REACTIONS OF 2,2'-BIPHENYLDICARBOXALDEHYDE

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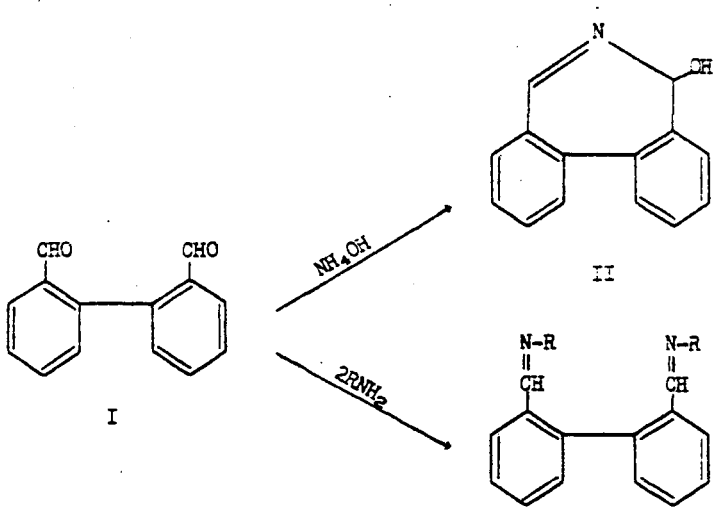
Although 2,2'-biphenyldicarboxaldehyde (I) was first reported by Kenner and Turner[1] in 1911 and later by other workers,[2] it has received only limited study because no simple method has existed for its preparation. Recent studies[3] on the ozonolysis of phenanthrene have resulted in a relatively simple preparation of the dialdehyde from a potentially abundant starting material. The ready availability of this dialdehyde thus served as a practical stimulus to our investigation of its chemical behavior.

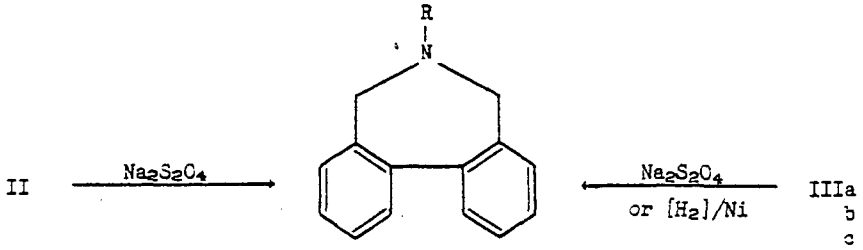
2,2'-Biphenyldicarboxaldehyde, I, was reacted with ammonia and primary amines to give Schiff-type bases. When I was heated with ammonium hydroxide, 5-hydroxy-5H-dibenz[c,e]azepine (II) was formed. The structure of II was assigned from elemental analysis and its infrared and NMR spectra. Infrared adsorption bands appeared at 6.15 μ (-N=C-) and 3.2-3.3 μ (-C-H). When I was reacted with benzylamine, methylamine, or aniline, 2,2'-bi(N-benzylbenzylidenimine) (IIIa), 2,2'-bi(N-methylbenzylidenimine) (IIIb), or 2,2'-bi(N-phenylbenzylidenimine) (IIIc) were the respective products. F. Mayer[2a] reported IIIc from the reaction of N-(o-iodobenzylidene)aniline and "Naturkupfer C". Infrared adsorption bands for the -N=C- linkage in these compounds occurred at 6.10 to 6.15 μ.



III (a) R = Benzyl
(b) R = Methyl
(c) R = Phenyl

When II, IIIa, and IIIb were refluxed with aqueous sodium hydrosulfite, 6,7-dihydro-5H-dibenz[c,e]azepine (IVa) and the 6-substituted derivatives (IVb and IVc) were the respective products. Hydrosulfite reduction of 2,2'-biphenyldicarboxaldehyde monoxime also gave IVa.

Raney nickel catalyst was sufficiently active for the low-pressure hydrogenation of IIIc to IVd but not II to IVa. However, hydrogenation at higher pressure of an ethanolic solution of I and methylamine over Raney nickel yielded IVc. Low-pressure hydrogenation of I with benzylamine and methylamine over palladium catalyst gave the respective products, IVb and IVc. Only representative azepines were prepared by the various methods of reduction, and no attempt was made to study exhaustively the several different possible combinations.



IVa R = H (from II)
b R = Benzyl (from IIIa)
c R = Methyl (from IIIb)
d R = Phenyl (from IIIc)

It was found unnecessary to isolate the Schiff bases prior to reduction by sodium hydrosulfite. By first refluxing I with the proper amine in methanol followed by treatment with the hydrosulfite, 6-allyl (V), 6-(3-dimethylaminopropyl) (VI), 6-(3-diethylaminopropyl) (VII), and 6-(2-aminoethyl)-6,7-dihydro-5H-dibenz[c,e]azepine (VIII) were also prepared.

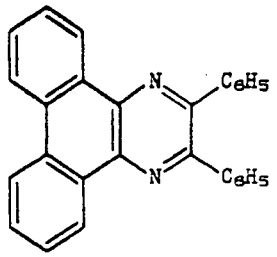
With the exception of the latter three derivatives, these 6,7-dihydroazepines had been prepared by the reaction of o,o'-bis(bromomethyl)biphenyl with ammonia or with primary amines.[4] A second method involved the reaction of diphenic anhydride with ammonia to give diphenamic acid. Diphenamic acid was cyclized to diphenimide, which was in turn reduced by lithium aluminum hydride to IVa.[5]

The present method of synthesizing these azepines is superior to previous methods because of the availability of the initial starting material, phenanthrene. The yields of the azepines, isolated as acid salts, ranged from 57 to 92%.

During the present work, a British patent[6] was granted to Hoffman-LaRoche Company for the reductive amination of the dialdehyde to azepines. However, the use of sodium hydrosulfite in reductive amination of an aldehyde appears to be novel.

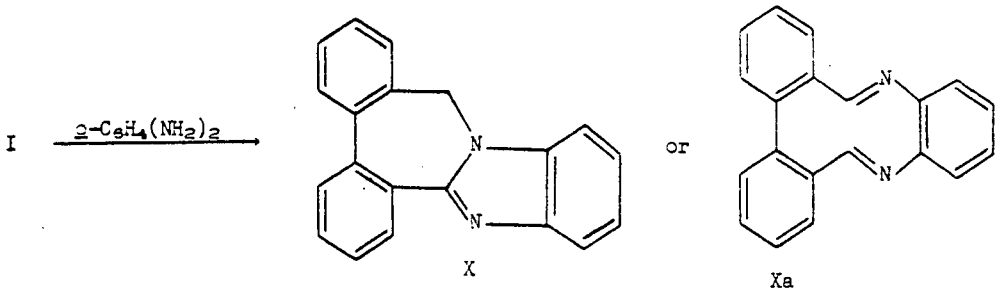
Randall and Smith[7] screened the 6-substituted azepines for pharmacological activity and demonstrated their antiepinephrine properties. V was the most effective member of the group tested.

When a solution of IIIa in N,N-dimethylformamide was refluxed with copper chromite, dehydrocyclization occurred to yield 2,3-diphenyldibenz[f,h]quinoxaline (IX).[8]



IX

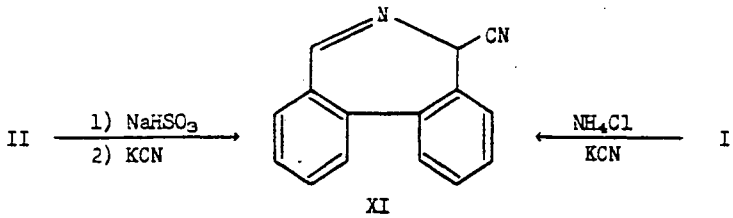
Sparatore[9] reacted I and o-phenylenediamine in methanol for 48 hours and obtained a glass, m.p. 52-57° C, for which he assigned the probable structure of 15H-dibenzo[c,e]benzimidazo[1,2-a]azepine (X). An uncharacterized hydrochloride melted at 260-265° C.



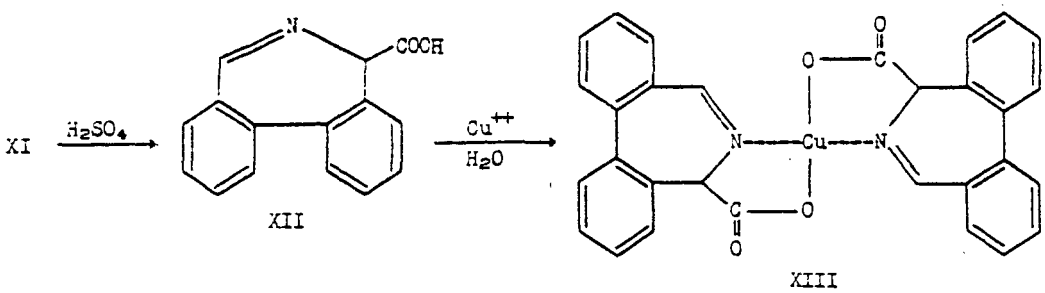
In our hands, the product from this reaction was obtained as a crystalline solid, m.p. 189-190° C, and was thought to exhibit polymorphism. Two different crystal forms were isolated which had different infrared spectra as Nujol mulls but the same spectrum in carbon disulfide and the same empirical formula. The NMR spectrum confirmed structure X rather than Xa.

A more convenient synthesis is to react the dialdehyde with o-phenylenediamine dihydrochloride in isopropyl alcohol, wherein the azepine precipitates presumably as the dihydrochloride monohydrate. The free base can be regenerated by treatment with alkali. The melting point of the hydrochloride is not definitive because it is believed to exist as the dihydrochloride, the monohydrochloride monohydrate, as well as the dihydrochloride monohydrate. Decomposition occurs during melting point determination, and the recorded melting point may be that of a decomposition product.

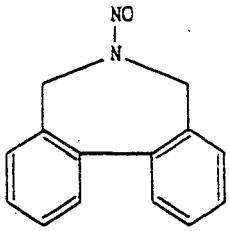
When II was treated with aqueous sodium bisulfite and then reacted with potassium cyanide, 5-cyano-5H-dibenz[c,e]azepine (XI) was obtained. When the dialdehyde was reacted with ammonium chloride and potassium cyanide, XI was isolated in almost quantitative yield.



Acid hydrolysis of XI gave a product, 5H-dibenz[c,e]azepine-5-carboxylic acid (XII), which could not be sufficiently separated from inorganics for characterization. The acid complexed with metallic ions to give colored, water-insoluble chelates. The copper chelate (XIII) was characterized.

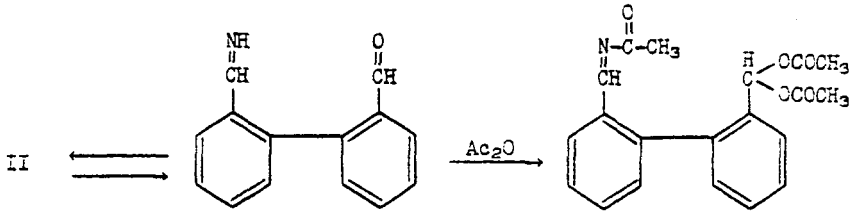


Nitrosation of IVa resulted in 6-nitroso-6,7-dihydro-5H-dibenz[c,e]azepine (XIV).

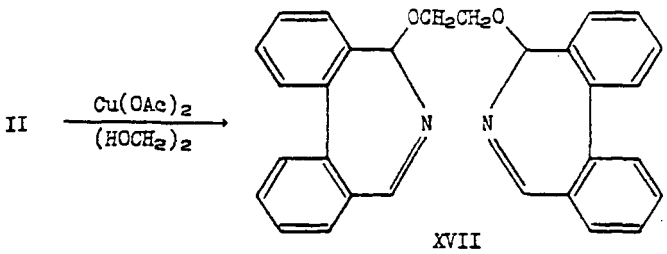


XIV

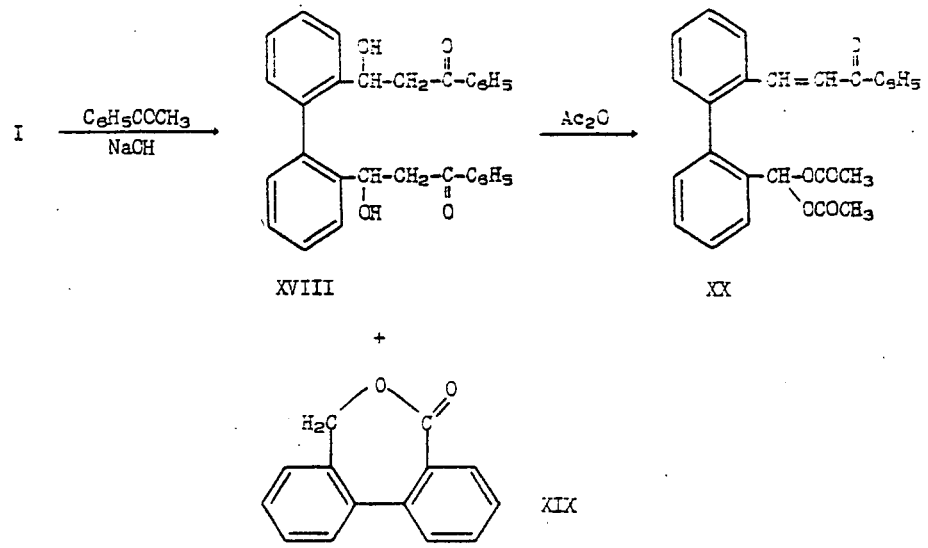
On acetylation of II by acetic anhydride, the 5-acetoxyazepine was not isolated, but rather 2-diacetoxymethyl-2'-acetyliminomethylbiphenyl (XV). The reaction might involve the isomeric structure, XVI.



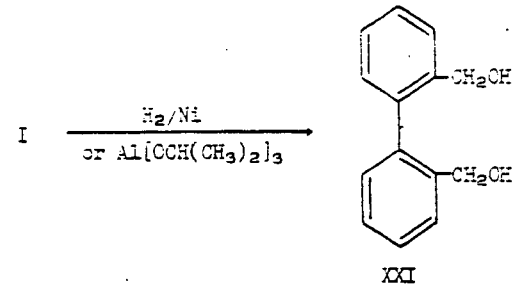
II was reacted with copper ion to give an insoluble complex, the structure of which could not be determined. However, II was reacted with ethylene glycol and cupric acetate to form 5,5'-ethylenedioxybis(5H-dibenz[c,e]azepine) (XVII). Monohydric alcohols gave oils which were not identified.



When I was reacted with two molecular equivalents of acetophenone in the presence of sodium hydroxide, a 55% yield of 2,2'-bis(1-hydroxy-2-benzoylethyl)-biphenyl (XVIII) was isolated, and 2,2'-diphenide (XIX) was identified as a by-product. With an equal molecular ratio of reactants, a 35% yield of XVIII and a 57% yield of XIX, resulting from a competing Cannizzaro reaction, were isolated. Reaction of XVIII with acetic anhydride afforded 2-diacetoxymethyl-2'-(benzoylvinylene)biphenyl (XX).



2,2'-Bis(hydroxymethyl)biphenyl (XXI) was obtained from I by either catalytic hydrogenation over Raney nickel or reduction by aluminum isopropoxide. The diol has been prepared by lithium aluminum hydride reduction of dimethyl diphenate[10] and diphenic acid[11] or by lithium borohydride reduction of dimethyl diphenate.[12]



Mayer[2a] had prepared 9,10-phenanthraquinone by a cyanide-catalyzed benzoin-type condensation of 2,2'-biphenyldicarboxaldehyde. It was found, however, that the intramolecular condensation was also light-catalyzed, although a peroxide, such as benzoyl peroxide, was necessary as an initiator.[13] The choice of solvent had a marked effect upon the yield of the quinone (Table I).

Table I

Yield of Phenanthraquinone Obtained from Irradiation of 2,2'-Biphenyldicarboxaldehyde in Various Solvents

Solvent	Yield of Phenanthraquinone, %	Reaction Conditions
t-Butyl Alcohol	5	Irradiation (Mercury Arc) for 48 hours at room temperature; 3 hours at reflux. One weight per cent benzoyl peroxide catalyst.
Acetic Acid	15	
Benzene	5	
Ethyl Ether	0	
Tetrahydrofuran	0	
Xylene	0	
Acetone	32	

The yield in acetone was increased from 32% to 50% by reflux for 72 hours. The remaining material was unreacted dialdehyde.

Experimental[14]

5-Hydroxy-5H-dibenz[c,e]azepine (II). Four grams of I was refluxed with 28% ammonium hydroxide (60 ml.) for 15 min. The mixture was cooled, and the colorless 5-hydroxy-5H-dibenz[c,e]azepine (3.7 g.; 97%), m.p. 126.8-128.8° C, was collected.

Anal. calcd. for $C_{14}H_{11}NO$: C, 80.36; H, 5.20; N, 6.70. Found: C, 80.59; H, 5.59; N, 7.00.

2,2'-Bi(N-benzylbenzylidenimine) (IIIa). I (2.1 g.; 0.01 mole), dissolved in toluene (30 ml.), was refluxed with benzylamine (2.20 ml.; 0.02 mole) for 15 min. The toluene was evaporated under reduced pressure, leaving an oil. Trituration with water afforded the solid 2,2'-bi(N-benzylbenzylidenimine) (3.86 g.; 99%), m.p. 94-97° C. Recrystallization from n-heptane gave crystals with a m.p. of 96-97° C.

Anal. calcd. for $C_{28}H_{24}N_2$: C, 86.56; H, 6.23; N, 7.21. Found: C, 86.53; H, 6.25; N, 7.21.

2,2'-Bi(N-methylbenzylidenimine) (IIIb). I (4.2 g.; 0.02 mole) was heated at 75-80° C in 15% aqueous monomethylamine (45 ml.) for 1 hr. with stirring. The colorless crystals (4.66 g.; 98%), m.p. 144-146° C, were collected. Recrystallization from n-heptane gave the pure 2,2'-bi(N-methylbenzylidenimine), m.p. 151.0-152.2° C.

Anal. calcd. for $C_{16}H_{16}N_2$: C, 81.32; H, 6.82; N, 11.86. Found: C, 81.32; H, 6.84; N, 11.84.

2,2'-Bi(N-phenylbenzylidenimine) (IIIc). I (2.1 g.; 0.01 mole) and aniline (2.04 g.; 0.021 mole) were refluxed in toluene (30 ml.) for 2 hr., with water being collected in a Dean-Stark trap. After evaporation of the toluene, the residue was dissolved in boiling n-heptane and the solution cooled. Light-yellow crystals (3.22 g.; 89%) of 2,2'-bi(N-phenylbenzylidenimine), m.p. 95.4-97.2° C, were obtained. Further recrystallization from n-heptane gave the pure compound, m.p. 97.6-99.0° C (lit., 98-99° C).[2a]

6,7-Dihydro-5H-dibenz[c,e]azepine (IVa), Method A. II (3.0 g.) and sodium hydrosulfite (9.0 g.) were refluxed in water (100 ml.) for 30 min. On cooling the solution, colorless crystals separated and were collected. Additional material was separated by adding sodium chloride to the filtrate. The combined solids were dissolved in water (200 ml.) containing concentrated hydrochloric acid (20 ml.), and the solution was refluxed for 30 min. After concentrating the solution to 50 ml. and cooling,

6,7-dihydro-5H-dibenz[c,e]azepine hydrochloride (3.0 g.; 92%), m.p. 290.2-291.2° C (lit., 286-288° C),[4b] separated.

Method B. I (2.1 g.; 0.01 mole) in methanol (30 ml.) was added to a solution of hydroxylamine hydrochloride (0.7 g.; 0.10 mole) in water (300 ml.). The precipitated 2,2'-biphenyldicarboxaldehyde monoxime (2.0 g.; 91%), m.p. 97-99° C, was collected.

Anal. calcd. for $C_{14}H_{11}NO_2$: C, 74.65; H, 4.92; N, 6.21. Found: C, 74.63; H, 4.96; N, 6.30.

The monoxime (1.0 g.; 0.005 mole) and sodium hydrosulfite (4.0 g.; 0.023 mole) were refluxed in water (50 ml.) for 30 min. The solid which separated on cooling was collected and refluxed for 30 min. in 10% hydrochloric acid (50 ml.). The solution was cooled and neutralized with sodium bicarbonate to precipitate 6,7-dihydro-5H-dibenz[c,e]azepine (0.7 g.; 81%), m.p. 88-93° C. Since the amine had not been reported as a solid, it was dissolved in ethyl ether, and the hydrochloride, m.p. 290-291° C, precipitated with hydrogen chloride. The infrared spectrum was identical to that of the product from Method A.

6-Benzyl-6,7-dihydro-5H-dibenz[c,e]azepine (IVb). I (2.1 g.; 0.01 mole) and benzylamine (1.6 ml.; 0.015 mole) were refluxed in toluene (15 ml.) for 1 hr. Water of reaction was collected in a Dean-Stark trap. The toluene was removed under an air blast, and the remaining oil, dissolved in methanol, was refluxed for 45 min. with sodium hydrosulfite (10 g.) in water (50 ml.). The methanol was distilled from the mixture and the cooled aqueous phase decanted from the semisolid material. The latter was refluxed with 3% hydrochloric acid (100 ml.) and the solution filtered. The cooled filtrate was made basic (pH 12) with sodium hydroxide. The precipitated oil was extracted into ether and the ether dried over potassium hydroxide pellets. Anhydrous hydrogen chloride was passed into the ether until the precipitation of 6-benzyl-6,7-dihydro-5H-dibenz[c,e]azepine hydrochloride hemihydrate (2.99 g.; 87%), m.p. 203-205° C (lit., 205° C),[4c] was complete.

Methiodide. 6-Methyl-6-benzyl-6,7-dihydro-5H-dibenz[c,e]azepinium iodide, m.p. 186-188° C (lit., 188-189° C).[4b]

6-Methyl-6,7-dihydro-5H-dibenz[c,e]azepine (IVc). I (4.2 g.; 0.02 mole) was heated at 85° C with stirring in 30% monomethylamine (25 ml.) for 30 min. The 2,2'-bi(N-methylbenzylidenimine) was collected and boiled with sodium hydrosulfite (12 g.) and water (75 ml.) for 30 min., allowing the volume to be reduced to 20 ml. When cool, the aqueous phase was decanted from the semisolid product. After washing and drying, this material was dissolved in n-heptane, and anhydrous hydrogen chloride was passed into the solution until precipitation of 6-methyl-6,7-dihydro-5H-dibenz-[c,e]azepine hydrochloride (4.0 g.; 81%), m.p. 221-224° C, was complete.

Methiodide. 6,6-Dimethyl-6,7-dihydro-5H-dibenz[c,e]azepinium iodide, m.p. 287-289° C (lit., 287-288° C).[4c]

Hydrogenation. A solution of I (0.0238 mole) and two molecular equivalents of the appropriate amine in ethanol (35 ml.) with the appropriate catalyst (10% on the dialdehyde) was subjected to hydrogenation in a low-pressure (50-60 p.s.i.g.) autoclave (Parr Instrument Company) or in a Magne-Dash autoclave (Autoclave Engineers) at higher pressures. After hydrogenation and removal of catalyst and solvent, the residue was refluxed with water (300 ml.) and sufficient hydrochloric acid to give pH 2. Any unreacted dialdehyde was collected by filtration, and the filtrate was concentrated to allow crystallization of the azepine hydrochloride.

Product	Catalyst	Hydrogen Pressure, p.s.i.g.	Temperature, °C	Time, hr.	Yield, %	m.p., °C
IVa	Raney Ni	850	75	17	51	287-290
IVa	5% Pt on Carbon	800	85	24	84	284-290
IVb	5% Pd on Carbon	60	50	18	91	202-208
IVc	5% Pd on Carbon	60	50	7	97	221-227

6-Phenyl-6,7-dihydro-5H-dibenz[c,e]azepine (IVd). 2,2'-Bi(N-phenylbenzylidenimine) (2.27 g.) in ethanol (50 ml.) was hydrogenated over Raney nickel (0.1 g.) at room temperature and 50 p.s.i. pressure for 7 hr. After removal of catalyst and evaporation of the ethanol, the semisolid product was crystallized from n-heptane to give 6-phenyl-6,7-dihydro-5H-dibenz[c,e]azepine (1.3 g.; 76%), m.p. 87-90° C. Upon recrystallization, the m.p. was 89.5-91.6° C.

Anal. calcd. for $C_{20}H_{17}N$: N, 5.17. Found: N, 5.38.

6-Allyl-6,7-dihydro-5H-dibenz[c,e]azepine (V). I (4.2 g.; 0.02 mole) and allylamine (3.1 ml.; 0.041 mole) were refluxed in methanol for 5 min. A solution of sodium hydrosulfite (15 g.) in water (75 ml.) was added to the cooled solution and the mixture refluxed for 30 min. After distilling over the methanol, the suspended oil was extracted into ethyl ether from the cooled aqueous phase. After drying the ether extract over potassium hydroxide, crude 6-allyl-6,7-dihydro-5H-dibenz[c,e]azepine hydrochloride (4.88 g.; 90%), m.p. 190-200° C, was precipitated by hydrogen chloride. Recrystallization from methanol-ethyl ether gave a 57% yield, m.p. 214-215° C (lit., 214-215° C).[4a]

6-(3-Dimethylaminopropyl)-6,7-dihydro-5H-dibenz[c,e]azepine (VI). Dimethylaminopropylamine (Union Carbide Chemicals Company) (4.90 g.; 0.048 mole) was added to a solution of I (10 g.; 0.048 mole) in methanol (15 ml.). After 5 min., a solution of sodium hydrosulfite (30 g.) in water (330 ml.) was added and the solution refluxed for 1 hr. After removing two-thirds of the solvent by distillation, 10% aqueous sodium hydroxide (75 ml.) was added to the cooled solution to precipitate the azepine as an oil. The oil was extracted into ethyl ether. The ether phase was washed well with water, separated, and evaporated from the amine. The azepine was dissolved in isopropyl alcohol and reacted with excess hydrogen chloride. Crystalline 6-(3-dimethylaminopropyl)-6,7-dihydro-5H-dibenz[c,e]azepine dihydrochloride monohydrate, m.p. 227-230° C (dec.), separated from the solution. The yield was 10.9 g. (62%). This material was recrystallized from isopropyl alcohol to a m.p. of 231.2-232.3° C (dec.).

Anal. calcd. for $C_{19}H_{24}N_2 \cdot 2HCl \cdot H_2O$: C, 61.45; H, 7.60; Cl, 19.10; N, 7.55. Found: C, 61.29; H, 7.91; Cl, 18.64; N, 7.35.

6-(3-Diethylaminopropyl)-6,7-dihydro-5H-dibenz[c,e]azepine (VII). The 6-(3-diethylaminopropyl) derivative was prepared similarly to the previous compound. The dihydrochloride was too deliquescent for easy handling, so the diphosphate was prepared by dissolving the amine in methanol (40 ml.) and 85% phosphoric acid (8.5 g.). After crystallization was complete, 17.4 g. (70% yield) of 6-(3-diethylaminopropyl)-6,7-dihydro-5H-dibenz[c,e]azepine diphosphate monohydrate, m.p. 220-223° C (dec.) (lit., 220-222° C),[5] was obtained. After recrystallization from ethanol-water, the pure compound melted at 221.5-223.5° C (dec.).

Anal. calcd. for $C_{21}H_{28}N_2 \cdot 2H_3PO_4 \cdot H_2O$: C, 48.27; H, 6.94; N, 5.36. Found: C, 48.82; H, 6.72; N, 5.19.

6-(2-Aminoethyl)-6,7-dihydro-5H-dibenz[c,e]azepine (VIII). Ethylenediamine (2.0 ml.; 0.02 mole) was added to a solution of I (4.2 g.; 0.02 mole) in methanol at room temperature. After 5 min., sodium hydrosulfite (10 g.) in water (50 ml.) was added and the mixture refluxed for 1 hr. After cooling, the aqueous phase was decanted and the residue refluxed with 5% aqueous sodium hydroxide (20 ml.) and toluene

(20 ml.) for a few minutes, dissolving the product in the toluene layer. The organic phase was separated, washed with water, and dried over potassium hydroxide pellets. The crude 6-(2-aminoethyl)-6,7-dihydro-5H-dibenz[c,e]azepine dihydrochloride (4.6 g.; 74%), m.p. 225-260° C, was precipitated by hydrogen chloride. Recrystallization from methanol gave the pure compound (3.9 g.; 63%), m.p. 268-270° C.

Anal. calcd. for $C_{16}H_{18}N_2 \cdot 2HCl$: C, 61.73; H, 6.47; N, 9.00. Found: C, 61.42; H, 6.29; N, 9.38.

2,3-Diphenyldibenz[f,h]quinoxaline (IX). I (5.0 g.) and benzylamine (5.1 g.) were refluxed in toluene (20 ml.) for 30 min. The water of reaction was collected in a Dean-Stark trap. After evaporation of the toluene, the residual oil, in N,N-dimethylformamide (35 ml.), was refluxed with powdered copper chromite (0.5 g.) for 2 hr. After removal of catalyst and solvent, the oily residue was triturated with methanol (15 ml.). The insoluble portion (1.5 g.), m.p. 260-265° C, was crystallized from benzene to give crystals (1.4 g.; 15%), m.p. 272-275° C (lit., 272° C).[15]

15H-Dibenzo[c,e]benzimidazo[1,2-a]azepine (X), Method A. A solution of I (2.10 g.) and o-phenylenediamine (1.08 g.) in methanol (40 ml.) remained at ambient temperature for 48 hr. After removal of the solvent by vacuum evaporation, a benzene (25 ml.) solution of the residual oil was absorbed on a column (2 × 16 cm.) of neutral alumina (Bio Rad AG7, 100-200 mesh). Elution with benzene gave 2.35 g. of a solid, m.p. 135-150° C. Recrystallization from benzene gave the product (1.37 g.; 50%), m.p. 189-190° C. Picrate, 279-281° C (dec.) (lit., 278-280° C).[9]

Anal. calcd. for $C_{20}H_{14}N_2$: C, 85.08; H, 4.99; N, 9.93. Found: C, 85.08; H, 5.34; N, 10.15.

NMR: The chemical shift value for the aliphatic protons was 5.03 τ (area ratio: aromatic to aliphatic protons, 5.5; theory, 6.0). A comparison of 1.82 τ for the methine proton in salicaldoxime and 6.38 τ for the methylene protons adjacent to the phenyl group in N,N,N',N'-tetrabenzylmethylene diamine[16] led to the assignment of structure X rather than structure Xa.

The dialdehyde (2.10 g.) and o-phenylenediamine dihydrochloride (1.81 g.), dissolved in methanol (25 ml.) (a deep-red solution), were heated at reflux for 20 min. (red color was discharged). The volume was reduced by one-half and the mixture cooled. The crystals thus formed (2.36 g.), m.p. 252-256° C beginning at ambient temperature, were collected. If a sample were introduced into the melting poing block at 240° C, the sample melted with gas evolution, solidified, and remelted at 252-256° C. The infrared spectrum contained peaks at 2.8 μ, 3.8 μ, and 4.3 μ. Thus the composition $X \cdot 2HCl \cdot H_2O$ was assigned. A sample of the above, heated at 140° C under vacuum, lost 4.34% in weight (theory for $1H_2O$: 4.83%) and now melted at 256-260° C. The 2.8 μ peak was now missing in the infrared spectrum of the dihydrochloride. $X \cdot 2HCl$ (1.0 g.) was recrystallized from isopropyl alcohol (25 ml.) and water (1 ml.). The crystals (0.5 g.) now melted at 263-267° C when placed in the apparatus at 240° C (m.p. 240-245° C from ambient temperature). The infrared spectrum now contained peaks at 2.8 μ and 3.8 μ but none at 4.3 μ, giving support to the composition $X \cdot HCl \cdot H_2O$.

Anal. calcd. for $C_{20}H_{14}N_2 \cdot HCl \cdot H_2O$: N, 8.32; Cl, 10.53. Found: N, 8.40; Cl, 10.40.

Method B. I (2.10 g.; 0.01 mole) and o-phenylenediamine dihydrochloride (1.81 g.; 0.01 mole) in isopropyl alcohol (50 ml.) were refluxed for 2 hr. The reaction mixture was cooled to 0° C and filtered. The residue (2.34 g.) was washed with cold isopropyl alcohol (10 ml.) and dried. The hydrochloride was dissolved in boiling 95% ethanol (30 ml.), and water (60 ml.) was added. The solution was made alkaline (pH 8) with aqueous 20% sodium hydroxide solution. The azepine base separated. After concentrating to one-half of the volume, the free base was collected. The yield was

1.99 g. (70%) of buff-colored product melting at 185-188° C. Crystallization from benzene gave rhomboid-like crystals, m.p. 186-189° C. Recrystallization from n-heptane gave mixed crystals, which on repeated recrystallization from n-heptane gave solely a needle form, m.p. 189-192° C.

Anal. calcd. for $C_{20}H_{14}N_2$: C, 85.08; H, 4.99; N, 9.93. Found: C, 85.26; H, 5.28; N, 10.19.

The needle form of X could be reconverted to the rhomboid form by dissolving in methanol, evaporating to an oily semisolid, and crystallizing from ethyl acetate. A few repetitions of this process gave solely the rhomboid form of X, m.p. 188-191° C.

Anal. calcd. for $C_{20}H_{14}N_2$: C, 85.08; H, 4.99; N, 9.93. Found: C, 85.24; H, 5.05; N, 9.85.

Comparison of the infrared spectra of the two forms in Nujol mulls showed sufficient dissimilarity to suggest polymorphism. The rhomboid form showed bands at 6.2 μ and 14.1 μ, which were absent in the needle form. The needle form showed bands at 10.8 μ and 11.9 μ, which were absent in the rhomboid form. Solution infrared spectra of the crystal forms in carbon bisulfide were identical, with no absorption at the above wave lengths.

5-Cyano-5H-dibenz[c,e]azepine (XI), Method A. A solution of II (6.3 g.; 0.03 mole) in acetic acid (30 ml.) was added to a solution of sodium bisulfite (3.1 g.; 0.03 mole) in water (75 ml.) and evaporated to dryness. A solution of potassium cyanide (1.9 g.; 0.03 mole) in water (30 ml.) was added to the residue dissolved in water (200 ml.). The solution was heated at 90° C for 1 hr. 5-Cyano-5H-dibenz[c,e]-azepine (5.0 g.; 82%), m.p. 150-152° C, precipitated. Recrystallization from ethyl acetate-n-heptane gave a m.p. of 154-156° C.

Anal. calcd. for $C_{15}H_{10}N_2$: C, 82.56; H, 4.62; N, 12.83. Found: C, 82.46; H, 5.21; N, 12.84.

Method B. A solution of I (21.0 g.; 0.1 mole) in methanol (300 ml.) was slowly poured into water (3 l.) containing ammonium chloride (16 g.; 0.33 mole) and potassium cyanide (6.5 g.; 0.01 mole). The solution was refluxed for 30 min. and cooled. The 5-cyano-5H-dibenz[c,e]azepine (20 g.; 99%), m.p. 150-153° C, was collected, washed with water, and dried.

5H-Dibenz[c,e]azepine-5-carboxylic Acid (XII). 5-Cyano-5H-dibenz[c,e]azepine (2.6 g.; 0.012 mole) was refluxed for 2 hr. in 67% sulfuric acid (50 ml.). The cooled reaction solution was poured into cold water (100 ml.) containing sodium hydroxide (34.6 g.). The pH of the solution was then adjusted to 6.8, and the solids, consisting of the product and sodium sulfate, which separated were collected and dried. 5H-Dibenz-[c,e]azepine-5-carboxylic acid was extracted from the solid into hot methanol. Evaporation of the methanol gave 2.4 g. (87%) of the acid, m.p. 249-253° C. Since the acid was difficult to free of sodium sulfate, an analytical sample was prepared in the form of a water-insoluble copper chelate, XIII. A solution of copper sulfate pentahydrate (0.628 g.; 0.0025 mole) in water (25 ml.) was added to a solution of the acid (1.1 g.; 0.005 mole) in water (25 ml.). The lavender-colored complex (1.2 g.), m.p. 221-222° C, which precipitated was collected, washed, and dried.

Anal. calcd. for $(C_{15}H_{10}NO_2)_2Cu \cdot 2H_2O$: C, 62.98; H, 4.22; Cu, 11.10; H_2O, 6.29. Found: C, 63.10; H, 4.20; Cu, 10.77; H_2O, 6.12.

6-Nitroso-6,7-dihydro-5H-dibenz[c,e]azepine (XIV). Sodium nitrite (2.8 g.; 0.04 mole) was added to a solution of 6,7-dihydro-5H-dibenz[c,e]azepine hydrochloride (2.0 g.; 0.009 mole) in water (150 ml.) and hydrochloric acid (2.0 ml.). 6-Nitroso-6,7-dihydro-5H-dibenz[c,e]azepine (1.8 g.; 93%), m.p. 107-112° C (dec.), which crystallized from solution, was collected and dried.

Anal. calcd. for $C_{14}H_{12}N_2O$: C, 75.00; H, 5.36; N, 12.50. Found: C, 74.90; H, 5.55; N, 12.53.

2-Diacetoxymethyl-2'-acetyliminobiphenyl (XV). II (2.3 g.) was refluxed in acetic anhydride (50 ml.) for 30 min. After removing the excess acetic anhydride by vacuum distillation, the crude product (3.5 g.), m.p. 132-160° C, was washed with ethyl acetate (15 ml.). The undissolved material was 2-diacetoxymethyl-2'-acetyliminomethylbiphenyl (2.0 g.; 51%), m.p. 177-181° C. Recrystallization from ethyl acetate gave the pure compound, m.p. 184-186° C.

Anal. calcd. for $C_{20}H_{19}NO_5$: C, 67.97; H, 5.42; N, 3.98. Found: C, 67.81; H, 5.40; N, 4.26.

5,5'-Ethylenedioxybis(5H-dibenz[c,e]azepine) (XVII). Cupric acetate monohydrate (7.5 g.; 0.038 mole) was added to a solution of II (15 g.; 0.072 mole) in ethylene glycol (150 ml.) and water (30 ml.) and the mixture refluxed for 1.5 hr. Precipitated cupric hydroxide was removed by filtration and chloroform added to the filtrate. The chloroform was washed with 7% aqueous sodium bicarbonate (300 ml.) and then with water. After separation, the chloroform layer was evaporated to a volume of 200 ml., and n-heptane was added to cause crystallization of the crude product (11.7 g.; 71%), m.p. 227-232° C. Recrystallization from chloroform-acetone gave the pure compound, m.p. 244-246° C.

Anal. calcd. for $C_{30}H_{24}N_2O_2$: C, 80.96; H, 5.44; N, 6.30. Found: C, 80.79; H, 5.58; N, 6.26.

2,2'-Bis(1-hydroxy-2-benzoylethyl)biphenyl (XVIII). A solution of sodium hydroxide (2.1 g.) in water (80 ml.) was added to a solution of I (4.6 g.; 0.022 mole) in ethanol (80 ml.). Acetophenone (5.2 g.; 0.044 mole) was added to the resulting solution over a 1-min. period. Colorless crystals soon formed and after only several minutes were collected, washed with ethanol (-5 to 0° C), and dried. This crude 2,2'-bis(1-hydroxy-2-benzoylethyl)biphenyl weighed 5.5 g. (55%), m.p. 175-185° C. Recrystallization from methanol gave the pure compound, m.p. 238.5-239.0° C (dec.).

Anal. calcd. for $C_{30}H_{26}O_4$: C, 79.75; H, 5.81. Found: C, 79.74; H, 5.69.

The use of one molar equivalent of acetophenone as above gave 35% yield of XVIII and 57% yield of diphenide, m.p. 124-130° C (lit., 132° C).[1] The infrared spectrum was identical with that of authentic diphenide.

2-Diacetoxymethyl-2'-(benzoylvinylene)biphenyl (XX). 2,2'-Bis(1-hydroxy-2-benzoylethyl)biphenyl (6.0 g.) was refluxed in acetic anhydride (100 ml.) for 1 hr. The acetic anhydride was removed by flash evaporation. The residual oil was dissolved in ethanol, from which, on concentration, 3.9 g. (70%) of crude 2-diacetoxymethyl-2'-(benzoylvinylene)biphenyl, m.p. 197-204° C, was obtained. Recrystallization from ethyl acetate gave the pure compound, m.p. 208.5-209.5° C.

Anal. calcd. for $C_{26}H_{22}O_5$: C, 75.30; H, 5.36; N, 19.34. Found: C, 74.92; H, 5.46; N, 19.62.

2,2'-Bis(hydroxymethyl)biphenyl (XXI), Method A. Aluminum isopropoxide (2.8 g.; 0.014 mole) was mixed with anhydrous isopropyl alcohol (100 ml.) containing I (4.2 g.; 0.02 mole). Acetone was distilled from the reaction through a 12-in. Vigreaux column followed by the majority of the isopropyl alcohol. The cooled reaction mixture was poured into 20% hydrochloric acid (100 ml.). The precipitated 2,2'-bis(hydroxymethyl)biphenyl (4.01 g.), m.p. 92-100° C, was collected, washed, and dried. Recrystallization from benzene gave 2.79 g. (65%) of material melting at 109.4-109.8° C (lit., 112-113° C).[10]

Method B. I (15 g.) in ethanol (100 ml.) was hydrogenated (50 p.s.i.) over Raney nickel catalyst (0.5 g.) at 52° C for 18 hr. After removal of the catalyst by filtration, the ethanol was flash evaporated and the residue recrystallized from benzene to give 12.4 g. (81%) of 2,2'-bis(hydroxymethyl)biphenyl, m.p. 109.0-109.8° C.

9,10-Phenanthraquinone. A solution of I (2.1 g.; 0.01 mole) in acetone (100 ml.) containing benzoyl peroxide (0.02 g.) was refluxed for 72 hr. with continuous irradiation from a mercury vapor lamp (Hanovia Chemical and Manufacturing Company, Type 16200; filter removed) at a distance of 5-6 in. The solution was aerated at the rate of approximately 0.06 S.C.F.M. The acetone was flash evaporated, and a 50% yield of 9,10-phenanthraquinone, m.p. 196-206° C (lit., 206-207° C),[17] was recovered by washing the residue with ethyl ether. The material dissolved in the ether was largely unchanged dialdehyde, identified by an infrared spectrum.

Other solvents—t-butyl alcohol, acetic acid, benzene, ethyl ether, tetrahydrofuran, and xylene—were employed similarly, except that the reaction time was 48 hr. at room temperature followed by 3 hr. at reflux.

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