α-1,3-Dimethyl-4-phenyl-4-propionoxyazacyclooctane (XVII). To a solution of phenyllithium prepared by adding 7.1 g. of bromobenzene to a mixture of 0.635 g. (0.091 g.-atom) of lithium shot and 50 ml. of anhydrous ether under nitrogen, followed by 2 hr. of reflux, was added at −20°, 2.0 g. (0.0129 mol.) of XIV in 25 ml. of toluene. After 0.5 hr., the reaction mixture was warmed to room temperature and allowed to stand overnight. A solution of 6.66 g. (0.0475 mol.) of propionic anhydride in 25 ml. of toluene with 2 drops of concentrated sulfuric acid as a catalyst was added and the solution was concentrated until the temperature of the distillate reached 105°, when the temperature was held at this point for 3 hr. After the solution was cooled and made alkaline by adding 20 ml. of 5% sodium hydroxide solution, the product was extracted from the toluene layer by washing with dilute hydrochloric acid, the acid extract washed with ether to remove traces of neutral material, and made alkaline by adding cold 4*N* sodium hydroxide. The product was taken up in ether, dried over anhydrous potassium carbonate, filtered, concentrated, and distilled to give 1.0 g. (27%) of amber liquid (XVII) boiling from 90–92° at 0.20 mm., n_D^{24} 1.5262. While two DL mixtures are possible, no evidence for more than one form, designated α, has been found in this product.

Anal. Calcd. for $C_{18}H_{27}NO_2$: C, 74.70; H, 9.41. Found: C, 74.88; H, 9.76.

The *picrate*, melting at 128–130°, was formed in ether and was recrystallized from 1-butanol.

Anal. Calcd. for $C_{24}H_{30}N_4O_9$: C, 55.60; H, 5.85; N, 10.80. Found: C, 55.73; H, 5.49; N, 10.41.

The *acid citrate*, melting at 134–135°, was formed in absolute ethanol.

Anal. Calcd. for $C_{24}H_{35}NO_9$: C, 59.90; H, 7.31; N, 2.91. Found: C, 60.97; H, 7.13; N, 2.98.

PHILADELPHIA, PA.

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY, GEORGIA INSTITUTE OF TECHNOLOGY]

Reaction of 2-Phenylquinoxaline and of 2,3-Diphenylquinoxaline with Dimethyl Acetylenedicarboxylate[1]

ERLING GROVENSTEIN, JR., WILLIAM POSTMAN, AND JAMES W. TAYLOR

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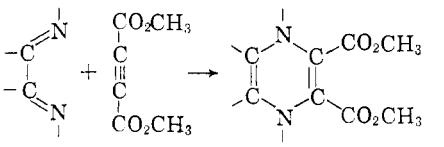
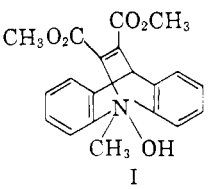
2,3-Diphenylquinoxaline reacts with dimethyl acetylenedicarboxylate in methanol to give a yellow product which consists of 1 mole each of 2,3-diphenylquinoxaline, dimethyl acetylenedicarboxylate, and methanol. On the basis of its reactions and ultraviolet absorption spectra, this product is assigned the structure 1-(1,2-dicarbomethoxyvinyl)-2,3-diphenyl-2-methoxy-1,2-dihydroquinoxaline (IV) in neutral or basic solution in methanol, while in acidic methanol it exists as 1-(1,2-dicarbomethoxyvinyl)-2,3-diphenylquinoxalinium cation (VI). 2-Phenylquinoxaline reacts similarly with dimethyl acetylenedicarboxylate to give a product which after long exposure to the atmosphere was isolated as 1-(1,2-dicarbomethoxyvinyl)-3-phenyl-2-hydroxy-1,2-dihydroquinoxaline (VIII). Reaction of 2,3-diphenylquinoxaline with hydrogen peroxide in acetic acid gave under the present conditions *N,N'*-dibenzoyl-*o*-phenylenediamine in addition to the previously reported *N,N'*-dioxo-2,3-diphenylquinoxaline.

The addition of dienophiles to 1-aza- and 1,4-diaza-1,3-dienes might be expected to occur in a manner analogous to the ordinary Diels-Alder reaction, thus for a 1,4-diaza-1,3-diene with dimethyl acetylenedicarboxylate as indicated in Equation 1. Such reactions, however, generally



(1)

appear to proceed in other ways if reaction occurs at all.[2] However, dehydroindigo undergoes 1,4-addition of dienophiles such as styrene to its two heterocyclic nitrogens[3] and acridine adds dimethyl acetylenedicarboxylate in methanol, according to Diels and Thiele,[4] to give chiefly an adduct which was formulated as stucture I. The report of Diels and Thiele encouraged us to investigate the reaction of dimethyl acetylenedicarboxylate with 2-phenyl- and 2,3-diphenylquinoxaline. During the course of the present work, Acheson and Burstall[5] showed that the product of Diels and Thiele had structure IIa in neutral



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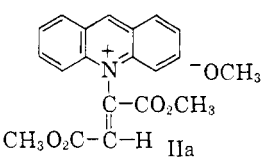
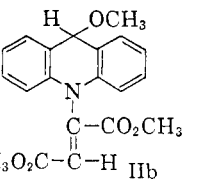


IIa



IIb

(1) Based chiefly upon the following theses at the Georgia Institute of Technology: W. Postman, Ph.D. Thesis, June, 1953; J. W. Taylor, M.S. thesis, June, 1958.

(2) M. C. Kloetzal, *Org. Reactions*, **4**, 1 (1948); H. L. Homes, *Org. Reactions*, **4**, 60 (1948).

(3) R. Pummerer, H. Fiesselmann, and O. Müller, *Ann.*, **544**, 206 (1940); R. Pummerer and E. Stieglitz, *Ber.*, **75**, 1072 (1942).

(4) O. Diels and W. E. Thiele, *Ann.*, **543**, 79 (1940).

(5) R. M. Acheson and M. L. Burstall, *J. Chem. Soc.*, 3240 (1954).

methanol and IIb in alkaline methanol. Similar structures were reported by Acheson and Bond[6] for the product from phenanthridine and by Acheson and Jefford[7] for the product from 2,3-benzacridine with dimethyl acetylenedicarboxylate in methanol.

Adduct from 2,3-Diphenylquinoxaline. Dimethyl acetylenedicarboxylate and 2,3-diphenylquinoxaline in methanol upon standing gave a yellow adduct whose elemental analysis, methoxyl content, and molecular weight were in agreement with that required for an adduct from 1 mol. each of dimethyl acetylenedicarboxylate, diphenylquinoxaline, and methyl alcohol. The adduct could be distilled *in vacuo* with little decomposition and could be recrystallized from solvents such as acetonitrile and carbon tetrachloride. The methanol in the adduct is, therefore, rather firmly bound, a fact which is also required by molecular weight determination in triphenylmethane. On the other hand, reaction of the adduct in ether solution with perchloric acid, picric acid, or ferric chloride gave crystalline products of composition expected for replacement of one methoxyl by perchlorate, picrate, or tetrachloroferrate(III) anion. A chloride could apparently be obtained by a similar procedure, but it proved too unstable for analysis.

When the yellow adduct was refluxed with ethanolic hydrochloric acid, 2,3-diphenylquinoxaline was recovered in nearly 70% yield. Reaction of the adduct with two molar equivalents of ethanolic potassium hydroxide gave some 45% yield of 2,3-diphenylquinoxaline, 16% of desoxybenzoin (benzyl phenyl ketone), 17% of quinoxaline-2-carboxylic acid, and 22% yield of carbon dioxide.

The adduct in acetone showed no reaction with a dilute solution of potassium permanganate at room temperature. The adduct, however, was oxidized by a hot solution of sodium dichromate in acetic acid; only 2,3-diphenylquinoxaline was recovered from the oxidation mixture. The adduct was oxidized by hydrogen peroxide in acetic acid in low yield to *N,N'*-dibenzoyl-*o*-phenylenediamine; this same product was obtained along with *N,N'*-dioxo-2,3-diphenylquinoxaline by oxidation of 2,3-diphenylquinoxaline under similar conditions.

The most outstanding result from the cleavage of the adduct by acid, base, or oxidizing agents—in so far as it relates to the structure of the adduct—was the isolation of 2,3-diphenylquinoxaline or its oxidation product. This result suggests that the adduct retains the structural skeleton of 2,3-diphenylquinoxaline and provides evidence against the attachment of dimethyl acetylenedicarboxylate to 2,3-diphenylquinoxaline by way of a C—C bond.

(6) R. M. Acheson and G. J. F. Bond, *J. Chem. Soc.*, 246 (1956).

(7) R. M. Acheson and G. W. Jefford, *J. Chem. Soc.*, 2676 (1956).

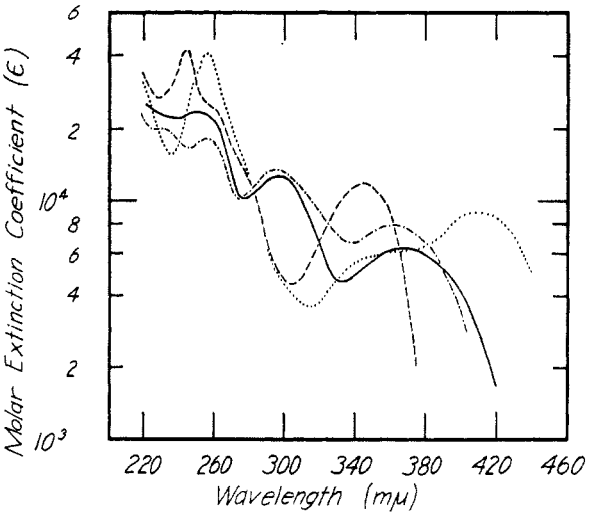
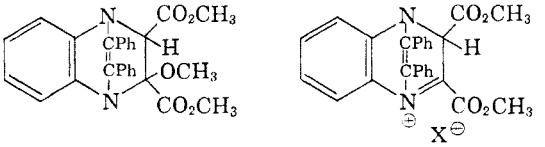


Fig. 1. Ultraviolet absorption spectra of adduct (IV) from 2,3-diphenylquinoxaline in methanol or in methanolic 0.1*N* $NaOCH_3$ (———) and in methanolic 0.1*N* $HClO_4$ or HCl (.....); adduct (VIII) from 2-phenylquinoxaline in methanol (-·-·-·); 2,3-diphenylquinoxaline in methanol (- - - -)

The isolation of quinoxaline-2-carboxylic acid suggests that at least one (possibly two) of the acetylenic carbon atoms of dimethyl acetylenedicarboxylate is joined to a heterocyclic nitrogen atom of 2,3-diphenylquinoxaline.

In Fig. 1 are presented the ultraviolet absorption spectra of the adduct in neutral, alkaline, and acidic methanol. The adduct gives the same spectrum in neutral methanol as in 0.1*N* methanolic $NaOCH_3$; however, the spectrum is appreciably altered in 0.1*N* methanolic $HClO_4$ or HCl. By way of comparison the spectrum of 2,3-diphenylquinoxaline differs significantly from that of its adduct with acetylenic ester; moreover, the spectrum of 2,3-diphenylquinoxaline is essentially the same in neutral methanol and in 0.1*N* methanolic HCl. The adduct and especially its derivatives with acids absorb more intensely at longer wave lengths than does 2,3-diphenylquinoxaline.

These data cannot be explained satisfactorily in terms of a structure such as IIIa for the adduct Structure IIIa could not undergo a ready ionization



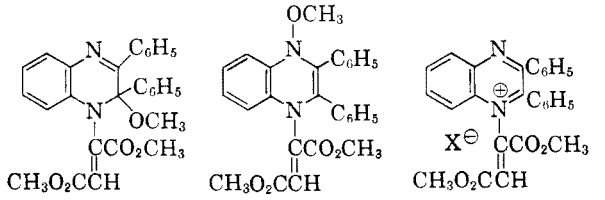
IIIa IIIb

(Ph = C_6H_5, X^- = Cl^-, ClO_4^-, *etc.*)

with dilute acids to give IIIb because IIIb is a highly strained structure, having a double bond at a bridgehead in violation of Bredt's rule. Conceivably III might undergo a more complex ionization to give VI. A more decisive argument against IIIa is that such a compound would not be

expected to be colored,[8a] as it has merely a *cis*-stilbene unit as its most extended chromophore (the nitrogen atoms of IIIa are not conjugated with the double bonds because of unfavorable geometry[8b] for orbital overlap).

Structure IV is therefore proposed for the adduct from 2,3-diphenylquinoxaline with dimethyl acetylenedicarboxylate in methanol. This structure is analogous to those proposed by Acheson[5,6,7] and co-workers and moreover offers an explanation for the ready ionization by dilute acids, as IV would be expected to combine with acids to give the more fully aromatic structure VI. Structure IV is favored



IV V VI

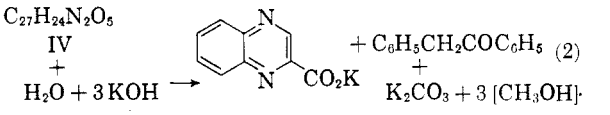
a, X = $FeCl_4$
b, X = Picrate
c, X = ClO_4

over V for the adduct because it more satisfactorily accounts for the color of the adduct,[8a] because bond energy calculations[9] indicate that IV should be about 6 kcal. per mole more stable than V, and because IV might be expected to have more resonance energy than V because of more effective conjugation. The relationship between IV and VI is analogous to the tautomeric change recognized by Hantzsch[10] and by Kehrmann.[11]

Dilute solutions ($2\times10^{-5}M$) of the perchlorate VIc in absolute methanol showed ultraviolet absorption which was almost identical with that of the adduct IV under similar conditions. This result indicates that VI undergoes extensive methanolysis to give IV under even weakly acidic conditions.

No direct evidence concerning the stereochemistry of IV was established, but the structure of IV suggests that it was formed by a type of Michael addition. Such additions frequently take place with acetylenic compounds[12] to give mainly products of *trans* addition. Moreover a *trans* structure was suggested for the closely related addition products of Acheson[5,6,7] and co-workers.

The alkaline hydrolysis of IV follows two routes: one regenerates 2,3-diphenylquinoxaline while the other follows Equation 2. The reaction leading to

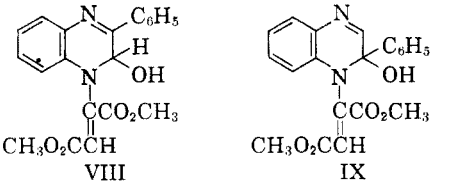


(2)

quinoxaline-2-carboxylic acid is of interest but the present results cannot distinguish between the several likely paths.

Adduct from 2-Phenylquinoxaline. 2-Phenylquinoxaline with dimethyl acetylenedicarboxylate in methanol gave a viscous oil under conditions similar to those employed with 2,3-diphenylquinoxaline. While the oil resisted usual methods of crystallization, upon solution in carbon tetrachloride followed by standing in an open evaporating dish for three weeks the oil was converted into a yellow crystalline product. This product, after recrystallization from carbon tetrachloride and methyl ethyl ketone, had the correct analysis, molecular weight, and methoxyl content for an adduct composed of 1 mol. each of 2-phenylquinoxaline, dimethyl acetylenedicarboxylate, and water. Oxidation of the adduct by potassium permanganate in aqueous acetone gave 2-hydroxy-3-phenylquinoxaline and 2-phenylquinoxaline. 2-Phenylquinoxaline was not oxidized by potassium permanganate under similar conditions. Reaction of the adduct with two molar equivalents of alcoholic potassium hydroxide gave some 2-phenylquinoxaline but mostly yielded a dibasic acid which resisted attempts at purification. The crude dibasic acid reacted with potassium hydroxide to give 2-phenylquinoxaline.

The ultraviolet absorption spectrum of the adduct from 2-phenylquinoxaline is shown in Fig. 1. This spectrum is similar to that of the adduct (IV) from 2,3-diphenylquinoxaline. The adduct from 2-phenylquinoxaline is accordingly assigned structure VIII and the dibasic acid is evidently the free acid corresponding to VIII, as it possesses a



VIII IX

similar ultraviolet absorption spectrum. The isomeric structure IX for the adduct is improbable both because of the ultraviolet absorption spectrum and because IX, unlike VIII, would not be expected to undergo ready oxidation by potassium permanganate to give 2-hydroxy-3-phenylquinoxaline.

(8) a. *cf.* J. N. Murrell, *J. Chem. Soc.*, 296 (1959). b. *cf.* B. M. Wepster, *Rec. trav. chim.*, **71**, 1159 (1952).

(9) Based on values given by Y. K. Syrkin as quoted by A. E. Remick, "Electronic Interpretation of Organic Chemistry," 2nd ed., John Wiley and Sons, New York, 1949, p. 142.

(10) A. Hantzsch, *Ber.*, **32**, 575 (1899); A. Hantzsch and M. Kalb, *Ber.*, **32**, 3109 (1899). For a recent survey see C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell Univ. Press, Ithaca, N. Y., 1953, pp. 575–586.

(11) F. Kehrmann and C. Natcheff, *Ber.*, **31**, 2425 (1898); F. Kehrmann and M. Woulfson, *Ber.*, **32**, 1042 (1899). For recent examples with quinoxaline derivatives see: K. Brand and E. Wild, *Ber.*, **56**, 105 (1923); J. Druey and A. Huni, *Helv. Chim. Acta*, **35**, 2301 (1952).

(12) A. W. Johnson, "The Chemistry of the Acetylenic Compounds," Edwards Arnold and Co., London, 1950, Vol. II, pp. 201, 218.

EXPERIMENTAL[13]

Dimethyl acetylenedicarboxylate was prepared from the monopotassium salt of acetylenedicarboxylic acid by the procedure of Huntress, Lesslie, and Bornstein.[14] 2,3-Diphenylquinoxaline was prepared in 81% yield from equimolar quantities of *o*-phenylenediamine and benzil in refluxing glacial acetic acid by the method of Bost and Towell.[15]

2-Phenylquinoxaline. Phenylglyoxal hydrate,[16] prepared from 147 g. (1.10 mol.) of phenylglyoxal, and *o*-phenylenediamine (119 g., 1.10 mol.) were refluxed in 700 ml. of 95% ethyl alcohol for 2.5 hr. The reaction mixture was chilled in an ice bath and filtered to give, after drying, 177 g. (78% yield) of crude product. Recrystallization from 800 ml. of alcohol with aid of animal charcoal for decolorization gave 131 g. of product of m.p. 76–77°. The most highly purified sample had m.p. 77.5–78.5° (recorded,[17] m.p. 78°).

1-(1,2-Dicarbomethoxyvinyl)-2,3-diphenyl-2-methoxy-1,2-dihydroquinoxaline (IV). Dimethyl acetylenedicarboxylate (34.2 g., 0.241 mol.) and 2,3-diphenylquinoxaline (34.0 g., 0.121 mol.) were mixed in 240 ml. of anhydrous methanol and were kept in a stoppered flask at room temperature with occasional shaking for 6 days. The yellow precipitate which formed was separated by filtration and weighed 33.2 g. (m.p. 144–148°). By concentration of the filtrate *in vacuo* an additional 8.7 g. of crude product was obtained to give a total yield of 76%. Recrystallization of the first batch of crystals once and the second batch twice from acetonitrile gave 34.0 g. (61.5% yield) of yellow crystals of IV, m.p. 156–157°. Compound IV, for analysis, was also recrystallized from carbon tetrachloride and from methyl ethyl ketone.

Anal. Calcd. for $C_{27}H_{24}N_2O_6$: C, 71.04; H, 5.30; N, 6.14; CH_3O, 20.41 (three methoxyl groups per mole); mol. wt., 456.5. Found: C, 71.19; H, 5.58; N, 6.26; CH_3O, 20.24; mol. wt. 465 ± 50 (in triphenylmethane after procedure described by Schneider[18]).

In working up the mother liquors from the preparation of IV sometimes about 1 g. of a red product was obtained. This red compound after recrystallization from acetonitrile had m.p. 214.5–215° (dec.) but was not further characterized.

Compound IV could be distilled with some decomposition at a pressure of 0.05 to 0.1 mm. and a bath temperature of about 250°. Compound IV underwent slow decomposition upon storage at room temperature.

Tetrachloroferrate(III) *of IV.* A solution prepared from 1.4 g. of ferric chloride hexahydrate and 45 ml. of anhydrous ethyl ether was filtered to remove undissolved ferric chloride and was then mixed with 25 ml. of an ether solution containing 1.5 g. of IV. Yellow crystals precipitated in the form of needles. The crystals were dissolved in acetonitride and were reprecipitated by addition of anhydrous ether. The product had m.p. 182–183°.

Anal. Calcd. for $C_{26}H_{21}Cl_4FeN_2O_4$: C, 50.19; H, 3.40; Cl, 22.80; N, 4.50; ash (Fe_2O_3), 12.84. Found: C, 50.31; H, 3.34; Cl, 22.69; N, 4.61; ash, 12.81.

Picrate of IV. Compound IV (1.3 g.) was dissolved in 20 ml. of a saturated solution of picric acid in anhydrous ethyl ether. Minute yellow crystals formed. These were dissolved in acetonitrile and precipitated by addition of ethyl ether. Repetition of this recrystallization technique gave a product of m.p. 169.3–170.5°.

Anal. Calcd. for $C_{32}H_{23}N_5O_{11}$: C, 58.80; H, 3.55; N, 10.72. Found: C, 58.33; H, 3.60; N, 10.72.

Perchlorate of IV. In 25 ml. of anhydrous ethyl ether 1.5 g. of compound IV was dissolved and the solution was added to an ethereal solution of perchloric acid, prepared by shaking 20 ml. of 70% perchloric acid with 25 ml. of anhydrous ethyl ether and separating the ether phase. The yellow product (1.0 g.) which precipitated had m.p. 222.5–223° (dec.). Solution of the product in 20 ml. of methyl ethyl ketone and addition of anhydrous ethyl ether gave 0.89 g. of purified product, m.p. 228–229° (dec.).

Anal. Calcd. for $C_{26}H_{21}ClN_2O_8$: C, 59.49; H, 4.03; Cl, 6.76; N, 5.34. Found: C, 59.84; H, 4.05; Cl, 6.81; N, 5.35.

The perchlorate undergoes decomposition on storage, thus after 12 days a sample had m.p. about 219°.

Use of the same procedure with 1.5 g. of 2,3-diphenylquinoxaline resulted in the formation of 0.92 g. of a yellow perchlorate of m.p. 254–255.5°. A mixture of equal parts of this solid with the perchlorate of IV had m.p. 205–216°.

Reaction of IV with HCl. Compound IV (1.5 g.) in 25 ml. of anhydrous ethyl ether was added to 50 ml. of anhydrous ether which was 0.6*M* in hydrogen chloride. A yellow solid immediately precipitated. Suction filtration gave a solid which on momentary contact with air was converted to an oil.

Compound IV (2.0 g.) was stirred with 10 ml. of 95% ethyl alcohol to give a slurry, 1.0 ml. of concentrated hydrochloric acid was added, and the mixture was refluxed on the steam bath for 1 hr. The solvent was allowed to evaporate partially at room temperature. A product (0.87 g., 70% yield calculated as 2,3-diphenylquinoxaline) was separated by filtration and had m.p. near 105°. Recrystallization from ethyl alcohol gave a product of m.p. 124.5–125.5° which showed no depression of melting point when admixed with a sample of pure 2,3-diphenylquinoxaline (m.p. 125.5–126.5°). Continued evaporation of the reaction mixture gave a dark red semisolid mass.

Reaction of IV with KOH. Compound IV (20.0 g., 0.0439 mol.) was refluxed on a steam bath for 2 hr. with 125 ml. of ethyl alcohol and 53 ml. (0.088 mol.) of 1.66*N* aqueous KOH. The mixture was cooled in an ice bath and filtered. The crystalline precipitate was washed well with water and after drying weighed 5.6 g. (45% yield calculated as 2,3-diphenylquinoxaline). The product was recrystallized from ethyl alcohol to give 4.4 g. of crystals of m.p. 125.8–126.6°, which showed no depression of melting point when mixed with 2,3-diphenylquinoxaline. The mother liquors from washing the 5.6 g. of crude 2,3-diphenylquinoxaline were found to liberate upon acidification 106 ml. (S.T.P.) of carbon dioxide (22% yield on the assumption that 1 mol. of IV should yield 1 mol. of CO_2).

The filtrate from which the 2,3-diphenylquinoxaline had been removed was evaporated *in vacuo*. The concentrated solution deposited 3.3 g. of a brown solid which upon recrystallization from ethyl alcohol gave 1.4 g. (16% yield calculated as desoxybenzoin) of pale yellow crystals, m.p. 47–50°. The product was recrystallized from benzene-cyclohexane, *n*-hexane, and finally twice from ethyl alcohol to give white crystals of m.p. 55–56°. This product was identified as desoxybenzoin by its m.p. and mixed m.p. with an authentic sample of desoxybenzoin[19] and by the identity of its ultraviolet absorption spectrum with that of desoxybenzoin.

The mother liquor from which the crude desoxybenzoin had been removed was further concentrated on the steam

(13) Melting points are corrected. Analyses are by Clark Microanalytical Laboratory, Urbana, Ill. Ultraviolet absorption spectra were determined by means of a Beckmann quartz spectrophotometer, model DU or DK.

(14) E. H. Huntress, T. E. Lesslie, and J. Bornstein, *Org. Syntheses*, **32**, 55 (1952). We are indebted to the authors for supplying us with these directions before their publication.

(15) R. W. Bost and E. E. Towell, *J. Am. Chem. Soc.*, **70**, 904 (1948).

(16) H. A. Riley and A. R. Gray, *Org. Syntheses*, **Coll. Vol. II**, 509 (1943).

(17) O. Hinsberg, *Ann.*, **292**, 246 (1896); O. Fischer and E. Schindler, *Ber.*, **39**, 2243 (1906).

(18) F. Schneider, "Qualitative Organic Microanalysis," John Wiley and Sons, New York, N. Y., 1946, p. 112.

(19) Prepared by the procedure of C. F. H. Allen and W. E. Barker, *Org. Syntheses*, **Coll. Vol. II**, 156 (1943).

bath. There deposited, on cooling, a dark yellow solid (3.0 g.) which was separated by filtration and was then converted into a slurry with 25 ml. of water and again filtered. The aqueous filtrate was strongly acidified with hydrochloric acid. The precipitate which formed weighed 1.3 g. (17% yield calculated as quinoxaline-2-carboxylic acid) and melted at about 204°. After decolorization with charcoal and three recrystallizations from ethyl alcohol the pure white product melted at 212° (dec.). This compound was identified as quinoxaline-2-carboxylic acid on the basis of its m.p. and mixed m.p. with authentic quinoxaline-2-carboxylic,[20] and by comparison of its ultraviolet absorption spectrum with that of the authentic sample.

Oxidation of IV. Solutions of IV in methanol or acetone showed no reaction at room temperature when treated with a dilute aqueous solution of $KMnO_4$. When 3.0 g. (0.0066 mol.) of IV was refluxed for 15 min. with 3.0 g. (0.011 mol.) of sodium dichromate in 21 ml. of glacial acetic acid, a green solution resulted. The solution was poured onto ice and extracted with ether and the ether extract was washed with ammonium hydroxide. From the ether extract 1.1 g. of semisolid residue was obtained. Two recrystallizations from methanol gave white crystals of m.p. 122–123° which gave no depression of m.p. with a pure sample of 2,3-diphenylquinoxaline.

To a slurry of 8.0 g. of IV in 27 ml. of glacial acetic acid was added a solution of 67 ml. of 30% hydrogen peroxide in 40 ml. of acetic acid. The mixture was heated on a steam bath for 2 hr., cooled to room temperature, and filtered. The insoluble product weighed 0.57 g. and after two recrystallizations from acetophenone was a white compound of m.p. 309–310° (dec.) and gave the following analysis.

Anal. Calcd. for $C_{20}H_{16}N_2O_2$: C, 75.92; H, 5.10; N, 8.86. Found: C, 75.78; H, 5.38; N, 9.06.

This compound (VII) had the same melting point and mixed melting point and the same infrared absorption spectrum as a sample of *N,N'*-dibenzoyl-*o*-phenylenediamine prepared by oxidation (see below) of 2,3-diphenylquinoxaline with hydrogen peroxide.

Oxidation of 2,3-diphenylquinoxaline. To a mixture of 25 ml. of acetic acid and 50 ml. of 30% hydrogen peroxide was added 3.0 g. of 2,3-diphenylquinoxaline partially dissolved in 25 ml. of ethanol. The mixture was subjected to reflux for 40 hr. and was then allowed to cool undisturbed for 24 hr. The crystals which precipitated were separated by filtration and were washed with enough hot methanol to dissolve an orange impurity and leave 1.33 g. of white crystals. The combined mother liquor and methanol wash from these crystals upon evaporation gave 1.58 g. of yellow crystals (m.p. 193–195°). A repetition of this preparation gave 1.55 g. of the yellow product but only 0.08 g. of the white product; the cause for the variation in yield is unknown. After two recrystallizations from ethyl alcohol the yellow product had m.p. 210–211° (dec.) and gave the following analysis:

Anal. Calcd. for $C_{20}H_{14}N_2O_2$: C, 76.42; H, 4.49; N, 8.91. Found: C, 76.59; H, 4.62; N, 8.94.

This analysis agrees with that expected for *N,N'*-dioxo-2,3-diphenylquinoxaline. This amine oxide has been analyzed previously only for carbon and hydrogen and is reported[21] to melt in the range of 208 to 216°.

The white product from the hydrogen peroxide oxidation after several recrystallizations from acetic acid or acetophenone had m.p. 309–310° (dec.). This substance as noted above was identical with compound VII from oxidation of IV. Previous reports[21] of the reaction of 2,3-diphenylquinoxaline with hydrogen peroxide under milder conditions than the present have not indicated the formation of a high melting product of properties analogous to VII, although 2,3-diphenylquinoxaline monoxide (m.p. 197°) has been found under some conditions. Compound VII corresponds in elementary analyses to a monohydrate of 2,3-diphenylquinoxaline monoxide; however VII could be recrystallized from acetic acid or acetophenone and could be sublimed at 260° (0.02 mm.) without loss of water. The white product of m.p. 309–310° (dec.) was eventually found[22] to be identical, as indicated by mixed melting point and infrared spectral determinations, with a sample of *N,N'*-dibenzoyl-*o*-phenylenediamine, prepared[23] from *o*-phenylenediamine.

1-(1,2-Dicarbomethoxyvinyl)-2-hydroxy-3-phenyl-1,2-dihydroquinoxaline (VIII). Dimethyl acetylenedicarboxylate (66.8 g., 0.470 mol.) and 2-phenylquinoxaline (97.0 g., 0.471 mol.) were dissolved in 760 ml. of anhydrous methanol and the solution was allowed to stand in a stoppered flask for 1 week at room temperature. The solvent was removed *in vacuo* and there remained a dark red viscous oil. Attempts to crystallize the product from acetonitrile under customary conditions were unsuccessful; however, crystals were obtained by the following procedure. The oil was dissolved in 170 ml. of carbon tetrachloride and the solution was left at room temperature for 3 weeks in an evaporating dish which was open to the atmosphere. During this period, the solid material which formed a crust over the solution was broken up from time to time. The residue in the evaporating dish was filtered and washed thoroughly with ether. The insoluble portion consisted of yellow crystals whose surface was red in color. The crude solid after removal of solvent weighed 114 g. (66% yield calculated as VIII) and had m.p. 128–138°. Five recrystallizations alternately from carbon tetrachloride and then methyl ethyl ketone gave yellow crystals of VIII of m.p. 139.5–140.5° (with some decomposition to give a red melt).

Anal. Calcd. for $C_{20}H_{18}N_2O_5$: C, 65.56; H, 4.95; N, 7.65; CH_3O, 16.94 (two methoxyl groups per mole); mol. wt., 366.4. Found: C, 65.87; H, 4.90; N, 7.57; CH_3O, 16.1; mol. wt., 387 ± 40 (in triphenylmethane after procedure described by Schneider[18]).

Compound VIII undergoes slow decomposition upon storage.

Reaction of VIII with KOH. While VIII dissolved to only a small extent in a mixture of equal parts of water and methanol, solution was complete after shaking for 5 min. in a mixture of equal parts of 10% aqueous KOH and methanol. Under similar conditions adduct IV was not visibly more soluble in presence than in absence of KOH.

Compound VIII (10.0 g., 0.0273 mol.) in 60 ml. of ethyl alcohol and 32.0 ml. (0.0552 mol.) of 1.725*N* aqueous potassium hydroxide was heated on a steam bath under conditions for reflux for 2.5 hr. The reaction mixture was cooled to room temperature, diluted with 250 ml. of water, and extracted with ether until the ether extracts acquired only a pale yellow color. The ether extracts yielded 0.76 g. (13.5% yield calculated as 2-phenylquinoxaline) of a brown residue which after recrystallization from ethyl alcohol and decolorization with animal charcoal had m.p. 74–76°. A mixed melting point with a pure sample of 2-phenylquinoxaline (m.p. 77.5–78.5°) showed no depression. The aqueous solution from the ether extractions was acidified with hydrochloric acid. The brown precipitate which separated was filtered and washed well with water. This brown product after drying at room temperature in a dessicator over Drierite weighed 9.2 g. and had m.p. 143–145° (dec. with evolution of gas). All attempts to obtain this product in a purer condition by recrystallization were unsuccessful. The titration curve for this acid showed two end points as expected for the dibasic acid corresponding to VIII and the ultraviolet absorption spectrum had maxima

(20) Prepared by the procedure of B. R. Brown, *J. Chem. Soc.*, 2577 (1949).

(21) S. Maffei, *Gazz. chim. ital.*, **76**, 239 (1946); F. Linsker and R. L. Evans, *J. Am. Chem. Soc.*, **68**, 403 (1946); J. K. Landquist and G. J. Stacey, *J. Chem. Soc.*, 2828 (1953).

(22) We wish to acknowledge helpful discussions from Dr. J. W. Huffman and Dr. J. R. Dyer concerning the structure of this product.

(23) O. Hinsberg and L. v. Udránsky, *Ann.*, **254**, 254 (1889); E. Bamberger and B. Berlé, *Ann.*, **273**, 346 (1893).

at the same locations as for VIII but with somewhat altered intensities. A 5.0 g. sample of the crude acid was heated under reflux for 1.5 hr. with 30 ml. of ethyl alcohol and 25.0 ml. of 1.72*N* aqueous KOH. The reaction mixture after dilution with water gave 1.25 g. of crude 2-phenylquinoxaline in the ether extract.

Oxidation of VIII. Compound VIII (10.0 g., 0.0273 mol.) was dissolved in 150 ml. of acetone and a saturated aqueous solution of $KMnO_4$ (170 ml. in all) was added in small portions, with shaking, until the color of the permanganate persisted for a few minutes. During this addition the reaction mixture warmed spontaneously to 35–40°. The precipitate which separated was filtered, was made into a slurry with water, and was acidified with hydrochloric acid. Sodium bisulfite was then added until the manganese dioxide dissolved. The resulting solution was filtered and the precipitate was washed well with water. The precipitate weighed 1.4 g. (23% yield calculated as 2-hydroxy-3-phenylquinoxaline) and after one recrystallization from methyl ethyl ketone had m.p. 244–245°. Recrystallization from methyl ethyl ketone and then from ethyl alcohol gave a very pale yellow product of m.p. 248.5–249.0°.

Anal. Calcd. for $C_{14}H_{10}N_2O$: C, 75.65; H, 4.54; N, 12.61. Found: C, 75.62; H, 4.60; N, 12.52. This compound is identified as 2-hydroxy-3-phenylquinoxaline and gave no depression of melting point with an authentic sample prepared[24] by condensation of *o*-phenylenediamine with benzoylformic acid.[25]

The acetone solution, from which the 2-hydroxy-3-phenylquinoxaline had been removed by filtration, upon evaporation deposited 2.44 g. (24% yield) of crude 2-phenylquinoxaline (m.p. *ca.* 76–78°) contaminated somewhat with 2-hydroxy-3-phenylquinoxaline.

To a solution of 2-phenylquinoxaline (0.56 g.) in 15 ml. of acetone was added a few drops of a saturated aqueous solution of $KMnO_4$. No color change was evident upon mixing at room temperature or even when the solution was boiled for a few minutes.

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(24) J. Buraczewski and L. Marchlewski, *Ber.*, **34**, 4009 (1901).

(25) B. B. Corson *et al.*, *Org. Syntheses*, **Coll. Vol. I**, 244 (1941).

[CONTRIBUTION FROM WALKER LABORATORY, RENSSELAER POLYTECHNIC INSTITUTE]

Cyclopropyl Analogs of Hexestrol and Diethylstilbestrol[1,2]

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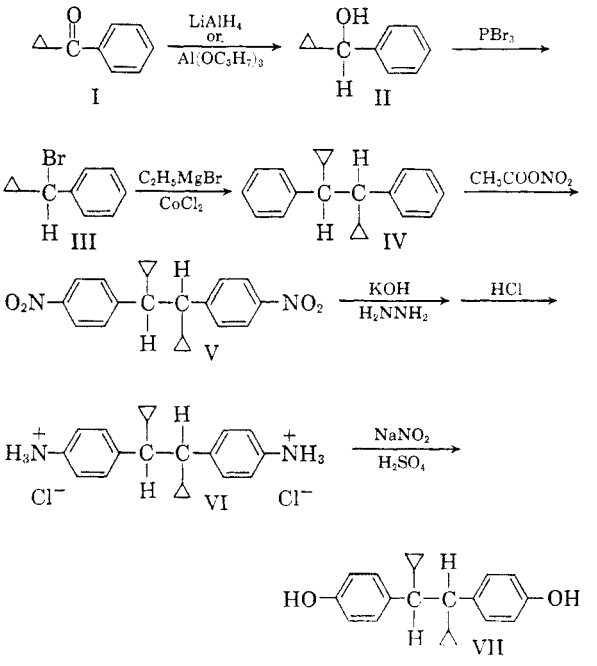
1,2-Dicyclopropyl-1,2-di-*p*-hydroxyphenylethane and 1,2-dicyclopropyl-1,2-di-*p*-anisylethylene, which are cyclopropyl analogs of hexestrol and of the dimethyl ether of diethylstilbestrol, have been prepared.

The purpose of this research was to investigate synthetic routes for the preparation of several cyclopropyl compounds which are structurally related to hexestrol, diethylstilbestrol, and estradiol, namely, 1,2-dicyclopropyl-1,2-di-*p*-hydroxyphenylethane (VII), 1,2-dicyclopropyl-1,2-di-*p*-hydroxyphenylethylene (XI), and 1,1′-di-*p*-hydroxyphenylbicyclopropyl.

The interest in these compounds lies in their possible estrogenic activity and possible action in relation to tumor initiation or cancer chemotherapy.

1,2-Dicyclopropyl-1,2-di-p-hydroxyphenylethane (VII) was successfully synthesized by the sequence of reactions illustrated in 1.1% over-all yield from γ-butyrolactone.

Cyclopropyl phenyl ketone (I), prepared from γ-butyrolactone by the method of Close,[4] was reduced to cyclopropylphenylcarbinol (II) by means of aluminum isopropoxide in 94% yield and also by means of lithium aluminum hydride[4] in 75% aver-



(1) Abstracted from the Ph.D. thesis of James G. Bennett, Jr., Rensselaer Polytechnic Institute, 1959.

(2) Presented before the Division of Organic Chemistry at the 135th National Meeting of the American Chemical Society, Boston, Mass., April 1959.

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(4) W. J. Close, *J. Am. Chem. Soc.*, **79**, 1455 (1957).