The following statement is a full description of this invention, including the best method of performing it known to us.

X741-80-ND-25P.C.
The present invention is concerned with 1-[3-(5,6,7,8-tetrahydronaphth-1-yloxy)-propyl]-piperazine derivatives and with the preparation thereof.

The 1-[3-(5,6,7,8-tetrahydronaphth-1-yloxy)-propyl]-piperazine derivatives according to the present invention are compounds of the general formula:

\[
\text{O-CH}_2\text{-CH-CH}_2\text{-N} \text{(CH}_2\text{)}_n\text{-N-(CH}_2\text{)}_n\text{-X}
\]

wherein A is a hydrogen atom or a hydroxyl group, X is a hydrogen or halogen atom or an alkyl, alkoxy, alkylthio, trifluoromethyl, hydroxyl, nitro, amino, acylamino or alkylsulphonylamino radical and \( n \) is 0, 1 or 2, and the pharmacologically compatible salts thereof.

The new compounds according to the present invention possess an outstanding blood pressure-lowering action and thus have anti-hypertensive properties. Furthermore, in rats they inhibit the anaphylactoid reactions released by dextran.

The new compounds according to the present invention can be prepared, for example, by one of the following methods:

a) reaction of a compound of the general formula:
wherein A has the same meaning as above and Y and Z are reactive groups, which can be the same or different, with 5,6,7,8-tetrahydro-1-naphthol and a piperazine of the general formula:

$$\text{HN} \quad \text{N} \quad \text{(III)}$$

wherein X and n have the same meanings as above, optionally with intermediate protection of the group A; or

b) when A is a hydroxyl group, reaction of a compound of the general formula:

$$\text{O-CH}_2\text{-CH}_2\text{-R}_2$$

wherein R₁ is a hydrogen atom and R₂ is a halogen atom or R₁ and R₂ together represent a valency bond, with a piperazine of general formula (III), whereafter, if desired, the residue X is subsequently converted into a different residue X and the compounds obtained are, if desired, converted into pharmacologically compatible salts.

In the case of method a), all 3 components can, if desired, be reacted together simultaneously. Preferably, however, the reaction is carried out in two steps: first, 5,6,7,8-tetrahydro-1-naphthol is reacted with a compound (II) and the condensation product obtained is then condensed with
the compound (III) or the compounds (II) and (III) are first condensed and the product obtained subsequently reacted with 5,6,7,8-tetrahydro-1-naphthol.

These condensation reactions are carried out in the presence of an acid-binding agent, for example of a tertiary amine, such as triethylamine, or of an alkali metal carbonate or bicarbonate, or there is used the sodium or potassium salt of 5,6,7,8-tetrahydro-1-naphthol, which can be obtained in known manner. As solvent, there can be used, for example, a lower ketone, for example methyl ethyl ketone, or a lower alcohol, for example isopropanol, or tetrahydrofuran. When A signifies a hydroxyl group, it is preferable temporarily to block this by a protective group which can easily be split off, for example an acyl radical or a benzyl, triphenyl-methyl or tetrahydropyranyl-(2) radical. These protective groups can subsequently be again removed by acidic or alkaline hydrolysis or hydrogenolytically.

The reactive groups Y and Z in the compounds of general formula (II) are preferably acid residues, for example of hydrohalic or sulphonic acids.

The reaction according to method b) can be carried out by mixing molar amounts of the reaction components and leaving the mixture to stand at ambient temperature; by briefly heating, optionally in a pressure vessel, the reaction can be accelerated and, if desired, a solvent, for example a lower alcohol, can be added thereto.

If desired, the residues X can, after the condensation according to method a) or b), be converted into a different residue X; for example, a nitro group can be reduced to an amino group or an amino group can be acylated.
For the preparation of salts, the compounds (I) according to the present invention are reacted with pharmacologically compatible organic or inorganic acids, for example with hydrochloric acid, sulphuric acid, phosphoric acid, lactic acid, citric acid or an alkyl-sulphonic acid.

For the preparation of pharmaceutical compositions, the compounds (I) are mixed in the usual manner with solid or liquid pharmaceutical diluents or carriers and optionally also with odoriferous, flavouring and colouring materials and then shaped into, for example, tablets or dragees or, by the addition of appropriate adjuvants, suspended or dissolved in water or oil, for example in olive oil.

The following Examples are given for the purpose of illustrating the present invention:-

Example 1

4-(4-Chlorophenyl)-1-[3-(5,6,7,8-tetrahydronaphth-1-yloxy)-prop-1-yl]-piperazine.

53.2 g. (0.385 mole) powdered, dry potassium carbonate are added, with stirring, over the course of 3 hours to a boiling mixture of 51.8 g. (0.35 mole) 5,6,7,8-tetrahydro-1-naphthol, 350 ml. anhydrous methyl ethyl ketone and 212.0 g (1.05 mole) 1,3-dibromopropane. Subsequently, the reaction mixture is boiled under reflux for a further 6 hours, then filtered with suction and the filter cake washed with acetone. The combined organic filtrates are evaporated in a vacuum, the evaporation residue is taken up in chloroform and the chloroform solution is extracted several times with a dilute aqueous solution of sodium hydroxide, then washed neutral with water and dried. The chloroform is evaporated off and the residue, which is an oil of low viscosity, is distilled.
at oil pump vacuum. Between 125 and 135°C./ 0.05 mm. Hg., there are obtained 33.1 g. 1-((5,6,7,8-tetrahydronaphth-1-yloxy)-3-bromopropane. The yield is 35% of theory, which corresponds to a yield of 77.5%, calculated from the amount of reacted tetrahydro-1-naphthol; \( n_D^{20} = 1.5626 \).

A mixture of 8.9 g. (33 mMole) 1-((5,6,7,8-tetrahydronaphth-1-yloxy)-3-bromopropane, 6.5 g. (33 mMole) 1-(4-chlorophenyl)-piperazine, 4.20 g. (50 mMole) sodium bicarbonate and 35 ml. anhydrous alcohol are heated under reflux for 18 hours and the reaction mixture then evaporated in a vacuum. The evaporation residue is stirred with 1N aqueous sodium hydroxide solution and the undissolved material is filtered off with suction, washed with water, dried and recrystallised from alcohol, with the addition of charcoal. There are obtained 7.1 g. (56% of theory) colourless 4-(4-chlorophenyl)-1-[3-(5,6,7,8-tetrahydronaphth-1-yloxy)-prop-1-yl]-piperazine, which has a melting point of 97°C. The dihydrochloride obtained herefrom in the usual manner melts, with decomposition, at 200 - 203°C.

Example 2

4-(2-Chlorophenyl)-1-[3-(5,6,7,8-tetrahydronaphth-1-yloxy)-prop-1-yl]-piperazine

A mixture of 10.7 g. (40 mMole) 1-((5,6,7,8-tetrahydronaphth-1-yloxy)-3-bromopropane (prepared in the manner described in Example 1), 7.9 g. (40 mMole) 2-chlorophenyl-piperazine, 8.1 g. (80 mMole) anhydrous triethylamine and 40 ml. anhydrous tetrahydrofuran is stirred at reflux temperature for 24 hours. After cooling, the reaction mixture is filtered with suction, the precipitate is washed with tetrahydrofuran and the combined filtrates obtained are
evaporated in a vacuum. The evaporation residue is taken up in chloroform, washed twice with 0.5N aqueous sodium hydroxide solution and twice with an aqueous solution of sodium chloride and then dried over anhydrous sodium sulphate. After evaporation in a vacuum, there is obtained a non-crystallising oil which is dissolved in warm isopropanol. After filtering, hydrogen chloride-containing dioxan is added to the filtrate to precipitate out 13.4 g. (80% of theory) 4-(2-chlorophenyl)-1-[3-(5,6,7,8-tetrahydronaphth-1-yloxy)-prop-1-yl]-piperazine hydrochloride, which has a melting point of 228 - 230°C.

The following compounds are obtained in an analogous manner:

4-(2-methylthiophenyl)-1-[3-(5,6,7,8-tetrahydronaphth-1-yloxy)-prop-1-yl]-piperazine from 1-(5,6,7,8-tetrahydronaphth-1-yloxy)-3-bromopropane and 1-(2-methylthiophenyl)-piperazine; yield 64% of theory; m.p. of the hydrochloride 224 - 225°C. (decomp.);

4-(3-trifluoromethylphenyl)-1-[3-(5,6,7,8-tetrahydronaphth-1-yloxy)-prop-1-yl]-piperazine from 1-(5,6,7,8-tetrahydronaphth-1-yloxy)-3-bromopropane and 1-(3-trifluoromethylphenyl)-piperazine; yield 84% of theory; m.p. of the dihydrochloride: 182 - 183°C.

Example 3

4-(2-Methylphenyl)-1-[3-(5,6,7,8-tetrahydronaphth-1-yloxy)-prop-1-yl]-piperazine.

40.4 g. (0.4 mole) triethylamine and 31.5 g. (0.2 mole) 1-chloro-3-bromopropane are added to a solution of 35.3 g. 0.2 mole) 1-(2-methylphenyl)-piperazine in 100 ml. anhydrous tetrahydrofuran and the reaction mixture then...
heated under reflux for 14 hours. After cooling, the reaction mixture is mixed with 10 ml. anhydrous ether, the crystals which separate out are filtered off with suction and the filtrate is evaporated in a vacuum. 46.2 g. of an oily substance remain behind which consists of crude 4-(2-methylphenyl)-1-(3-chloropropyl)-piperazine; the corresponding hydrochloride decomposes between 185 and 210°C.

A mixture of 8.15 g. (55 mMole) 5,6,7,8-tetrahydro-1-naphthol, 7.60 g. (55 mMole) powdered dry potassium carbonate and 100 ml. anhydrous methyl ethyl ketone is heated under reflux for 2 hours and then cooled somewhat. 0.2 g. potassium iodide are added thereto and a solution of 12.64 g. (50 mMole) 4-(2-methylphenyl)-1-(3-chloropropyl)-piperazine in 50 ml. anhydrous methyl ethyl ketone then added dropwise, whereafter the reaction mixture is heated under reflux for a further 16 hours. After filtering with suction, the filter cake obtained is washed with acetone. The combined organic filtrates are evaporated in a vacuum, the oily evaporation residue is taken up in chloroform and the chloroform solution is extracted several times with a dilute aqueous solution of sodium hydroxide and then with distilled water. After drying and evaporating in a vacuum, there is obtained an oily product which is dissolved in ether and treated with dry hydrogen chloride. The precipitated 4-(2-methylphenyl)-1-[3-(5,6,7,8-tetrahydro-naphth-1-yloxy)-prop-1-yl]-piperazine hydrochloride thus obtained is filtered off with suction, washed with some ether and finally with alcohol to which some concentrated hydrochloric acid had been added. The yield is 72% of theory and the product has a melting point of 243-244°C.
The following compounds are obtained in an analogous manner:

1-[3-(5,6,7,8-tetrahydronaphth-1-yl oxy)-propyl]-4-phenyl-piperazine from 5,6,7,8-tetrahydro-1-naphthol and 1-(3-chloropropyl)-4-phenyl-piperazine; yield 72% of theory; m.p. of the dihydrochloride 210 - 211°C (decomp.);

1-[3-(5,6,7,8-tetrahydronaphth-1-yl oxy)-propyl]-4-(2-methoxy-phenyl)-piperazine from 5,6,7,8-tetrahydro-1-naphthol and 1-(3-chloropropyl)-4-(2-methoxyphenyl)-piperazine; yield 48% of theory; m.p. of the dihydrochloride 202 - 203°C (decomp.).

Example 4

1-[3-(5,6,7,8- tetrahydronaphth-1-yl oxy)-2-hydroxyprop-1-yl]-4-(2-methoxyphenyl)-piperazine

A mixture of 11.24 g. (55 mMole) 1-(5,6,7,8-tetrahydronaphth-1-yl oxy)-2,3-epoxypropene and 9.62 g. (50 mMole) 1-(2-methoxyphenyl)-piperazine is stirred for 5 hours in an oil bath at a bath temperature of 120°C. Subsequently, the reaction mixture is dissolved in 350 ml. hot isopropanol, cooled and the precipitated crystals filtered off with suction. After repeated recrystallisation from isopropanol, there are obtained 12.8 g. (64% of theory) pure 1-[3-(5,6,7,8-tetrahydronaphth-1-yl oxy)-2-hydroxyprop-1-yl]-4-(2-methoxyphenyl)-piperazine, which has a melting point of 123 - 124°C. The dihydrochloride melts, with decomposition, at 212 - 213°C.

The epoxide used as starting material is prepared in the following manner:

A solution of 10.0 g. (0.25 mole) sodium hydroxide in 34 ml. water is added dropwise to a mixture, heated to
72°C., of 37.1 g. (0.25 mole) 5,6,7,8-tetrahydro-1-naphthol and 46.2 g. (0.5 mole) epichlorhydrin, the temperature being maintained between 72 and 75°C. by occasional cooling. Subsequently, the reaction mixture is maintained for 2.5 hours at 75°C. After cooling and the addition of 50 ml. water, it is extracted several times with chloroform and the combined chloroform extracts are washed with distilled water, dried over anhydrous sodium sulphate and then freed from chloroform in a vacuum. The oily residue obtained is distilled. Between 124 and 128°C./0.3 mm.Hg., there are obtained 40.4 g. (79% of theory) 1-(5,6,7,8-tetrahydronaphth-1-yloxy)-2,3-epoxypropane.

The following compounds are obtained in an analogous manner:

1-[3-(5,6,7,8-tetrahydronaphth-1-yloxy)-2-hydroxyprop-1-yl]-4-phenyl-piperazine from 1-(5,6,7,8-tetrahydronaphth-1-yloxy)-2,3-epoxypropane and 1-phenyl-piperazine; yield 68% of theory; m.p. of the dihydrochloride 213 - 214°C. (decomp.).

1-[3-(5,6,7,8-tetrahydronaphth-1-yloxy)-2-hydroxyprop-1-yl]-4-(2-methylphenyl)-piperazine from 1-(5,6,7,8-tetrahydronaphth-1-yloxy)-2,3-epoxypropane and 1-(2-methyl-phenyl)-piperazine; yield 73% of theory; m.p. of the dihydrochloride 202 - 2-4°C.;

1-[3-(5,6,7,8-tetrahydronaphth-1-yloxy)-2-hydroxyprop-1-yl]-4-(2-chlorophenyl)-piperazine from 1-(5,6,7,8-tetrahydronaphth-1-yloxy)-2,3-epoxypropane and 1-(2-chlorophenyl)-piperazine; yield 87% of theory; m.p. 90 - 91°C. (recrystallised from isopropanol); m.p. of the hydrochloride 132 - 133°C.;

1-[3-(5,6,7,8-tetrahydronaphth-1-yloxy)-2-hydroxyprop-1-yl]-
4-(3-methoxyphenyl)-piperazine from 1-(5,6,7,8-tetrahydro-naphth-1-yloxy)-2,3-epoxypropane and 1-(3-methoxyphenyl)-piperazine; yield 76% of theory; m.p. of the dihydrochloride 208° C. (decomp.);

1-[3-(5,6,7,8-tetrahydronaphth-1-yloxy)]-4-(4-methoxyphenyl)-piperazine from 1-(5,6,7,8-tetrahydronaphth-1-yloxy)-2,3-epoxypropane and 1-(4-methoxyphenyl)-piperazine; yield 72% of theory; m.p. 83 - 84° C. (re-crystallised from isopropanol); m.p. of the dihydrochloride 230 - 231° C. (decomp.).

Example 5

1-[3-(5,6,7,8-tetrahydronaphth-1-yloxy)]-2-hydroxyprop-1-yl-4-(2-methylthio)phenyl)piperazine.

A mixture of 10.2 g. (50 mMole) 1-(5,6,7,8-tetrahydronaphth-1-yloxy)-2,3-epoxypropane and 10.4 g. (50 mMole) 1-(2-methylthiophenyl)-piperazine is left to stand for 24 hours in a closed vessel and then brought to crystallisation by the addition of ligroin. After filtering off with suction, there are obtained 19.8 g. (96% of theory) 1-[3-(5,6,7,8-tetrahydronaphth-1-yloxy)]-4-(2-methylthiophenyl)-piperazine which is recrystallised from 300 ml. of a mixture of ligroin and ethyl acetate (4:6 v/v). The yield is 15.6 g. (76% of theory); m.p. 120 - 121° C.

The following compounds are obtained in an analogous manner:

1-[3-(5,6,7,8-tetrahydronaphth-1-yloxy)]-2-hydroxyprop-1-yl]-4-(3-trifluoromethylphenyl)-piperazine from 1-(5,6,7,8-tetrahydronaphth-1-yloxy)-2,3-epoxypropane and 1-(3-trifluoromethylphenyl)-piperazine; yield 74% of theory; m.p. 104 -
105°C. (recrystallised from ligroin and ethyl acetate (8:2 v/v);
1-[3-(5,6,7,8-tetrahydronaphth-1-yloxy)-2-hydroxyprop-1-yl]-4-(4-chlorophenyl)-piperazine from 1-(5,6,7,8-tetrahydronaphth-1-yloxy)-2,3-epoxypropane and 1-(4-chlorophenyl)-piperazine; yield 67% of theory; m.p. 94°C. (recrystallised from ethyl acetate and ligroin (2:8 v/v);
1-[3-(5,6,7,8-tetrahydronaphth-1-yloxy)-2-hydroxyprop-1-yl]-4-benzyl-piperazine from 1-(5,6,7,8-tetrahydronaphth-1-yloxy)-2,3-epoxypropane and 1-benzyl-piperazine; yield 64% of theory; m.p. of the hydrochloride 236 - 237°C.
Example 6
1-[3-(5,6,7,8-Tetrahydronaphth-1-yloxy)-prop-1-yl]-4-(2-nitrophenyl)-piperazine.
A mixture of 75.0 g. (0.29 mole) 1-(5,6,7,8-tetrahydronaphth-1-yloxy)-3-bromopropene (prepared in the manner described in Example 1), 60.0 g. (0.29 mole) 1-(o-nitrophenyl)-piperazine, 59 g. (0.58 mole) anhydrous triethylamine and 250 ml. anhydrous tetrahydrofuran is stirred for 28 hours under reflux, then cooled and the precipitated triethylamine hydrobromide is filtered off with suction. The filtrate is evaporated in a vacuum, a viscous, deep red oil remaining behind. For purification, this crude product is dissolved in dioxan, converted into the hydrochloride by passing in gaseous hydrogen chloride and the hydrochloride thus obtained is recrystallised from ethanol. In this manner, there is obtained 1-[3-(5,6,7,8-tetrahydronaphth-1-yloxy)-prop-1-yl]-4-(2-nitrophenyl)-piperazine hydrochloride in a yield of 73% of theory; m.p. 214 - 215°C.
Example 7

1-\((5,6,7,8\text{-tetrahydronaphth-1-yloxy})\text{-prop-1-yl}\)-4-(2-aminophenyl)-piperazine.

22.7 g. (57.5 mMole) 1-\([3-(5,6,7,8\text{-tetrahydronaphth-1-yloxy})\text{-prop-1-yl}]\)-4-(2-nitrophenyl)-piperazine (obtained by the liberation of the base from the hydrochloride obtained according to Example 6 by means of a concentrated aqueous solution of sodium hydroxide) are dissolved in 150 ml. anhydrous tetrahydrofuran, about 20 g. Raney nickel are added thereto, followed by hydrogenation at atmospheric pressure on a shaking device until the theoretical amount of hydrogen has been taken up. After filtering off the catalyst, the filtrate obtained is freed from tetrahydrofuran in a vacuum and the oily residue converted into the hydrochloride by treatment with gaseous hydrogen chloride. In this manner, there is obtained 1-\([3-(5,6,7,8\text{-tetrahydronaphth-1-yloxy})\text{-prop-1-yl}]\)-4-(2-aminophenyl)-piperazine dihydrochloride in a yield of 20.4 g. (89% of theory); m.p. 256 - 258°C.

Example 8

1-\([3-(5,6,7,8\text{-Tetrahydronaphth-1-yloxy})\text{-prop-1-yl}]\)-4-(2-acetaminophenyl)-piperazine.

6.1 g. (60 mMole) acetic anhydride are added, with stirring, to a solution of 18.3 g. (50 mMole) 1-\([3-(5,6,7,8\text{-tetrahydronaphth-1-yloxy})\text{-prop-1-yl}]\)-4-(aminophenyl)-piperazine (obtained by liberation of the base from the dihydrochloride prepared according to Example 7 by means of a concentrated aqueous solution of sodium hydroxide) in 100 ml. anhydrous pyridine, whereafter the reaction mixture is heated for 1 hour on a steambath. Thereafter, the reaction
mixture is substantially evaporated in a vacuum, some water is added to the evaporation residue and then it is left to stand for 1 hour at 30 - 35°C. Subsequently, the reaction mixture is extracted several times with ether, the combined ethereal phases are dried over anhydrous sodium sulphate and the ether is finally distilled off. The oily evaporation residue is brought to crystallisation by stirring with a very small amount of ether. There are obtained 16.4 g. (80% of theory) 1-(3-(5,6,7,8-tetrahydronaphth-1-yloxy)-prop-1-yl)-4-(2-acetaminophenyl)-piperazine, which has a melting point of 100 - 101°C.

Example 9

1-[3-(5,6,7,8-Tetrahydronaphth-1-yloxy)-2-hydroxy-prop-1-yl]-4-(2-nitrophenyl)-piperazine.

54.4 g. (268 mMole) 1-(5,6,7,8-tetrahydronaphth-1-yloxy)-2,3-epoxypropane (prepared in the manner described in Example 4) are mixed with 55.5 g. (268 mMole) 1-(o-nitrophenyl)-piperazine and left to stand in a closed vessel for a day. The product is brought to crystallisation by the addition of some isopropanol. After recrystallisation from 500 ml. isopropanol, there are obtained 88.9 g. (81% of theory) pure 1-[3-(5,6,7,8-tetrahydronaphth-1-yloxy)-2-hydroxyprop-1-yl]-4-(2-nitrophenyl)-piperazine, which has a melting point of 88 - 89°C. The hydrochloride thereof, prepared in the usual manner, has a melting point of 186 - 187°C.

Example 10.

1-[3-(5,6,7,8-Tetrahydronaphth-1-yloxy)-2-hydroxy-prop-1-yl]-4-(2-aminophenyl)-piperazine.

20.6 g. (50 mMole) 1-[3-(5,6,7,8-,tetrahydronaphth-
l-yloxy)-2-hydroxy-prop-1-yl]-4-(2-nitrophenyl)-piperazine (prepared in the manner described in Example 9) are hydrogenated in tetrahydrofuran, in the presence of Raney nickel in a manner analogous to that described in Example 7. There are thus obtained 19.4 g. (85% of theory) 1-[3-(5,6,7,8-tetrahydronaphth-1-yloxy)-2-hydroxy-prop-1-yl]-4-(2-aminophenyl)-piperazine, which has a melting point of 268 - 271°C. The free base obtained herefrom in the usual manner melts at 103 - 104°C.

Example 11.

1-[3-(5,6,7,8-Tetrahydronaphth-1-yloxy)-2-hydroxy-prop-1-yl]-4-(2-acetaminophenyl)-piperazine.

9.5 g. (25 mMole) 1-[3-(5,6,7,8-tetrahydronaphth-1-yloxy)-2-hydroxy-prop-1-yl]-4-(2-aminophenyl)-piperazine (prepared in the manner described in Example 10) in 50 ml. anhydrous pyridine are acetylated by the addition of 5.1 g. (50 mMole) acetic anhydride and, after treatment with hydrogen chloride, there are obtained 11.6 g. (93% of theory) of a very deliquescent product which commences to decompose at 70°C. A solution of 11 g. of this hydrochloride in 100 ml. methanol is mixed dropwise with 30 ml. 2N aqueous potassium hydroxide solution, the temperature being kept at 20°C. After leaving to stand overnight, the methanol is distilled off in a vacuum. The residue is mixed with some water, dilute hydrochloric acid is added thereto until the pH is 5 and the oily phase is taken up in isopropanol. By the addition of hydrogen chloride-containing ether, 1-[3-(5,6,7,8-tetrahydronaphth-1-yloxy)-2-hydroxyprop-1-yl]-4-(2-acetaminophenyl)-piperazine dihydrochloride precipitates out; the yield is 76% of theory; m.p. 179-183°C. (decomp.).
The claims defining the invention are as follows:

1. 1-[(3-(5,6,7,8-Tetrahydroanaphth-1-yloxy)-propyl]-piperazine derivatives of the general formula:

   \[
   O-CH_2-CH-CH_2-N\bigg(\bigg(CH_2\bigg)^n\bigg)\bigg(\bigg(CH_2\bigg)^n\bigg)N-CH(X)A
   \]

   wherein A is a hydrogen atom or a hydroxyl group, X is a hydrogen or halogen atom or alkyl, alkoxy, alkylthio, trifluoromethyl, hydroxy, nitro, amino, acylamino or alklyloxynaphthyl amino radical and n is 0, 1 or 2; and the pharmacologically compatible salts thereof.

2. A compound selected from the group comprising:

   4-(4-Chlorophenyl)-1-[(3-(5,6,7,8-tetrahydroanaphth-1-yloxy)-propyl]-piperazine,
   4-(2-Chlorophenyl)-1-[(3-(5,6,7,8-tetrahydroanaphth-1-yloxy)-propyl]-piperazine,
   4-(2-Methylthiophenyl)-1-[(3-(5,6,7,8-tetrahydroanaphth-1-yloxy)-propyl]-piperazine,
   4-(3-Trifluoromethylphenyl)-1-[(3-(5,6,7,8-tetrahydroanaphth-1-yloxy)-propyl]-piperazine,
   4-(2-Methylphenyl)-1-[(3-(5,6,7,8-tetrahydroanaphth-1-yloxy)-propyl]-piperazine,
   1-[(3-(5,6,7,8-Tetrahydroanaphth-1-yloxy)-propyl]-4-phenyl-piperazine,
   1-[(3-(5,6,7,8-Tetrahydroanaphth-1-yloxy)-propyl]-4-
(2-methoxyphenyl)-piperazine,

1-[[3-(5,6,7,8-Tetrahydrophenanthryloxy)prop-1-yl]4-(2-methoxyphenyl)-piperazine,

1-[[3-(5,6,7,8-Tetrahydrophenanthryloxy)prop-1-yl]4-phenyl-piperazine,

1-[[3-(5,6,7,8-Tetrahydrophenanthryloxy)prop-1-yl]4-(2-methylphenyl)-piperazine,

1-[[3-(5,6,7,8-Tetrahydrophenanthryloxy)prop-1-yl]4-(2-chlorophenyl)-piperazine,

1-[[3-(5,6,7,8-Tetrahydrophenanthryloxy)prop-1-yl]4-(3-methoxyphenyl)-piperazine,

1-[[3-(5,6,7,8-Tetrahydrophenanthryloxy)prop-1-yl]4-(4-methoxyphenyl)-piperazine,

1-[[3-(5,6,7,8-Tetrahydrophenanthryloxy)prop-1-yl]4-(2-methylthiophenyl)-piperazine,

1-[[3-(5,6,7,8-Tetrahydrophenanthryloxy)prop-1-yl]4-(3-trifluoromethyphenyl)-piperazine,

1-[[3-(5,6,7,8-Tetrahydrophenanthryloxy)prop-1-yl]4-(4-chlorophenyl)-piperazine,

1-[[3-(5,6,7,8-Tetrahydrophenanthryloxy)prop-1-yl]4-benzyl-piperazine,

1-[[3-(5,6,7,8-Tetrahydrophenanthryloxy)prop-1-yl]4-(2-nitrophenyl)-piperazine,

1-[[3-(5,6,7,8-Tetrahydrophenanthryloxy)prop-1-yl]4-(2-aminophenyl)-piperazine,

1-[[3-(5,6,7,8-Tetrahydrophenanthryloxy)prop-1-yl]4-(2-acetaminophenyl)-piperazine,

1-[[3-(5,6,7,8-Tetrahydrophenanthryloxy)prop-1-yl]4-(2-nitrophenyl)-piperazine,
3. Process for the preparation of compounds of the general formula given in Claim 1, wherein a compound of the general formula:

\[ Y-\text{CH}_2-\text{CH}-\text{CH}_2-Z \]

in which \( A \) has the same meaning as in Claim 1 and \( Y \) and \( Z \), which may be the same or different, are reactive groups, is reacted with 5,6,7,8-tetrahydro-1-naphthol and with a piperazine of the general formula:

\[
\begin{array}{c}
\text{HN} \\
\text{N-(CH}_2)^n \\
\text{X}
\end{array}
\]

in which \( X \) and \( n \) have the same meaning as in Claim 1, optionally with temporary protection of the group \( A \).

4. Process for the preparation of compounds of the general formula given in Claim 1, in which \( A \) is a hydroxyl group, wherein a compound of the general formula:

\[
\begin{array}{c}
\text{O-CH}_2-\text{CH}-\text{CH}_2-R_2 \\
\text{OR}_1
\end{array}
\]
in which $R_1$ is a hydrogen atom and $R_2$ is a halogen atom
or in which $R_1$ and $R_2$ together represent a valency bond,
is reacted with a piperazine of the general formula given
in Claim 3.

5. Process according to Claim 3 or 4, wherein the
substituent $X$ in the product obtained is subsequently
converted into a different substituent $X$.

6. Process according to any of Claims 3 to 5, wherein
the product obtained is reacted with a pharmacologically
compatible inorganic or organic acid to give the
 corresponding salt.

7. Process for the preparation of compounds according
to Claim 1, substantially as hereinbefore described and
exemplified.

8. Pharmaceutical compositions, comprising at least
one compound according to Claim 1, in admixture with a solid
or liquid pharmaceutical diluent or carrier.

Dated this 7th day of January, 1974.

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By its Patent Attorneys
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