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NO DRAWINGS

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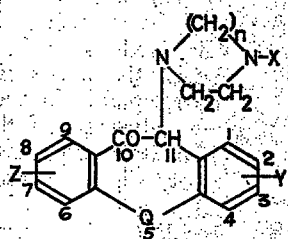
COMPLETE SPECIFICATION

New Thiepin and Oxepin Derivatives, their Production and Use

We, J. R. GEIGY A.G., a body corporate organised according to the laws of Switzerland, of 215, Schwarzwaldallee, Basle Switzerland, 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 concerns new thiepin and oxepin derivatives, their addition salts with inorganic and organic acids, processes for the production thereof, medicaments which contain the new compounds and their use as medicaments.

Compounds of general formula I (numbering according to Chemical abstracts)



(I)

wherein Q represents an oxygen or sulphur atom;

X represents hydrogen, an alkyl or hydroxyalkyl group having at most 4 carbon atoms in the alkyl moieties, or an alkanoyloxyalkyl group having, in all, at most 8 carbon atoms;

Y and Z each represent a hydrogen atom, a halogen atom up to the atomic

number 35, or alkyl or alkoxy groups having at most 4 carbon atoms in the alkyl moieties; and n represents 2 or 3;

have not been known hitherto.

It has now been found that such compounds and their salts with inorganic or organic acids have valuable central depressant properties. They potentiate the action of anaesthetics and have a catatonic, sedative, relaxing and anti-convulsive action which characterises the compounds as tranquilisers (neuroleptics) for use for the treatment of mental disorders as well as of states of anxiety and tension. In addition to the central properties, the compounds also have peripheral pharmacological properties such as antihistaminic and musculotropic spasmolytic action.

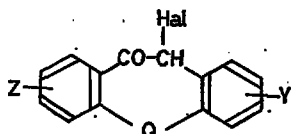
In the compounds of general formula I, X as an alkyl group can be the methyl, ethyl, propyl, isopropyl, butyl, isobutyl or the sec. butyl group; as an hydroxyalkyl group it can be the 2 - hydroxyethyl, 3 - hydroxypropyl or the 2 - methyl - 3 - hydroxypropyl group, and as an alkanoyloxyalkyl group it can be the 2 - acetoxyethyl, 2 - propionyloxyethyl, 3 - acetoxypropyl, 2 - methyl - 3 - acetoxypropyl, 3 - propionyloxypropyl, 2 - methyl - 3 - propionyloxypropyl, 2 - pivaloyloxyethyl or the 3 - pivaloyloxypropyl group.

Y and Z can be both identical or different and, as substituents of the benzene rings, can be in the 1-, 2-, 3- or 4-position or in the 6-, 7-, 8- or 9-position, the 2- and 8-positions being preferred; as alkyl radicals they represent, e.g., the methyl, ethyl

[Price 4s. 6d.]

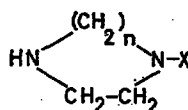
propyl, isopropyl, butyl or isobutyl group and, as alkoxy radicals they represent, e.g., the methoxy, ethoxy, propoxy, isopropoxy, butoxy or the isobutoxy group.

- 5 The new compounds of general formula I are produced by reacting a compound of general formula II



(II)

- 10 wherein Hal represents a halogen atom, especially a chlorine or bromine atom, and
Q, Y and Z have the meanings given in formula I,
with a compound of general formula III



(III)

- 15 wherein X and n have the meanings given in formula I, the reaction being performed in the presence of a basic condensing agent, preferably in a solvent or diluent, if desired, treating a compound of general formula I in which X represents hydrogen with an alkylene oxide having at most 4 carbon atoms, a reactive monoester of an alkane diol having at most 4 carbon atoms in the alkyl moiety, a reactive ester of an alkanoyloxy-
20 alkanol having, in all, at most 8 carbon atoms, or with a reactive ester of an alkanol having at most 4 carbon atoms in the alkyl moiety, e.g., methanol, and, if desired, converting a compound of general formula I into an addition salt with an inorganic or organic acid.

- 25 Suitable solvents or diluents are hydrocarbons such as benzene, toluene or xylene, alkanols such as methanol or ethanol, or an alkanolic acid amide such as dimethyl formamide. The reaction can be performed at a temperature of about 60—200°C; sometimes it is to be performed in a closed vessel depending on the boiling point of the solvent
40 and on the reaction temperature necessary. It is of advantage to use excess amine of the general formula III or a tertiary organic base such as pyridine, lutidine, collidine, quinoline or quinaldine as acid binding agent. Such
45 bases, used in excess, can also serve as solvents. Also, alkali or alkaline earth carbon-

ates such as sodium carbonate or calcium carbonate are suitable as acid binding agents; these are preferably used in acetone or in an aqueous alkanol such as ethanol.

In order to introduce an hydroxyalkyl, alkanoyloxyalkyl group or alkyl group into the 4-position of the piperazine or hexahydro-1H - 1,4 - diazepine group of compounds of general formula I in which X represents hydrogen, such compounds are reacted, e.g., with β - bromoethanol, β - p - toluene sulphonyloxy ethanol, β - bromoethyl acetate or methyl or ethyl bromide in the presence of a suitable acid binding agent such as potassium or sodium carbonate in an organic solvent such as benzene, toluene, acetone or butanone, or with an alkylene oxide such as ethylene oxide or propylene oxide, in an inert organic solvent.

The starting materials of the general formula II are obtained, e.g., by starting from the known dibenzo[b,f]thiepin - 10(11H)-one or derivatives substituted in the benzene nuclei which are produced analogously and reacting these, preferably in a solvent or diluent such as carbon disulphide, with a halogen, especially with bromine or chlorine.

The compounds of general formula I obtained according to the process of the invention are then converted in the usual way, of desired, into their addition salts with inorganic or organic acids. For example, the acid desired as salt component or a solution thereof, is added to a solution of a compound of general formula I in an organic solvent. Preferably organic solvents are chosen for the reaction in which the salt formed dissolves with difficulty so that it can be isolated by filtration. Such solvents are, e.g., methanol, methanol/ether and ethanol/ether.

Instead of the free bases, non-toxic acid addition salts can be used as medicaments, i.e. salts with those acids the anions of which are pharmaceutically acceptable in the usual dosages. Also, it is of advantage if the salts to be used as medicaments crystallise well and are not or are only slightly hygroscopic. For salt formation with compounds of general formula I, e.g., hydrochloric acid, hydrobromic acid, sulphuric acid, phosphoric acid, methane sulphonc acid, ethane sulphonc acid, β -hydroxyethane sulphonc acid, acetic acid, malic acid, tartaric acid, citric acid, lactic acid, oxalic acid, succinic acid, fumaric acid, maleic acid, benzoic acid, salicylic acid, phenylacetic acid, mandelic acid and embonic acid, can be used.

As mentioned above, the new active substances can be administered orally, rectally or parenterally. The daily dosages of the free bases or of non-toxic acid addition salts thereof vary between 10 and 800 mg for adult patients. Suitable dosage units such as dragees (sugar coated tablets), tablets, suppositories or ampoules preferably contain 5—

50 mg of an active substance according to the invention or of a non-toxic acid addition salt thereof. Also, corresponding amounts of forms for administration not made up into single dosages can be used.

Dosage units for oral administration preferably contain between 1—90% of a compound of general formula I or a non-toxic acid addition salt thereof as active substance.

- 10 They are produced, e.g., by combining the active substance with solid, pulverulent carriers such as lactose, saccharose, sorbitol, mannitol; starches such as potato starch, maize starch or amylopectin, also laminaria powder or citrus pulp powder; cellulose derivatives or gelatine, optionally with the addition of lubricants such as magnesium or calcium stearate or polyethylene glycols (Carbowaxes) of suitable molecular weights, to form tablets or dragee cores. The latter are coated, e.g. with concentrated sugar solutions which can also contain, e.g., gum arabic, talcum and/or titanium dioxide, or with a lacquer dissolved in easily volatile organic solvents or mixtures of solvents. Dyestuffs can be added to these coatings, e.g., to distinguish between varying dosages of active substance.

- 20 Dosage units for rectal administration are, e.g., suppositories which consist of a combination of an active substance or a suitable acid addition salt thereof with a neutral fatty foundation, or also gelatine rectal capsules which contain a combination of the active substance or a suitable acid addition salt thereof with polyethylene glycols (Carbowaxes) of suitable molecular weight.

- 25 Ampoules for parenteral, particularly intramuscular, administration preferably contain a water soluble acid addition salt of an active substance in a concentration of, preferably, 0.5—5%, in aqueous solution, optionally together with suitable stabilisers and buffer substances.

- 30 The following prescriptions further illustrate the production of tablets and dragees:

- 35 a) 250 g of 11 - (4 - methyl - 1 - piperazinyl) - dibenzo[b,f]thiepin - 10(11H) - one are mixed with 175.80 g of lactose and 169.70 g of potato starch, the mixture is moistened with an alcoholic solution of 10 g of stearic acid and granulated through a sieve. After drying, 160 g of potato starch, 200 g of talcum, 2.50 g of magnesium stearate and 32 g of colloidal silicon dioxide are mixed in and the mixture is pressed into 10,000 tablets each weighing 100 mg and containing 25 mg of active substance. If desired, the tablets can be grooved for better adaptation of the dosage.

- 40 b) A granulate is produced from 250 g of 11 - [4 - (2 - hydroxy - ethyl) - 1 - piperazinyl] - dibenzo[b,f]thiepin - 10(11H) - one dihydrochloride, 175.90 g of lactose and an alcoholic solution of 10 g of stearic acid. After drying, the granulate is mixed with

56.60 g of colloidal silicon dioxide, 165 g of talcum, 20 g of potato starch and 2.50 g of magnesium stearate and the mixture pressed into 10,000 dragee cores. These are then coated with a concentrated syrup from 502.28 g of crystallised saccharose, 6 g of shellac, 10 g of gum arabic, 0.22 g of dyestuff and 1.5 g of titanium dioxide and dried. The dragees obtained each weigh 120 mg and contain 25 mg of active substance.

The following examples illustrate the production of the new compounds of general formula I and of hitherto undescribed intermediate products, but in no way limit the scope of the invention. The temperatures are given in degrees Centigrade.

EXAMPLE 1

a) 45 g of dibenzo[b,f]thiepin - 10(11H) - one are dissolved in 250 ml of carbon disulphide and 9.6 ml of bromine in 50 ml of carbon disulphide are added dropwise to the solution at 0 to 5° while stirring. The brown reaction mixture, which is stirred for another hour, loses its colour. It is then evaporated in vacuo, the residue is recrystallised from ethanol and 11 - bromo - dibenzo[b,f]thiepin - 10(11H) - one is obtained, M.P. 105—106°.

b) A solution of 30.5 g of the bromoketone prepared according to a) and a solution of 20 ml of 4-methylpiperazine in 20 ml of dimethyl formamide are heated for half an hour at 100° and then poured into a large quantity of water. The reaction mixture is made alkaline with concentrated sodium hydroxide solution and extracted with diethyl ether. The basic parts are removed from the ethereal extract with 2N hydrochloric acid. The acid solution is made alkaline with concentrated sodium hydroxide solution and the free bases are extracted with diethyl ether. The ethereal solution is washed with water, dried over sodium sulphate and concentrated in vacuo. The residue is distilled under high vacuum at 197°/0.02 Torr and the distillate is fractionally crystallised from ethanol. A first fraction from 80 ml of ethanol, which melts at 210°, consists of a by product. After concentrating the mother liquor, 11 - (4 - methyl - 1 - piperazinyl) - dibenzo[b,f]thiepin - 10(11H) - one is obtained which, after recrystallisation from benzene, melts at 101.5°.

EXAMPLE 2

30 g of the bromoketone obtained according to Example 1a) and 35 g of 2 - (1 - piperazinyl)ethanol are heated at 160—170° for 20 hours. After cooling to room temperature, the reaction solution is extracted with ether. The ether extract is washed with water, dried over sodium sulphate, evaporated and ethanolic hydrochloric acid is added to the residue. The 11 - [4 - (2 - hydroxyethyl) -

1 - piperazinyl] - dibenzo[b,f]thiopin - 10(11H) - one dihydrochloride obtained is recrystallised from ethanol; it melts at 174—175°.

EXAMPLE 3

Starting from one of the 11 - bromo - dibenzo[b,f]thiopin - 10(11H) - ones given below under a) to d) and reacting this bromo-keto-compound according to the procedure of Example 1b) with 4 - methyl - piperazine, the final compounds also given below are obtained:

a) with 11 - bromo - 2 - chlorodibenzo[b,f]thiopin - 10(11H) - one, 2 - chloro - 11 - (4 - methyl - 1 - piperazinyl) - dibenzo[b,f]thiopin - 10(11H) - one, M.P. 167—170° (from ethanol),

b) with 11 - bromo - 3 - chlorodibenzo[b,f]thiopin - 10(11H) - one, 3 - chloro - 11 - (4 - methyl - 1 - piperazinyl) - dibenzo[b,f]thiopin - 10(11H) - one, M.P. 136—139° (from benzene),

c) with 11 - bromo - 8 - chlorodibenzo[b,f]thiopin - 10(11H) - one, 8 - chloro - 11 - (4 - methyl - 1 - piperazinyl) - dibenzo[b,f]thiopin - 10(11H) - one, M.P. 153—157° (from acetonitrile), with decomposition, and

d) with 11 - bromo - 2 - methoxydibenzo[b,f]thiopin - 10(11H) - one, 2 - methoxy - 11 - (4 - methyl - 1 - piperazinyl) - dibenzo[b,f]thiopin - 10(11H) - one, M.P. 122—124.5° (from nitromethane).

EXAMPLE 4

Starting from one of the 11 - bromo - dibenzo[b,f]thiopin - 10(11H) - ones given below under a) to d) and reacting this bromo-keto-compound according to the procedure of Example 2 with 2 - (1 - piperazinyl)ethanol, the final compounds also given below are obtained:

a) with 11 - bromo - 2 - chloro - dibenzo[b,f]thiopin - 10(11H) - one, 2 - chloro - 11 - [4 - (2 - hydroxyethyl) - 1 - piperazinyl] dibenzo[b,f]thiopin - 10(11H) - one, M.P. 195—197° (hydrochloride),

b) with 11 - bromo - 3 - chloro - dibenzo[b,f]thiopin - 10(11H) - one, 3 - chloro - 11 - [4 - (2 - hydroxyethyl) - 1 - piperazinyl]dibenzo[b,f]thiopin - 10(11H) - one, M.P. (base) 147—151° (from cyclohexane/benzol),

c) with 11 - bromo - 8 - chloro - dibenzo[b,f]thiopin - 10(11H) - one, 8 - chloro - 11 - [4 - (2 - hydroxyethyl) - 1 - piperazinyl] dibenzo[b,f]thiopin - 10(11H) - one, M.P. (base) 144—148° (from acetonitrile) and

d) with 11 - bromo - 2 - methoxy - dibenzo[b,f]thiopin - 10(11H) - one, 2 - methoxy - 11 - [4 - (2 - hydroxyethyl) - 1 - piperazinyl]dibenzo[b,f]thiopin - 10(11H) - one, M.P. (base) 140—143° (from nitromethane).

EXAMPLE 5

a) A solution of 29 g of 11 - bromo -

dibenz[b,f]oxepin - 10(11H) - one in 200 ml of abs. benzene is added dropwise within half an hour to a stirred solution of 22 g of 4-methyl piperazine in 80 ml of abs. benzene and the mixture is stirred for 20 hours at 50—55°. The reaction solution is then washed with 500 ml of water and the organic phase is extracted with 2N hydrochloric acid. The acid extract is made alkaline with concentrated sodium hydroxide solution and the precipitated base is extracted with ether. The ether extract is washed with water, dried over sodium hydroxide and evaporated in vacuo. The residue is taken up in dry acetone and abs. ethanolic hydrochloric acid is added until it has a reaction acid to congo paper. The precipitated 11 - (4 - methyl - 1 - piperazinyl) - dibenz[b,f]oxepin - 10(11H) - one dihydrochloric dihydrate is filtered off under suction, washed with dry acetone and recrystallised from abs. ethanol; it melts at 177—198° with decomposition.

The starting material, 11 - bromo - dibenz[b,f]oxepin - 10(11H) - one, is obtained as follows:

b) 52.5 g of dibenz[b,f]oxepin - 10(11H) - one are dissolved in 250 ml of carbon disulphide and, while stirring the solution at 0—5°, 40 g of bromine in 140 ml of carbon disulphide are added dropwise within 1 hour. The brown reaction mixture is stirred for 1 hour during which it loses its colour. It is then evaporated in vacuo, the residue is recrystallised from ethanol and 11 - bromodibenz[b,f]oxepin - 10(11H) - one is obtained, M.P. 94.5—96.8°.

EXAMPLE 6

29 g of 11 - bromo - dibenz[b,f]oxepin - 10(11H) - one in 180 ml of dry acetone are added dropwise within 30 minutes to 29 g of 2 - (1 - piperazinyl)ethanol in 100 ml of dry acetone, the addition being made while stirring. The reaction solution is boiled for 5 hours. The reaction mixture is then concentrated in vacuo and the residue is taken up in ether. The ether solution is washed with water, extracted with 2N hydrochloric acid and the acid extract is made alkaline with concentrated sodium hydroxide solution. The precipitated base is taken up in ether, the ether solution is washed with water, dried over sodium hydroxide and concentrated in vacuo. The pale orange residue is taken up in dry acetone and abs. ethanolic hydrochloric acid is added to the acetone solution until there is a congo acid reaction. The precipitated 11 - [4 - (2 - hydroxyethyl) - 1 - piperazinyl] - dibenz[b,f]oxepin - 10(11H) - one dihydrochloride is filtered off under suction, washed with dry acetone and recrystallised from ethanol; it melts at 185—189° with decomposition.

EXAMPLE 7

The following compounds are obtained in an analogous manner according to Example 5 a) and 5 b):

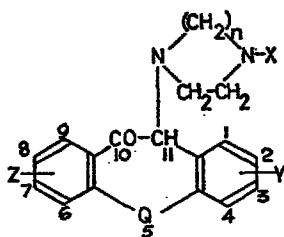
- 5 a) from 2 - chloro - 11 - bromo - dibenz[b,f]oxepin - 10(11H) - one with 4-methyl piperazine, 2 - chloro - 11 - (4-methyl - 1 - piperazinyl) - dibenz[b,f]oxepin - 10(11H) - one dihydrochloride hydrate, M.P. 218—225° with decomposition, and
- 10 b) from 2 - chloro - dibenz[b,f]oxepin - 10(11H) - one with bromine, the intermediate product 2 - chloro - 11 - bromo - dibenz[b,f]oxepin - 10(11H) - one, M.P. 111—113.8° from ethanol.

EXAMPLE 8

- Starting from 2 - chloro - 11 - bromo - dibenz[b,f]oxepin - 10(11H) - one and reacting it analogously to Example 6 with 2 - (1-piperazinyl)ethanol, the 2 - chloro - 11 - [4-(2 - hydroxyethyl) - 1 - piperazinyl] - dibenz[b,f]oxepin - 10(11H) - one is obtained; M.P. (hydrochloride) 189—193° (from abs. ethanol), with decomposition.

25 WHAT WE CLAIM IS:—

1. Thiepin and oxepin derivatives of the general formula I



(I)

wherein Q represents an oxygen or a sulphur atom;

- 30 X represents a hydrogen atom, an alkyl or hydroxyalkyl group having at most 4 carbon atoms in the alkyl moieties, or an alkanoyloxyalkyl group having, in all, at most 8 carbon atoms;

- 35 Y and Z each represent a hydrogen atom, a halogen atom up to the atomic number 35, or an alkyl or alkoxy group having at most 4 carbon atoms in the alkyl moiety; and

- 40 n represents 2 or 3; and their addition salts with inorganic and organic acids.

- 45 2. Thiepin and oxepin derivatives of the general formula I set forth in claim 1 wherein X represents a hydrogen atom or the methyl or the 2 - hydroxyethyl group,

50

Y and Z each represent a hydrogen atom, a chlorine atom or an alkoxy groups having not more than 4 carbon atoms, and

Q and n have the meanings given in claim 1,

and their salts with inorganic and organic acids.

3. 11 - (4 - Methyl - 1 - piperazinyl) - dibenzo[b,f]thiepin - 10(11H) - one.

4. 2 - Chloro - 11 - (4 - methyl - 1 - piperazinyl) - dibenzo[b,f]thiepin - 10(11H) - one.

5. 2 - Methoxy - 11 - (4 - methyl - 1 - piperazinyl) - dibenzo[b,f]thiepin - 10(11H) - one.

6. 11 - [4 - (2 - Hydroxyethyl) - 1 - piperazinyl] - dibenzo[b,f]thiepin - 10(11H) - one.

7. 2 - Chloro - 11 - [4 - (2 - hydroxyethyl) - 1 - piperazinyl] - dibenzo[b,f]thiepin - 10(11H) - one.

8. 11 - (4 - Methyl - 1 - piperazinyl) - dibenz[b,f]oxepin - 10(11H) - one and its dihydrochloride salt.

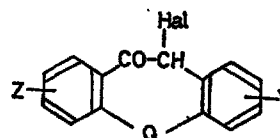
9. 11 - [4 - (2 - Hydroxyethyl) - 1 - piperazinyl] - dibenz[b,f]oxepin - 10(11H) - one and its dihydrochloride salt.

10. 2 - Chloro - 11 - (4 - methyl - 1 - piperazinyl) - dibenz[b,f]oxepin - 10(11H) - one and its hydrochloride salt.

11. 2 - Chloro - 11 - [4 - (2 - hydroxyethyl) - 1 - piperazinyl] - dibenz[b,f]oxepin - 10(11H) - one and its hydrochloride salt.

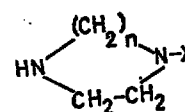
12. Thiepin and oxepin derivatives of the general formula I as defined in claim 1, substantially as herein described with reference to and as illustrated in any of the foregoing examples.

13. Process for the production of thiepin and oxepin derivatives according to claim 1, which comprises reacting, in the presence of a basic condensing agent, a compound of the general formula II

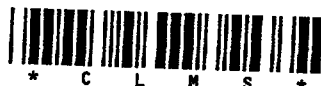


(II)

wherein Hal represents a halogen atom and Q, Y and Z have the meanings given in claim 1, with a compound of the general formula III



(III)



EXAMPLE 7

The following compounds are obtained in an analogous manner according to Example 5 a) and 5 b):

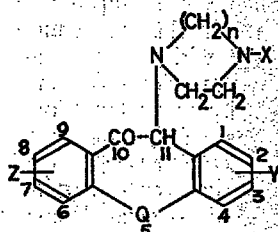
- 5 a) from 2 - chloro - 11 - bromo - dibenz[b,f]oxepin - 10(11H) - one with 4-methyl piperazine, 2 - chloro - 11 - (4-methyl - 1 - piperazinyl) - dibenz[b,f]oxepin - 10(11H) - one dihydrochloride hydrate, M.P. 218—225° with decomposition, and
- 10 b) from 2 - chloro - dibenz[b,f]oxepin - 10(11H) - one with bromine, the intermediate product 2 - chloro - 11 - bromo - dibenz[b,f]oxepin - 10(11H) - one, M.P. 111—113.8° from ethanol.

EXAMPLE 8

- Starting from 2 - chloro - 11 - bromo - dibenz[b,f]oxepin - 10(11H) - one and reacting it analogously to Example 6 with 2 - (1-piperazinyl)ethanol, the 2 - chloro - 11 - [4-(2 - hydroxyethyl) - 1 - piperazinyl] - dibenz[b,f]oxepin - 10(11H) - one is obtained; M.P. (hydrochloride) 189—193° (from abs. ethanol), with decomposition.

WHAT WE CLAIM IS:—

1. Thiepin and oxepin derivatives of the general formula I



(I)

wherein Q represents an oxygen or a sulphur atom;

- 30 X represents a hydrogen atom, an alkyl or hydroxyalkyl group having at most 4 carbon atoms in the alkyl moieties, or an alkanoyloxyalkyl group having, in all, at most 8 carbon atoms;

- 35 Y and Z each represent a hydrogen atom, a halogen atom up to the atomic number 35, or an alkyl or alkoxy group having at most 4 carbon atoms in the alkyl moiety; and

- 40 n represents 2 or 3; and their addition salts with inorganic and organic acids.

- 45 2. Thiepin and oxepin derivatives of the general formula I set forth in claim 1 wherein X represents a hydrogen atom or the methyl or the 2 - hydroxyethyl group,

Y and Z each represent a hydrogen atom, a chlorine atom or an alkoxy groups having not more than 4 carbon atoms, and

Q and n have the meanings given in claim 1,

and their salts with inorganic and organic acids.

3. 11 - [4 - Methyl - 1 - piperazinyl] - dibenzo[b,f]thiepin - 10(11H) - one.

4. 2 - Chloro - 11 - [4 - methyl - 1 - piperazinyl] - dibenzo[b,f]thiepin - 10(11H) - one.

5. 2 - Methoxy - 11 - [4 - methyl - 1 - piperazinyl] - dibenzo[b,f]thiepin - 10(11H) - one.

6. 11 - [4 - (2 - Hydroxyethyl) - 1 - piperazinyl] - dibenzo[b,f]thiepin - 10(11H) - one.

7. 2 - Chloro - 11 - [4 - (2 - hydroxyethyl) - 1 - piperazinyl] - dibenzo[b,f]thiepin - 10(11H) - one.

8. 11 - [4 - Methyl - 1 - piperazinyl] - dibenz[b,f]oxepin - 10(11H) - one and its dihydrochloride salt.

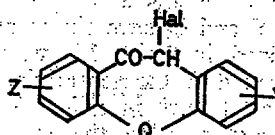
9. 11 - [4 - (2 - Hydroxyethyl) - 1 - piperazinyl] - dibenz[b,f]oxepin - 10(11H) - one and its dihydrochloride salt.

10. 2 - Chloro - 11 - [4 - methyl - 1 - piperazinyl] - dibenz[b,f]oxepin - 10(11H) - one and its hydrochloride salt.

11. 2 - Chloro - 11 - [4 - (2 - hydroxyethyl) - 1 - piperazinyl] - dibenz[b,f]oxepin - 10(11H) - one and its hydrochloride salt.

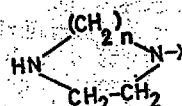
12. Thiepin and oxepin derivatives of the general formula I as defined in claim 1, substantially as herein described with reference to and as illustrated in any of the foregoing examples.

13. Process for the production of thiepin and oxepin derivatives according to claim 1, which comprises reacting, in the presence of a basic condensing agent, a compound of the general formula II



(II)

wherein Hal represents a halogen atom and Q, Y and Z have the meanings given in claim 1, with a compound of the general formula III



(III)



- wherein X and n have the meanings given in claim 1, if desired, treating a compound of general formula I in which X is hydrogen, with an alkylene oxide having at most 4 carbon atoms, with a reactive monoester of an alkane diol having at most 4 carbon atoms in the alkyl moiety, or with a reactive ester of an alkanoyloxyalkanol having, in all, at most 8 carbon atoms, or with a reactive ester of an alkanol having at most 4 carbon atoms in the alkyl moiety and, if desired, converting a compound of the general formula I into an addition salt with an inorganic or organic acid.
14. Thiepin derivatives of the general formula I set forth in claim 1 wherein Q represents a sulphur atom; X represents an alkyl or hydroxyalkyl group having at most 4 carbon atoms in the alkyl moieties or an alkanoyloxyalkyl group having, in all, at most, 8 carbon atoms; Y and Z each represent a hydrogen atom, a halogen atom up to the atomic number 35, or an alkyl or alkoxy group having at most 4 carbon atoms in the alkyl moiety, and n represents 2 or 3; and their addition salts with inorganic and organic acids.
15. Thiepin derivatives as claimed in claim 14, wherein X in the general formula I represents a methyl or 2-hydroxyethyl group, Y and Z each represent a hydrogen atom, a chlorine atom or an alkoxy groups having at most 4 carbon atoms, and Q and n have the meaning defined in claim 14, and their salts with inorganic and organic acids.
16. A process for the production of thiepin derivatives as claimed in claim 14 which comprises reacting, in the presence of a basic condensing agent, a compound of the general formula II, as set forth in claim 13, wherein Hal represents a halogen atom and Q, Y and Z have the meanings defined in claim 14, with a compound of the general formula III, as set forth in claim 13, wherein X and n have the meanings defined in claim 14, and, if desired, converting the compound of the general formula I into an addition salt with an inorganic or organic acid.
17. Thiepin derivatives having the general formula I, as set forth in claim 1, wherein Q is a sulphur atom, X represents a hydrogen atom, an alkyl or hydroxyalkyl group having at most 4 carbon atoms in the alkyl moieties or an alkanoyloxyalkyl group having, in all, at most 8 carbon atoms, Y and Z each represent a hydrogen atom, a halogen atom up to the atomic number 35, or an alkyl or alkoxy group having at most 4 carbon atoms in the alkyl moieties, and n represents 2 or 3; and their addition salts with inorganic and organic acids.
18. Thiepin derivatives as claimed in claim 17, wherein X represents a hydrogen atom or a methyl or 2-hydroxyethyl group, Y and Z each represent a hydrogen atom, a chlorine atoms or an alkoxy groups having at most 4 carbon atoms, and Q and n have the meanings given in claim 17, and their salts with inorganic and organic acids.
19. A process for the production of thiepin derivatives as claimed in claim 17, which comprises reacting, in the presence of a basic condensing agent, a compound of the formula II, as set forth in claim 13, wherein Hal represents a halogen atom and Q, Y and Z have the meanings given in claim 17 with a compound of the general formula III, as set forth in claim 13, wherein X and n have the meanings given in claim 17, if desired, treating a compound of general formula I in which X is hydrogen, with an alkylene oxide having at most 4 carbon atoms, with a reactive monoester of an alkane diol having at most 4 carbon atoms, in the alkyl moiety, or with a reactive ester of an alkanoyloxyalkanol having, in all, at most 8 carbon atoms, or with a reactive ester of an alkanol having at most 4 carbon atoms in the alkyl moiety and, if desired, converting a compound of the general formula I, defined in claim 17, into an addition salt with an inorganic or organic acid.
20. Oxepin derivatives of the general formula I set forth in claim 1, wherein Q is an oxygen atom, X is hydrogen, an alkyl or hydroxyalkyl group having at most 4 carbon atoms in the alkyl moieties or an alkanoyloxyalkyl group having, in all, at most 8 carbon atoms, Y and Z each represent a hydrogen atom, a halogen atom up to the atomic number 35, or an alkyl or alkoxy group having at most 4 carbon atoms in the alkyl moieties, and n represents 2 or 3; and their addition salts with inorganic and organic acids.
21. Oxepin derivatives as claimed in claim 20 wherein X represents a hydrogen atom or a

5 methyl or 2-hydroxyethyl group,
Y and Z each represent a hydrogen
atom, a chlorine atom or an
alkoxy group having at most 4
carbon atoms, and

Q and n have the meanings given
in claim 20, and their salts with
inorganic and organic acids.

10 22. A process for the production of oxepin
derivatives as claimed in claim 20 which
comprises reacting, in the presence of a basic
condensing agent, a compound having the
general formula II as set forth in claim 13,

15 wherein Hal represents a halogen atom and
Q, Y and Z have the meanings
defined in claim 20 with a com-
pound of the general formula III,
as set forth in claim 13,

20 wherein X and n have the meanings given
in claim 20, and if desired, treat-
ing a compound of general form-
ula I, defined in claim 20, in
which X is hydrogen, with and
25 alkylene oxide having at most 4
carbon atoms, with a reactive mono-
ester of an alkane diol hav-
ing at most 4 carbon atoms in
the alkyl moiety, or with a reactive
30 ester of an alkanoyloxyalkanoyl
having, in all, at most 8 carbon
atoms, or with a reactive ester
of an alkanol having at most
4 carbon atoms in the alkyl moiety
and, if desired, converting a com-
35 pound of general formula I defined
in claim 20 into an addition salt
with an inorganic or organic acid.

23. A process for the production of thie-
pin derivatives of the general formula I
40 defined in claim 14, as claimed in claim 16,

substantially as hereinbefore described with
reference to and as illustrated in Example 1.

24. A process for the production of thie-
pin derivatives of the general formula 1,
defined in claim 17, as claimed in claim 19,
substantially as hereinbefore described with
reference to and as illustrated in any one of
Examples 2 to 4. 45

25. A process for the production of oxe-
pin derivatives of the general formula I
defined in claim 20, as claimed in claim
22, substantially as hereinbefore described in
any one of Examples 5 to 8. 50

26. Thiepin derivatives as claimed in claim
17 as described in any one of Examples 2
to 4. 55

27. Oxepin derivatives as claimed in claim
20 as described in any of Examples 5 to
8.

28. A pharmaceutical preparation in dos-
age unit form comprising a compound claimed
in claim 1 and at least one inert pharma-
ceutical carrier. 60

29. A pharmaceutical preparation in dos-
age unit form comprising a compound claimed
in claim 14 and at least one inert pharma-
ceutical carrier. 65

30. A pharmaceutical preparation in dos-
age unit form comprising a compound claimed
in claim 17 and at least one inert pharma-
ceutical carrier. 70

31. A pharmaceutical preparation in dos-
age unit form comprising a compound claimed
in claim 20 and at least one inert pharma-
ceutical carrier. 75

W. P. THOMPSON & CO.,
12, Church Street,
Liverpool, 1.
Chartered Patent Agents.

