United States Patent Office 3,105,854 Patented Oct. 1, 1963

3,105,854

META-SUBSTITUTED PHENOXYETHYLAMINES

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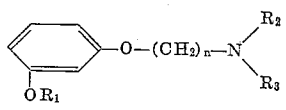
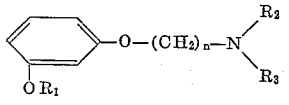
No Drawing. Filed Sept. 23, 1959, Ser. No. 841,688
Claims priority, application Switzerland Nov. 6, 1958
21 Claims. (Cl. 260—570.7)

The present invention relates to the manufacture of amines of the formula

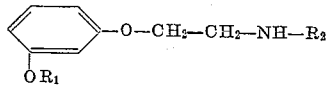


in which R_1 represents a hydrocarbon radical of aliphatic character containing 3 to 7 carbon atoms, R_2 a hydrocarbon radical, R_3 has the same meaning or advantageously represents hydrogen, and R_2 and R_3 together with the nitrogen atom may form a ring, and n represents a whole low number, but at least 2, and salts thereof.

The invention relates more especially to compounds of the formula



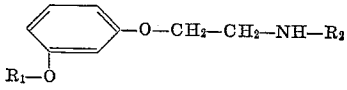
In which R_1 to R_3 have the meanings given above but contain together at least 5 carbon atoms, but preferably 7 to 10 carbon atoms, and n is a number from 2 to 4, and salts thereof, and more particularly to compounds of the formula



and their salts, in which R_1 and R_2 have the meanings given above and contain together at least 5 carbon atoms, but preferably 7 to 10 carbon atoms.

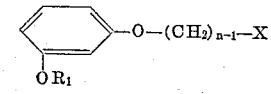
The hydrocarbon radical of aliphatic character, R_1, with 3 to 7 carbon atoms is for example an alkyl group, such as propyl, isopropyl, butyl, secondary butyl, pentyl, isopentyl, hexyl or heptyl, a cycloalkyl radical such as cyclopentyl or cyclohexyl, or an unsaturated radical, such as allyl, cyclopentenyl or cyclohexenyl. R_2 is advantageously also of aliphatic character, more especially an aliphatic or cycloaliphatic hydrocarbon radical having 1 to 10 carbon atoms, and especially 3 to 6 carbon atoms, preferably a straight or branched lower alkyl or alkenyl radical, e.g. methyl, ethyl, propyl, isopropyl, allyl, methallyl, butyl, secondary butyl, pentyl or hexyl, or also a cycloalkyl radical, e.g. cyclopentyl or cyclohexyl. R_3 can have the same meanings, but advantageously stands for hydrogen. Together with the nitrogen atom R_2 and R_3 can represent for example a pyrrolidino or piperidino radical.

The new compounds, more especially those of the formula



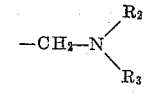
in which R_1 stands for a butyl or pentyl radical and R_2 for methyl or ethyl or, more preferred for a propyl or butyl radical, as well as their salts are useful, local anaesthetics and are thus intended to be used as medicaments. Special mention deserve in this connection N-[β-(meta-n-pentyloxy-phenoxy)-ethyl]-N-methyl amine, N-[β-(meta-n-pentyloxyphenoxy)-ethyl]-N-isobutylamine and N-[β-(meta-n-butoxyphenoxy)-ethyl]-N-n-butylamine as well as their salts.

The new amines are obtained by customary methods. It is of advantage to proceed in such a way that in phenol ethers of the formula



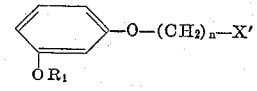
(I)

in which n and R_1 have the meanings given above and X stands for a radical convertible into the group



in which R_2 and R_3 have the meanings given above, X is converted into the latter group.

A preferred modification of this process consists in converting in compounds of the formula



(II)

in which n has the meaning given above and X' represents a radical convertible directly or in stages into the group

X' directly or in stages into the latter group.

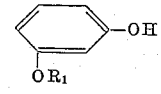
The preferred form of the process consists in reacting a compound of the Formula II in which X' represents a radical exchangeable for an amino group, with an amine of the formula

in which R_2 and R_3 have the meanings given above. X' is preferably a reactively esterified hydroxyl group esterified with a strong inorganic acid, for example hydrohalic acid, such as hydrochloric acid, hydrobromic acid or hydriodic acid, or sulfuric acid, or a strong organic acid such as sulfonic acid, e.g. an alkane- or aryl-sulfonic acid.

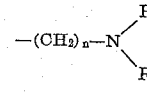
Furthermore, in compounds of the Formula II in which X' stands for the group

in which R_2 has the meaning given above and Y represents a radical splittable by hydrolysis or hydrogenolysis, Y is split in the manner indicated. Y is, for example, an acyl radical, e.g. lower alkanoyl, aroyl or aryl sulfonyl which can be split in the customary manner by hydrolysis, for example with a dilute alkali, or an arylmethyl or arylmethyloxycarbonyl radical, such as a carbobenzoxy radical which may be removed by hydrogenolysis, for example by catalytically activated hydrogen in the presence of a palladium or platinum catalyst.

Finally, the tertiary amines of this invention can be prepared in such a way that in compounds of the formula

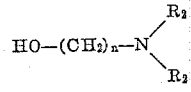


wherein R_1 has the meaning given above, the radical



in which R_2 has the meaning given above is introduced

directly in a customary manner e.g. by reaction with a reactive ester of an alcohol of the formula



such as a corresponding halide.

The above reactions are carried out in the usual manner, in the presence or absence of a diluent and/or condensing agent, at a low, ordinary or raised temperature, under atmospheric or superatmospheric pressure.

Depending on the method of working, the new compounds are obtained in the form of their bases or salts. The free amine bases can be obtained from the salts in a manner known per se. Again, from these amine bases it is possible to obtain salts by reaction with acids which are suitable for forming therapeutically usable salts, such as, for instance salts of hydrohalic acids, sulfuric acid, nitric acid, phosphoric acid, thiocyanic acid, acetic acid, propionic acid, oxalic acid, malonic acid, tartaric acid, succinic acid, malic acid, methane-sulfonic acid, ethane-sulfonic acid, hydroxyethane-sulfonic acid, benzene- or toluene-sulfonic acid or of therapeutically active acids.

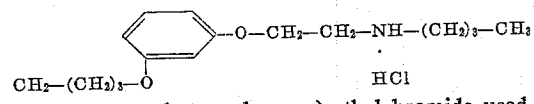
The starting materials are known or can be produced by methods known per se.

The new compounds may be used as medicaments, for example in the form of pharmaceutical preparations which contain them or their salts in admixture with a pharmaceutical organic or inorganic solid or liquid carrier suitable for enteral, topical or parenteral administration. For making the carrier there are used substances which do not react with the new compounds, such as, for example, water, gelatine, lactose, starch, magnesium stearate, talc, vegetable oils, benzyl alcohols, gums, polyalkylene glycols, white petroleum jelly, chloesterol or other known carriers for medicaments. The pharmaceutical preparations may be in the form, for example, of tablets, dragees or in liquid form as solutions, suspensions or emulsions. If desired, they are sterilized and/or contain auxiliary substances, such as preserving, stabilizing, wetting or emulsifying agents, salts for varying the osmotic pressure or buffers. They may also contain other therapeutically valuable substances. The preparations are produced by conventional methods.

The following examples illustrate the invention:

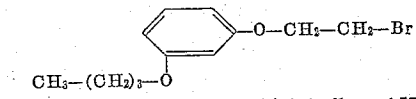
Example 1

13.6 grams (0.05 mol) of β-(meta-n-butoxyphenoxy)-ethylbromide and 7.3 grams (0.1 mol) of n-butylamine are heated for 1½ hours at 120° C. After cooling, the reaction mixture is taken up in 100 cc. of chloroform and the solution is extracted with 25 cc. of 2 N-sodium hydroxide solution and then with water. The chloroformic solution is dried over anhydrous sodium sulfate and then evaporated in a water-jet vacuum, leaving N-[β-(meta-n-butoxy-phenoxy)-ethyl]-N-n-butylamine as a yellow oil which is neutralized with a 2 N-solution of hydrogen chloride in ethyl acetate. The solution is evaporated and the resulting hydrochloride is twice recrystallized from ethanol-ether. The product is obtained in colorless crystals melting at 157–158° C.; it corresponds to the formula



The β-(meta-n-butoxyphenoxy)-ethyl bromide used as starting material can be prepared as follows:

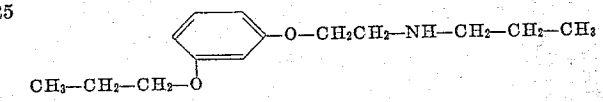
A solution of 83 grams (0.5 mol) of meta-butoxyphenol in 100 cc. of absolute ethanol is run into a solution of 11.5 grams (0.5 mol) of sodium in 250 cc. of absolute ethanol. The mixture is cooled to 0° C. and mixed with 282 grams (1.5 mols) of ethylene bromide. The content of the flask is refluxed with vigorous stirring until it gives a neutral reaction (2–3 hours), then cooled and the sodium bromide formed is filtered off and the filtrate is evaporated in a water-jet vacuum. The residue is taken up in 200 cc. of chloroform, extracted twice with 50 cc. of 2 N-sodium hydroxide solution on each occasion, and the extracts are washed with water until neutral and then dried over anhydrous sodium sulfate. The solvent is removed and the residue is distilled in a water-jet vacuum, to yield β-(meta-n-butoxyphenoxy)-ethyl-bromide of the formula



in the form of a pale-yellow oil which boils at 157–160° C. under 12 mm. Hg pressure.

Example 2

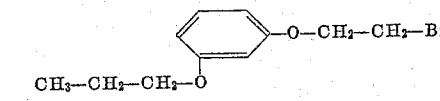
11.0 grams (0.043 mol) of β-(meta-n-propoxyphenoxy)-ethyl bromide and 11.8 grams (0.2 mol) of n-propylamine are refluxed for 12 hours in 20 cc. of ethanol, evaporated in a water-jet vacuum, treated with 50 cc. of N-sodium hydroxide solution and extracted with chloroform. Evaporation of the chloroformic extracts yields N-[β-(meta-n-propoxyphenoxy)-ethyl]-N-n-propyl-amine of the formula



as a yellowish oil which is directly converted into the hydrochloride by neutralization with hydrochloric acid in ethyl acetate. On recrystallization from ethanol-ethyl acetate it forms colorless crystals melting at 148–150° C.

The β-(meta-n-propoxyphenoxy)-ethyl bromide used as starting material is prepared as follows:

83.8 grams (0.55 mol) of resorcinol-mono-n-propyl ether are added to a solution of 12.8 grams (0.56 mol) of sodium in 400 cc. of ethanol. The whole is heated to the boil and 310 grams (1.65 mols) of ethylene bromide are run in with vigorous stirring. The contents of the flask are then refluxed until it gives a neutral reaction (2–3 hours), cooled to 0° C., the precipitated sodium bromide is filtered off, and the filtrate is evaporated in a water-jet vacuum. The residue is taken up in 200 cc. of chloroform, extracted twice with 50 cc. of 2 N-sodium hydroxide solution on each occasion, washed with water until it is neutral and then dried over anhydrous sodium sulfate. The solvent is removed and the residue is distilled in a high vacuum, β-(meta-n-propoxyphenoxy)-ethylbromide of the formula



is an almost colorless oil boiling at 75–83° C. under a pressure of 0.02 mm. Hg.

The new resorcinol ethers used as starting material in this example and in the following examples are obtained in the following manner:

A solution of 110 grams (1 mol) of resorcinol in 300 cc. of ethanol is run into a solution of 23 grams (1 mol) of sodium in 400 cc. of ethanol. The mixture is stirred for 30 minutes, 200 grams (1.18 mols) of n-propyl iodide are added, and the whole is refluxed with stirring for 3 hours. The solvent is evaporated, and the dark-colored residue is taken up in chloroform, the chloroformic solution is extracted with dilute hydrochloric acid and water and the extracts are dried over anhydrous sodium sulfate. The solvent is evaporated and the residue is fractionated under a high vacuum through a Vigreux-Hickman column, to yield the resorcinol-mono-n-propyl ether as a pale-yellow oil boiling at 80–89° C. under a pressure of 0.07 mm. Hg, n_D^{24}: 1.5232.

The identical procedure, starting from 23 grams (1.0 mol) of sodium and 110 grams (1.0 mol) of resorcinol

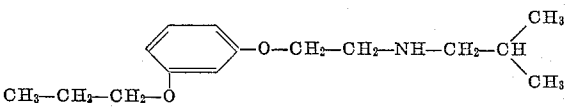
and carrying out the reaction in 400 cc. of ethanol, yield by reaction with 165 grams (1.2 mols) of isobutylbromide the meta-isobutoxyphenol as a colorless liquid boiling at 80–87° C. under a pressure of 0.06 mm. Hg.

When 110 grams (1.0 mol) of resorcinol are added to a solution of 23 grams (1.0 mol) of sodium in 400 cc. of ethanol, and the reaction described above is performed with 180 grams (1.0 mol) of n-amylbromide, meta-pentyl-oxyphenol is obtained; it boils at 100–105° C. under a pressure of 0.05 mm. Hg.

Finally, in the same manner by reacting 110 grams (1.0 mol) of resorcinol with 23 grams (1.0 mol) of sodium and then with 145 grams (1.20 mols) of allyl bromide there is obtained meta-allyloxyphenol boiling at 145–150° under a pressure of 12 mm. Hg.

Example 3

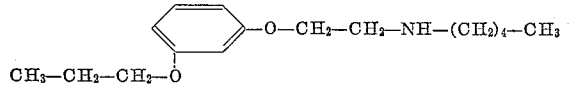
11.0 grams (0.043 mol) of β-(meta-n-propoxyphenoxy)-ethyl-bromide and 14.6 grams (0.2 mol) of isobutylamine yield by the process described in Example 2, the N-[β-(meta-n-propoxyphenoxy)-ethyl]-N-isobutylamine of the formula



as a yellow oil which is then converted as described in Example 1 into its hydrochloride which on recrystallization from ethanol-ethyl acetate is obtained in colorless crystals melting at 139–140° C.

Example 4

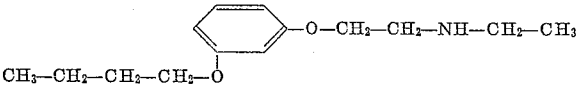
11.0 grams (0.043 mol) of β-(meta-n-propoxyphenoxy)-ethyl-bromide and 17.4 grams (0.2 mol) of n-pentylamine yield by the process described in Example 2 N-[β-(meta-n-propoxyphenoxy)-ethyl]-N-pentylamine of the formula



which is converted into its hydrochloride. The latter product is recrystallized from ethanol-ethyl acetate to form colorless crystals melting at 148–150° C.

Example 5

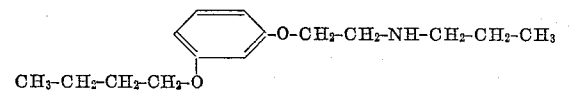
A mixture of 12.0 grams (0.044 mol) of β-(meta-n-butoxy-phenoxy)-ethylbromide and 9.0 grams (0.2 mol) of ethylamine is treated with 50 cc of ethanol and heated for 14 hours at 100° C. in a closed tube. Working up as described in Example 2 yields N-[β-(meta-n-butoxy-phenoxy)-ethyl]-N-ethylamine of the formula



Its hydrochloride melts at 160–162° C. after having been recrystallized from ethanol-ethyl acetate.

Example 6

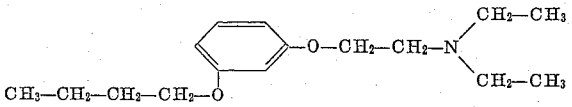
12.0 grams (0.044 mol) of β-(meta-n-butoxyphenoxy)-ethyl bromide and 11.8 grams (0.02 mol) of n-propyl-amine yield by the process described in Example 2 N-[β-(meta-n-butoxyphenoxy)-ethyl]-N-n-propylamine of the formula



in the form of a yellow oil. Its hydrochloride, prepared in the usual manner, forms colorless scales melting at 147.5° C. after having been recrystallized from ethanol-ethyl acetate.

Example 7

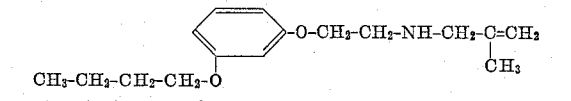
10.0 grams (0.037 mol) of β-(mono-n-butoxyphenoxy)-ethyl-bromide and 14.6 grams (0.2 mol) of diethylamine are refluxed for 12 hours; working up in the manner described in Example 2 yields N-[β-(meta-n-butoxyphenoxy)-ethyl]-N:N-diethylamine of the formula



in the form of a colorless oil. The hydrochloride, prepared in the usual manner, yields on crystallization from ethyl acetate colorless flakes melting at 109–110° C.

Example 8

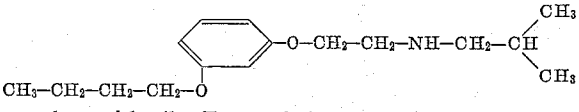
12.0 grams (0.044 mol) of β-(meta-n-butoxyphenoxy)-ethyl-bromide and 14.2 grams (0.2 mol) of methallyl-amine yield by the process described in Example 2 N-[β-(meta-n-butoxyphenoxy)-ethyl]-N-methallylamine of the formula



as a colorless liquid boiling at 125–128° C. under a pressure of 0.05 mm. Hg. Its hydrochloride is obtained in colorless scales melting at 109 to 111° C. on crystallization from ethanol-ethyl acetate.

Example 9

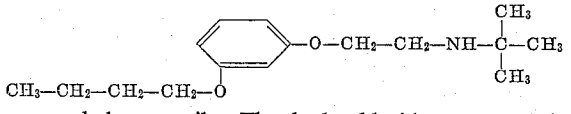
6.1 grams (0.022 mol) of β-(meta-n-butoxyphenoxy)-ethyl-bromide and 7.3 grams (0.1 mol) of isobutylamine are reacted as described in Example 2 to yield N-[β-(meta-n-butoxyphenoxy)-ethyl]-N-isobutylamine of the formula



as a brownish oil. From ethyl acetate the hydrochloride is obtained in colorless crystals melting at 137–138° C.

Example 10

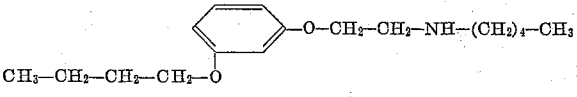
8.0 grams (0.029 mol) of β-(meta-n-butoxyphenoxy)-ethyl-bromide and 14.6 grams (0.2 mol) of tertiary butyl-amine yield by the process described in Example 2, N-[β-(meta-n-butoxyphenoxy)-ethyl]-N-tertiary butylamine of the formula



as a pale-brown oil. The hydrochloride, prepared in the usual manner, melts at 108° C. after having been recrystallized from ethyl acetate-ether.

Example 11

8.0 grams (0.029 mol) of β-(meta-n-butoxyphenoxy)-ethyl-bromide and 17.4 grams (0.2 mol) of n-pentylamine yield by the process described in Example 2, N-[β-(meta-n-butoxyphenoxy)-ethyl]-N-n-pentylamine of the formula

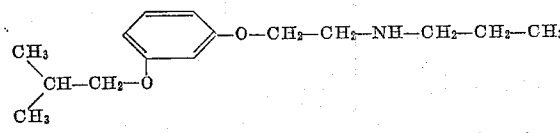


its hydrochloride melts at 142–144° C. after recrystallization from ethyl acetate.

Example 12

12.5 grams (0.046 mol) of β-(meta-isobutoxyphenoxy)-ethyl bromide and 11.8 grams (0.2 mol) of n-propyl-amine yield by the process described in Example 2, N-[β-

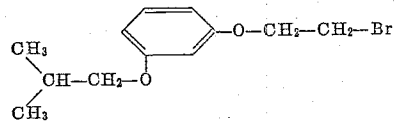
(meta-isobutoxyphenoxy)-ethyl]-N-n-propylamine of the formula



Its hydrochloride is obtained on recrystallization from ethyl acetate-ethanol in colorless needles melting at 138–140° C.

The β(meta-isobutoxyphenoxy)-ethyl bromide used as starting material is prepared as follows:

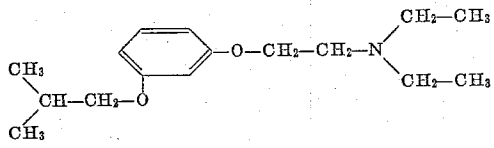
75.0 grams (0.45 mol) of meta-isobutoxyphenol are treated with a solution of 10.4 grams (0.45 mol) of sodium in 400 cc. of ethanol for conversion into the sodium salt which is then converted with 255 grams (1.35 mols) of ethylene bromide, as described in Example 2, into the β-(meta-isobutoxyphenoxy)-ethyl-bromide of the formula



which is obtained in the form of a pale-yellow oil boiling at 82–90° C. under a pressure of 0.06 mm. Hg.

Example 13

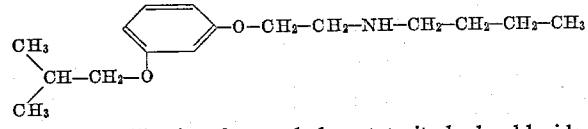
12.5 grams (0.046 mol) of β-(meta-isobutoxyphenoxy)-ethylbromide and 20 cc. of diethylamine yield by the process described in Example 2, N-[β-(meta-isobutoxyphenoxy)-ethyl]-N:N-diethylamine of the formula



Its hydrochloride forms colorless crystals melting at 104–106° C. after having been recrystallized from ethyl acetate.

Example 14

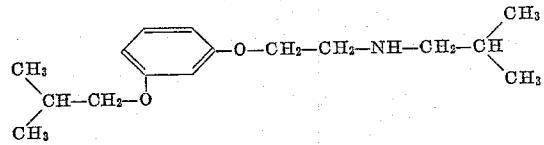
The reaction analogous to that described in Example 2 of 12.5 grams (0.046 mol) of β-(meta-isobutoxyphenoxy)-ethyl-bromide with 20 cc. of n-butyl-amine yields N-[β-(meta-isobutoxyphenoxy)-ethyl]-N-n-butylamine of the formula



On recrystallization from ethyl acetate its hydrochloride melts at 136–138° C.

Example 15

12.5 grams (0.046 mol) of β-(meta-isobutoxyphenoxy)-ethyl-bromide and 20 cc. of isobutylamine yield by the process described in Example 2, N-[β-(meta-isobutoxyphenoxy)-ethyl]-N-isobutylamine of the formula

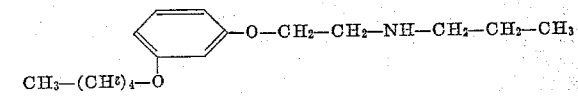


as a brownish oil. On recrystallization from ethyl acetate its hydrochloride forms colorless needles melting at 140–142° C.

Example 16

12.0 grams (0.043 mol) of β-(meta-n-pentyloxyphenoxy)-ethylbromide and 11.8 grams (0.2 mol) of n-propylamine yield by the process described in Example 2, N-

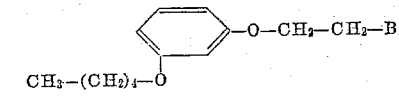
[β-(meta-n-pentyloxyphenoxy)-ethyl]-N-n-propylamine of the formula



as a pale-yellow oil. Its hydrochloride forms on recrystallization from ethanol-ethyl acetate colorless scales melting at 146–147° C.

The β-(meta-n-pentyloxyphenoxy)-ethyl bromide used as starting material can be prepared as follows:

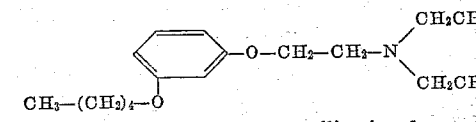
120 grams of meta-n-pentyloxy-phenol are converted with a solution of 15.4 grams (0.67 mol) of sodium in 400 cc. of ethanol into the sodium salt which is then reacted with 376 grams (2.0 mols) of ethylene bromide as described in Example 2. The product, the β-(meta-n-pentyloxyphenoxy)-ethylbromide of the formula



forms a colorless oil boiling at 102–112° C. under a pressure of 0.08 mm. Hg.

Example 17

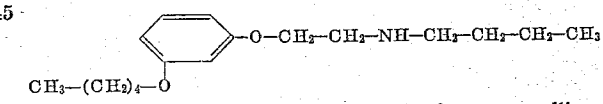
The reaction analogous to that described in Example 2 of 12.0 grams (0.043 mol) of β-(meta-n-pentyloxyphenoxy)ethylbromide with 20 cc of diethylamine yields N-[β - (meta - n - pentyloxyphenoxy)-ethyl]-N:N-diethylamine of the formula



Its hydrochloride forms on recrystallization from ethanol-ethyl acetate colorless hydroscopic crystals melting at 90° C.

Example 18

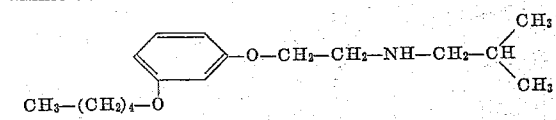
10.0 grams (0.035 mol) of β-(meta-n-pentyloxyphenoxy)-ethylbromide and 14.5 grams (0.2 mol) of n-butylamine yield by the process described in Example 2, N - [β-(meta-n-pentyloxyphenoxy)-ethyl]-N-n-butylamine of the formula



Its hydrochloride melts at 151–153° C. after recrystallization from methanol-ethyl acetate.

Example 19

12.0 grams (0.043 mol) of β-(meta-n-pentyloxyphenoxy)-ethylbromide and 14.6 grams (0.2 mol) of isobutylamine yield by the process described in Example 2, N - [β - (meta-n-pentyloxyphenoxy)-ethyl]-N-isobutylamine of the formula

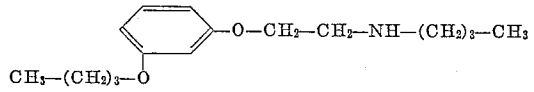


Its hydrochloride forms on recrystallization from ethanol-ethyl acetate colorless crystals melting at 135–136° C.

Example 20

20.0 grams (0.065 mol) of N-[β-(meta-n-butoxyphenoxy)-ethyl]-N-acetyl-N-butylamine boiling at 132–134° C. under 0.04 mm. of pressure which can be obtained, for example, by reacting the sodium salt of resorcinol monobutyl ether with N-(β-chloro-ethyl)-N-acetyl-butylamine in absolute benzene, are boiled under reflux overnight with 30 cc. of methanol and 30 cc. of 2 N-sodium hydroxide solution. After cooling, the mixture is acidified with 100 cc. of 2 N-hydrochloric acid and the neutral products

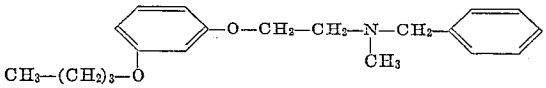
are removed by extraction with ether. The aqueous phase is agitated with active charcoal and, after filtering, rendered alkaline with concentrated ammonia. The precipitating base is taken up in chloroform and, after distilling off the solvent, is distilled in a high vacuum. N-[β-(meta-n-butoxyphenoxy)-ethyl]-N-butylamine of the formula



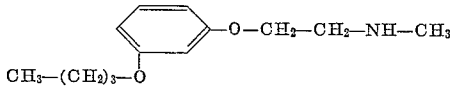
is a colorless oil boiling at 123–126° C. under 0.05 mm. of pressure. Its hydrochloride crystallizes from a mixture of ethanol and ether in the form of colorless crystals melting at 157–158° C. It is identical in every respect with the hydrochloride described in Example 1.

Example 21

27.2 grams (0.10 mol) of β-(meta-n-butoxyphenoxy)-ethyl bromide are dissolved in 30 cc. of ethanol; 12.0 grams (0.10 mol) of N-methyl-benzylamine are added and the whole is heated under reflux for 12 hours. After cooling, 150 cc. of water are added, extraction is carried out with methylene chloride after adding 50 cc. of 2 N-sodium-hydroxide solution, and the extracts are washed neutral with water. After evaporating the solvent, N-[β-(meta - n - butoxy-phenoxy)-ethyl]-N-methyl-N-benzylamine of the formula



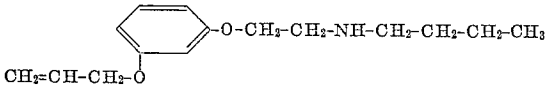
remains as a yellow, highly viscous oil which is debenzylated catalytically. For this purpose the base is dissolved in 200 cc. of ethyl acetate and the solution agitated in the presence of 0.5 gram of palladium charcoal (10% Pd) in a hydrogen atmosphere. After 2.1 liters of hydrogen have been taken up, the absorption of hydrogen ceases. The catalyst is filetered off and the solvent evaporated. The residue is distilled in a high vacuum. N-[β-(meta-n-butoxyphenoxy)-ethyl]-N-methylamine of the formula



is a colorless oil boiling at 110–112° C. under 0.08 mm. of pressure. When recrystallized from a mixture of ethanol and ethyl acetate the hydrochloride forms colorless crystals melting at 138–139° C.

Example 22

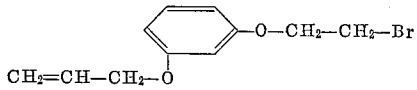
From 16.0 grams (0.062 mol) of β-(meta-allyoxyphenoxy)-ethyl bromide and 30 cc. of n-butylamine there is obtained by the method described in Example 2 N-[β-(meta-allyloxyphenoxy)-ethyl]-N-n-butylamine of the formula



as a colorless oil boiling at 118–125° C. under 0.1 mm. of pressure. Hydrochloride: colorless crystals from ethyl acetate melting at 140–142° C.

The β-(meta-allyloxyphenoxy)-ethyl bromide used as starting material can be obtained as follows:

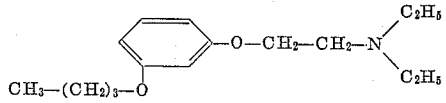
34.6 grams (0.23 mol) of meta-allyloxyphenol are dissolved in 100 cc. of absolute ethanol and by adding 5.4 grams (0.23 mol) of sodium converted into the sodium salt. 130 grams (0.69 mol) of ethylene bromide are introduced and the same procedure followed as described in Example 2. The products, β-(meta-allyloxyphenoxy)-ethyl bromide of the formula



is a yellowish liquid boiling at 102–110° C. under 0.08 mm. of pressure.

Example 23

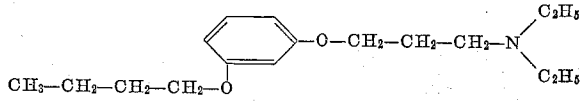
33.2 grams (0.20 mol) of meta-n-butoxyphenol, 41.3 grams (0.24 mol) of β-chloroethyl-diethylamine hydrochloride and 83 grams (0.6 mol) of potassium carbonate are heated at the boil in 400 cc. of acetone for 12 hours with vigorous stirring. The reaction mixture is cooled, the inorganic salts are suction filtered and the filtrate evaporated nearly to dryness. The residue is taken up in chloroform and liberated from the starting phenol by being extracted several times with dilute sodium hydroxide solution. The chloroform solution is then washed several times with water and dried over anhydrous sodium sulfate. After evaporattion the solvent, a dark residue remains which on distillation yields N-[β-(meta-n-butoxyphenoxy)-ethyl]-N:N-diethylamine of the formula



in the form of a pale yellow liquid boiling at 126–134° C. under 0.03 mm. of pressure. Hydrochloride: colorless flakes from ethyl acetate melting at 109–110° C. The hydrochloride is identical with the hydrochloride having the same melting point and described in Example 7.

Example 24

83 grams (0.50 mol) of meta-n-butoxyphenol, 110 grams (0.59 mol) of N-(γ-chloropropyl)-diethylamine hydrochloride and 208 grams (1.50 mols) of anhydrous potassium carbonate are heated under reflux in 800 cc. of acetone for 15 hours with vigorous stirring. After cooling, the inorganic constituents are filtered off, the filtrate evaporated and the residue dissolved in chloroform. In order to remove the starting phenol the reaction solution is extracted several times with dilute sodium hydroxide solution. The chloroform solution is finally washed neutral with water, dried over sodium sulfate and the solvent evaporated. On distillation the residue yields N-[γ - (meta-n-butoxyphenoxy)-propyl]-N:N-diethylamine of the formula

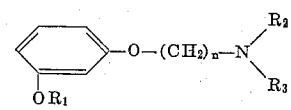


in the form of a yellow oil boiling at 116–120° C. under 0.08 mm. of pressure.

The citrate crystallized from a mixture of ethanol and ethyl acetate in the form of very fine crystals melting at 87–88° C.

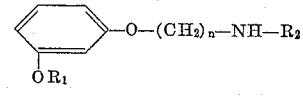
What is claimed is:

1. A member of the group consisting of amines of the formula



in which R_1 stands for a member of the group consisting of alkyl having from 3 to 7 carbon atoms, and alkenyl having from 3 to 7 carbon atoms, R_2 represents a member of the group consisting of alkyl containing 1 to 10 carbon atoms, and alkenyl containing 3 to 10 carbon atoms, R_3 stands for hydrogen, and n means a whole number from 2 to 4, and addition salts of said compounds with therapeutically usable acids.

2. Compounds of the formula

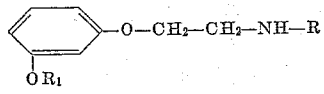


in which R_1 stands for alkyl containing from 3 to 7 car-

bon atoms, R_2 represents alkyl containing from 3 to 6 carbon atoms, and *n* represents a whole number from 2 to 4.

3. Addition salts of the compounds in claim 2 with therapeutically usable acids.

4. Secondary amines of the formula



in which R stands for alkyl containing from 3 to 6 carbon atoms, and R_1 represents alkyl containing from 3 to 7 carbon atoms.

5. Addition salts of the compounds in claim 4 with therapeutically usable acids.

6. N - [β - (meta - n - pentyloxyphenoxy) - ethyl] - N-isobutylamine.

7. Addition salts of the compound in claim 6 with therapeutically usable acids.

8. N - [β - (meta - n - butoxyphenoxy) - ethyl] - N - n-butylamine.

9. Addition salts of the compound in claim 8 with therapeutically usable acids.

10. N - [β - (meta - n - butoxyphenoxy) - ethyl] - N-ethylamine.

11. Addition salts of the compound in claim 10 with therapeutically usable acids.

12. N - [β - (meta - n - butoxyphenoxy) - ethyl] - N-n-propylamine.

13. Addition salts of the compound in claim 12 with therapeutically usable acids.

14. N - [β - (meta - n - butoxyphenoxy) - ethyl] - N-methallylamine.

15. Addition salts of the compound in claim 14 with therapeutically usable acids.

16. N - [β - (meta - n - butoxyphenoxy) - ethyl] - N-isobutylamine.

17. Addition salts of the compound in claim 16 with therapeutically usable acids.

18. N - [β - (meta - isobutoxyphenoxy) - ethyl] - N-n-propylamine.

19. Addition salts of the compound in claim 18 with therapeutically usable acids.

20. N - [β - (meta - n - pentyloxyphenoxy) - ethyl]-N-n-propylamine.

21. Addition salts of the compound in claim 20 with therapeutically usable acids.

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