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[54] Title: PROPANOLAMINE DERIVATIVES AND PHARMACEUTICAL PREPARATION THEREOF

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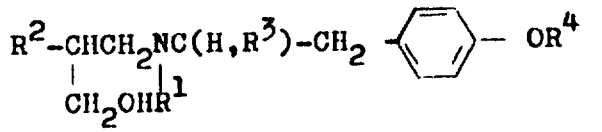
[57]

A B S T R A C T

The propanolamine derivatives of the formula



I

wherein R^1, R^2, R^3 and R^4 have the significances given in the description, and the physiologically compatible salts thereof have catabolic activity and can be used for the treatment of obesity, of diabetes and of conditions which are associated with high protein breakdown or as feed additives for fattening animals.

The can be manufactured by reducing corresponding malonic acid monoester monoamides or corresponding propanolamides.

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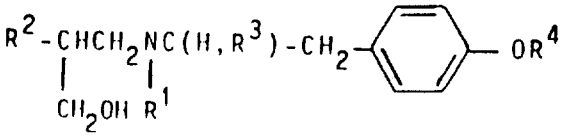
PROPANOLAMINE DERIVATIVES

Abstract

The propanolamine derivatives of the formula



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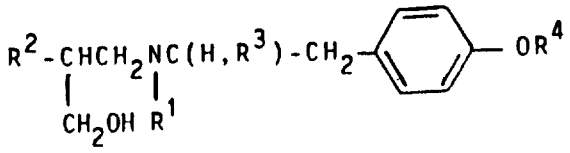
wherein R^1, R^2, R^3 and R^4 have the significances given in the description, and the physiologically compatible salts thereof have catabolic activity and can be used for the treatment of obesity, of diabetes and of conditions which are associated with high protein breakdown or as feed additives for fattening animals.

They can be manufactured by reducing corresponding malonic acid monoester monoamides or corresponding propanolamides.

PROPANOLAMINE DERIVATIVES

The present invention is concerned with novel propanolamine derivatives per se and as therapeutically active substances, especially for the treatment of obesity, of diabetes mellitus and of conditions which are associated with high protein breakdown; further, pharmaceutical preparations and feedstuffs for fattening animals which contain such a propanolamine derivative, a process for the manufacture of these derivatives and, respectively, of these preparations and feedstuffs, as well as the use of said propanolamine derivatives for the manufacture of the above pharmaceutical preparations.

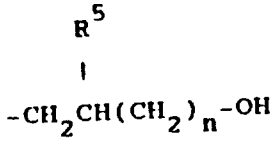
The propanolamine derivatives of the present invention are compounds of the formula



I

wherein

R^1 is hydrogen or a group of the formula



(a)

n is the number 0 or 1

R^2 and R^5 are phenyl, m-halophenyl, m-trifluoromethylphenyl, thienyl or pyridyl

R^3 is hydrogen or methyl

R^4 is hydrogen, $-CH_2COOH$, $-CH_2COO-C_{1-4}$-alkyl, $-(CH_2)_2O-C_{1-4}$-alkyl or $-(CH_2)_2O(CH_2)_{1-4}-C_6H_5$,

and physiologically compatible salts thereof.

m-Chlorophenyl is preferred among the m-halophenyl groups R^2 or R^5, and 2-thienyl and, respectively, 2-pyridyl are preferred under the thienyl and pyridyl groups. C_{1-4}-Alkyl denotes straight-chain or branched residues with 1-4 C-atoms such as methyl, ethyl, propyl, isopropyl, butyl and isobutyl.

The compounds of formula I form salts with acids, and these salts are also an object of the invention. Examples of such salts are salts with physiologically compatible mineral acids such as hydrochloric acid, hydrobromic acid, sulphuric acid, phosphoric acid; or with organic acids such as oxalic acid, methanesulphonic acid, acetic acid, propionic acid, citric acid, maleic acid, succinic acid, malic acid, fumaric acid, phenylacetic acid or salicylic acid. Carboxylic acids of formula I can also be present as salts. Examples of such salts are alkali metal, alkaline earth metal, ammonium and ethanolammonium salts.

The compounds in accordance with the invention contain at least one asymmetric carbon atom and can accordingly be present as optically active enantiomers, as diastereomers or as racemates.

Among the compounds of formula I there are preferred those in which R^1 is hydrogen, R^2 is phenyl, m-halophenyl, especially m-chlorophenyl, or m-trifluoromethylphenyl, thienyl or pyridyl, especially 2- or 3-pyridyl, R^4 is hydrogen, 2-ethoxyethyl, 2-phenethoxyethyl or ethoxycarbonylmethyl, especially those in which the C-atom

attached to a methyl group R^3 which may be present has the R-configuration. Those compounds in which R^2 is phenyl or 2-thienyl and R^4 is 2-ethoxyethyl or ethoxycarbonylmethyl are especially preferred. The following are examples of such compounds

(R or S)-ß-[[[p-(2-ethoxyethoxy)phenethyl]amino]-methyl]phenethyl alcohol,

ethyl [p-[2-[[ß-(hydroxymethyl)phenethyl]amino]ethyl]-phenoxy]acetate,

ß-[[[(R)-p-(2-ethoxyethoxy)-α-methylphenethyl]amino]-methyl]phenethyl alcohol and

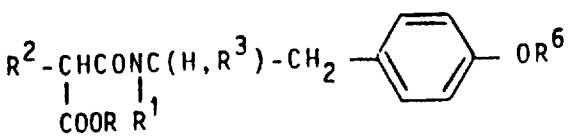
ß-[[[p-(2-ethoxyethoxy)phenethyl]amino]methyl]-2-thiopheneethanol.

Further, there are preferred the compounds of formula I in which R^1 represents a group of formula (a) in which either n is the number 1 and R^5 is phenyl or m-halophenyl, especially m-chlorophenyl, or n is the number 0 and R^5 is phenyl, especially in which the C-atom attached to the group R^5 has the R-configuration, R^2 is phenyl or m-halophenyl, especially m-chlorophenyl, R^3 is hydrogen and R^4 is 2-ethoxyethyl, e.g.

(RS)-m-chloro-ß-[p-(2-ethoxyethoxy)phenethyl][[[(R)-ß--hydroxyphenethyl]amino]methyl]phenethyl alcohol.

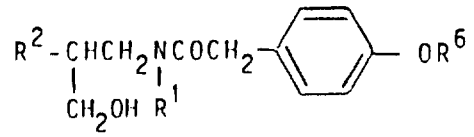
The products of the present invention can be manufactured in a manner known per se by

a) reducing an amide of the formula



II

or



III

wherein R^1, R^2 or R^3 have the above significance and R^6 is hydrogen, $-(CH_2)_2O-C_{1-4}$-alkyl or $-(CH_2)_2O(CH_2)_{1-4}-C_6H_5$,

and

b) if desired, etherifying a phenol of formula I in which R^4 is hydrogen to a compound of formula I in which R^4 is a group $-CH_2-COOH$ or $-CH_2COO-C_{1-4}$-alkyl, and

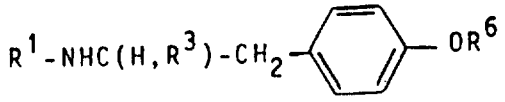
c) if desired, converting a compound of formula I into a salt.

The reduction according to process variant a) can be carried out conveniently by means of a complex metal hydride such as lithium aluminium hydride ($LiAlH_4$) in a solvent such as an ether, e.g. diethyl ether, monoglyme, diglyme or tetrahydrofuran (THF), at a temperature up to the reflux temperature of the reaction mixture, preferably at room temperature.

The etherification according to variant b) can be carried out with a compound of the formula $X-R^{40}$ in which R^{40} is a group $-CH_2COOH$ or $-CH_2COO-C_{1-4}$-alkyl and X is halogen, conveniently iodine, or a sulphonate group, e.g. methanesulphonate. The reaction is conveniently carried out in a solvent such as a ketone, e.g. acetone, an ether such as THF or in dimethylformamide in the presence of a base such as an alkali metal hydroxide, e.g. potassium hydroxide or sodium hydroxide, at a temperature up to the reflux temperature, preferably at room temperature.

The amides of formulae II and III can be prepared in a manner known per se.

Thus, the amides II are obtained by reacting an amine of the formula



IV

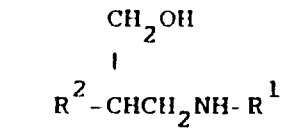
with a diester of the formula

$$R^2\text{-}CH(COOR)_2 \qquad V$$

wherein R is C_{1-4}-alkyl.
Amides of formula II in which R^1 is a group (a) can also be obtained by reacting a secondary amine of formula I in which R^1 is hydrogen with a diester V.

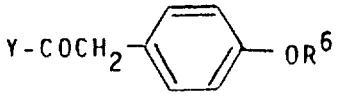
These reactions can be carried out in a solvent such as an ether, e.g. diglyme, at temperatures up to the reflux temperature, conveniently at about 90-100°C. For the preparation of the amide starting material of Example 1 hereinafter, a solution of diethyl phenylmalonate in 50 mg of diglyme was treated in this manner with 25 g of p-(2-ethoxyethoxy)phenethylamine and stirred at 95°C for 48 hrs. After cooling the excess solvent was evaporated. The residue was chromatographed on silica gel with ethyl acetate/hexane (1:2). There was obtained ethyl [[[p-(2-ethoxyethoxy)phenethyl]carbamoyl]phenyl]acetate, m.p. 80°C. The amide starting materials of Examples 2.a), 2.l) and 2.o) were also obtained in crystalline form (m.p. 108°C, 94-95°C and 110-111°C, respectively).

The amides III are obtained by reacting an alcohol of the formula



VI

with a compound of the formula

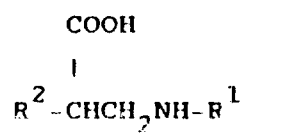


VII

wherein Y is halogen, especially chlorine, or lower-alkoxy.

This reaction can be carried out in the same manner as the reaction of an amine IV with a diester V described above. For the preparation of the amide starting materials III of Examples 3.a) and 3.b), 50 g of ethyl p-(2-ethoxyethoxy)-phenyl acetate in 50 ml of diglyme were treated slowly with 25 g of (R or S)-ß-(aminomethyl)phenethyl alcohol and stirred at 95°C for 48 hrs. The mixture was then cooled and evaporated and the residue was chromatographed on silica gel with ethyl acetate/hexane (1:2).

The alcohols VI can be prepared by reducing the corresponding acids of the formula



VIII.

This reduction can be carried out analogously to the reduction of an amide II or III described above.

A racemate of formula VI can be resolved readily by salt formation with an optically active acid such as L- or D-dibenzoyltartaric acid and is therefore especially suitable as an intermediate in the manufacture of optically active compounds III and I.

For the preparation of the alcohols VI used in Examples 3.a) and 3.b), 10 g of 3-amino-2-phenylpropanecarboxylic acid in 150 ml of monoglyme were stirred with 3 g of $LiAlH_4$ for 20 hrs. Then, 12 ml of water and 3 ml of 10% sodium hydroxide solution were slowly added thereto. The mixture was filtered and the filtrate was again evaporated with toluene. There were obtained 8.4 g of ß-(aminomethyl)phenethyl alcohol.

For the preparation of the R- and S-enantiomers of this alcohol, this was dissolved in 200 ml of THF and treated with a solution of dibenzoyl-L-tartaric acid. After one day crystals were filtered off and recrystallized from ethanol until the rotation was constant. There was obtained (R or S)-ß-(aminomethyl)phenethyl alcohol (S,S)-2,3-di-O-benzoyltartrate, m.p. 172 173°C, $[\alpha]_D$ -28.4° (DMSO, c = 1%).

The mother liquors were treated with a strongly basic ion exhanger, filtered and evaporated. The oily residue of the free amine enriched with the enantiomers was treated as described above, but this time with dibenzoyl-D--tartaric acid. There was obtained (R or S)-ß-(aminomethyl)phenethyl alcohol (R,R)-2,3-di-O-benzoyltartrate, m.p. 172-173°C, $[\alpha]_D$ +28.2° (DMSO, c = 1%).

The compounds IV, V, VII and VIII, insofar as they are not known, can be prepared in a manner known per se, e.g. in analogy to known compounds. Thus, the diesters V can be obtained from the corresponding acetic acid esters

according to the methods described in Organic Synthesis, Collective Vol. 2, Edited by A.H. Blatt (1943) 288-289.

The propanolamine derivatives in accordance with the invention can be used as active substances in pharmaceutical preparations for the treatment of obesity and/or of diabetes mellitus, especially of obese adult diabetics. In an animal experiment an increased catabolism, primarily of fat, has been observed upon the aministration of the said derivatives. Furthermore, it has been observed that the propanolamine derivatives in accordance with the invention stimulate the formation of brown adipose tissue in rats and obese-hyperglycaemic mice. It is known that defects of the brown adipose tissue play a substantial role in the origin of obesity. In obese-hyperglycaemic mice and in streptozotocin-diabetic rats these derivatives have a pronouned antidiabetic effect, in that they have hypoglycaemic activity and reduce glycosuria. The propanolamine derivatives in accordance with the invention exhibit only a slight activity on the working of the heart and circulation. Moreover, they have only a slight activity on insulin distribution. This is of significance, since as is known high plasma insulin plays an important role in the pathogenesis of obesity. The dosage can amount to 0.5-1000 mg, preferably 2-200 mg, per day for an adult depending on the strength of activity of the individual compounds and on the individual requirements of the patients, whereby the dosage can be administered as a single dosage or in several dosages over the day.

In addition, in an animal experiment with the propanolamine derivatives in accordance with the invention an increase in the body protein content and a decrease in the body fat content could be detected. The said derivatives therefore lead to an increase in the lean

composition of the body at the expense of fat. Accordingly, they can be used in human medicine for the treatment of conditions which are associated with high protein breakdown, e.g. in convalescence after operations. In this case the dosages administered are the same as in the treatment of obesity and/or of diabetes mellitus.

The propanolamine derivatives in accordance with the invention can also be used in the maintenance of fattening animals such as beef cattle, pigs, sheep and poultry. In this case the dosage forms are the same as in the case of vitamins. The said derivatives can also be used as feed additives in dosages of 0.01-100 mg/kg depending on the substance, kind of animal and age.

The pharmaceutical preparations contain the active substances together with a compatible pharmaceutical, organic or inorganic carrier material such as water, gelatine, gum arabic, lactose, starch, magnesium stearate, talc, vegetable oils, polyalkylene glycols or Vaseline. The pharmaceutical preparations are preferably administered orally, e.g. in the form of tablets, capsules, pills, powders, granulates, solutions, syrups, suspensions or elixirs. The administration can, however, also be effected parenterally, e.g. in the form of sterile solutions, suspensions or emulsions. The pharmaceutical preparations can be sterilized and/or can contain ingredients such as preserving agents, stabilizing agents, wetting agents, emulsifiers, salts for varying the osmotic pressure and buffer substances.

The activity of the novel compounds of formula I is evident from the following test results:

1) Activity on oxygen consumption

Male albino rats weighing 160-180 g were placed in metabolic cages after fasting for 24 hours. The cages were ventilated with a constant 6 litre room air/minute which was equilibrated at a dew point of 11°C. Samples of the spent air were collected during periods of in each case 14 minutes after again equilibrating and the oxygen content and CO_2 content were analyzed. After an adaptation time of 4 hours the animals, divided into groups of 6, received either placebo (5% gum arabic) or the test substance (suspended in 5% gum arabic) per os. Thereafter, the determinations were carried out for a period of 12 hours. In Table I there is given the percentage of the average oxygen consumption after medication during the first 3 hours and the entire test duration (12 hours) of the oxygen consumption of the adaptation period, corresponding corrections for variations in the placebo group having been taken into consideration.

Table I

Compound of Example No.	Dosage µM/kg	O_2 consumption % of the value of the pre-period 1st-3rd hour	1st-12th hour
2.a)	10	149	113
2.b)	3	124	107
2.c)	3	132	108
2.d)	3	152	127
2.j)	10	137	113
2.o)	10	147	115
3.a)	3	152	112
4	3	145	112

2) Activity on heart rate

Male albino rats weighing 250-320 g received 6 hours after withdrawal of food either placebo (5% gum arabic) or the test substance (suspended in 5% gum arabic) per os. The animals were subsequently immobilized in perforated plastic tubes. The electrocardiogram was derived by means of bipolar subcutaneous needle electrodes. The R-point was used to activate an impact counter. The heart rate measured 1 and 3 hours after completion is given in Table II as a percentage of the control value (placebo).

Table II

Compound of Example	Dosage (mg/kg)	Heart rate (% of controls) 1 hour	3 hours
2a	30	105	100
	100	121	112
2b	30	106	99
	100	114	105
2c	10	103	102
	30	111	104
2d	10	103	100
	30	111	104
2j	100	110	-
2o	30	108	-
	100	111	
3a	10	108	-
	30	115	-

Example 1

A solution of 15 g of $LiAlH_4$ in 600 ml of diethyl ether is treated while stirring with a solution of 20 g of ethyl [[[p-(2-ethoxyethoxy)phenethyl]carbamoyl]phenyl]-acetate. After stirring for 12 hours 15 ml of water and 5 ml of 10% sodium hydroxide solution are added to the mixture. The mixture is filtered through silica gel and the filtrate is evaporated. The residue is dissolved in ethanol and treated with the equivalent amount of oxalic acid dissolved in ethanol. After adding ethyl acetate there is obtained ß-[[[p-(2-ethoxyethoxy)phenethyl]amino]-methyl]phenethyl alcohol oxalate
m.p. 145°C.

Example 2

Analogously to Example 1,

2a) from ethyl [[(R)-p-(2-ethoxyethoxy)-α-methyl-phenethyl]carbamoyl]phenylacetate there was manufactured ß-[[[(R)-p-(2-ethoxyethoxy)-α-methylphenethyl]amino]-methyl]phenethyl alcohol oxalate
m.p. 145°C (decomposition).

2b) from ethyl [[p-(2-ethoxyethoxy)phenethyl]carbamoyl]-m--chlorophenylacetate there was manufactured m-chloro-ß-[[[p-(2-ethoxyethoxy)phenethyl]amino]methyl]-phenethyl alcohol oxalate
m.p. 148°C.

2c) from (RS)-2-phenyl-N-[(RS)-ß-(hydroxymethyl)-phenethyl]-N-[p-(2-ethoxyethoxy)phenethyl]ethylmalonamate there was manufactured ß,ß'-[[[p-(2-ethoxyethoxy)phenethyl]imino]dimethylene]bis-[(RS)-phenethyl alcohol] hydrochloride
m.p. 94°C.

2d) from (RS)-2-(m-chlorophenyl)-N-[p-(2-ethoxyethoxy)-phenethyl]-N-[(R)-ß-hydroxyphenethyl]malonamate there was manufactured
(RS)-m-chloro-ß-[p-(2-ethoxyethoxy)phenethyl][[[(R)-ß--hydroxyphenethyl]amino]methyl]phenethyl alcohol oxalate
m.p. 130°C.

2e) from ethyl (RS)-[[[(R)-α-methyl-p-(2-phenethoxy)-ethoxy]phenethyl]carbamoyl]-m-chlorophenyl acetate there was manufactured
(RS)-m-chloro-ß-[[[(R)-α-methyl-p-[2-(phenethoxy)ethoxy]-phenethyl]amino]methyl]phenethyl alcohol oxalate
m.p. 164-166°C.

2f) from (RS)-2-(m-chlorophenyl)-N-[(RS)-m-chloro-ß--(hydroxymethyl)phenethyl]-N-[p-(2-ethoxyethoxy)phenethyl]-ethylmalonamate there was manufactured
ß,ß'-[[[p-(2-ethoxyethoxy)phenethyl]imino]dimethylene]-bis[(RS)-m-chlorophenethyl alcohol] hydrochloride
m.p. 148°C.

2g) from ethyl (RS)-[[[(R)-α-methyl-p-(2-ethoxyethoxy)-phenethyl]carbamoyl]-m-chlorophenyl acetate there was manufactured
(RS)-m-chloro-ß-[[[(R)-p-(2-ethoxyethoxy)-α-methyl-phenethyl]amino]methyl]phenethyl alcohol oxalate
m.p. 145°C.

2h) from ethyl [[p-hydroxyphenethyl]carbamoyl]phenyl acetate there was manufactured
ß-[[(p-hydroxyphenethyl)amino]methyl]phenethyl alcohol oxalate
m.p. 136-137°C.

2i) from ethyl (RS)-[[[(R)-α-methyl-p-(2-phenethoxy)-ethoxy]phenethyl]carbamoyl]phenyl acetate there was manufactured

ß-[[[(R)-α-methyl-p-(2-phenethoxy)ethoxy]phenethyl]amino]-methyl]phenethyl alcohol oxalate
m.p. 165-179°C.

2j) from ethyl [[p-(2-phenethoxy)ethoxy]phenethyl]-carbamoyl]phenyl acetate there was manufactured ß-[[[p-(2-phenethoxy)ethoxy]phenethyl]amino]methyl]-phenethyl alcohol oxalate
m.p. 145°C.

2k) from ethyl [[p-(2-ethoxyethoxy)phenethyl]carbamoyl]-m--trifluoromethylphenyl acetate there was manufactured ß-[[[p-(2-ethoxyethoxy)phenethyl]amino]methyl]-m-trifluoromethylphenethyl alcohol oxalate
m.p. 148°C.

2l) from ethyl α-[[p-(2-ethoxyethoxy)phenethyl]-carbamoyl]-3-thiopheneacetate there was manufactured ß-[[[p-(2-ethoxyethoxy)phenethyl]amino]methyl]-3-thiopheneethanol oxalate
m.p. 153-155°C.

2m) from ethyl α-[[p-(2-ethoxyethoxy)phenethyl]-carbamoyl]-2-pyridine acetate there was manufactured ß-[[[p-(2-ethoxyethoxy)phenethyl]amino]methyl]-2-pyridineethanol oxalate
m.p. 128-129°C.

2n) from ethyl α-[[p-(2-ethoxyethoxy)phenethyl]-carbamoyl]-3-pyridineacetate there was manufactured ß-[[[p-(2-ethoxyethoxy)phenethyl]amino]methyl]-3-pyridineethanol oxalate
m.p. 170°C (decomposition).

2o) from ethyl α-[[p-(2-ethoxyethoxy)phenethyl]-carbamoyl]-2-thiopheneacetate there was manufactured

ß-[[[p-(2-ethoxyethoxy)phenethyl]amino]methyl]-2-thiophene-ethanol oxalate
m.p. 145°C (decomposition).

Example 3

Analogously to Example 1,

3a) from N-[(R or S)-3-hydroxy-2-phenylpropyl]-p-(2--ethoxyethoxy)phenylacetamide there is manufactured (R or S)-ß-[[[p-(2-ethoxyethoxy)phenethyl]amino]methyl]-phenethyl alcohol oxalate
m.p. 152-154°C, $[\alpha]_D$ -9° (DMSO, c = 1%)

3b) from the enantiomer corresponding to Example 3a) there is manufactured the enantiomer (R or S) ß-[[[p-(2-ethoxy-ethoxy)phenethyl]amino]methyl]phenethyl alcohol oxalate
m.p. 151-154°C, $[\alpha]_D$ +8.3° (DMSO, c = 1%).

Example 4

3.62 g of the product of Example 2h) are stirred for 24 hours in 200 ml of acetone with 2.5 g of ethyl iodo-acetate and 2 g of potassium hydroxide. The mixture is then evaporated, the residue is taken up in water and ethyl acetate. The organic phase is separated, dried over sodium sulphate and evaporated. The residue is chromato-graphed on silica gel. The product is dissolved in ethanol, treated with 1 ml of concentrated hydrochloric acid and evaporated with ethanol. Crystallization of the residue from ethanol/ether gives ethyl [p-[2-[[ß-(hydroxy-methyl)phenethyl]amino]ethyl]phenoxy]acetate hydrochloride
m.p. 104-105°C.

Example 5

Tablets of the following composition are manufactured in the usual manner:

Active substance of formula I, e.g. (RS)-m-chloro-ß-[p-(2-ethoxyethoxy)-phenethyl][[[(R)-ß-hydroxyphenethyl]-amino]methyl]phenethyl alcohol oxalate	250 mg
Lactose	200 mg
Maize starch	300 mg
Maize starch paste	50 mg
Calcium stearate	5 mg
Dicalcium phosphate	45 mg

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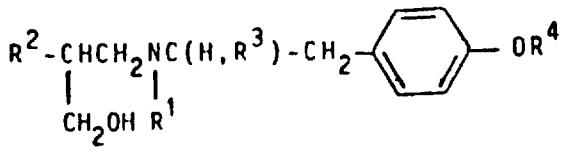
CLAIMS

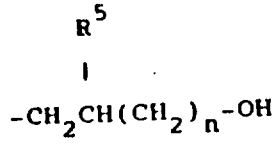
1. Propanolamine derivatives of the formula



I

wherein

R^1 is hydrogen or a group of the formula



(a)

n is the number 0 or 1

R^2 and R^5 are phenyl, m-halophenyl, m-trifluoro methylphenyl, thienyl or pyridyl.

R^3 is hydrogen or methyl

R^4 is hydrogen, $-CH_2COO-C_{1-4}$-alkyl, $-(CH_2)_2O-C_{1-4}$-alkyl or $-(CH_2)_2O(CH_2)_{1-4}-C_6H_5$,

and physiologically compatible salts thereof.

2. Compunds according to claim 1, wherein R^1 is hydrogen or a group (a) in which n and R^5 have the significance given in claim 1.

3. Compounds according to claim 1 wherein R^1 is hydrogen, R^2 is phenyl, m-chlorophenyl, or m-trifluoromethylphenyl, thienyl or 2- or 3-pyridyl, R^4 is hydrogen, 2-ethoxyethyl, 2-phenethoxyethyl or ethoxycarbonylmethyl, and in which the C-atom attached to a methyl group R^3 has the R-configuration.

4. Compounds according to claim 1 wherein R^1 represents a group (a) in which n is the number 1 and R^5 is phenyl or m-chlorophenyl, or n is the number 0

and R^5 is phenyl and in which the C-atom attached to the group R^5 has the R-configuration. R^2 is phenyl or m-chlorphenyl, R^3 is hydrogen and R^4 is 2-ethoxyethyl.

5. (RS)-m-Chloro-β-[p-(2-ethoxyethoxy)phenethyl]-[[[(R)-β-hydroxyphenethyl]amino]methyl]phenethyl alcohol.

6. (R or S)-β-[[[p-(2-Ethoxyethoxy)phenethyl]-amino]methyl]phenethyl alcohol.

7. Ethyl [p-[2-[[β-(hydroxymethyl)phenethyl]-amino]ethyl]phenoxy]acetate.

8. β-[[[(R)-p-(2-Ethoxyethoxy)-α-methyl-phenethyl]amino]methyl]phenethyl alcohol.

9. β-[[[p-(2-Ethoxyethoxy)phenethyl]amino]methyl] 2-thio-pheneethanol.

10. A pharmaceutical preparation which contains a compound according to claim 1 and a therapeutically acceptable carrier.

11. A feedstuff for fattening animals containing a compound according to claim 1 as therapeutically active ingredient.

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