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PATENT SPECIFICATION

NO DRAWINGS

931,555

Date of Application and filing Complete Specification: Aug. 28, 1959.

No. 29490/59.

Application made in United States of America (No. 763,809) on Sept. 29, 1958.

Application made in United States of America (No. 826,493) on July 13, 1959.

Complete Specification Published: July 17, 1963.

Index at acceptance:—Class 2(3), C1E3K(3:6), C1E6K(3:6), C1G5(A:B), C1G6B(4:6), C1H2(A7:B:C2), B1Q(1A:4:6B2:6C:7A:8A:9B:9D2:11D:11J), C2A(3:5:9), C2B4(A2:A3:D:G3:M), C2R17, C2T16, C3A7V3(A2:E1:J3), C3A12A(3:4B), C3A12(B1:C5:C6), C3A13A3(A4:B1:C:K), C3A13C(1C:3C:9:10F:10H), C3(A16:C10).

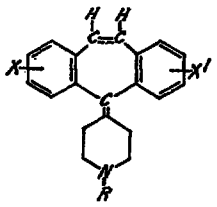
International Classification:—C07d.

COMPLETE SPECIFICATION

Dibenzocycloheptatriene Derivatives

We, MERCK & CO., INC., a corporation duly organised and existing under the laws of the State of New Jersey, United States of America, of Rahway, New Jersey, United States of America, 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:—

This invention is concerned with derivatives of dibenzo[a,e]cycloheptatriene, and provides compounds having the general formula:



Compound II

in which R is a hydrogen atom or a lower alkyl or alkenyl radical containing up to 4 carbon atoms which may be straight-chain or branched-chain.

When there is a double bond between the 10 and 11 Cs and when R is alkyl, the compounds may be designated as 1-alkyl-4-(5-dibenzo[a,e]cycloheptatrienylidene)-piperidines.

The alkyl or alkenyl radical R may be substituted, for example, with a hydroxy, a mesyloxy or an amino group. The presence of either a single bond or a double bond between the 10 and 11 carbon atoms is indicated by the dotted line. The numbering of the dibenzocycloheptatriene ring system conforms to the Ring Index, No. 2077.

The symbols X and X^1 represent a hydrogen or a halogen atom, particularly chlorine, bromine or fluorine, or a trifluoromethyl, C_{1-4} alkyl, C_{1-4} alkoxy or mononuclear aryl (e.g. phenyl) radical. The atoms or radicals X and X^1 may be similar or may be dissimilar and each benzene ring may have one or two of the aforementioned atoms or radicals attached to it.

One or more of the hydrogens in positions 2,3,5 and 6 of the piperidine ring may be replaced by alkyl groups so long as the total number of carbon atoms in all such substituent alkyl groups does not exceed four. The invention also includes the N-oxides of the compounds, which may be prepared from the bases by methods known for the preparation of N-oxides of bases.

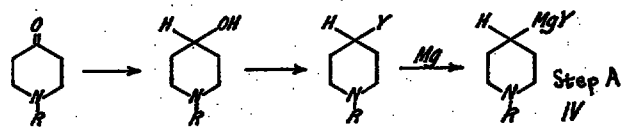
The compounds of the invention possess antiserotonin and antihistamine activity. They may be administered to persons in any of the usual pharmaceutical oral forms such as powders, capsules, tablets, elixirs and aqueous suspensions, in the amount of from 1 to 250 mg. per dose taken 2 to 4 times a day. For sterile solutions, for injection, from 0.1 to 50 mg. would be injected per dose 2 to 4 times a day. The compounds

may most easily be administered as a salt: a salt of any convenient non-toxic acid such as hydrochloric acid may be used for this purpose and these salts are considered to be equivalent to the bases.

To prepare the compounds of the invention, the known compound dibenzo[a,e]-cycloheptatrien-5-one and its 10,11-dihydro derivative are used as starting materials and they are herein referred to generically as dibenzo[a,e]cycloheptatrien-5-ones. The preparation of specific starting materials is referred to in the subsequent examples.

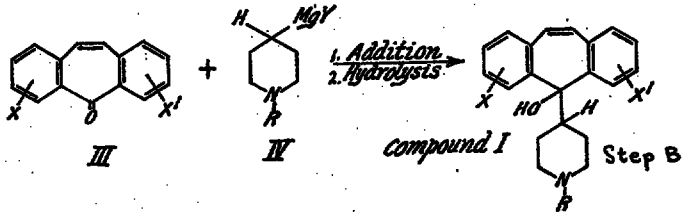
The selected dibenzo[a,e]cycloheptatrien-5-one (III) is condensed with a 1-alkyl-4-piperidylmagnesium halide (IV), desirably in a tetrahydrofuran solvent, the precautions usually taken to exclude air and moisture from the apparatus during Grignard reactions being observed. (See Step B hereinafter). This 1-alkyl-4-piperidyl-magnesium halide may be either the bromide or the chloride but is preferably the chloride.

The Grignard reagent may be prepared as follows: The selected 1-alkyl-4-piperidone is reduced to the carbinol by known methods. The 1-alkyl-4-piperidinol then may be converted to the 1-alkyl-4-chloropiperidine or to the 1-alkyl-4-bromopiperidine by known methods. The Grignard reagent is then prepared by combining the 1-alkyl-4-halopiperidine with magnesium, preferably using tetrahydrofuran as the solvent. Dry conditions should, as is usual, be maintained. This may be represented as follows:



in which Y is a halogen such as chlorine or bromine.

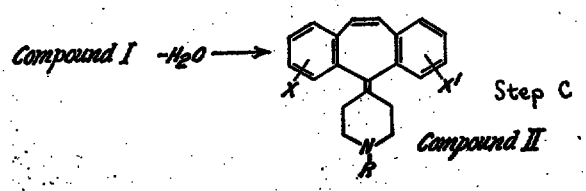
The Grignard reagent and the dibenzo[a,e]cycloheptatrien-5-one are combined according to the following equation:



The condensation reaction of Step B is preferably initially carried at low temperature, for example cooling by means of an ice-bath, and finally may continue at room temperature. It has been found that tetrahydrofuran is an excellent solvent for carrying out the reaction of Step B and the source of this may be the solution obtained in Step A. The dibenzo[a,e]cycloheptatrien-5-one can be added directly to the reaction mixture in which the Grignard reagent IV was prepared. However, any inert solvent for the reactants of Step B may be used.

After the reaction of Step B is completed the bulk of the solvent is removed by vacuum distillation, and the Grignard adduct is dissolved in benzene and hydrolysed by the addition of water or ammonium chloride solution with cooling. Compound I is recovered from the benzene solution. It should be noted that these 5-hydroxy compounds corresponding to the compounds of the present invention, and the above method for their preparation, are claimed in the specification of our copending application No. 7308/63 (Serial No. 931,556).

In accordance with the present invention, Compound I is dehydrated to produce Compound II, the compound of the present invention, as is represented by the following:



The dehydration of compound I may be effected by means of such commonly used dehydrating agents as acetyl chloride or acetic anhydride but preferably *o*-sulphobenzoic anhydride is used. The alcohol may be dehydrated directly or may be first converted to a salt such as hydrochloride, hydrobromide, or sulphate. Conversion to a salt prior to dehydration is preferable in some cases. The reaction may be carried out in an excess of dehydrating agent as solvent, or using a solvent such as chloroform or glacial acetic acid. The solvent then is removed by vacuum distillation and the compound II in the form of a salt is crystallized from a suitable solvent.

The following examples will further illustrate the invention.

EXAMPLE I

1-methyl-4-(5-dibenzo[a,e]cycloheptatrienylidene)-piperidine hydrochloride and 1-methyl-4-(5-dibenzo[a,e]cycloheptatrienylidene-piperidine

Step A. Preparation of 1-methyl-4-piperidylmagnesium chloride.

5.45 g. (0.22 g. atom) of magnesium turnings were placed in a 500 ml. 3-necked flask provided with a condenser, Hershberg stirrer and dropping funnel and protected with a drying tube. An atmosphere of dry nitrogen was maintained in the apparatus throughout the reaction. The magnesium was covered with 20 ml. of dry tetrahydrofuran. A crystal of iodine and 1.2 g. of ethyl bromide were added and after the reaction had subsided (formation of ethylmagnesium bromide) a solution of 29.4 g. (0.22 mole) of 4-chloro-1-methyl-piperidine in dry tetrahydrofuran (total volume, 103 ml.) was added dropwise at such a rate that gentle reflux was maintained. The solution of 4-chloro-1-methyl-piperidine in tetrahydrofuran was dried over calcium hydride at ice-bath temperature prior to use. When the addition of the halide was complete the reaction mixture was refluxed with stirring for 1 hour. In some subsequent experiments this period of refluxing was omitted with no deleterious result.

Step B. Preparation of 1-methyl-4-(5-hydroxy-5-dibenzo[a,e]cycloheptatrienyl)-piperidine.

The solution of the Grignard reagent prepared in Step A was cooled to 5 to 10°C. and stirred while 22.7 g. (0.11 mole) of dibenzo[a,e]cycloheptatrien-5-one was added in ~~proportions~~ portions. After stirring for 1 hour during which time the reaction mixture was allowed to warm up to room temperature, the bulk of the tetrahydrofuran was distilled at 40—50°C. under reduced pressure. 150 ml. of benzene was added and the reaction mixture stirred and cooled in an ice-bath while 100 ml. of water was added gradually. The benzene layer was separated by decantation and the gelatinous residue extracted three times with 75-ml. portions of boiling benzene. The solvent was evaporated from the combined benzene extracts to give 33.4 g. of a clear light brown resin. Crystallization from an alcohol-water mixture gave 19.5 g. of 1-methyl-4-(5-hydroxy-5-dibenzo-[a,e]cycloheptatrienyl)-piperidine, m.p. 156—157°C. Two recrystallizations from alcohol-water mixtures followed by two recrystallizations from benzene-hexane mixtures gave analytically pure product, m.p. 166.7—167.7°C.

Analysis Calc'd. for $C_{21}H_{23}NO$: C, 82.59; H, 7.59; N, 4.59.
Found: C, 82.39; H, 7.67; N, 4.54.

Step C. Preparation of 1-methyl-4-(5-dibenzo[a,e]cycloheptatrienylidene)piperidine hydrochloride.

3.05 g. (0.01 mole) of 1-methyl-4-(5-hydroxy-5-dibenzo[a,e]cycloheptatrienyl)-piperidine was dissolved in 15 ml. of glacial acetic acid. The solution was saturated with dry hydrogen chloride with external cooling. A white solid separated. 3.07 g. (0.03 mole) of acetic anhydride was added and the mixture heated on the steam-bath for 1 hour. The solid dissolved in the first 5 minutes of the heating period. The reaction mixture was poured into 25 ml. of water and the mixture made strongly alkaline with 10*N* sodium hydroxide solution. The mixture was extracted three times with 50-ml. portions of benzene, the combined extracts were washed with water and concentrated to a volume of approximately 50 ml. The solution was saturated with dry hydrogen chloride and the white crystalline product collected and dried. The yield of product, m.p. 251.6—252.6°C. (dec.) was 2.5 g. Recrystallization from a mixture of absolute alcohol and absolute ether gave product, m.p. 252.6—253.6°C. A sample was analysed after drying for 7 hours at 110° over phosphorus pentoxide *in vacuo*.

Analysis Calc'd. for $C_{21}H_{21}N.HCl$: C, 77.88; H, 6.85; N, 4.33.
Found: C, 77.60; H, 6.80; N, 4.31.

Step D. Preparation of 1-methyl-4-(5-dibenzo[a,e]cycloheptatrienylidine)-piperidine.

4.3 g. of the hydrochloride salt was suspended in 100 ml. of warm water and the mixture made strongly alkaline by the addition of 15 ml. of 5% sodium hydroxide. The mixture was extracted with four 50-ml. portions of benzene and the extract dried over sodium sulphate. Evaporation of the benzene on the steam-bath at reduced pressure left 3.7 g. (97%) of the base, m.p., 110.3—111.3° C. Recrystallization from a mixture of alcohol and water gave product, m.p. 112.3—113.3°C.

Analysis Calc'd. for $C_{21}H_{21}N$: C, 87.76; H, 7.37; N, 4.88.
Found: C, 87.77; H, 7.47; N, 4.87.

EXAMPLE Ia

1-methyl-4(5-dibenzo[a,e]cycloheptatrienylidene)-piperidine hydrochloride hydrate

0.400 g. (0.00139 mole) of 1-methyl-4-(5-dibenzo[a,e]cycloheptatrienylidene)-piperidine, obtained as in Example I, was dissolved in 55 ml. of 1*N* hydrochloric acid at the boiling point. The solution was allowed to cool to room temperature and to stand for 24 hours. The crystalline product was collected and dried in a vacuum desiccator over concentrated sulphuric acid and soda-lime for 6 hours. The product then was pulverized and dried over calcium chloride and soda lime at 0.1 mm. for approximately 65 hours. The yield of dried product was 0.420 g. In a melting point determination, this substance sintered at 180°C. and melted at 214—216°C. when heated at a rate of 6° per minute ~~form~~ from 180°C.

Analysis Calc'd. for $C_{21}H_{21}N.HCl.H_2O$: C, 73.76; H, 7.08; N, 4.10; Cl, 10.37.
Found: C, 73.69; H, 7.31; N, 4.19; Cl, 10.36.

EXAMPLE Ib

1-methyl-4-(5-dibenzo[a,e]cycloheptatrienylidene)-piperidine hydrogen maleate

0.400 g. (0.00139 mole) of methyl-4-(5-dibenzo[a,e]cycloheptatrienylidene)-piperidine as obtained in Example I, was dissolved in 8 ml. of absolute alcohol. A solution of 0.170 g. (0.00147 mole) of maleic acid in 4 ml. of absolute alcohol was added and the resulting solution diluted to incipient crystallization with absolute ether. The product melted at 187—188°C. It was recrystallized from a mixture of isopropyl alcohol and ether with no change in melting point.

Analysis Calc'd. for $C_{21}H_{21}N.C_4H_4O_4$: C, 74.41; H, 6.25; N, 3.47.
Found: C, 74.17; H, 6.31; N, 3.64.

EXAMPLE II

1-isopropyl-4-(5-dibenzo[a,e]cycloheptatrienylidene-piperidine

Step A. Preparation of 1-isopropyl-4-piperidylmagnesium chloride.

By substituting an equimolecular quantity of 4-chloro-1-isopropylpiperidine for the 4-chloro-1-methyl-piperidine of Example 1, Step A and following substantially the procedure of Example 1, Step A, a solution of 1-isopropyl-4-piperidylmagnesium chloride in tetrahydrofuran is obtained.

Step. B. Preparation of 1-isopropyl-4-(5-hydroxy-5-dibenzo[a,e]cycloheptatrineyl)-piperidine.

Dibenzo[a,e]cycloheptatriene-5-one is added to the solution of the Grignard reagent obtained in Step A, and the product isolated as described in Example 1, Step B.

Step C. Preparation of 1-isopropyl-4-(5-dibenzo[a,e]cycloheptatrienylidene)-piperidine.

The 1-isopropyl-4-(5-hydroxy-5-dibenzo[a,e]cycloheptatrienyl)-piperidine obtained in Step B is dehydrated as described in Example I, step C, to give 1-isopropyl-4-(5-dibenzo[a,e]cycloheptatrienylidene)-piperidine, which is isolated in the form of the hydrochloride salt.

EXAMPLE III

1-butyl-4-(5-dibenzo[a,e]cycloheptatrienylidene)-piperidine

Step A. Preparation of 1-butyl-4-piperidylmagnesium chloride.

By substituting an equimolecular quantity of 4-chloro-1-butylpiperidine for the 4-chloro-1-methylpiperidine of Example I Step A and following substantially the procedure of Example I, Step A a solution of 1-butyl-4-piperidylmagnesium chloride in tetrahydrofuran is obtained.

Step B. Preparation of 1-butyl-4-(5-hydroxy-5-dibenzo-[a,e]cycloheptatrienyl)-piperidine.

Dibenzo[a,e]cycloheptatrien-5-one is added to the solution of the Grignard reagent obtained in Step A and the product isolated as described in Example I, step B.

Step C. Preparation of 1-butyl-4-(5-dibenzo[a,e]cycloheptatrienylidene)-piperidine.

The 1-butyl-4-(5-hydroxy-5-dibenzo[a,e]cycloheptatrienyl)-piperidine obtained in Step B is dehydrated as described in Example I step C to give 1-butyl-4-(5-dibenzo[a,e]cycloheptatrienylidene)-piperidine, which is isolated in the form of the hydrochloride salt.

EXAMPLE IV

1-Methyl-4-(5-dibenzo[a,e]cycloheptatrienylidene)-piperidine N-oxide

A solution of 3.0 g. (0.0104 mole) of 1-methyl-4-(5-dibenzo[a,e]cycloheptatrienylidene)-piperidine in 30 ml. of absolute methanol was stirred and cooled in an ice-bath while 3.5 g. of 30% hydrogen peroxide was added dropwise over a 5-minute period. A colourless solid separated while the mixture was being stirred in the cold. After 15 minutes the ice-bath was removed and stirring was continued for 3 hours at room temperature. During this period the solid dissolved to give a clear pale-yellow solution. After 22 hours the solution was cooled in an ice-bath and treated with an aqueous suspension of platinum black. After stirring for 1 hour at room temperature a test for peroxide was negative and the mixture was filtered through a mat of diatomaceous earth. The solvent then was evaporated under reduced pressure keeping the temperature below 35°C. The residue, a glass-like resin, was pulverized. It became partially crystalline on further drying. After additional drying over phosphorus pentoxide at 0.1 mm. pressure the product gave elementary analyses agreeing well with the values calculated for the hemihydrate.

Analysis Calc'd for $C_{21}H_{21}No.\frac{1}{2}H_2O$: C, 80.71; H, 7.10; N, 4.48.
Found: C, 80.77; H, 7.36; N, 4.58.

A sample from another experiment that was subjected to further drying gave the following analyses:

Anal. Calc'd for $C_{21}H_{21}NO$: C, 83.00; H, 6.97; N, 4.61.
Found: C, 82.58; H, 7.37; N, 4.59.

EXAMPLE V

1-methyl-4-(10,11-dihydro-5-dibenzo[a,e]cycloheptatrienylidene-piperidine hydrochloride

Step A. Preparation of 1-methyl-4-piperidylmagnesium chloride.

The Grignard reagent was prepared from 2.27 g. (0.0921 g. atom) of magnesium and 12.3 g. (0.0921 mole) of 1-methyl-4-piperidyl chloride in approximately 85 ml. of tetrahydrofuran, following the procedure of Example 1, Step A.

Step B. Preparation of 1-methyl-4-(10,11-dihydro-5-hydroxy-5-dibenzo[a,e]cycloheptatrienyl)-piperidine.

9.58 g. (0.046 mole) of 10,11-dihydrodibenzo[a,e]cycloheptatrien-5-one was added to the Grignard solution of step A and the product was isolated substantially as described in Example I, Step B. The 1-methyl-4-(10,11-dihydro-5-hydroxy-5-dibenzo[a,e]cycloheptatrienyl)-piperidine, m.p. 179—181°C. weighed 8.3 g. (59%) after recrystallization from a mixture of alcohol and water. A further recrystallization gave product m.p. 180—181°C.

Anal. Calc'd. for $C_{21}H_{25}NO$: C, 82.04; H, 8.20; N, 4.56.
Found: C, 81.79; H, 7.93; N, 4.64.

Step C. Preparation of 1-methyl-4-(10,11-dihydro-5-dibenzo[a,e]cycloheptatrienylidene)-piperidine hydrochloride.

6.3 g. (0.0205 mole) of 1-methyl-4-(10,11-dihydro-5-hydroxy-5-dibenzo[a,e]cycloheptatrienyl)-piperidine was dehydrated following substantially the procedure of Example I, step C. The hydrochloride of 1-methyl-4-(10,11-dihydro-5-dibenzo[a,e]cycloheptatrienylidene)-piperidine was obtained in a yield of 5.89 g. (99%), m.p. 273—274°C. (with decomposition). Recrystallization from a mixture of isopropyl alcohol and ether did not change the m.p.

Anal. Calc'd. for $C_{21}H_{23}N.HCl$: C, 77.40; H, 7.42; N, 4.29; Cl, 10.88.
Found: C, 77.23; H, 7.46; N, 4.45; Cl. 10.76.

EXAMPLE VI

1-methyl-4-(3-chloro-5-dibenzo[a,e]cycloheptatrienylidene)-piperidine hydrogen maleate

Step A. Preparation of 1-methyl-4-piperidylmagnesium chloride.

The Grignard reagent was prepared from 2.43 g. (0.1 g. atom) of magnesium and 13.36 g. (0.1 mole) of 1-methyl-4-chloropiperidine in approximately 90 ml. of tetrahydrofuran, following the procedure of Example 1, Step A and omitting the final period of heating.

Step. B. Preparation of 1-methyl-4-(3-chloro-5-hydroxy-5-dibenzo[a,e]cyclohepta-trienyl)-piperidine.

The solution of the Grignard reagent prepared in Step A was cooled to 5—10°C. and stirred at this temperature while 3-chlorodibenzo[a,e]cycloheptatrien-5-one (12.03 g., 0.05 mole) was added. The product was isolated essentially as described in Example I, ~~Step~~ B. The yield of product, m.p. 94.5—95.5°C. was 9.6 g. (54%). Recrystallization from a mixture of alcohol and water raised the m.p. to 95—97°C. After a second recrystallization the m.p. was increased to 199—200°C. The yield of this material was 5.4 g. (32%). A further recrystallization from a mixture of alcohol and water followed by a recrystallization from benzene and hexane did not change the m.p.

Anal. Calc'd. for $C_{21}H_{22}ClNO$: C, 74.21; H, 6.53; N, 4.12.
Found: C, 73.90; H, 6.39; N, 4.01.

The 3-chlorodibenzo[a,e]cycloheptatrien-5-one employed in Step B was prepared by the following sequence. 3-(β-Chlorobenzylidene)-phthalide was prepared from *p*-chlorophenylacetic acid and phthalic anhydride following essentially the known method for the preparation of benzalphthalide described in Organic Syntheses Collective Volume II, page 61 (John Wiley and Sons, 1948). The 3-*p*-chlorobenzylidene)-phthalide was reduced to 2-(*p*-chlorophenethyl)-benzoic acid with phosphorus and hydriodic acid, essentially as described by A. G. Cope and S. W. Fenton [J. Am. Chem. Soc. *73*, 1673 (1951)] for the reduction of benzalphthalide. The cyclization of 2-(*p*-chlorophenethyl)-benzoic acid to 3-chloro-10,11-dihydrodibenzocycloheptatrien-5-one was accomplished by heating with polyphosphoric acid substantially as described by T. W. Campbell, R. Ginsig and H. Schmid, Helv. Chim. Acta, *36* 1489 (1953). The 3-chloro-10,11-dihydrodibenzocycloheptatrien-5-one was brominated with N-bromosuccinimide and converted to 3-chlorodibenzo[a,e]cycloheptatrien-5-one essentially as described by Cope and Fenton [J. Am. Chem. Soc. *73*, 1673 (1951)].

Step. C. Preparation of 1-methyl-4-(3-chloro-5-dibenzo[a,e]cycloheptatrienylidene)-piperidine hydrogen maleate.

0.65 g. (0.00192 mole) of 1-methyl-4-(3-chloro-5-hydroxy-5-dibenzo[a,e]cyclo-heptatrienyl)-piperidine and 3.68 g. (0.02 mole) of *o*-sulphobenzoic anhydride were mixed and heated to 135—140°C. for 90 minutes. The solid that formed on cooling was ground up and mixed with water. The mixture was made strongly alkaline and extracted with benzene. After washing with water the benzene was evaporated on the steam-bath under reduced pressure. The residue, a clear brown gum, was dissolved in benzene and the solution diluted with hexane. A small quantity of an insoluble solid was separated by filtration and the solvent evaporated. The clear light-yellow residue weighed 0.16 g. It was dissolved in 15 ml. of absolute ether and treated with a solution of 0.064 g. of maleic acid in 3 ml. of absolute alcohol. The white crystalline product, m.p. 197—198°C. weighed 0.08 g. Recrystallization from a mixture of alcohol and ether did not change the m.p.

Anal. Calc'd. for $C_{21}H_{20}ClN.C_4H_4O_4$: C, 68.57; H, 5.52; N, 3.20; Cl, 8.10.
Found: C, 68.39; H, 5.47; N, 3.27; Cl, 7.91.

EXAMPLE VII

4-(5-dibenzo[a,e]cycloheptatrienylidene)-piperidine

Step A. Preparation of 1-cyano-4-(5-dibenzo[a,e]cycloheptatrienylidene)-piperidine.

A solution of 8.9 g. (0.031 mole) of 1-methyl-4-(5-dibenzo[a,e]cycloheptatrienyl-idene)-piperidine in 20 ml. of dry benzene was added dropwise to a stirred solution of 3.6 g. (0.034 mole) of cyanogen bromide in 15 ml. of benzene at room temperature. When approximately half of the solution had been added a white solid began to separate. When the addition was complete, 15 ml. of benzene was added to facilitate stirring and the mixture stirred for 75 minutes, then allowed to stand overnight. After the addition of 50 ml. of absolute ether the product was collected and recrystallized from

a mixture of acetone and absolute alcohol. The yield of product, m.p. 203—205°C. was 6.18 g. (67%).

An analytical sample, prepared by recrystallizing the product from a similar experiment from acetone and subsequently from ethyl acetate, melted at 203.5—204.5°C.

Anal. Calc'd. for $C_{21}H_{18}N_2$: C, 84.53; H, 6.08; N, 9.39.
Found: C, 84.62; H, 6.30; N, 9.58.

Step B. Preparation of 4-(5-dibenzo[a,e]cycloheptatrienylidene)-piperidine hydrochloride.

6.18 g. (0.0206 mole) of 1-cyano-4-(5-dibenzo[a,e]cycloheptatrienylidene)-piperidine was heated to refluxing in a mixture of 150 ml. of glacial acetic acid, 100 ml. of water and 15 ml. of concentrated hydrochloric acid for 16 hours. The solution was concentrated until solid began to separate (volume approximately 150 ml.) and diluted with 100 ml. of water. The white crystalline product was collected and dried at 65°C. The yield of product, m.p. 290—292°C. (with decomposition) was 5.8 g. (91%).

Anal. Calc'd. for $C_{20}H_{19}N.HCl$: C, 77.53; H, 6.51; N, 4.52.
Found: C, 77.46; H, 6.51; N, 4.54.

Step. C. Preparation of 4-(5-dibenzo[a,e]cycloheptatrienylidene)-piperidine.

The hydrochloride of 4-(5-dibenzo[a,e]cycloheptatrienylidene)-piperidine was converted to the base by suspending it in water, adding benzene and an excess of sodium hydroxide, and shaking the mixture till the solid dissolved. Evaporation of the benzene left the crystalline base that was purified by recrystallization from a mixture of alcohol and water, followed by recrystallization from a mixture of benzene and hexane.

Anal. Calc'd. for $C_{20}H_{19}N$: C, 87.87; H, 7.01; N, 5.12.
Found: C, 88.13; H, 7.05; N, 5.09.

Example VIII

1-Ethyl-4-(5-dibenzo[a,e]cycloheptatrienylidene)-piperidine hydrogen maleate

1.093 g. (0.004 mole) of 4-(5-dibenzo[a,e]cycloheptatrienylidene)-piperidine was dissolved in 25 ml. of dry *t*-butyl alcohol. 4.5 ml. of a 0.97 molar solution of potassium *t*-butoxide in *t*-butyl alcohol was added followed by 0.624 g. (0.004 mole) of ethyl iodide. The solution was allowed to stand at room temperature for 20 hours and then heated on the steam bath for 2 hours. In order to remove unreacted starting material, 0.5 ml. of ethyl chlorocarbonate and 0.5 ml. of pyridine were added to the cooled solution which was then stirred 30 minutes at room temperature, heated on the steam-bath for 15 minutes, cooled and treated with 10 ml. of water followed by 10 ml. of 1.25*N* sodium hydroxide solution. Benzene was added and the benzene extract separated and washed with water. The basic material was extracted into 200 ml. of 0.05 molar citric acid solution. The acidic extract then was made basic and the basic material extracted into benzene. Evaporation of the benzene and drying the residue on the steam-bath under reduced pressure gave 0.48 g. of a viscous yellow oil that was dissolved in 95% ethanol and added to a solution of 0.203 g. of maleic acid in 95% ethanol. The solution was concentrated and diluted with ether. The white crystalline product, m.p. 202.5—203.5°C. weighed 0.57 g. Further recrystallization from mixtures of alcohol and ether gave material melting at 203.5—204.5°C.

Anal. Calc'd. for $C_{22}H_{23}N.C_4H_4O_4$: C, 74.80; H, 6.52; N, 3.36.
Found: C, 74.59; H, 6.54; N, 3.44.

Example IX

1-propyl-4-(5-dibenzo[a,e]cycloheptatrienylidene)-piperidine hydrogen maleate

5.47 g. (0.02 mole) of 4-(5-dibenzo[a,e]cycloheptatrienylidene)-piperidine and 0.78 g. (0.02 mole) of sodamide were heated to refluxing in 50 ml. of toluene for 15 hours. The light brown turbid solution was cooled to room temperature and 3.40 g. (0.02 mole) of *n*-propyl iodide was added. The mixture was stirred at room temperature for 1 hour during which time a flocculent light-brown precipitate separated. The mixture then was heated on the steam-bath for 1 hour and finally at reflux for 30 minutes. After cooling to room temperature, 50 ml. of water was added to the reaction mixture which was then diluted with 200 ml. of hexane. The aqueous layer was separated and the organic layer washed with additional portions of water. After standing for 10 days at room temperature the solution had deposited some prismatic crystals that were separated by filtration. The solution then was concentrated to a volume of approximately 25 ml. In order to remove unreacted starting material, 4.70 g. (0.05 mole) of maleic anhydride in 35 ml. of benzene was added and the solution refluxed for 20 minutes.

5 ml. of methanol was then added to destroy the excess of maleic anhydride and the solution was concentrated to a volume of approximately 25 ml., and transferred to a separatory funnel. 200 ml. of hexane, 200 ml. of water, and 14.9 g. (0.1 mole) of triethanolamine were added and the mixture shaken. After the separation was complete the clear yellow organic layer was separated and washed with water. Evaporation of the solvent and drying the residue on the steam-bath under reduced pressure gave 4.42 g. of a clear light-brown residue. This material was dissolved in absolute alcohol and treated with a solution of 1.79 g. (0.0154 mole) of maleic acid in absolute alcohol. The hydrogen maleate of 1-propyl-4-(5-dibenzo[a,e]cycloheptatrienylidene)-piperidine, m.p. 214—215°C. weighed 5.42 g. Recrystallization from *n*-propyl alcohol gave product m.p. 214—216°C. (sintered at 213°C.).

Anal. Calc'd. for $C_{23}H_{25}N.C_4H_4O_4$: C, 75.15; H, 6.77; N, 3.25.
Found: C, 75.34; H, 6.86; N, 3.23.

EXAMPLE X

1-allyl-4-(5-dibenzo[a,e]cycloheptatrienylidene)-piperidine hydrogen maleate

The procedure of Example IX was followed, substituting 2.42 g. (0.02 mole) of allyl bromide for the *n*-propyl iodide. The product was isolated by substantially the same procedure. The product melted at 175—177°C. after recrystallization from a mixture of alcohol and ether followed by recrystallization from *n*-propyl alcohol.

Anal. Calc'd. for $C_{23}H_{23}N.C_4H_4O_4$: C, 75.50; H, 6.34; N, 3.26.
Found: C, 75.21; H, 6.42; N, 3.28.

EXAMPLE XI

1-(2-hydroxyethyl)-4-(5-dibenzo[a,e]cycloheptatrienylidene)-piperidine

5.47 g. (0.02 mole) of 4-(5-dibenzo[a,e]cycloheptatrienylidene)-piperidine was dissolved in 109 ml. of 95% ethanol. The solution was cooled to 0°C. and ethylene oxide was passed in until the gain in weight was 1.76 g. The container was then stoppered and heated to 65—70°C. in an autoclave for 1 hour. The solvent was then distilled and the last traces of alcohol and water removed by azeotropic distillation with benzene. The crystalline residue was extracted with boiling hexane and recrystallized from a mixture of benzene and hexane. Further recrystallization from mixtures of alcohol and water gave product, m.p. 158—159°C.

Anal. Calc'd. for $C_{22}H_{23}NO$: C, 83,24; H, 7.30; N, 4.41.
Found: C, 83.00; H, 7.29; N, 4.38.

EXAMPLE XII

1-(2-mesyloxyethyl)-4-(5-dibenzo[a,e]cycloheptatrienylidene)-piperidine hydrochloride

2.10 g. (0.00662 mole) of 1-(2-hydroxyethyl)-4-(5-dibenzo[a,e]cycloheptatrienylidene)-piperidine was dissolved in 100 ml. of dry acetonitrile. A solution of 1.22 g. (0.007 mole) of methane-sulphonic anhydride in 4 ml. of acetonitrile was added and the solution allowed to stand at room temperature for 48 hours. Some crystals that had been deposited were separated by decantation and approximately 50 ml. of acetonitrile was distilled at 35—45°C. under reduced pressure. After 3 days in the refrigerator the solution was filtered to remove the solid that had separated and the solvent evaporated at 25—35°C. under reduced pressure. The syrupy residue, the methanesulphonic acid salt of the product, weighed 3.32 g. It was dissolved in 13 ml. of absolute alcohol and treated with 0.84 ml. of an 8.9*N* solution of dry hydrogen chloride in absolute alcohol. Absolute ether was added portionwise to precipitate the hydrochloride. The product was recrystallized by dissolving it in absolute methanol, warming the solution in a bath at 30°C. and cautiously adding ether to incipient turbidity. The product melted at 130.5°—134°C. with effervescence.

Anal. Calc'd. for $C_{23}H_{25}O_3NS:HCl$: C, 63.95; H, 6.07; Cl, 8.21; N, 3.24; S, 7.42.
Found: C, 64.47; H, 6.22; Cl, 8.02; N, 3.24; S, 7.35.

EXAMPLE XIII

1-(β-dimethylaminoethyl)-4-(5-dibenzo[a,e]cycloheptatrienylidene)-piperidine dihydrogen dimaleate

5.47 g. (0.02 mole) of 4-(5-dibenzo[a,e]cycloheptatrienylidene)-piperidine and 1.64 g. (0.042 mole) of sodamide were heated to refluxing in 50 ml. of toluene for 3 hours. 3.17 g. (0.022 mole) of β-dimethylaminoethyl chloride hydrochloride was added to the warm solution. Stirring and refluxing then were resumed and were continued for 12 hours. The reaction mixture was then filtered and the solvent evaporated on the steam-bath under reduced pressure. The residue contained a white crystalline solid.

It was taken up in ether and shaken with water till the solid dissolved. The ether layer then was separated, washed with water and evaporated. The residue, a clear dark brown resin, weighed 6.31 g. It was dissolved in 25 ml. of benzene and treated with a solution of 4.70 g. (0.05 mole) of maleic anhydride in 50 ml. of benzene. The dark-brown solution was refluxed on the steam-bath for 20 minutes. The warm mixture was then treated with 5 ml. of absolute methanol. The dark brown solution was decanted from a black tarry solid that had separated. The solid was shaken with a solution of 6 g. (0.15 mole) of sodium hydroxide in 100 ml. of water. Nearly all the black solid dissolved. This solution was added to the benzene layer. A heavy emulsion resulted. 100 ml. of water and 100 ml. of benzene were added without effecting a separation. 100 ml. of ether was added. A clear yellow organic phase separated and a tan precipitate collected in the aqueous layer. The organic layer was separated and the aqueous layer filtered. The precipitate dissolved readily in water. This solution was extracted with ether and the extract combined with the organic layer. The combined organic layers were then washed with water. Evaporation of the solvent and drying the residue on the steam-bath under reduced pressure left 3.35 g. of residue. The residue was dissolved in absolute alcohol and treated with a solution of 2.48 g. (0.021 mole) of maleic acid in absolute alcohol. The product separated as a white crystalline solid, m.p. 192—193°C. (sintered at 190°C.) in a yield of 4.29 g. Recrystallization from absolute alcohol raised the m.p. to 193—194.5°C.

Anal. Calc'd. for $C_{24}H_{28}N_2.2C_4H_4O_4$: C, 66.65; H, 6.29; N, 4.86.
Found: C, 66.51; H, 6.26; N, 4.80.

EXAMPLE XIV

1-methyl-4-(3-methoxy-5-dibenzo[a,e]cycloheptatrienylidene)-piperidine hydrogen maleate

By substituting 3-methoxydibenzo[a,e]cycloheptatrien-5-one for the 3-chlorodibenzo[a,e]cycloheptatrien-5-one of Example VI and following substantially the method of Example VI, 1-methyl-4-(3-methoxy-5-dibenzo[a,e]cycloheptatrienylidene)-piperidine hydrogen maleate is obtained.

The 3-methoxydibenzo[a,e]cycloheptatrien-5-one is obtained by the sequence used for the preparation of 3-chlorodibenzo[a,e]cycloheptatrien-5-one except that 3-(*p*-methoxybenzylidene)-phthalide is reduced to 2-(*p*-methoxyphenethyl)-benzoic acid.

EXAMPLE XV

1-Methyl-4-(3-fluoro-5-dibenzo[a,e]cycloheptatrienylidene)-piperidine hydrogen maleate

By substituting 3-fluorodibenzo[a,e]cycloheptatrien-5-one for the 3-chlorodibenzo[a,e]cycloheptatrien-5-one of Example VI and following substantially the method of Example VI, 1-methyl-4-(3-fluoro-5-dibenzo[a,e]cycloheptatrienylidene)-piperidine hydrogen maleate is obtained.

The 3-fluorodibenzo[a,e]cycloheptatrien-5-one is obtained by the sequence used for the preparation of 3-chlorodibenzo[a,e]cycloheptatrien-5-one.

EXAMPLE XVI

1-Methyl-4-(1-bromo-5-dibenzo[a,e]cycloheptatrienylidene)-piperidine hydrogen maleate

By substituting 1-bromodibenzo[a,e]cycloheptatrien-5-one for the 3-chlorodibenzo[a,e]cycloheptatrien-5-one of Example VI and following substantially the method of Example VI, 1-methyl-4-(1-bromo-5-dibenzo[a,e]cycloheptatrienylidene)-piperidine hydrogen maleate is obtained.

The 1-bromodibenzo[a,e]cycloheptatrien-5-one is prepared from 2-(*o*-bromophenethyl)-aniline by the following procedure. The amino group is replaced by cyano, by means of the Sandmeyer reaction. Hydrolysis of this nitrile gives 2-(*o*-bromophenethyl)-benzoic acid, which is converted to 1-bromodibenzo[a,e]cycloheptatrien-5-one by the same sequence used for the preparation of 3-chlorodibenzo[a,e]cycloheptatrien-5-one.

EXAMPLE XVII

1-methyl-4-(3,7-dichloro-5-dibenzo[a,e]cycloheptatrienylidene)-piperidine

By substituting 3,7-dichlorodibenzo[a,e]cycloheptatrien-5-one for the 3-chlorodibenzo[a,e]cycloheptatrien-5-one of Example VI and following substantially the method of Example VI, 1-methyl-4-(3,7-dichloro-5-dibenzo[a,e]cycloheptatrienylidene)-piperidine is obtained.

The 3,7-dichlorodibenzo[a,e]cycloheptatrien-5-one is prepared from 3,7-dinitro-

dibenzo[a,e]cycloheptatrien-5-one by reducing the nitro groups to amino and replacing the amino groups by chlorine, employing the Sandmeyer reaction. The dinitrodibenzocycloheptatrienone is prepared by known methods.

EXAMPLE XVIII

1-methyl-4-(4-methyl-10,11-dihydro-5-dibenzo[a,e]cycloheptatrienylidene)-piperidine hydrogen maleate

By substituting 4-methyl-10,11-dihydrodibenzo[a,e]cycloheptatrien-5-one for the 10,11-dihydrodibenzo[a,e]cycloheptatrien-5-one of Example V and following substantially the same procedure as that of Example V, 1-methyl-4-(4-methyl-10,11-dihydro-5-dibenzo[a,e]cycloheptatrienylidene)-piperidine is obtained. The product is isolated as the hydrogen maleate salt.

The 4-methyl-10,11-dihydro-5-dibenzo[a,e]cycloheptatrien-5-one is prepared by the cyclization of 2-methyl-6-phenethylbenzoic acid with polyphosphoric acid under the conditions for the cyclization of 2-phenethylbenzoic acid.

EXAMPLE XIX

1-Methyl-4-(10,11-dihydro-2,3-dimethyl-7-isopropyl-5-dibenzo[a,e]cycloheptatrienylidene)-piperidine hydrochloride

By substituting 10,11-dihydro-2,3-dimethyl-7-isopropyldibenzo[a,e]cycloheptatrien-5-one for the 10,11-dihydro-dibenzo[a,e]cycloheptatrien-5-one of Example V and following substantially the same procedure as that of Example V, 1-methyl-4-(10,11-dihydro-2,3-dimethyl-7-isopropyl-5-dibenzo[a,e]cycloheptatrienylidene)-piperidine hydrochloride is obtained.

The 10,11-dihydro-2,3-dimethyl-7-isopropyl-dibenzo[a,e]cycloheptatrien-5-one is prepared by the following sequence. 4,5-Dimethylphthalic anhydride is condensed with *p*-isopropylphenyl-acetic acid to give 3-(*p*-isopropylbenzylidene)phthalide. Reduction with phosphorus and hydroiodic acid gives 2-(*p*-isopropylphenethyl)-4,5-dimethylbenzoic acid. The acid is cyclized to the desired ketone by the action of polyphosphoric acid.

EXAMPLE XX

1-Methyl-4-(10.11)-dihydro-2,3-dichloro-7-methyl-5-dibenzo[a,e]cycloheptatrienylidene)-piperidine hydrochloride

By substituting 10,11-dihydro-2,3-dichloro-7-methyl-dibenzo[a,e]cycloheptatrien-5-one for the 10,11-dihydrodibenzo[a,e]cycloheptatrien-5-one of Example V and following substantially the same procedure as that of Example V, 1-methyl-4-(10,11-dihydro-2,3-dichloro-7-methyl-5-dibenzo[a,e]cycloheptatrienylidene)-piperidine hydrochloride is obtained.

The 10,11-dihydro-2,3-dichloro-7-methyldibenzo[a,e]cycloheptatrien-5-one is prepared by the sequence of reactions for the preparation of 10,11-dihydro-2,3-dimethyl-7-isopropyl-dibenzo[a,e]cycloheptatrien-5-one described in Example XIX, using 4,5-dichlorophthalic anhydride and *p*-methylphenylacetic acid as starting materials.

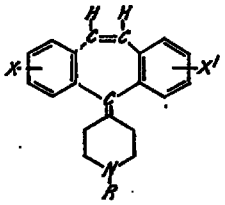
The following compounds can also be obtained in accordance with the present invention by processes analogous to those set forth above:

1-methyl-4(3-trifluoromethyl-5-dibenzo[a,e]cycloheptatrienylidine)piperidine;
1,3-dimethyl-4(3-trifluoromethyl-5-dibenzo[a,e]cycloheptatrienylidine)piperidine;
1,2-dimethyl-4(3-trifluoromethyl-5-dibenzo[a,e]cycloheptatrienylidine)piperidine;
1-methyl-2-ethyl-4(3-trifluoromethyl-5-dibenzo[a,e]cycloheptatrienylidine)piperidine;
1,2,6-trimethyl-4(3-trifluoromethyl-5-dibenzo[a,e]cycloheptatrienylidine)piperidine;
1-methyl-4(2-trifluoromethyl-5-dibenzo[a,e]cycloheptatrienylidine)piperidine;
1,3-dimethyl-4(2-trifluoromethyl-5-dibenzo[a,e]cycloheptatrienylidine)piperidine;
1,2-dimethyl-4(2-trifluoromethyl-5-dibenzo[a,e]cycloheptatrienylidine)piperidine;
1-methyl-2-ethyl-4(2-trifluoromethyl-5-dibenzo[a,e]cycloheptatrienylidine)piperidine;
1,2,6-trimethyl-4(2-trifluoromethyl-5-dibenzo[a,e]cycloheptatrienylidine)piperidine;
1-methyl-4(3-phenyl-5-dibenzo[a,e]cycloheptatrienylidine)piperidine;
1,3-dimethyl-4(3-phenyl-5-dibenzo[a,e]cycloheptatrienylidine)piperidine;
1,2-dimethyl-4(3-phenyl-5-dibenzo[a,e]cycloheptatrienylidine)piperidine;
1-methyl-2-ethyl-4(3-phenyl-5-dibenzo[a,e]cycloheptatrienylidine)piperidine;
1,2,6-trimethyl-4(3-phenyl-5-dibenzo[a,e]cycloheptatrienylidine)piperidine;
1-methyl-4(3-*p*-tolyl-5-dibenzo[a,e]cycloheptatrienylidine)piperidine;
1,3-dimethyl-4(3-*p*-tolyl-5-dibenzo[a,e]cycloheptatrienylidine)piperidine;
1,2-dimethyl-4(3-*p*-tolyl-5-dibenzo[a,e]cycloheptatrienylidine)piperidine;
1-methyl-2-ethyl-4(3-*p*-tolyl-5-dibenzo[a,e]cycloheptatrienylidine)piperidine;
1,2,6-trimethyl-4(3-*p*-tolyl-5-dibenzo[a,e]cycloheptatrienylidine)piperidine;

1 - methyl - 4(3 - trifluoromethyl - 10,11 - dihydro - 5 - dibenzo[a,e]cyclohepta-trienylidine)piperidine;
1,3 - dimethyl - 4(3 - trifluoromethyl - 10,11 - dihydro - 5 - dibenzo[a,e]cyclohepta-trienylidine)piperidine;
1,2 - dimethyl - 4(3 - trifluoromethyl - 10,11 - dihydro - 5 - dibenzo[a,e]cyclohepta-trienylidine)piperidine;
1 - methyl - 2 - ethyl - 4(3 - trifluoromethyl - 10,11 - dihydro - 5 - dibenzo[a,e]-cycloheptatrienylidine)piperidine;
1,2,6 - trimethyl - 4(3 - trifluoromethyl - 10,11 - dihydro - 5 - dibenzo[a,e]cyclo-heptatrienylidine)piperidine;
1-methyl-4(3-phenyl-10,11-dihydro-5-dibenzo[a,e]cycloheptatrienylidine)piperidine;
1,3 - dimethyl - 4(3 - phenyl - 10,11 - dihydro - 5 - dibenzo[a,e]cycloheptatrienyl-idine)piperidine;
1,2 - dimethyl - 4(3 - phenyl - 10,11 - dihydro - 5 - dibenzo[a,e]cycloheptatrienyl-idine)piperidine;
1 - methyl - 2 - ethyl - 4(3 - phenyl - 10,11 - dihydro - 5 - dibenzo[a,e]cyclohepta-trienylidine)piperidine;
1,2,6 - trimethyl - 4(3 - phenyl - 10,11 - dihydro - 5 - dibenzo[a,e]cycloheptatrienyl-idine)piperidine;

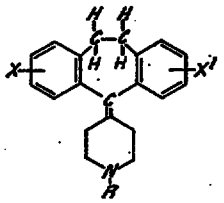
WHAT WE CLAIM IS:—

1. A compound having the general formula:



in which X and X^1 are hydrogen, halogen, trifluoromethyl, C_{1-4} alkyl, C_{1-4} alkoxy or mononuclear aryl, there being one or more such atom or group in each ring, and R is hydrogen, C_{1-4} alkyl C_{1-4} alkenyl, or their hydroxy, mesyloxy and amino substituted derivatives, and derivatives alkylated in one or more of positions 2,3,5 and 6 of the piperidine ring so that the total number of carbon atoms in all such substituent alkyl groups does not exceed four.

2. A compound having the general formula:



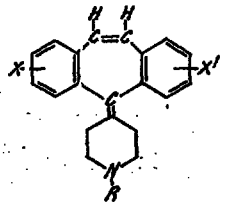
in which X, X^1 and R are as defined in Claim 1.

3. 1-Isopropyl-4-(5-dibenzo[a,e]cycloheptatrienylidene)-piperidine.
4. 1-Butyl-4-(5-dibenzo[a,e]cycloheptatrienylidene)-piperidine.
5. 1-methyl-4-(5-dibenzo[a,e]cycloheptatrienylidene)-piperidine.
6. 1-Methyl-4-(10,11-dihydro-5-dibenzo[a,e]cycloheptatrienylidene)-piperidine.
7. 1-Methyl-4-(3-chloro-5-dibenzo[a,e]cycloheptatrienylidene)-piperidine.
8. 4-(5-dibenzo[a,e]cycloheptatrienylidene)-piperidine.
9. 1-(2-hydroxyethyl)-4-(5-dibenzo[a,e]cycloheptatrienylidene)-piperidine.
10. A hydrogen maleate salt of a 1-R-4(5-dibenzo[a,e]cycloheptatrienylidene) piperidine in which R is ethyl, *n*-propyl, allyl or dimethylaminoethyl.
11. 1 - (2 - methanesulphonyloxyethyl) - 4 - (5 - dibenzo[a,e]cycloheptatrienyl-idene)-piperidine.
12. An acid-addition salt of a compound as claimed in any one of Claims 1, 3, 4 and 5.

1 - methyl - 4(3 - trifluoromethyl - 10,11 - dihydro - 5 - dibenzo[a,e]cyclohepta-trienylidine)piperidine;
1,3 - dimethyl - 4(3 - trifluoromethyl - 10,11 - dihydro - 5 - dibenzo[a,e]cyclohepta-trienylidine)piperidine;
1,2 - dimethyl - 4(3 - trifluoromethyl - 10,11 - dihydro - 5 - dibenzo[a,e]cyclohepta-trienylidine)piperidine;
1 - methyl - 2 - ethyl - 4(3 - trifluoromethyl - 10,11 - dihydro - 5 - dibenzo[a,e]-cycloheptatrienylidine)piperidine;
1,2,6 - trimethyl - 4(3 - trifluoromethyl - 10,11 - dihydro - 5 - dibenzo[a,e]cyclo-heptatrienylidine)piperidine;
1-methyl-4(3-phenyl-10,11-dihydro-5-dibenzo[a,e]cycloheptatrienylidine)piperidine;
1,3 - dimethyl - 4(3 - phenyl - 10,11 - dihydro - 5 - dibenzo[a,e]cycloheptatrienyl-idine)piperidine;
1,2 - dimethyl - 4(3 - phenyl - 10,11 - dihydro - 5 - dibenzo[a,e]cycloheptatrienyl-idine)piperidine;
1 - methyl - 2 - ethyl - 4(3 - phenyl - 10,11 - dihydro - 5 - dibenzo[a,e]cyclohepta-trienylidine)piperidine;
1,2,6 - trimethyl - 4(3 - phenyl - 10,11 - dihydro - 5 - dibenzo[a,e]cycloheptatrienyl-idine)piperidine;

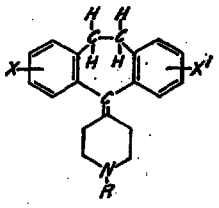
WHAT WE CLAIM IS:—

1. A compound having the general formula:



in which X and X^1 are hydrogen, halogen, trifluoromethyl, C_{1-4} alkyl, C_{1-4} alkoxy or mononuclear aryl, there being one or more such atom or group in each ring, and R is hydrogen, C_{1-4} alkyl C_{2-4} alkenyl, or their hydroxy, mesyloxy and amino substituted derivatives, and derivatives alkylated in one or more of positions 2,3,5 and 6 of the piperidine ring so that the total number of carbon atoms in all such substituent alkyl groups does not exceed four.

2. A compound having the general formula:



in which X, X^1 and R are as defined in Claim 1.

3. 1-Isopropyl-4-(5-dibenzo[a,e]cycloheptatrienylidene)-piperidine.
4. 1-Butyl-4-(5-dibenzo[a,e]cycloheptatrienylidene)-piperidine.
5. 1-methyl-4-(5-dibenzo[a,e]cycloheptatrienylidene)-piperidine.
6. 1-Methyl-4-(10,11-dihydro-5-dibenzo[a,e]cycloheptatrienylidene)-piperidine.
7. 1-Methyl-4-(3-chloro-5-dibenzo[a,e]cycloheptatrienylidene)-piperidine.
8. 4-(5-dibenzo[a,e]cycloheptatrienylidene)-piperidine.
9. 1-(2-hydroxyethyl)-4-(5-dibenzo[a,e]cycloheptatrienylidene)-piperidine.
10. A hydrogen maleate salt of a 1-R-4(5-dibenzo[a,e]cycloheptatrienylidene) piperidine in which R is ethyl, *n*-propyl, allyl or dimethylaminoethyl.
11. 1 - (2 - methanesulphonyloxyethyl) - 4 - (5 - dibenzo[a,e]cycloheptatrienyl-idene)-piperidine.
12. An acid-addition salt of a compound as claimed in any one of Claims 1, 3, 4 and 5.

* C L M S *

13. An acid-addition salt of a compound as claimed in any one of Claims 2 and 6—8.

14. The hydrochloride of the compound claimed in Claim 3, 4 or 5.

15. The hydrochloride of the compound claimed in Claim 6 or 8.

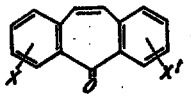
16. A hydrogen maleate salt of the compound claimed in Claim 5 or 7.

17. An N-oxide of a compound as claimed in Claim 1.

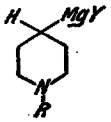
18. The N-oxide of the compound claimed in Claim 5.

19. An N-oxide of a compound as claimed in Claim 2.

20. A method of making a compound as claimed in Claim 1, which comprises mixing a compound having the general formula:

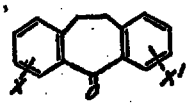


with a Grignard reagent having the general formula:

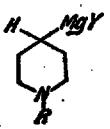


in which Y is a halogen and X, X^1, and R are as in Claim 1, hydrolysing the resulting Grignard adduct and dehydrating the resulting product.

21. A method of making a compound as claimed in Claim 2 which comprises mixing a compound having the general formula:

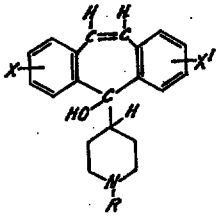


with a Grignard reagent having the general formula:



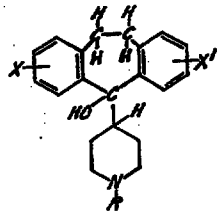
in which Y is halogen and R, X and X^1 are as in Claim 1, hydrolysing the resulting Grignard adduct and dehydrating the resulting product.

22. The process that comprises dehydrating a compound having the general formula:



in which X, X^1 and R are as defined in Claim 1 to produce a compound as claimed in Claim 1.

23. The process that comprises dehydrating a compound having the general formula:



* C L M S *

in [illegible], X^1 and R are as defined in Claim 1, to produce a compound as claimed in Claim 2.

24. A process as claimed in Claim 20 or 22, in which the dehydration is effected by means of *o*-sulphobenzoic anhydride.

25. A process as claimed in Claim 21 or 23, in which the dehydration is effected by means of *o*-sulphobenzoic anhydride.

26. A process as claimed in Claim 20 or 22, substantially as hereinbefore described with reference to any one of Examples I—IV.

27. A process as claimed in Claim 20 or 22, substantially as hereinbefore described with reference to any one of Examples VI, XIV, XV, XVI and XVII.

28. A process as claimed in Claim 21 or 23 substantially as hereinbefore described with reference to any one of Example V, XVIII, XIX and XX.

29. A process as claimed in any one of Claims 22—25, in which the starting material is prepared by a process as claimed in the specification of our copending application No. 7308/63 (Serial No. 931,556).

30. A process for preparing the compound claimed in Claim 8, which comprises reacting 1-methyl-4-(5-dibenzo[a,e]cycloheptatrienylidene)-piperidine with cyanogen bromide to produce 1-cyano-4-(5-dibenzo[a,e]cycloheptatrienylidene)-piperidine, and heating the latter under strongly acid conditions.

31. A process as claimed in Claim 30, in which the starting material is prepared by a process as claimed in Claim 20, 22 or 24.

32. A process as claimed in Claim 30 or 31, substantially as hereinbefore described with reference to Example VII.

33. A process for preparing a compound as claimed in Claim 10, which comprises reacting 4-(5-dibenzo[a,e]cycloheptatrienylidene)-piperidine with a halide R.hal, where R is as defined in Claim 10 and hal is a halogen, under strongly basic conditions, and acidifying the reaction product with maleic acid.

34. A process as claimed in Claim 33, in which the starting material is prepared by a process as claimed in any one of Claims 30 to 32.

35. A process as claimed in Claim 33 or 34, substantially as hereinbefore described with reference to any one of Examples VIII, IX, X and XIII.

36. A process for preparing the compound claimed in Claim 9, which comprises reacting 4-(5-dibenzo[a,e]cycloheptatrienylidene)-piperidine with ethylene oxide.

37. A process as claimed in Claim 36, in which the starting material is prepared by a process as claimed in any one of Claims 30 to 32.

38. A process as claimed in Claim 36 or 37, substantially as hereinbefore described with reference to Example XI.

39. A process as claimed in any one of Claims 36 to 38, including the additional step of reacting the product with methanesulphonyl chloride to produce the compound claimed in Claim 11.

40. A process as claimed in Claim 39, in which the reaction with methanesulphonyl chloride is carried out substantially as hereinbefore described with reference to Example XII.

41. A compound as claimed in Claim 1 or 2, when prepared by a process as claimed in any one of Claims 20 to 40 or are an obvious chemical equivalent of such a process.

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Leamington Spa: Printed for Her Majesty's Stationery Office, by the Courier Press (Leamington) Ltd.—1963. Published by The Patent Office, 25 Southampton Buildings, London, W.C.2, from which copies may be obtained.

* C L M S *