PATENT SPECIFICATION

NO DRAWINGS

908,788

Date of Application and filing Complete Specification: Sept. 2, 1960.

No. 30261/60.

Application made in Switzerland (No. 77806) on Sept. 4, 1959.

Complete Specification Published: Oct. 24, 1962.

Index at acceptance:—Class 2(3), C1F1(B:D3), C1G(5B:6B3), C1H1(A2:C3), C1H2(A9:C3), C2A(3:5:6:8:9:14), C2(B43D1:R16:T18).

International Classification:—C07d.

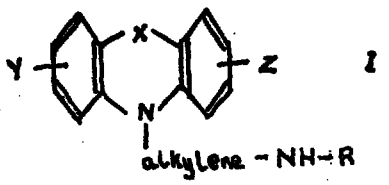
COMPLETE SPECIFICATION

Substituted 5H-Dibenz[b,f]Azepines and their 10,11-Dihydro Derivatives

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 N-heterocyclic compounds having valuable pharmacological properties, as well as processes for the production thereof.

It has surprisingly been found that derivatives of imino - dibenzyl (10,11 - dihydro-5H - dibenzo[b,f]azepine) and iminostilbene (5H - dibenzo[b,f]azepine) of the general formula



I

wherein X represents the ethylene or vinylene group $-CH_2-CH_2-$ or $-CH=CH-$ respectively,

Y represents hydrogen, a halogen atom or an alkyl radical of at most 4 carbon atoms,

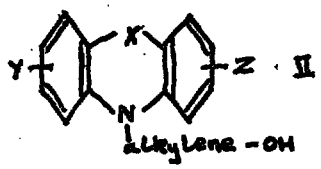
Z represents hydrogen, a halogen atom or an alkyl radical of at most 4 carbon atoms,

alkylene represents an alkylene radical having a straight or branched chain of 2—6 carbon atoms,

R represents an alkyl or alkenyl radical or a cycloalkyl radical each of which may contain at most 8 carbon atoms,

have valuable pharmacological properties, in particular antiallergic, spasmolytic, anticonvulsive and sedative activity.

To produce the new compounds of the general formula I a reactive ester of a hydroxy compound of the general formula



II

wherein X, Y, Z and alkylene have the meanings given above, in particular a halide, is reacted with a primary amine of the general formula

$$NH_2 — R \qquad III$$

wherein R has the meaning given above. The reaction can be performed, for example, at moderately raised temperatures of from 70—120° in an organic solvent such as, e.g. a low molecular weight alkanol, benzene or toluene, using at least a second mol of the amine reacted as acid-binding agent. Depending on the boiling point of the amine used and of the solvent as well as on the reaction temperature necessary, the reaction is sometimes performed in a closed vessel. In particular, in reactions with primary amines the boiling points of which are within the range of the reaction temperature, an excess of the amine can be used as sole diluent.

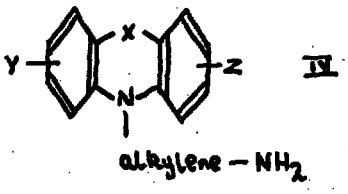
Reactive esters of hydroxy compounds of the general formula II are obtained, for example, by reacting alkali metal compounds of iminodibenzyl or iminostilbene, possibly substituted according to the meanings of Y and Z, with reactive, advantageously mixed, diesters of alkylene glycols such as, e.g. 1-chloro - 2 - bromoethane, 1 - chloro - 3-bromopropane, 1,2 - dichloropropane, 1,2-dibromopropane, 1 - chloro - 4 - bromo -n-butane, 1,4 - dibromobutane, 3 - bromo - 2-methyl - propyl chloride or ω - halogen alkyl esters of toluene *p* - sulphonic acid or methane

[*Price 4s. 6d.*]

sulphonic acid, or by reacting the alkali metal compounds mentioned above with alkylene oxides and treating the hydroxyalkyl compounds obtained with inorganic acid halides, aryl sulphonic acid chlorides or methane sulpho - chloride, whereupon 5 - halogen alkyl, 5 - aryl sulphonyloxyalkyl or 5-methane sulphonyloxyalkyl derivatives of possibly substituted iminodibenzyl or iminostilbene are obtained.

Methylamine, ethylamine, n - propylamine, isopropylamine, n - butylamine, isobutylamine, sec. butylamine, tert. butylamine, n - amylamine, isoamylamine, 3 - aminopentane, tert. amylamine, n - hexylamine, n - heptylamine, n - octylamine, allylamine, crotylamine and methallylamine are examples of primary amines of the general formula III.

Compounds of the general formula I are obtained by a second process by reacting compounds of the general formula



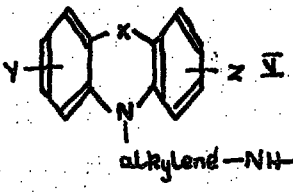
IV

wherein X, Y, Z and alkylene have the meanings given above, with low molecular weight, aliphatic oxo compounds which can be saturated or can contain a double linkage, and then, subsequently or simultaneously, reducing the reaction products.

This process is of particular practical interest for the production of 5 - (α - alkylaminomethyl - alkyl) - iminodibenzyls and -iminostilbenes which are possibly substituted in the benezene nuclei. The 5 - (α - aminomethyl-alkyl) - iminodibenzyls and -iminostilbenes necessary as starting materials in this process are easily obtained by Strecker's method by condensation of possibly substituted iminodibenzyls or iminostilbenes with aldehydes and alkali cyanides in acetic acid to form 5-(α - cyanoalkyl) - iminodibenzyls or 5 - (α-cyanoalkyl) - iminostilbenes, respectively, followed by hydrogenation thereof, for example in the presence of Raney nickel at 60—100° and 30—140 atm. pressure in aqueous dioxan containing ammonia, or reduction thereof, e.g. with lithium aluminium hydride in ether-like solvents such as diethyl ether, dibutyl ether or tetrahydrofuran. Hydrogenation of the cyano compounds, reaction of the amino compounds formed with aliphatic oxo compounds and hydrogenation of the reaction products obtained can possibly be performed simultaneously (this process is known as reduction alkylation). Suitable starting materials of the general formula IV are, for example, 5 - (β-aminoethyl) - iminodibenzyl (hydrochloride M.P. 256°), 5 - (γ - aminopropyl) - iminodibenzyl, 5 - (δ - aminobutyl) - iminodibenzyl, 5 - (α - aminomethyl - ethyl) - iminodibenzyl (hydrochloride M.P. 228—230°), 5-(α - aminomethyl - isobutyl) - iminodibenzyl, 5 - (α - aminomethyl - n - amyl) - iminodibenzyl, 3 - chloro - 5 - (α - aminomethyl-ethyl) - iminodibenzyl (hydrochloride M.P. 250—252°), 5 - (β - aminoethyl) - iminostilbene and 5 - (α - aminomethyl - ethyl)-iminostilbene (hydrochloride M.P. 266—268°).

Formaldehyde, acetaldehyde, propionaldehyde, butyraldehyde, isobutyraldehyde, acetone, butanone, isopropylmethyl ketone, pinacolin, crotonaldehyde, α - methylacrolein and mesityloxide are mentioned as aliphatic oxo compounds. If end products having an alkenyl radical R are desired, the imines are reduced advantageously with chemical agents, e.g. with sodium borohydride, lithium aluminium hydride or formic acid. On the other hand, because of their reactivity, also the use of unsaturated oxo compounds as starting materials for the production of end products having an alkyl radical R can be of interest. In this case, catalytic methods are used for the simultaneous hydrogenation of the imino group and of the aliphatic double linkage.

In addition, compounds of the general formula I can also be produced by reducing, advantageously by means of alkali metal-earth metal hydrides such as, e.g. lithium aluminium hydride in diethyl ether, dibutyl ether or tetrahydrofuran, compounds of the general formula



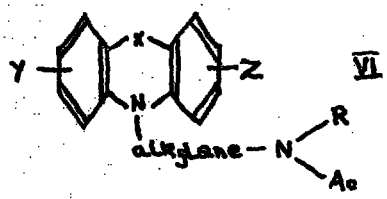
V

wherein X, Y and Z have the meanings given above, and alkylene[1] and R[1] differ from alkylene and R as defined above only in that in at least one of these radicals the methylene group bound to a nitrogen atom is replaced by a carbonyl group. As starting materials of the general formula V can be used, for example, the possibly substituted 5 - alkanoylaminoalkyl- or 5 - alkenoylaminoalkyliminodibenzyls or -iminostilbenes which are obtained by reacting the 5 - (α - aminomethyl - alkyl)-iminodibenzyls and -iminostilbenes mentioned above or reacting other 5 - aminoalkyl - iminodibenzyls or -iminostilbenes with reactive functional derivatives or low molecular weight alkanoic or alkenoic acids, for example with their esters, halides or anhydrides. In addi-

tion, such starting materials are also, for example, the possibly substituted 5 - alkylcarbamyl - alkyl- or 5 - alkenylcarbamylalkyl - iminodibenzyls or -iminostilbenes obtained by reacting possibly substituted 5-carbalkoxyalkyl - iminodibenzyls or -iminostilbenes such as, e.g. iminodibenzyl- or iminostilbene - 5 - acetic acid alkyl esters, with primary amines of the general formula III.

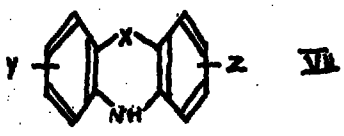
A further group of starting materials of the general formula V is obtained by reacting possibly substituted 5 - halogenalkanoyliminodibenzyls or -iminostilbenes with primary amines of the general formula III.

In addition, compounds of the general formula I are obtained by a fourth process by splitting into acid and into a secondary amine, amides of the general formula



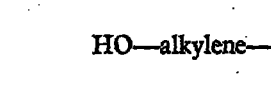
VI

wherein Ac represents an acyl radical, in particular a low ~~alkanyl~~ alkanoyl radical, the toluene *p* - sulphonyl radical or methane sulphonyl radical, and X, Y and Z, alkylene and R have the meanings given above. If Ac is a low molecular alkanoyl radical, the amide can be split by, for example, acid or alkaline hydrolysis, and if Ac is a methane sulphonyl or a toluene *p* - sulphonyl radical, it can be split by, for example, treatment with sodium in ammonia. Compounds of the general formula VI are obtained in their turn, for example, by reacting metal compounds of the possibly substituted 5 - alkanoylaminoalkyl- iminodibenzyls or -iminostilbenes embraced by the general formula V, with reactive esters of low molecular weight alkanols or alkenols, for example reacting sodium compounds of 5 - (α - formylaminomethyl - alkyl) - iminodibenzyls with methyl iodide, dimethyl sulphate, ethyl iodide, diethyl sulphate, n - butyl bromide, allyl bromide or methallyl chloride. In addition, compounds of the general formula VI can be obtained, for example, by condensing possibly substituted iminodibenzyl or iminostilbene of the general formula



VII

with a reactive ester of an N - acyl - alkylaminoalkanol or -alkenylaminoalkanol of the general formula



VIII

wherein X, Y, Z, alkylene, R and Ac have the meanings given above, the condensation being performed in the presence of an acid-binding agent such as, e.g. sodium amide, lithium amide, potassium amide, sodium potassium, butyl lithium, phenyl lithium or lithium hydride in the presence or absence of an inert organic solvent such as, e.g. benzene, toluene or xylene. For example in this way, an iminodibenzyl, 3,7 - dichloroiminodibenzyl, 3 - chloro - iminodibenzyl, 3-bromo - iminodibenzyl, 3,7 - dimethyliminodibenzyl, iminostilbene, 3 - chloroiminostilbene or 3,7 - dichloro - iminostilbene can be reacted with N - formyl-, N-isibutyryl-, N - benzoyl-, N - carbethoxy- or N - methane sulphonyl -β - methylaminoethyl ~~choride~~ chloride, -β - ethylamino - ethyl chloride, -β - methylamino - propyl chloride, -β-amino - propyl chloride or - γ ethylamino - n-ethylamino - propyl chloride -γ - methyl propyl chloride.

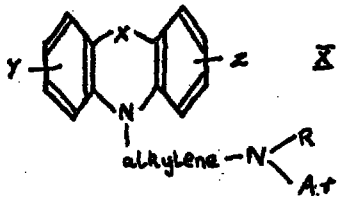
Another possibility for the production of starting materials of the general formula VI consists in reacting reactive esters of hydroxy compounds of the general formula II, for example halides, with amides of the general formula



IX

wherein R and Ac have the meanings given above, the reaction being performed in the presence of acid-binding agents or reacting such esters with metal compounds of such amides.

Finally, compounds of the general formula I can be produced by a fifth process by hydrogenolysing, for example in the presence of Raney nickel or noble metal catalysts, compounds of the general formula



X

wherein Ar represents an arylmethyl radical, in particular the benzyl radical and X, Y, Z, alkylene and R have the meanings given above. Starting materials of the general formula X can be obtained for example by reacting reactive esters of hydroxy compounds of the general formula II with N - alkyl-

arylmethylamines, in particular with N - alkylbenzylamines. Although this process necessitates two steps starting from compounds of the general formula II until the end products are obtained, compared with the one-step process first mentioned it can sometimes be of interest because it avoids tertiary side products with two iminodibenzyl radicals in the molecule. Starting materials of the general formula X can also be obtained in another manner, for example, by reducing 5 - (N-alkyl - benzoylaminoalkyl) - iminodibenzyls with lithium-aluminium hydride, or by condensing possibly substituted iminodibenzyl of the general formula VII with a reactive ester of an N - arylmethyl - alkylaminoalkanol analogously to the reactions described above of possibly substituted iminodibenzyl with N-acyl - alkylaminoalkanols.

The secondary bases obtained according to the invention form water soluble salts with inorganic or organic ~~acides~~ acids such as hydrochloric acid, hydrobromic acid, sulphuric acid, phosphoric acid, methane sulphonic acid, ethane disulphonic acid, acetic acid, citric acid, malic acid, succinic acid, fumaric acid, maleic ~~acid~~, tartaric acid, benzoic acid and phthalic acid.

The following examples further illustrate the production of the new compounds. Parts are given therein as parts by weight and their relationship to parts by volume is as that of grammes to cubic centimetres. The temperatures are in degrees Centigrade.

EXAMPLE 1

19 Parts of iminostilbene and 20 parts of 1 - chloro - 3 - bromopropane are dissolved in 800 parts by volume of anhydrous benzene and 4.4 parts of sodium amide in 13.2 parts by volume toluene are added dropwise at 50° over a period of half an hour while stirring well. The whole is stirred for 3 hours at 50—60° and then refluxed for 3 hours. After the reaction mixture has cooled, water is added and the benzene phase is separated, washed with water, dried and concentrated. The oily residue is taken up in 400 parts by volume of petroleum ether (boiling range 40°—60°), any undissolved iminostilbene is filtered off and the filtrate is evaporated, whereupon the 5 - (γ - chloropropyl) - iminostilbene remains which, after recrystallisation from anhydrous ether, melts at 67°.

30 Parts of 5 - (γ - chloropropyl) - iminostilbene and 100 parts by volume of a solution of methylamine in methanol, saturated at 0—5°, are heated for 12 hours at 100—110° in an autoclave. The solvent is then distilled off, water is added to the residue and it is extracted with ether. The ethereal solution is washed with water and then extracted with 2N - hydrochloric acid or with dilute acetic acid. The acid extract is made alkaline with concentrated sodium hydroxide solution and the substance that separates is taken up in petroleum ether (boiling range 40—60°C). After the solution has been washed with water and dried over potassium carbonate, the petroleum ether is evaporated off and the residue is distilled in a high vacuum. The 5 - (γ - methylamino - propyl) - iminostilbene passes over at 150—152° under 0.005 mm pressure. The hydrochloride melts at 205—206°.

5 - (γ - methylamino - propyl) - iminodibenzyl ($B.P._{0.02}$ 172—174°) is obtained in an analogous manner on using 30 parts of the oily 5 - (γ - chloropropyl) - iminodibenzyl (produced analogously to 5 - (γ - chloropropyl) - iminostilbene but using the oily residue of the benzene phase direct). The hydrochloride melts at 214—218°.

Also 5 - (β - methylamino - ethyl) - iminodibenzyl is obtained in an analogous manner starting from 5 - (β - chloroethyl) - iminodibenzyl. Its hydrochloride melts at 214—216°.

EXAMPLE 2

40 Parts of 5 - (γ - chloropropyl) - iminodibenzyl and 150 parts by volume of an about 20% solution of ethylamine in benzene are heated for 15 hours in an autoclave at 110—120°. The benzene and the excess ethylamine are then distilled off, water is added to the residue and it is extracted with ether. The ether solution is washed with water and then extracted with 2N - acetic acid. The acetic acid solution is made alkaline with concentrated sodium hydroxide solution and the separated substance is taken up in petroleum ether (boiling range 40°—60°C), the solution is washed with water, dried over potassium carbonate and concentrated. On distilling the residue, 5 - (γ - ethylaminopropyl) - iminodibenzyl ($B.P._{0.01}$ 168—170°) is obtained. The hydrochloride melts at 246°. 3,7 - Dichloro - 5 - (γ - ethylamino - propyl) - iminodibenzyl ($B.P._{0.01}$ 192°) is obtained in an analogous manner starting from 50 parts of 3,7 - dichloro - 5 - (γ - chloropropyl) - iminodibenzyl. The hydrochloride melts at 174°.

5 - (γ - Ethylamino - propyl) - iminostilbene ($B.P._{0.005}$ 153—155°) is obtained in an analogous manner on using 40 parts of 5 - (γ - chloropropyl) - iminostilbene. The hydrochloride melts at 153°.

The same compounds are obtained if, instead of the chloro compounds, the corresponding toluene p - sulphonic acid or methane sulphonic acid esters are used and otherwise analogous procedure is followed.

EXAMPLE 3

30 Parts of 5 - (γ - chloropropyl) - iminostilbene in 100 parts by volume of n - butylamine are refluxed for 16 hours. The excess amine is then distilled off, water is added to the residue and it is extracted with ether. The ether extract is washed with water and then extracted with 2N - acetic acid. The

acetic acid extract is then made alkaline with concentrated sodium hydroxide solution and the substance that separates is taken up in petroleum ether (boiling range 40°—60°C). The solution is washed with water and dried over potassium carbonate. The residue which remains after distilling off the petroleum ether is distilled in a high vacuum whereupon 5-(γ - n - butylaminopropyl) - iminostilbene passes over at 180—182° under 0.02 mm pressure. The hydrochloride melts at 153°.

On using 40 parts of 5 - (γ - chloropropyl)-iminodibenzyl, 5 - (γ - n - butylaminopropyl) - iminodibenzyl (B.P. $_{0.01}$ 177—179°) is obtained in an analogous manner. The hydrochloride melts at 120°.

EXAMPLE 4

40 Parts of 5 - (γ - chloropropyl)-iminodibenzyl and 100 parts by volume of isopropylamine are heated for 16 hours in an autoclave at 100—110° and the reaction mixture is worked up analogously to example 3. 5 -(γ - isopropylamino - propyl) - iminodibenzyl (B.P.$_{0.01}$ 168—170°) is obtained. The hydrochloride melts at 253°.

5 - (γ - allylamino - propyl) - iminostilbene (B.P.$_{0.01}$ 171—173°) is obtained in an analogous manner from 40 parts of 5 - (γ - chloropropyl) - iminostilbene and 100 parts by volume of allylamine. This base, with an anhydrous ethanolic hydrogen chloride solution, produces the hydrochloride which, after recrystallisation from anhydrous ethanol, melts at 150—152°.

EXAMPLE 5

A solution of 10 parts of 5 - (α - acetylaminomethyl - ethyl) - iminodibenzyl (M.P. 145°), is produced from 5 - (α - aminomethylethyl) - iminodibenzyl by acetylation (either with acetyl chloride and aqueous sodium hydroxide solution according to Schotten-Baumann, [See Chem. Rev. *53*, 272 (1953)], or by means of acetic anhydride or by heating with ethyl acetate) in 150 parts of tetrahydrofuran is added dropwise at 60° while stirring to a suspension of 2 parts of lithium aluminium hydride in 50 parts of tetrahydrofuran and the whole is then stirred for 2 hours at 60°. 1 Part of methanol is then added, after which 2 parts of water, then 2 parts of 15% sodium hydroxide solution and then 6 parts of water are added. The granular precipitate which forms is filtered off and the filtrate is evaporated to dryness. The residue is taken up in ether and the ether solution is well shaken with 2N - hydrochloric acid whereupon a part of the 5 - (α-ethylaminomethylethyl) - iminodibenzyl hydrochloride precipitates in crystalline form. The crystals are filtered off (M.P. 238—240°) and recrystallised from methanol/ether (M.P. 242—243°).

The filtrate, which consists of an ethereal and an acid aqueous phase, is separated into phases, the aqueous phase is made alkaline with sodium hydroxide solution, extracted with ether and the ether extract is dried and evaporated to dryness. The evaporation residue consists of 5 - (α - ethylaminomethylethyl) - iminodibenzyl which is converted into the hydrochloride by means of ethanolic hydrochloric acid.

In an analogous manner, starting from 5-(α - aminomethylisobutyl) - iminodibenzyl (hydrochloride M.P. 248—250°), 5 - (α acetylaminomethyl - isobutyl) - iminodibenzyl (M.P. 111—113°) is obtained and from the latter, 5-(α - ethylaminomethyl - isobutyl)-iminodibenzyl (hydrochloride M.P. 223—224°) is obtained and starting from 5 - (α-aminomethyl - n - amyl) - iminodibenzyl (hydrochloride M.P. 209°), 5 - (α - acetylaminomethyl - n - amyl) - iminodibenzyl (M.P. 148°) is obtained and from the latter 5 - (α - ethylaminomethyl - n -amyl) - iminodibenzyl (hydrochloride M.P. 160°) is obtained.

EXAMPLE 6

25 Parts of 5 - (γ - aminopropyl) - iminodibenzyl and 7.2 parts of butyraldehyde are dissolved in 300 parts by volume of dioxan the solution is heated for a short time and then hydrogenated over 10 parts of Raney nickel at 80° and 30 atm. After the theoretical amount of hydrogen has been taken up, the reaction mixture is filtered, the filtrate is concentrated, the residue is taken up in 2N-hydrochloric acid, the hydrochloric acid solution is extracted with ether, the aqueous phase is made alkaline and extracted with ether, the ether phase is dried over potassium carbonate and concentrated and the residue is distilled. The 5 - (γ - butylaminopropyl)-iminodibenzyl passes over at 180—183° under 0.03 mm pressure.

In an analogous manner, 5 - (α - isopropylamino - methyl - ethyl) - iminodibenzyl (B.P.$_{0.05}$ 170—173°) is obtained from 5 - (α - aminomethylethyl) - iminodibenzyl and acetone in ethanol, and 5 - (α - cyclohexylamino - methyl - isobutyl) - iminodibenzyl is obtained from 5 - (α - aminomethylisobutyl) - iminodibenzyl and cyclohexanone.

EXAMPLE 7

14 Parts of 5 - (α - ethylideneiminomethylethyl) - iminodibenzyl (produced from 5 - (α-aminomethyl - ethyl) - iminodibenzyl and acetaldehyde) dissolved in 100 parts of ether are added dropwise while stirring to 2.5 parts of lithium aluminium hydride in 100 parts of anhydrous ether whereupon the whole is refluxed for 3 hours. 2 Parts of methanol, then 2 parts of water, 2 parts of 15% sodium hydroxide solution and, finally, 6 parts of water are added; the precipitate which forms is filtered off. The filtrate is evaporated to dryness and the residue is taken up in 2N-hydrochloric acid. The solution is extracted with ether, the aqueous phase is made alkaline and extracted with ether, the ether phase is

washed with water, dried over potassium carbonate and evaporated to dryness. The residue is treated with ethanolic hydrochloric acid and the hydrochloride of 5 - (α - ethylaminomethyl - ethyl) - iminodibenzyl (M.P. 242°C) is isolated.

In an analogous manner, 3 - chloro - 5-(α - cyclopentylidene - iminomethyl - ethyl)-iminodibenzyl is obtained from 3 - chloro-5 - (α - aminomethyl - ethyl) - iminodibenzyl and cyclopentanone and, by reducing it with lithium aluminium hydride, 3 - chloro - 5-(α - cyclopentylaminomethyl - ethyl) - iminodibenzyl is obtained. In the same way, from 3 - ethyl - 5 - (γ - aminopropyl) - iminostilbene and acetone, 3 - ethyl - 5 - (γ-isopropylideneimino - propyl) - iminostilbene is obtained and, from it, by reduction with lithium aluminium hydride, 3 - ethyl-5 - (γ - isopropylamino - propyl) - imino stilbene is obtained.

EXAMPLE 8

3 Parts of 5 - (α - N - formyl - N-methylaminomethyl - ethyl) - iminodibenzyl are dissolved in 40 parts by volume of dioxan and, after the addition of 40 parts of 2N sodium hydroxide solution, the solution is refluxed for 4 hours. It is then concentrated, the residue is taken up in 2N - hydrochloric acid, the hydrochloric acid solution is extracted with ether, the aqueous phase is made alkaline and extracted with ether, the ether phase is washed with water, dried over potassium carbonate and evaporated to dryness. The residue is converted with ethanolic hydrochloric acid into the hydrochloride of 5 - (α - methylaminomethyl - ethyl) - iminodibenzyl, M.P. 226°.

In an analogous manner, 2,8 - dimethyl-5 - (γ - methylaminopropyl) - iminostilbene is obtained from 2,8 - dimethyl - 5 -(γ - N-acetyl - N - methylamino - propyl) - iminostilbene on saponifying in ethylene glycol as solvent.

EXAMPLE 9

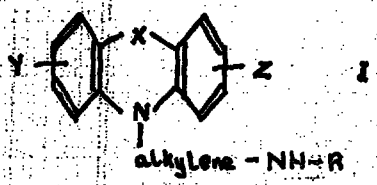
8.5 Parts of 5 - (α - N - benzyl - N-methylaminomethyl - ethyl) - iminodibenzyl, 190 parts of dioxan, 10 parts of water and 10 parts of Raney nickel are hydrogenated for 2 hours at 80° and 30 atm. pressure. The catalyst is removed and then the reaction solution is evaporated to dryness. The residue contains the desired 5 - (α - methylaminomethyl - ethyl) - iminodibenzyl which is isolated in the form of the hydrochloride (M.P. 226°) after converting the crude bases into the hydrochlorides by fractionally crystallising the salt mixture, for example, from methanol/ether.

5 - (α - cyclopentylamino - methyl - isobutyl) - iminodibenzyl is obtained in an analogous manner from 5 - (α - N - benzyl-N - cyclopentylamino - methyl - isobutyl)-iminodibenzyl.

The 5 - (α - methylaminomethyl - ethyl)-iminodibenzyl can also be separated in the form of its N - acetyl derivative by treating the crude bases according to Schotten-Baumann [See Chem. Rev. *53*, 272 (1953)] with acetyl chloride, filtering the neutral portions formed in benzene solution over 60—100 parts of aluminium oxide, concentrating the benzene filtrate and crystallising the residue from ether/petroleum ether; the 5 - (α - N-methyl - acetamidomethyl - ethyl) - iminodibenzyl obtained melts at 84—85°.

WHAT WE CLAIM IS:—

1. N - heterocyclic compounds of the general formula



I

wherein X represents the ethylene or vinylene group, $-CH_2-CH_2-$ or $-CH=CH-$ respectively,

Y represents hydrogen, a halogen atom or an alkyl radical of at most 4 carbon atoms,

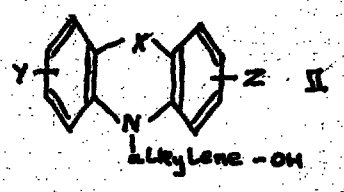
Z represents hydrogen, a halogen atom or an alkyl radical of at most 4 carbon atoms,

alkylene represents an alkylene radical having a straight or branched chain with 2—6 carbon atoms, and

R represents an alkyl, or alkenyl radical or a cycloalkyl radical each of which may contain at most 8 carbon atoms.

2. N - heterocyclic compounds as claimed in claim 1 in which R is an alkyl or alkenyl radical.

3. A process for the production of N-heterocyclic compounds claimed in claim 1 which comprises reacting a reactive ester of a hydroxyl compound of the general formula



II

with a primary amine of the general formula

$$NH_2 - R \qquad III$$

4. A process for the production of N-heterocyclic compounds claimed in claim 1 which comprises reacting a compound of the general formula

washed with water, dried over potassium carbonate and evaporated to dryness. The residue is treated with ethanolic hydrochloric acid and the hydrochloride of 5 - (α - ethylaminomethyl - ethyl) - iminodibenzyl (M.P. 242°C) is isolated.

In an analogous manner, 3 - chloro - 5-(α - cyclopentylidene - iminomethyl - ethyl)-iminodibenzyl is obtained from 3 - chloro-5 - (α - aminomethyl - ethyl) - iminodibenzyl and cyclopentanone and, by reducing it with lithium aluminium hydride, 3 - chloro - 5-(α - cyclopentylaminomethyl - ethyl) - iminodibenzyl is obtained. In the same way, from 3 - ethyl - 5 - (γ - aminopropyl) - iminostilbene and acetone, 3 - ethyl - 5 - (γ-isopropylideneimino - propyl) - iminostilbene is obtained and, from it, by reduction with lithium aluminium hydride, 3 - ethyl-5 - (γ - isopropylamino - propyl) - imino stilbene is obtained.

EXAMPLE 8

3 Parts of 5 - (α - N - formyl - N-methylaminomethyl - ethyl) - iminodibenzyl are dissolved in 40 parts by volume of dioxan and, after the addition of 40 parts of 2N sodium hydroxide solution, the solution is refluxed for 4 hours. It is then concentrated, the residue is taken up in 2N - hydrochloric acid, the hydrochloric acid solution is extracted with ether, the aqueous phase is made alkaline and extracted with ether, the ether phase is washed with water, dried over potassium carbonate and evaporated to dryness. The residue is converted with ethanolic hydrochloric acid into the hydrochloride of 5 - (α - methylaminomethyl - ethyl) - iminodibenzyl, M.P. 226°.

In an analogous manner, 2,8 - dimethyl-5 - (γ - methylaminopropyl) - iminostilbene is obtained from 2,8 - dimethyl - 5 -(γ - N-acetyl - N - methylamino - propyl) - iminostilbene on saponifying in ethylene glycol as solvent.

EXAMPLE 9

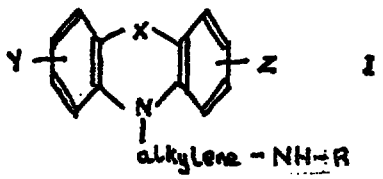
8.5 Parts of 5 - (α - N - benzyl - N-methylaminomethyl - ethyl) - iminodibenzyl, 190 parts of dioxan, 10 parts of water and 10 parts of Raney nickel are hydrogenated for 2 hours at 80° and 30 atm. pressure. The catalyst is removed and then the reaction solution is evaporated to dryness. The residue contains the desired 5 - (α - methylaminomethyl - ethyl) - iminodibenzyl which is isolated in the form of the hydrochloride (M.P. 226°) after converting the crude bases into the hydrochlorides by fractionally crystallising the salt mixture, for example, from methanol/ether.

5 - (α - cyclopentylamino - methyl - isobutyl) - iminodibenzyl is obtained in an analogous manner from 5 - (α - N - benzyl-N - cyclopentylamino - methyl - isobutyl)-iminodibenzyl.

The 5 - (α - methylaminomethyl - ethyl)-iminodibenzyl can also be separated in the form of its N - acetyl derivative by treating the crude bases according to Schotten-Baumann [See Chem. Rev. *53*, 272 (1953)] with acetyl chloride, filtering the neutral portions formed in benzene solution over 60—100 parts of aluminium oxide, concentrating the benzene filtrate and crystallising the residue from ether/petroleum ether; the 5 - (α - N-methyl - acetamidomethyl - ethyl) - iminodibenzyl obtained melts at 84—85°.

WHAT WE CLAIM IS:—

1. N - heterocyclic compounds of the general formula



I

wherein X represents the ethylene or vinylene group, $-CH_2-CH_2-$ or $-CH=CH-$ respectively,

Y represents hydrogen, a halogen atom or an alkyl radical of at most 4 carbon atoms,

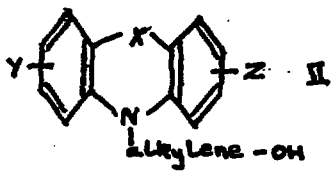
Z represents hydrogen, a halogen atom or an alkyl radical of at most 4 carbon atoms,

alkylene represents an alkylene radical having a straight or branched chain with 2—6 carbon atoms, and

R represents an alkyl, or alkenyl radical or a cycloalkyl radical each of which may contain at most 8 carbon atoms.

2. N - heterocyclic compounds as claimed in claim 1 in which R is an alkyl or alkenyl radical.

3. A process for the production of N-heterocyclic compounds claimed in claim 1 which comprises reacting a reactive ester of a hydroxyl compound of the general formula

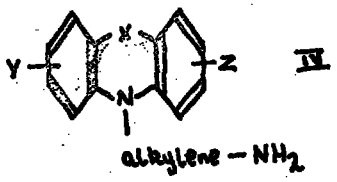


II

with a primary amine of the general formula

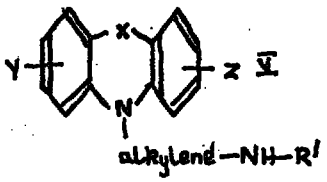
$$NH_2 — R \qquad III$$

4. A process for the production of N-heterocyclic compounds claimed in claim 1 which comprises reacting a compound of the general formula



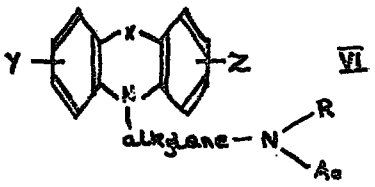
wherein X, Y, Z and alkylene have the meanings given in claim 1 with a low molecular weight aliphatic oxo compound which is saturated or contains a double linkage, and either subsequently or simultaneously reducing the reaction product.

5. A process for the production of N-heterocyclic compounds claimed in claim 1 which comprises reducing a compound of the general formula



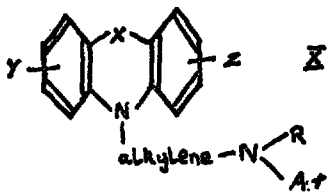
wherein X, Y and Z have the meanings given in claim 1, and alkylene[1] and R[1] differ from alkylene and R as defined in claim 1 only in that in at least one of these radicals the methylene group bound to a nitrogen atom is replaced by a carbonyl group.

6. A process for the production of N-heterocyclic compounds as claimed in claim 1 characterised by splitting into an acid and a secondary amine, an amide of the general formula



wherein Ac represents a acyl radical and X, Y, Z, alkylene and R have the meanings given in claim 1.

7. A process for the production of N-heterocyclic compounds claimed in claim 1 which comprises hydrogenolysing a compound of the general formula



wherein Ar represents an arylmethyl radical and X, Y, Z, alkylene and R have the meanings given in claim 1.

8. Process as claimed in any of claims 3 to 7 in which R is an alkyl or alkenyl group.

9. Process for the production of N - heterocyclic compounds as claimed in any of claims 3 to 7 substantially as hereinbefore described in any one of the foregoing Examples.

10. New N - heterocyclic compounds as claimed in claim 2 as hereinbefore described in any one of the foregoing Examples.

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Leamington Spa: Printed for Her Majesty's Stationery Office, by the Courier Press (Leamington) Ltd.—1962. Published by The Patent Office, 25 Southampton Buildings, London, W.C.2, from which copies may be obtained.

