

PATENT SPECIFICATION

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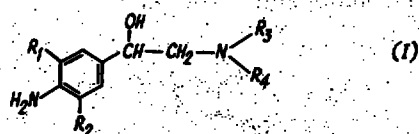
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(54) ETHANOLAMINE DERIVATIVES

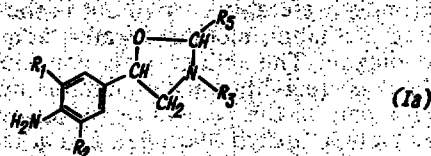
(71) We, DR. KARL THOMAE G.M.B.H., a German Body Corporate, of Biberach an der Riss, Germany, do hereby declare the invention, for which we pray that a patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement:—

The present invention relates to new amino-phenyl-ethanolamines having interesting physiological properties.

According to one feature of the present invention there are provided compounds of general formula



and oxazolidines thereof of general formula



[wherein R₁ represents a hydrogen, fluorine, chlorine, bromine or iodine atom or a cyano group, R₂ represents a fluorine atom, a straight or branched alkyl group containing from 1 to 5 carbon atoms or a hydroxyalkyl, aminoalkyl, dialkylaminoalkyl, trifluoromethyl, alkoxy, nitro, cyano, carboxy, carbalkoxy or carbamoyl group, R₃ and R₄, which may be the same or different, each represents a hydrogen atom, a straight or branched alkyl group containing from 1 to 6 carbon atoms, or a hydroxyalkyl, cycloalkyl, cycloalkylalkyl, alkenyl, alkynyl or optionally substituted aralkyl group and R₅ represents a hydrogen atom or a straight or branched alkyl group] and acid addition salts thereof.

The compounds of general formula I exist in the form of optically active isomers and all forms of the compounds of general formula I including optically active and racemic forms are included within the scope of the present invention.

In general the compounds of general formula I and Ia possess valuable pharmacological properties, in particular a mimetic activity of the β_2 -receptors and/or a blocking activity on the β_1 -receptors, as well as an analgetic, utero-spasmolytic and an antispastic activity on the skeletal muscles. It is generally found that the predominance of the β_2 -mimetic activity or the β_1 -blocking activity is dependent on the substitution of the compound of formula I or Ia. It has also been found that the d(+)-stereoisomers of compounds of general formula I have an especially selective activity on the β_1 -receptors and the l(-)-stereoisomers have a selective activity on the β_2 -receptors.

Preferred compounds of general formula I and oxazolidines of general formula Ia by virtue of their particularly favourable pharmacological properties are those wherein R_1 represents a hydrogen, chlorine, bromine or iodine atom or a cyano group; R_2 represents a fluorine atom or a trifluoromethyl, nitro or cyano group with the proviso that R_1 is not hydrogen when R_2 represents a fluorine atom; R_3 represents a straight or branched alkyl group containing from 3 to 5 carbon atoms optionally substituted by a hydroxyl group, a cycloalkyl group containing from 3 to 5 carbon atoms or a 3,4-methylenedioxyphenylisopropyl group; R_4 represents a hydrogen atom; and R_5 represents a hydrogen atom or a straight or branched alkyl group containing from 1 to 5 carbon atoms and physiologically compatible acid addition salts thereof. Particularly preferred compounds of general formula I are the following:—

1 - (4 - Amino - 3 - bromo - 5 - fluoro - phenyl) - 2 - tert. - butylamino - ethanol and physiologically compatible acid addition salts thereof;

1 - (4 - amino - 3 - chloro - 5 - cyano - phenyl) - 2 - tert. - butylamino - ethanol and physiologically compatible acid addition salts thereof;

1 - (4 - amino - 3 - fluoro - 5 - iodo - phenyl) - 2 - cyclopropylamino - ethanol and physiologically compatible acid addition salts thereof;

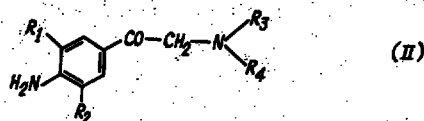
1 - (4 - amino - 3 - fluoro - 5 - cyano - phenyl) - 2 - isopropylamino - ethanol and physiologically compatible acid addition salts thereof;

1 - (4 - amino - 3,5 - dicyano - phenyl) - 2 - tert. - butylamino - ethanol and physiologically compatible acid addition salts thereof; and

1 - (4 - amino - 3 - bromo - 5 - nitro - phenyl) - 2 - tert. - butylamino - ethanol and physiologically compatible acid addition salts thereof.

The compounds of general formula I as hereinbefore defined may be prepared according to the following processes, which processes constitute further features of the present invention:—

a) Reduction of a compound of formula



(wherein R_1 , R_2 , R_3 and R_4 are as hereinbefore defined).

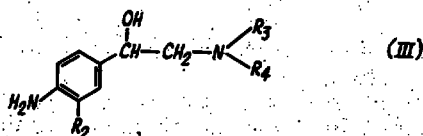
The reduction is preferably carried out in the presence of a solvent, suitable solvents including methanol, methanol/water, ethanol, isopropanol, ether, tetrahydrofuran and dioxan. The reduction is conveniently effected by means of a complex metal hydride (e.g. lithium aluminium hydride or sodium borohydride), aluminium isopropylate in the presence of a primary or secondary alcohol or by means of catalytically activated hydrogen and at temperatures from -20°C up to the boiling temperature of the solvent used.

The reduction with complex metal hydrides is, however, preferably carried out with sodium borohydride, and at room temperature. If a reactive complex metal hydride such as lithium aluminium hydride is used, particularly if the reduction is carried out at elevated temperatures, any cyano, carboxy, carbalkoxy or carbamoyl groups present may also be reduced at the same time.

If the reduction is effected with hydrogen in the presence of a catalyst, for example Raney nickel, platinum or palladium/animal charcoal, any alkenyl or alkynyl groups may be converted into the corresponding alkyl groups, and/or any benzyl groups present may be split off hydrogenolytically.

b) For the preparation of compounds of general formula I (wherein R_3 and R_4 are

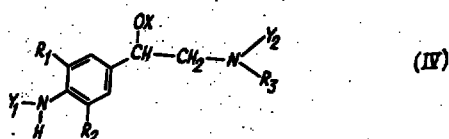
as hereinbefore defined, except that they do not represent alkynyl or alkenyl groups and R_1 represents a chlorine, bromine or iodine atom):
Halogenation of a compound of formula:—



(wherein R_2 to R_4 are as hereinbefore defined with the proviso that they cannot represent alkenyl or alkynyl groups).

The reaction is effected by means of a halogenating agent, e.g. with chlorine, bromine, iodine, tribromophenol hypobromite or iodosobenzene dichloride, preferably in the presence of a solvent, e.g. in 50 to 100% acetic acid or in tetrahydrofuran in the presence of a tertiary organic base, optionally in the presence of a heavy metal salt, for example, mercury(II) oxide, and conveniently at temperatures from 0 to 50°C. Advantageously 1 mol of the halogenating agent or a small excess thereof is employed per mol of the compound of formula III, which may be used as the free base or in salt form, e.g. as the mono-, di- or tri-hydrochloride. If a hydrogen halide salt is obtained during the reaction, the salt may be directly isolated or, if desired, it may be further purified via the base.

c) Removal of one or more protective groups from a compound of formula



(wherein R_1 , R_2 and R_3 are as hereinbefore defined, X represents a protective group for a hydroxyl group or a hydrogen atom, Y_1 represents a protective group for an amino group or a hydrogen atom, and Y_2 represents a protective group for an amino group or has the meanings given above for R_4 , with the proviso that at least one of the groups X, Y_1 and Y_2 represents one of the above mentioned protective groups).

Y_1 and/or Y_2 may for example represent acyl groups, (e.g. acetyl, benzoyl or p-toluenesulfonyl groups) or benzyl groups and X may for example represent an acyl group, (e.g. an acetyl, benzoyl or p-toluenesulfonyl group) or a trimethylsilyl, benzyl or tetrahydropyranyl-(2)-group.

If Y_1 and/or Y_2 for example represent acyl groups, the removal of these groups is conveniently effected hydrolytically, e.g. with ethanolic hydrochloric acid or with sodium hydroxide solution at temperatures up to the boiling point of the solvent used. If in a compound of formula IV R_2 represents a cyano group, this group may be simultaneously saponified to a carbamoyl or carboxyl group; if R_2 represents a carbalkoxy or carbamoyl group, these groups may be saponified at the same time to carboxyl groups.

If X, Y_1 and/or Y_2 in the compound of formula IV wherein R_2 does not represent a nitro group for example represent benzyl groups the removal of these groups is conveniently effected hydrogenolytically, for example with hydrogen in the presence of a catalyst, e.g. palladium on charcoal, palladium oxide hydrate on barium sulfate, platinum or Raney nickel. The hydrogenolysis is preferably effected in the presence of a solvent, for example methanol, methanol/hydrochloric acid or ethanol, at room temperature or at slightly elevated temperatures and at normal pressure or slightly elevated pressure. Any alkynyl or alkenyl groups present may be at the same time be converted into the corresponding alkyl groups during the reaction.

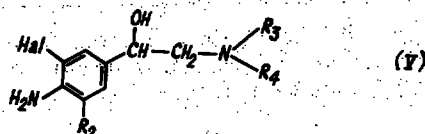
If for example X represents an acyl group, a trimethylsilyl or a tetrahydropyranyl-(2)-group, the removal of these groups is conveniently effected hydrolytically, preferably in the presence of an acid, and at temperatures up to the boiling temperature of the solvent used.

d) For the preparation of compounds of formula I (wherein R_1 represents a hydrogen atom, and R_2 , R_3 and R_4 are as hereinbefore defined): Dehalogenation of a compound of the formula:

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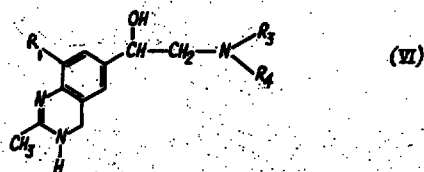
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(wherein R_2 , R_3 and R_4 are as hereinbefore defined and Hal represents a chlorine, bromine or iodine atom).

The dehalogenation is preferably effected in the presence of a solvent and advantageously either by means of triphenylphosphine in benzene or toluene as solvent or by means of hydrogen in methanol, ethanol, ethyl acetate or tetrahydrofuran as solvent and in the presence of a hydrogenation catalyst. The reaction is usually carried out at room temperature or at elevated temperatures for example at temperatures from 100 to 150°C. and at normal pressure or at a moderately elevated pressure. If, for example, Raney nickel or palladium/charcoal is used as catalyst, the dehalogenation is performed at room temperature and at normal pressure. In the compound of formula V if R_3 and/or R_4 represent alkenyl or alkynyl groups, these groups may be hydrogenated to the corresponding alkyl groups during the hydrogenolytic dehalogenation, and/or, if R_4 represents a benzyl group, the benzyl group may be simultaneously removed hydrogenolytically. In the compound of formula V if R_2 represents a nitro group, the dehalogenation is preferably carried out with triphenylphosphine.

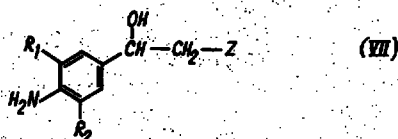
e) For the preparation of compounds of general formula I, (wherein R_2 represents the aminomethyl group and R_1 , R_3 and R_4 are as hereinbefore defined): Reducing and subsequently hydrolysing a compound of formula



(wherein R_1 , R_3 and R_4 are as hereinbefore defined).

The reaction is preferably carried out in the presence of a solvent, conveniently by reduction with sodium in pentyl alcohol at temperatures from 0 to 50°C. The subsequent hydrolysis of the 1,2,3,4-tetrahydro-quinazoline so formed, which need not be isolated, is preferably carried out by means of hydrochloric acid at elevated temperatures, e.g. at the boiling temperature of the hydrochloric acid.

f) Reaction of a compound of formula



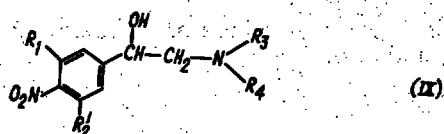
(wherein R_1 and R_2 are as hereinbefore defined and Z represents a chlorine, bromine or iodine atom or a p-toluene-sulfonyloxy group) with an amine of formula



(wherein R_3 and R_4 are as hereinbefore defined).

The reaction is conveniently carried out in the presence of a solvent, suitable solvents including methanol, ethanol, chloroform, carbon tetrachloride and dioxan. Alternatively the reaction may be carried out with an excess of the amine of formula VIII used. The reaction may, however, also be carried out in the absence of a solvent. The reaction temperature is conveniently from 0 to 100°C.

g) For the preparation of compounds of general formula I (wherein R_1 , R_2 , R_3 and R_4 are as hereinbefore defined with the proviso that R_2 does not represent a nitro group): Reduction of a compound of formula

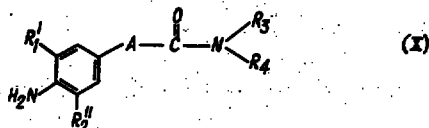


(wherein R_1 , R_3 and R_4 are as hereinbefore defined and R_2' is as hereinbefore defined for R_2 with the proviso that it cannot represent a nitro group).

The reduction is conveniently carried out in the presence of a solvent, for example in water, methanol, ethanol, water/methanol or ethyl acetate, and is preferably effected by means of nascent hydrogen (e.g. from zinc/glacial acetic acid or iron/hydrochloric acid) hydrogen in the presence of a catalyst, (e.g. Raney nickel, platinum or palladium/charcoal) a complex metal hydride (e.g. lithium aluminium hydride) or tin (II) chloride and hydrochloric acid. The reduction is preferably effected at temperatures from 0 to 100°C.

h) For the preparation of compounds of general formula I, (wherein R_1 , R_2 , R_3 and R_4 are as hereinbefore defined with the proviso that R_1 does not represent a cyano group and R_2 does not represent a nitro, cyano, carboxy, carbalkoxy or carbamoyl group):

Reduction of a compound of formula

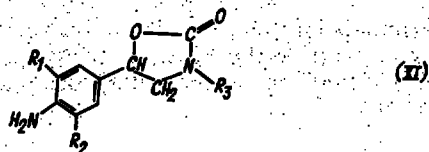


(wherein R_3 and R_4 are as hereinbefore defined, R_1' is as hereinbefore defined for R_1 with the proviso that it cannot represent a cyano group, R_2'' is as hereinbefore defined for R_2 with the proviso that it cannot represent a nitro, cyano, carboxy, carbalkoxy or carbamoyl group and A represents a carbonyl or a hydroxy-methylene group).

The reaction is conveniently performed in the presence of a solvent, e.g. in ether, tetrahydrofuran, dioxane or tetrahydrofuran/benzene, preferably by means of a reducing agent such as a complex metal hydride, (e.g. lithium aluminium hydride, sodium borohydride in the presence of a Lewis acid or sodium borohydride in pyridine) conveniently at temperatures from 0 to 120°C, preferably at the boiling point of the solvent used.

i) For the preparation of compounds of general formula I, (wherein R_1 , R_2 and R_3 are as hereinbefore defined and R_4 represents a hydrogen atom):

Hydrolysis of an oxazolidone of formula

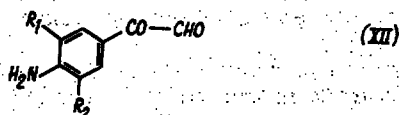


(wherein R_1 , R_2 and R_3 are as hereinbefore defined).

The hydrolysis is conveniently carried out in the presence of a solvent, for example in water, methanol, ethanol, ethanol/water or glacial acetic acid, preferably in the presence of an acid (e.g. hydrochloric acid, hydrobromic acid or sulfuric acid) or in the presence of a base (e.g. sodium hydroxide or potassium hydroxide) and conveniently at temperatures from 0 to 110°C depending to the nature of the hydrolyzing agent used, preferably at room temperature or at the boiling temperature of the solvent used.

j) For the preparation of compounds of general formula I (wherein R_1 , R_2 and R_3 are as hereinbefore defined and R_4 represents a hydrogen atom):

Reduction of an aldehyde of formula



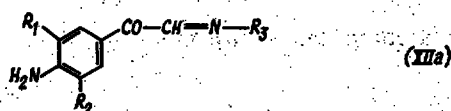
(wherein R_1 and R_2 are as hereinbefore defined), or of the hydrate thereof, in the presence of an amine of formula



(wherein R_3 is as hereinbefore defined).

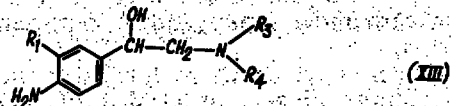
The reduction is conveniently carried out in the presence of a solvent, for example in methanol, ethanol, ether or tetrahydrofuran, preferably by means of a complex metal hydride (e.g. sodium borohydride or lithium aluminium hydride), nascent hydrogen or hydrogen in the presence of a catalyst (e.g. Raney nickel, palladium/charcoal or platinum) conveniently at temperatures from -20 to 100°C , preferably, however, at temperatures up to the boiling temperature of the solvent used.

The reaction may, however, also be carried out by first forming a compound of formula



(wherein R_1 , R_2 and R_3 are as hereinbefore defined) in situ and subsequently reducing it.

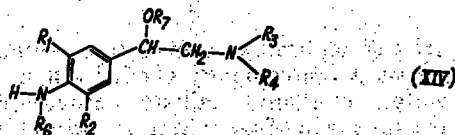
k) For the preparation of compounds of general formula I (wherein R_1 , R_3 and R_4 are as hereinbefore defined and R_2 represents a nitro group): Nitration of a compound of formula



(wherein R_1 , R_3 and R_4 are as hereinbefore defined).

The reaction is effected by means of a nitrating agent, preferably nitric acid or a mixture of concentrated nitric acid and concentrated sulfuric acid, conveniently at temperatures from -20° to 100°C .

According to a yet further feature of the invention there is provided a process for the preparation of the optical isomers of compounds of general formula I as hereinbefore defined which comprises resolving a racemic mixture of the compound of formula I into its optically active isomers. Advantageously this may be performed by converting the racemic mixture of the compound of formula I into a racemic mixture of the compound of formula I into a racemic mixture of a compound of formula



(wherein R_1 , R_2 , R_3 and R_4 are as hereinbefore defined, R_6 represents a hydrogen atom or an acyl group and R_7 represents a chiral acyl group), resolving this mixture into its constituent optical isomers and subsequently splitting off the groups R_7 and R_6 , if R_6 represents an acyl group and, if desired, the group R_4 , if R_4 represents an optionally substituted benzyl group, from each pure isomer.

Appropriate chiral acyl groups R_7 are for example optically active α -amino-acyl-groups protected at the nitrogen atom, (e.g. N-benzyl-oxycarbonyl-L-alanyl-group) or optically active terpenyl-oxycarbonyl-groups, (e.g. the (-)-methyl-oxycarbonyl-group).

The separation of racemic mixture of formula XIV into the pure diastereoisomeric compounds is conveniently carried out by fractional crystallization and/or by column chromatography over an inert carrier.

The subsequent splitting off of the radicals R_1 and R_2 is appropriately effected by means of hydrolysis or solvolysis in the presence of water or of a suitable alcohol such as methanol, optionally in the presence of an acid or a base and conveniently at temperatures from 0 to 100°C.

The removal of the radical R_1 can also be conveniently effected by hydrogenolysis by means of a complex metal hydride, e.g. lithium aluminium hydride, in the presence of a suitable solvent, e.g. in ether, tetrahydrofuran or dioxane, and conveniently at temperatures from -20 to 20°C. If R_2 in the compound of formula XIV represents a cyano group, this group may be reduced at the same time. According to the nature of the substituents R_1 and R_2 , their removal may be effected separately or in a single stage.

If R_1 represents an optionally substituted benzyl group, the removal of this group from compounds in which R_2 does not represent a nitro group, is conveniently effected by means of hydrogenolysis in the presence of a suitable catalyst such as palladium on charcoal or barium sulfate, in the presence of a suitable solvent, for example an alcohol e.g. methanol, ethanol or acetic acid, optionally with the addition of a mineral acid e.g. hydrochloric acid and at elevated hydrogen pressure and preferably at temperatures from 20 to 50°C. If R_2 in the compound of formula XIV represents a cyano group, this group may be reduced simultaneously. The removal of R_1 may be effected before or after the radicals R_1 and R_2 have been split off.

The resolution of a racemic mixture of a compound of formula I is preferably carried out by fractional crystallization of a mixture of the diastereoisomeric salts therefrom with an optically active acid, e.g. with D(-)-tartaric acid, L(+)-tartaric acid, dibenzoyl - D - tartaric acid, dibenzoyl - L - tartaric acid, (+) - camphor - 10 - sulfonic acid, L(-) - malic acid, L(+) - mandelic acid, d - α -bromocamphor- π -sulfonic acid or l-quinic acid. The resolution may, however, also be effected by column chromatography over an optically active carrier, e.g. acetylcellulose.

A compound of formula I (wherein R_1 , R_2 and R_3 are as hereinbefore defined and R_4 represents a cyano group) obtained for example by one of the processes a) to k) may be converted into the corresponding compound of formula I (wherein R_4 represents a carbamoyl or carboxy group) by partial or complete hydrolysis. In addition a compound of formula I (wherein R_1 , R_2 and R_3 are as hereinbefore defined and R_4 represents a carbamoyl or carbalkoxy group) may be converted into the corresponding compound or formula I (wherein R_4 represents a carboxy group) by hydrolysis.

According to a still further feature of the present invention there is provided a process for the preparation of oxazolidines of general formula Ia as hereinbefore defined which comprises reacting a compound of formula I (wherein R_1 and R_2 are as hereinbefore defined and one of R_3 and R_4 represents a hydrogen atom and the other is as hereinbefore defined) with an aldehyde of formula



(wherein R_5 is as hereinbefore defined).

The reaction is conveniently effected in the presence of a solvent for example ethanol, benzene, toluene or dioxane, advantageously under dehydrating conditions, e.g. in the presence of anhydrous copper(II) sulfate, at temperatures up to the boiling temperature of the solvent used, e.g. at temperatures from 20 to 100°C. The reaction may, however, also be carried out in the absence of a solvent. Especially preferred is the reaction using an apparatus incorporating a water separator funnel in the presence of a solvent such as benzene or toluene.

The compounds of general formulae I and Ia thus obtained may be converted, if desired, into their physiologically compatible acid addition salts with 1, 2 or 3 equivalents of the corresponding inorganic or organic acid. Suitable acids are for example hydrochloric acid, hydrobromic acid, sulfuric acid, phosphoric acid, lactic acid, citric acid, tartaric acid, maleic acid and fumaric acid.

The compounds of general formulae II and XIV used as starting compounds may for example be obtained according to methods known from the literature.

Thus the compounds of general formula II used as starting materials may for example be obtained by reaction of the corresponding 2-halogeno-acetophenones with the corresponding amines.

The compounds of general formulae III, IV and V may for example be obtained by reaction of the corresponding 2-halogeno-acetophenones with the

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corresponding amines and subsequent reduction of the ketones thus formed for example with sodium borohydride. A starting compound of general formula V may also be obtained by halogenation of the corresponding compound or by catalytic reduction of a corresponding 4-nitro-phenyl-compound.

The compounds of general formula VI may for example be obtained by reduction of the corresponding aminoacetylquinazolines with sodium borohydride.

The starting compounds of general formula VII may for example be obtained by reaction of the corresponding phenylethyleneglycol with p-toluenesulfonyl chloride in the presence of pyridine or by reduction of a corresponding aminophenacyl halide by means of sodium borohydride.

A starting compound of general formula IX may for example be obtained by reduction of the corresponding ketone with sodium borohydride.

A starting compound of general formula X may for example be obtained by reaction of the corresponding acid with the corresponding amine in the presence of a condensation agent (e.g. N,N'-dicyclohexyl-carbodiimide or N,N'-carbonyl-diimidazole) optionally with activation of the acid via the acid chloride or a mixed anhydride, and subsequent reduction of the corresponding ketocarboxylic acid amide so formed.

A starting compound of formula XI may for example be obtained by halogenation of the corresponding oxazolidone (wherein R₁ represents a hydrogen atom) or by alkylation of the corresponding oxazolidone (wherein R₁ represents a hydrogen atom).

A starting compound of general formula XII may for example be obtained by oxidation of the corresponding acetophenone with selenium dioxide or by oxidation of the corresponding phenylacetyl bromide with dimethylsulfoxide.

A starting compound of general formula XIII may be conveniently obtained according to a process of the present application.

The starting compounds of general formulas II to XIII used for processes a) to k) need not always be purified before reaction to produce a compound of formula I or Ia.

As already above mentioned, the new compounds of general formulae I and Ia possess in general valuable pharmacological properties, especially a mimetic activity on the β_2 -receptors and/or a blocking activity on the β_1 -receptors, whereby according to their substitution the one or the other activity is more predominant. The d(+)-isomers which have been tested show a selective activity on the β_1 -receptors and the l(-)-isomers a preferred activity on the β_2 -receptors.

The following compounds have been tested with regard to their activity on the β -receptors:

- A=1 - (4 - Amino - 3 - bromo - 5 - fluoro - phenyl) - 2 - tert. - butylamino - ethanol hydrochloride,
- B=5 - (4 - Amino - 3 - bromo - 5 - fluoro - phenyl) - 3 - tert. - butyl - oxazolidine dihydrochloride,
- C=1 - (4 - Amino - 3 - chloro - 5 - fluoro - phenyl) - 2 - cyclopropylamino - ethanol hydrochloride,
- D=1 - (4 - Amino - 3 - chloro - 5 - fluoro - phenyl) - 2 - tert. - butylamino - ethanol hydrochloride,
- E=1 - (4 - Amino - 3 - fluoro - phenyl) - 2 - tert. - butylamino - ethanol hydrochloride,
- F=1 - (4 - Amino - 3 - trifluoromethyl - phenyl) - 2 - tert. - pentylamino - ethanol hydrobromide,
- G=1 - (4 - Amino - 3 - chloro - 5 - trifluoromethyl - phenyl) - 2 - tert. - butylamino - ethanol hydrochloride,
- H=1 - (4 - Amino - 3 - chloro - 5 - trifluoromethyl - phenyl) - 2 - cyclobutylamino - ethanol hydrochloride,
- I=1 - (4 - Amino - 3 - chloro - 5 - cyano - phenyl) - 2 - tert. - butylamino - ethanol,
- J=1 - (4 - Amino - 3 - bromo - 5 - cyano - phenyl) - 2 - tert. - butylamino - ethanol hydrochloride,
- K=1 - (4 - Amino - 3 - bromo - 5 - fluoro - phenyl) - 2 - cyclobutylamino - ethanol hydrochloride,
- L=1 - (4 - Amino - 3 - fluoro - 5 - iodo - phenyl) - 2 - cyclopropylamino - ethanol hydrochloride,
- M=1 - (4 - Amino - 3 - fluoro - 5 - cyano - phenyl) - 2 - isopropylamino - ethanol hydrochloride,

	N=F - (4 - Amino - 3 - fluoro - 5 - cyano - phenyl) - 2 - tert. - butylamino - ethanol hydrochloride,	
	O=1 - (4 - Amino - 3 - cyano - phenyl) - 2 - cyclobutylamino - ethanol hydrobromide,	
5	P=1 - (4 - Amino - 3 - cyano - phenyl) - 2 - tert. - pentylamino - ethanol,	5
	Q=1 - (4 - Amino - 3 - chloro - 5 - cyano - phenyl) - 2 - propylamino - ethanol hydrochloride,	
	R=1 - (4 - Amino - 3 - chloro - 5 - cyano - phenyl) - 2 - sec. - butylamino - ethanol hydrochloride,	
10	S=1 - (4 - Amino - 3 - chloro - 5 - cyano - phenyl) - 2 - (hydroxy - tert. - butylamino) - ethanol hydrochloride,	10
	T=1 - (4 - Amino - 3 - chloro - 5 - cyano - phenyl) - 2 - tert. - pentylamino - ethanol hydrochloride,	
15	U=1 - (4 - Amino - 3 - chloro - 5 - cyano - phenyl) - 2 - cyclopentylamino - ethanol hydrochloride,	15
	V=1 - (4 - Amino - 3 - chloro - 5 - cyano - phenyl) - 2 - [1 (3,4 - methylenedioxyphenyl) - 2 - propylamino] - ethanol hydrochloride,	
	W=1 - (4 - Amino - 3 - bromo - 5 - cyano - phenyl) - 2 - cyclobutylamino - ethanol hydrochloride,	
20	X=1 - (4 - Amino - 3,5 - dicyano - phenyl) - 2 - tert. - butylamino - ethanol hydrochloride,	20
	Y=1 - (4 - Amino - 3 - bromo - 5 - nitro - phenyl) - 2 - tert. - butylamino - ethanol and	
	Z=1 - (4 - Amino - 3 - chloro - 5 - nitro - phenyl) - 2 - tert. - butylamino - ethanol.	
25	The β_1 -blocking activity was tested as antagonism to tachycardia in narcotized cats provoked by a standard dose of 1.0 μ /kg i.v. of N-isopropyl-noradrenalin sulfate. From the average percentage decrease in increase of heart rate, caused by N-isopropyl-noradrenalin sulfate, obtained by various doses of the compounds in question an ED ₅₀ was determined by graphical extrapolation (see Tables II and	25
30	III).	30
	The β -mimetic activity was tested as antagonism to bronchospasm provoked by intravenous application of 20 μ of acetylcholine per kg of body weight in narcotized guinea pigs (according to the method of Konzett-Rössler) on the intravenous administration of compounds of the present invention. From the average percentage decrease of the bronchospasm produced by various doses of the compounds of the present invention, an ED ₅₀ was determined by graphical extrapolation (see table I).	
35		35
	The β_2 -blocking activity was tested as antagonism to the broncholytic activity which is observed on the administration of 5 μ /kg of body weight i.v. of N-isopropyl-noradrenalin sulfate in the test arrangement according to Konzett-Rössler using narcotized guinea pigs, following the inducement of a bronchospasm caused by a standard dose of 20 μ /kg of body weight i.v. of acetylcholine (see table III).	
40		40
	The acute toxicity of the substances was determined on groups of 10 mice. The LD ₅₀ , i.e. the dose administered intravenously after which 50% of the animals died within a period of 14 days, was calculated according to the method of Litchfield and Wilcoxon (see tables II and III).	
45		45

TABLE I

Substance	β_2 -mimetic activity			Duration of activity in minutes
	n_1	n_2	ED ₅₀ γ /kg i.v.	
A	9	5	8.3	>150
B	5	4	6.7	>110
C	5	4	24.0	> 50
D	5	4	19.0	>120
E	6	3	18.0	> 80
G	10	5	19.5	>130
H	5	5	6.8	>125
I	11	4	0.20	> 95
J	5	4	4.8	> 40
K	6	3	58.0	> 50
M	6	4	0.08	> 40
N	5	3	0.32	> 40
O	5	3	6.9	40
P	5	4	3.6	65
Q	5	3	27.0	50
R	5	3	5.7	> 80
S	5	3	10.0	> 65
T	5	3	1.9	> 40
U	4	4	9.8	> 50
V	6	4	2.7	> 65
W	5	3	20.5	> 50
X	6	3	11.3	> 65
Z	5	3	31.5	> 80

n_1 = number of animals/dose;

n_2 = number of the doses taken into consideration for the calculation of the ED₅₀.

TABLE II

Substance	Activity on the β_1 -receptors			LD ₅₀ mg/kg i.v.
	n ₁	n ₂	ED ₅₀ γ /kg i.v.	
A	3	5	18.5	34.5
B	—	—	—	27.2
C	4	5	14.0	57.0
D	4	5	8.0	35.1
E	4	5	13.5	69.2
F	3	5	35.0	—
G	5	5	11.5	36.5
H	—	—	—	36.5
I	5	5	0.74	60.0
J	—	—	—	67.0
K	4	4	1.5	26.4
L	6	5	1.3	45.2
M	5	3	0.27	66.4
N	6	4	0.022	58.4
O	5	5	0.070	61.8
P	5	5	0.086	62.0
Q	6	5	0.76	53.4
R	6	6	0.32	40.4
S	5	4	0.76	81.8
T	5	4	0.45	33.7
U	6	4	0.70	39.1
V	6	4	1.4	13.5
W	6	5	0.078	38.5
X	6	4	0.92	166.0
Y	5	4	2.8	35.8
Z	6	4	4.5	42.4

n₁ = number of animals/dosen₂ = number of doses

TABLE III

Substance	Blocking activity on the β_1 -receptors			Blocking activity on the β_2 -receptors			LD ₅₀ mg/kg i.v.
	n ₁	n ₂	ED ₅₀ γ /kg i.v.	n ₁	n ₂	ED ₅₀ γ /kg i.v.	
A-d(+)	7	4	8.4	5	1	>2 000	37.2
D-d(+)	6	4	6.2	5	1	>2 000	34.2
E-d(+)	8	3	1.5	4	1	>2 000	—
G-d(+)	8	4	12.5	4	1	>2 000	33.2

n₁ = number of animals

n₂ = number of doses tested per number of animals

According to a further feature of the present invention there are provided pharmaceutical compositions comprising as active ingredient at least one compound of formula I or Ia as hereinbefore defined or a physiologically compatible acid or basic addition salt thereof in association with a pharmaceutical carrier or excipient.

The compositions may, for example, be presented in a form suitable for oral, rectal or parenteral administration. Thus for example compositions for oral administration may be solid or liquid and may take the form of tablets, coated tablets, and gelatine capsules, such compositions comprising carriers or excipients conventionally used in the pharmaceutical art.

For parenteral administration, the carrier may be a parenterally acceptable liquid, such as sterile water, a parenterally acceptable oil, e.g. arachis oil, contained in ampoules. For rectal administration compositions may take the form of suppositories, the carrier comprising a suppository base.

Advantageously the compositions may be formulated as dosage units. Each dosage unit preferably contains from 1 to 100 γ , preferably however from 5 to 50 γ of active ingredient.

The following Examples serve to illustrate the preparation of compounds according to the invention and of pharmaceutical compositions containing the same.

Example 1.

1-(4-Amino-3-bromo-5-fluoro-phenyl)-2-diethylamino-ethanol

3.4 g of 4'-amino-3'-bromo-2-diethylamino-5'-fluoroacetophenone hydrochloride were dissolved in 20 ml of methanol. A solution of 570 mg of sodium borohydride in 5 ml of water were slowly added whilst stirring at room temperature. The pH was adjusted to between 3 and 6 by simultaneous addition of 3N hydrochloric acid. After the addition of the sodium borohydride solution was completed, the mixture was stirred for 30 minutes at room temperature. Subsequently, 3N hydrochloric acid was added until a pH of 1 was reached. The acidic solution was extracted twice with chloroform and the chloroform extracts were thrown away. The aqueous solution was made alkaline with ammonia and exhaustively extracted with chloroform. The chloroform extracts were combined, dried over sodium sulfate and evaporated to dryness in vacuo. A colorless oil was obtained, which was dissolved in ethyl acetate. Ethereal hydrochloric acid was added and a colorless precipitate was obtained, which was suction filtered and dissolved in water. The aqueous solution was made alkaline with sodium hydroxide and extracted with chloroform. The chloroform extract was washed with water, dried over sodium sulfate and evaporated in vacuo. A colorless oil was obtained.

Proof of structure by NMR-spectra (CDCl₃): 0.85 to 1.2 ppm, triplet [6 protons, N(CH₂-CH₂)₂]; 2.4 to 2.9 ppm, multiplet [6 protons, N(CH₂-) ₃]; 4.15 ppm, singlet (2 protons NH₂); 4.4 to 4.7 ppm, multiplet (1 proton, CH); 4.85 ppm singlet (1 proton, OH); 6.9 to 7.4 ppm, multiplet (2 aromatic protons).

Example 2.

1 - (4 - Amino - 3 - chloro - 5 - trifluoromethyl - phenyl) - 2 - tert. - butylamino-ethanol hydrochloride

80 g of 4'-amino-2-tert.-butylamino-3'-chloro-5'-trifluoromethyl-acetophenone hydrochloride (decomposition between 223 and 231°C) were dissolved in 500 ml of methanol and cooled to -15°C. 9.5 g of sodium borohydride were added in small amounts over a period of one hour whilst stirring at temperatures from -5 to -15°C. One hour later the mixture was acidified with 2N hydrochloric acid at -15°C and the methanol was removed in vacuo. The remaining aqueous solution was made alkaline with 2N ammonia and extracted with ethyl acetate. The organic layer was washed with water, dried and 50 ml of 4.5N isopropanolic hydrochloric acid were added. The title compound precipitated from the solution and this precipitate was suction filtered and washed with ethyl acetate and ether.

M.p.: 205 to 207°C (decomp.).

By concentration of the mother liquor a further yield of the product was obtained.

Example 3.

1-(4-Amino-3-bromo-5-cyano-phenyl)-2-dimethylamino-ethanol hydrochloride

15.2 g of 4'-amino-3'-bromo-5'-cyano-2-dimethylamino-acetophenone were dissolved in 300 ml of methanol and a solution of 10 g of sodium borohydride in 100 ml of water was added dropwise at room temperature whilst stirring. The solution was allowed to stand overnight, the excess of sodium borohydride was destroyed by acidification with hydrochloric acid, the methanol was evaporated in vacuo and the residue obtained was dissolved in water. The solution was made alkaline with ammonia, extracted three times with about 150 ml of chloroform each time, the chloroform solution was washed twice with a small quantity of water, dried over sodium sulfate and evaporated to dryness.

The residue was dissolved in ethanol and weakly acidified with alcoholic hydrochloric acid, whereupon the 1-(4-amino-3-bromo-5-cyano-phenyl)-2-dimethylamino-ethanol hydrochloride was obtained. The reaction product was recrystallized from ethanol.

M.p.: 187 to 190°C.

Example 4.

1 - (4 - Amino - 3 - chloro - 5 - trifluoromethyl - phenyl) - 2 - tert. - pentylamino - ethanol hydrochloride

0.37 g of 1-(4-amino-3-trifluoromethyl-phenyl)-2-tert.-pentylamino-ethanol hydrobromide and 0.2 ml of pyridine were dissolved in 30 ml of tetrahydrofuran and cooled to 0°C. 0.3 g of iodosobenzene dichloride were added, the mixture was kept at 0°C for 2 hours and a further 0.1 g of iodosobenzene dichloride were added. After 20 hours at about 4°C the solution was evaporated and distributed between ethyl acetate and water. The aqueous extract was made alkaline with 2N ammonia, and the solution was again extracted with ethyl acetate. The organic layer was washed with water, dried and a few drops of 4N hydrochloric acid in isopropanol were added. The title compound precipitated from the solution and this precipitate was suction filtered and washed with ether.

M.p.: 176-178°C (decomp.).

Example 5.

1 - (4 - Amino - 3 - bromo - 5 - methyl - phenyl) - 2 - tert. - butylamino - ethanol dihydrochloride

2.6 g of 1-(4-amino-3-methyl-phenyl)-2-tert.-butylamino-ethanol hydrochloride were dissolved in 90 ml of 50% acetic acid and 1.6 g of bromine, dissolved in 5 ml of glacial acetic acid and 1 ml of water, were added at 0 to 5°C. After 15 minutes the excess of bromine was destroyed with sodium hydrogen sulfite. The reaction mixture was diluted with water and insoluble by-products were removed by filtration through charcoal. The filtrate was made alkaline with sodium hydroxide solution whilst cooling and the solution was extracted with chloroform. After drying over sodium sulfate, the chloroform solution was filtered through charcoal and evaporated to dryness in vacuo. The oily base thus obtained was

dissolved in isopropanol and acidified with isopropanolic hydrochloric acid. After evaporating and cooling, the precipitated 1-(4-amino-3-bromo-5-methyl-phenyl)-2-tert.-butylamino-ethanol dihydrochloride was suction filtered and recrystallized from isopropanol/ether.

M.p.: 148°C.

Example 6.

1-(4-Amino-5-bromo-3-hydroxymethyl-phenyl)-2-tert.-butylamino-ethanol

2.0 g of 1-(4-amino-3-hydroxymethyl-phenyl)-2-tert.-butylamino-ethanol were dissolved in 18 ml of glacial acetic acid and 2 ml of water and 1.3 g of bromine were added dropwise. Subsequently the reaction mixture was evaporated, the residue was dissolved in water, made alkaline with 2N ammonia and extracted four times with chloroform. The organic layer was dried over sodium sulfate and evaporated and the residue was purified over a silica gel column with ethanol and eluent. The fractions containing the substance were combined and evaporated in vacuo. After mixing the evaporation residue with ether, the title compound crystallized after a short time.

M.p.: 121—124°C.

Example 7.

1-(4-Amino-3-trifluoromethyl-phenyl)-2-tert.-butylamino-ethanol

5.05 g of 1-(4-acetyl-amino-3-trifluoromethyl-phenyl)-2-tert.-butylamino-ethanol hydrochloride were refluxed for 3 hours in a mixture of 50 ml of ethanol and 50 ml of 4N sodium hydroxide solution. The ethanol was removed in vacuo and the precipitated crystals were suction filtered.

M.p.: 145 to 147°C (from ethanol/water).

For conversion into the monohydrochloride the product was dissolved in the calculated quantity of 1N hydrochloric acid; the mixture was evaporated to dryness in vacuo and the solid residue was recrystallized from isopropanol/ether.

M.p.: of the hydrochloride: 172—174°C (decomp.).

Example 8.

1-(4-Amino-3-trifluoromethyl-phenyl)-2-(N-benzyl-N-tert.-butyl)-amino-ethanol

0.5 g of 1-(4-acetyl-amino-3-trifluoromethyl-phenyl)-2-(N-benzyl-N-tert.-butyl)-amino-ethanol (m.p.: 98—100°C) were refluxed for 1½ hours in a mixture of 10 ml of ethanol and 10 ml of 4N sodium hydroxide solution. The ethanol was distilled off in vacuo and the aqueous layer was extracted with ethyl acetate. The organic extract was washed with water, dried and evaporated in vacuo. Thin-layer chromatography indicated 1 product only in the oily residue (silica gel: chloroform:methanol=19:1. R_F-value: about 0.5).

Example 9.

1-(4-Amino-3-carboxy-phenyl)-2-tert.-butylamino-ethanol.

0.3 g of 1-(4-acetyl-amino-3-carboxy-phenyl)-2-tert.-butylamino-ethanol were dissolved in 6 ml of ethanol and 4 ml of concentrated hydrochloric acid were added. The mixture was heated for 40 minutes at 70°C, evaporated to dryness in vacuo and the product was purified by column chromatography (silica gel; chloroform:methanol = 3:2 as eluent). The product was shown to be 1-(4-amino-3-carboxy-phenyl)-2-tert.-butylamino-ethanol by NMR-spectroscopy (CD₃OD): 1.4 ppm, singlet [9 protons, C(CH₃)₃]; 3.3 ppm, multiplet (2 protons, CH₂); 4.5 ppm, multiplet (1 proton, CH); 6.8—7.8 ppm, multiplet (3 aromatic protons).

Example 10.

1-(4-Amino-3-trifluoromethyl-phenyl)-2-tert.-butylamino-ethanol.

0.45 g of 1-(4-amino-3-trifluoromethyl-phenyl)-2-(N-benzyl-N-tert.-butyl)-amino-ethanol were dissolved in a hydrogenation vessel in 10 ml of methanol and 1.4 ml of 1N hydrochloric acid. The solution was hydrogenated in the presence of 50 mg of palladium/charcoal (10%) as catalyst until 1 mol of hydrogen was absorbed. The catalyst was removed by filtration, the solution was evaporated in vacuo and the residue was distributed between ethyl acetate and 2N ammonia. The organic layer was washed with water, dried and again evaporated in vacuo. The residue was crystallized from ethanol/water.

M.p.: 145 to 147°C.

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Example 11.

1 - (4-Amino-3-chloro-5-trifluoromethyl-phenyl)-2-tert.-butylamino-ethanol hydrochloride.

0.76 g of 1-(4-amino-3-chloro-5-trifluoromethyl-phenyl)-2-(N-benzyl-N-tert.-butyl)-amino-ethanol were dissolved in a hydrogenation vessel in 20 ml of methanol and 1.95 ml of 1N hydrochloric acid. The solution was hydrogenated in the presence of 80 mg of palladium/charcoal (10%) as catalyst until 1 mol of hydrogen had been absorbed. Afterwards the catalyst was removed by filtration and the filtrate was evaporated to dryness in vacuo. The oily residue was purified by column chromatography (silica gel; chloroform:methanol:concentrated ammonia = 80:20:1 as eluent). The fractions containing the title compound were combined and the solvent was removed in vacuo. The crystalline base of the title compound remained and was converted into the hydrochloride with the calculated quantity of 1.07N hydrochloric acid in isopropanol. The hydrochloride was recrystallized from ethyl acetate/ether.

M.p.: 205 to 207°C (decomp.).

Example 12.

1-(4-Amino-3-chloro-5-methyl-phenyl)-2-tert.-butylamino-ethanol dihydrochloride.

0.7 g of 1-(4-amino-3-chloro-5-methyl-phenyl)-2-(N-benzyl-N-tert.-butyl)-amino-ethanol hydrochloride were dissolved in 50 ml of methanol and 0.92 ml of 2N hydrochloric acid and the solution was hydrogenated in the presence of 50 mg of palladium on charcoal (10%). The hydrogenation was interrupted after absorption of 41 ml of hydrogen; the catalyst was filtered off and the filtrate was evaporated to dryness in vacuo. The residue was dissolved in ethanol and precipitated as the dihydrochloride by the addition of ether.

M.p.: >95°C (decomposition).

Example 13.

1-(4-Amino-3-methoxy-phenyl)-2-tert.-butylamino-ethanol.

8.5 g of 1-(4-amino-3-methoxy-phenyl)-2-(N-benzyl-N-tert.-butyl)-amino-ethanol were dissolved in 150 ml of methanol and acidified to a pH of 6 with ethanolic hydrochloric acid. 1 g of palladium on charcoal (10%) was added to this solution and the mixture was hydrogenated in a shaking device at room temperature and at atmospheric pressure until the calculated quantity of hydrogen had been absorbed. After the catalyst had been removed by suction filtration, the mixture was concentrated. The precipitated crystals were suction filtered and recrystallized from ethanol. The colorless crystals of the hydrochloric of the title compound melted at 174—176°C (decomp.).

Example 14.

1 - (4 - Amino - 3 - trifluoromethyl-phenyl) - 2 - cyclopropylamino-ethanol dihydrochloride.

4.1 g of 1-(4-amino-3-bromo-5-trifluoromethyl-phenyl)-2-cyclopropyl-amino-ethanol were dissolved in a hydrogenation vessel in 200 ml of methanol and 2 g of palladium oxide/barium sulfate (5%) were added as catalyst. The mixture was hydrogenated until 1 mol of hydrogen had been absorbed; the catalyst was filtered off and the filtrate was evaporated to dryness in vacuo. The residue was dissolved in water, made alkaline with 2N ammonia, and the aqueous layer was extracted with ethyl acetate. The organic extracts were washed with water, dried and evaporated again. The solid residue was dissolved in isopropanol and 2 equivalents of 4N hydrochloric acid in isopropanol were added to the solution. The dihydrochloride of the title compound crystallized out and the crystals were suction filtered and washed with isopropanol and ether.

M.P.: 141.5 to 142°C (decomp.).

Example 15.

1-(4-Amino-3-trifluoromethyl-phenyl)-2-tert.-pentylamino-ethanol hydrobromide.

5 g of 1-(4-amino-3-bromo-5-trifluoromethyl-phenyl)-2-tert.-pentylamino-ethanol hydrochloride were distributed between ethyl acetate and 2N ammonia. The organic layer was dried and evaporated in vacuo. The remaining base was dissolved in 100 ml of methanol in a hydrogenation vessel and 2.5 g of palladium oxide/barium sulfate (5%) were added as catalyst. The mixture was hydrogenated until 1 mol of hydrogen had been absorbed. After the catalyst had been removed by filtration, the filtrate was evaporated in vacuo and the solid residue was recrystallized from isopropanol. The hydrobromide of the title compound was obtained and the crystals melted at 174 to 175°C (decomp.).

Example 16.

1-(4-Amino-3-methyl-phenyl)-2-(N-benzyl-N-tert.-butyl)-amino-ethanol.

4.5 g of 1-(4-amino-3-bromo-5-methyl-phenyl)-2-(N-benzyl-N-tert.-butyl)-amino-ethanol were dissolved in 100 ml of methanol and 11.6 ml of 2N hydrochloric acid were added. The mixture was hydrogenated in the presence of 250 mg of palladium on charcoal (5%). After absorption of 315 ml of hydrogen the hydrogenation was interrupted, the catalyst was removed by suction filtration, the solvent was distilled off in vacuo, the residue was dissolved in water and the base was liberated with ammonia. Subsequently the base was extracted with chloroform and purified chromatographically by passing it through a silica gel column. The title compound had a melting point between 96 and 98°C and the dihydrochloride was obtained therefrom (m.p.: >145°C decomposition).

Example 17.

1-(4-Amino-3-aminomethyl-phenyl)-2-tert.-butylamino-ethanol.

2.0 g of 6-(2-tert.-butylamino-1-hydroxy-ethyl)-3,4-dihydro-2-methyl-quinazoline were dissolved in 80 ml of pentyl alcohol. 7.5 g of sodium were added in small quantities over a period of one hour and the mixture was slowly heated up to the boiling temperature after a further $\frac{1}{2}$ hour. After refluxing for 5 hours, the solution was cooled and 100 ml of water were added. 60 ml of concentrated hydrochloric acid were then added dropwise and the reaction mixture was stirred for 2 hours and extracted twice with ether. The acidic layer was made alkaline with 10N sodium hydroxide solution, the base was extracted with ether, and the ethereal layer was dried over sodium sulfate and evaporated. The crude product was purified by column chromatography over silica gel with methanol:chloroform (2:1).

Evaporation of the selected fractions yielded 1-(4-amino-3-aminomethyl-phenyl)-2-tert.-butylamino-ethanol as an amorphous substance.

Elementary analysis:

$C_{13}H_{23}N_3O$ (237.34)

Calculated: C 65.78 H 9.76 N 17.70

Found: 65.50 9.61 17.58

Example 18.

1-(4-Amino-3-bromo-5-carbamoyl-phenyl)-2-dimethylamino-ethanol.

2 g of 1-(4-amino-3-bromo-5-cyano-phenyl)-2-dimethylamino-ethanol were boiled for 4 hours with a solution of 5 g of sodium hydroxide in 120 ml of 50% ethanol. The ethanol was distilled off and the remaining aqueous solution was diluted with 100 ml of water and extracted three times with chloroform. The chloroform layer was dried over sodium sulfate and evaporated in vacuo. The obtained residue was recrystallized from chloroform.

M.p.: >93°C (decomp.).

Example 19.

1-(4-Amino-3-bromo-5-carboxy-phenyl)-2-dimethylamino-ethanol.

2 g of 1-(4-amino-3-bromo-5-cyano-phenyl)-2-dimethylamino-ethanol were boiled for 4 hours with a solution of 5 g of sodium hydroxide in 120 ml of 50% ethanol. The ethanol was distilled off and the remaining aqueous solution was diluted with 100 ml of water and extracted three times with chloroform. The aqueous layer was neutralized and evaporated to dryness. The residue was treated with ethanol, suction filtered and the filtrate was evaporated. The obtained residue was again treated with ethanol and suction filtered. Evaporation of this last filtrate yielded a residue of 1-(4-amino-3-bromo-5-carboxy-phenyl)-2-dimethylamino-ethanol, which had a melting point between 240 and 250°C (decomp.). Its structure was established from its IR- and UV-spectra:

IR (KBr): COO^- at 1620 cm^{-1} ; NH^+ at $2000-3500\text{ cm}^{-1}$.

UV (ethanol): maxima at 220 and 330-340 nm, shoulder at 250 nm.

Example 20.

5-(4-Amino-3-chloro-5-trifluoromethyl-phenyl)-3-tert.-butyl-1,3-oxazolidine.

1.35 g of 1-(4-amino-3-chloro-5-trifluoromethyl-phenyl)-2-tert.-butyl-amino-ethanol were dissolved in 30 ml of benzene and 1.2 ml of 40% aqueous formaldehyde solution were added. The mixture was evaporated to half the volume at normal pressure, 35 ml of benzene were added and the reaction mixture was refluxed for 5 hours. A further 1.5 ml of formaldehyde solution were then added and the above-described process was repeated 3 times. The mixture was then evaporated to dryness in vacuo, dissolved in ether and the insoluble residue

was filtered off. The filtrate was weakly acidified with ethereal hydrochloric acid and the precipitated product was crystallized by trituration. The crystals were suction filtered and recrystallized from acetone/ether. The obtained hydrochloride of the above mentioned compound melted at 163 to 165°C (decomp.).

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Example 21.

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1-(4-Amino-3-fluoro-phenyl)-2-tert.-butylamino-ethanol.

M.p. of the hydrochloride: 196 to 197°C (decomp.).

Prepared according to process a) from 4'-amino-2-tert.-butylamino-3'-fluoro-acetophenone hydrochloride and sodium borohydride analogously to Example 1.

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Example 22.

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1-(4-Amino-3-bromo-5-fluoro-phenyl)-2-tert.-butylamino-ethanol.

M.p. of hydrochloride: 207 to 208°C (decomp.).

Prepared according to process a) from 4'-amino-3'-bromo-2-tert.-butylamino-5'-fluoro-acetophenone hydrochloride and sodium borohydride analogously to Example 1.

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Example 23.

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1-(4-Amino-3-chloro-5-trifluoromethyl-phenyl)-2-cyclobutylamino-ethanol.

M.p. of the hydrochloride: 177 to 178°C.

Prepared according to process a) from 4'-amino-3'-chloro-2-cyclobutylamino-5'-trifluoromethyl-acetophenone hydrochloride and sodium borohydride analogously to Example 2.

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Example 24.

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1-(4-Amino-3-fluoro-phenyl)-2-cyclopropylamino-ethanol.

M.p. of the hydrochloride: 157 to 158°C (decomp.).

Prepared according to process c) from 1-(4-acetylamino-3-fluoro-phenyl)-2-cyclopropylamino-ethanol and sodium hydroxide solution analogously to Example 7.

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Example 25.

1-(4-Amino-3-fluoro-phenyl)-2-tert.-butylamino-ethanol.

M.p. of the hydrochloride: 196 to 197°C (decomp.).

Prepared according to process c) from 1-(4-amino-3-fluoro-phenyl)-2-(N-benzyl-N-tert.-butyl)-amino-ethanol hydrochloride and catalytically activated hydrogen analogously to Example 13.

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Example 26.

2-Ethylamino-1-(4-amino-3-chloro-5-fluoro-phenyl)-ethanol.

M.p. of the hydrochloride: 186 to 188°C (decomp.).

Prepared according to process a) from 2-ethylamino-4'-amino-3'-chloro-5'-acetophenone and sodium borohydride analogously to Example 1.

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Example 27.

1-(4-Amino-3-chloro-5-fluoro-phenyl)-2-isopropylamino-ethanol.

M.p. of the hydrochloride: 152 to 154°C (decomp.).

Prepared according to process a) from 4'-amino-3'-chloro-5'-fluoro-2-isopropylamino-acetophenone hydrochloride and sodium borohydride analogously to Example 1.

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Example 28.

1-(4-Amino-3-chloro-5-fluoro-phenyl)-2-cyclopropylamino-ethanol.

M.p. of the hydrochloride: 175 to 177°C (decomp.).

Prepared according to process a) from 4'-amino-3'-chloro-2-cyclopropylamino-5'-fluoro-acetophenone hydrochloride and sodium borohydride analogously to Example 1.

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Example 29.

1-(4-Amino-3-chloro-5-fluoro-phenyl)-2-tert.-butylamino-ethanol.

M.p. of the hydrochloride: 206 to 208°C (decomp.).

Prepared according to process a) from 4'-amino-2-tert.-butylamino-3'-chloro-5'-fluoro-acetophenone hydrochloride and sodium borohydride analogously to Example 1.

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Example 30.

1-(4-Amino-3-chloro-5-fluoro-phenyl)-2-tert.-pentylamino-ethanol.

M.p. of the hydrochloride: 187 to 188°C (decomp.).

Prepared according to process a) from 4'-amino-3'-chloro-5'-fluoro-2-tert.-pentylamino-acetophenone hydrochloride and sodium borohydride analogously to Example 1.

Example 31.

1-(4-Amino-3-chloro-5-fluoro-phenyl)-2-[1-(3,4-methylenedioxyphenyl)-2-propylamino]-ethanol.

M.p. of the hydrochloride: 119 to 121°C (decomp.).

Prepared according to process a) from 4'-amino-3'-chloro-5'-fluoro-2-[1-(3,4-methylenedioxyphenyl)-2-propylamino]-acetophenone and sodium borohydride analogously to Example 1.

Example 32.

1-(4-Amino-3-chloro-5-fluoro-phenyl)-2-dimethylamino-ethanol.

M.p. of the hydrochloride: 208 to 210°C (decomp.).

Prepared according to process a) from 4'-amino-3'-chloro-2-dimethylamino-5'-fluoro-acetophenone hydrochloride and sodium borohydride analogously to Example 1.

Example 33.

1-(4-Amino-3-chloro-5-fluoro-phenyl)-2-diethylamino-ethanol.

M.p.: 39 to 41°C.

Prepared according to process a) from 4'-amino-3'-chloro-2-diethylamino-5'-fluoro-acetophenone hydrochloride and sodium borohydride analogously to Example 1.

Example 34.

2-Ethylamino-1-(4-amino-3-bromo-5-fluoro-phenyl)-ethanol.

M.p.: of the hydrochloride: 167 to 169°C (decomp.).

Prepared according to process a) from 2-ethylamino-4'-amino-3'-bromo-5'-fluoro-acetophenone hydrochloride and sodium borohydride analogously to Example 1.

Example 35.

1-(4-Amino-3-bromo-5-fluoro-phenyl)-2-isopropylamino-ethanol.

M.p. of the hydrochloride: 171 to 173°C (decomp.).

Prepared according to process a) from 4'-amino-3'-bromo-5'-fluoro-2-isopropylamino-acetophenone hydrochloride and sodium borohydride analogously to Example 1.

Example 36.

1-(4-Amino-3-bromo-5-fluoro-phenyl)-2-cyclopropylamino-ethanol.

M.p. of the hydrochloride: 185 to 187°C (decomp.).

Prepared according to process a) from 4'-amino-3'-bromo-2-cyclopropylamino-5'-fluoro-acetophenone and sodium borohydride analogously to Example 1.

Example 37.

1-(4-Amino-3-bromo-5-fluoro-phenyl)-2-(hydroxy-tert.-butylamino)-ethanol.

M.p.: 122 to 125°C.

Prepared according to process a) from 4'-amino-3'-bromo-5'-fluoro-2-(hydroxy-tert.-butylamino)-acetophenone hydrochloride and sodium borohydride analogously to Example 1.

Example 38.

1-(4-Amino-3-bromo-5-fluoro-phenyl)-2-tert.-pentylamino-ethanol.

M.p. of the hydrochloride: 185 to 187°C (decomp.).

Prepared according to process a) from 4'-amino-3'-bromo-5'-fluoro-2-tert.-pentylamino-acetophenone hydrochloride and sodium borohydride analogously to Example 1.

Example 39.

1-(4-Amino-3-bromo-5-fluoro-phenyl)-2-[1-(3,4-methylenedioxyphenyl)-2-propylamino]-ethanol.

M.p.: 126 to 128°C.

Prepared according to process a) from 4'-amino-3'-bromo-5'-fluoro-2-[1-(3,4-

methylenedioxy-phenyl)-2-propylamino]-acetophenone and sodium borohydride analogously to Example 1.

Example 40.

1-(4-Amino-3-chloro-5-trifluoromethyl-phenyl)-2-isopropylamino-ethanol.

M.p.: 104 to 106°C.

M.p. of the hydrochloride: 185 to 187°C.

Prepared according to process a) from 4'-amino-3'-chloro-2-isopropylamino-5'-trifluoromethyl-acetophenone hydrochloride and sodium borohydride analogously to Example 2.

Example 41.

1-(4-Amino-3-chloro-5-trifluoromethyl-phenyl)-2-cyclopropylamino-ethanol.

M.p.: 138 to 139°C.

Prepared according to process a) from 4'-amino-3'-chloro-2-cyclopropylamino-5'-trifluoromethyl-acetophenone and sodium borohydride analogously to Example 2.

Example 42.

1-(4-Amino-3-chloro-5-trifluoromethyl-phenyl)-2-(hydroxy-tert.-butylamino)-ethanol.

M.p. of the hydrochloride: 219 to 220°C.

Prepared according to process a) from 4'-amino-3'-chloro-2-(hydroxy-tert.-butylamino)-5'-trifluoromethyl-acetophenone hydrochloride and sodium borohydride analogously to Example 2.

Example 43.

1-(4-Amino-3-chloro-5-trifluoromethyl-phenyl)-2-tert.-pentylamino-ethanol.

M.p. of the hydrochloride: 176 to 178°C (decomp.).

Prepared according to process a) from 4'-amino-3'-chloro-2-tert.-pentylamino-5'-trifluoromethyl-acetophenone hydrochloride and sodium borohydride analogously to Example 2.

Example 44.

1-(4-Amino-3-chloro-5-trifluoromethyl-phenyl)-2-[2-methyl-4-hydroxy-butyl-(2)-amino]-ethanol.

M.p. of the hydrochloride: 148 to 150°C (decomp.).

Prepared according to process a) from 4'-amino-3'-chloro-2-[2-methyl-4-hydroxy-butyl-(2)-amino]-5'-trifluoromethyl-acetophenone and sodium borohydride analogously to Example 2.

Example 45.

2-[3-Ethynyl-pentyl-(3)-amino]-1-(4-amino-3-chloro-trifluoromethyl-phenyl)-ethanol.

M.p. of the hydrochloride: 185 to 187°C (decomp.).

Prepared according to process a) from 2-[3-ethynyl-pentyl-(3)-amino]-4'-amino-3'-chloro-5'-trifluoromethyl-acetophenone hydrochloride and sodium borohydride analogously to Example 2.

Example 46.

1-(4-Amino-3-chloro-5-trifluoromethyl-phenyl)-2-[1-(3,4-methylenedioxy-phenyl)-2-propylamino]-ethanol.

M.p. of the hydrochloride: 206 to 207°C (decomp.).

Prepared according to process a) from 4'-amino-3'-chloro-2-[1-(3,4-methylenedioxy-phenyl)-2-propylamino]-5'-trifluoromethyl-acetophenone hydrochloride and sodium borohydride analogously to Example 2.

Example 47.

1-(4-Amino-3-chloro-5-trifluoromethyl-phenyl)-2-dimethylamino-ethanol.

M.p. of the hydrochloride: 162 to 164°C.

Prepared according to process a) from 4'-amino-3'-chloro-2-dimethylamino-5'-trifluoromethyl-acetophenone hydrochloride and sodium borohydride analogously to Example 2.

Example 48.

1-(4-Amino-3-chloro-5-trifluoromethyl-phenyl)-2-(N-methyl-ethylamino)-ethanol.

M.p.: 48 to 49°C.

Prepared according to process a) from 4'-amino-3'-chloro-2-(N-methylethyl-

amino)-5'-trifluoromethyl-acetophenone hydrochloride and sodium borohydride analogously to Example 2.

Example 49.

1-(4-Amino-3-chloro-5-trifluoromethyl-phenyl)-2-diethylamino-ethanol.

M.p. of the hydrochloride: 149 to 151°C.

Prepared according to process a) from 4'-amino-3'-chloro-2-diethylamino-5'-trifluoromethyl-acetophenone hydrochloride and sodium borohydride analogously to Example 2.

Example 50.

1-(4-Amino-3-chloro-5-trifluoromethyl-phenyl)-2-(N-benzyl-N-tert-butyl)-amino-ethanol.

Oil; pure by thin-layer chromatography (SiO₂; chloroform:methanol = 15:1; R_F-value: about 0.75).

Prepared according to process a) from 2'-amino-2-(N-benzyl-N-tert-butyl)-amino-3'-chloro-5'-trifluoromethyl-acetophenone and sodium borohydride analogously to Example 2.

Example 51.

1-(4-Amino-3-bromo-5-trifluoromethyl-phenyl)-2-isopropylamino-ethanol.

M.p.: 102 to 103°C.

M.p. of the hydrochloride: 177 to 179°C (decomp.).

Prepared according to process a) from 4'-amino-3'-bromo-2-isopropylamino-5'-trifluoromethyl-acetophenone hydrochloride and sodium borohydride analogously to Example 2.

Example 52.

1-(4-Amino-3-bromo-5-trifluoromethyl-phenyl)-2-cyclopropylamino-ethanol.

M.p.: 141.5 to 142.5°C.

M.p. of the hydrochloride: 195 to 195.5°C (decomp.).

Prepared according to process a) from 4'-amino-3'-bromo-2-cyclopropylamino-5'-trifluoromethyl-acetophenone hydrochloride and sodium borohydride analogously to Example 2.

Example 53.

1-(4-Amino-3-bromo-5-trifluoromethyl-phenyl)-2-tert-butylamino-ethanol.

M.p.: 85 to 87°C.

M.p. of the hydrochloride: 205 to 206°C (decomp.).

Prepared according to process a) from 4'-amino-3'-bromo-2-tert-butylamino-5'-trifluoromethyl-acetophenone hydrochloride and sodium borohydride analogously to Example 2.

Example 54.

1-(4-Amino-3-bromo-5-trifluoromethyl-phenyl)-2-cyclobutylamino-ethanol.

M.p. of the hydrochloride: 189 to 191°C (decomp.).

Prepared according to process a) from 4'-amino-3'-bromo-2-cyclobutylamino-5'-trifluoromethyl-acetophenone hydrochloride and sodium borohydride analogously to Example 2.

Example 55.

1-(4-Amino-3-bromo-5-trifluoromethyl-phenyl)-2-tert-pentylamino-ethanol.

M.p. of the hydrochloride: 166.5 to 168°C (decomp.).

Prepared according to process a) from 4'-amino-3'-bromo-2-tert-pentylamino-5'-trifluoromethyl-acetophenone hydrochloride and sodium borohydride analogously to Example 2.

Example 56.

2-[3-Ethynyl-pentyl-(3)-amino]-1-(4-amino-3-bromo-trifluoromethyl-phenyl)-ethanol.

M.p. of the hydrochloride: 189 to 190°C (decomp.).

Prepared according to process a) from 2-[3-ethynyl-pentyl-(3)-amino]-4'-amino-3'-bromo-5'-trifluoromethyl-acetophenone hydrochloride and sodium borohydride analogously to Example 2.

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Example 57.

1-(4-Amino-3-bromo-5-trifluoromethyl-phenyl)-2-dimethylamino-ethanol.

M.p. of the hydrochloride: 149 to 151°C.

Prepared according to process a) from 4'-amino-3'-bromo-2-dimethylamino-5'-trifluoromethyl-acetophenone hydrochloride and sodium borohydride analogously to Example 2.

Example 58.

1-(4-Amino-3-bromo-5-trifluoromethyl-phenyl)-2-(N-methyl-ethylamino)-ethanol.

M.p.: 52.5 to 53.5°C.

Prepared according to process a) from 4'-amino-3'-bromo-2-(N-methylethylamino)-5'-trifluoromethyl-acetophenone hydrochloride and sodium borohydride analogously to Example 2.

Example 59.

1-(4-Amino-3-bromo-5-trifluoromethyl-phenyl)-2-diethylamino-ethanol.

M.p. of the hydrochloride: 159 to 160°C.

Prepared according to process a) from 4'-amino-3'-bromo-2-diethylamino-5'-trifluoromethyl-acetophenone hydrochloride and sodium borohydride analogously to Example 2.

Example 60.

1-(4-Amino-3-methyl-phenyl)-2-tert.-butylamino-ethanol.

M.p. of the hydrochloride: 108°C (decomp.).

Prepared according to process a) from 4'-amino-3'-methyl-2-tert.-butylamino-acetophenone and sodium borohydride analogously to Example 3.

Example 61.

1-(4-Amino-3-chloro-5-methyl-phenyl)-2-methylamino-ethanol.

M.p.: 95 to 96°C.

Prepared according to process a) from 4'-amino-3'-chloro-5'-methyl-2-methylamino-acetophenone and sodium borohydride analogously to Example 3.

Example 62.

2-Ethylamino-1-(4-amino-3-chloro-5-methyl-phenyl)-ethanol.

M.p.: 107 to 108.5°C.

Prepared according to process a) from 2-ethylamino-4'-amino-3'-chloro-5'-methyl-acetophenone and sodium borohydride analogously to Example 3.

Example 63.

1-(4-Amino-3-chloro-5-methyl-phenyl)-2-dimethylamino-ethanol.

M.p. of the hydrochloride: 120 to 125°C (decomp.).

Prepared according to process a) from 4'-amino-3'-chloro-2-dimethylamino-5'-methyl-acetophenone hydrochloride and sodium borohydride analogously to Example 1.

Example 64.

1-(4-Amino-3-chloro-5-methyl-phenyl)-2-(N-methyl-ethylamino)-ethanol.

M.p. of the hydrochloride: 93 to 96°C.

Prepared according to process a) from 4'-amino-3'-chloro-5'-methyl-2-(N-methyl-ethylamino)-acetophenone hydrochloride and sodium borohydride analogously to Example 1.

Example 65.

1-(4-Amino-3-chloro-5-methyl-phenyl)-2-diethylamino-ethanol.

M.p. of the hydrochloride: 118 to 122°C (decomp.).

Prepared according to process a) from 4'-amino-3'-chloro-2-diethylamino-5'-methyl-acetophenone hydrochloride and sodium borohydride analogously to Example 1.

Example 66.

1-(4-Amino-3-chloro-5-methyl-phenyl)-2-(N-benzyl-N-tert.-butyl)-amino-ethanol.

M.p. of the hydrochloride: 200 to 201°C.

Prepared according to process a) from 4'-amino-2-(N-benzyl-N-tert.-butyl)-amino-3'-chloro-5'-methyl-acetophenone and sodium borohydride analogously to Example 3.

Example 67.

1-(4-Amino-3-bromo-5-methyl-phenyl)-2-dimethylamino-ethanol.

M.p. of the hydrochloride: 123 to 125°C (decomp.).

Prepared according to process a) from 4'-amino-3'-bromo-2-dimethylamino-5'-methyl-acetophenone and sodium borohydride analogously to Example 3.

Example 68.

1-(4-Amino-3-bromo-5-methyl-phenyl)-2-diethylamino-ethanol.

M.p.: 48 to 50°C.

Prepared according to process a) from 4'-amino-3'-bromo-2-diethylamino-5'-methyl-acetophenone and sodium borohydride analogously to Example 3.

Example 69.

1-(4-Amino-3-bromo-5-methyl-phenyl)-2-(N-benzyl-N-tert.-butyl)-amino-ethanol.

Prepared according to process a) from 4'-amino-3'-bromo-2-(N-benzyl-N-tert.-butyl)-amino-5'-methyl-acetophenone and sodium borohydride analogously to Example 3.

The substance was purified by thin-layer chromatography (SiO₂; chloroform:methanol = 9:1, R_F-value: about 0.9).

Example 70.

1-(3-Ethyl-4-amino-5-chloro-phenyl)-2-diethylamino-ethanol.

M.p. of the hydrochloride: 121 to 124°C.

Prepared according to process a) from 3'-ethyl-4'-amino-5'-chloro-2-diethylamino-acetophenone and sodium borohydride analogously to Example 3.

Example 71.

1-(3-Ethyl-4-amino-5-bromo-phenyl)-2-diethylamino-ethanol.

M.p. of the hydrochloride: 132 to 134°C.

Prepared according to process a) from 3'-ethyl-4'-amino-5'-bromo-2-diethylamino-acetophenone and sodium borohydride analogously to Example 3.

Example 72.

1-(4-Amino-3-tert.-butyl-5-chloro-phenyl)-2-tert.-butylamino-ethanol.

M.p. of the hydrochloride: >218°C (decomp.).

Prepared according to process a) from 4'-amino-3'-tert.-butyl-2-tert.-butylamino-5'-chloro-acetophenone and sodium borohydride analogously to Example 1.

Example 73.

1-(4-Amino-3-hydroxymethyl-phenyl)-2-dimethylamino-ethanol.

Prepared from 4'-amino-2-dimethylamino-3'-hydroxymethyl-acetophenone and sodium borohydride analogously to Example 1.

Structure established by UV- and IR-spectra. UV (ethanol): maximum at 250 nm ($\epsilon=0.5$), shoulder at 275—305 nm ($\epsilon=0.11$); IR (CH₂Cl₂): OH at 3600 cm⁻¹; NH₂ at 3380 and 3450 cm⁻¹; N(CH₃)₂ at 2780 and 2830 cm⁻¹.

Example 74.

1-(4-Amino-3-hydroxymethyl-phenyl)-2-diethylamino-ethanol.

M.p. of the hydrochloride: >125°C (decomp.).

Prepared according to process a) from 4'-amino-2-diethylamino-3'-hydroxymethyl-acetophenone and sodium borohydride analogously to Example 1.

Example 75.

1-(4-Amino-3-chloro-5-cyano-phenyl)-2-isopropylamino-ethanol.

M.p. of the hydrochloride: 185 to 188°C.

Prepared according to process a) from 4'-amino-3'-chloro-5'-cyano-2-isopropylamino-acetophenone and sodium borohydride analogously to Example 3.

Example 76.

1-(4-Amino-3-chloro-5-cyano-phenyl)-2-tert.-butylamino-ethanol.

M.p.: 125 to 133°C.

Prepared according to process a) from 4'-amino-3'-chloro-5'-cyano-2-tert.-butylamino-acetophenone and sodium borohydride analogously to Example 3.

Example 77.

1-(4-Amino-3-chloro-5-cyano-phenyl)-2-dimethylamino-ethanol.

M.p. of the hydrochloride: 187 to 189°C.

Prepared according to process a) from 4'-amino-3'-chloro-5'-cyano-2-dimethylamino-acetophenone and sodium borohydride analogously to Example 3.

Example 78.

1-(4-Amino-3-chloro-5-cyano-phenyl)-2-diethylamino-ethanol.

M.p.: 69 to 71°C.

Prepared according to process a) from 4'-amino-3'-chloro-5'-cyano-2-diethylamino-acetophenone and sodium borohydride analogously to Example 3.

Example 79.

1-(4-Amino-3-bromo-5-cyano-phenyl)-2-isopropylamino-ethanol.

M.p. of the hydrochloride: 186 to 189°C.

Prepared according to process a) from 4'-amino-3'-bromo-5'-cyano-2-isopropylamino-acetophenone and sodium borohydride analogously to Example 3.

Example 80.

1-(4-Amino-3-bromo-5-cyano-phenyl)-2-tert.-butylamino-ethanol.

M.p. of the hydrochloride: 213 to 215°C.

Prepared according to process a) from 4'-amino-3'-bromo-2-tert.-butylamino-5'-cyano-acetophenone and sodium borohydride analogously to Example 3.

Example 81.

1-(4-Amino-3-bromo-5-cyano-phenyl)-2-diethylamino-ethanol.

M.p.: 72 to 74°C.

Prepared according to process a) from 4'-amino-3'-bromo-5'-cyano-2-diethylamino-acetophenone and sodium borohydride analogously to Example 3.

Example 82.

1-(4-Amino-3-bromo-5-carboxy-phenyl)-2-tert.-butylamino-ethanol.

M.p.: >218°C (decomp.).

Prepared according to process a) from 4'-amino-3'-bromo-2-tert.-butylamino-5'-carboxy-acetophenone and sodium borohydride analogously to Example 3.

Example 83.

1-(4-Amino-3-chloro-5-methoxy-phenyl)-2-tert.-butylamino-ethanol.

M.p. of the hydrochloride: 175 to 178°C (decomp.).

Prepared according to process a) from 4'-amino-2-tert.-butylamino-3'-chloro-5'-methoxy-acetophenone hydrochloride and sodium borohydride analogously to Example 1.

Example 84.

1-(4-Amino-5-bromo-3-hydroxymethyl-phenyl)-2-dimethylamino-ethanol.

M.p.: 87 to 92°C.

Prepared according to process b) by bromination of 1-(4-amino-3-hydroxymethyl-phenyl)-2-dimethylamino-ethanol analogously to Example 6.

Example 85.

1-(4-Amino-5-bromo-3-dimethylaminomethyl-phenyl)-2-tert.-butylamino-ethanol.

M.p.: 127 to 129°C.

Prepared according to process b) by bromination of 1-(4-amino-3-dimethylaminomethyl-phenyl)-2-tert.-butylamino-ethanol analogously to Example 6.

Example 86.

1-(4-Amino-5-bromo-3-dimethylaminomethyl-phenyl)-2-dimethylamino-ethanol.

Prepared according to process b) by bromination of 1-(4-amino-3-dimethylaminomethyl-phenyl)-2-dimethylamino-ethanol analogously to Example 6.

Proof of structure by NMR-spectra (CDCl₃/CD₃OD): 2.2 ppm, singlet [6 protons, N(CH₃)₂]; 2.35 ppm, singlet [6 protons, N(CH₃)₂]; 1.8—3.0 ppm, multiplet (2 protons, CH₂); 3.45 ppm, singlet (2 protons, CH₂); 4.4—4.8 ppm, multiplet (1 proton, CH); 6.96 ppm, doublet and 7.4 ppm, doublet (2 aromatic protons).

Example 87.

2-Ethylamino-1-(4-amino-3-fluoro-phenyl)-ethanol.

M.p. of the hydrochloride: 187 to 188°C (decomp.).

Prepared according to process c) from 1-(4-acetylamino-3-fluoro-phenyl)-2-ethylamino-ethanol and sodium hydroxide solution analogously to Example 7.

Example 88.

1-(4-Amino-3-fluoro-phenyl)-2-isopropylamino-ethanol.

M.p. of the hydrochloride: 156 to 158°C (decomp.).

Prepared according to process c) from 1-(4-acetylamino-3-fluoro-phenyl)-2-isopropylamino-ethanol and sodium hydroxide solution analogously to Example 7.

Example 89.

1-(4-Amino-3-fluoro-phenyl)-2-tert.-pentylamino-ethanol.

M.p. of the hydrochloride: 153 to 155°C (decomp.).

Prepared according to process c) from 1-(4-acetylamino-3-fluoro-phenyl)-2-tert.-pentylamino-ethanol and sodium hydroxide solution analogously to Example 7.

Example 90.

1-(4-Amino-3-fluoro-phenyl)-2-dimethylamino-ethanol.

Prepared according to process c) from 1-(4-acetylamino-3-fluoro-phenyl)-2-dimethylamino-ethanol and sodium hydroxide solution analogously to Example 7.

Oil: structure established by IR- and UV-spectra. IR (CH₂Cl₂): OH free at 3500 cm⁻¹; NH₂ at 3370 and 3450 cm⁻¹; OH associated at 3200—3500 cm⁻¹; N(CH₃)₂ at 2780 and 2830 cm⁻¹; aromatic C=C at 1635 cm⁻¹. UV (ethanol): maxima at 238 nm (ϵ = 0.6) and 288 nm (ϵ = 0.13).

Example 91.

1-(4-Amino-3-fluoro-phenyl)-2-diethylamino-ethanol.

M.p. of the hydrochloride: 122 to 125°C (decomp.).

Prepared according to process c) from 1-(4-acetylamino-3-fluoro-phenyl)-2-diethylamino-ethanol and sodium hydroxide solution analogously to Example 7.

Example 92.

1-(4-Amino-3-dimethylaminomethyl-phenyl)-2-tert.-butylamino-ethanol.

M.p.: 55 to 59°C.

Prepared according to process c) by saponification of 1-(4-acetylamino-3-dimethylaminomethyl-phenyl)-2-tert.-butylamino-ethanol with ethanolic sodium hydroxide solution analogously to Example 7.

Example 93.

1-(4-Amino-3-dimethylaminomethyl-phenyl)-2-dimethylamino-ethanol.

Prepared according to process c) by saponification of 1-(4-acetylamino-3-dimethylaminomethyl-phenyl)-2-dimethylamino-ethanol with ethanolic sodium hydroxide solution analogously to Example 7.

Structure established by NMR-spectrum (CDCl₃): 2.2 ppm, singlet [6 protons, N(CH₃)₂]; 2.35 ppm, singlet [6 protons, N(CH₃)₂]; 1.6—2.9 ppm, multiplet (2 protons, CH₂); 3.42 ppm, singlet (2 protons, CH₂); 4.4—4.8 ppm, multiplet (1 proton, CH); 6.6—7.18 ppm, multiplet (3 aromatic protons).

Example 94.

1-(4-Amino-3-hydroxymethyl-phenyl)-2-tert.-butylamino-ethanol.

M.p.: 123 to 128°C.

Prepared according to process c) from 1-(4-amino-3-hydroxymethyl-phenyl)-2-(N-benzyl-N-tert.-butyl)-amino-ethanol with hydrogen in the presence of palladium on charcoal analogously to Example 13.

Example 95.

1-(4-Amino-3-chloro-5-hydroxymethyl-phenyl)-2-tert.-butylamino-ethanol.

Prepared according to process c) from 1-(4-amino-3-chloro-5-hydroxymethyl-phenyl)-2-(N-benzyl-N-tert.-butyl)-amino-ethanol with hydrogen in the presence of palladium on charcoal analogously to Example 13.

Proof of structure by NMR-spectrum (CDCl₃): 1.1 ppm, singlet [9 protons, C(CH₃)₃]; 2.0—3.6 ppm, multiplet (2 protons, CH₂); 4.6 ppm, singlet (2 protons, CH₂); 4.2—4.6 ppm, multiplet (1 proton, CH); 6.9 ppm, doublet and 7.2 doublet (2 aromatic protons).

Example 96.

1-(4-Amino-3-trifluoromethyl-phenyl)-2-isopropylamino-ethanol.

M.p.: 136 to 137.5°C.

Prepared according to process d) from 1-(4-amino-3-bromo-5-trifluoromethyl-phenyl)-2-isopropylamino-ethanol and catalytically activated hydrogen analogously to Example 14.

Example 97.

1-(4-Amino-3-trifluoromethyl-phenyl)-2-dimethylamino-ethanol.

M.p.: 64 to 66.5°C.

Prepared according to process d) from 1-(4-amino-3-bromo-5-trifluoromethyl-phenyl)-2-dimethylamino-ethanol hydrochloride and catalytically activated hydrogen analogously to Example 14.

Example 98.

1-(4-Amino-3-trifluoromethyl-phenyl)-2-(N-methyl-ethylamino)-ethanol.

Prepared according to process d) from 1-(4-amino-3-bromo-5-trifluoromethyl-phenyl)-2-(N-methyl-ethylamino)-ethanol and catalytically activated hydrogen analogously to Example 14.

Oil; pure by thin-layer chromatography (R_f -value: 0.2; SiO_2 ; chloroform:methanol:concentrated ammonia = 90:10:1);

Elementary analysis:

 $\text{C}_{12}\text{H}_{17}\text{F}_3\text{N}_2\text{O}$ (262.3)

Calculated: C 54.95 H 6.53 N 10.68

Found: C 54.70 H 6.55 N 10.68

Example 99.

1-(4-Amino-3-trifluoromethyl-phenyl)-2-diethylamino-ethanol.

Prepared according to process d) from 1-(4-amino-3-bromo-5-trifluoromethyl-phenyl)-2-diethylamino-ethanol hydrochloride and catalytically activated hydrogen analogously to Example 14.

Oil; pure by thin-layer chromatography (R_f -value: about 0.3; SiO_2 ; chloroform:methanol:concentrated ammonia = 90:10:1); structure established by NMR-spectrum (CDCl_3): 1.1 ppm, triplet [6 protons, $\text{N}(\text{CH}_2-\text{CH}_3)_2$]; 2.55 ppm, multiplet [6 protons, $\text{N}(\text{CH}_2-\text{CH}_3)_2$]; 4.5 ppm, multiplet (1 proton, CH); 6.7 ppm, doublet and 7.3 ppm, doublet (2 aromatic protons).

Example 100.

1-(4-Amino-3-methyl-phenyl)-2-(N-benzyl-N-tert.-butyl)-amino-ethanol.

M.p. of the dihydrochloride: $>145^\circ\text{C}$ (decomp.).

Prepared according to process d) from 1-(4-amino-3-bromo-5-methyl-phenyl)-2-(N-benzyl-N-tert.-butyl)-amino-ethanol with catalytically activated hydrogen analogously to Example 16.

Example 101.

1-(4-Amino-3-cyano-phenyl)-2-isopropylamino-ethanol.

M.p.: 159 to 161°C.

Prepared according to process d) from 1-(4-amino-3-bromo-5-cyano-phenyl)-2-isopropylamino-ethanol and catalytically activated hydrogen analogously to Example 16.

Example 102.

1-(4-Amino-3-cyano-phenyl)-2-tert.-butylamino-ethanol.

M.p.: 181 to 185°C.

Prepared according to process d) from 1-(4-amino-3-bromo-5-cyano-phenyl)-2-tert.-butylamino-ethanol and catalytically activated hydrogen analogously to Example 16.

Example 103.

1-(4-Amino-3-cyano-phenyl)-2-dimethylamino-ethanol.

M.p. of the dihydrochloride: 130 to 133°C (decomp.).

Prepared according to process d) from 1-(4-amino-3-bromo-5-cyano-phenyl)-2-dimethylamino-ethanol with catalytically activated hydrogen analogously to Example 16.

Example 104.

1-(4-Amino-3-cyano-phenyl)-2-diethylamino-ethanol.

Prepared according to process d) from 1-(4-amino-3-bromo-5-cyano-phenyl)-2-diethylamino-ethanol and catalytically activated hydrogen analogously to Example 16.

Oil; elementary analysis:

$C_{13}H_{19}N_3O$ (233.3)

Calculated: C 67.00 H 8.20 N 18.00

Found: 67.00 8.40 17.81

Example 105.

5-(4-Amino-3-bromo-5-fluoro-phenyl)-3-tert.-butyl-oxazolidine.

M.p. of the dihydrochloride: 164 to 178°C (decomp.).

Prepared from 1-(4-amino-3-bromo-5-fluoro-phenyl)-2-tert.-butyl-amino-ethanol and 40% formaldehyde solution analogously to Example 20.

Example 106.

1-(4-Amino-3-chloro-5-trifluoromethyl-phenyl)-2-tert.-butylamino-ethanol.

M.p. of the hydrochloride: 205 to 207°C (decomp.).

Prepared according to process c) from 2-tert.-butylamino-1-[3-chloro-4-(p-chloro-benzoylamino)-5-trifluoromethyl-phenyl]-ethanol and sodium hydroxide solution analogously to Example 8.

Example 107.

1-(4-Amino-3-fluoro-phenyl)-2-tert.-butylamino-ethanol.

M.p. of the hydrochloride: 196 to 197°C (decomp.).

Prepared according to process c) from 1-(4-benzoylamino-3-fluoro-phenyl)-2-tert.-butylamino-ethanol and sodium hydroxide solution analogously to Example 7.

Example 108.

1-(4-Amino-3-chloro-5-fluoro-phenyl)-2-tert.-butylamino-ethanol.

M.p. of the hydrochloride: 206 to 208°C (decomp.).

Prepared according to process c) from 2-tert.-butylamino-1-(3-chloro-5-fluoro-4-propionylamino-phenyl)-ethanol and sodium hydroxide solution analogously to Example 7.

Example 109.

1-(4-Amino-3-bromo-5-trifluoromethyl-phenyl)-2-cyclopentylamino-ethanol.

M.p.: 100 to 102.5°C (decomp.).

Prepared according to process a) from 4'-amino-3'-bromo-2-cyclopentyl-amino-5'-trifluoromethyl-acetophenone hydrochloride and sodium borohydride analogously to Example 2.

Example 110.

1-(4-Amino-3-bromo-5-cyano-phenyl)-2-cyclopropylamino-ethanol.

3 g of sodium borohydride were added at room temperature to 7.5 g of 4'-amino-3'-bromo-5'-cyano-2-cyclopropylamino-acetophenone, dissolved in 200 ml of tetrahydrofuran and 100 ml of water, and the mixture was stirred for 1 hour. The excess of sodium borohydride was destroyed by addition of acetone. The insoluble material in the mixture was filtered off and the solvents were distilled off in vacuo. The residue was dissolved in hot isopropanol and the hydrochloride of 1-(4-amino-3-bromo-5-cyano-phenyl)-2-cyclopropylamino-ethanol was obtained by addition of isopropanolic hydrochloric acid, and was recrystallized from isopropanol.

M.p.: 190 to 193°C (decomp.).

Example 111.

1-(4-Amino-3-bromo-5-fluoro-phenyl)-2-cyclobutylamino-ethanol.

a) 20 g of 4'-amino-3'-bromo-5'-fluoro-acetophenone were dissolved in 300 ml of chloroform. The solution was heated to boiling and then a solution of 4.3 ml of bromine in 20 ml of chloroform was slowly added dropwise whilst stirring. Afterwards the mixture was stirred for a further 5 minutes at the boiling temperature of the mixture and was then cooled to room temperature. To the solution of 4'-amino-3',2-dibromo-5'-fluoro-acetophenone a mixture of 15 g of cyclobutylamine and 14 ml of triethylamine was added dropwise whilst stirring the mixture and with ice-cooling. Afterwards, the mixture was refluxed for 2 hours and

washed with water after cooling. The organic layer was evaporated to dryness in vacuo. The residue consisted of crude 4'-amino-3'-bromo-2-cyclobutylamino-5'-fluoro-acetophenone.

b) The crude ketone obtained as described in Example IIIa) was dissolved in 30 ml of tetrahydrofuran. 5 ml of water were added to the solution and afterwards 4.5 g of sodium borohydride were added in small amounts whilst stirring the mixture and cooling with ice. The solution was stirred for 3 hours whilst cooling and left to stand overnight at room temperature. Subsequently, the excess of sodium borohydride was destroyed with acetone and the solution was evaporated to dryness in vacuo. The residue was distributed between water and chloroform, the organic layer was extracted three times with 100 ml portions of 2N-hydrochloric acid, the combined hydrochloric acid-extracts were made alkaline with sodium hydroxide and extracted with chloroform. The chloroform solution was washed with water, dried over sodium sulfate and evaporated to dryness in vacuo. The remaining residue of crude 1-(4-amino-3-bromo-5-fluoro-phenyl)-2-cyclobutylamino-ethanol was dissolved in isopropanol and acidified to a pH of 5 with ethereal hydrochloric acid. The product crystallized after addition of ether. The precipitated hydrochloride of the title compound was recrystallized from isopropanol.

M.p.: 164 to 166°C (decomp.).

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Example 112.

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1-(4-Amino-3-fluoro-5-iodo-phenyl)-2-isopropylamino-ethanol hydrochloride.

5.15 g of 1-(4-amino-3-fluoro-phenyl)-2-isopropylamino-ethanol were dissolved in 300 ml of acetic acid, 80 g of iodine and 4.0 g of mercuric (II) oxide were added and the mixture was stirred vigorously for 24 hours at room temperature. The solid was subsequently filtered off, the dark-brown colour of the filtrate was removed with saturated sodium hydrogen sulfite solution and the solution was diluted to about 1 l with water. The mixture was made alkaline with 10N sodium hydroxide solution whilst cooling and extracted with chloroform. The chloroform layer was dried over sodium sulfate and evaporated to dryness in vacuo. The residue was dissolved in methanol and acidified to a pH of 4.5 with ethereal hydrochloric acid. The solution was evaporated to dryness in vacuo and the solid residue was recrystallized from absolute ethanol.

M.p.: 203 to 205°C (decomp.).

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Example 113.

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1-(4-Amino-3-diethylaminomethyl-phenyl)-2-tert.-butylamino-ethanol.

6.0 g of 1-(4-acetylaminomethyl-3-diethylaminomethyl-phenyl)-2-tert.-butylamino-ethanol were refluxed for 35 hours in a mixture of 50 ml of ethanol and 50 ml of 4N sodium hydroxide solution. The ethanol was subsequently distilled off, and the mixture was diluted with water and extracted twice with chloroform. The organic layer was dried with sodium sulfate and evaporated. After column chromatographical purification the 1-(4-amino-3-diethylaminomethyl-phenyl)-2-tert.-butylamino-ethanol was first purified by column chromatography (silica gel; methanol) and was then crystallized from petroleum ether.

M.p.: 86 to 90°C.

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Example 114.

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1-(4-Amino-3-cyano-phenyl)-2-cyclopropylamino-ethanol.

4 g of 1-(4-amino-3-bromo-5-cyano-phenyl)-2-cyclopropylamino-ethanol were dissolved in methanol and hydrogenated at room temperature at a hydrogen pressure of 3 to 5 atm. in the presence of 1 g of palladium on charcoal (10%). After the hydrogen has been absorbed, the catalyst was removed by suction filtration, the filtrate was evaporated to dryness in vacuo and the residue was distributed between dilute sodium hydroxide solution and chloroform. After evaporation of the chloroform layer, 1-(4-amino-3-cyano-phenyl)-2-cyclopropylamino-ethanol was obtained as an oil, which was purified chromatographically over silica gel (eluent: chloroform:methanol = 9:1). The dihydrochloride was obtained by addition of ethereal hydrochloric acid and was recrystallized from isopropanol.

M.p.: 148 to 151°C (decomp.).

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Example 115.

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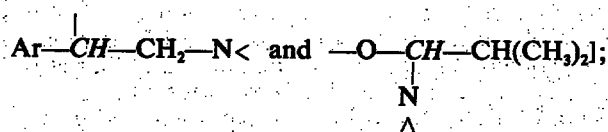
2-Ethyl-5-(4-amino-3-bromo-5-fluoro-phenyl)-3-tert.-butyl-oxazolidine.

5 g of 1-(4-amino-3-bromo-5-fluoro-phenyl)-2-tert.-butylamino-ethanol were dissolved in 100 ml of benzene. 5 g of propionaldehyde were added and the

mixture was refluxed for 6 hours using an apparatus incorporating a water separator funnel. A further 5 g of propionaldehyde were then added and the mixture was heated for a further 3 hours. After cooling the reaction mixture was evaporated to dryness in vacuo and the residue was purified by column chromatography. The column was filled with 50 g of silica gel and benzene was used as the eluent. The eluates containing the substance were combined and evaporated to dryness in vacuo, whereby the title compound was obtained as a foam.

Structure established by NMR-spectrum (CDCl_3):

0.7—1.8 ppm, multiplet [14 protons, $-\text{C}(\text{CH}_3)_2$ and $-\text{CH}_2-\text{CH}_3$];
2.5—2.95 and 3.1—3.7 ppm, 2 multiplets [2 protons $\text{Ar}-\text{CH}-\text{CH}_2-\text{N}<$];
4.0—4.3 ppm, singlet [2 protons, NH_2];
4.4—5.2 ppm, multiplet [2 protons,



6.8—7.35 ppm, multiplet [2 aromatic protons].

Example 116.

1-(4-Amino-3-bromo-5-fluoro-phenyl)-2-cyclopentylamino-ethanol.

M.p. of the hydrochloride: 167 to 170°C (decomp.).

Prepared according to process a) from 4'-amino-3'-bromo-2-cyclopentyl-amino-5'-fluoro-acetophenone and sodium borohydride analogously to Example 111.

Example 117.

1-(4-Amino-3-bromo-5-fluoro-phenyl)-2-cyclohexylamino-ethanol.

M.p. of the hydrochloride: 191 to 195°C (decomp.).

Prepared according to process a) from 4'-amino-3'-bromo-2-cyclohexyl-amino-5'-fluoro-acetophenone and sodium borohydride analogously to Example 111.

Example 118.

1-(4-Amino-3-bromo-5-fluoro-phenyl)-2-cycloheptylamino-ethanol.

M.p. of the hydrochloride: 187 to 189°C (decomp.).

Prepared according to process a) from 4'-amino-3'-bromo-2-cycloheptyl-amino-5'-fluoro-acetophenone and sodium borohydride analogously to Example 111.

Example 119.

1-(4-Amino-3-fluoro-5-iodo-phenyl)-2-cyclopropylamino-ethanol.

M.p. of the hydrochloride: 199 to 201°C (decomp.).

Prepared according to process a) from 4'-amino-2-cyclopropylamino-3'-fluoro-5'-iodo-acetophenone and sodium borohydride analogously to Example 111.

Example 120.

1-(4-Amino-3-fluoro-5-iodo-phenyl)-2-isopropylamino-ethanol.

M.p. of the hydrochloride: 203 to 205°C (decomp.).

Prepared according to process a) from 4'-amino-3'-fluoro-2-isopropylamino-5'-iodo-acetophenone and sodium borohydride analogously to Example 111.

Example 121.

1-(4-Amino-3-fluoro-5-iodo-phenyl)-2-cyclobutylamino-ethanol.

M.p. of the hydrochloride: 197 to 199°C (decomp.).

Prepared according to process a) from 4'-amino-2-cyclobutylamino-3'-fluoro-5'-iodo-acetophenone and sodium borohydride analogously to Example 111.

Example 122.

1-(4-Amino-3-fluoro-5-iodo-phenyl)-2-tert.-butylamino-ethanol.

M.p. of the hydrochloride: 207 to 209°C (decomp.).

Prepared according to process a) from 4'-amino-2-tert.-butylamino-3'-fluoro-5'-iodo-acetophenone and sodium borohydride analogously to Example 111.

Example 123.

1-(4-Amino-3-fluoro-5-iodo-phenyl)-2-(hydroxy-tert.-butylamino)-ethanol

M.p. of the hydrochloride: 200 to 202°C (decomp.).

Prepared according to process a) from 4'-amino-3'-fluoro-2-(hydroxy-tert.-butylamino)-5'-iodo-acetophenone and sodium borohydride analogously to Example 111.

Example 124.

2-Ethylamino-1-(4-amino-3-cyano-5-fluoro-phenyl)-ethanol

M.p. of the hydrochloride: 216 to 218°C (decomp.).

Prepared according to process a) from 2-ethylamino-4'-amino-3'-cyano-5'-fluoro-acetophenone and sodium borohydride analogously to Example 111.

Example 125.

1-(4-Amino-3-cyano-5-fluoro-phenyl)-2-cyclopropylamino-ethanol

M.p. of the hydrochloride: 188 to 190°C (decomp.).

Prepared according to process a) from 4'-amino-3'-cyano-2-cyclopropylamino-5'-fluoro-acetophenone and sodium borohydride analogously to Example 111.

Example 126.

1-(4-Amino-3-cyano-5-fluoro-phenyl)-2-isopropylamino-ethanol

M.p. of the hydrochloride: 182 to 184°C (decomp.).

Prepared according to process a) from 4'-amino-3'-cyano-5'-fluoro-2-isopropylamino-acetophenone and sodium borohydride analogously to Example 111.

Example 127.

1-(4-Amino-3-cyano-5-fluoro-phenyl)-2-cyclobutylamino-ethanol

M.p. of the hydrochloride: 222 to 224°C (decomp.).

Prepared according to process a) from 4'-amino-3'-cyano-2-cyclobutylamino-5'-fluoro-acetophenone and sodium borohydride analogously to Example 111.

Example 128.

1-(4-Amino-3-cyano-5-fluoro-phenyl)-2-tert.-butylamino-ethanol

M.p. of the hydrochloride: 242 to 243°C (decomp.).

Prepared according to process a) from 4'-amino-2-tert.-butylamino-3'-cyano-5'-fluoro-acetophenone and sodium borohydride analogously to Example 111.

Example 129.

1-(4-Amino-3-cyano-5-fluoro-phenyl)-2-cyclopentylamino-ethanol

M.p. of the hydrochloride: 184 to 186°C (decomp.).

Prepared according to process a) from 4'-amino-3'-cyano-2-cyclopentylamino-5'-fluoro-acetophenone and sodium borohydride analogously to Example 111.

Example 130.

1-(4-Amino-3-cyano-5-fluoro-phenyl)-2-tert.-pentylamino-ethanol

M.p. of the hydrochloride: 172 to 175°C (decomp.).

Prepared according to process a) from 4'-amino-3'-cyano-5'-fluoro-2-tert.-pentylamino-acetophenone and sodium borohydride analogously to Example 111.

Example 131.

1-(4-Amino-3-cyano-5-fluoro-phenyl)-2-dimethylamino-ethanol

Prepared according to process a) from 4'-amino-3'-cyano-2-dimethylamino-5'-fluoro-acetophenone and sodium borohydride analogously to Example 111.

Oil; Structure established by NMR-spectrum (CD₃OD): 2.2—2.65 ppm, multi-

OH

plet, [8 protons; N—CH₃ and N—CH—CH₂—N<]; 4.6—4.9 ppm, multiplet, [4 pro-

OH

tons; 3 exchange protons and —CH—CH₂—N<]; 7.15—7.4 ppm, multiplet [2 aromatic protons].

Example 132.

1-(4-Amino-3-cyano-5-fluoro-phenyl)-2-diethylamino-ethanol

Prepared according to process a) from 4'-amino-3'-cyano-2-diethylamino-5'-fluoro-acetophenone and sodium borohydride analogously to Example 111.

Oil; structure established by NMR-spectrum (CD₃OD): 0.85—1.2 ppm, triplet, [6 protons; —N(CH₂—CH₃)₂]; 2.45—2.85 ppm, multiplet [6 protons; —N(CH₂—CH₃)₂ and —CH—CH₂—N<d]; 4.5—4.85 ppm, singlet and triplet [4 pro-

OH

tons; 3 exchange protons and —CH—CH₂—]; 7.1—7.4 ppm, multiplet [2 aromatic protons].

Example 133.

1-(4-Amino-3-trifluoromethyl-phenyl)-2-(cyclopropylmethyl-amino)-ethanol

M.p. of the hydrochloride: 122 to 127°C (decomp.; > 110°C discoloration).

Prepared according to process d) from 1-(4-amino-3-bromo-5-trifluoromethyl-phenyl)-2-(cyclopropylmethyl-amino)-ethanol and catalytically activated hydrogen analogously to Example 114.

Example 134.

1-(4-Amino-3-trifluoromethyl-phenyl)-2-cyclopentylamino-ethanol

M.p. of the hydrochloride: 144 to 145°C.

Prepared according to process d) from 1-(4-amino-3-bromo-5-trifluoromethyl-phenyl)-2-cyclopentylamino-ethanol and catalytically activated hydrogen analogously to Example 114.

Example 135.

1-(4-Amino-3-chloro-5-trifluoromethyl-phenyl)-2-(cyclopropylmethyl-amino)-ethanol

M.p. of the hydrochloride: 186 to 187°C (decomp.).

Prepared according to process a) from 4'-amino-3'-chloro-2-(cyclopropylmethyl-amino)-5'-trifluoromethyl-acetophenone and sodium borohydride analogously to Example 110.

Example 136.

1-(4-Amino-3-chloro-5-trifluoromethyl-phenyl)-2-cyclopentylamino-ethanol

M.p. of the hydrochloride: 188 to 190°C (decomp.).

Prepared according to process a) from 4'-amino-3'-chloro-2-cyclopentylamino-5'-trifluoromethyl-acetophenone and sodium borohydride analogously to Example 110.

Example 137.

1-(4-Amino-3-chloro-5-trifluoromethyl-phenyl)-2-cyclohexylamino-ethanol

M.p. of the hydrochloride: 213 to 214°C (decomp.).

Prepared according to process a) from 4'-amino-3'-chloro-2-cyclohexylamino-5'-trifluoromethyl-acetophenone and sodium borohydride analogously to Example 110.

Example 138.

1-(4-Amino-3-chloro-5-trifluoromethyl-phenyl)-2-cycloheptylamino-ethanol

M.p. of the hydrochloride: 163 to 165°C.

Prepared according to process a) from 4'-amino-3'-chloro-2-cycloheptylamino-5'-trifluoromethyl-acetophenone and sodium borohydride analogously to Example 110.

Example 139.

1-(4-Amino-3-bromo-5-trifluoromethyl-phenyl)-2-(cyclopropylmethyl-amino)-ethanol

M.p. of the hydrochloride: 173 to 175°C (decomp.).

Prepared according to process a) from 4'-amino-3'-bromo-2-(cyclopropylmethyl-amino)-5'-trifluoromethyl-acetophenone and sodium borohydride analogously to Example 110.

Example 140.

1-(4-Amino-3-cyano-phenyl)-2-cyclobutylamino-ethanol

M.p. of the hydrobromide: > 193°C decomposition.

Prepared according to process d) from 1-(4-amino-3-bromo-5-cyano-phenyl)-2-cyclobutylamino-ethanol and catalytically activated hydrogen analogously to Example 110.

Example 141.

1-(4-Amino-3-cyano-phenyl)-2-cyclopentylamino-ethanol

M.p.: 158 to 160°C.

Prepared according to process d) from 1-(4-amino-3-bromo-5-cyano-phenyl)-2-cyclopentylamino-ethanol and catalytically activated hydrogen analogously to Example 110.

Example 142.

1-(4-Amino-3-cyano-phenyl)-2-tert.-pentylamino-ethanol

M.p.: 143°C.

Prepared according to process d) from 1-(4-amino-3-bromo-5-cyano-phenyl)-2-tert.-pentylamino-ethanol and catalytically activated hydrogen analogously to Example 110.

Example 143.

1-(4-Amino-3-chloro-5-cyano-phenyl)-2-cyclopropylamino-ethanol

M.p. of the hydrochloride: 175 to 177°C.

Prepared according to process a) from 4'-amino-3'-chloro-5'-cyano-2-cyclopropylamino-acetophenone and sodium borohydride analogously to Example 110.

Example 144.

1-(4-Amino-3-chloro-5-cyano-phenyl)-2-propylamino-ethanol

M.p. of the hydrochloride: 187 to 189°C.

Prepared according to process a) from 4'-amino-3'-chloro-5'-cyano-2-propylamino-acetophenone and sodium borohydride analogously to Example 110.

Example 145.

1-(4-Amino-3-chloro-5-cyano-phenyl)-2-cyclobutylamino-ethanol

M.p. of the hydrochloride: 178 to 180°C (decomp.).

Prepared according to process a) from 4'-amino-3'-chloro-5'-cyano-2-butylamino-acetophenone and sodium borohydride analogously to Example 110.

Example 146.

1-(4-Amino-3-chloro-5-cyano-phenyl)-2-sec.-butylamino-ethanol

M.p. of the dihydrochloride: 190 to 191°C.

Prepared according to process a) from 4'-amino-2-sec.-butylamino-3'-chloro-5'-cyano-acetophenone and sodium borohydride analogously to Example 110.

Example 147.

1-(4-Amino-3-chloro-5-cyano-phenyl)-2-(hydroxy-tert.-butylamino)-ethanol

M.p. of the hydrochloride: 228 to 230°C (decomp.).

Prepared according to process a) from 4'-amino-3'-chloro-5'-cyano-2-(hydroxy-tert.-butylamino)-acetophenone and sodium borohydride analogously to Example 110.

Example 148.

1-(4-Amino-3-chloro-5-cyano-phenyl)-2-cyclopentylamino-ethanol

M.p. of the hydrochloride: 138 to 144°C.

Prepared according to process a) from 4'-amino-3'-chloro-5'-cyano-2-cyclopentylamino-acetophenone and sodium borohydride analogously to Example 110.

Example 149.

1-(4-Amino-3-chloro-5-cyano-phenyl)-2-tert.-pentylamino-ethanol

M.p. of the hydrochloride: 218 to 220°C (decomp.).

Prepared according to process a) from 4'-amino-3'-chloro-5'-cyano-2-tert.-pentylamino-acetophenone and sodium borohydride analogously to Example 110.

Example 150.

1-(4-Amino-3-chloro-5-cyano-phenyl)-2-cycloheptylamino-ethanol

M.p. of the hydrochloride: 235 to 237°C (decomp.).

Prepared according to process a) from 4'-amino-3'-chloro-5'-cyano-2-cycloheptylamino-acetophenone and sodium borohydride analogously to Example 110.

Example 151.

1 - (4 - Amino - 3 - chloro - 5 - cyano - phenyl) - 2 - [1 - (3,4 - methylenedioxy - phenyl) - 2 - propylamino] - ethanol

M.p. of the hydrochloride: 189 to 192°C.

Prepared according to process a) from 4'-amino-3'-chloro-5'-cyano-2-[1-(3,4-methylenedioxy-phenyl)-2-propylamino]-acetophenone and sodium borohydride analogously to Example 110.

Example 152.

1-(4-Amino-3-bromo-5-cyano-phenyl)-2-cyclobutylamino-ethanol

M.p. of the hydrochloride: 215 to 216°C (decomp.).

Prepared according to process a) from 4'-amino-3'-bromo-5'-cyano-2-cyclobutylamino-acetophenone and sodium borohydride analogously to Example 110.

Example 153.

1-(4-Amino-3-bromo-5-cyano-phenyl)-2-(hydroxy-tert.-butylamino)-ethanol

M.p. of the hydrochloride: 221 to 222°C.

Prepared according to process a) from 4'-amino-3'-bromo-5'-cyano-2-(hydroxy-tert.-butylamino)-acetophenone and sodium borohydride analogously to Example 110.

Example 154.

1-(4-Amino-3-bromo-5-cyano-phenyl)-2-cyclopentylamino-ethanol

M.p. of the hydrochloride: 177°C.

Prepared from 4'-amino-3'-bromo-5'-cyano-2-cyclopentylamino-acetophenone and sodium borohydride analogously to Example 110.

Example 155.

1-(4-Amino-3-bromo-5-cyano-phenyl)-2-tert.-pentylamino-ethanol

M.p. of the hydrochloride: 202 to 204°C (decomp.).

Prepared according to process a) from 4'-amino-3'-bromo-5'-cyano-2-tert.-pentylamino-acetophenone and sodium borohydride analogously to Example 110.

Example 156.

1-(4-Amino-3-bromo-5-cyano-phenyl)-2-cyclohexylamino-ethanol

M.p. of the hydrochloride: 209 to 210°C (decomp.).

Prepared according to process a) from 4'-amino-3'-bromo-5'-cyano-2-cyclohexylamino-acetophenone and sodium borohydride analogously to Example 110.

Example 157.

1-(4-Amino-3,5-dicyano-phenyl)-2-cyclopropylamino-ethanol

M.p. of the hydrochloride: 222 to 223°C (decomp.).

Prepared according to process a) from 4'-amino-2-cyclopropylamino-3',5'-dicyano-acetophenone and sodium borohydride analogously to Example 110.

Example 158.

1-(4-Amino-3,5-dicyano-phenyl)-2-isopropylamino-ethanol

M.p. of the hydrochloride: 224 to 226°C (decomp.).

Prepared according to process a) from 4'-amino-3',5'-dicyano-2-isopropylamino-acetophenone and sodium borohydride analogously to Example 110.

Example 159.

1-(4-Amino-3,5-dicyano-phenyl)-2-cyclobutylamino-ethanol

M.p. of the hydrochloride: 258°C (decomp.).

Prepared according to process a) from 4'-amino-2-cyclobutylamino-3',5'-dicyano-acetophenone and sodium borohydride analogously to Example 110.

Example 160.

1-(4-Amino-3,5-dicyano-phenyl)-2-sec.-butylamino-ethanol

M.p. of the hydrochloride: 197 to 199°C.

Prepared according to process a) from 4'-amino-2-sec.-butylamino-3',5'-dicyano-acetophenone and sodium borohydride analogously to Example 110.

Example 161.

1-(4-Amino-3,5-dicyano-phenyl)-2-tert.-butylamino-ethanol

M.p. of the hydrochloride: 251 to 253°C (decomp.).

Prepared according to process a) from 4'-amino-2-tert.-butylamino-3',5'-dicyano-acetophenone and sodium borohydride analogously to Example 110.

Example 162.

1-(4-Amino-3,5-dicyano-phenyl)-2-(hydroxy-tert.-butylamino)-ethanol

M.p. of the hydrochloride: 240 to 241°C (decomp.).

Prepared according to process a) from 4'-amino-3',5'-dicyano-2-(hydroxy-tert.-butylamino)-acetophenone and sodium borohydride analogously to Example 110.

Example 163.

1-(4-Amino-3,5-dicyano-phenyl)-2-cyclopentylamino-ethanol

M.p. of the hydrochloride: 214 to 216°C.

Prepared according to process a) from 4'-amino-2-cyclopentylamino-3',5'-dicyano-acetophenone and sodium borohydride analogously to Example 110.

Example 164.

1-(4-Amino-3,5-dicyano-phenyl)-2-tert.-pentylamino-ethanol

M.p. of the hydrochloride: 231 to 233°C (decomp.).

Prepared according to process a) from 4'-amino-3',5'-dicyano-2-tert.-pentylamino-acetophenone and sodium borohydride analogously to Example 110.

Example 165.

1-(4-Amino-3,5-dicyano-phenyl)-2-[1-(3,4-methylenedioxy-phenyl)-2-propylamino]-ethanol

M.p. of the hydrochloride: 219 to 222°C (decomp.).

Prepared according to process a) from 4'-amino-3',5'-dicyano-2-[1-(3,4-methylenedioxy-phenyl)-2-propylamino]-acetophenone and sodium borohydride analogously to Example 110.

Example 166.

1-(4-Amino-3-chloro-5-diethylaminoethyl-phenyl)-2-tert.-butylamino-ethanol

M.p.: 65 to 69°C.

Prepared according to process a) from 4'-amino-2-tert.-butylamino-3'-chloro-5'-diethylaminoethyl-acetophenone and sodium borohydride analogously to Example 110.

Example 167.

1-(4-Amino-3-bromo-5-diethylaminomethyl-phenyl)-2-tert.-butylamino-ethanol

M.p.: 96 to 100°C.

Prepared according to process a) from 4'-amino-3'-bromo-2-tert.-butylamino-5'-diethylaminomethyl-acetophenone and sodium borohydride analogously to Example 110.

Example 168.

1-(4-Amino-3-chloro-5-nitro-phenyl)-2-tert.-butylamino-ethanol

M.p.: 148 to 149°C.

Prepared according to process a) from 4'-amino-2-tert.-butylamino-3'-chloro-5'-nitro-acetophenone and sodium borohydride analogously to Example 110.

Example 169.

1-(4-Amino-3-bromo-5-nitro-phenyl)-2-tert.-butylamino-ethanol

M.p.: 151 to 152°C.

Prepared according to process a) from 4'-amino-3'-bromo-2-tert.-butylamino-5'-nitro-acetophenone and sodium borohydride analogously to Example 110.

Example 170.

5-(4-Amino-3-bromo-5-fluoro-phenyl)-3-tert.-butyl-2-isopropyl-oxazolidine

Prepared from 1-(4-amino-3-bromo-5-fluoro-phenyl)-2-tert.-butylamino-ethanol and isobutyraldehyde analogously to Example 115.

Amorphous substance; structure established by NMR-spectrum (CDCl₃): 0.85—1.2 ppm, multiplet [15 protons, —C(CH₃)₃ and >CH—CH(CH₃)₂]; 1.5—1.85 ppm, multiplet [1 proton, >CH—CH(CH₃)₂]; 2.5—2.9 and 3.2—3.7 ppm, 2 multiplets [2 protons, Ar—CH—CH₂—N<]; 3.9—4.2 ppm, singlet [2 protons, NH₂]; 4.4—4.9 ppm, multiplet [2 protons, Ar—CH—CH₂—N> and —O—CH—CH(CH₃)₂];

6.8—7.3 ppm, multiplet [2 aromatic protons].



Example 171.

5-(4-Amino-3-bromo-5-fluoro-phenyl)-3-tert.-butyl-oxazolidine

M.p. of the dihydrochloride: 164 to 178°C (decomp.).

Prepared from 1-(4-amino-3-bromo-5-fluoro-phenyl)-2-tert.-butylamino-ethanol and formaldehyde analogously to Example 115.

Example 172.

5-(4-Amino-3-chloro-5-trifluoromethyl-phenyl)-3-tert.-butyl-2-methyl-oxazolidine

M.p. of the hydrochloride: 199 to 202°C (decomp.).

Prepared from 1-(4-amino-3-chloro-5-trifluoromethyl-phenyl)-2-tert.-butylamino-ethanol and acetaldehyde analogously to Example 115.

Example 173.

1-1-(4-Amino-3-fluoro-phenyl)-2-tert.-butylamino-ethanol and d-1-(4-amino-3-fluoro-phenyl)-2-tert.-butylamino-ethanol.

a.) 1-(4-Acetylamino-3-fluoro-phenyl)-2-(N-benzyl-N-tert.-butyl)-amino-O-(N-carbobenzoxy-L-alanyl)-ethanol and d-1-(4-acetylamino-3-fluoro-phenyl)-2-(N-benzyl-N-tert.-butyl)-amino-O-(N-carbobenzoxy-L-alanyl)-ethanol

14.5 g of N,N'-carbonyl-diimidazole were added to a solution of 15 g of N-carbobenzoxy-L-alanine in 300 ml of absolute tetrahydrofuran and the mixture was stirred for 3 hours at room temperature. Subsequently a solution of 10 g of d, 1-1-(4-acetylamino-3-fluoro-phenyl)-2-(N-benzyl-N-tert.-butyl)-aminoethanol in 200 ml of absolute tetrahydrofuran and a small piece of sodium were added and the mixture was stirred for 12 days at room temperature and then evaporated to dryness in vacuo. The residue was distributed between chloroform and water. The chloroform layer was dried over sodium sulfate and evaporated to dryness in vacuo. The diastereisomeric esters thus obtained in the mixture have different R_f -values on the thin-layer chromatogram (silica gel G, Merck; chloroform:acetone = 10:1). The above evaporation residue was purified by passing it through a silica gel chromatography column without separating the diastereisomeric esters (500 g of silica gel; eluent: chloroform:acetone = 10:1).

The fractions containing the title compounds were evaporated to dryness in vacuo and 1-1-(4-Acetylamino-3-fluoro-phenyl)-2-(N-benzyl-N-tert.-butyl)-amino-O-(N-carbobenzoxy-L-alanyl)-ethanol crystallised out of an ether solution (colorless crystals).

 $[\alpha]_{364}^{20} = -101^\circ$ (c = 2.0; methanol); R_f -value = 0.27.

The mother liquor was evaporated to dryness in vacuo. The diastereomeric ester with the larger R_f -value (R_f = 0.33) was isolated by passage through a chromatography column (100 g of silica gel; eluent: chloroform:acetone = 20:1): d-1-(4-Acetylamino-3-fluoro-phenyl)-2-(N-benzyl-N-tert.-butyl)-amino-O-(N-carbobenzoxy-L-alanyl)-ethanol was thus obtained as a colorless oil.

 $[\alpha]_{364}^{20} = -65^\circ$ (c = 2.0; methanol); R_f -value = 0.33.

b.) 1-1-(4-Amino-3-fluoro-phenyl)-2-tert.-butylamino-ethanol

2 g of 1-1-(4-acetylamino-3-fluoro-phenyl)-2-(N-benzyl-N-tert.-butyl)-amino-O-(N-carbobenzoxy-L-alanyl)-ethanol were dissolved in 60 ml of ethanol. 20 ml of 5N sodium hydroxide solution were added and the solution was refluxed for 4 hours. After cooling the solution was distributed between chloroform and water and the aqueous layer was extracted four times with chloroform. The combined chloroform extracts were dried over sodium sulfate and evaporated to dryness in vacuo. The residue consisting of 1-1-(4-amino-3-fluoro-phenyl)-2-(N-benzyl-N-tert.-butyl)-aminoethanol, was dissolved in 50 ml of methanol and acidified to a pH of 6 with ethereal hydrochloric acid. 0.2 g of palladium on charcoal (10%) were added and the reaction product was hydrogenated in a Parr-apparatus at room temperature and at a pressure of 5 atmospheres until all hydrogen had been absorbed. After the catalyst had been removed by suction filtration, the reaction product was evaporated to dryness in vacuo and the solid residue, consisting of 1-1-(4-amino-3-fluoro-phenyl)-2-tert.-butylamino-ethanol hydrochloride, was crystallized from isopropanol solution by addition of ether.

M.p.: 199 to 200°C (decomposition)

 $[\alpha]_{364}^{20} = -123.3^\circ$ (c = 1.0; methanol).

c.) d-1-(4-Amino-3-fluoro-phenyl)-2-tert.-butylamino-ethanol

The oily d-1-(4-acetylamino-3-fluoro-phenyl)-2-(N-benzyl-N-tert.-butyl)-amino-O-(N-carbobenzoxy-L-alanyl)-ethanol prepared as described above, was dissolved in 30 ml of ethanol. 10 ml of 5N sodium hydroxide solution were added and the solution was refluxed for 4 hours. After cooling the reaction solution was distributed between chloroform and water and the aqueous layer was extracted four times with chloroform. The combined chloroform extracts were dried over sodium and evaporated to dryness in vacuo. The residue, consisting of d-1-(4-amino-3-fluoro-phenyl)-2-(N-benzyl-N-tert.-butyl)-amino-ethanol, was dissolved in 25 ml of methanol and acidified to a pH of 6 with ethereal hydrochloric acid, 0.1 g of palladium on charcoal (10%) were added and the reaction product was hydrogenated in a Parr-apparatus at room temperature and at a pressure of 5 atmospheres, until all the hydrogen has been absorbed. After the catalyst has been suction filtered, the mixture was evaporated to dryness in vacuo and the solid residue, consisting of d-1-(4-amino-3-fluoro-phenyl)-2-tert.-butylamino-ethanol hydrochloride, was crystallized from isopropanol solution by addition of ether.

M.p.: 198 to 200°C (decomposition).

$[\alpha]_{364}^{20} + 1224.4^{\circ}$ (c = 1.142; methanol).

Example 174.

d-1-(4-Amino-3-chloro-5-trifluoromethyl-phenyl)-2-tert.-butylamino-ethanol and 1-1-(4-amino-3-chloro-5-trifluoromethyl-phenyl)-2-tert.-butylamino-ethanol

a.) d, l-1-(4-Amino-3-chloro-5-trifluoromethyl-phenyl)-2-tert.-butylamino-O-[(*-*)-menthoxy-carbonyl]-ethanol

56.6 ml of a 0.5 molar solution of (*-*)-menthyl chloroformate in toluene were added dropwise whilst stirring and at 20°C to a solution of 8.8 g of d, l-1-(4-amino-3-chloro-5-trifluoromethyl-phenyl)-2-tert.-butylamino-ethanol in 50 ml of pyridine. After two hours the solution was evaporated to dryness in vacuo. The oily residue was triturated with water, the aqueous solution was decanted and the residue was subsequently dissolved in ether. The ethereal solution was successively washed with water, 2N ammonia (whereupon a precipitate which had formed between the layers dissolved) and again with water. The ethereal solution was dried with magnesium sulfate and adjusted to a pH of 6 with 4N isopropanolic hydrochloric acid. A mixture of the hydrochlorides of the diastereoisomeric title compounds crystallized out. The reaction product was suction filtered and washed with ether.

Thin-layer chromatography of the crystals on silica gel G, Merck, with butyl acetate:cyclohexane = 9:1 as eluent showed two spots of the same concentration with the approximate R_f -values of 0.45 and 0.55.

b.) Separation of d- and l-1-(4-amino-3-chloro-5-trifluoromethyl-phenyl)-2-tert.-butylamino-O-[(*-*)-menthoxy-carbonyl]-ethanol

3.0 g of the mixture of the hydrochlorides of d- and l-1-(4-amino-3-chloro-5-trifluoromethyl-phenyl)-2-tert.-butylamino-O-[(*-*)-methoxy-carbonyl]-ethanol obtained as described above were suspended in a small quantity of water. Ether was added and then 5.0 ml of 2N ammonia were added and the mixture was shaken until all solid matter was in solution. The ethereal layer was separated, washed with water, dried over magnesium sulfate and evaporated in vacuo. The oily residue thus obtained was chromatographed through a silica gel column (6.5 cm diameter, 107 cm length, 2.2 kg of silica gel) with a mixture of butyl acetate and cyclohexane (19:1) as eluent (flow speed 120 ml/hour). The fractions containing the pure substance with R_f -value 0.55 were combined and the solvent was removed in vacuo. d-1-(4-Amino-3-chloro-5-trifluoromethyl-phenyl)-2-tert.-butylamino-O-[(*-*)-menthoxy-carbonyl]-ethanol was crystallized from petroleum ether (boiling point: 40 to 60°C).

M.p.: 95.5 to 96.5°C

$[\alpha]_{364}^{20} = +74.1^{\circ}$ (c = 1.0; chloroform).

The fractions containing a mixture of the diastereoisomeric compounds were discarded. The fractions containing the almost pure substance with the R_f -value 0.45 were subsequently continued and evaporated in vacuo. The residue was recrystallized once from petroleum ether and chromatographically pure 1-1-(4-amino-3-chloro-5-trifluoromethyl-phenyl)-2-tert.-butylamino-O-[(*-*)-menthoxy-carbonyl]-ethanol was obtained.

M.p.: 102 to 104°C.

$[\alpha]_{364}^{20} = -273.5^{\circ}$ (C = 1.0; chloroform).

c.) d - 1 - (4 - Amino - 3 - chloro - 5 - trifluoromethyl - phenyl) - 2 - tert. - butyl - amino-ethanol

1.6 g of d-1-(4-amino-3-chloro-5-trifluoromethyl-phenyl)-2-tert.-butylamino-O-[(*-*)-menthoxy-carbonyl]-ethanol were dissolved in 16 ml of methanol and allowed to stand for 65 hours at about 20°C. The mixture was evaporated in vacuo and the residue was purified by column chromatography (silica gel; chloroform:methanol:concentrated ammonia = 90:10:1). The fractions containing the desired substance were combined and evaporated in vacuo. The residue was dissolved in ethyl acetate and the calculated quantity of 4N hydrochloric acid in isopropanol was added, whereupon the hydrochloride of the title compound crystallized out.

M.p.: > 194°C slow decomposition.

$[\alpha]_{364}^{20} = +154.9^{\circ}$ (c = 1.0; methanol).

d.) 1 - 1 - (4 - Amino - 3 - chloro - 5 - trifluoromethyl - phenyl) - 2 - tert. - butylamino - ethanol

Prepared from 1.58 g of 1-1-(4-amino-3-chloro-5-trifluoromethyl-phenyl)-2-tert.-butylamino-O-[(*-*)-menthoxy-carbonyl]-ethanol by solvolysis with methanol and purification by chromatography analogously to Example 174c).

M.p. of the hydrochloride: > 194°C slow decomposition.

$[\alpha]_{364}^{20} = -154.8^{\circ}$ (c = 1.0; methanol).

Example 175.

d - 1 - (4 - Amino - 3 - bromo - 5 - fluoro - phenyl) - 2 - tert. - butylamino - ethanol and 1 - 1 - (4 - amino - 3 - bromo - 5 - fluoro - phenyl) - 2 - tert. - butylamino - ethanol

205 g of d,1-1-(4-amino-3-bromo-5-fluoro-phenyl)-2-tert.-butylamino-ethanol 118 g of dibenzoyl-D-tartaric acid were dissolved in 2.5 l of hot ethanol. The mixture was filtered and the filtrate was left to stand for one day at room temperature for crystallization. The crude product thus obtained was recrystallized six times from methanol-ether, whereby pure d-1-(4-amino-3-bromo-5-fluoro-phenyl)-2-tert.-butylamino-ethanol-dibenzoyl-D-tartrate of m.p. 206 to 208°C (decomposition) was obtained.

$[\alpha]_{364}^{20} = +332.9^{\circ}$ (c = 2.0; methanol).

The salt was dissolved in methanol and concentrated ammonia whilst heating and the base was crystallized out by addition of water. The free base thus obtained was dissolved in absolute ethanol and neutralized with absolute ethanolic hydrochloric acid. d-1-(4-amino-3-bromo-5-fluoro-phenyl)-2-tert.-butylamino-ethanol hydrochloride crystallized on addition of ether.

M.p.: 234 to 235°C (decomposition).

$[\alpha]_{364}^{20} = +132.0^{\circ}$ (c = 2.0; methanol).

The mother liquors of the precipitation of the d-1-(4-amino-3-bromo-5-fluoro-phenyl)-2-tert.-butylamino-ethanol-dibenzoyl-D-tartrate and of the first recrystallization were combined and evaporated to a smaller volume. Concentrated ammonia and water were added and 140 g of the 1-(4-amino-3-bromo-5-fluoro-phenyl)-2-tert.-butylamino-ethanol (1-form enriched) were obtained. This stereoisomeric mixture was dissolved in 1.8 l of absolute ethanol and a solution of 82 g of dibenzoyl-L-tartaric acid in 500 ml of absolute ethanol were added. The mixture was evaporated to a volume of 1 l and left to stand for three days at room temperature for crystallization. The obtained product was recrystallized 6 times from methanol/ether. Pure 1-1-(4-amino-3-bromo-5-fluoro-phenyl)-2-tert.-butylamino ethanol-dibenzoyl-L-tartrate was obtained.

M.p.: 204 to 206°C (decomposition).

$[\alpha]_{364}^{20} = 133.9^{\circ}$ (c = 2.0; methanol).

The salt was dissolved in methanol and concentrated ammonia whilst heating and the free base was precipitated by the addition of water. The base was dissolved in absolute ethanol, neutralized with absolute ethanolic hydrochloric acid and 1-1-(4-amino-3-bromo-5-fluoro-phenyl)-2-tert.-butylamino-ethanol hydrochloride crystallized out on addition of ether.

M.p.: 218 to 220°C (decomposition).

$[\alpha]_{364}^{20} = 133.9^{\circ}$ (c = 2.0; methanol).

Example 176.

d-1-(4-Amino-3-chloro-5-fluoro-phenyl)-2-tert.-butylamino-ethanol
Mp. of the hydrochloride: 210 to 211°C (decomposition).
 $[\alpha]_{364}^{20} = +139.7^{\circ}$ (c = 2.0; methanol).

Prepared from d,1-1-(4-amino-3-chloro-5-fluoro-phenyl)-2-tert.-butylamino-ethanol by fractional crystallization of the dibenzoyl-D-tartrate analogously to Example 175.

1-1-(4-Amino-3-chloro-5-fluoro-phenyl)-2-tert.-butylamino-ethanol
M.p. of the hydrochloride 209 to 210°C (decomp.).
 $[\alpha]_{364}^{20} = -139.2^{\circ}$ (c = 2.0; methanol).

Prepared from d,1-1-(4-amino-3-chloro-5-fluoro-phenyl)-2-tert.-butylamino-ethanol by fractional crystallization of the dibenzoyl-L-tartrate analogously to Example 175.

Example 177.

d-1-(4-Amino-3-chloro-5-cyano-phenyl)-2-tert.-butylamino-ethanol
M.p. of the hydrochloride: 197 to 199°C (decomposition).
 $[\alpha]_{364}^{20} = +59.9^{\circ}$ (c = 2.0; methanol).

Prepared from d,1-1-(4-amino-3-chloro-5-cyano-phenyl)-2-tert.-butylamino-ethanol by fractional crystallization of the dibenzoyl-D-tartrate analogously to Example 175.

1-1-(4-Amino-3-chloro-5-cyano-phenyl)-2-tert.-butylamino-ethanol
M.p. of the hydrochloride: 199 to 202°C (decomposition).
 $[\alpha]_{364}^{20} = 59.85^{\circ}$ (c = 2.0; methanol).

Prepared from d,1-1-(4-amino-3-chloro-5-cyano-phenyl)-2-tert.-butylamino-ethanol by fractional crystallization of the dibenzoyl-L-tartrate analogously to Example 175.

Example 178.

d-1-(4-Amino-3-chloro-5-fluoro-phenyl)-2-tert.-butylamino-ethanol
0.26 g of d-1-(4-amino-3-fluoro-phenyl)-2-tert.-butylamino-ethanol hydrochloride and 0.2 ml of pyridine were dissolved in 30 ml of tetrahydrofuran and cooled to 0°C. 0.3 g of iodosobenzene dichloride were added, the mixture was held at 0°C for 2 hours and a further 0.1 g of iodosobenzene dichloride was added. After 20 hours at about 4°C, the solution was evaporated and the residue was distributed between ethyl acetate and water. The aqueous extract was made alkaline with 2N ammonia and the aqueous mixture was again extracted with ethyl acetate. The organic layer was washed with water, dried and evaporated to dryness in vacuo. The residue was dissolved in absolute ethanol, neutralized with ethanolic hydrochloric acid and the hydrochloride of the title compound was crystallized by the addition of ether.

M.p. 210—211°C (decomposition).
 $[\alpha]_{364}^{20} = +139.6^{\circ}$ (c = 2.0; methanol).

Example 179.

d-1-(4-Amino-3-bromo-5-fluoro-phenyl)-2-tert.-butylamino-ethanol
0.26 g of d-1-(4-amino-3-fluoro-phenyl)-2-tert.-butylamino-ethanol hydrochloride were dissolved in 30 ml of 50% ethyl acetate and 0.16 g of bromine, dissolved in 5 ml of ethyl acetate and 1 ml of water, were added at 0 to 5°C. After 15 minutes, the reaction mixture was evaporated, the residue was dissolved in water, made alkaline with 2N ammonia and extracted with chloroform. The chloroform solution was dried over sodium sulfate and evaporated to dryness in vacuo. The residue was converted into the hydrochloride of the title compound by dissolving in ethanol, neutralizing with ethanolic hydrochloric acid and adding ether.

M.p. 234 to 235°C (decomposition).
 $[\alpha]_{364}^{20} = +132.0^{\circ}$ (c = 2.0; methanol).

Example 180.

1-(4-Amino-3-cyano-phenyl)-2-cyclobutylamino-ethanol
M.p. of the hydrobromide: > 193°C (decomp.).
Prepared from 4'-amino-3'-cyano-2-cyclobutylamino-acetophenone hydrochloride and sodium borohydride analogously to Example 1.

- The following compounds have also been prepared analogously to Example 1.
- 1 - (4 - Amino - 3 - cyano - phenyl) - 2 - tert. - pentylamino - ethanol
M.p.: 143°C.
- 5 1 - (4 - Amino - 3 - trifluoromethyl - phenyl) - 2 - tert. - butylamino - ethanol
M.p. of the hydrochloride: 172 to 174°C (decomp.).
- 1 - (4 - Amino - 3 - trifluoromethyl - phenyl) - 2 - tert. - pentylamino - ethanol
M.p. of the hydrobromide: 174 to 175°C (decomp.).

Example 181.

- 10 1 - (4 - Amino - 3 - chloro - 5 - fluoro - phenyl) - 2 - isopropylamino - ethanol
M.p. of the hydrochloride: 152 to 154°C (decomp.).
Prepared from 1 - (4 - amino - 3 - fluoro - phenyl) - 2 - isopropylamino - ethanol hydrochloride and chlorine analogously to Example 4.

The following compounds have been prepared analogously to Examples 4, 5 or 112:

- 15 1 - (4 - Amino - 3 - chloro - 5 - fluoro - phenyl) - 2 - cyclopropylamino - ethanol hydrochloride
M.p.: 175 to 177°C (decomp.).
- 20 1 - (4 - Amino - 3 - chloro - 5 - fluoro - phenyl) - 2 - tert. - butylamino - ethanol hydrochloride
M.p.: 206 to 208°C (decomp.).
- 1 - (4 - Amino - 3 - chloro - 5 - fluoro - phenyl) - 2 - tert. - pentylamino - ethanol hydrochloride
M.p.: 187 to 188°C (decomp.).
- 25 1 - (4 - Amino - 3 - bromo - 5 - fluoro - phenyl) - 2 isopropylamino - ethanol hydrochloride
M.p.: 171 to 173°C (decomp.).
- 1 - (4 - Amino - 3 - bromo - 5 - fluoro - phenyl) - 2 - tert. - butylamino - ethanol hydrochloride
M.p.: 207 to 208°C (decomp.).
- 30 1 - (4 - Amino - 3 - bromo - 5 - fluoro - phenyl) - 2 - cyclobutylamino - ethanol hydrochloride
M.p.: 164 to 166°C (decomp.).
- 1 - (4 - Amino - 3 - fluoro - 5 - iodo - phenyl) - 2 - cyclopropylamino - ethanol hydrochloride
M.p.: 199 to 201°C (decomp.).
- 35 1 - (4 - Amino - 3 - chloro - 5 - cyano - phenyl) - 2 - propylamino - ethanol hydrochloride
M.p.: 187 to 189°C.
- 40 1 - (4 - Amino - 3 - chloro - 5 - cyano - phenyl) - 2 - sec. - butylamino - ethanol hydrochloride
M.p.: 190 to 191°C.
- 1 - (4 - Amino - 3 - chloro - 5 - cyano - phenyl) - 2 - tert. - butylamino - ethanol hydrochloride
M.p.: 125 to 133°C.
- 45 1 - (4 - Amino - 3 - chloro - 5 - cyano - phenyl) - 2 - (hydroxy - tert. - butylamino) - ethanol hydrochloride
M.p.: 228 to 230°C (decomp.).
- 1 - (4 - Amino - 3 - chloro - 5 - cyano - phenyl) - 2 - tert. - pentylamino - ethanol hydrochloride
M.p.: 218 to 220°C (decomp.).
- 50 1 - (4 - Amino - 3 - chloro - 5 - cyano - phenyl) - 2 - cyclopentylamino - ethanol hydrochloride
M.p.: 138 to 144°C.
- 1 - (4 - Amino - 3 - chloro - 5 - cyano - phenyl) - 2 - [1 - (3,4 - methylenedioxy - phenyl) - 2 - propylamino] - ethanol hydrochloride
M.p.: 189 to 192°C.
- 55 1 - (4 - Amino - 3 - bromo - 5 - cyano - phenyl) - 2 - isopropylamino - ethanol hydrochloride
M.p.: 186 to 189°C.
- 1 - (4 - Amino - 3 - bromo - 5 - cyano - phenyl) - 2 - tert. - butylamino - ethanol hydrochloride
M.p.: 213 to 215°C.
- 60 1 - (4 - Amino - 3 - bromo - 5 - cyano - phenyl) - 2 - cyclobutylamino - ethanol hydrochloride
M.p.: 215 to 216°C (decomp.).

	1 - (4 - Amino - 3 - chloro - 5 - trifluoromethyl - phenyl) - 2 - isopropylamino - ethanol M.p.: 104 to 106°C.	
5	1 - (4 - Amino - 3 - chloro - 5 - trifluoromethyl - phenyl) - 2 - tert. - butylamino - ethanol hydrochloride M.p.: 205 to 207°C (decomp.).	5
	1 - (4 - Amino - 3 - chloro - 5 - trifluoromethyl - phenyl) - 2 - cyclobutylamino - ethanol hydrochloride M.p.: 177 to 178°C.	
10	1 - (4 - Amino - 3 - chloro - 5 - trifluoromethyl - phenyl) - 2 - tert. - pentylamino - ethanol hydrochloride M.p.: 176 to 178°C (decomp.).	10
	1 - (4 - Amino - 3 - bromo - 5 - trifluoromethyl - phenyl) - 2 - isopropylamino - ethanol hydrochloride M.p.: 177 to 179°C (decomp.).	
15	1 - (4 - Amino - 3 - chloro - 5 - nitro - phenyl) - 2 - tert. - butylamino - ethanol M.p.: 148 to 149°C.	15
	1 - (4 - Amino - 3 - bromo - 5 - nitro - phenyl) - 2 - tert. - butylamino - ethanol M.p.: 151 to 152°C.	
20	Example 182. 1-(4-Amino-3-chloro-5-fluoro-phenyl)-2-isopropylamino-ethanol M.p. of the hydrochloride: 152 to 154°C (decomp.). Prepared from 1-(4-acetylamino-3-chloro-5-fluoro-phenyl)-2-isopropylamino-ethanol hydrochloride analogously to Example 7 or from 1-(4-amino-3-chloro-5-fluoro-phenyl)-2-(N-benzyl-N-isopropyl)-amino-ethanol analogously to Example 10.	20
25	The following compounds have been prepared analogously to Examples 7 or 10.	25
	1 - (4 - Amino - 3 - chloro - 5 - fluoro - phenyl) - 2 - cyclopropylamino - ethanol hydrochloride M.p.: 175 to 177°C (decomp.).	
30	1 - (4 - Amino - 3 - chloro - 5 - fluoro - phenyl) - 2 - tert. - pentylamino - ethanol hydrochloride M.p.: 187 to 188°C (decomp.).	30
	1 - (4 - Amino - 3 - bromo - 5 - fluoro - phenyl) - 2 - isopropylamino ethanol hydrochloride M.p.: 171 to 173°C (decomp.).	
35	1 - (4 - Amino - 3 - bromo - 5 - fluoro - phenyl) - 2 - tert. - butylamino - ethanol hydrochloride M.p.: 207 to 208°C (decomp.).	35
	1 - (4 - Amino - 3 - bromo - 5 - fluoro - phenyl) - 2 - cyclobutylamino - ethanol hydrochloride M.p.: 164 to 166°C (decomp.).	
40	1 - (4 - Amino - 3 - fluoro - 5 - iodo - phenyl) - 2 - cyclopropylamino - ethanol hydrochloride M.p.: 199 to 201°C (decomp.).	40
45	1 - (4 - Amino - 3 - trifluoromethyl - phenyl) - 2 - tert. - pentylamino - ethanol hydrobromide M.p.: 174 to 175°C (decomp.).	45
	1 - (4 - Amino - 3 - chloro - 5 - trifluoromethyl - phenyl) - 2 - isopropylamino - ethanol M.p.: 104 to 106°C.	
50	1 - (4 - Amino - 3 - chloro - 5 - trifluoromethyl - phenyl) - 2 - tert. - butylamino - ethanol hydrochloride M.p.: 205 to 207°C (decomp.).	50
	1 - (4 - Amino - 3 - chloro - 5 - trifluoromethyl - phenyl) - 2 - cyclobutylamino - ethanol hydrochloride. M.p.: 177 to 178°C.	
55	1 - (4 - Amino - 3 - chloro - 5 - trifluoromethyl - phenyl) - 2 - tert. - pentylamino - ethanol hydrochloride M.p.: 176 to 178°C (decomp.).	55
	1 - (4 - Amino - 3 - bromo - 5 - trifluoromethyl - phenyl) - 2 - isopropylamino - ethanol hydrochloride M.p.: 177 to 179°C (decomp.).	
60		60

Example 183.

1-(4-Amino-3-chloro-5-nitro-phenyl)-2-tert.-butylamino-ethanol
M.p.: 148 to 149°C.

Prepared from 1-(4-acetylamino-3-chloro-5-nitro-phenyl)-2-tert.-butylamino-ethanol hydrochloride analogously to Example 7.

The following compound has also been prepared analogously to Example 7.
1 - (4 - Amino - 3 - bromo - 5 - nitro - phenyl) - 2 - tert. - butylamino - ethanol
M.p.: 151 to 152°C.

Example 184.

1-(4-Amino-3-fluoro-phenyl)-2-tert.-butylamino-ethanol
M.p. of the hydrochloride: 196 to 197°C (decomp.).

Prepared from 1-(4-amino-3-bromo-5-fluoro-phenyl)-2-tert.-butylamino-ethanol analogously to Example 14.

The following compound has also been prepared analogously to Example 14.
1 - (4 - Amino - 3 - trifluoromethyl - phenyl) - 2 - tert. - butylamino - ethanol
M.p. of the hydrochloride: 172 to 174°C (decomp.).

Example 185.

1-(4-Amino-3-chloro-5-trifluoromethyl-phenyl)-2-tert.-butylamino-ethanol

3.4 g of 1-(4-amino-3-chloro-5-trifluoromethyl-phenyl)-2-bromoethanol were dissolved in 25 ml of tert.-butylamine and allowed to stand for 20 hours at room temperature. The excess of tert.-butylamine was removed in vacuo and the residue was dissolved in ether. The ethereal solution was washed with water, dried over magnesium sulfate and evaporated in vacuo. The evaporation residue was purified chromatographically by passage through a silica gel column (chloroform:methanol:concentrated ammonia = 90:10; 1). The combined fractions containing the title compound thus obtained were evaporated to dryness in vacuo. The residue was dissolved in ether, and the solution was adjusted to a pH of 4 with isopropanolic hydrochloric acid. 1-(4-Amino-3-chloro-5-trifluoromethyl-phenyl)-2-tert.-butylamino-ethanol hydrochloride crystallized out. The crystals were filtered and washed with ether and melted at 205 to 207°C (decomp.).

Example 186.

1-(4-Amino-3-chloro-5-trifluoromethyl-phenyl)-2-tert.-butylamino-ethanol
M.p. of the hydrochloride: 205 to 207°C (decomp.).

Prepared according to process f) from 1-(4-amino-3-chloro-5-trifluoromethyl-phenyl)-2-(p-toluenesulfonyloxy)-ethanol and an excess of tert.-butylamine analogously to Example 186.

The following compounds have been prepared analogously to Examples 185 and 186.

1 - (4 - Amino - 3 - fluoro - phenyl) - 2 - tert. - butylamino - ethanol hydrochloride
M.p.: 196 to 197°C (decomp.).

1 - (4 - Amino - 3 - chloro - 5 - fluoro - phenyl) - 2 - isopropylamino - ethanol hydrochloride
M.p.: 152 to 154°C (decomp.).

1 - (4 - Amino - 3 - chloro - 5 - fluoro - phenyl) - 2 - cyclopropylamino - ethanol hydrochloride
M.p.: 175 to 177°C (decomp.).

1 - (4 - Amino - 3 - chloro - 5 - fluoro - phenyl) - 2 - tert. - butylamino - ethanol hydrochloride
M.p.: 206 to 208°C (decomp.).

1 - (4 - Amino - 3 - chloro - 5 - fluoro - phenyl) - 2 - tert. - pentylamino - ethanol hydrochloride
M.p.: 187 to 188°C (decomp.).

1 - (4 - Amino - 3 - bromo - 5 - fluoro - phenyl) - 2 - isopropylamino - ethanol hydrochloride
M.p.: 171 to 173°C (decomp.).

1 - (4 - Amino - 3 - bromo - 5 - fluoro - phenyl) - 2 - tert. - butylamino - ethanol hydrochloride
M.p.: 207 to 208°C (decomp.).

1 - (4 - Amino - 3 - bromo - 5 - fluoro - phenyl) - 2 - cyclobutylamino - ethanol hydrochloride
M.p.: 164 to 166°C (decomp.).

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	1 - (4 - Amino - 3 - fluoro - 5 - iodo - phenyl) - 2 - cyclopropylamino - ethanol hydrochloride M.p.: 199 to 201°C (decomp.).	
5	1 - (4 - Amino - 3 - cyano - 5 - fluoro - phenyl) - 2 - isopropylamino - ethanol hydrochloride M.p.: 182 to 184°C (decomp.).	5
	1 - (4 - Amino - 3 - cyano - 5 - fluoro - phenyl) - 2 - tert. - butylamino - ethanol hydrochloride M.p.: 242 to 243°C (decomp.).	
10	1 - (4 - Amino - 3 - cyano - phenyl) - 2 - cyclobutylamino - ethanol hydrobromide M.p.: > 193°C (decomp.).	10
	1 - (4 - Amino - 3 - cyano - phenyl) - 2 - tert. - pentylamino - ethanol M.p.: 143°C.	
15	1 - (4 - Amino - 3 - chloro - 5 - cyano - phenyl) - 2 - propylamino - ethanol hydrochloride M.p.: 187 to 189°C.	15
	1 - (4 - Amino - 3 - chloro - 5 - cyano - phenyl) - 2 - sec. - butylamino - ethanol dihydrochloride M.p.: 190 to 191°C.	
20	1 - (4 - Amino - 3 - chloro - 5 - cyano - phenyl) - 2 - tert. - butylamino - ethanol M.p.: 125 to 133°C.	20
	1 - (4 - Amino - 3 - chloro - 5 - cyano - phenyl) - 2 - (hydroxy - tert. - butylamino) - ethanol hydrochloride M.p.: 228 to 230°C (decomp.).	
25	1 - (4 - Amino - 3 - chloro - 5 - cyano - phenyl) - 2 - tert. - pentylamino - ethanol hydrochloride M.p.: 218 to 220°C (decomp.).	25
	1 - (4 - Amino - 3 - chloro - 5 - cyano - phenyl) - 2 - cyclopentylamino - ethanol hydrochloride M.p.: 138 to 144°C.	
30	1 - (4 - Amino - 3 - chloro - 5 - cyano - phenyl) - 2 - [1 - (3,4 - methylenedioxy - phenyl)-2-propylamino]-ethanol hydrochloride M.p.: 189 to 192°C.	30
35	1 - (4 - Amino - 3 - bromo - 5 - cyano - phenyl) - 2 - isopropylamino - ethanol hydrochloride M.p.: 186 to 189°C.	35
	1 - (4 - Amino - 3 - bromo - 5 - cyano - phenyl) - 2 - tert. - butylamino - ethanol hydrochloride M.p.: 213 to 215°C.	
40	1 - (4 - Amino - 3 - bromo - 5 - cyano - phenyl) - 2 - cyclobutylamino - ethanol hydrochloride M.p.: 215 to 216°C (decomp.).	40
	1 - (4 - Amino - 3,5 - dicyano - phenyl) - 2 - tert. - butylamino ethanol hydrochloride M.p.: 251 to 253°C (decomp.).	
45	1 - (4 - Amino - 3 - trifluoromethyl - phenyl) - 2 - tert. - butylamino - ethanol hydrochloride M.p.: 172 to 174°C (decomp.).	45
	1 - (4 - Amino - 3 - trifluoromethyl - phenyl) - 2 - tert. - pentylamino - ethanol hydrobromide M.p.: 174 to 175°C (decomp.).	
50	1 - (4 - Amino - 3 - chloro - 5 - trifluoromethyl - phenyl) - 2 - isopropylamino - ethanol hydrochloride M.p.: 185 to 187°C.	50
	1 - (4 - Amino - 3 - chloro - 5 - trifluoromethyl - phenyl) - 2 - cyclobutylamino - ethanol hydrochloride M.p.: 177 to 178°C.	
55	1 - (4 - Amino - 3 - chloro - 5 - trifluoromethyl - phenyl) - 2 - tert. - pentylamino - ethanol hydrochloride M.p.: 176 to 178°C (decomp.).	55
	1 - (4 - Amino - 3 - bromo - 5 - trifluoromethyl - phenyl) - 2 - isopropylamino - ethanol hydrochloride M.p.: 177 to 179°C (decomp.).	
60		60

1 - (4 - Amino - 3 - chloro - 5 - nitro - phenyl) - 2 - tert. - butylamino - ethanol
M.p.: 148 to 149°C.

1 - (4 - Amino - 3 - bromo - 5 - nitro - phenyl) - 2 - tert. - butylamino - ethanol
M.p.: 151 to 152°C.

Example 187.

1-(4-Amino-3-bromo-5-fluoro-phenyl)-2-tert.-butylamino-ethanol-hydrochloride
1.5 g of 2-tert.-butylamino-1-(3-bromo-5-fluoro-4-nitro-phenyl)-ethanol hydrochloride were dissolved in 40 ml of methanol. After addition of 0.6 g of platinum dioxide, the mixture was hydrogenated whilst shaking at room temperature and normal pressure until the theoretical quantity of hydrogen had been absorbed. The catalyst was removed and the solution was evaporated to dryness in vacuo. The crude, solid residue of 1-(4-amino-3-bromo-5-fluoro-phenyl)-2-tert.-butylamino-ethanol hydrochloride was distributed between 2N sodium hydroxide solution and methylene chloride. The organic layer was separated, washed with water, dried over sodium sulfate and evaporated to dryness in vacuo. The remaining oily residue was purified chromatographically by passing it through a chromatography column filled with 80 g of silica gel, using a mixture of chloroform and methanol = 10:1 as eluent. The eluates containing the desired product were combined and evaporated to dryness in vacuo. The residue was dissolved in a small quantity of isopropanol and acidified to a pH of 5 with ethereal hydrochloric acid. After addition of a small quantity of ether the product crystallized. The crystals were suction filtered and washed with a mixture of isopropanol and ether.

M.p.: 207 to 208°C (decomp.).

The following compounds have been prepared analogously to Example 187:

1 - (4 - Amino - 3 - fluoro - phenyl) - 2 - tert. - butylamino - ethanol hydrochloride

M.p.: 196 to 197°C (decomp.).

1 - (4 - Amino - 3 - chloro - 5 - fluoro - phenyl) - 2 - isopropylamino - ethanol hydrochloride

M.p.: 152 to 154°C (decomp.).

1 - (4 - Amino - 3 - chloro - 5 - fluoro - phenyl) - 2 - cyclopropylamino - ethanol hydrochloride

M.p.: 175 to 177°C (decomp.).

1 - (4 - Amino - 3 - chloro - 5 - fluoro - phenyl) - 2 - tert. - butylamino - ethanol hydrochloride

M.p.: 206 to 208°C (decomp.).

1 - (4 - Amino - 3 - chloro - 5 - fluoro - phenyl) - 2 - tert. - pentylamino - ethanol hydrochloride

M.p.: 187 to 188°C (decomp.).

1 - (4 - Amino - 3 - bromo - 5 - fluoro - phenyl) - 2 - isopropylamino - ethanol hydrochloride

M.p.: 171 to 173°C (decomp.).

1 - (4 - Amino - 3 - bromo - 5 - fluoro - phenyl) - 2 - cyclobutylamino - ethanol hydrochloride

M.p. 164 to 166°C (decomp.).

1 - (4 - Amino - 3 - fluoro - 5 - iodo - phenyl) - 2 - cyclopropylamino - ethanol hydrochloride

M.p.: 199 to 201°C (decomp.).

1 - (4 - Amino - 3 - cyano - 5 - fluoro - phenyl) - 2 - isopropylamino - ethanol hydrochloride

M.p.: 182 to 184°C (decomp.).

1 - (4 - Amino - 3 - cyano - 5 - fluoro - phenyl) - 2 - tert. - butylamino - ethanol hydrochloride

M.p.: 242 to 243°C (decomp.).

1 - (4 - Amino - 3 - cyano - phenyl) - 2 - cyclobutylamino - ethanol hydrobromide

M.p.: > 193°C (decomp.).

1 - (4 - Amino - 3 - cyano - phenyl) - 2 - tert. - pentylamino - ethanol hydrochloride

M.p.: 143°C.

1 - (4 - Amino - 3 - chloro - 5 - cyano - phenyl) - 2 - propylamino - ethanol hydrochloride

M.p.: 187 to 189°C.

1 - (4 - Amino - 3 - chloro - 5 - cyano - phenyl) - 2 - sec. - butylamino - ethanol dihydrochloride

M.p.: 190 to 191°C.

- 1 - (4 - Amino - 3 - chloro - 5 - cyano - phenyl) - 2 - tert. - butylamino - ethanol
M.p.: 125 to 133°C.
- 1 - (4 - Amino - 3 - chloro - 5 - cyano - phenyl) - 2 - (hydroxy - tert. - butylamino) - ethanol hydrochloride
M.p.: 228 to 230°C (decomp.).
- 1 - (4 - Amino - 3 - chloro - 5 - cyano - phenyl) - 2 - tert. - pentylamino - ethanol hydrochloride
M.p.: 218 to 220°C (decomp.).
- 1 - (4 - Amino - 3 - chloro - 5 - cyano - phenyl) - 2 - cyclopentylamino - ethanol hydrochloride
M.p.: 138 to 144°C.
- 1 - (4 - Amino - 3 - chloro - 5 - cyano - phenyl) - 2 - [1 - (3,4 - methylenedioxy - phenyl)-2-propylamino]-ethanol hydrochloride
M.p.: 189 to 192°C.
- 1 - (4 - Amino - 3 - bromo - 5 - cyano - phenyl) - 2 - isopropylamino - ethanol hydrochloride
M.p.: 186 to 189°C.
- 1 - (4 - Amino - 3 - bromo - 5 - cyano - phenyl) - 2 - tert. - butylamino - ethanol hydrochloride
M.p.: 213 to 215°C.
- 1 - (4 - Amino - 3 - bromo - 5 - cyano - phenyl) - 2 - cyclobutylamino - ethanol hydrochloride
M.p.: 215 to 216°C (decomp.).
- 1 - (4 - Amino - 3,5 - dicyano - phenyl) - 2 - tert. - butylamino - ethanol hydrochloride
M.p.: 251 to 253°C (decomp.).
- 1 - (4 - Amino - 3 - trifluoromethyl - phenyl) - 2 - tert. - butylamino - ethanol hydrochloride
M.p.: 172 to 174°C (decomp.).
- 1 - (4 - Amino - 3 - trifluoromethyl - phenyl) - 2 - tert. - pentylamino - ethanol hydrobromide
M.p.: 174 to 175°C (decomp.).
- 1 - (4 - Amino - 3 - chloro - 5 - trifluoromethyl - phenyl) - 2 - isopropylamino - ethanol
M.p.: 104 to 106°C.
- 1 - (4 - Amino - 3 - chloro - 5 - trifluoromethyl - phenyl) - 2 - tert. - butylamino - ethanol hydrochloride
M.p.: 205 to 207°C (decomp.).
- 1 - (4 - Amino - 3 - chloro - 5 - trifluoromethyl - phenyl) - 2 - cyclobutylamino - ethanol hydrochloride
M.p.: 177 to 178°C.
- 1 - (4 - Amino - 3 - chloro - 5 - trifluoromethyl - phenyl) - 2 - tert. - pentylamino - ethanol hydrochloride
M.p.: 176 to 178°C (decomp.).
- 1 - (4 - Amino - 3 - bromo - 5 - trifluoromethyl - phenyl) - 2 - isopropylamino - ethanol hydrochloride
M.p.: 177 to 179°C (decomp.).

Example 188.

1-(4-Amino-3-bromo-5-fluoro-phenyl)-2-tert.-butylamino-ethanol
1.2 g of lithium aluminium hydride were added to 4.8 g of 4-amino-3-bromo-5-fluoro-phenylglycolic acid N-(tert-butyl)-amide in 100 ml of absolute ether and refluxed for 2 hours with stirring. Subsequently the excess of lithium aluminium hydride was decomposed with ethyl acetate. Water and 2N sodium hydroxide solution were added and the two layers were separated. The aqueous layer was extracted with chloroform, and the combined organic layers were dried and evaporated in vacuo. The residue was purified by column chromatography over silica gel (chloroform:methanol:concentrated ammonia = 90:10:1). The evaporation residue of the fractions containing the substance was dissolved in isopropanol and acidified to a pH of 5 with ethereal hydrochloric acid. After addition of ether the product crystallized. The precipitated hydrochloride of the title compound was recrystallized from isopropanol.
M.p.: 207 to 208°C (decomp.).

The following compounds have been prepared analogously to Example 188.

- 1 - (4 - Amino - 3 - fluoro - phenyl) - 2 - tert. - butylamino - ethanol hydrochloride
M.p.: 196 to 197°C (decomp.).

- 5 1 - (4 - Amino - 3 - chloro - 5 - fluoro - phenyl) - 2 - isopropylamino - ethanol hydrochloride
M.p.: 152 to 154°C (decomp.).
- 5 1 - (4 - Amino - 3 - chloro - 5 - fluoro - phenyl) - 2 - cyclopropylamino - ethanol hydrochloride
M.p.: 175 to 177°C (decomp.).
- 10 1 - (4 - Amino - 3 - chloro - 5 - fluoro - phenyl) - 2 - tert. - butylamino - ethanol hydrochloride
M.p.: 206 to 208°C (decomp.).
- 10 1 - (4 - Amino - 3 - chloro - 5 - fluoro - phenyl) - 2 - tert. - pentylamino - ethanol hydrochloride
M.p.: 187 to 188°C (decomp.).
- 15 1 - (4 - Amino - 3 - bromo - 5 - fluoro - phenyl) - 2 - isopropylamino - ethanol hydrochloride
M.p.: 171 to 173°C (decomp.).
- 15 1 - (4 - Amino - 3 - bromo - 5 - fluoro - phenyl) - 2 - cyclobutylamino - ethanol hydrochloride
M.p.: 164 to 166°C (decomp.).
- 20 1 - (4 - Amino - 3 - fluoro - 5 - iodo - phenyl) - 2 - cyclopropylamino - ethanol hydrochloride
M.p.: 199 to 201°C (decomp.).
- 20 1 - (4 - Amino - 3 - trifluoromethyl - phenyl) - 2 - tert. - butylamino - ethanol hydrochloride
M.p.: 172 to 174°C (decomp.).
- 25 1 - (4 - Amino - 3 - trifluoromethyl - phenyl) - 2 - tert. - pentylamino - ethanol hydrobromide
M.p.: 174 to 175°C (decomp.).
- 25 1 - (4 - Amino - 3 - chloro - 5 - trifluoromethyl - phenyl) - 2 - isopropylamino - ethanol
M.p.: 104 to 106°C.
- 30 1 - (4 - Amino - 3 - chloro - 5 - trifluoromethyl - phenyl) - 2 - tert. - butylamino - ethanol hydrochloride
M.p.: 205 to 207°C (decomp.).
- 35 1 - (4 - Amino - 3 - chloro - 5 - trifluoromethyl - phenyl) - 2 - cyclobutylamino - ethanol hydrochloride
M.p.: 177 to 178°C.
- 35 1 - (4 - Amino - 3 - chloro - 5 - trifluoromethyl - phenyl) - 2 tert. - pentylamino - ethanol hydrochloride
M.p.: 176 to 178°C (decomp.).
- 40 1 - (4 - Amino - 3 - bromo - 5 - trifluoromethyl - phenyl) - 2 - isopropylamino - ethanol hydrochloride
M.p.: 177 to 179°C (decomp.).

Example 189.

- 45 1-(4-Amino-3-bromo-5-fluoro-phenyl)-2-tert.-butylamino-ethanol
0.75 g of powdered lithium aluminium hydride were added to 4.2 g of 4-amino-3-bromo-5-fluoro-phenylglyoxylic acid N-(tert.-butyl)-amide in 100 ml of absolute ether, and the mixture was stirred mechanically and refluxed for 2 hours. 2.0 ml of water, 2.4 ml of 2N sodium hydroxide solution and 6.0 ml of water were carefully added. The reaction mixture was suction filtered, the inorganic residue was washed with chloroform and the combined filtrates were evaporated in vacuo. The residue was purified by chromatography using silica gel (eluent: chloroform:methanol:concentrated ammonia = 90:10:1). The evaporation residue of the fractions containing the desired compound was obtained by vacuum distillation of the solvents. The residue was dissolved in isopropanol and ethereal hydrochloric acid was added until the pH was 5. Further ether was added whereby the hydrochloride of the title compound crystallized. The crystals were suction filtered and recrystallized from isopropanol. M.p.: 207 to 208°C (decomp.).
- 50
- 55

The following compounds have been prepared analogously to Example 189:

- 60 1 - (4 - Amino - 3 - fluoro - phenyl) - 2 - tert. - butylamino - ethanol hydrochloride
M.p.: 196 to 197°C (decomp.).
- 60 1 - (4 - Amino - 3 - chloro - 5 - fluoro - phenyl) - 2 - isopropylamino - ethanol hydrochloride
M.p.: 152 to 154°C (decomp.).

- 1 - (4 - Amino - 3 - chloro - 5 - fluoro - phenyl) - 2 - cyclopropylamino - ethanol hydrochloride
M.p.: 175 to 177°C (decomp.).
- 5 1 - (4 - Amino - 3 - chloro - 5 - fluoro - phenyl) - 2 - tert. - butylamino - ethanol hydrochloride
M.p.: 206 to 208°C (decomp.).
- 1 - (4 - Amino - 3 - chloro - 5 - fluoro - phenyl) - 2 - tert. - pentylamino - ethanol hydrochloride
M.p.: 187 to 188°C (decomp.).
- 10 1 - (4 - Amino - 3 - bromo - 5 - fluoro - phenyl) - 2 - isopropylamino - ethanol hydrochloride
M.p.: 171 to 173°C (decomp.).
- 1 - (4 - Amino - 3 - bromo - 5 - fluoro - phenyl) - 2 - cyclobutylamino - ethanol hydrochloride
M.p.: 164 to 166°C (decomp.).
- 15 1 - (4 - Amino - 3 - fluoro - 5 - iodo - phenyl) - 2 - cyclopropylamino - ethanol hydrochloride
M.p.: 199 to 210°C (decomp.).
- 20 1 - (4 - Amino - 3 - trifluoromethyl - phenyl) - 2 - tert. - butylamino - ethanol hydrochloride
M.p.: 172 to 174°C (decomp.).
- 1 - (4 - Amino - 3 - trifluoromethyl - phenyl) - 2 - tert. - pentylamino - ethanol hydrobromide
M.p.: 174 to 175°C (decomp.).
- 25 1 - (4 - Amino - 3 - chloro - 5 - trifluoromethyl - phenyl) - 2 - isopropylamino - ethanol
M.p.: 104 to 106°C.
- 1 - (4 - Amino - 3 - chloro - 5 - trifluoromethyl - phenyl) - 2 - tert. - butylamino - ethanol hydrochloride
M.p.: 205 to 207°C (decomp.).
- 30 1 - (4 - Amino - 3 - chloro - 5 - trifluoromethyl - phenyl) - 2 - cyclobutylamino - ethanol hydrochloride
M.p.: 177 to 178°C.
- 1 - (4 - Amino - 3 - chloro - 5 - trifluoromethyl - phenyl) - 2 - tert. - pentylamino - ethanol hydrochloride
M.p.: 176 to 178°C (decomp.).
- 35 1 - (4 - Amino - 3 - bromo - 5 - trifluoromethyl - phenyl) - 2 - isopropylamino - ethanol hydrochloride
M.p.: 177 to 179°C (decomp.).
- 40 **Example 190.**
1-(4-Amino-3-chloro-5-trifluoromethyl-phenyl)-2-tert.-butylamino-ethanol
13 ml of 45% hydrobromic acid in glacial acetic acid were added at room temperature to 3.5 g of 5-(4-amino-3-chloro-5-trifluoromethyl-phenyl)-3-tert.-butyl-oxazolidone-(2) dissolved in 13 ml of glacial acetic acid. The mixture was allowed to stand for one hour. The reaction mixture was then poured on to ice, made alkaline with concentrated ammonia and extracted with ethyl acetate. The organic layer was extracted with 2N hydrochloric acid, the acidic solution was made alkaline with concentrated ammonia and the reaction product was again extracted with ethyl acetate. After evaporation of the organic solvent in vacuo a crude product was obtained, which was purified chromatographically by passing it through a silica gel column (eluent: chloroform: methanol: concentrated ammonia = 90:10:1). The 1-(4-amino-3-chloro-5-trifluoromethyl-phenyl)-2-tert.-butylamino-ethanol thus obtained was dissolved in ether and isopropanolic hydrochloric acid was added, whereby the hydrochloride was obtained of melting point 205 to 207°C (decomp.).
- 45
- 50
- 55 **Example 191.**
1-(4-Amino-3-bromo-5-fluoro-phenyl)-2-tert.-butylamino-ethanol
1.5 g of 5-(4-Amino-3-bromo-5-fluoro-phenyl)-3-tert.-butyl-oxazolidone-(2) were heated for 3 hours at 90°C in 25 ml of 3N hydrochloric acid. After cooling, the slightly turbid solution was filtered, the pH was adjusted to 9 with sodium hydroxide solution and the mixture was extracted with chloroform. The chloroform layer was washed with water, dried over sodium sulfate and evaporated to dryness in vacuo. The oily residue was dissolved in a small quantity of isopropanol and acidified to a pH of 5 with ethereal hydrochloric acid.
- 60

After addition of a small quantity of ether, the product crystallized. The crystals were suction filtered and washed with a mixture of isopropanol and ether.
M.p. 207 to 208°C (decomp.).

Example 192.

1-(4-Amino-3-chloro-5-cyano-phenyl)-2-tert.-butylamino-ethanol.

0.5 g of 5-(4-amino-3-chloro-5-cyano-phenyl)-3-tert.-butyl-oxazolidone-(2) (m.p. 115 to 119°C) were refluxed for 30 minutes with 5 ml of concentrated hydrochloric acid. The mixture was cooled, ice was added, and the mixture was then made alkaline with sodium hydroxide solution. The 1-(4-amino-3-chloro-5-cyano-phenyl)-2-tert.-butylamino-ethanol was extracted with chloroform. The product was purified by chromatography using silica gel (eluent: chloroform:methanol = 7:3).

M.p.: 131 to 135°C; m.p. of the hydrochloride: 204 to 207°C.

The following compounds have been prepared analogously to Examples 190 to 192:

1 - (4 - Amino - 3 - fluoro - phenyl) - 2 - tert. - butylamino - ethanol hydrochloride

M.p.: 196 to 197°C (decomp.).

1 - (4 - Amino - 3 - chloro - 5 - fluoro - phenyl) - 2 - isopropylamino - ethanol hydrochloride

M.p.: 152 to 154°C (decomp.).

1 - (4 - Amino - 3 - chloro - 5 - fluoro - phenyl) - 2 - cyclopropylamino - ethanol hydrochloride

M.p.: 175 to 177°C (decomp.).

1 - (4 - Amino - 3 - chloro - 5 - fluoro - phenyl) - 2 - tert. - butylamino - ethanol hydrochloride

M.p.: 206 to 208°C (decomp.).

1 - (4 - Amino - 3 - chloro - 5 - fluoro - phenyl) - 2 - tert. - pentylamino - ethanol hydrochloride

M.p.: 187 to 188°C (decomp.).

1 - (4 - Amino - 3 - bromo - 5 - fluoro - phenyl) - 2 - isopropylamino - ethanol hydrochloride

M.p.: 171 to 173°C (decomp.).

1 - (4 - Amino - 3 - bromo - 5 - fluoro - phenyl) - 2 - cyclobutylamino - ethanol hydrochloride

M.p.: 164 to 166°C (decomp.).

1 - (4 - Amino - 3 - fluoro - 5 - iodo - phenyl) - 2 - cyclopropylamino - ethanol hydrochloride

M.p.: 199 to 210°C (decomp.).

1 - (4 - Amino - 3 - cyano - 5 - fluoro - phenyl) - 2 - isopropylamino - ethanol hydrochloride

M.p.: 182 to 184°C (decomp.).

1 - (4 - Amino - 3 - cyano - 5 - fluoro - phenyl) - 2 - tert. - butylamino - ethanol hydrochloride

M.p.: 242 to 243°C (decomp.).

1 - (4 - Amino - 3 - cyano - phenyl) - 2 - cyclobutylamino - ethanol hydrobromide

M.p.: >193°C (decomp.).

1 - (4 - Amino - 3 - cyano - phenyl) - 2 - tert. - pentylamino - ethanol

M.p.: 143°C.

1 - (4 - Amino - 3 - chloro - 5 - cyano - phenyl) - 2 - propylamino - ethanol hydrochloride

M.p.: 187 to 189°C.

1 - (4 - Amino - 3 - chloro - 5 - cyano - phenyl) - 2 - sec. - butylamino - ethanol dihydrochloride

M.p.: 190 to 191°C.

1 - (4 - Amino - 3 - chloro - 5 - cyano - phenyl) - 2 - (hydroxy - tert. - butylamino) - ethanol hydrochloride

M.p.: 228 to 230°C (decomp.).

1 - (4 - Amino - 3 - chloro - 5 - cyano - phenyl) - 2 - tert. - pentylamino - ethanol hydrochloride

M.p.: 218 to 220°C (decomp.).

1 - (4 - Amino - 3 - chloro - 5 - cyano - phenyl) - 2 - cyclopentylamino - ethanol hydrochloride

M.p.: 138 to 144°C.

85

- 1 - (4 - Amino - 3 - chloro - 5 - cyano - phenyl) - 2 - [1 - (3,4 - methylenedioxy - phenyl) - 2 - propylamino] - ethanol hydrochloride
M.p.: 189 to 192°C.
- 5 1 - (4 - Amino - 3 - bromo - 5 - cyano - phenyl) - 2 - isopropylamino - ethanol hydrochloride
M.p.: 186 to 189°C.
- 10 1 - (4 - Amino - 3 - bromo - 5 - cyano - phenyl) - 2 - tert. - butylamino - ethanol hydrochloride
M.p.: 213 to 215°C (decomp.).
- 15 1 - (4 - Amino - 3 - bromo - 5 - cyano - phenyl) - 2 - cyclobutylamino - ethanol hydrochloride
M.p.: 215 to 216°C (decomp.).
- 1 - (4 - Amino - 3,5 - dicyano - phenyl) - 2 - tert. - butylamino - ethanol hydrochloride
M.p.: 251 to 253°C (decomp.).
- 20 1 - (4 - Amino - 3 - trifluoromethyl - phenyl) - 2 - tert. - butylamino - ethanol hydrochloride
M.p.: 172 to 174°C (decomp.).
- 1 - (4 - Amino - 3 - trifluoromethyl - phenyl) - 2 - tert. - pentylamino - ethanol hydrobromide
M.p.: 174 to 175°C (decomp.).
- 25 1 - (4 - Amino - 3 - chloro - 5 - trifluoromethyl - phenyl) - 2 - isopropylamino - ethanol
M.p.: 104 to 106°C.
- 1 - (4 - Amino - 3 - chloro - 5 - trifluoromethyl - phenyl) - 2 - cyclobutylamino - ethanol hydrochloride
M.p.: 177 to 178°C.
- 30 1 - (4 - Amino - 3 - chloro - 5 - trifluoromethyl - phenyl) - 2 - tert. - pentylamino - ethanol hydrochloride
M.p.: 176 to 178°C (decomp.).
- 1 - (4 - Amino - 3 - bromo - 5 - trifluoromethyl - phenyl) - 2 - isopropylamino - ethanol hydrochloride
M.p.: 177 to 179°C (decomp.).
- 35 1 - (4 - Amino - 3 - chloro - 5 - nitro - phenyl) - 2 - tert. - butylamino - ethanol
M.p.: 148 to 149°C.
- 1 - (4 - Amino - 3 - bromo - 5 - nitro - phenyl) - 2 - tert. - butylamino - ethanol
M.p.: 151 to 152°C.

40 Example 193. 40

1-(4-Amino-3-cyano-5-fluoro-phenyl)-2-tert.-butylamino-ethanol.
10 g of 4'-amino-3'-cyano-5'-fluoro-acetophenone were added in small amounts to a mixture of 6 g of selenium dioxide in 36 ml of dioxane and 1 ml of water at 60°C whilst stirring. Subsequently the mixture was refluxed for 45 4 hours. The mixture was cooled and the reaction vessel was then put in an ice pail. 30 ml of tert.-butylamine were then added dropwise to the solution of 4-amino-3-cyano-5-fluoro-phenylglyoxal thus obtained. The reaction mixture was subsequently diluted with 150 ml of ethanol and the insoluble residue was filtered off. 6 g of sodium borohydride were added in small amounts to the 50 solution containing the crude 4-amino-3-cyano-5-fluoro-phenyl-glyoxylidene-tert.-butylamine whilst stirring and cooling with ice. The mixture was left to stand overnight. Subsequently the excess of sodium borohydride was destroyed with acetone, water was added and the organic solvents were removed in vacuo. The precipitate was suction filtered, washed with water and dissolved 55 in 200 ml of 2N hydrochloric acid. The hydrochloric acid solution was filtered and subsequently 10N sodium hydroxide solution was added until the pH was 6. The aqueous phase was washed with chloroform and 10N sodium hydroxide solution was again added until a clearly alkaline reaction occurred. The precipitate was extracted with chloroform, the chloroform solution was washed 60 with water, dried over sodium sulfate and evaporated to dryness in vacuo. The solid residue of 1-(4-amino-3-cyano-5-fluoro-phenyl)-2-tert.-butylamino-ethanol was dissolved in 100 ml of absolute ethanol and acidified to a pH of 6 with ethereal hydrochloric acid. The hydrochloride started to precipitate as

colorless crystals and crystallization was completed by addition of ether. The crystals were suction filtered and washed with ether.

M.p.: 242 to 243°C (decomp.).

Example 194.

1-(4-Amino-3-chloro-5-trifluoromethyl-phenyl)-2-tert.-butylamino ethanol.

0.4 g of 4-amino-3-chloro-5-trifluoromethyl-phenylglyoxal-hydrate were dissolved in 10 ml of methanol. 0.23 g of tert.-butylamine were added and the mixture was allowed to stand for 3 hours at room temperature. Subsequently the solution was cooled to -20°C, 0.1 g of sodium borohydride were added and the reaction mixture was stirred for 20 minutes at -10 to -20°C. The pH of the solution was adjusted to 2 with 2N hydrochloric acid and was then adjusted to 9 with 2N ammonia. The solution was diluted with water and the methanol was removed in vacuo. The aqueous mixture was extracted with ether, the ethereal extract was washed with water, dried over magnesium sulfate and evaporated in vacuo. The oily evaporation residue was dissolved in a small quantity of ether and the pH was adjusted to 4 with isopropanolic hydrochloric acid. Crystalline 1-(4-amino-3-chloro-5-trifluoromethyl-phenyl)-2-tert.-butylamino-ethanol hydrochloride was obtained, which was suction filtered and washed with ether. M.p.: 205 to 207°C (decomp.).

The following compounds have been prepared analogously to Examples 193 to 194:

1 - (4 - Amino - 3 - fluoro - phenyl) - 2 - tert. - butylamino - ethanol hydrochloride

M.p.: 196 to 197°C (decomp.).

1 - (4 - Amino - 3 - chloro - 5 - fluoro - phenyl) - 2 - isopropylamino - ethanol hydrochloride

M.p.: 152 to 154°C (decomp.).

1 - (4 - Amino - 3 - chloro - 5 - fluoro - phenyl) - 2 - cyclopropylamino - ethanol hydrochloride

M.p.: 175 to 177°C (decomp.).

1 - (4 - Amino - 3 - chloro - 5 - fluoro - phenyl) - 2 - tert. - butylamino - ethanol hydrochloride

M.p.: 206 to 208°C (decomp.).

1 - (4 - Amino - 3 - chloro - 5 - fluoro - phenyl) - 2 - tert. - pentylamino - ethanol hydrochloride

M.p.: 187 to 188°C (decomp.).

1 - (4 - Amino - 3 - bromo - 5 - fluoro - phenyl) - 2 - isopropylamino - ethanol hydrochloride

M.p.: 171 to 173°C (decomp.).

1 - (4 - Amino - 3 - bromo - 5 - fluoro - phenyl) - 2 - tert. - butylamino - ethanol hydrochloride

M.p.: 207 to 208°C (decomp.).

1 - (4 - Amino - 3 - bromo - 5 - fluoro - phenyl) - 2 - cyclobutylamino - ethanol hydrochloride

M.p.: 164 to 166°C (decomp.).

1 - (4 - Amino - 3 - fluoro - 5 - iodo - phenyl) - 2 - cyclopropylamino - ethanol hydrochloride

M.p.: 199 to 201°C (decomp.).

1 - (4 - Amino - 3 - cyano - 5 - fluoro - phenyl) - 2 - isopropylamino - ethanol hydrochloride

M.p.: 182 to 184°C (decomp.).

1 - (4 - Amino - 3 - cyano - phenyl) - 2 - cyclobutylamino - ethanol hydrobromide

M.p.: >193°C (decomp.).

1 - (4 - Amino - 3 - cyano - phenyl) - 2 - tert. - pentylamino - ethanol

M.p.: 143°C.

1 - (4 - Amino - 3 - chloro - 5 - cyano - phenyl) - 2 - propylamino - ethanol hydrochloride

M.p.: 187 to 189°C.

1 - (4 - Amino - 3 - chloro - 5 - cyano - phenyl) - 2 - sec. - butylamino - ethanol dihydrochloride

M.p.: 190 to 191°C.

1 - (4 - Amino - 3 - chloro - 5 - cyano - phenyl) - 2 - tert. - butylamino - ethanol

M.p.: 125 to 133°C.

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	1- (4 - Amino - 3 - chloro - 5 - cyano - phenyl) - 2 - (hydroxy - tert. - butylamino) - ethanol hydrochloride M.p.: 228 to 230°C (decomp.).	
5	1 - (4 - Amino - 3 - chloro - 5 - cyano - phenyl) - 2 - tert. - pentylamino - ethanol hydrochloride M.p.: 218 to 220°C (decomp.).	5
	1 - (4 - Amino - 3 - chloro - 5 - cyano - phenyl) - 2 - cyclopentylamino - ethanol hydrochloride M.p.: 138 to 144°C.	
10	1 - (4 - Amino - 3 - chloro - 5 - cyano - phenyl) - 2 - [1 - (3,4 - methylenedioxy - phenyl) - 2 - propylamino] - ethanol hydrochloride M.p.: 189 to 192°C.	10
	1 - (4 - Amino - 3 - bromo - 5 - cyano - phenyl) - 2 - isopropylamino - ethanol hydrochloride M.p.: 186 to 189°C.	
15	1 - (4 - Amino - 3 - bromo - 5 - cyano - phenyl) - 2 - tert. - butylamino - ethanol hydrochloride M.p.: 213 to 215°C.	15
	1 - (4 - Amino - 3 - bromo - 5 - cyano - phenyl) - 2 - cyclobutylamino - ethanol hydrochloride M.p.: 215 to 216°C (decomp.).	
20	1 - (4 - Amino - 3,5 - dicyano - phenyl) - 2 - tert. - butylamino - ethanol hydrochloride M.p.: 251 to 253°C (decomp.).	20
	1 - (4 - Amino - 3 - trifluoromethyl - phenyl) - 2 - tert. - butylamino - ethanol hydrochloride M.p.: 172 to 174°C (decomp.).	
25	1 - (4 - Amino - 3 - trifluoromethyl - phenyl) - 2 - tert. - pentylamino - ethanol hydrobromide M.p.: 174 to 175°C (decomp.).	25
	1 - (4 - Amino - 3 - chloro - 5 - trifluoromethyl - phenyl) - 2 - isopropylamino - ethanol M.p.: 104 to 106°C.	
30	1 - (4 - Amino - 3 - chloro - 5 - trifluoromethyl - phenyl) - 2 - cyclobutylamino - ethanol hydrochloride M.p.: 177 to 178°C.	30
	1 - (4 - Amino - 3 - chloro - 5 - trifluoromethyl - phenyl) - 2 - tert. - pentylamino - ethanol hydrochloride M.p.: 176 to 178°C (decomp.).	
35	1 - (4 - Amino - 3 - bromo - 5 - trifluoromethyl - phenyl) - 2 - isopropylamino - ethanol hydrochloride M.p.: 177 to 179°C (decomp.).	35
	1 - (4 - Amino - 3 - chloro - 5 - nitro - phenyl) - 2 - tert. - butylamino - ethanol M.p.: 148 to 149°C.	
40	1 - (4 - Amino - 3 - bromo - 5 - nitro - phenyl) - 2 - tert. - butylamino - ethanol M.p.: 151 to 152°C.	40
45		45

Example 195.

	1-(4-Amino-3-bromo-5-nitro-phenyl)-2-tert.-butylamino-ethanol.	
50	2.9 g of 1-(4-amino-3-bromo-phenyl)-2-tert.-butylamino-ethanol were dissolved in 15 ml of a mixture of concentrated nitric acid and concentrated sulfuric acid. The solution was heated for one minute at 80 to 85°C and was then poured onto ice. The mixture was made alkaline by addition of ammonia and was subsequently extracted with chloroform. The chloroform solution was washed with water, dried and evaporated to dryness in vacuo. The title compound was isolated by chromatography using silica gel (eluent: chloroform:methanol = 8:2), and the crude product thus obtained was recrystallized from ethyl acetate. M.p. of the 1-(4-Amino-3-bromo-5-nitro-phenyl)-2-tert.-butylamino-ethanol: 151 to 152°C.	50
55		55

Example 196.

60	1-(4-Amino-3-chloro-5-nitro-phenyl)-2-tert.-butylamino-ethanol. M.p.: 148 to 149°C. Prepared from 1-(4-amino-3-chloro-phenyl)-2-tert.-butylamino-ethanol and nitric acid/sulfuric acid analogously to Example 195.	60
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Example 197.

1-(4-Amino-3-chloro-5-cyano-phenyl)-2-dimethylamino-ethanol.

0.5 g of 1-acetoxy-1-(4-amino-3-chloro-5-cyano-phenyl)-2-dimethylamino-ethane (m.p.: 120 to 124°C) were stirred for 1 hour at 20°C in methanolic sodium hydroxide solution. Water was added, the methanol was distilled off in vacuo and the remaining aqueous layer was extracted with chloroform. The chloroform layer was dried over sodium sulfate and evaporated to dryness in vacuo. The residue was dissolved in isopropanol and the hydrochloride of 1-(4-amino-3-chloro-5-cyano-phenyl)-2-dimethylamino-ethanol was crystallized by the addition of isopropanolic hydrochloric acid. M.p.: 187 to 189°C.

Example 198.

1-(4-Amino-3-cyano-5-fluoro-phenyl)-2-dimethylamino-ethanol.

7 g of 1-acetoxy-1-(4-amino-3-cyano-5-fluoro-phenyl)-2-dimethylamino-ethane were dissolved in 100 ml of methanol. 5 ml of 10N aqueous NaOH-solution were added and the solution was allowed to stand for 1 hour at room temperature. Subsequently the reaction mixture was diluted with saturated sodium chloride solution and extracted exhaustively with chloroform. The chloroform solution was washed with saturated sodium chloride solution, dried over sodium sulfate and evaporated to dryness in vacuo. A colourless oil was obtained.

Structure established by NMR-spectrum(CD₃OD):

2.2—2.65 ppm, multiplet [8 protons; N—CH₃ and N—CH—CH₂—N<],

4.6—4.9 ppm, multiplet [4 protons; 3 exchange protons and —CH—CH₂—N<],

7.15—7.4 ppm, multiplet [2 aromatic protons].

Example 199.

1-(4-Amino-3-chloro-5-cyano-phenyl)-2-tert.-butylamino-ethanol.

0.5 g of N-acetyl-N-[2-acetoxy-2-(4-amino-3-chloro-5-cyano-phenyl)-ethyl]-tert.-butylamine (m.p.: 160 to 162°C) were stirred for 1 hour at 20°C with methanolic sodium hydroxide solution. Water was added, the methanol was distilled off in vacuo and the remaining aqueous layer was extracted with chloroform. The chloroform layer was dried over sodium sulphate and evaporated to dryness in vacuo. The residue was crystallized from ethanol; 1-(4-amino-3-chloro-5-cyano-phenyl)-2-tert.-butylamino-ethanol was obtained.

M.p.: 131 to 135°C; m.p. of the hydrochloride: 204 to 207°C.

The following compounds have been prepared analogously to Examples 197 to 199:

1 - (4 - Amino - 3 - fluoro - phenyl) - 2 - tert. - butylamino - ethanol hydrochloride

M.p.: 196 to 197°C (decomp.).

1 - (4 - Amino - 3 - chloro - 5 - fluoro - phenyl) - 2 - isopropylamino - ethanol hydrochloride

M.p.: 152 to 154°C (decomp.).

1 - (4 - Amino - 3 - chloro - 5 - fluoro - phenyl) - 2 - cyclopropylamino - ethanol hydrochloride

M.p.: 175 to 177°C (decomp.).

1 - (4 - Amino - 3 - chloro - 5 - fluoro - phenyl) - 2 - tert. - butylamino - ethanol hydrochloride

M.p.: 206 to 208°C (decomp.).

1 - (4 - Amino - 3 - chloro - 5 - fluoro - phenyl) - 2 - tert. - pentylamino - ethanol hydrochloride

M.p.: 187 to 188°C (decomp.).

1 - (4 - Amino - 3 - bromo - 5 - fluoro - phenyl) - 2 - isopropylamino - ethanol hydrochloride

M.p.: 171 to 173°C (decomp.).

1 - (4 - Amino - 3 - bromo - 5 - fluoro - phenyl) - 2 - tert. - butylamino - ethanol hydrochloride

M.p.: 207 to 208°C (decomp.).

	1 - (4 - Amino - 3 - bromo - 5 - fluoro - phenyl) - 2 - cyclobutylamino - ethanol hydrochloride M.p.: 164 to 166°C (decomp.).	
5	1 - (4 - Amino - 3 - fluoro - 5 - iodo - phenyl) - 2 - cyclopropylamino - ethanol hydrochloride M.p.: 199 to 201°C (decomp.).	5
	1 - (4 - Amino - 3 - cyano - 5 - fluoro - phenyl) - 2 - isopropylamino - ethanol hydrochloride M.p.: 182 to 184°C (decomp.).	
10	1 - (4 - Amino - 3 - cyano - 5 - fluoro - phenyl) - 2 - tert. - butylamino - ethanol hydrochloride M.p.: 242 to 243°C (decomp.).	10
	1 - (4 - Amino - 3 - cyano - phenyl) - 2 - cyclobutylamino - ethanol hydrobromide M.p.: >193°C (decomp.).	
15	1 - (4 - Amino - 3 - cyano - phenyl) - 2 - tert. - pentylamino - ethanol M.p.: 143°C.	15
	1 - (4 - Amino - 3 - chloro - 5 - cyano - phenyl) - 2 - propylamino - ethanol hydrochloride M.p.: 187 to 189°C.	
20	1 - (4 - Amino - 3 - chloro - 5 - cyano - phenyl) - 2 - sec. - butylamino - ethanol dihydrochloride M.p.: 190 to 191°C.	20
	1 - (4 - Amino - 3 - chloro - 5 - cyano - phenyl) - 2 - (hydroxy - tert. - butylamino) - ethanol hydrochloride M.p.: 228 to 230°C (decomp.).	
25	1 - (4 - Amino - 3 - chloro - 5 - cyano - phenyl) - 2 - tert. - pentylamino - ethanol hydrochloride M.p.: 218 to 220°C (decomp.).	25
	1 - (4 - Amino - 3 - chloro - 5 - cyano - phenyl) - 2 - cyclopentylamino - ethanol hydrochloride M.p.: 138 to 144°C.	
30	1 - (4 - Amino - 3 - chloro - 5 - cyano - phenyl) - 2 - [1 - (3,4 - methylenedioxy - phenyl) - 2 - propylamino] - ethanol hydrochloride M.p.: 189 to 192°C.	30
	1 - (4 - Amino - 3 - bromo - 5 - cyano - phenyl) - 2 - isopropylamino - ethanol hydrochloride M.p.: 186 to 189°C.	
35	1 - (4 - Amino - 3 - bromo - 5 - cyano - phenyl) - 2 - tert. - butylamino - ethanol hydrochloride M.p.: 213 to 215°C.	35
	1 - (4 - Amino - 3 - bromo - 5 - cyano - phenyl) - 2 - cyclobutylamino - ethanol hydrochloride M.p.: 215 to 216°C (decomp.).	
40	1 - (4 - Amino - 3,5 - dicyano - phenyl) - 2 - tert. - butylamino - ethanol hydrochloride M.p.: 251 to 253°C (decomp.).	40
	1 - (4 - Amino - 3 - trifluoromethyl - phenyl) - 2 - tert. - butylamino - ethanol hydrochloride M.p.: 172 to 174°C (decomp.).	
45	1 - (4 - Amino - 3 - trifluoromethyl - phenyl) - 2 - tert. - pentylamino - ethanol hydrobromide M.p.: 174 to 175°C (decomp.).	45
	1 - (4 - Amino - 3 - chloro - 5 - trifluoromethyl - phenyl) - 2 - isopropylamino - ethanol M.p.: 104 to 106°C.	
50	1 - (4 - Amino - 3 - chloro - 5 - trifluoromethyl - phenyl) - 2 - tert. - butylamino - ethanol hydrochloride M.p.: 205 to 207°C (decomp.).	50
	1 - (4 - Amino - 3 - chloro - 5 - trifluoromethyl - phenyl) - 2 - cyclobutylamino - ethanol hydrochloride M.p.: 177 to 178°C.	
55	1 - (4 - Amino - 3 - chloro - 5 - trifluoromethyl - phenyl) - 2 - tert. - pentylamino - ethanol hydrochloride M.p.: 176 to 178°C (decomp.).	55
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- 1 - (4 - Amino - 3 - bromo - 3 - trifluoromethyl - phenyl) - 2 - isopropylamino - ethanol hydrochloride
M.p.: 177 to 179°C (decomp.).
- 1 - (4 - Amino - 3 - chloro - 5 - nitro - phenyl) - 2 - tert. - butylamino - ethanol
M.p.: 148 to 149°C.
- 1 - (4 - Amino - 3 - bromo - 5 - nitro - phenyl) - 2 - tert. - butylamino - ethanol
M.p.: 151 to 152°C.

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Example 200.

Tablets containing 10 γ of 1-(4-amino-3-chloro-5-cyano-phenyl)-2-tert.-butylamino-ethanol hydrochloride.

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Composition:

1 tablet contains:

Active ingredient	0.01 mg
lactose	82.49 mg
potato starch	33.00 mg
polyvinylpyrrolidone	4.00 mg
magnesium stearate	0.50 mg
	120.00 mg

15

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Method of preparation:

The active ingredient and polyvinylpyrrolidone were dissolved in ethanol. The mixture of lactose and potato starch was homogeneously moistened with this solution. The moist-screening was carried out with a screen of 1.5 mm mesh-size. Subsequently the mixture was dried at 50°C and the dry-screening effected with a screen of 1.0 mm mesh-size. The granulate thus obtained was mixed with magnesium stearate and compressed to form the tablets.

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Weight of tablet: 120 mg
Punch: 7 mm, flat

Example 201.

Coated tablets containing 5 γ of 1-(4-amino-3-chloro-5-cyano-phenyl)-2-tert.-butylamino-ethanol.

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Composition:

1 coated tablet core contains:

Active ingredient	0.005 mg
lactose	82.495 mg
potato starch	33.000 mg
polyvinylpyrrolidone	4.000 mg
magnesium stearate	0.500 mg
	120.000 mg

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Method of preparation:

The tablet cores were prepared analogously to Example 200.

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Weight of core: 120 mg
Punch: 7 mm, arched

The cores were covered according to known methods with a coating consisting substantially of sugar and talcum. The finished pills were polished with beeswax. Weight of coated tablet: 200.0 mg.

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Example 202.

Gelatine capsules containing 10% of 1-(4-amino-3-chloro-5-cyano-phenyl)-2-tert.-butylamino-ethanol.

Composition:

1 capsule contains:

Active ingredient	0.010 mg
lactose	59.990 mg
corn starch	60.000 mg
	120.000 mg

10 *Method of preparation:*

The active ingredient was intimately mixed with lactose and corn starch and filled into gelatine capsules of suitable size.

Capsule filling: 120.0 mg

Example 203.

15 Ampoules containing 10% of 1-(4-amino-3-bromo-5-fluoro-phenyl)-2-tert.-butylamino-ethanol hydrochloride. 15

Composition:

1 ampoule contains:

Active ingredient	0.01 mg	
citric acid	2.5 mg	
sodium hydrogen phosphate	7.5 mg	
sodium chloride	4.6 mg	
distilled water	ad	2.0 ml

25 *Method of preparation:*

The active ingredient, buffer substances and sodium chloride were dissolved in distilled water and filtered sterile.

Filling: into brown ampoules of 2 ml capacity in a protective gas atmosphere (N₂)
Sterilisation: 20 minutes at 120°C.

Example 204.

30 Suppositories containing 10% of 1-(4-amino-3-chloro-5-cyano-phenyl)-2-tert.-butylamino-ethanol. 30

Composition:

1 suppository contains:

Active ingredient	0.01 mg
suppository mass (e.g. "Witepsol" W 45)	1 669.99 mg
("Witepsol" is a registered Trade Mark)	
	1 700.00 mg

Method of preparation:

40 The finely pulverized active ingredient was stirred into the molten suppository mass, cooled to 40°C, with the aid of an immersion homogenizer. 40
At 37°C the mass was poured into slightly pre-cooled moulds.

Weight of suppository: 1.7 g.

Example 205.

45 Syrup containing 10% of 1-(4-amino-3-bromo-5-fluoro-phenyl)-2-tert.-butylamino-ethanol hydrochloride per 100 ml. 45

Composition:

100 ml of syrup contain:

Active ingredient	0.00001	g
benzoic acid	0.1	g
tartaric acid	1.0	g
sugar	50.0	g
orange flavouring	1.0	g
red food colouring	0.05	g
distilled water	ad	100.0 ml

Method of preparation:

About 60 g of distilled water were heated to 80°C and the benzoic acid, tartaric acid, active ingredient, food colouring and sugar were dissolved successively therein. After cooling to room temperature, the flavouring was added and the mixture was made up to the given volume. The syrup was filtered.

Example 206.

Coated tablets containing 25% of 1-(4-amino-3-chloro-5-trifluoromethyl-phenyl)-2-tert.-butylamino-ethanol hydrochloride.

Composition:

1 coated tablet core contains:

Active ingredient	0.025	mg
lactose	82.475	mg
potato starch	33.000	mg
polyvinylpyrrolidone	4.000	mg
magnesium stearate	0.500	mg
	120.000	mg

Method of preparation:

The coated tablets were prepared analogously to Example 200.

Example 207.

Ampoules containing 20% of 1-(4-amino-3-chloro-5-trifluoromethyl-phenyl)-2-tert.-butylamino-ethanol hydrochloride.

Composition:

1 ampoule contains:

Active ingredient	0.02	mg
citric acid	2.5	mg
sodium hydrogen phosphate	7.5	mg
sodium chloride	4.6	mg
distilled water	ad	2.0 ml

Method of preparation:

Analogously to Example 203.

Example 208.

Tablets containing 50% of D-1-(4-amino-3-fluoro-phenyl)-2-tert.-butylamino-ethanol hydrochloride.

Composition:

1 tablet contains:

Active ingredient	0.05	mg
lactose	82.45	mg
potato starch	33.00	mg
polyvinylpyrrolidone	4.00	mg
magnesium stearate	0.50	mg
	120.00	mg

Method of preparation:

The tablets were prepared analogously to Example 200.

Weight of tablet: 120 mg,
Punch: 7 mm, flat

Example 209.

Coated tablets containing 25% of D-1-(4-amino-3-fluoro-phenyl)-2-tert.-butyl-amino-ethanol hydrochloride.

Composition:

1 coated tablet core contains:

Active ingredient	0.025 mg
lactose	82.475 mg
potato starch	33.000 mg
polyvinylpyrrolidone	4.000 mg
magnesium stearate	0.500 mg

120.000 mg

Method of preparation:

The tablet cores were prepared analogously to Example 201.

Weight of core: 120 mg
Punch: 7 mm, arched

The cores were covered according to known methods with a coating consisting substantially of sugar and talcum. The finished pills were polished with beeswax.

Weight of coated tablet: 200.0 mg

Example 210.

Gelatine capsules containing 25% of D-1-(4-amino-3-fluoro-phenyl)-2-tert.-butyl-amino-ethanol hydrochloride.

Composition:

1 capsule contains:

Active ingredient	0.025 mg
lactose	59.975 mg
corn starch	60.000 mg

120.000 mg

Method of preparation:

Analogously to Example 202.

Example 211.

Ampoules containing 20% of D-1-(4-amino-3-fluoro-phenyl)-2-tert.-butylamino-ethanol hydrochloride.

Composition:

1 ampoule contains:

Active ingredient	0.02 mg
citric acid	2.5 mg
sodium hydrogen phosphate	7.5 mg
sodium chloride	4.6 mg
distilled water	ad 2.0 ml

Method of preparation:

Analogously to Example 203.

Example 212.

Suppositories containing 50% of D-1-(4-amino-3-fluoro-phenyl)-2-tert.-butylamino-ethanol hydrochloride.

Composition:

1 suppository contains:

Active ingredient	0.05 mg
suppository mass	1 699.95 mg
	1 700.00 mg

Method of preparation:

Analogously to Example 204.

Example 213.

Syrup containing 25% of D-1-(4-amino-3-fluoro-phenyl)-2-tert.-butylamino-ethanol hydrochloride per 5 ml.

Composition:

100 ml of syrup contain:

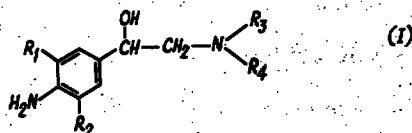
Active ingredient	0.0005 g
benzoic acid	0.1 g
tartaric acid	1.0 g
sugar	50.0 g
orange flavouring	1.0 g
red food colouring	0.05 g
distilled water ad	100.0 ml

Method of preparation:

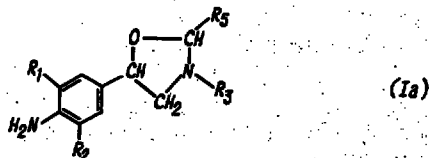
Analogously to Example 205.

WHAT WE CLAIM IS:—

1. Compounds of general formula



and oxazolidines thereof of general formula



[wherein R_1 represents a hydrogen, fluorine, chlorine, bromine or iodine atom or a cyano group, R_2 represents a fluorine atom, a straight or branched alkyl group containing from 1 to 5 carbon atoms or a hydroxyalkyl, aminoalkyl, dialkylaminoalkyl, trifluoromethyl, alkoxy, nitro, cyano, carboxy, carbalkoxy or carbamoyl group, R_3 and R_4 , which may be the same or different, each represents a hydrogen atom, a straight or branched alkyl group containing from 1 to 6 carbon atoms, or a hydroxyalkyl, cycloalkyl, cycloalkylalkyl, alkenyl, alkynyl or optionally substituted aralkyl group and R_5 represents a hydrogen atom or a straight or branched alkyl group] and acid addition salts thereof.

2. Optical isomers of compounds of general formula I as defined in claim 1 and physiologically compatible acid addition salts thereof.

3. Compounds of general formula I and oxazolidines thereof of general formula Ia [wherein R_1 represents a hydrogen, chlorine, bromine or iodine atom or

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Example 212.

Suppositories containing 50% of D-1-(4-amino-3-fluoro-phenyl)-2-tert.-butylamino-ethanol hydrochloride.

Composition:

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1 suppository contains:

Active ingredient	0.05 mg
suppository mass	1 699.95 mg
	1 700.00 mg

5

Method of preparation:

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Analogously to Example 204.

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Example 213.

Syrup containing 25% of D-1-(4-amino-3-fluoro-phenyl)-2-tert.-butylamino-ethanol hydrochloride per 5 ml.

Composition:

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100 ml of syrup contain:

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Active ingredient	0.0005 g
benzoic acid	0.1 g
tartaric acid	1.0 g
sugar	50.0 g
orange flavouring	1.0 g
red food colouring	0.05 g
distilled water ad	100.0 ml

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Method of preparation:

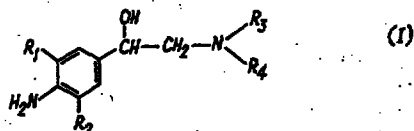
Analogously to Example 205.

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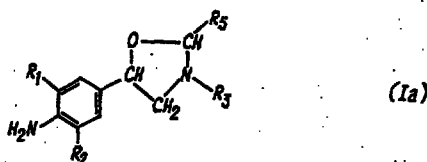
WHAT WE CLAIM IS:—

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1. Compounds of general formula



and oxazolidines thereof of general formula



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[wherein R₁ represents a hydrogen, fluorine, chlorine, bromine or iodine atom or a cyano group, R₂ represents a fluorine atom, a straight or branched alkyl group containing from 1 to 5 carbon atoms or a hydroxyalkyl, aminoalkyl, dialkylaminoalkyl, trifluoromethyl, alkoxy, nitro, cyano, carboxy, carbalkoxy or carbamoyl group, R₃ and R₄, which may be the same or different, each represents a hydrogen atom, a straight or branched alkyl group containing from 1 to 6 carbon atoms, or a hydroxyalkyl, cycloalkyl, cycloalkylalkyl, alkenyl, alkynyl or optionally substituted aralkyl group and R₅ represents a hydrogen atom or a straight or branched alkyl group] and acid addition salts thereof.

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2. Optical isomers of compounds of general formula I as defined in claim 1 and physiologically compatible acid addition salts thereof.

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3. Compounds of general formula I and oxazolidines thereof of general formula Ia [wherein R₁ represents a hydrogen, chlorine, bromine or iodine atom or

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a cyano group; R_2 represents a fluorine atom or a trifluoromethyl, nitro or cyano group with the proviso that R_1 is not hydrogen when R_2 represents a fluorine atom; R_3 represents a straight or branched alkyl group containing from 3 to 5 carbon atoms optionally substituted by a hydroxyl group, a cycloalkyl group containing from 3 to 5 carbon atoms or a 3,4-methylenedioxyphenylisopropyl group; R_4 represents a hydrogen atom; and R_5 represents a hydrogen atom or a straight or branched alkyl group containing from 1 to 5 carbon atoms] and physiologically compatible acid addition salts thereof.

4. d(+) and l(-) stereoisomers of compounds of general formula I as defined in claim 3 and physiologically compatible acid addition salts thereof.

5. 1-(4-Amino-3-bromo-5-fluoro-phenyl)-2-tert.-butylamino-ethanol and physiologically compatible acid addition salts thereof.

6. 1-(4-Amino-3-chloro-5-cyano-phenyl)-2-tert.-butylamino-ethanol and physiologically compatible acid addition salts thereof.

7. 1-(4-Amino-3-fluoro-5-iodo-phenyl)-2-cyclopropylamino-ethanol and physiologically compatible acid addition salts thereof.

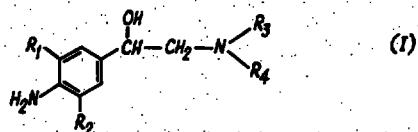
8. 1-(4-Amino-3-fluoro-5-cyano-phenyl)-2-isopropylamino-ethanol and physiologically compatible acid addition salts thereof.

9. 1-(4-Amino-3,5-dicyano-phenyl)-2-tert.-butylamino-ethanol and physiologically compatible acid addition salts thereof.

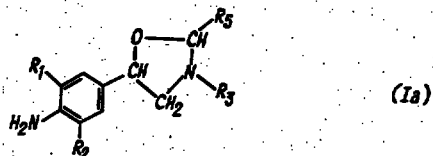
10. 1-(4-Amino-3-bromo-5-nitro-phenyl)-2-tert.-butylamino-ethanol and physiologically compatible acid addition salts thereof.

11. 1-(4-Amino-3-fluoro-phenyl)-2-tert.-butylamino-ethanol and physiologically active acid addition salts thereof.

12. Compounds of general formula

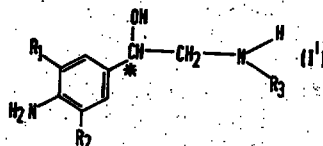


and oxazolidines thereof of general formula



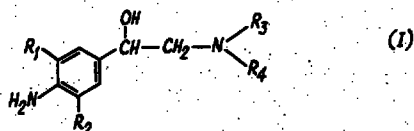
[wherein R_1 represents a hydrogen, chlorine or bromine atom; R_2 represents a fluorine atom, a straight or branched alkyl group containing from 1 to 5 carbon atoms, or a hydroxyalkyl, aminoalkyl, dialkylaminoalkyl, trifluoromethyl, alkoxy, cyano, carboxy, carbalkoxy or carbamoyl group; R_3 and R_4 , which may be the same or different, each represents a hydrogen atom, a straight or branched alkyl group containing from 1 to 6 carbon atoms, or a cycloalkyl, alkenyl, alkynyl or an optionally substituted aralkyl group; and R_5 represents a hydrogen atom] and physiologically compatible acid addition salts thereof.

13. Optical isomers of compounds of general formula



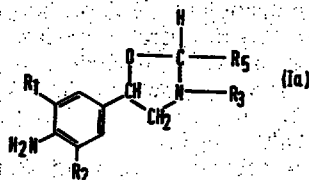
[wherein R_1 represents a hydrogen, chlorine, or bromine atom; R_2 represents a fluorine atom or a trifluoromethyl or cyano group; and R_3 represents a straight or branched alkyl group containing from 3 to 5 carbon atoms or a cycloalkyl group containing from 3 to 5 carbon atoms] and physiologically compatible acid addition salts thereof.

14. Compounds of general formula





and oxazolidines thereof of general formula



[wherein R_1 represents a hydrogen, fluorine, chlorine, bromine or iodine atom or a cyano group; R_2 represents a fluorine atom or a cyano, trifluoromethyl, nitro or dialkylaminoalkyl group; R_3 represents a straight or branched alkyl group containing from 1 to 6 carbon atoms optionally substituted by a hydroxyl group, a cycloalkyl group containing from 3 to 7 carbon atoms, or a cycloalkylalkyl or (methylenedioxyphenyl)-alkyl group; R_4 represents a hydrogen atom or an alkyl group containing from 1 to 3 carbon atoms; and R_5 represents a hydrogen atom or a straight or branched alkyl group containing from 1 to 5 carbon atoms] and physiologically compatible acid addition salts thereof.

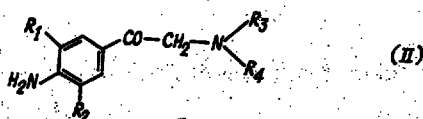
15. Compounds as claimed in claims 1 and 2 other than those claimed in claims 5 to 11 as herein specifically disclosed.

16. Compounds as claimed in claim 12 other than those claimed in claims 5 and 6 as herein specifically disclosed.

17. Compounds as claimed in claim 13 and herein specifically disclosed.

18. Compounds as claimed in claim 14 other than those claimed in claims 5 to 11 as herein specifically disclosed.

19. A process for the preparation of compounds of general formula I as defined in claim 1 which comprises reducing a compound of formula



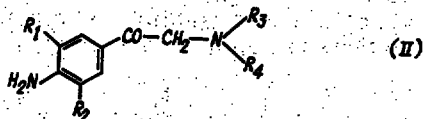
(wherein R_1 , R_2 , R_3 and R_4 are as defined in claim 1).

20. A process as claimed in claim 19 wherein the reduction is effected in the presence of a solvent.

21. A process as claimed in claim 19 or claim 20 wherein the reduction is effected by means of a complex metal hydride, aluminium isopropoxide or catalytically activated hydrogen.

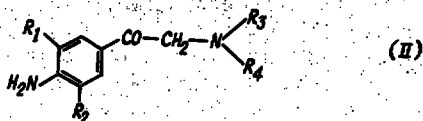
22. A process as claimed in any of claims 19 to 21 wherein the reduction is effected at temperatures from -20° up to the boiling point of the solvent used.

23. A process for the preparation of compounds of general formula I as defined in claim 12 which comprises reducing a compound of formula



(wherein R_1 , R_2 , R_3 and R_4 are as defined in claim 12) in the presence of a solvent.

24. A process for the preparation of compounds of general formula I as defined in claim 14 which comprises reducing a compound of formula



(wherein R_1 , R_2 , R_3 and R_4 are as defined in claim 14) in the presence of a solvent.

25. A process for the preparation of compounds of general formula I (wherein R_1 represents a chlorine, bromine or iodine atom and R_2 , R_3 and R_4 are as defined in claim 1 with the proviso that R_3 and R_4 cannot represent alkenyl or alkynyl groups) which comprises halogenating a compound of formula

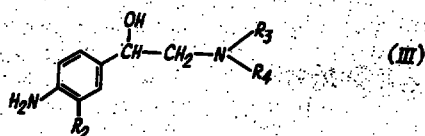


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(wherein R_2 , R_3 and R_4 are as defined in claim 1 with the proviso that R_3 and R_4 cannot represent alkenyl or alkynyl groups).

26. A process as claimed in claim 25 wherein the reaction is effected in the presence of a solvent.

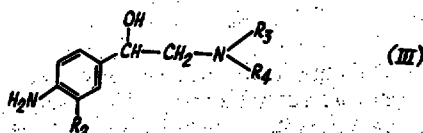
27. A process as claimed in claim 25 or claim 26 wherein the halogenation is effected with chlorine, bromine, iodine, tribromophenol hypobromite or iodosobenzene dichloride.

28. A process as claimed in any of claims 25 to 27 wherein the halogenation is effected in the presence of a tertiary organic base or a heavy metal oxide.

29. A process as claimed in claim 28 wherein the heavy metal oxide is mercury (II) oxide.

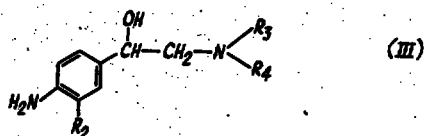
30. A process as claimed in any of claims 25 to 29 wherein the reaction is effected at temperatures from 0 to 50°C.

31. A process for the preparation of compounds of general formula I (wherein R_1 represents a chlorine or bromine atom and R_2 , R_3 and R_4 are as defined in claim 12 with the proviso that R_3 and R_4 cannot represent alkenyl or alkynyl groups) which comprises halogenating a compound of formula



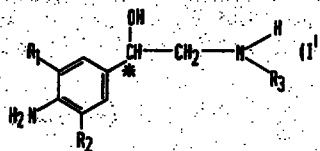
(wherein R_2 , R_3 and R_4 are as defined in claim 12 with the proviso that R_3 and R_4 cannot represent alkenyl or alkynyl groups) in the presence of a solvent.

32. A process for the preparation of compounds of general formula I (wherein R_1 represents a chlorine, bromine or iodine atom and R_2 , R_3 and R_4 are as defined in claim 14) which comprises halogenating a compound of formula



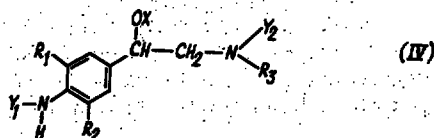
(wherein R_2 , R_3 and R_4 are as defined in claim 14) in the presence of a solvent.

33. A process for the preparation of the optical isomers of a compound of formula



(wherein R_1 represents a chlorine or bromine atom and R_2 and R_3 are as defined in claim 13) which comprises chlorinating or brominating corresponding optical isomers of a compound of formula I' (wherein R_1 represents a hydrogen atom and R_2 and R_3 are as defined in claim 13).

34. A process for the preparation of compounds of general formula I as defined in claim 1 which comprises splitting off one or more protecting groups from a compound of formula





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(wherein R_1 , R_2 and R_3 are as defined in claim 1; X represents a protecting group for a hydroxyl group or a hydrogen atom; Y_1 represents a protecting group for an amino group or a hydrogen atom; and Y_2 represents a protecting group for an amino group or is as defined in claim 1 for R_4 , with the proviso that at least one of the groups X , Y_1 and Y_2 represents one of the above-identified protecting groups).

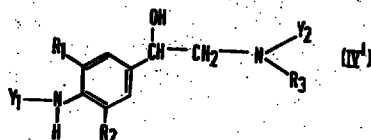
35. A process as claimed in claim 34 wherein the reaction is effected in the presence of a solvent.

36. A process as claimed in claim 34 or claim 35 wherein X , Y_1 and/or Y_2 in the compound of formula IV represents (an) acyl group(s) or X represents a trimethylsilyl or tetrahydropyran-2-yl group and these protecting groups are split off hydrolytically.

37. A process as claimed in claim 34 or claim 35 wherein X , Y_1 and/or Y_2 in the compound of formula IV represent(s) (a) benzyl group(s) and these groups are split off hydrogenolytically.

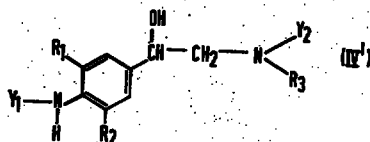
38. A process as claimed in any of claims 35 to 37 wherein the reaction is effected at temperatures up to the boiling point of the solvent used.

39. A process for the preparation of general formula I as defined in claim 12 which comprises splitting off one or two protecting groups from a compound of formula



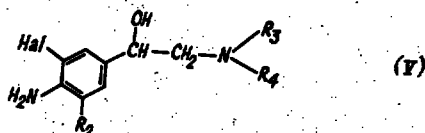
(wherein R_1 , R_2 and R_3 are as defined in claim 12, Y_1 represents a protecting group for an amino group or a hydrogen atom and Y_2 represents a protecting group for an amino group or is as defined in claim 12 for R_4 , with the proviso that at least one of Y_1 and Y_2 represents a protecting group for an amino group) in the presence of a solvent.

40. A process for the preparation of compounds of general formula I as defined in claim 14 which comprises splitting off one or two protecting groups from a compound of formula



(wherein R_1 , R_2 and R_3 are as defined in claim 14, Y_1 represents a protecting group for an amino group or a hydrogen atom and Y_2 represents a protecting group for an amino group or is as defined in claim 14 for R_4 , with the proviso that at least one of Y_1 and Y_2 represents a protecting group for an amino group) in the presence of a solvent.

41. A process for the preparation of compounds of general formula I (wherein R_1 represents a hydrogen and R_2 , R_3 and R_4 are as defined in claim 1) which comprises dehalogenating a compound of formula



(wherein R_2 , R_3 and R_4 are as defined in claim 1 and Hal represents a chlorine, bromine or iodine atom).

42. A process as claimed in claim 41 wherein the dehalogenation is effected in the presence of a solvent.

43. A process as claimed in claim 41 or claim 42 wherein the dehalogenation is effected by means of triphenylphosphine.

44. A process as claimed in claim 41 or claim 42 wherein the dehalogenation is effected by means of hydrogen in the presence of a hydrogenation catalyst.

45. A process as claimed in any of claims 41 to 44 wherein the dehalogenation is effected at temperatures from room temperature up to 150°C.

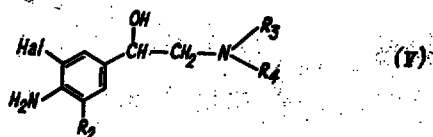


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46. A process for the preparation of compounds of general formula I (wherein R_1 represent a hydrogen atom and R_2 , R_3 and R_4 are as defined in claim 12) which comprises dehalogenating a compound of formula

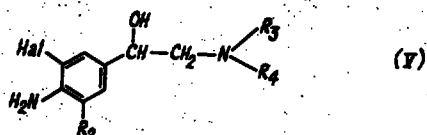


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(wherein Hal represents a chlorine, bromine or iodine atom and R_2 , R_3 and R_4 are as defined in claim 12) in the presence of a solvent.

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47. A process for the preparation of compounds of general formula I (wherein R_1 represents a hydrogen atom and R_2 , R_3 and R_4 are as defined in claim 14) which comprises dehalogenating a compound of formula



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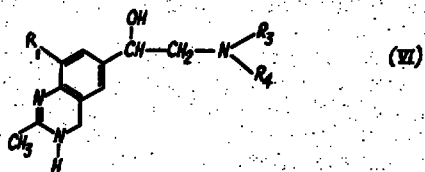
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(wherein Hal represents a chlorine, bromine or iodine atom and R_2 , R_3 and R_4 are as defined in claim 14) in the presence of a solvent.

48. A process for the preparation of compounds of general formula I (wherein R_1 , R_3 and R_4 are as defined in claim 1 and R_2 represents an aminomethyl group) which comprises reducing and subsequently hydrolysing a compound of formula

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(wherein R_1 , R_3 and R_4 are as defined in claim 1).

49. A process as claimed in claim 48 wherein both stages of the reaction are effected in the presence of a solvent.

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50. A process as claimed in claim 48 or claim 49 wherein the reduction is effected by means of sodium and pentyl alcohol.

51. A process as claimed in claim 50 wherein the reduction is effected at temperatures from 0 to 50°C.

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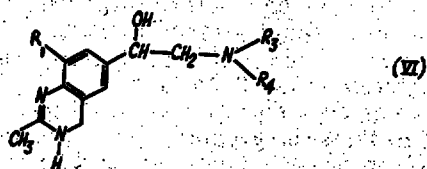
52. A process as claimed in any of claims 48 to 51 wherein the hydrolysis is effected by means of hydrochloric acid.

53. A process as claimed in claim 52 wherein the hydrolysis is effected at temperatures up to the boiling point of hydrochloric acid.

54. A process for the preparation of compounds of general formula I (wherein R_1 , R_3 and R_4 are as defined in claim 12 and R_2 represents an aminomethyl group) which comprises reducing and subsequently hydrolysing a compound of formula

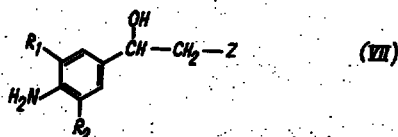
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(wherein R_1 , R_3 and R_4 are as defined in claim 12) in the presence of a solvent.

55. A process for the preparation of compounds of general formula I as defined in claim 1 which comprises reacting a compound of formula



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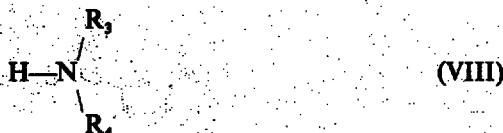
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(wherein R_1 and R_2 are as defined in claim 1 and Z represents a chlorine, bromine or iodine atom or a p-toluenesulfonyloxy group) with an amine of formula

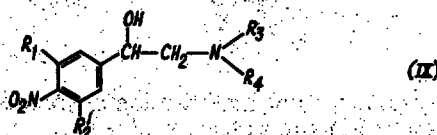


(wherein R_3 and R_4 are as defined in claim 1).

56. A process as claimed in claim 55 wherein the reaction is effected in the presence of a solvent.

57. A process as claimed in claim 55 or claim 56 wherein the reaction is effected at temperatures from 0 to 100°C.

58. A process for the preparation of compounds of general formula I (wherein R_1 , R_2 , R_3 and R_4 are as defined in claim 1 with the proviso that R_2 does not represent a nitro group) which comprises reducing a compound of formula



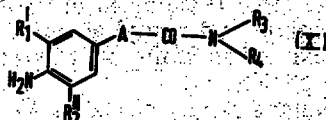
(wherein R_1 , R_3 and R_4 are as defined in claim 1 and R_2' is as defined in claim 1 for R_2 with the proviso that it does not represent a nitro group).

59. A process as claimed in claim 58 wherein the reduction is effected in the presence of a solvent.

60. A process as claimed in claim 58 or claim 59 wherein the reduction is effected by means of nascent hydrogen, hydrogen in the presence of a catalyst, tin (II) chloride and hydrochloric acid, or a complex metal hydride.

61. A process as claimed in any of claims 58 to 60 wherein the reduction is effected at temperatures from 0 to 100°C.

62. A process for the preparation of compounds of general formula I as defined in claim 1 with the proviso that R_1 does not represent a cyano group and R_2 does not represent a nitro, cyano, carboxy, carbalkoxy or carbamoyl group which comprises reducing a compound of formula



(wherein R_3 and R_4 are as defined in claim 1, R_1' is as defined in claim 1 for R_1 but does not represent a cyano group, R_2' is as defined in claim 1 for R_2 but does not represent a nitro, cyano, carboxyl, carbalkoxy or carbamoyl group, and A represents a carbonyl or hydroxymethylene group).

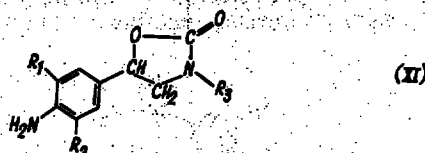
63. A process as claimed in claim 62 wherein the reduction is effected in the presence of a solvent.

64. A process as claimed in claim 62 or claim 63 wherein the reduction is effected by means of a complex metal hydride.

65. A process as claimed in any of claims 62 to 64 wherein the reduction is effected at temperatures from 0 to 120°C.

66. A process as claimed in claim 65 wherein the reduction is effected at temperatures up to the boiling point of the solvent used.

67. A process for the preparation of compounds of general formula I (wherein R_1 , R_2 and R_3 are as defined in claim 1 and R_4 represents a hydrogen atom) which comprises hydrolysing an oxazolidone of formula



(wherein R_1 , R_2 and R_3 are as defined in claim 1).



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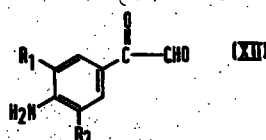
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68. A process as claimed in claim 67 wherein the hydrolysis is effected in the presence of a solvent.

69. A process as claimed in claim 67 or claim 68 wherein the hydrolysis is effected in the presence of an acid or a base.

70. A process as claimed in any of claims 67 to 69 wherein the hydrolysis is effected at temperatures from 0 to 110°C.

71. A process for the preparation of compounds of general formula I (wherein R_1 , R_2 and R_3 are as defined in claim 1 and R_4 represents a hydrogen atom) which comprises reducing a compound of formula

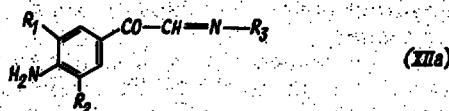


(wherein R_1 and R_2 are as defined in claim 1) or the hydrate thereof in the presence of an amine of formula



(wherein R_3 is as defined in claim 1).

72. A process for the preparation of compounds of general formula I (wherein R_1 , R_2 and R_3 are as defined in claim 1 and R_4 represents a hydrogen atom) which comprises reducing a compound of formula



(wherein R_1 , R_2 and R_3 are as defined in claim 1) prepared in situ.

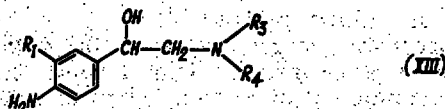
73. A process as claimed in claim 71 or claim 72 wherein the reduction is effected in the presence of a solvent.

74. A process as claimed in any of claims 71 to 73 wherein the reduction is effected by means of a complex metal hydride, nascent hydrogen or hydrogen in the presence of a catalyst.

75. A process as claimed in any of claims 71 to 74 wherein the reduction is effected at temperatures from -20 to 100°C.

76. A process as claimed in claim 75 wherein the reduction is effected at temperatures up to the boiling point of the solvent used.

77. A process for the preparation of compounds of general formula I (wherein R_1 , R_3 and R_4 are as defined in claim 1 and R_2 represents a nitro group) which comprises nitrating a compound of formula



(wherein R_1 , R_3 and R_4 are as defined in claim 1).

78. A process as claimed in claim 77 wherein the nitration is effected in the presence of a solvent.

79. A process as claimed in claim 77 or claim 78 wherein the nitration is effected by means of nitric acid or a mixture of concentrated nitric acid and concentrated sulfuric acid.

80. A process as claimed in any of claims 77 to 79 wherein the reduction is effected at temperatures from -20 to 100°C.

81. A process for the preparation of compounds of general formula I (wherein R_1 , R_3 and R_4 are as defined in claim 1 and R_2 represents a carbamoyl or carboxyl group) which comprises partially or fully hydrolysing a compound of formula I (wherein R_1 , R_3 and R_4 are as defined in claim 1 and R_2 represents a cyano group).



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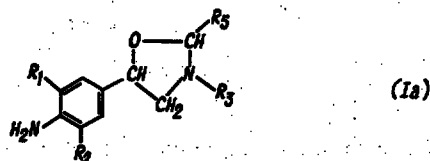
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82. A process for the preparation of compounds of general formula I (wherein R_1 , R_2 and R_3 are as defined in claim 12 and R_4 represents a carbamoyl or carboxyl group) which comprises partially or fully hydrolysing a compound of formula I (wherein R_1 , R_2 and R_3 are as defined in claim 12 and R_4 represents a cyano group).

83. A process for the preparation of compounds of general formula I (wherein R_1 , R_2 and R_3 are as defined in claim 1 and R_4 represents a carboxyl group) which comprises hydrolysing a compound of formula I (wherein R_1 , R_2 and R_3 are as defined in claim 1 and R_4 represents a carbamoyl or carbalkoxy group).

84. A process for the preparation of oxazolidines of general formula



(wherein R_1 , R_2 , R_3 and R_4 are as defined in claim 1) which comprises reacting a compound of formula I (wherein R_1 , R_2 and R_3 are as defined in claim 1 and R_4 represents a hydrogen atom) with an aldehyde of formula



(wherein R_5 represents a hydrogen atom or a straight or branched alkyl group).

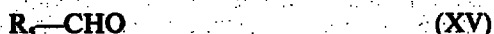
85. A process as claimed in claim 84 wherein the reaction is effected in the presence of a solvent.

86. A process as claimed in claim 84 or claim 85 wherein the reaction is effected under dehydrating conditions.

87. A process as claimed in claim 86 wherein the reaction is effected in the presence of anhydrous copper (II) sulphate or using an apparatus incorporating a water separator funnel.

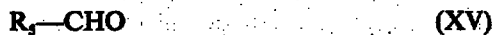
88. A process as claimed in any of claims 84 to 87 wherein the reaction is effected at temperatures up to the boiling point of the solvent used.

89. A process for the preparation of oxazolidines of general formula Ia (wherein R_1 , R_2 , R_3 and R_4 are as defined in claim 12) which comprises reacting a compound of formula I (wherein R_1 , R_2 and R_3 are as defined in claim 12 and R_4 represents a hydrogen atom) with an aldehyde of formula



(wherein R_5 represents a hydrogen atom).

90. A process for the preparation of oxazolidines of general formula Ia as defined in claim 14 which comprises reacting a compound of formula I (wherein R_1 , R_2 and R_3 are as defined in claim 14 and R_4 represents a hydrogen atom) with an aldehyde of formula

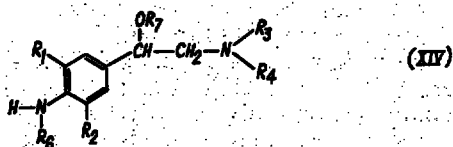


(wherein R_5 is as defined in claim 14).

91. A process for the preparation of the optical isomers of compounds of general formula I as defined in claim 1 which comprises resolving a racemic mixture of the compound of formula I into its optical isomers.

92. A process for the preparation of the d(+)- and l(-)-stereoisomers of compounds of general formula I' as defined in claim 13 which comprises resolving a racemic mixture of the compound of formula I into its optical isomers.

93. A process as claimed in claim 91 wherein the resolution is achieved by converting the racemic mixture of the compound of formula I into a racemic mixture of a compound of formula





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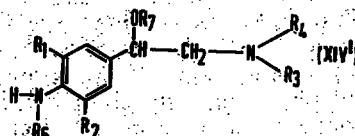
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(wherein R_1 , R_2 , R_3 and R_4 are as defined in claim 1, R_5 represents a hydrogen atom or an acyl group and R_6 represents a chiral acyl group), resolving this racemic mixture into its constituent optical isomers, and subsequently splitting off the groups R_5 and R_6 , if R_5 represents an acyl group, and if desired the group R_4 , if R_4 represents an optionally substituted benzyl group, from each pure optical isomer.

94. A process as claimed in claim 93 wherein the resolution of the racemic mixture of the compound of formula XIV is achieved by fractional crystallization and/or column chromatography over an inert carrier.

95. A process as claimed in claim 92 wherein the resolution is achieved by converting the racemic mixture of the compound of formula I' into a racemic mixture of a compound of formula



(wherein R_1 , R_2 and R_3 are as defined in claim 13, R_4 represents a hydrogen atom or a benzyl group, R_5 represents a hydrogen atom or an acyl group and R_6 represents a chiral acyl group), resolving this racemic mixture into its constituent optical isomers and subsequently splitting off the groups R_5 , R_6 if R_5 represents an acyl group, and R_4 , if R_4 represents a benzyl group, from each pure optical isomer.

96. A process as claimed in claim 91 wherein the resolution of the racemic mixture of the compound of formula I is achieved by column chromatography over an optically active carrier.

97. A process as claimed in claim 91 wherein the resolution of the racemic mixture of the compound of formula I is achieved by fractional crystallization of the diastereoisomeric salts therefrom with an optically active acid.

98. A process as claimed in claim 97 wherein the optically active acid is D(-)-tartaric acid, L(+)-tartaric acid, dibenzoyl-D-tartaric acid, dibenzoyl-L-tartaric acid, (+)-camphor-10-sulfonic acid, L(-)-malic acid, L(+)-mandelic acid, D- α -bromo-camphor- π -sulfonic acid or L-quinic acid.

99. A process as claimed in any of claims 19 to 98 wherein the compound of formula I (including the pure d(+) and l(-)-stereoisomers thereof) or of formula Ia as defined in claim 1 is subsequently converted into an acid addition salt thereof.

100. A process as claimed in claim 99 wherein the compound of formula I (including the pure d(+) and l(-)-stereoisomers thereof) or of formula Ia as defined in claim 1 is subsequently converted into a physiologically compatible acid addition salt thereof.

101. A process as claimed in any of claims 23, 31, 39, 46, 54, 82 and 89 wherein the compound of formula I or of formula Ia as defined in claim 12 is subsequently converted into a physiologically compatible acid addition salt thereof.

102. A process as claimed in any of claims 33, 92 and 95 wherein the d(+) or l(-) stereoisomer of a compound of formula I' as defined in claim 13 is subsequently converted into a physiologically compatible acid addition salt thereof.

103. A process as claimed in any of claims 24, 32, 40, 47, and 90, wherein the compound of formula I or of formula Ia as defined in claim 14 is subsequently converted into a physiologically compatible acid addition salt thereof.

104. A process as claimed in any of claims 34, 55, 58, 62, 67, 71, 72, 77, 81, 83 and 84 wherein the compound of formula I or of formula Ia as defined in claim 1 is subsequently converted into a physiologically compatible acid addition salt thereof.

105. A process as claimed in any of claims 19 to 104 substantially as herein described.

106. A process as claimed in any of claims 23, 31, 39, 46, 54, 82, 89 and 101 substantially as herein described.

107. A process as claimed in any of claims 33, 92, 95 and 102, substantially as herein described.

108. A process as claimed in any of claims 24, 32, 40, 47, 90 and 103 substantially as herein described.

109. A process as claimed in any of claims 34, 55, 58, 62, 67, 71, 72, 77, 81, 83, 84 and 104, substantially as herein described.

110. A process for the preparation of compounds as claimed in claim 1 substantially as herein described with reference to Examples 1 to 199.



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111. A process for the preparation of compounds as claimed in claim 12 substantially as herein described with reference to Examples 1 to 109.

112. A process for the preparation of compounds as claimed in claim 13 substantially as herein described with reference to Examples 173 to 179.

113. A process for the preparation of compounds as claimed in claim 14 substantially as herein described with reference to Examples 110 to 172.

114. A process for the preparation of compounds as claimed in claim 1 substantially as herein described with reference to Examples 185 to 199.

115. Compounds of general formula I (including the pure d(+)- and l(-)-stereoisomers thereof) and of general formula Ia as defined in claim 1 and acid addition salts thereof when prepared by a process as claimed in any of claims 19 to 114.

116. Compounds of general formula I and Ia as defined in claim 12 and physiologically compatible acid addition salts thereof when prepared by a process as claimed in any of claims 23, 31, 39, 46, 54, 82, 89, 101, 106 and 111.

117. d(+)- and l(-)-stereoisomers of compounds of general formula I' as defined in claim 13 and physiologically compatible acid addition salts thereof when prepared by a process as claimed in any of claims 23, 92, 95, 102, 107 and 112.

118. Compounds of general formulae I and Ia as defined in claim 14 and physiologically compatible acid addition salts thereof when prepared by a process as claimed in any of claims 24, 32, 40, 47, 90, 103, 108 and 113.

119. Compounds of general formulae I and Ia as defined in claim 1 and physiologically compatible acid addition salts thereof when prepared by a process as claimed in any of claims 34, 55, 58, 62, 67, 71, 72, 77, 81, 83, 84, 104, 109 and 114.

120. Pharmaceutical compositions comprising as active ingredient at least one compound of formula I or Ia as defined in claim 1 or physiologically compatible acid addition salts thereof in association with a pharmaceutical carrier or excipient.

121. Compositions as claimed in claim 120 in a form suitable for oral, rectal or parenteral administration.

122. Compositions as claimed in claim 120 or claim 121 in the form of tablets, coated tablets, gelatine capsules, ampoules, suppositories and syrups.

123. Compositions as claimed in any of claims 120 to 122 in the form of dosage units.

124. Compositions as claimed in claim 123 wherein each dosage unit contains from 1 to 100 μ of active ingredient.

125. Compositions as claimed in claim 123 wherein each dosage unit contains from 5 to 50 μ of active ingredient.

126. Compositions as claimed in any one of claims 120 to 125 wherein the active ingredient is a compound as claimed in claim 12.

127. Compositions as claimed in any of claims 120 to 125 wherein the active ingredient is a compound as claimed in claim 13.

128. Compositions as claimed in any of claims 120 to 125 wherein the active ingredient is a compound as claimed in claim 14.

129. Pharmaceutical compositions substantially as herein described.

130. Pharmaceutical compositions substantially as herein described with reference to Examples 200 to 213.

131. Pharmaceutical compositions substantially as herein described with reference to Examples 200 to 207.

132. Pharmaceutical compositions substantially as herein described with reference to Examples 208 to 213.

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