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NO DRAWINGS

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Int. Cl.:—C 07 c, d // C 07 f

COMPLETE SPECIFICATION

Dibenzocycloheptene Derivatives and their Preparation

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:—

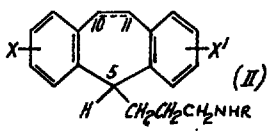
This invention relates to derivatives of dibenzocycloheptenes and processes for making them. More particularly, the invention provides 5H-dibenzo-[a,d]-cycloheptenes and 10,11-dihydro-5H-dibenzo-[a,d]-cycloheptenes which are substituted at their 5-carbon atom with an aminopropyl or an aminopropylidene radical.

The compounds of the invention are useful in the treatment of mental health conditions as they are antidepressants and serve as mood elevators or psychic energizers. For this purpose the daily dosage is within the range of 5 mg. to 250 mg., preferably taken in divided amounts over the day. The compounds are preferably administered in the form of their acid-addition salts and these salts are included in the scope of this invention.

The compounds of the invention may be represented by the general formulae:



(I)



(II)

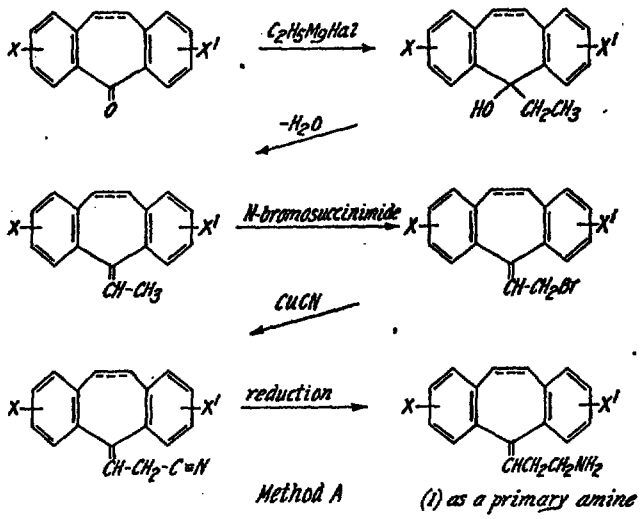
in which R is a hydrogen atom or a C_{1-6} alkyl radical, and each of X and X^1 is a hydrogen or halogen atom or a trifluoromethyl, C_{1-6} alkyl, C_{1-4} alkoxy, mercapto, C_{1-4} alkylmercapto, C_{1-4} alkylsulphonyl, sulphamoyl, C_{1-4} alkylsulphamoyl or C_{2-6} dialkylsulphamoyl radical.

The dotted line between the 10 and 11 carbon atoms indicates that the compounds may be saturated or unsaturated at this location, the saturated compound being indentified by the 10,11-dihydro designation.

The compounds I and II differ from each other in that the side chain of compounds I is attached to the nucleus by a double bond.

To obtain the primary amines of compounds I, i.e. in which R is hydrogen, the following general method may be followed;

[Price 4s. 6d.]

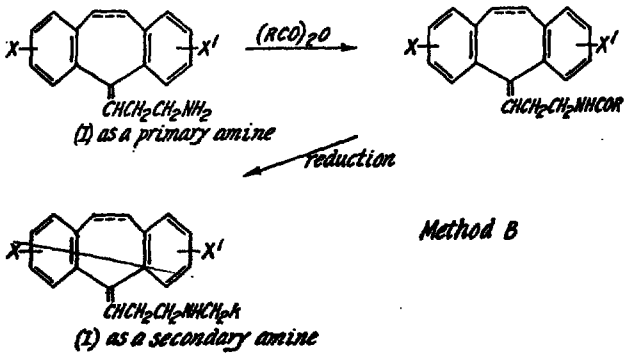


This method A begins with the known ketone which may be prepared by using known processes. Or, the starting compounds, particularly those having substituents on the benzene rings, may be prepared by methods described in the literature.

Method A involves the attachment of an ethylidene chain to the 5-carbon of the nucleus and its subsequent expansion to a propylidene chain having a terminal amino group. The Grignard reagent and the reaction using it are conventional and an inert solvent, e.g., ether, is used, preferably under reflux. The Grignard adduct is hydrolysed in the usual manner but it is preferable that it be under approximately neutral conditions such as produced by the addition of ammonium chloride solution. The dehydration step which next follows is carried out by a chemical dehydrating agent, *e.g.*, acetyl chloride, acetic anhydride or trifluoroacetic anhydride, which can subsequently be removed by evaporation. N-bromo-succinimide is used for the next step as it is a selective brominating agent and avoids adding bromine to the olefinic linkage. This bromination is carried on at the refluxing temperature of a low boiling inert solvent, *e.g.* benzene. A substantial excess of N-bromosuccinimide is to be avoided, particularly with compounds of the 10,11-dihydro series. The resulting succinimide precipitates and is removed.

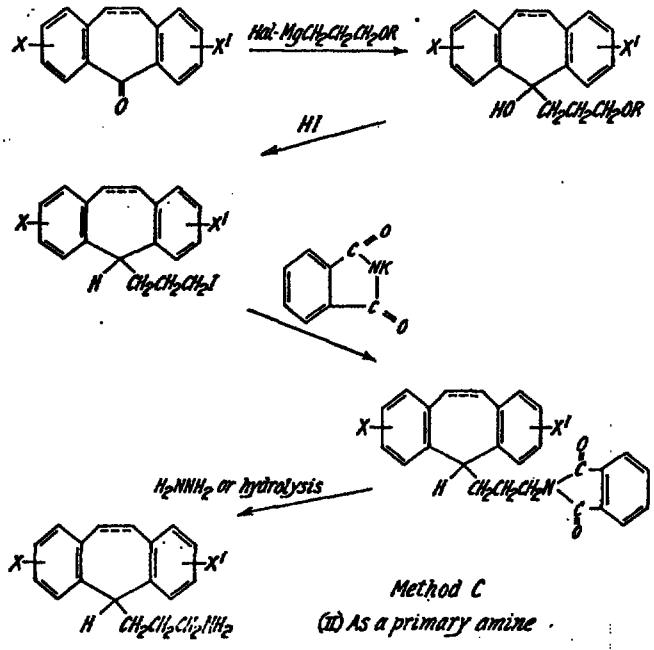
The bromo compound need not be isolated from the filtrate, and a cyanide salt, preferably cuprous cyanide, may be added directly to the filtrate. The substitution of the cyanide group for the bromine will occur at room temperature but to hasten it heat is preferably applied. The resulting cyanoethylidene derivative in method A is then isolated by evaporation of the solvent and is then subjected to the reduction step. To avoid simultaneous reduction at the aliphatic double bond it is best to use a chemical reducing agent, *e.g.*, lithium aluminium hydride, in the presence of a solvent, *e.g.* anhydrous ether. After hydrolysis, for example, by the addition of an aqueous solution of caustic alkali, the ethereal layer is recovered and the product obtained from it by distillation.

The primary amine which is so obtained in method A can readily be converted to a secondary amine type of compound I by the following reactions, in which R is a C_{1-5} alkyl radical:



The conversion to the amide is readily carried out by the addition of an acyl halide or anhydride, such as acetic anhydride. This is carried on at room temperature with stirring or by heating. The amide is isolated by removal of the excess acylating agent and the reduction is carried out by the use of a metal hydride as explained above, to avoid reduction of the olefinic double bond.

As noted above, method A is useful to obtain compounds I having an olefinic linkage to the side chain. To obtain the compounds of type II, the following series of reactions may be carried out:



Method C

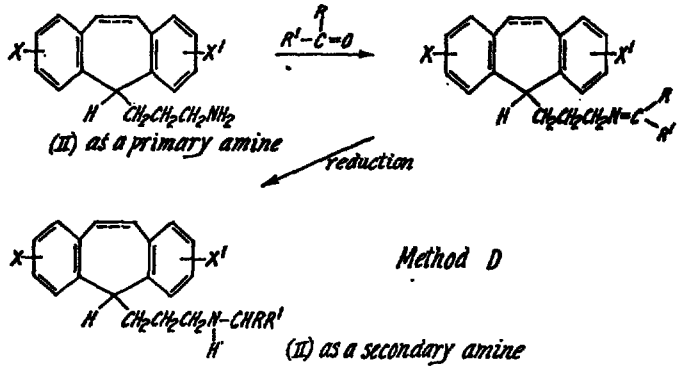
(II) As a primary amine

This method C, in which R is a C_{1-6} alkyl radical, in general involves the initial attachment of an alkoxypropyl radical at the 5-carbon of the nucleus by a Grignard reaction, the simultaneous reduction of the 5-hydroxy compound and replacement of the alkoxy group by an iodine atom, and then the replacement of this iodine atom by an amino group.

The ketone used as the starting material in method C is the same as that used in method A. It is reacted according to conventional procedures with a Grignard reagent having a terminal ether group. R may be any lower alkyl radical having up to 6 carbons. The resulting Grignard adduct is hydrolysed, preferably under neutral conditions, *e.g.*, by using an ammonium chloride solution. The resulting product is recovered from the solvent by evaporation and is treated with hydriodic acid in the presence of a solvent, *e.g.*, acetic acid or acetic anhydride. The iodinated compound is extracted into a solvent, *e.g.*, benzene, and recovered from it by evaporation of the solvent. The addition to this iodo compound of the potassium phthalimide is carried on with a solvent, *e.g.*, dimethylformamide, and after the complete addition slight heat may be applied to increase the reaction rate. The phthalimido compound is isolated by extraction.

The subsequent reaction with hydrazine hydrate is carried out in absolute methanol or ethanol and heat may be applied up to the refluxing temperature to hasten the reaction. The phthalhydrazide is separated and the primary amino compound II is recovered from the solution. Instead of hydrazinolysis, the phthalimido compound can be converted to the amine by hydrolysis.

This produces the aminopropyl compounds II as primary amines, and they can be converted to secondary amines by the following procedure, in which each of R and R^1 is a hydrogen atom or an alkyl radical, the total number of carbon atoms in R and R^1 not exceeding five:

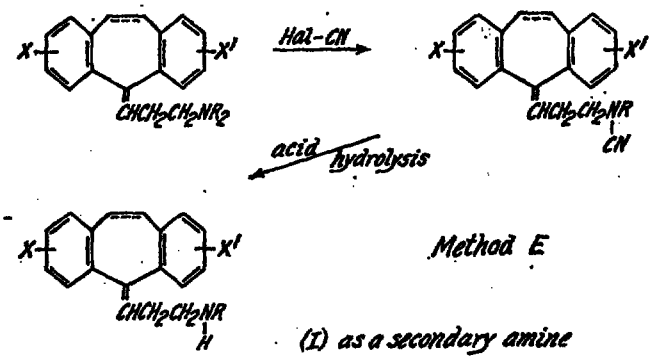


Method D

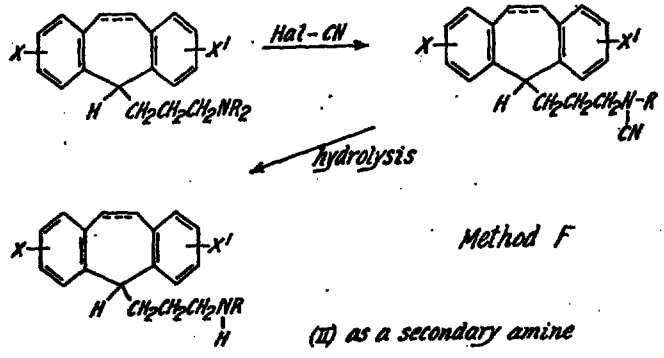
In method D the primary amine II is combined with a ketone or an aldehyde in a solvent, *e.g.*, benzene or toluene, and heated, preferably to refluxing temperature. The resulting alkylideneaminopropyl compound is then recovered by evaporating off the solvent and it is reduced by catalytic hydrogenation to the resulting secondary aminopropyl compound. The reduction may also be accomplished with a metal hydride as described in method B. Instead of isolating the alkylideneamino compound the primary amine and the selected carbonyl compound can be dissolved in a suitable solvent, *e.g.*, a lower alcohol, and catalytic hydrogenation carried out.

The primary amine II may also be converted to the secondary amine II by following method B. Likewise, the primary amine I may be converted to the secondary amine I by following method D.

The foregoing methods for preparing the secondary amines I and II are especially suited to those cases where groups larger than methyl are present. Where methyl or ethyl aminopropylidene and methyl or ethyl aminopropyl substituents are desired they are conveniently prepared from the corresponding dialkylamino compounds by treatment with a cyanogen halide. This monodealkylation process may be represented as follows, as applied to compounds I and compounds II:



Method E

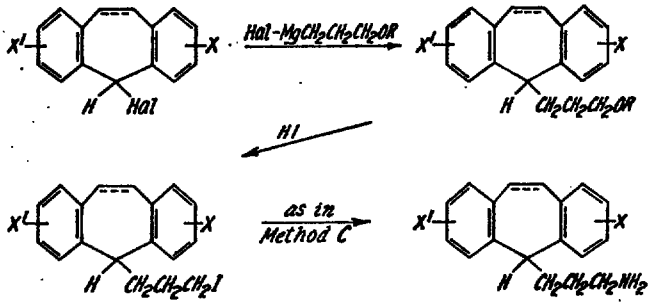


Method F

The tertiary amine is dissolved in a non-hydroxylic solvent, *e.g.* benzene or ether, and this solution is added slowly to a solution of cyanogen halide in the same solvent, while stirring and permitting the alkyl halide to escape. After the reaction is complete the basic material is separated by washing with dilute acid and the cyanamide isolated by evaporating the solvent. The cyanamide is hydrolysed to the secondary amine in an acidic or alkaline medium. This is illustrated in Examples 10 and 11.

A variation of Method C to produce compounds II as a primary amine involves starting with a 5-halo (preferably chloro or bromo) derivative of the selected 5H-dibenzo[a,d]cycloheptene.

This method involves the following series of steps:

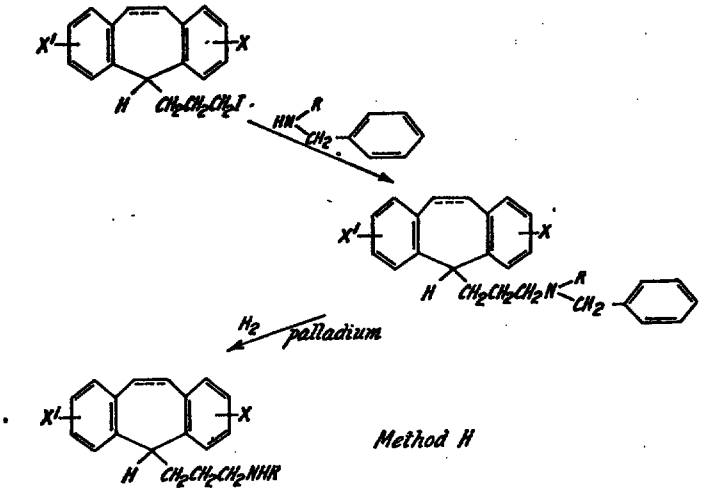


Method G

The R portion of the Grignard reagent is any radical, *e.g.* a lower alkyl radical, which will react with the hydriodic acid to result in replacement of the ether group with an iodine atom. The resulting 5H-dibenzo[a,d]cycloheptene having an iodopropyl group at the 5-carbon is the same as the one in Method C, and as in Method C, may be converted to the primary amine of Compound II.

In Method G, the reaction with the Grignard reagent may be carried out in the presence of a common solvent, *e.g.*, dry ether or tetrahydrofuran, the addition being slow to prevent a substantial rise above room temperature. The usual procedures then are carried out. The primary amine of the end product of Method G can be converted to a secondary amine by employing Method B as is illustrated in Example 18.

Still another method for producing the secondary amines of compound II involves a catalytic debenzylation procedure. This may be represented as follows:



Method H

The starting compound of Method H will be recognized as the iodo derivative produced by Method C and Method G. It is gradually combined with the N-alkyl-benzylamine to prevent a substantial rise above room temperature, a solvent, e.g., absolute alcohol, being used. Heat to a refluxing temperature should be applied for from 15 to

60 minutes and the solvent distilled off. The selective debenzylation action of hydrogen in the presence of palladium is utilized to remove the benzyl moiety and produce the secondary amine of compounds II. The alkyl radical of the N-alkylbenzylamine is selected to produce the radical R of compound II. This is illustrated in Examples 19 and 20.

The following examples are illustrative of the many compounds contemplated by the invention and falling within the scope of the claims.

EXAMPLE 1

5-(3-Aminopropylidene)-5H-dibenzo[a,d]cycloheptene

A. *5-Ethyl-5-hydroxy-5H-dibenzo[a,d]cycloheptene*

5H - Dibenzo[a,d]cyclohepten - 5 - one (15.5g., 0.075 mole) is added in portions to a solution of ethylmagnesium bromide, prepared from 3.64g. (0.15 mole) of magnesium and 16.4g. of ethyl bromide in ether. After stirring for one hour at room temperature the mixture is heated to refluxing for 15 minutes then cooled and the Grignard adduct is hydrolysed by cautiously adding ammonium chloride solution. The crude 5-ethyl-5-hydroxy-5H-dibenzo[a,d]cycloheptene is recovered from the ethereal layer in a yield of 16.78g. (95%), m.p., 63—65°C. (clearing at 70°C.). After recrystallization from petroleum ether, hexane and finally isopropyl alcohol, an analytical sample melted at 63—65°C.

Analysis, Calculated for $C_{17}H_{16}O$: C, 86.40; H, 6.83.
Found: C, 86.31; H, 6.50

B. *5-Ethylidene-5H-dibenzo[a,d]cycloheptene*

5 - Ethyl - 5 - hydroxy - 5H - dibenzo[a,d]cycloheptene (13.7g., 0.058 mole) is dissolved in 80 ml. of acetyl chloride and the solution refluxed for 90 minutes. The acetyl chloride is evaporated under reduced pressure and the residue dissolved in benzene. After washing with alkali followed by a water wash, the benzene is removed and the product distilled under reduced pressure. The desired 5 - ethylidene - 5H - dibenzo-[a,d]cycloheptene is obtained as the fraction boiling at 130—135°C. (0.02 mm.). It crystallized on cooling. The compound was purified further by recrystallization from 95% alcohol.

C. *5-(2-Cyanoethylidene)-5H-dibenzo[a,d]cycloheptene*

5 - Ethylidene - 5H - dibenzo[a,d]cycloheptene is treated with one molar equivalent of N-bromosuccinimide in refluxing benzene. After refluxing for 2 hours, the mixture is cooled and the precipitated succinimide is separated by filtration. An excess of finely pulverized dried cuprous cyanide then is added and the mixture is stirred for 2 hours at room temperature, then for 12 hours at reflux. The solids are separated by filtration and the 5 - (2 - cyanoethylidene) - 5H - dibenzo[a,d]cycloheptene is isolated by evaporation of the benzene filtrate and purified by distillation under reduced pressure.

D. *5-(3-Aminopropylidene)-5H-dibenzo[a,d]cycloheptene*

5 - (2 - Cyanoethylidene) - 5H - dibenzo[a,d]cycloheptene (0.1 mole) is dissolved in absolute ether and the solution added to a solution of 3.8g. (0.10 mole) of lithium aluminum hydride in 200 ml. of anhydrous ether while stirring and cooling. After stirring for 1 hour, water and 20% sodium hydroxide solution are added with continued stirring and cooling. The 5 - (3 - aminopropylidene) - 5H - dibenzo[a,d]cycloheptene is isolated from the ether layer by distillation.

EXAMPLE 2

5-(3-Aminopropylidene)-10,11-dihydro-5H-dibenzo[a,d]cycloheptene

This compound is obtained by following the procedure of Example 1 but starting with 10,11-dihydro-5H-dibenzo[a,d]cyclohepten-5-one as the ketone.

EXAMPLE 3

5-(3-ethylaminopropylidene)-5H-dibenzo[a,d]cycloheptene

A. *5-(3-Acetamidopropylidene)-5H-dibenzo[a,d]cycloheptene*

5 - (3 - Aminopropylidene) - 5H - dibenzo[a,d]cycloheptene is dissolved in acetic anhydride and the solution is heated to refluxing for 20 minutes. The solution is then cooled and poured into a large volume of water. The mixture is stirred until the excess of acetic anhydride is hydrolysed. The product is extracted into ether, the extract

washed with sodium bicarbonate solution, followed by water, and dried over sodium sulfate. The product is isolated by evaporating the ether.

B. *5-(3-Ethylaminopropylidene)-5H-dibenzo[a,d]cycloheptene*

5 - (3 - Acetamidopropylidene) - 5H - dibenzo[a,d] - cycloheptene is dissolved in absolute ether. The solution is added dropwise to a stirred solution of lithium aluminium hydride in ether, containing 1.25 molar equivalents of the hydride. The mixture is stirred for 2 hours at room temperature, then for 15 hours at reflux. The mixture is then cooled and stirred while water is added cautiously, followed by sodium hydroxide solution. The ether layer is separated, washed with water and dried over sodium sulphate. The product is obtained by evaporation of ether and purified by vacuum distillation.

EXAMPLE 4

5-(3-Aminopropyl)-5H-dibenzo[a,d]cycloheptene

A. *5-(3-Ethoxypropyl)-5-hydroxy-5H-dibenzo[a,d]cycloheptene*

The Grignard reagent is prepared from 12.55g. (0.075 mole) of 3-ethoxypropyl bromide and 1.82g. (0.075 mole) of magnesium in ether. The solution is cooled in an ice-bath and a solution of 5.15g. (0.025 mole) of 5H-dibenzo[a,d]cyclohepten-5-one in dry ether is added dropwise with stirring. The mixture is stirred at room temperature for 2 hours, then at reflux for 30 minutes. The Grignard adduct then is decomposed by pouring the reaction mixture into a mixture of ice and ammonium chloride solution. The ethereal layer is separated and the aqueous layer extracted further with ether. Evaporation of the ether gives the product as an oily crystalline solid. Two recrystallizations from alcohol gave product, m.p., 129—130°C.

Analysis, Calculated for $C_{20}H_{22}O_2$: C, 81.60; H, 7.54.
Found: C, 81.28; H, 7.50.

B. *5-(3-Iodopropyl)-5H-dibenzo[a,d]cycloheptene*

A solution of 9.25g. (0.0314 mole) of 5 - (3 - ethoxypropyl) - 5 - hydroxydibenzo-[a,d]cycloheptene prepared as above in 45 ml. of acetic anhydride is heated on the steam-bath for 90 minutes then cooled to 65°C. A stream of nitrogen is passed through the solution while 30 ml. of hydriodic acid (sp. gr., 1.5) is added in portions, keeping the temperature below 90°C. The solution develops a dark brown iodine colour during the addition. The solution is heated to 80°C. for 30 minutes, then cooled and poured into ice-water. The brown oil that separates is extracted into benzene and the extract washed with water, dilute sodium thiosulphate solution and finally with water. Evaporation of the benzene gives the product 5 - (3 - iodopropyl) - 5H - dibenzo[a,d]cycloheptene as a yellow oil. A sample gives a precipitate with alcoholic silver nitrate solution.

C. *5-(3-Phthalimidopropyl)-5H-dibenzo[a,d]cycloheptene*

5 - (3 - Iodopropyl) - 5H - dibenzo[a,d]cycloheptene 1.8 g. (0.005 mole) is dissolved in 10 ml. of dimethylformamide. The solution is stirred while 930 mg. (0.0051 mole) of potassium phthalimide is added. When the addition is complete, the mixture is heated to 85—90° for 40 minutes, then cooled, diluted with chloroform and poured into water. The chloroform layer is separated and the aqueous layer extracted further with chloroform. Evaporation of the chloroform gives the product as an oily crystalline solid. Several recrystallizations from isopropyl alcohol gave product, m.p. 125.5—131.5°C.

Analysis, Calculated for $C_{26}H_{21}O_2N$: C, 82.30; H, 5.58; N, 3.69.
Found: C, 82.46; H, 5.60; N, 3.70.

D. *5-(3-Aminopropyl)-5H-dibenzo[a,d]cycloheptene*

5 - (3 - Phthalimidopropyl) - 5H - dibenzo[a,d]cycloheptene, 2.15g. (0.0054 mole) is dissolved in 50 ml. of hot 95% ethanol. Hydrazine hydrate, 0.6 ml., is added and the solution heated to refluxing for 2 hours. The solution then is cooled, acidified, and the precipitate of phthalhydrazide removed by filtration. Ethanol is distilled from the filtrate under reduced pressure and the residue dissolved in 40 ml. of water. The filtered solution is evaporated by heating under reduced pressure to a volume of approximately 20 ml. Upon cooling, the hydrochloride salt of 5 - (3 - aminopropyl) - 5H - dibenzo-[a,d]cycloheptene is precipitated in a yield of 1.35g. (87.5%). After recrystallization from a mixture of ethanol and ether and from isopropyl alcohol, an analytical sample melted at 263—265°C. dec.

Analysis, Calculated for $C_{18}H_{19}N.HCl$: C, 75.64; H, 7.05; N, 4.90.
Found: C, 75.54; H, 6.77; N, 4.78.

EXAMPLE 5

5-(3-Aminopropyl)-10,11-dihydro-5H-dibenzo[a,d]cycloheptene

If the starting compound is 10,11-dihydro-5H-dibenzo[a,d]cyclohepten-5-one, the resulting end compound is 5-(3-aminopropyl)-10,11-dihydro-5H-dibenzo[a,d]cycloheptene. The process of Example 4 is to be followed.

EXAMPLE 6

5-(3-Butylaminopropyl)-5H-dibenzo[a,d]cycloheptene

Butyraldehyde is added to a solution of 5 - (3 - aminopropyl) - 5H - dibenzo-[a,d]cycloheptene in benzene. The mixture is heated to refluxing under a continuous water separator until separation of the water is complete. The benzene then is distilled and the 5 - (3 - butylideneaminopropyl) - 5H - dibenzo[a,d]cycloheptene distilled under reduced pressure. The latter is dissolved in absolute alcohol and hydrogenated over a platinum catalyst. The catalyst is separated, the solvent distilled and the product purified by distillation under reduced pressure.

EXAMPLE 7

5-(3-Isopropylaminopropyl)-5H-dibenzo[a,d]cycloheptene

A solution of 5 - (3 - aminopropyl) - 5H - dibenzo[a,d]cycloheptene and acetone in ethanol, the acetone being in excess over the amine, is hydrogenated and isolated by following the procedure given in Example 6. The product obtained is 5-(3-isopropylaminopropyl)-5H-dibenzo[a,d]cycloheptene.

EXAMPLE 8

5-(3-Methylaminopropyl)-5H-dibenzo[a,d]cycloheptene

A. *5-(3-N-Cyano-N-methylaminopropyl)-5H-dibenzo[a,d]cycloheptene*

A solution of 0.0834 mole of 5 - (3 - dimethylaminopropyl) - 5H - dibenzo[a,d]-cycloheptene in 61 ml. of benzene is added dropwise to a stirred solution of 9.80 g. (0.0917 mole) of cyanogen bromide in 38 ml. of benzene. Some heat is evolved. The mixture is stirred for 3 hours at room temperature, and filtered to remove any precipitate which forms. The filtrate, together with a benzene wash of the precipitate, is evaporated to dryness on a steam bath under reduced pressure to remove excess cyanogen bromide and solvent. The residual crude cyanamide is dissolved in benzene, and the solution is washed with dilute hydrochloric acid to remove any unchanged amine, then with water. The benzene solution is then evaporated under reduced pressure leaving 5 - (3 - N - cyano - N - methylaminopropyl) - 5H - dibenzo[a,d]cycloheptene as a yellow oil weighing about 19.6 g.

B. *5-(3-methylaminopropyl)-5H-dibenzo-[a,d]cycloheptene*

The oily cyanamide (19.6 g.) prepared in A above, together with 500 ml. of glacial acetic acid, 330 ml. of water, and 50 ml. of concentrated hydrochloric acid is heated under reflux for 16 hours, thereby effecting hydrolysis and decarboxylation and forming the product. The reaction mixture is concentrated to a small volume by heating under reduced pressure and the residue is dissolved in 250 ml. of water containing 1 ml. of concentrated hydrochloric acid. The aqueous solution is washed with benzene, and rendered alkaline by the addition of excess potassium carbonate. The free base thus liberated is extracted into ether and the ethereal solution dried over anhydrous potassium carbonate. Evaporation of the ether under reduced pressure on the steam bath leaves a residue of 5-(3-methylaminopropyl)-5H-dibenzo[a,d]cycloheptene, as an oil.

The free base may be reconverted to the hydrochloride salt by treatment with ethanolic hydrogen chloride and precipitation by addition of ether. After recrystallization from a mixture of isopropyl alcohol and ether, the hydrochloride salt melts at 166.5—167.5°C.

Analysis, Calculated for $C_{19}H_{21}N.HCl$: C, 76.11; H, 7.40; N, 4.67.
Found: C, 76.14; H, 7.30; N, 4.64.

Alternatively the cyanamide can be hydrolysed under alkaline conditions as follows:

The cyanamide, obtained as described in Step A, (2.0 g., 0.007 mole) is mixed with a hot solution of 25 g. of potassium hydroxide in 38 ml. of absolute methanol. The mixture is heated to refluxing with stirring for 45 hours. The reaction mixture then is diluted with water and the yellow oil that separates is extracted into benzene. After washing with water and drying over sodium sulphate the benzene is evaporated to give 1.75 g. of a yellow oily residue. The basic material is extracted into 1N hydrochloric acid and after separating the neutral material by extracting with ether, the basic material is recovered by making the aqueous layer basic and extracting with ether.

Evaporation of the ether gives 1.46 g. of the base 5-(3-methylaminopropyl)-5H-dibenzo[a,d]cycloheptene. Conversion to the hydrochloride is carried out as described above.

Preparation of starting material.

Step C. *Preparation of 3-dimethylaminopropylmagnesium chloride*

Magnesium turnings (1.08g., 0.0442g. atom) are placed in a 200 ml. 3-necked flask equipped with a stirrer, a dropping funnel and a reflux condenser carrying a drying tube. An atmosphere of dry nitrogen is maintained in the apparatus throughout the reaction. A crystal of iodine is added followed by 10 ml. of dry tetrahydrofuran. 3 ml. of 3-dimethylaminopropylmagnesium chloride solution is added and the mixture heated to refluxing on the steam-bath. A solution of 3-dimethylaminopropyl chloride (5.37g., 0.0442 mole) in 35 ml. of dry tetrahydrofuran is added dropwise, refluxing being maintained by the application of heat when necessary. When the addition is complete the mixture is refluxed for 2 hours when almost all of the magnesium is dissolved.

Instead of using 3-dimethylaminopropylmagnesium chloride to initiate the reaction, ethyl bromide can be used in a quantity of 0.05 mole per mole of magnesium.

Step D. *Preparation of 5-(3-Dimethylaminopropyl)-5H-dibenzo[a,d]cycloheptene Hydrochloride*

The Grignard solution prepared in step C is cooled to room temperature and stirred while a solution of 5.05g. (0.0221 mole) of 5-chloro-5H-dibenzo[a,d]cycloheptene in 25 ml. of dry tetrahydrofuran is added dropwise, external cooling being applied as required to maintain the temperature close to room temperature. When the addition is complete the mixture is heated to refluxing for 15 minutes. The bulk of the tetrahydrofuran then is distilled under reduced pressure, keeping the water-bath temperature at 50—60°C. The syrupy mixture is dissolved in 75 ml. of benzene and water, 15 ml., is added dropwise with stirring. The benzene layer is decanted from the gelatinous precipitate which then is re-extracted with three 20 ml. portions of boiling benzene. The combined benzene extracts are washed with water and extracted with three 15 ml. portions of 3 *N* hydrochloric acid. The acid extract is made basic with sodium hydroxide and the yellow oily base that separates is extracted into hexane. After washing the combined extracts with water the hexane is evaporated and the product obtained as a yellow oil in a yield of 4.61g. The base is converted to the hydrochloride by dissolving it in a mixture of 15 ml. of absolute alcohol and 15 ml. of absolute ether and adding 1.8 ml. of a 10.28 N solution of dry hydrogen chloride in absolute alcohol. The solution then is diluted to incipient crystallization by the addition of 25 ml. of absolute ether. The yield of 5 - (3 - dimethylaminopropyl) - 5H - dibenzo[a,d]cycloheptene hydrochloride, m.p., 186—190°C. is 4.17 g. Recrystallization from mixtures of absolute alcohol and absolute ether gives the product, m.p. 191—193°C.

Analysis: Calculated for $C_{20}H_{23}N.HCl$: C, 76.53; H, 7.71; N, 4.46.
Found: C, 76.23; H, 7.83; N, 4.45.

EXAMPLE 9

10,11-Dihydro-5-(3-methylaminopropyl)-5H-dibenzo[a,d]cycloheptene

10,11 - Dihydro - 5 - (3 - dimethylaminopropyl) - 5H - dibenzo[a,d]cycloheptene is converted to the corresponding cyanamide by following the procedure of Example 8A. The cyanamide (5.03g.) together with 60 ml. of glacial acetic acid, 40 ml. of water and 8 ml. of concentrated hydrochloric acid is heated to refluxing for 16 hours. The reaction mixture is evaporated to dryness by heating under reduced pressure. Crystallization of the residual solid from isopropyl alcohol gives 4.48g. (86%) of the hydrochloride salt of 10,11 - dihydro - 5 - (3 - methylaminopropyl) - 5H - dibenzo[a,d]cycloheptene melting at 174—175°C.

Analysis, Calculated for $C_{19}H_{23}N.HCl$: C, 75.60; H, 8.01; N, 4.64
Found: C, 75.89; H, 8.05; N, 4.61.

The starting 10,11 - dihydro - 5 - (3 - dimethylaminopropyl) - 5H - dibenzo[a,d]-cycloheptene used in this Example may be prepared by following steps C and D in Example 8 but using 5-chloro-10,11-dihydro-5H-dibenzo[a,d]cycloheptene as the starting compound.

EXAMPLE 10

3-Chloro-10,11-dihydro-5-(3-methylaminopropyl)-5H-dibenzo[a,d]cycloheptene

3 - Chloro - 10,11 - dihydro - 5 - (3 - dimethylaminopropyl) - 5H - dibenzo[a,d]-cycloheptene is converted to the corresponding cyanamide by following the procedure of

Example 8A. Upon hydrolysis according to the procedure of Example 8B, there is obtained 3 - chloro - 10,11 - dihydro - 5 - (3 - methylaminopropyl) - 5H - dibenzo-[a,d]cycloheptene. This may be converted to its hydrochloride salt directly by treatment with ethanolic hydrogen chloride as described in Example 8B. After recrystallization from a mixture of isopropyl alcohol and ether, the hydrochloride salt melts at 192.5—193.5°C. dec.

Analysis, Calculated for $C_{19}H_{22}NCl.HCl$: C, 67.85; H, 6.89; N, 4.17.
Found: C, 68.09; H, 6.94; N, 4.13.

The starting 3 - chloro - 10,11 - dihydro - 5 - (3 - dimethylaminopropyl) - 5H-dibenzo[a,d]cycloheptene used in this Example may be prepared by following steps C and D of the above Example 8 using 3,5 - dichloro - 10,11 - dihydro - 5H - dibenzo-[a,d]cycloheptene as the starting compound.

EXAMPLE 11

By following the procedure of Example 10 but starting with the corresponding 10,11 unsaturated compound, 3,5 - dichloro - 5H - dibenzo[a,d]cycloheptene, there is obtained 3 - chloro - 5 - (3 - methylaminopropyl) - 5H - dibenzo[a,d]cycloheptene.

EXAMPLE 12

5-(3-Aminopropyl)-5H-dibenzo[a,d]cycloheptene

A. *5-(3-Ethoxypropyl)-5H-dibenzo[a,d]cycloheptene*

The Grignard reagent is prepared from 6.44g. (0.0386 mole) of 3-ethoxypropyl bromide and 940 mg. (0.0386g. atom) of magnesium in ether. A solution of 5.67g. (0.025 mole) of 5 - chloro - 5H - dibenzo[a,d]cycloheptene in a mixture of dry ether and tetrahydrofuran is added dropwise with stirring. The mixture is stirred at room temperature for 1 hour. The Grignard adduct then is decomposed by pouring the reaction mixture into a mixture of ice and ammonium chloride solution. The ethereal layer is separated, the aqueous layer extracted further with ether. Evaporation of the ether and distillation of the residue under reduced pressure gives the product as a yellow oil, b.p., 145—148°C. (0.1 mm.)

Analysis, Calculated for $C_{20}H_{22}O$: C, 86.28; H, 7.97.
Found: C, 86.84; H, 7.97.

B. *5-(3-Iodopropyl)-5H-dibenzo[a,d]cycloheptene*

This product is obtained by following the procedure of Example 4B, but starting with 5 - (3 - ethoxypropyl) - 5H - dibenzo[a,d]cycloheptene. To obtain as the end product the compound of the title of this Example, the remaining procedure of Example 4 is followed.

EXAMPLE 13

3-Chloro-5-(3-aminopropyl)-5H-dibenzo[a,d]cycloheptene

A. *3-Chloro-5-(3-ethoxypropyl)-5H-dibenzo[a,d]cycloheptene*

3,5 - Dichloro - 5H - dibenzo[a,d]cycloheptene, dissolved in absolute ether, is added dropwise with stirring to a solution containing one equivalent of 3-ethoxypropyl-magnesium bromide in ether. The mixture is stirred at room temperature for 1 hours, then at reflux for 2 hours. The mixture then is cooled, treated with dilute hydrochloric acid and the ether separated, washed with water and dried. The product is isolated by evaporation of the ether.

B. *3-Chloro-5-(3-iodopropyl)-5H-dibenzo[a,d]cycloheptene*

3 - Chloro - 5 - (3 - ethoxypropyl) - 5H - dibenzo[a,d]cycloheptene (0.03 mole) is dissolved in 45 ml. of acetic anhydride. The solution is heated to 65°C. and nitrogen is passed through while 30 ml. of hydriodic acid (sp. gr., 1.5) is added gradually, keeping the temperature below 90°C. The solution is heated to approximately 80°C. for 30 minutes, then cooled and poured into ice-water. The product is extracted into ether, the extract washed with dilute sodium thiosulphate solution, followed by dilute sodium bicarbonate solution and finally with water. The product is isolated by evaporation of the ether.

C. *3-Chloro-5-(3-phthalimidopropyl)-5H-dibenzo[a,d]cycloheptene*

3 - Chloro - 5 - (3 - iodopropyl) - 5H - dibenzo[a,d]cycloheptene is converted to 3 - chloro - 5 - (3 - phthalimidopropyl) - 5H - dibenzo[a,d]cycloheptene by following the procedure of Example 4, step C.

D. *3-Chloro-5-(3-aminopropyl)-5H-dibenzo[a,d]cycloheptene*

3 - Chloro - 5 - (3 - phthalimidopropyl) - 5H - dibenzo[a,d]cycloheptene is converted to 3 - chloro - 5 - (3 - aminopropyl) - 5H - dibenzo[a,d]cycloheptene by following the procedure of Example 4, step D.

EXAMPLE 14

3-Chloro-5-(3-ethylaminopropyl)-5H-dibenzo[a,d]cycloheptene

A. *3-Chloro-5-(3-acetamidopropyl)-5H-dibenzo[a,d]cycloheptene*

3 - Chloro - 5 - (3 - aminopropyl) - 5H - dibenzo[a,d]cycloheptene is dissolved in acetic anhydride and the solution heated to refluxing for 20 minutes. The solution then is cooled and poured into a large volume of water. The mixture is stirred until the excess of reagent has been hydrolysed. The product then is extracted into ether, the extract washed with sodium bicarbonate solution, followed by water, and dried over sodium sulphate. The product is isolated by evaporating the ether.

B. *3-Chloro-5-(3-ethylaminopropyl)-5H-dibenzo[a,d]cycloheptene*

3 - Chloro - 5 - (3 - acetamidopropyl) - 5H - dibenzo[a,d]cycloheptene is dissolved in absolute ether. The solution is added dropwise to a stirred solution of lithium aluminium hydride in ether, containing 1.25 molar equivalents of the hydride. The mixture is stirred for 2 hours at room temperature, then for 15 hours at reflux. The mixture then is cooled and stirred while water is added cautiously followed by sodium hydroxide solution. The ether layer is separated, washed with water and dried over sodium sulphate. The product is obtained by evaporation of the ether and purified by vacuum distillation.

EXAMPLE 15

5-(3-Ethylaminopropyl)-5H-dibenzo[a,d]cycloheptene

5-[3-(N-Benzyl-N-ethylamino)-propyl]-5H-dibenzo[a,d]cycloheptene

5 - (3 - Iodopropyl) - 5H - dibenzo[a,d]cycloheptene is added gradually to an excess of N-ethyl benzylamine in absolute alcohol with stirring and cooling. The reaction mixture then is heated to refluxing for 30 minutes and the alcohol distilled under reduced pressure. The residue is warmed with dilute acid and the acid-insoluble material separated. The aqueous layer then is rendered alkaline with sodium hydroxide and the liberated bases extracted into ether. The ether is evaporated and the product isolated by vacuum distillation.

5-(3-Ethylaminopropyl)-5H-dibenzo[a,d]cycloheptene

5 - [3 - (N - Benzyl - N - ethylamino - propyl] - 5H - dibenzo - [a,d]cycloheptene is dissolved in absolute alcohol and hydrogenated over palladium-on-alumina catalyst at 40—60°C. The catalyst is separated and the product isolated by evaporating the solvent.

EXAMPLE 16

By starting with 5 - (3 - iodopropyl) - 10,11 - dihydro - 5H - dibenzo[a,d]cycloheptene, the end product obtained is the corresponding 10,11-dihydro derivative, namely 10,11 - dihydro - 5 - (3 - ethylamino - propyl) - dibenzo[a,d]cycloheptene.

EXAMPLE 17

3-Dimethylsulfamoyl-5-(3-methylaminopropyl)-5H-dibenzo[a,d]cycloheptene

A. *3-Bromo-7-fluorosulfonyl-10,11-dihydro-5H-dibenzo[a,d]-cyclohepten-5-one*

Fluorosulfonic acid, 100 ml., is placed in a 300 ml. 3-necked round bottom flask equipped with polyethylene inlet tube and polyethylene exit tube with drying tube half-filled with anhydrous sodium fluoride. A nitrogen atmosphere is maintained throughout the reaction. With stirring, 17.0 g. (0.059 mole) of 3 - bromo - 10,11 - dihydro - 5H-dibenzo[a,d]cycloheptene - 5 - one is added in portions over 20 minutes. After stirring another 10 minutes, the dark green solution is heated on the steam-bath for 6½ hours. The mixture then is cooled to room temperature, poured cautiously with stirring into 1.5 kg. of crushed ice, and allowed to stand overnight at room temperature. The brown solid is collected, washed with water, dried in a vacuum desiccator over sodium hydroxide, and then extracted in a Soxhlet extractor with 700 ml. of boiling cyclohexane for 16 hours. On cooling, the cyclohexane extract deposits 11.65 g. (53%) of 3 - bromo-7 - fluorosulfonyl - 10,11 - dihydro - 5H - dibenzo[a,d] - cyclohepten - 5 - one as dark

yellow flakes, m.p. 148—151°C. Recrystallizations from ether and cyclohexane give an analytical sample, m.p. 150—152°C.

Analysis, Calcd. for $C_{15}H_{10}O_3FBrS$: C, 48.79; H, 2.73; S, 8.69.
Found: C, 48.78; H, 2.83; S, 8.87.

B. *3-Bromo-7-dimethylsulfamoyl-10,11-dihydro-5H-dibenzo-[a,d]cyclohepten-5-one*

3 - Bromo - 7 - fluorosulfonyl - 10,11 - dihydro - 5H - dibenzo[a,d]cyclohepten-5-one (2.5 g., 0.00677 mole) together with 30 ml. of 25% aqueous dimethylamine and 30 ml. of *p*-dioxane is heated to refluxing for 3 hours. The brown solution is evaporated to dryness under reduced pressure and the residue partitioned between benzene and water. After washing with water, the benzene layer is evaporated to dryness under reduced pressure, leaving 3 - bromo - 7 - dimethylsulfamoyl - 10,11 - dihydro - 5H-dibenzo[a,d]cyclohepten - 5 - one as a tan solid, m.p. 142—145°C., in a yield of 2.1 g. (80%). An analytical sample melts at 146—148°C. after crystallizations from mixtures of benzene and hexane and from methanol.

Analysis, Calcd. for $C_{17}H_{16}O_3NBrS$: C, 51.78; H, 4.09; N, 3.55.
Found: C, 51.71; H, 4.12; N, 3.53.

C. *3-Dimethylsulfamoyl-10,11-dihydro-5H-dibenzo[a,d]-cyclohepten-5-one*

3 - Bromo - 7 - dimethylsulfamoyl - 10,11 - dihydro - 5H - dibenzo[a,d]cyclohepten - 5 - one, 8.0 g. (0.0203 mole), is dissolved in a mixture of 100 ml. of absolute ethanol, 70 ml. of dimethylformamide, and 5 ml. of triethylamine. The solution is hydrogenated at atmospheric pressure and in the presence of 600 mg. of 10% palladium on charcoal catalyst until hydrogen uptake is complete. Catalyst is removed by filtration and washed with absolute ethanol. The filtrate is evaporated to dryness under reduced pressure and the residue triturated with benzene. The insoluble triethylamine hydrobromide is filtered and the benzene filtrate evaporated to dryness under reduced pressure. Crystallization of the residual white solid from absolute ethanol affords 6.1 g. (97%) of 3 - dimethylsulfamoyl - 10,11 - dihydro - 5H - dibenzo[a,d]cyclohepten - 5-one, m.p. 122—124°C. The melting point is unchanged after crystallization from absolute ethanol.

Analysis, Calcd. for $C_{17}H_{17}O_3NS$: C, 64.74; H, 5.44; N, 4.44.
Found: C, 64.20; H, 5.47; N, 4.16.

D. *3-Dimethylsulfamoyl-5H-dibenzo[a,d]cyclohepten-5-one*

A mixture of 3 - dimethylsulfamoyl - 10,11 - dihydro - 5H - dibenzo[a,d]cyclohepten - 5 - one (6.1 g., 0.0194 mole), N-bromosuccinimide (3.6 g., 0.029 mole), benzoyl peroxide (50 mg.) and 50 ml. of benzene is stirred and heated to refluxing for 3 hours. The precipitated succinimide is filtered and washed with warm benzene. After washing with 5% aqueous sodium hydroxide and then with water, the benzene filtrate is evaporated to dryness under reduced pressure. The residual oily solid is suspended in 75 ml. of triethylamine and the mixture stirred at reflux for 16 hours. Triethylamine is evaporated under reduced pressure and the residual solid partitioned between benzene and water. The benzene layer is separated, washed with 3N hydrochloric acid and then with water, and evaporated to dryness under reduced pressure. Crystallization of the residual solid from 95% ethanol gives 2.83 g. (46.5%) of 3 - dimethylsulfamoyl - 5H-dibenzo[a,d]cyclohepten-5-one, m.p. 129.5—135.5°C. An analytical sample melts at 138.5—139.5°C. after repeated crystallizations from 95% ethanol.

Analysis, Calcd. for $C_{17}H_{15}O_3NS$: C, 65.16; H, 4.83; N, 4.47.
Found: C, 64.88; H, 4.85; N, 4.11.

E. *3-Dimethylsulfamoyl-5H-dibenzo[a,d]cyclohepten-5-ol*

3 - Dimethylsulfamoyl - 5H - dibenzo[a,d]cyclohepten - 5 - one (6.9 g., 0.022 mole) and 100 ml. of absolute methanol are stirred and heated to refluxing. A solution of 1.6 g. (0.0296 mole) of potassium borohydride in 12 ml. of water containing 1 pellet of potassium hydroxide is added dropwise at a rate such that reflux is maintained without external heating. After another 1-1/2 hours at reflux, the solution is evaporated to dryness under reduced pressure. The residual white solid is suspended in water, collected, and crystallized from 95% ethanol. The yield of 3-dimethylsulfamoyl-5H-dibenzo-[a,d]cyclohepten-5-ol is 6.05 g. (87%), m.p. 150—152°C. The melting point is unchanged by further recrystallization.

Analysis, Calcd. for $C_{17}H_{17}O_3NS$: C, 64.74; H, 5.44; N, 4.44.
Found: C, 64.22; H, 5.44; N, 4.40.

F. *5-Chloro-3-dimethylsulfamoyl-5H-dibenzo[a,d]cycloheptene*

A solution of 1.0 g. (0.00317 mole) of 3 - dimethylsulfamoyl - 5H - dibenzo[a,d]-cyclohepten - 5 - ol in a mixture of 2 ml. of dry dioxane and 2 ml. of absolute ether is cooled in ice and saturated with dry hydrogen chloride. The mixture is allowed to stand at room temperature for 5 hours and then is refrigerated overnight. The white crystalline product is collected, washed with petroleum ether, and dried in a vacuum desiccator over calcium chloride. The yield of 5 - chloro - 3 - dimethylsulfamoyl - 5H-dibenzo - [a,d]cycloheptene is 600 mg., m.p. 139.5—143.5°C. Dilution of the mother liquor with petroleum ether gives a second crop which is recrystallized from a mixture of ether and petroleum ether affording 250 mg., m.p. 138.5—142.5°C.

Analysis, Calcd. for $C_{17}H_{16}O_2NClS$: C, 61.16; H, 4.83; N, 4.20.
Found: C, 61.15; H, 4.57; N, 4.11.

G. *3-Dimethylsulfamoyl-5-(3-dimethylaminopropyl)-5H-dibenzo[a,d]cycloheptene*

By replacing the 5 - chloro - 5H - dibenzo[a,d] - cycloheptene used in Example 8, step D., with an equimolecular amount of 5 - chloro - 3 - (dimethylsulfamoyl) - 5H-dibenzo[a,d]cycloheptene and following substantially the same procedure described in Example 8, step D., there is obtained 3 - dimethylsulfamoyl - 5 - (3 - dimethylaminopropyl) - 5H - dibenzo[a,d]cycloheptene. The yield of yellow oily base is 50%.

H. *3-Dimethylsulphamoyl-5-(3-methylaminopropyl)-5H-dibenzo[a,d]cycloheptene*

3 - Dimethylsulphamoyl - 5 - (3 - dimethylaminopropyl) - 5H - dibenzo[a,d]-cycloheptene is converted to the corresponding cyanamide by following the procedure of Example 8 Step A. The cyanamide (0.28 g. 0.00071 mole) together with 2.8 ml. of glacial acetic acid, 2.0 ml. of water and 0.4 ml. of concentrated hydrochloric acid is heated to refluxing for 29 hours. The reaction mixture is evaporated to dryness under reduced pressure and the residue is dissolved in water. The aqueous solution is made alkaline with sodium hydroxide and the oily base that separates is extracted into ether. The washed and dried ether extract is evaporated under reduced pressure, leaving 3-dimethylsulphamoyl - 5 - (3 - methylaminopropyl) - 5H - dibenzo[a,d]cycloheptene as an oil weighing 170 mg. The base may be converted to the hydrogen oxalate salt by dissolution in absolute ethanol, addition of an equimolar quantity of oxalic acid dissolved in ethanol, and precipitation by the addition of ether. After repeated recrystallizations from absolute ethanol and from isopropyl alcohol, the hydrogen oxalate melts at 133.5—135.5°C., dec.

Analysis, Calcd. for $C_{21}H_{26}O_2N_2S.C_2H_2O_4$; C, 59.98; H, 6.13; N, 6.08.
Found: C, 60.00; H, 6.42; N, 6.09.

EXAMPLE 18

5-(3-Methylaminopropylidene)-3-methylsulphonyl-5H-dibenzo[a,d]cycloheptene

A. *Preparation of Cuprous methylmercaptide*

Concentrated ammonium hydroxide solution, 300 ml., is placed in a 1 liter, 3-necked flask fitted with a stirrer and gas inlet tube. The apparatus is cooled in an ice-bath and flushed with dry nitrogen while 40.0 g. (0.40 mole) of cuprous chloride is added portion-wise with stirring. To the dark blue solution is added 95% ethanol, 300 ml., and then methylmercaptan is bubbled into the cooled solution until precipitation is complete and the supernatant solution becomes yellow. The solid is collected and washed by centrifugation with four portions of dilute ammonium hydroxide solution, followed by four portions of absolute ethanol. The yellow product is dried under reduced pressure at 45—50°C. and finally in a vacuum desiccator over concentrated sulfuric acid. The yield of product is 41.4 g. (93%).

B. *Preparation of 3-methylmercapto-5H-dibenzo[a,d]-cyclohepten-5-one*

3 - Bromo - 5H - dibenzo[a,d]cyclohepten - 5 - one, 7.93 g., (0.028 mole), and cuprous methylmercaptide, 4.01 g. (0.036 mole), prepared as described in Step A., are put in a 100 ml. flask fitted with a stirrer and reflux condenser. Quinoline, 44.8 ml., and pyridine, 4.0 ml., are added and the slurry is heated at 200°C. with stirring for six hours. The reaction mixture is poured into 6 *N* hydrochloric acid, 120 ml., and ice and extracted with five 150 ml. portions of boiling benzene. The combined extracts are washed with three 200 ml. portions of 3 N. hydrochloric acid. After washing with water, the solvent is evaporated under reduced pressure leaving a brown oil, weight 7.41 g., as residue. The oil is dissolved in absolute methanol, 125 ml., and boiled with 370 mg. decolorizing carbon for thirty minutes. The filtrate is concentrated to 50 ml. and a yellow solid separates, along with a brown oil. The solid is mechanically separated from

the oil and dried in a vacuum desiccator over concentrated sulfuric acid. The product weighs 2.77 g. and melts at 66.5—67.5°C. The brown oil is evaporatively distilled at 146°C./0.1 mm .and the sublimate is crystallized from 25 ml. of absolute methanol to give 2.65 g. of material melting at 66.5—67.5°C. (77% yield).

Analysis, Calcd. for $C_{16}H_{12}OS$: C, 76.16; H, 4.80; S, 12.71.
Found: C, 76.35; H, 4.61; S, 12.60.

C. *Preparation of 5-(3-dimethylaminopropyl)-5-hydroxy-3-methylmercapto-5H-dibenzo[a,d]cycloheptene*

The Grignard reagent is prepared from 4.86 g. (0.2 g. atom) of magnesium and 24.34 g. (0.2 mole) of 3-dimethylaminopropyl chloride in 100 ml. of tetrahydrofuran as described in U.S. Patent No. 3,046,283, Step A. of Example 2. The solution is standardized by determination of the magnesium content. A volume of the solution containing 0.043 mole of Grignard reagent is cooled in an ice-bath and stirred while a solution of 3 - methylmercapto - 5H - dibenzo[a,d]cyclohepten - 5 - one, 5.38 g. (0.0213 mole) in 28 ml. tetrahydrofuran, is added over a period of twenty minutes. The reaction mixture is stirred in an ice-bath for 30 minutes and at room temperature for ninety minutes. The bulk of the solvent is then distilled at 45°C. under reduced pressure and benzene, 70 ml., is added to the residue. The solution is cooled in an ice-bath and the Grignard adduct is hydrolysed by the dropwise addition of water, 20 ml., with stirring. The benzene solution is separated and the gelatinous residue is extracted three times with 50-ml. portions of boiling benzene. The combined benzene extracts are extracted with three 45-ml. portions of 0.5 *M* citric acid solution and washed once with 50 ml. H_2O. The combined aqueous solutions are made basic with sodium hydroxide solution and extracted with ether. The combined extracts are washed with water and evaporated under reduced pressure. The yellow solid residue, m.p. 127—129°C., weighs 6.88 g. (95%). Recrystallization from ethanol-water yields 6.50 g. of product melting at 128—129°C.

Analysis, Calcd. for $C_{21}H_{25}NOS$: C, 74.29; H, 7.42; N, 4.13
Found: C, 74.60; H, 7.56; N, 3.94

D. *Preparation of 5-(3-dimethylaminopropyl)-5-hydroxy-3-methylsulfonyl-5H-dibenzo[a,d]cycloheptene*

5 - (3 - Dimethylaminopropyl) - 5 - hydroxy - 3 - methylmercapto - 5H - dibenzo-[a,d]cycloheptene, 21.53 g. (0.063 mole), is dissolved in glacial acetic acid, 250 ml., and the solution is cooled in an ice-bath while 30% hydrogen peroxide, 25.8 ml., is added dropwise with stirring. After standing at room temperature for twenty-two hours, the solution is saturated with sulfur dioxide for one hour with periodic cooling in an ice-bath. The solution is made basic with 10 *N* sodium hydroxide solution, 625 ml., and extracted with three 300 ml. portions of benzene. After washing the combined extracts with water, solvent is distilled under reduced pressure leaving a yellow oily residue, weight 23.20 g. The oil solidifies on standing at room temperature. Four recrystallizations from methanol-water give 13.22 g. (57%) of product melting at 170.5—171.5°C.

Analysis, Calcd. for $C_{21}H_{25}NO_3S$: C, 67.89; H, 6.78; N, 3.77.
Found: C, 67.72; H, 6.78; N, 3.59.

E. *5 - (3 - Dimethylaminopropylidene) - 3 - methylsulfonyl - 5H - dibenzo[a,d]-cycloheptene (mixed geometric isomers)*

5 - (3 - Dimethylaminopropyl) - 5 - hydroxy - 3 - methylsulfonyl - 5H - dibenzo-[a,d]cycloheptene (13.62 g., 0.037 mole) is dissolved in 136 ml. of trifluoroacetic acid. Trifluoroacetic anhydride, 68 ml., is added and the solution heated under reflux for 1 hour in a water-bath at 70°C. The dark green solution is cooled and poured into 250 ml. of ice-water. The mixture is rendered alkaline with 10 *N* sodium hydroxide solution while stirring and cooling and extracted with benzene. The benzene extract is washed with water and dried over sodium sulfate and the benzene distilled under reduced pressure. The mixed geometric isomers of 5 - (3 - dimethylaminopropylidene) - 3-methylsulfonyl - 5H - dibenzo - [a,d]cycloheptene are obtained as a brown oily residue in a yield of 13.19 g. (theory, 13.08 g.).

F. *α-Isomer of 5-(3-dimethylaminopropylidene)-3-methyl-sulfonyl-5H-dibenzo-[a,d]cycloheptene Hydrochloride*

The mixture of geometric isomers is dissolved in alcohol. One-half molar equivalent of dry hydrogen chloride dissolved in absolute alcohol is added and the solvent evaporated on a water-bath under reduced pressure. The residue is taken up in iso-

propyl alcohol and an equal volume of acetone is added. Absolute ether then is added to incipient cloudiness. The α-isomer separates as the crystalline hydrochloride, and is recrystallized to constant melting point. In one experiment the product so obtained sintered at 217°C. and melted at 218.5—219.5°C., clearing at 220.5°C.

Analysis, Calcd. for $C_{21}H_{23}O_2S.HCl$: C, 64.68; H, 6.20; N, 3.59; Cl, 9.09.
Found: C, 64.32; H, 6.35; N, 3.38; Cl, 8.78.

G. *β-Isomer of 5-(3-dimethylaminopropylidene)-3-methylsulfonyl-5H-dibenzo[a,d]cycloheptene*

The mother liquors from the separation of the hydrochloride of the α-isomer are evaporated and treated with one-quarter of a molar equivalent of hydrogen chloride in absolute alcohol. After evaporating the solvent, the residue is treated with isopropyl alcohol and acetone and another crop of solid precipitates with ether as described in Step F. The mother liquors then are evaporated under reduced pressure and the residue shaken with dilute sodium hydroxide and benzene. The benzene layer is separated, washed with water and the benzene distilled under reduced pressure. The base of the β-isomer is covered with hexane and allowed to stand until partially crystalline. The base then is recrystallized to constant melting point from cyclohexane. The product obtained in a typical experiment sintered at 141°C., melted at 142.5—143°C., clearing at 144°C.

Analysis, Calcd. for $C_{21}H_{23}NO_2S$: C, 71.36; H, 6.56; N, 3.96.
Found: C, 71.37; H, 6.52; N, 3.97.

H. *5-(3-Methylaminopropylidene)-3-methylsulfonyl-5H-dibenzo[a,d]cycloheptene (α-isomer)*

By substituting 5-(3-dimethylaminopropylidene)-3-methylsulfonyl-5H-dibenzo[a,d]cycloheptene (α-isomer), (product of Step F.), for the 5-(3-dimethylaminopropyl)-5H-dibenzo[a,d]cycloheptene of Example 8, and following substantially the procedure of Example 8, Steps A and B., 5-(3-methylaminopropylidene)-3-methylsulfonyl-5H-dibenzo[a,d]cycloheptene (α-isomer) is obtained in the form of a yellow oil. The product is converted to the hydrochloride that melts at 273—274.5°C. (sintered, 271.5°C.) after recrystallization from mixtures of methanol and ether.

Analysis, Calcd. for $C_{20}H_{21}NO_2S.HCl$: C, 63.90; H, 5.90; N, 3.73; Cl, 9.43.
Found: C, 63.67; H, 5.72; N, 3.59; Cl, 9.36.

I. *5-(3-Methylaminopropylidene)-3-methylsulfonyl-5H-dibenzo[a,d]cycloheptene (β-isomer)*

By substituting 5-(3-dimethylaminopropylidene)-3-methylsulfonyl-5H-dibenzo[a,d]cycloheptene (β-isomer), (Product of Step G.), for the 5-(3-dimethylaminopropyl)-5H-dibenzo[a,d]cycloheptene of Example 8, and following substantially the procedure of Example 8, Steps A and B., 5-(3-methylaminopropylidene)-3-methylsulfonyl-5H-dibenzo[a,d]cycloheptene (β-isomer) is obtained in the form of a yellow oil. The product is converted to the hydrogen maleate, which melts at 175—176°C.

Analysis, Calcd. for $C_{20}H_{21}NO_2S.C_4H_4O_4$: C, 63.28; H, 5.53; N, 3.08.
Found: C, 63.20; H, 5.39; N, 2.98.

EXAMPLE 19

10,11-Dihydro-5-(3-methylaminopropylidene)-3-methyl-sulfonyl-5H-dibenzo[a,d]cycloheptene (α-isomer)

A. *Hydrogenation of 5-(3-dimethylaminopropylidene)-3-methylsulfonyl-5H-dibenzo[a,d]cycloheptene (α-isomer)*

5-(3-Dimethylaminopropylidene)-3-methylsulfonyl-5H-dibenzo[a,d]-cycloheptene (α-isomer), (1.39 g., 0.0039 mole), dissolved in 20 ml. of ethanol, is hydrogenated over Raney nickel at 65°C. under an initial hydrogen pressure of 440 p.s.i. The catalyst is separated and the solvent evaporated under reduced pressure. Recrystallization from cyclohexane gives 10,11-dihydro-5-(3-dimethylaminopropylidene)-3-methylsulfonyl-5H-dibenzo[a,d]cycloheptene (α-isomer), m.p. 121—121.5°C. (sintered, 120°C.; cleared, 122.5°C.).

Analysis, Calcd. for $C_{21}H_{25}NO_2S$: ~~C, 70.96~~; H, 7.09; N, 3.94. C, 70.95;
Found: C, 70.75; H, 7.13; N, 3.84.

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B. *Demethylation of 10,11-dihydro-5-(3-dimethylaminopropylidene)-3-methylsulfonyl-5H-dibenzo[a,d]cycloheptene (α-isomer)*

By substituting 10,11 - dihydro - 5 - (3 - dimethylaminopropylidene) - 3 - methylsulfonyl - 5H - dibenzo[a,d]cycloheptene (α-isomer) for the 5 - (3 - dimethylaminopropyl) - 5H - dibenzo[a,d]cycloheptene of Example 8, and following substantially the procedure of Example 8, Steps A and B., 10,11 - dihydro - 5 - (3 - methylaminopropylidene) - 3 - methylsulfonyl - 5H - dibenzo[a,d]cycloheptene (α-isomer) is obtained as a yellow oil. The product is converted to the hydrochloride that melts at 275.5—276.5°C. (sintered, 274.5°C.) after recrystallization from methanol-ether mixtures.

Analysis, Calcd. for $C_{20}H_{23}NO_2S.HCl$: C, 63.56; H, 6.40; N, 3.71.
Found: C, 63.79; H, 6.22; N, 3.66.

EXAMPLE 20

10,11-Dihydro-5-(3-methylaminopropylidene)-3-methylsulfonyl-5H-dibenzo[a,d]cycloheptene (β-isomer)

A. *Hydrogenation of 5-(3-dimethylaminopropylidene)-3-methylsulfonyl-5H-dibenzo-[a,d]cycloheptene (β-isomer)*

The procedure of Example 19 Step A., is employed using the β-isomer instead of the α-isomer. The β-isomer of 10,11 - dihydro - 5 - (3 - dimethylaminopropylidene)-3 - methylsulfonyl - 5H - dibenzo[a,d]cycloheptene is obtained as the crystalline base, m.p. 109—110°C. (sintered, 108.5°C., cleared, 110.5°C.).

Analysis, Calcd. for $C_{21}H_{25}NO_2S$: C, 70.95; H, 7.09; N, 3.94.
Found: C, 71.20; H, 6.97; N, 3.88.

B. *Demethylation of 10,11-dihydro-5-(3-dimethylaminopropylidene)-3-methylsulfonyl-5H-dibenzo[a,d]cycloheptene (β-isomer)*

By substituting 10,11-dihydro-5-(3-dimethylaminopropylidene)-3-methylsulfonyl-5H-dibenzo[a,d]-cycloheptene (β-isomer) for the 5 - (3 - dimethylaminopropyl) - 5H-dibenzo[a,d]cycloheptene of Example 8, and following substantially the procedure of Example 8, Steps A and B., 10,11 - dihydro - 5 - (3 - methylaminopropylidene) - 3-methylsulfonyl - 5H - dibenzo[a,d]cycloheptene (β-isomer) is obtained in the form of a yellow oil. The product is converted to the hydrochloride that melts at 232.5—234.5°C. after recrystallization from isopropyl alcohol.

Analysis, Calcd. for $C_{20}H_{23}NO_2S.HCl$: C, 63.56; H, 6.40; N, 3.71.
Found: C, 63.49; H, 6.30; N, 3.66.

EXAMPLE 21

5-(3-Methylaminopropyl)-3-methylsulfonyl-5H-dibenzo-[a,d]cycloheptene

A. *3-Methylmercapto-5H-dibenzo[a,d]cyclohepten-5-ol*

3 - Methylmeracpto - 5H - dibenzo[a,d]cyclohepten - 5 - one, 27.9 g. (0.11 mole), is dissolved in 500 ml. of methanol. The solution is stirred and heated to refluxing while a solution of 14.9 g. (0.276 mole) of potassium borohydride in 150 ml. of water containing 0.2 ml. of 10 N. sodium hydroxide is added dropwise. After stirring at reflux for 2 hours, the solution is chilled and the precipitated product collected and washed with methanol yielding, typically, 27 g. (96%). An analytical sample melts at 117—118.5°C. after repeated recrystallizations from methanol.

Analysis, Calcd. for $C_{16}H_{14}OS$: C, 75.58; H, 5.55;
Found: C, 74.70; H, 5.56.

B. *5-Chloro-3-methylmercapto-5H-dibenzo[a,d]cycloheptene*

A solution of 18 g. (0.071 mole) of 3-methylmercapto-5H-dibenzo[a,d]cycloheptene-5-ol in 90 ml. of dry dioxane is cooled in an ice-bath and saturated with dry hydrogen chloride. A solid separates and, when precipitation appears to be complete, the mixture is stirred with 150 ml. of petroleum ether and the product collected, washed with petroleum ether, and dried in a vacuum desiccator over potassium hydroxide. The yield of 5 - chloro - 3 - methylmercapto - 5H - dibenzo[a,d]cycloheptene is 16g. (84%), m.p. 135—138°C. The melting point is unchanged by recrystallization from cyclohexane.

Analysis, Calcd. for $C_{16}H_{13}ClS$: C, 70.44; H, 4.80.
Found: C, 70.19; H, 4.81.

C. *5-(3-Dimethylaminopropyl)-3-methylmercapto-5H-dibenzo[a,d]cycloheptene*

The Grignard reagent is prepared from dimethylaminopropyl chloride (0.2 mole) and magnesium (0.2 g. atom) in 75 ml. of dry tetrahydrofuran following the method

described in U.S. Patent No. 2,996,503. A 15 ml. portion of this solution is cooled in an ice-bath and stirred while a solution of 4.7 g. (0.0172 mole) of 5-chloro-3-methylmercapto-5H-dibenzo[a,d]cycloheptene in 25 ml. of tetrahydrofuran is added dropwise. The usual precautions, such as careful drying of the apparatus and maintaining a nitrogen atmosphere, are observed. After stirring the mixture for 2 hours at room temperature, the bulk of the solvent is distilled at 30°C. under reduced pressure and the residue dissolved in benzene. The solution is cooled in an ice-bath and the excess of Grignard reagent hydrolysed by the dropwise addition of water. The benzene layer is decanted and the gelatinous precipitate washed with four 25 ml. portions of boiling benzene. After washing with water, the combined benzene solutions are extracted with 50 ml. of 0.5 M. citric acid. The acid extract is rendered alkaline with sodium hydroxide and the oily base extracted into benzene. Evaporation of the washed benzene extract under reduced pressure leaves 5 - (3 - dimethylaminopropyl) - 3 - methylmercapto-5H - dibenzo[a,d]cycloheptene as the oily residue weighing, typically, 4.2 g. (75%).

D. *5-(3-Dimethylaminopropyl)-3-methylsulfonyl-5H-dibenzo[a,d]cycloheptene*

5 - (3 - Dimethylaminopropyl) - 3 - methylmercapto - 5H - dibenzo[a,d]cycloheptene, 1.6 g. (0.0005 mole), is dissolved in 16 ml. of glacial acetic acid. The solution is cooled in an ice-bath at 15°C. and stirred while hydrogen peroxide, 2 ml. of 30%, is added dropwise. The ice-bath then is removed and the solution stirred while it warms to room temperature and then allowed to stand for 65 hours. The solution is cooled in an ice-bath and stirred while sulfur dioxide is introduced for 1 hour. After dilution with an equal volume of water and with stirring and cooling, the mixture is rendered alkaline with sodium hydroxide and the oily base extracted into benzene. Solvent is evaporated from the washed benzene extract under reduced pressure, leaving the product as a viscous oily residue in a yield of 1.75 g. (93%). The base may be converted to the hydrogen oxalate salt by treating a solution in ethanol with an equimolar quantity of oxalic acid dissolved in ethanol. 5 - (3 - Dimethylaminopropyl) - 3 - methylsulfonyl-5H - dibenzo[a,d]cycloheptene hydrogen oxalate separates as a white crystalline solid, m.p. 191—192°C. dec. The melting point is unchanged by recrystallization from ethanol.

Analysis, Calcd. for $C_{21}H_{25}NO_2S.C_2H_2O_4$: C, 62.00; H, 6.11; N, 3.15.
Found: ~~C, 61.39; H, 6.07; N, 3.14.~~

C 61.74; H, 5.95; N, 3.07.

E. *5-(3-Methylaminopropyl)-3-methylsulfonyl-5H-dibenzo-[a,d]cycloheptene*

By substituting 5 - (3 - dimethylaminopropyl) - 3 - methylsulfonyl - 5H - dibenzo-[a,d]cycloheptene for the 5 - (3 - dimethylaminopropyl) - 5H - dibenzo[a,d]cycloheptene of Example 8, Step A., and the following substantially the same procedure described in Example 8, Steps A and B., there is obtained 5 - (3 - methylaminopropyl)-3 - methylsulfonyl - 5H - dibenzo[a,d]cycloheptene as an oily residue. The base is converted to the hydrogen oxalate salt by treating an ethanolic solution of the base with a 10% excess of oxalic acid in ethanol. Dilution with absolute ether precipitates 5 - (3-methylaminopropyl) - 3 - methylsulfonyl - 5H - dibenzo[a,d]cycloheptene hydrogen oxalate as a white crystalline solid, m.p. 114—119°C. dec. An analytical sample melts at 114—115°C. dec. after two recrystallizations from mixtures of absolute ethanol and absolute ether.

Analysis, Calcd. for $C_{20}H_{23}NO_2S.C_2H_2O_4$: C, 61.24; H, 5.84; N, 3.25.
Found: C, 61.39; H, 6.07; N, 3.14.

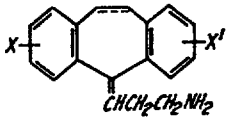
The following compounds can also be made by following the process of the present invention:

5-(methylaminopropylidene)-3-trifluoromethyl-5H-dibenzo[a,d]cycloheptene;
5-(methylaminopropyl)-3-trifluoromethyl-5H-dibenzo[a,d]cycloheptene;
5-(methylaminopropyl)-10,11-dihydro-3-trifluoromethyl-5H-dibenzo[a,d]cycloheptene;
5-(methylaminopropyl)-3-methyl-5H-dibenzo[a,d]cycloheptene;
5-(methylaminopropylidene)-3-methyl-5H-dibenzo[a,d]cycloheptene;
5-(methylaminopropyl)-3-methoxy-5H-dibenzo[a,d]cycloheptene;
5-(methylaminopropylidene)-3-methoxy-5H-dibenzo-[a,d]cycloheptene;
5-(methylaminopropylidene)-3-mercapto-5H-dibenzo[a,d]cycloheptene;
5-(methylaminopropyl)-3-mercapto-5H-dibenzo[a,d]cycloheptene;
5-(methylaminopropylidene)-3-methylmercapto-5H-dibenzo[a,d]cycloheptene;
5-(methylaminopropyl)-3-methylmercapto-5H-dibenzo[a,d]cycloheptene.

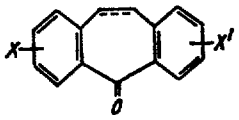
Certain of the starting materials used in one process of the present invention are claimed in Patent No. 858188.

WHAT WE CLAIM IS:—

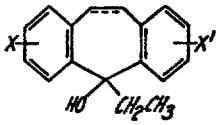
1. A process for the preparation of compounds of the formula:



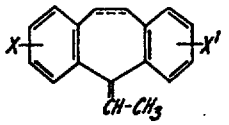
in which the dotted line between the 10 and 11 carbon atoms indicates that the compounds are saturated or unsaturated at this location, each of X and X^1 is a hydrogen or halogen atom or a trifluoromethyl, C_{1-6} alkyl, C_{1-4} alkoxy, mercapto, C_{1-4} alkylmercapto, C_{1-4} alkylsulphonyl, sulphamoyl, C_{1-4} alkylsulphamoyl or C_{2-6} dialkylsulphamoyl radical which comprises reacting a compound of the formula:



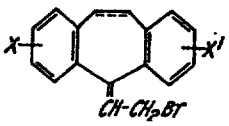
with an ethyl magnesium halide in an inert solvent, followed by hydrolysis, to form a compound of the formula:



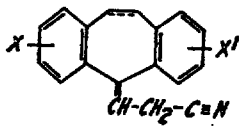
dehydrating the latter with a chemical dehydrating agent to form a compound of the formula:



reacting the latter with N-bromosuccinimide in the presence of a low-boiling solvent to form a compound of the formula:



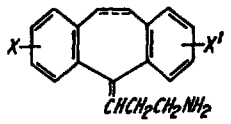
reacting the latter with a cyanide salt to form a compound of the formula:



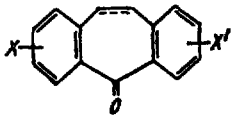
Certain of the starting materials used in one process of the present invention are claimed in Patent No. 858188.

WHAT WE CLAIM IS:—

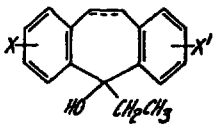
1. A process for the preparation of compounds of the formula:



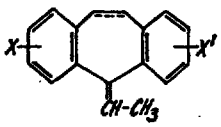
in which the dotted line between the 10 and 11 carbon atoms indicates that the compounds are saturated or unsaturated at this location, each of X and X^1 is a hydrogen or halogen atom or a trifluoromethyl, C_{1-6} alkyl, C_{1-4} alkoxy, mercapto, C_{1-4} alkylmercapto, C_{1-4} alkylsulphonyl, sulphamoyl, C_{1-4} alkylsulphamoyl or C_{2-8} dialkylsulphamoyl radical which comprises reacting a compound of the formula:



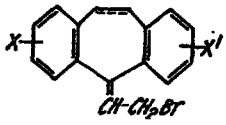
with an ethyl magnesium halide in an inert solvent, followed by hydrolysis, to form a compound of the formula:



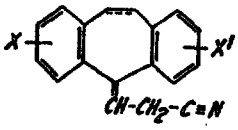
dehydrating the latter with a chemical dehydrating agent to form a compound of the formula:



reacting the latter with N-bromosuccinimide in the presence of a low-boiling solvent to form a compound of the formula:

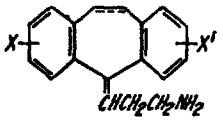


reacting the latter with a cyanide salt to form a compound of the formula:

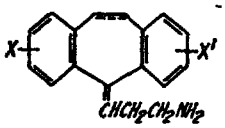


* C L M S *

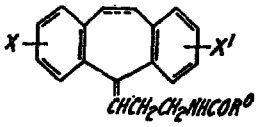
and reducing the latter with a metal hydride in the presence of a solvent to form a compound of the formula:



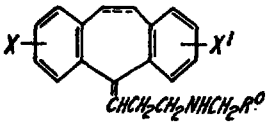
2. The process that comprises reacting a compound of the formula:



with an acyl halide or an acyl anhydride to form a compound of the formula:

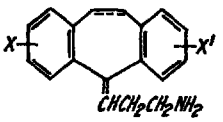


and reducing the latter with a metal hydride in a solvent to form a compound of the formula:

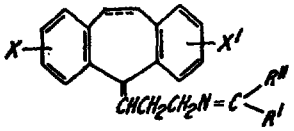


in which formulae the dotted line, X and X^1 are as defined in ~~Claim 1 and each of~~ R^1 C_{1-6} alkyl radical.

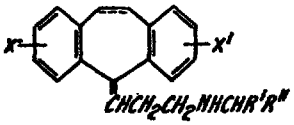
3. The process that comprises heating a compound of the formula:



with a ketone or an aldehyde in a solvent at reflux temperature to form a compound of the formula:



and reducing the latter with a metal hydride in a solvent to form a compound of the formula:

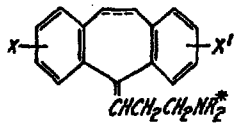


Claim 1 and R°

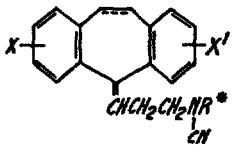
* C L M S *

in which formulae the dotted line, X and X^1 are as defined in Claim 1 and each of R^1 and R^{11} is a hydrogen atom or an alkyl radical, R^1 and R^{11} together containing not more than 5 carbon atoms.

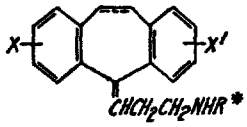
4. The process that comprises reacting a compound of the formula:



with a cyanogen halide to form a compound of the formula:

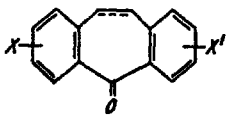


and hydrolysing the latter in an acid or alkaline medium to form a compound of the formula:

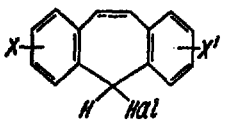


in which formulae the dotted line, X and X^1 are as defined in Claim 1, but with the proviso that when one of X and X^1 is hydrogen or halogen, the other is not hydrogen, and R* is a C_{1-6} alkyl radical.

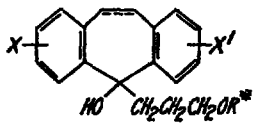
5. The process that comprises reacting a compound of the formula:



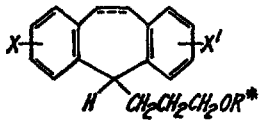
or



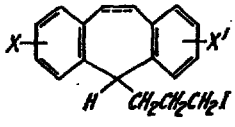
with an alkyl magnesium halide Grignard reagent having a terminal alkyl ether group to form a compound of the formula:



or

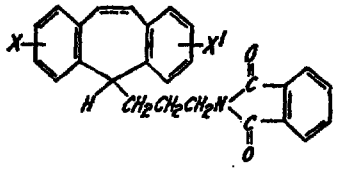


reacting the latter with hydriodic acid in the presence of a solvent to form a compound of the formula:

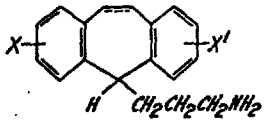


* C L M S *

reacting the latter in a solvent with potassium phthalimide to form a compound of the formula:

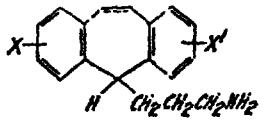


and either (A) reacting the latter with hydrazine hydrate in absolute alcohol or (B) hydrolysing the latter, to form a compound of the formula:

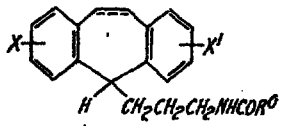


in which formulae Hal is a halogen atom, the dotted line, X and X^1 are as defined in claim 1 and R* is a C_{1-5} alkyl radical.

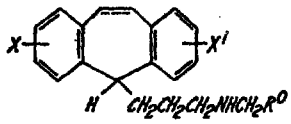
6. The process that comprises reacting a compound of the formula



with an acyl halide or an acyl anhydride to form a compound of the formula:

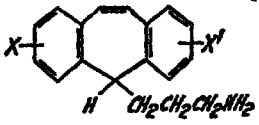


and reducing the latter with a metal hydride in a solvent to form a compound of the formula:

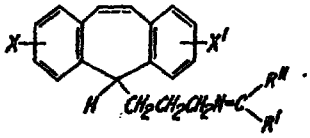


in which formulae the dotted line, X and X^1 are as defined in claim 1 and R° is a C_{1-5} alkyl radical.

7. The process that comprises reacting a compound of the formula:

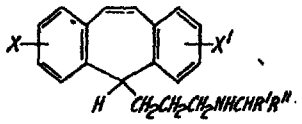


with a ketone or an aldehyde in a solvent to form a compound of the formula:



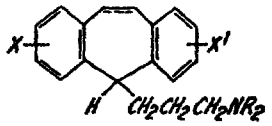
* C L M S *

and reducing the latter with a metal hydride in a solvent to form a compound of the formula:

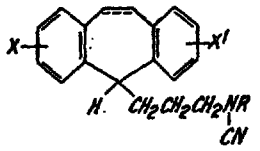


in which formulae the dotted line, X and X^1 are as defined in Claim 1 and R^1 and R^{11} are as defined in Claim 3.

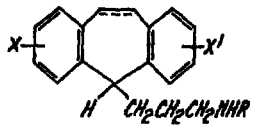
8. The process that comprises reacting a compound of the formula:



with cyanogen halide to form a compound of the formula:

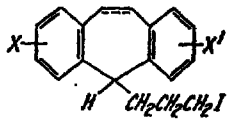


and hydrolysing the latter in an acid or alkaline medium to form a compound of the formula:

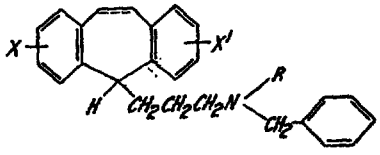


where the dotted line, X and X^1 are as defined in Claim 1 and R is a C_{1-6} alkyl radical.

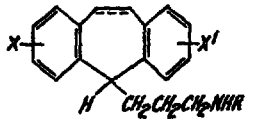
9. The process that comprises reacting a compound of the formula:



with an N-alkyl-benzylamine in a solvent to form a compound of the formula:



and catalytically debenzylating the latter to form a compound of the formula:

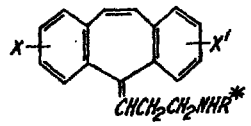


* C L M S *

where the dotted line X and X^1 are as defined in Claim 1, and R is a C_{1-6} alkyl radical.

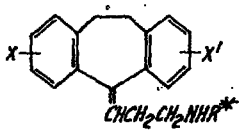
10. A process as claimed in any one of claims 1—9 substantially as hereinbefore described with reference to any appropriate foregoing Example.

11. A compound having the general formula:



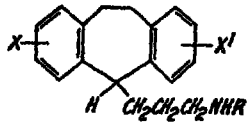
in which X and X^1 are as defined in claim 1 but with the proviso that when one of X and X^1 is hydrogen or halogen, the other is not hydrogen, and R* is a C_{1-6} alkyl radical.

12. A compound having the general formula:



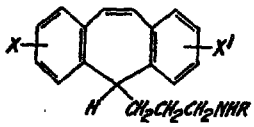
in which X and X^1 are as defined in claim 1 but with the proviso that when one of X and X^1 is hydrogen or halogen the other is not hydrogen, and R* is C_{1-6} alkyl radical.

13. A compound having the general formula:



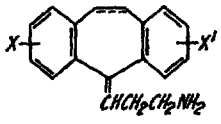
in which X and X^1 are as defined in Claim 1 and R is a hydrogen atom or a C_{1-6} alkyl radical.

14. A compound having the general formula:



in which X and X^1 are as defined in claim 1 and R is a hydrogen atom or a C_{1-6} alkyl radical.

15. A compound having the general formula:



in which the dotted line, X and X^1 are as defined in claim 1.

16. 5-(3-Aminopropylidene)-5H-dibenzo[a,d]cycloheptene.
17. 5-(3-Aminopropylidene)-10,11-dihydro-5H-dibenzo[a,d]cycloheptene.
18. 5-(3-Aminopropyl)-5H-dibenzo[a,d]cycloheptene.
19. 5-(3-Aminopropyl)-10,11-dihydro-5H-dibenzo-[a,d]cycloheptene.
20. 5-(3-butylaminopropyl)-5H-dibenzo[a,d]-cycloheptene.
21. 5-(3-methylaminopropyl)-5H-dibenzo[a,d]cycloheptene.
22. 5-(3-methylaminopropyl)-10,11-dihydro-5H-dibenzo[a,d]cycloheptene.
23. 5-(3-Methylaminopropyl)-3-methylsulfonyl-5H-dibenzo[a,d]cycloheptene.

* C L M S *

24. 5 - (3 - Methylaminopropylidene) - 10,11 - dihydro - 3 - methylsulfonyl-5H - dibenzo[a,d]cycloheptene.

25. 5 - (3 - Methylaminopropylidene) - 3 - methylsulfonyl - 5H - dibenzo[a,d]-cycloheptene.

26. 3 - Dimethylsulphamoyl - 5 - (3 - methylaminopropyl) - 5H - dibenzo[a,d]-cycloheptene.

27. Acid-addition salts of the compounds claimed in any one of claims 11—20 and 22—26.

28. Acid-addition salts of the compound claimed in claim 21.

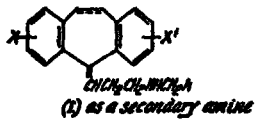
29. A compound as claimed in any one of claims 11—28 when prepared by a process as claimed in claims 1—10 or its obvious chemical equivalent.

For the Applicants,
D. YOUNG & CO.,
Chartered Patent Agents,
9, Staple Inn, London W.C.1.

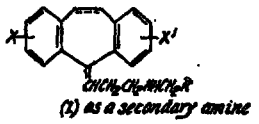
ERRATA

SPECIFICATION No. 1,008,263
Amendment No. 1

Page 2, line 30,
for



read



Page 15, line 57, *for* "C,70.96;" *read* "C 70.95;"

Page 17, line 32,
for "C 61.39; H, 6.07; N, 3.14."
read "C 61.74; H, 5.95; N, 3.07."

Page 19, line 11, *for* "Clai m1 and each of R^1" *read* "Claim 1 and R^o"

Page 19, line 12, *before* "C_{1-6}" *insert* "is a"

THE PATENT OFFICE
2nd December 1965

* C L M S *