenylethyl, 1,1-dimethyl-2-phenylethyl, 2-methyl-2-phenylethyl, 2,2-dimethyl-2-phenylethyl, 1,2-dimethyl-2-phenylethyl, 1-, 2- or 3-phenylpropyl, 1-methyl-3-phenylpropyl, 1-, 2-, 3- or 4-phenylbutyl, 1- or 2-naphthylmethyl, 2-(1-naphthyl)ethyl or 2-(2-naphthyl)-ethyl.

If R^2 is an aralkyl group, the aryl radical in this group can be mono- to tri-substituted by alkyl, alkoxy, OH, F and/or Cl or mono-substituted by methylenedioxy. If alkyl or alkoxy groups are substituted in the aryl radical, these have 1—8, preferably 1—4, C atoms; however, the substituted aralkyl radical may contain a total of not more than 15 C atoms. The substituted aralkyl radical preferably has a total of 7—11 C atoms. Suitable alkyl groups are, for example, methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, sec-butyl, tert-butyl, n-pentyl, isopentyl, n-hexyl, n-heptyl or n-octyl, and suitable alkoxy groups are, for example, methoxy, ethoxy, n-propoxy, isopropoxy, n-butoxy, isobutoxy, sec-butoxy, tert-butoxy, n-pentyloxy, isopentyloxy, n-hexyloxy, n-heptyloxy or n-octyloxy. Preferred substituted aryl radicals are, in particular, alkoxyphenyl, such as o-, m- or p-methoxyphenyl or o-, m- or p-ethoxyphenyl, dialkoxyphenyl, such as 2,3-, 2,4-, 2,5-, 2,6-, 3,5- or, particularly preferably, 3,4-dimethoxyphenyl, trialkoxyphenyl, such as 3,4,5-trimethoxyphenyl, methylenedioxyphenyl, such as 3,4-methylenedioxyphenyl, and also, for example, alkylphenyl, such as o-, m- or p-tolyl, o-, m- or p-ethylphenyl, o-, m- or p-isopropylphenyl or o-, m- or p-tert-butylphenyl, dialkylphenyl, such as 2,3-, 2,4-, 2,5-, 2,6-, 3,4- or 3,5-dimethylphenyl, trialkylphenyl, such as 2,4,6-trimethylphenyl or 2,6-dimethyl-4-tert-butylphenyl, o-, m- or p-hydroxyphenyl, dihydroxyphenyl, such as 3,4-dihydroxyphenyl, o-, m- or p-fluorophenyl or o-, m- or p-chlorophenyl. The aryl radicals can also carry two different substituents; examples of such radicals are 3-methoxy-4-hydroxyphenyl and 3-hydroxy-4-methoxyphenyl. 2-(3,4-Dimethoxyphenyl)-ethyl is a particularly preferred substituted aralkyl radical. Further particularly preferred substituted aralkyl radicals are, for example, 2-(p-methoxyphenyl)-ethyl, 2-(3,4,5-trimethoxyphenyl)-ethyl and 2-(3,4-methylenedioxyphenyl)-ethyl.

Preferred compounds according to the invention are compounds of formula I in which at least one of the R^1 and R^2 radicals has one of the preferred meanings indicated above.

Some preferred groups of compounds can be expressed by the following partial formulae Ia to Ip which correspond to formula I and wherein the radicals not described in more detail have the meanings indicated for formula I, but wherein

- in Ia, R^1 is alkenyl or alkynyl with 2—6 C atoms in each case;
- in Ib, R^1 is alkoxyalkyl with 2—6 C atoms or alkenyloxyalkyl with 3—6 C atoms;
- in Ic, R^1 is cycloalkyl with 3—8 C atoms;
- in Id, R^1 is allyl, propargyl, 2-alkoxyethyl with 3—5 C atoms, 2-allyloxyethyl or cyclopentyl;
- in Ie, R^1 is alkyl or hydroxyalkyl with 1—6 C atoms in each case or cycloalkyl with 3—8 C atoms;
- in If, R^2 is unsubstituted aralkyl or aralkyl which, in the aryl radical, is mono-

to tri-substituted by alkyl, alkoxy, OH, F and/or Cl or mono-substituted by methylenedioxy, with a total of 7—15 C atoms in each case;

in Ig, R² is isopropyl, tert.-butyl, 2-phenylethyl, 1,1-dimethyl-2-phenylethyl or 2-(3,4-dimethoxyphenyl)-ethyl;

in Ih, R² is isopropyl or tert.-butyl;

in Ii, R² is 2-phenylethyl or 2-(3,4-dimethoxyphenyl)-ethyl;

in Ij, R¹ is alkenyl or alkynyl with 2—6 C atoms in each case and R² is alkyl with 1—6 C atoms, phenylalkyl with 7—10 C atoms or phenylalkyl which, in the aryl radical, is mono- to tri-substituted by methoxy or mono-substituted by methylenedioxy, with a total of 9—13 C atoms;

in Ik, R¹ is allyl, propargyl, 2-alkoxyethyl with 3—5 C atoms, 2-allyloxyethyl or 2-cyclopentyl and R² is isopropyl, tert.-butyl, 2-phenylethyl, 1,1-dimethyl-2-phenylethyl or 2-(3,4-dimethoxyphenyl)-ethyl;

In Il, R¹ is allyl or propargyl and R² is isopropyl, tert.-butyl, 2-phenylethyl, 1,1-dimethyl-2-phenylethyl or 2-(3,4-dimethoxyphenyl)-ethyl;

in Im, R¹ is allyl or propargyl and R² is 2-(3,4-dimethoxyphenyl)-ethyl;

in In, R¹ is alkoxyalkyl with 2—6 C atoms, alkenyloxyalkyl with 3—6 C atoms or cycloalkyl with 3—8 C atoms and R² is alkyl with 1—6 C atoms, phenylalkyl with 7—10 C atoms or phenylalkyl which, in the aryl radical, is mono- to tri-substituted by methoxy or mono-substituted by methylene dioxy, with a total of 9—13 C atoms;

in Io, R¹ is 2-alkoxyethyl with 3—5 C atoms, 2-allyloxyethyl or cyclopentyl and R² is isopropyl, tert.-butyl, 2-phenylethyl, 1,1-dimethyl-2-phenylethyl or 2-(3,4-dimethoxyphenyl)-ethyl; and

in Ip, R¹ is 2-alkoxyethyl with 3—5 C atoms or 2-allyloxyethyl and R² is isopropyl or tert.-butyl.

The compounds of formula I have at least one asymmetric carbon atom and can contain further asymmetric carbon atoms in the R¹ and R² substituents. They can thus exist in the racemic or the optically active form. In general, they are obtained by synthesis as racemates, in the synthesis.

The present invention also comprises a process for the preparation of a phenoxy-amino-propanol of formula I, or a physiologically acceptable acid addition salt thereof, which comprises:

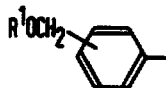
(i) reacting a compound of formula II:



with a compound of formula III:



wherein Ar is the group



one of the radicals Y and Z is NH₂, and the other is X, Q is OH or, together with X, an oxygen atom, X is Hal, OH, a functionally modified OH group or (in II), together with Q, an oxygen atom, and Hal is Cl, Br or I, and R¹ and R² have the above-stated meanings, or

(ii) reacting a phenol of formula IV:



wherein Ar has the above-stated meaning, with an amino-alcohol of formula V:



wherein R² and X have the above-stated meanings, or

(iii) reducing a compound of formula VI:



wherein W is a radical which can be reduced to the group —CHOH—CH₂—NHR² and Ar and R² have the above-stated meanings, or

(iv) treating a compound corresponding to formula I but which additionally

contains one or more groups which can be split off solvolytically or hydrogenolytically instead of one or more H atoms, with a solvolysing or hydrogenlysing agent.

A base of formula I obtained by any of the foregoing processes may, if desired, be converted into a physiologically acceptable acid addition salt thereof by treatment with an acid.

The radical X can be present in the starting materials of formulae II, III and V. This radical is preferably Cl or Br, and may also be I, OH or a functionally modified OH group. Suitable functionally modified OH groups are, in particular, reactive esterified OH groups, for example, alkylsulphonyloxy with preferably 1—6 C atoms, such as methanesulphonyloxy, or arylsulphonyloxy with preferably 6—10 C atoms, such as benzenesulphonyloxy, p-toluenesulphonyloxy or 1- or 2-naphthalene-sulphonyloxy.

The reactions forming the basis of the above-described methods for the preparation of the compounds of formula I are known in themselves and are described in the literature (for example in the standard works, such as Houben-Weyl, *Methoden der Organischen Chemie*, Georg-Thieme-Verlag, Stuttgart; and *Organic Reactions*, John Wiley and Sons, Inc., New York) and are preferably carried out under the conditions which are known to be suitable for the reactions in question. Use can also be made of known variants of such reactions which are not mentioned in more detail here.

Some of the starting materials for the preparation of the compounds of formula I are known and some are new. The new starting materials can be prepared by reactions which are known in themselves, in general analogously to the known starting materials.

If desired, the starting materials can also be formed *in situ* and are not isolated from the reaction mixture, but are immediately reacted further to give the compounds of formula I.

In the following text, the R¹, R², Ar, Hal, Q, W, X, Y and Z radicals have the meanings indicated for formula I to VI, unless something else is expressly indicated.

Most of the starting materials of formula II are new. They can be obtained, for example, by reacting phenols of the formula Ar—OH (IV) with compounds of the formula X—CH₂—CHQ—CH₂Y (for example, epichlorohydrin or epibromohydrin). Primary amines of formula II (Y=NH₂) can be prepared, for example, by reacting epoxides of formula II (Q and Y together forming an oxygen atom) with ammonia or with benzylamine and subsequently removing the benzyl group hydrogenolytically. Most of the starting materials of formula III are known. The amines of formula III (Z=NH₂) can be obtained from the corresponding halogen compounds of formula III (Z=Hal) by reaction with ammonia or by reaction with benzylamine and subsequent hydrogenolytic splitting-off of the benzyl group. Compounds of formulae II and III in which the radicals Y or Z are functionally modified OH groups can be obtained by functional modification of the corresponding alcohols, for example by reaction with alkyl- or arylsulphonyl halides in the presence of pyridine.

Most of the phenols of formula IV are new. They can be obtained by reacting o-, m- or p-hydroxybenzyl alcohol with compounds of the formula R¹—X, preferably by etherification with the corresponding alcohols of the formula R¹—OH, most of which are known. Aminoalcohols of formula V can be prepared, for example, by reacting compounds of the formula X—CH₂—CHQ—CH₂Y (preferably epoxides, such as epichlorohydrin) with amines of formula III (Z=NH₂).

In the starting materials of formula VI, the W substituent is a radical which can be reduced to the group —CHOH—CH₂—NHR², preferably one of the groups CO—CH₂—NHR² (=W¹), —CHOH—CH=NR² (=W²), —CHOH—CH₂—N=R² (=W³; the R² radical is an alkylidene, hydroxyalkylidene or cycloalkylidene group or an aralkylidene group which is unsubstituted or substituted as indicated in the definition of R², corresponding to the R² radical) or —CHOH—CH₂—NH—R⁴ (=W⁴; R⁴ is a radical which can be reduced to the R² group, for example a radical corresponding to the R² group, but which contains an additional C—C bond or an oxygen atom instead of two hydrogen atoms, for example alkanoyl, oxoalkyl, alkenyl, hydroxyalkanoyl or hydroxyalkenyl with up to 6 C atoms in each case, oxocycloalkyl or cycloalkenyl with 3—8 C atoms or aryl-alkanoyl, aryl-oxoalkyl or arylalkenyl, unsubstituted or substituted as indicated in the definition of the R² radical, with a total of 7—15 C atoms in each case).

The compounds of formula VI can be obtained, for example, by reacting the phenols of formula IV with compounds of the formula X—CH₂—W. The starting materials of formula VI (W=W¹) can also be obtained by reacting compounds of the formula Ar—O—CH₂—CO—CH₂—X with amines of the formula R²—NH₂; the compound of formula VI (W=W²) can be obtained by reacting aldehydes of the

formula $\text{Ar}-\text{O}-\text{CH}_2-\text{CHOH}-\text{CHO}$ with amines of the formula R^2-NH_2 ; the compounds of formula VI ($\text{W}=\text{W}'$) can be obtained by reacting amines of the formula $\text{Ar}-\text{O}-\text{CH}_2-\text{CHOH}-\text{CH}_2\text{NH}_2$ with aldehydes of the formula $\text{R}^3=\text{O}$; and the compounds of formula VI ($\text{W}=\text{W}'$) can be obtained by reacting compounds of the formula $\text{Ar}-\text{O}-\text{CH}_2-\text{CHOH}-\text{CH}_2-\text{X}$ with amines of the formula R^4-NH_2 .

The compounds of formula I are preferably prepared by reacting a compound of formula II with a compound of formula III. On the one hand, an epoxide of formula II (Q and Y together forming an oxygen atom), a halogeno-alcohol of formula II ($\text{Q}=\text{OH}$, $\text{Y}=\text{Hal}$) or a diol or a functional derivative thereof of formula II ($\text{Q}=\text{OH}$, $\text{Y}=\text{OH}$ or functionally modified OH) can be reacted with an amine of formula III ($\text{Z}=\text{NH}_2$); on the other hand, an amine of formula II ($\text{Q}=\text{OH}$, $\text{Y}=\text{NH}_2$) can be reacted with a compound of formula III ($\text{Z}=\text{X}$). The reaction of the epoxides mentioned with amines of the formula R^2-NH_2 is preferred.

The reaction of compounds of formula II with compounds of formula III may be carried out in the presence or absence of an inert solvent at a temperature of from 0° to 200°C , preferably from 20° to 120°C . Suitable inert solvents are those which are known, from the literature, for amination reactions of this type, for example, water; alcohols, such as methanol, ethanol, isopropanol or n-butanol; ethers, such as diethyl ether, diisopropyl ether, tetrahydrofuran (THF) or dioxan; hydrocarbons, such as benzene, toluene or xylene; halogenated hydrocarbons, such as dichloromethane, chloroform or trichloroethylene; nitriles, such as acetonitrile; amides, such as dimethylformamide (DMF); or sulphoxides, such as dimethylsulphoxide (DMSO). Mixtures of two or more of these solvents can also be used. The amines are preferably used in a molar ratio of at least 1:1 or in excess; if they are used in excess, they can simultaneously serve as the solvent. A further base, for example an inorganic base, such as sodium or potassium hydroxide, sodium carbonate, potassium carbonate, sodium bicarbonate or potassium bicarbonate can also be added to the reaction mixture. If starting compounds which have a structure such that one mol of acid is split off during the reaction (for example of a halohydrin is used, so that hydrogen halide is split off), it is preferable to use either an additional base or an excess of the amine.

If X is an OH group or an alkyl- or arylsulphonyloxy group, it may also be preferable to add an acid catalyst, for example an inorganic acid (such as sulphuric acid, polyphosphoric acid, hydrobromic acid or hydrochloric acid) and/or an organic acid (such as formic, acetic, propionic or p-toluenesulphonic acid). An excess of the acid can also simultaneously serve as the solvent.

The reaction times required are from 10 minutes to 7 days, depending on the starting materials used and the reaction temperature. The reaction can also be carried out under superatmospheric pressure (up to about 200 atmospheres); the reaction is thereby accelerated.

The compounds of formula I can also be obtained by reacting a phenol of formula IV with an aminoalcohol of formula V. For example, the phenol IV can first be converted into a salt, in particular a metal salt, for example an alkali metal salt (Li, Na or K salt). For this purpose, the phenol can be reacted with a reagent which forms metal salts, for example an alkali metal (for example, Na), an alkali metal hydride or amide (for example, LiH, NaH, NaNH_2 , or KNH_2), an alkali metal alcoholate (wherein the alcohol part preferably has 1-4 C atoms, for example, lithium methylate, ethylate or tert.-butylate, sodium methylate, ethylate or tert.-butylate or potassium methylate, ethylate or tert.-butylate), an organometallic compound (for example, butyllithium, phenyllithium or phenylsodium) or a metal hydroxide, carbonate or bicarbonate (for example of Li, Na, K or Ca). The preparation of the phenolate is advantageously carried out in the presence of a solvent or solvent mixture. Suitable solvents are, for example, hydrocarbons (such as hexane, benzene, toluene or xylene), ethers (such as diethyl ether, diisopropyl ether, THF, dioxan or diethylene glycol dimethyl ether), amides (such as DMF), alcohols (such as methanol or ethanol) or ketones (such as acetone or butanone). The phenol IV or its salt is preferably reacted with the compound V in the presence of a diluent, for example the solvent which has been used for the preparation of the salt, which may, however, be replaced by or diluted with another solvent. In general, the reaction is carried out at a temperature of from -20° to 150°C , preferably from 20° to 120°C .

The phenolate can also be formed *in situ*. In this case, the phenol IV and compound V are allowed to react with one another in the presence of a base. A particularly preferred method is to heat the compounds IV and V together with aqueous alcoholic sodium hydroxide for about 5 to 15 hours.

The compounds of formula I can also be prepared by reducing a compound of formula VI.

Suitable reducing agents are, for example, complex metal hydrides. The compounds of formula VI can also be reduced with catalytically activated or nascent hydrogen.

Amongst the complex metal hydrides, sodium borohydride and lithium aluminium hydride are preferred. The reaction is preferably carried out in a conventional solvent for such reductions, with NaBH_4 , preferably in an alcohol, such as methanol or ethanol, and with LiAlH_4 , preferably in an ether, such as diethyl ether or di-n-butyl ether, THF or ethylene glycol dimethyl ether. Suitable reaction temperatures are, in general, from -80° to 150°C , preferably from 15°C to the boiling point of the solvent used.

Suitable catalysts for catalytic hydrogenation are, for example, nickel and cobalt catalysts, and noble metal and mixed catalysts, such as copper/chromium oxide. Noble metal catalysts can be present on supports (for example, platinum- or palladium-on-charcoal or palladium-on-calcium carbonate or -strontium carbonate), in the form of oxide catalysts (for example, platinum oxide) or as finely divided metal catalysts. Nickel and cobalt catalysts are preferably employed as Raney metals, and nickel also on kieselghur or pumice as the support.

The hydrogenation can be carried out at room temperature and under normal pressure or at elevated temperature and/or under superatmospheric pressure. The reaction is preferably carried out under a pressure of from 1 to 100 atmospheres and at a temperature of from -80° to $+150^\circ\text{C}$, particularly from room temperature to $+100^\circ\text{C}$. The reaction may be carried out under acidic, neutral or alkaline conditions and preferably in the presence of a solvent, such as water, methanol, ethanol, isopropanol, n-butanol, ethyl acetate, dioxan, acetic acid or THF; or a mixture of two or more of these solvents. Raney metals are preferred catalysts for the catalytic hydrogenation of aminoketones of formula VI ($\text{W}=\text{W}^1$).

If nascent hydrogen is used as the reducing agent, it can be produced, for example, by treating metals with acids or bases. Thus, for example, a mixture of zinc and acid or alkali metal hydroxide solution, of iron and hydrochloric acid or acetic acid, or of tin and hydrochloric acid can be used. The use of sodium or another alkali metal in an alcohol, such as ethanol, isopropanol, butanol or amyl or isoamyl alcohol, or phenol is also suitable. An aluminium/nickel alloy in an aqueous alkaline solution, optionally with the addition of ethanol, can also be used. Sodium or aluminium amalgam in an aqueous alcoholic or aqueous solution is also suitable for producing the nascent hydrogen. The reaction can also be carried out in a heterogeneous phase, an aqueous and a benzene or toluene phase preferably being used. Suitable reaction temperatures are, for example, from room temperature to the boiling point of the solvent used.

The phenoxy-amino-propanols of formula I can also be obtained by solvolysis or hydrogenolysis of a compound which corresponds to formula I, but which additionally carries one or more group(s) which can be split off solvolytically or hydrogenolytically instead of one or more H atoms.

Suitable starting materials for this process variant are, in particular, compounds of the formula $\text{Ar}-\text{O}-\text{CH}_2-\text{CHOR}^1-\text{CH}_2-\text{NR}^2\text{R}^3$ (VII), wherein the R^1 radical is H or a hydroxyl protective group and the R^2 radical is H or an amino protective group, provided that the R^1 and R^2 radicals are not simultaneously H, and Ar and R^3 have the above-stated meanings.

The expressions "hydroxyl protective group" and "amino protective group" are generally known and relate to groups which are suitable for protecting (i.e. blocking) a hydroxyl group or an amino group from chemical reactions, but which can be readily removed after the desired chemical reaction at other positions in the molecule has been carried out. Since these protective groups are positioned in this course of this embodiment of the process according to the invention, their nature and size is in other respects not critical. However, R^1 and/or R^2 are preferably acyl with 1-20, in particular 1-8, C atoms (for example, alkanoyl, such as acetyl, aroyl such as benzoyl, aralkanoyl, such as phenylacetyl, alkoxycarbonyl, such as methoxycarbonyl, aralkyloxycarbonyl, such as benzyloxycarbonyl, or arylsulphonyl, such as p-toluene-sulphonyl) or optionally substituted benzyl (for example, benzyl, p-nitrobenzyl or triphenylmethyl).

Solvolysis of these compounds is preferably effected by the action of a solvent such as water (hydrolysis) or an alcohol with preferably 1-4 C atoms (alcoholysis) in the presence of an acidic or basic catalyst, for example a mineral acid, such as sulphuric acid or hydrochloric acid, a metal hydroxide, such as sodium, potassium,

calcium, barium, lead or silver hydroxide, or a metal salt or ammonium salt, such as sodium or potassium carbonate or ammonium chloride. Methanol, ethanol or isopropanol is preferably used as such an alcohol; mixtures of water with one of these alcohols can also be used. Solvolysis is preferably carried out at a temperature of from 0° to 120°C.

Hydrogenolysis can be carried out, for example, under the conditions described above for catalytic hydrogenation, preferably in the presence of a Raney nickel catalyst at a temperature of from 20° to 100°C and under a pressure of from 1 to 10 atmospheres.

A base of formula I obtained by any of the foregoing processes can be converted into an acid addition salt thereof by reaction with the appropriate acid. Suitable acids for this purpose are those which give physiologically acceptable salts. Thus, inorganic acids can be used, for example, sulphuric acid, nitric acid, hydrogen halide acids, such as hydrochloric acid or hydrobromic acid, and phosphoric acid, such as orthophosphoric acid and organic acids, in particular aliphatic, alicyclic, araliphatic, aromatic or heterocyclic monobasic or polybasic carboxylic or sulphonic acids, such as formic acid, acetic acid, propionic acid, pivalic acid, diethylacetic acid, malonic acid, succinic acid, pimelic acid, fumaric acid, maleic acid, lactic acid, tartaric acid, malic acid, benzoic acid, salicylic acid, 2-phenyl-propionic acid, citric acid, gluconic acid, ascorbic acid, nicotinic acid, isonicotinic acid, methane- or ethane-sulphonic acid, ethane-disulphonic acid, 2-hydroxyethanesulphonic acid, benzenesulphonic acid, p-toluenesulphonic acid and naphthalene-mono- and di-sulphonic acids. If desired, a free base of formula I can be liberated from a salt thereof by treating the latter with a strong base, such as sodium or potassium hydroxide or sodium or potassium carbonate.

The compounds of formula I are usually obtained in the racemic form. If the compounds have two or more centres of asymmetry, they are generally obtained as mixtures of racemates, from which the individual racemates can be isolated and obtained in the pure form, for example by recrystallising several times from suitable solvents.

Racemates can be mechanically or chemically resolved into their optical antipodes by known methods. Diastereomers are preferably formed from the racemic mixture by reaction with an optically active resolving agent. Suitable resolving agents are, for example, optically active acids, such as the D- and L-forms of tartaric acid, dibenzoyl tartaric acid, diacetyl tartaric acid, β -camphorsulphonic acid, mandelic acid, malic acid, or lactic acid.

It is possible to obtain optically active compounds by the methods described above by using starting materials which are already optically active.

The compounds of formula I and their physiologically acceptable salts can be used in human or veterinary medicine in admixture with suitable inert, physiologically acceptable carriers or excipients. Suitable carriers are organic or inorganic substances which are suitable for enteral (for example, oral) or parenteral administration or topical application and do not react with the new compounds, for example water, vegetable oils, benzyl alcohol, polyethylene glycols, glycerol triacetate, gelatin, carbohydrates, such as lactose or starch, magnesium stearate, talc or petroleum jelly. Compositions in the form of tablets, dragees, capsules, syrups, elixirs or drops are, for example, suitable for oral administration, compositions in the form of suppositories are used for rectal administration, compositions in the form of solutions, preferably oily or aqueous solutions, and suspensions, emulsions or implantates are used for parenteral administration, and compositions in the form of ointments, creams or powders are used for topical application. The new compounds can also be lyophilised and the resulting lyophilisates can be used, for example, for the preparation of injection formulations. Such compositions may be sterilised and/or contain adjuvants, such as lubricants, preservatives, stabilisers and/or wetting agents, emulsifiers, salts for influencing the osmotic pressure, buffers, dyestuffs, flavouring agents and/or aroma substances. If desired, they can also contain one or more further active compounds, for example one or more vitamins.

The compounds according to the invention are, in general, administered analogously to known, commercially available cardiac and circulatory formulations, in particular β -receptor blockers. The daily dosage is preferably from 0.01 and 4 mg/kg of body weight. However, the preferred dose for any particular patient depends on the most diverse factors, for example on the activity of the specific compound employed, on the age, body weight, general state of health and sex of the patient, on the diet, on the time and method of administration, on the rate of excretion and the medicament combination and on the severity of the particular disease for which therapy is given. Oral administration is preferred.

When the composition containing a compound according to the invention is in dosage unit form, each dosage unit preferably contains from 0.5 to 200, more preferably from 2 to 50 mg of the active compound.

Each of the compounds of formula I mentioned in the examples which follow is particularly suitable for the preparation of pharmaceutical compositions.

In order that the invention may be more fully understood, the following examples are given by way of illustration only. In these examples, all temperatures are in °C and the phrase "customary working up" means: water is added, if necessary, to the reaction mixture, the mixture is extracted with an organic solvent, such as ethyl acetate, chloroform or dichloromethane, and separated, the organic phase is dried over sodium sulphate and filtered, the filtrate is evaporated and the residue is purified by chromatography and/or crystallisation.

"Fumarate" is the neutral salt (from 2 mols of base and 1 mol of fumaric acid).

Example 1

A mixture of 22 g of crude oily 1-(p-allyloxymethylphenoxy)-2,3-epoxypropane [obtainable by heating p-hydroxybenzyl alcohol with allyl alcohol to 150° for 4 hours and reacting the resulting p-allyloxymethylphenol (boiling point 123—125[/0.01 mm Hg) with epichlorohydrin] and 20 g of 3,4-dimethoxyphenylethylamine is stirred for 12 hours at 25°. 60 ml of ethanol are added to the resulting 1-(p-allyloxymethylphenoxy)-3-[2-(3,4-dimethoxyphenyl)-ethylamino]-propan-2-ol and the precipitate is filtered off and recrystallised from isopropanol. Hydrochloride, melting point 126°.

Examples 2 to 27

Analogously to Example 1, the reaction of:

- 1-(o-allyloxymethyl-phenoxy)-2,3-epoxypropane,
- 1-(m-allyloxymethyl-phenoxy)-2,3-epoxypropane,
- 1-(p-allyloxymethyl-phenoxy)-2,3-epoxypropane,
- 1-(o-propargyloxymethyl-phenoxy)-2,3-epoxypropane,
- 1-(o-2-methoxyethoxymethyl-phenoxy)-2,3-epoxypropane,
- 1-(o-2-isopropoxyethoxymethyl-phenoxy)-2,3-epoxypropane,
- 1-(p-2-isopropoxyethoxymethyl-phenoxy)-2,3-epoxypropane,
- 1-(o-2-allyloxyethoxymethyl-phenoxy)-2,3-epoxypropane or
- 2-(o-cyclopentoxymethyl-phenoxy)-2,3-epoxypropane

(in each case obtainable from o-, m- or p-hydroxybenzyl alcohol by etherification with the corresponding alcohol and subsequent reaction with epichlorohydrin) with 2-phenylethylamine, 1,1-dimethyl-2-phenylethylamine or 2-(3,4-dimethoxyphenyl)-ethylamine gives:

2. 1 - (o - Allyloxymethyl - phenoxy) - 3 - (2 - phenylethylamino) - propan - 2 - ol, fumarate, m.p. 93°.
3. 1 - (o - Allyloxymethyl - phenoxy) - 3 - (1,1 - dimethyl - 2 - phenylethylamino) - propan - 2 - ol.
4. 1 - (o - Allyloxymethyl - phenoxy) - 3 - [2 - (3,4 - dimethoxyphenyl) - ethylamino] - propan - 2 - ol, fumarate, m.p. 110°.
5. 1 - (m - Allyloxymethyl - phenoxy) - (2 - phenylethylamino) - propan - 2 - ol.
6. 1 - (m - Allyloxymethyl - phenoxy) - (1,1 - dimethyl - 2 - phenylethylamino) - propan - 2 - ol.
7. 1 - (m - Allyloxymethyl - phenoxy) - [2 - (3,4 - dimethoxyphenyl)ethylamino] - propan - 2 - ol.
8. 1 - (p - Allyloxymethyl - phenoxy) - 3 - (2 - phenylethylamino) - propan - 2 - ol, hydrochloride, m.p. 150°.
9. 1 - (p - Allyloxymethyl - phenoxy) - 3 - (1,1 - dimethyl - 2 - phenylethylamino) - propan - 2 - ol, hydrochloride, m.p. 142°.
10. 1 - (o - Propargyloxymethyl - phenoxy) - 3 - (2 - phenylethylamino) - propan - 2 - ol, fumarate, m.p. 85°.
11. 1 - (o - Propargyloxymethyl - phenoxy) - 3 - (1,1 - dimethyl - 2 - phenylethylamino) - propan - 2 - ol.
12. 1 - (o - Propargyloxymethyl - phenoxy) - 3 - [2 - (3,4 - dimethoxyphenyl) - ethylamino] - propan - 2 - ol, fumarate, m.p. 115°.
13. 1 - (o - 2 - Methoxyethoxymethyl - phenoxy) - 3 - (2 - phenylethylamino) - propan - 2 - ol.

14. 1 - (o - 2 - Methoxyethoxymethyl - phenoxy) - 3 - (1,1 - dimethyl - 2 - phenylethylamino) - propan - 2 - ol.
15. 1 - (o - 2 - Methoxyethoxymethyl - phenoxy) - 3 - [2 - (3,4 - dimethoxyphenyl) - ethylamino] - propan - 2 - ol.
16. 1 - (o - 2 - Isopropoxyethoxymethyl - phenoxy) - 3 - (2 - phenylethylamino) - propan - 2 - ol.
17. 1 - (o - 2 - Isopropoxyethoxymethyl - phenoxy) - 3 - (1,1 - dimethyl - 2 - phenylethylamino) - propan - 2 - ol.
18. 1 - (o - 2 - Isopropoxyethoxymethyl - phenoxy) - 3 - [2 - (3,4 - dimethoxyphenyl) - ethylamino] - propan - 2 - ol, fumarate, m.p. 116°.
19. 1 - (p - 2 - Isopropoxyethoxymethyl - phenoxy) - 3 - (2 - phenylethylamino) - propan - 2 - ol.
20. 1 - (p - 2 - Isopropoxyethoxymethyl - phenoxy) - 3 - (1,1 - dimethyl - 2 - phenylethylamino) - propan - 2 - ol.
21. 1 - (p - 2 - Isopropoxyethoxymethyl - phenoxy) - 3 - [2 - (3,4 - dimethoxyphenyl) - ethylamino] - propan - 2 - ol, hydrochloride m.p. 126°.
22. 1 - (o - 2 - Allyloxyethoxymethyl - phenoxy) - 3 - (2 - phenylethylamino) - propan - 2 - ol.
23. 1 - (o - 2 - Allyloxyethoxymethyl - phenoxy) - 3 - (1,1 - dimethyl - 2 - phenylethylamino) - propan - 2 - ol, fumarate, m.p. 115°.
24. 1 - (o - 2 - Allyloxyethoxymethyl - phenoxy) - 3 - [2 - (3,4 - dimethoxyphenyl) - ethylamino] - propan - 2 - ol, fumarate, m.p. 95°.
25. 1 - (o - Cyclopentoxymethyl - phenoxy) - 3 - (2 - phenylethylamino) - propan - 2 - ol.
26. 1 - (o - Cyclopentoxymethyl - phenoxy) - 3 - (1,1 - dimethyl - 2 - phenylethylamino) - propan - 2 - ol.
27. 1 - (o - Cyclopentoxymethyl - phenoxy) - 3 - [2 - (3,4 - dimethoxyphenyl) - ethylamino] - propan - 2 - ol, hydrochloride, m.p. 127°.

Example 28

30. A solution of 22 g of 1 - (o - allyloxymethyl - phenoxy) - 2,3 - epoxypropane and 33 ml of isopropylamine in 45 ml of ethanol is allowed to stand for 15 hours at 20°. The solution is evaporated and the residue is dissolved in ethyl acetate and extracted with dilute hydrochloric acid. The aqueous phase is rendered alkaline and customary working up gives 1 - (o - allyloxymethyl - phenoxy) - 3 - isopropylamino - propan - 2 - ol; fumarate, m.p. 106°.

Examples 29 to 54

Analogously to Example 28, the epoxides indicated in Examples 2 to 27 and isopropylamine, tert.-butylamine or 1-methyl-2-hydroxyethylamine give:

29. 1 - (o - Allyloxymethyl - phenoxy) - 3 - tert. - butylamino - propan - 2 - ol.
30. 1 - (o - Allyloxymethyl - phenoxy) - 3 - (1 - methyl - 2 - hydroxyethylamino) - propan - 2 - ol.
31. 1 - (m - Allyloxymethyl - phenoxy) - 3 - isopropylamino - propan - 2 - ol, fumarate, m.p. 90°.
32. 1 - (m - Allyloxymethyl - phenoxy) - 3 - tert. - butylamino - propan - 2 - ol.
33. 1 - (m - Allyloxymethyl - phenoxy) - 3 - (1 - methyl - 2 - hydroxyethylamino) - propan - 2 - ol.
34. 1 - (p - Allyloxymethyl - phenoxy) - 3 - isopropylamino - propan - 2 - ol, fumarate, m.p. 103°.
35. 1 - (p - Allyloxymethyl - phenoxy) - 3 - tert. - butylamino - propan - 2 - ol, fumarate, m.p. 148°.
36. 1 - (p - Allyloxymethyl - phenoxy) - 3 - (1 - methyl - 2 - hydroxyethylamino) - propan - 2 - ol.
37. 1 - (o - Propargyloxymethyl - phenoxy) - 3 - isopropylamino - propan - 2 - ol, fumarate, m.p. 177°.
38. 1 - (o - Propargyloxymethyl - phenoxy) - 3 - tert. - butylamino - propan - 2 - ol, fumarate, m.p. 166°.
39. 1 - (o - Propargyloxymethyl - phenoxy) - 3 - (1 - methyl - 2 - hydroxyethylamino) - propan - 2 - ol.
40. 1 - (o - 2 - Methoxyethoxymethyl - phenoxy) - 3 - isopropylamino - propan - 2 - ol, fumarate, m.p. 95°.
41. 1 - (o - 2 - Methoxyethoxymethyl - phenoxy) - 3 - tert. - butylamino - propan - 2 - ol, fumarate, m.p. 115°.

42. 1 - (o - 2 - Methoxyethoxymethyl - phenoxy) - 3 - (1 - methyl - 2 - hydroxyethylamino) - propan - 2 - ol.
43. 1 - (o - 2 - Isopropoxyethoxymethyl - phenoxy) - 3 - isopropylamino - propan - 2 - ol, fumarate, m.p. 90°.
44. 1 - (o - 2 - Isopropoxyethoxymethyl - phenoxy) - 3 - tert. - butylamino - propan - 2 - ol, fumarate, m.p. 132°.
45. 1 - (o - 2 - Isopropoxyethoxymethyl - phenoxy) - 3 - (1 - methyl - 2 - hydroxyethylamino) - propan - 2 - ol.
46. 1 - (p - 2 - Isopropoxyethoxymethyl - phenoxy) - 3 - isopropylamino - propan - 2 - ol, fumarate, m.p. 100°.
47. 1 - (p - 2 - Isopropoxyethoxymethyl - phenoxy) - 3 - tert. - butylamino - propan - 2 - ol, hemifumarate, m.p. 105°.
48. 1 - (p - 2 - Isopropoxyethoxymethyl - phenoxy) - 3 - (1 - methyl - 2 - hydroxyethylamino) - propan - 2 - ol.
49. 1 - (o - 2 - Allyloxyethoxymethyl - phenoxy) - 3 - isopropylamino - propan - 2 - ol, fumarate, m.p. 92°.
50. 1 - (o - 2 - Allyloxyethoxymethyl - phenoxy) - 3 - tert. - butylamino - propan - 2 - ol, fumarate, m.p. 122°.
51. 1 - (o - 2 - Allyloxyethoxymethyl - phenoxy) - 3 - (1 - methyl - 2 - hydroxyethylamino) - propan - 2 - ol.
52. 1 - (o - Cyclopentoxymethyl - phenoxy) - 3 - isopropylamino - propan - 2 - ol, hydrochloride, m.p. 124°.
53. 1 - (o - Cyclopentoxymethyl - phenoxy) - 3 - tert. - butylamino - propan - 2 - ol, hydrochloride, m.p. 128°.
54. 1 - (o - Cyclopentoxymethyl - phenoxy) - 3 - (1 - methyl - 2 - hydroxyethyl amino) - propan - 2 - ol.

Examples 55 to 73

Analogously to Example 28, 1 - (o - 2 - methoxyethoxymethyl - phenoxy) - 2,3 - epoxyp propane with the corresponding amines gives:

55. 1 - (o - 2 - Methoxyethoxymethyl - phenoxy) - 3 - methylamino - propan - 2 - ol.
56. 1 - (o - 2 - Methoxyethoxymethyl - phenoxy) - 3 - (2 - hexylamino) - propan - 2 - ol.
57. 1 - (o - 2 - Methoxyethoxymethyl - phenoxy) - 3 - (3 - hydroxy - 2 - hexylamino) - propan - 2 - ol.
58. 1 - (o - 2 - Methoxyethoxymethyl - phenoxy) - 3 - cyclopropylamino - propan - 2 - ol.
59. 1 - (o - 2 - Methoxyethoxymethyl - phenoxy) - 3 - cyclopentylamino - propan - 2 - ol.
60. 1 - (o - 2 - Methoxyethoxymethyl - phenoxy) - 3 - cyclohexylamino - propan - 2 - ol.
61. 1 - (o - 2 - Methoxyethoxymethyl - phenoxy) - 3 - cyclooctylamino - propan - 2 - ol.
62. 1 - (o - 2 - Methoxyethoxymethyl - phenoxy) - 3 - benzylamino - propan - 2 - ol.
63. 1 - (o - 2 - Methoxyethoxymethyl - phenoxy) - 3 - (2 - p - tolylmethyl - propan - 2 - ol.
64. 1 - (o - 2 - Methoxyethoxymethyl - phenoxy) - 3 - (1 - methyl - 3 - phenyl - propylamino) - propan - 2 - ol.
65. 1 - (o - 2 - Methoxyethoxymethyl - phenoxy) - 3 - (2 - p - methoxyphenyl - ethylamino) - propan - 2 - ol.
66. 1 - (o - 2 - Methoxyethoxymethyl - phenoxy) - 3 - [2 - (3,4,5 - trimethoxy - phenyl) - ethylamino] - propan - 2 - ol.
67. 1 - (o - 2 - Methoxyethoxymethyl - phenoxy) - 3 - (2 - p - hydroxyphenyl - ethylamino) - propan - 2 - ol.
68. 1 - (o - 2 - Methoxyethoxymethyl - phenoxy) - 3 - (2 - p - fluorophenyl - ethylamino) - propan - 2 - ol.
69. 1 - (o - 2 - Methoxyethoxymethyl - phenoxy) - 3 - (2 - p - chlorophenyl - ethylamino) - propan - 2 - ol.
70. 1 - (o - 2 - Methoxyethoxymethyl - phenoxy) - 3 - [2 - (3,4 - methylenedioxyphenyl) - ethylamino] - propan - 2 - ol.
71. 1 - (o - 2 - Methoxyethoxymethyl - phenoxy) - 3 - [2 - (3 - methoxy - 4 - hydroxyphenyl) - ethylamino] - propan - 2 - ol.

72. 1 - (o - 2 - Methoxyethoxymethyl - phenoxy) - 3 - [1,1 - dimethyl - 2 - (3,4 - dimethoxyphenyl) - ethylamino] - propan - 2 - ol.
 73. 1 - (o - 2 - Methoxyethoxymethyl - phenoxy) - 3 - [1,1 - dimethyl - 4 - (3,4,5 - trimethoxyphenyl) - butylamino] - propan - 2 - ol.

Example 74

A mixture of 25.7 g of 1 - chloro - 3 - (p - allyloxymethyl - phenoxy) - propan - 2 - ol and 50 g of 2 - (3,4 - dimethoxyphenyl) - ethylamine is heated to 100° for 18 hours, and then cooled. Customary working up gives 1 - (p - allyloxymethyl - phenoxy) - 3 - [2 - (3,4 - dimethoxyphenyl) - ethylamino] - propan - 2 - ol. Hydrochloride, m.p. 126°.

Examples 75 to 83

Analogously to Example 74,

- 1 - chloro - 3 - (p - vinyloxymethyl - phenoxy) - propan - 2 - ol,
 1 - chloro - 3 - (p - 2 - hexen - 1 - yl - oxymethyl - phenoxy) - propan - 2 - ol,
 1 - chloro - 3 - (p - ethynyloxymethyl - phenoxy) - propan - 2 - ol,
 1 - chloro - 3 - (p - 5 - hexyn - 1 - yl - oxymethyl - phenoxy) - propan - 2 - ol,
 1 - chloro - 3 - (p - 2 - butoxyethoxymethyl - phenoxy) - propan - 2 - ol,
 1 - chloro - 3 - (p - 2 - vinyloxyethoxymethyl - phenoxy) - propan - 2 - ol,
 1 - chloro - 3 - [p - 2 - (2 - buten - 1 - yloxy) - ethoxymethyl - phenoxy] - propan - 2 - ol,
 1 - chloro - 3 - (p - cyclopropoxymethyl - phenoxy) - propan - 2 - ol or
 1 - chloro - 3 - (p - cyclohexyloxymethyl - phenoxy) - propan - 2 - ol

with 2 - (3,4 - dimethoxyphenyl) - ethylamine give:

75. 1 - (p - Vinyloxymethylphenoxy) - 3 - [2 - (3,4 - dimethoxyphenyl) - ethylamino] - propan - 2 - ol.
 76. 1 - (p - 2 - Hexen - 1 - yloxymethyl - phenoxy) - 3 - [2 - (3,4 - dimethoxyphenyl) - ethylamino] - propan - 2 - ol.
 77. 1 - (p - Ethynyloxymethyl - phenoxy) - 3 - [2 - (3,4 - dimethoxyphenyl) - ethylamino] - propan - 2 - ol.
 78. 1 - (p - 5 - Hexyn - 1 - yloxymethyl - phenoxy) - 3 - [2 - (3,4 - dimethoxyphenyl) - ethylamino] - propan - 2 - ol.
 79. 1 - (p - 2 - Butoxyethoxymethyl - phenoxy) - 3 - [2 - (3,4 - dimethoxyphenyl) - ethylamino] - propan - 2 - ol.
 80. 1 - (p - 2 - Vinyloxyethoxymethyl - phenoxy) - 3 - [2 - (3,4 - dimethoxyphenyl) - ethylamino] - propan - 2 - ol.
 81. 1 - [p - 2 - (2 - Buten - 1 - yloxy) - ethoxymethyl - phenoxy] - 3 - [2 - (3,4 - dimethoxyphenyl) - ethylamino] - propan - 2 - ol.
 82. 1 - (p - Cyclopropoxymethyl - phenoxy) - 3 - [2 - (3,4 - dimethoxyphenyl) - ethylamino] - propan - 2 - ol.
 83. 1 - (p - Cyclohexyloxymethyl - phenoxy) - 3 - [2 - (3,4 - dimethoxyphenyl) - ethylamino] - propan - 2 - ol.

Example 84

A mixture of 22.3 g of 1 - (p - allyloxymethylphenoxy) - 3 - amino - propan - 2 - ol [obtainable by reacting 1 - (p - allyloxymethylphenoxy) - 2,3 - epoxypropane with NH_3], 13.8 g of potassium carbonate, 27 g of 2 - (3,4 - dimethoxyphenyl) - ethyl bromide and 100 ml of n-butanol is boiled for 24 hours, whilst stirring. The mixture is filtered, the filtrate is evaporated and the residue is subjected to customary working up to give 1 - (p - allyloxymethylphenoxy) - 3 - [2 - (3,4 - dimethoxyphenyl) - ethylamino] - propan - 2 - ol, hydrochloride, m.p. 126°.

Example 85

A mixture of 16.4 g of p - allyloxymethyl - phenol, 27.4 g of 1 - chloro - 3 - [2 - (3,4 - dimethoxyphenyl) - ethylamino] - propan - 2 - ol [obtainable from epichlorohydrin and 2 - (3,4 - dimethoxyphenyl) - ethylamine], 8 g of sodium hydroxide, 400 ml of ethanol and 20 ml of water is heated to 100° for 10 hours. The mixture is evaporated to dryness, the residue is treated with dilute hydrochloric acid and ethyl acetate and separated and the aqueous phase is rendered alkaline with sodium hydroxide solution and then subjected to customary working up to give 1 - (p - allyloxymethyl - phenoxy) - 3 - [2 - (3,4 - dimethoxyphenyl) - ethylamino] - propan - 2 - ol, hydrochloride, m.p. 126°.

Example 86

A mixture of 39.9 g of 1 - (p - allyloxymethylphenoxy) - 3 - [2 - (3,4 - dimethoxyphenyl) - ethylamino] - acetone (obtainable from p - allyloxymethylphenol and 1 - bromo - 3 - [2 - (3,4 - dimethoxyphenyl) - ethylamino] - propan - 2 - one), 4 g of NaBH₄ and 2 l of methanol is stirred at 25° for 3 hours. It is then subjected to customary working up to give 1 - (p - allyloxymethyl - phenoxy) - 3 - [2 - (3,4 - dimethoxyphenyl) - ethylamino] - propan - 2 - ol, hydrochloride, m.p. 126°.

Example 87

A solution of 42.8 g of N - (2 - hydroxy - 3 - o - cyclopentylloxymethyl - phenoxy - propyl) - 3,4 - dimethoxyphenylacetamide [obtainable from 3,4 - dimethoxy - phenylacetyl chloride and 1 - (o - cyclopentylloxy - methylphenoxy) - 3 - amino - propan - 2 - ol] in 600 ml of THF is added dropwise to a suspension of 10 g of LiAlH₄ in 500 ml of absolute ether, whilst stirring. The mixture is subsequently boiled for 20 hours and subjected to customary working up to give 1 - (o - cyclopentylloxymethylphenoxy) - 3 - [2 - (3,4 - dimethoxyphenyl) - ethylamino] - propan - 2 - ol, hydrochloride, m.p. 127°.

Example 88

A solution of 10 g of 1 - (p - 2 - isopropoxyethoxy - methylphenoxy) - 3 - isopropylideneamino - propan - 2 - ol [obtainable by reacting 1 - (p - 2 - isopropoxyethoxymethylphenoxy) - 2,3 - epoxypropane with ammonia to give 1 - (p - 2 - isopropoxyethoxymethylphenoxy) - 3 - amino - propan - 2 - ol and subsequently reacting this with acetone] in 250 ml of ethanol is hydrogenated on 0.5 g of Raney nickel at 25° and under 1 atmosphere until 1 equivalent of H₂ has been absorbed. The mixture is filtered and the filtrate is evaporated to give 1 - (p - 2 - isopropoxyethoxymethyl - phenoxy) - 3 - isopropylamino - propan - 2 - ol, fumarate, m.p. 100°.

Example 89

10 g of N - [2 - hydroxy - 3 - (p - 2 - isopropoxyethoxymethyl - phenoxy) - propyl] - N - isopropyl - acetamide [obtainable by reacting Na p - (2 - isopropoxyethoxymethyl) - phenolate with N - (2 - hydroxy - 3 - bromo - propyl) - N - isopropyl - acetamide] are boiled for 4 hours with 250 ml of 20% hydrochloric acid and the mixture is evaporated. Customary working up gives 1 - (p - 2 - isopropoxyethoxymethyl - phenoxy) - 3 - isopropylamino - propan - 2 - ol, fumarate, m.p. 100°.

Example 90

10 g of 1 - (o - 2 - methoxyethoxymethyl - phenoxy) - 2 - acetoxy - 3 - tert. - butylamino - propane [obtainable from Na o - (2 - methoxyethoxymethyl) - phenolate and 1 - bromo - 2 - acetoxy - 3 - tert. - butylamino - propane] are boiled for 2 hours with 250 ml of 10% ethanolic NaOH and the mixture is evaporated and after customary working up 1 - (o - 2 - methoxyethoxymethyl - phenoxy) - 3 - tert. - butylamino - propan - 2 - ol, fumarate, m.p. 115°, is obtained.

In order that the invention may be more fully understood, the following examples of pharmaceutical compositions are given by way of illustration only:—

Example A: Tablets

A mixture of 1 kg of 1 - (p - allyloxymethylphenoxy) - 3 - [2 - (3,4 - dimethoxyphenyl) - ethylamino] - propan - 2 - ol hydrochloride, 4 kg of lactose, 1.2 kg of potato starch, 0.2 kg of talc and 0.1 kg of magnesium stearate is pressed in conventional manner to form tablets, each containing 10 mg of active compound.

Example B: Dragees

Tablets are pressed in the same way as in Example A and are then coated in conventional manner with a coating of sucrose, potato starch, talc, tragacanth and a dyestuff.

Example C: Capsules

2 kg of 1 - (o - 2 - methoxyethoxymethyl - phenoxy) - 3 - tert. - butylamino - propan - 2 - ol fumarate are filled into hard gelatine capsules in conventional manner to form capsules each containing 20 mg of the active compound.

Example D: Ampoules

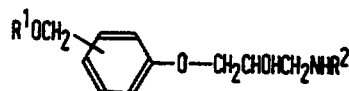
A solution of 1 kg of 1 - (o - allyloxymethyl - phenoxy) - 3 - [2 - (3,4 - dimethoxyphenyl) - ethylamino] - propan - 2 - ol fumarate in 30 l of doubly distilled water is

sterile filtered, filled into ampoules and lyophilised and sealed under sterile conditions. Each ampoule contains 1 mg of active compound.

Tablets, dragees, capsules and ampoules which contain one or more of the other compounds of formula I and/or their physiologically acceptable acid addition salts can be obtained analogously.

WHAT WE CLAIM IS:—

1. Phenoxy - amino - propanols of formula I:



I

wherein R¹ is alkenyl, alkynyl or alkoxyalkyl with 2—6 C atoms in each case, alkenyloxyalkyl with 3—6 C atoms or cycloalkyl with 3—8 C atoms, and R² is alkyl or hydroxyalkyl with 1—6 C atoms in each case, cycloalkyl with 3—8 C atoms or unsubstituted aralkyl or aralkyl which is mono- to trisubstituted in the aryl radical by alkyl, alkoxy, OH, F and/or Cl or mono-substituted by methylenedioxy, and having a total of 7—15 C atoms in each case, and their physiologically acceptable acid addition salts.

2. 1 - (p - Allyloxymethyl - phenoxy) - 3 - [2 - (3,4 - dimethoxyphenyl) - ethylamino] - propan - 2 - ol.

3. 1 - (o - Allyloxymethyl - phenoxy) - 3 - [2 - (3, 4- dimethoxyphenyl) - ethylamino] - propan - 2 - ol.

4. 1 - (o - 2 - Methoxyethoxymethyl - phenoxy) - 3 - tert. - butylamino - propan - 2 - ol.

5. 1 - (p - 2 - Isopropoxyethoxymethyl - phenoxy) - 3 - isopropylamino - propan - 2 - ol.

6. 1 - (o - 2 - Allyloxyethoxymethyl - phenoxy) - 3 - isopropylamino - propan - 2 - ol.

7. A process for the preparation of a phenoxyamino - propanol of formula I specified in claim 1, which comprises reacting a compound of formula II:



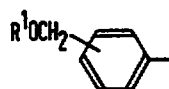
II

with a compound of formula III:



III

wherein Ar is the group



one of the radicals Y and Z is NH₂ and the other is X, Q is OH or, together with X, an oxygen atom, X is Hal, OH, a functionally modified OH group or (in II), together with Q, an oxygen atom, and Hal is Cl, Br or I, and R¹ and R² have the meanings specified in claim 1.

8. A process for the preparation of a phenoxy - amino - propanol of formula I specified in claim 1, which comprises reacting a phenol of formula IV:



IV

wherein Ar has the meaning specified in claim 7, with an aminoalcohol of formula V:



V

wherein R² has the meaning specified in claim 1 and X has the meaning specified in claim 7.

9. A process for the preparation of a phenoxyamino - propanol of formula I specified in claim 1, which comprises reducing a compound of formula VI:



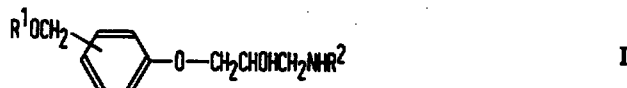
VI

sterile filtered, filled into ampoules and lyophilised and sealed under sterile conditions. Each ampoule contains 1 mg of active compound.

Tablets, dragees, capsules and ampoules which contain one or more of the other compounds of formula I and/or their physiologically acceptable acid addition salts can be obtained analogously.

WHAT WE CLAIM IS:—

1. Phenoxy - amino - propanols of formula I:



wherein R¹ is alkenyl, alkynyl or alkoxyalkyl with 2—6 C atoms in each case, alkenyloxyalkyl with 3—6 C atoms or cycloalkyl with 3—8 C atoms, and R² is alkyl or hydroxyalkyl with 1—6 C atoms in each case, cycloalkyl with 3—8 C atoms or unsubstituted aralkyl or aralkyl which is mono- to trisubstituted in the aryl radical by alkyl, alkoxy, OH, F and/or Cl or mono-substituted by methylenedioxy, and having a total of 7—15 C atoms in each case, and their physiologically acceptable acid addition salts.

2. 1 - (p - Allyloxymethyl - phenoxy) - 3 - [2 - (3,4 - dimethoxyphenyl) - ethylamino] - propan - 2 - ol.

3. 1 - (o - Allyloxymethyl - phenoxy) - 3 - [2 - (3, 4- dimethoxyphenyl) - ethylamino] - propan - 2 - ol.

4. 1 - (o - 2 - Methoxyethoxymethyl - phenoxy) - 3 - tert. - butylamino - propan - 2 - ol.

5. 1 - (p - 2 - Isopropoxyethoxymethyl - phenoxy) - 3 - isopropylamino - propan - 2 - ol.

6. 1 - (o - 2 - Allyloxyethoxymethyl - phenoxy) - 3 - isopropylamino - propan - 2 - ol.

7. A process for the preparation of a phenoxyamino - propanol of formula I specified in claim 1, which comprises reacting a compound of formula II:



with a compound of formula III:



wherein Ar is the group



one of the radicals Y and Z is NH₂ and the other is X, Q is OH or, together with X, an oxygen atom, X is Hal, OH, a functionally modified OH group or (in II), together with Q, an oxygen atom, and Hal is Cl, Br or I, and R¹ and R² have the meanings specified in claim 1.

8. A process for the preparation of a phenoxy - amino - propanol of formula I specified in claim 1, which comprises reacting a phenol of formula IV:



wherein Ar has the meaning specified in claim 7, with an aminoalcohol of formula V:



wherein R² has the meaning specified in claim 1 and X has the meaning specified in claim 7.

9. A process for the preparation of a phenoxyamino - propanol of formula I specified in claim 1, which comprises reducing a compound of formula VI:





wherein W is a radical which can be reduced to the group $-\text{CHOH}-\text{CH}_2-\text{NHR}^2$, Ar has the meaning specified in claim 7, and R^2 has the meaning specified in claim 1.

5 10. A process for the preparation of a phenoxyamino - propanol of formula I specified in claim 1, which comprises treating a compound corresponding to formula I, but which additionally contains one or more groups which can be split off solvolytically or hydrogenolytically instead of one or more H atoms, with a solvolysing or hydrogenolysing agent. 5

10 11. A process according to any of claims 7 to 10, in which the compound of formula I obtained is reacted with an acid in order to form a physiologically acceptable acid addition salt thereof. 10

12. A process for the preparation of a phenoxyamino - propanol of formula I specified in claim 1, or a physiologically acceptable acid addition salt thereof, substantially as herein described in any of Examples 1 to 90.

15 13. A pharmaceutical composition comprising at least one compound as claimed in any of claims 1 to 6 and an inert, physiologically acceptable carrier. 15

14. A pharmaceutical composition according to claim 13 which is in dosage unit form, each dosage unit containing from 2 to 50 mg of said compound(s).

15. A pharmaceutical composition substantially as herein described in any of Examples A to D.

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