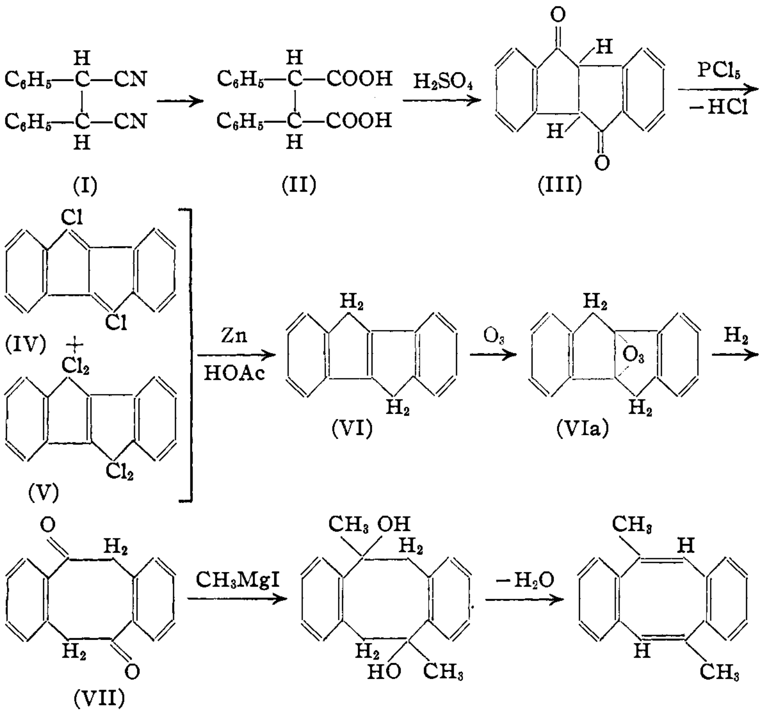
[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY OF THE UNIVERSITY OF MINNESOTA]

An Attempt to Synthesize a Substituted Cycloöctatetraene[1]

BY STANLEY WAWZONEK

Willstätter[2] has reported the synthesis of cyclooctatetraene. In view of the results obtained by Hurd and Drake[3] in their study of the pyrolysis of bis-quaternary ammonium hydroxides related to 1,2- and 1,3-butenes, and the striking similarity[4] in chemical and physical properties between styrene and its derivatives and the supposed cycloöctatetraene and its derivatives, the structure of the latter compound is questionable.

In the hope that a substituted cycloöctatetraene might be synthesized in an easier manner than cycloöctatetraene itself,[4] the following synthesis[5] of *sym*-dibenzocycloöctatetraene was attempted, and carried out successfully through the formation of the *sym*-dibenzocycloöctanedione-5,11 (VII).



In spite of the failure to complete the synthesis, it was thought that the properties and reactions of the cyclic diketone (VII) were of sufficient interest to be reported.

sym-Dibenzocycloöctanedione-5,11 (VII) is a white solid, difficultly soluble in aqueous alkali and easily soluble in alcoholic alkali to give a yellow solution. To determine the nature of this salt, an alkaline solution was treated with dimethyl sulfate and found to give a product that analyzed for a hydrated dimethyl ether. Since the ether would not brominate and could be cleaved by hydrobromic acid to the diketone (VII), its structure is that given by formula (VIII). The sodium salt is therefore a derivative of the hydrated form of the diketone (IX), a structure which is supported in part by the failure of the salt to react with benzenediazonium sulfate in alkaline solution.

All attempts to cause the diketone (VII) to react with butyl nitrite, *p*-nitrosodimethylaniline, bromine or selenium dioxide were either unsuccessful or gave oily products. That active methylene groups were present in the compound was shown by the formation of a dibenzal compound (X) from benzaldehyde in alcoholic alkali, and by the formation of a substituted quinoline (XI) from isatin in alkali.

The presence of two carbonyl groups was shown by the formation of a dioxime (XII) and a dichlorodiphosphinic acid (XIII) from phosphorus pentachloride. In the Grignard machine the cyclic diketone (VII) showed only one carbonyl group. The Grignard product in turn showed only one active hydrogen. Difficulty in dehydration of the Grignard product indicated that the compound was a dihydropyran (XIV). The formation of such a compound is analogous to the previously reported[6] formation of 2,4,4,6-tetraphenyl-

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[1] A portion of a thesis submitted in partial fulfillment of the requirements for the degree of Doctor of Philosophy by Stanley Wawzonek, August, 1939.

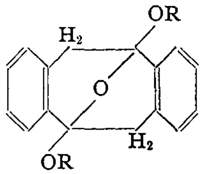
[2] (a) Willstätter and Waser, *Ber.*, **44**, 3433 (1911); (b) Willstätter and Heidelberger, *ibid.*, **46**, 517 (1913).

[3] Hurd and Drake, THIS JOURNAL, **61**, 1943 (1939).

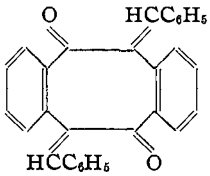
[4] Vincent, Thompson, Jr., and Smith, *J. Org. Chem.*, **3**, 603 (1939).

[5] Reactions up through the formation of diphensuccindene-10 (VI) have already been reported in part by Brand and Müller, *Ber.*, **55**, 601 (1922).

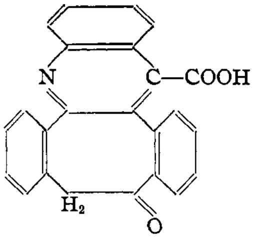
[6] Pere de Carvalho, *Ann. chim.*, **4**, 495 (1935).



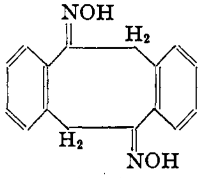
(VIII), R = CH_3
(IX), R = Na



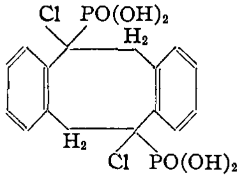
(X)



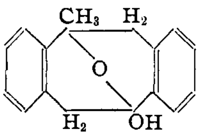
(XI)



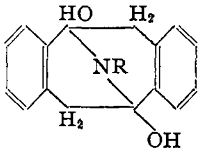
(XII)



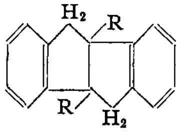
(XIII)



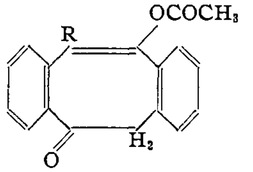
(XIV)



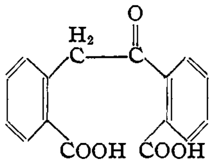
(XV), R = H
(XVI), R = $NHCONH_2$



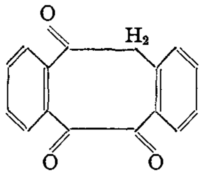
(XVII), R = H
(XVIII), R = OH



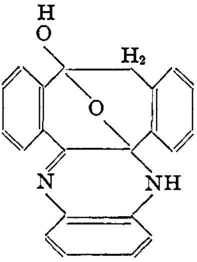
(XIX), R = H
(XXI), R = Br



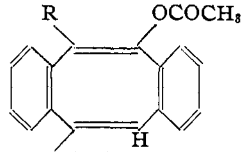
(XX)



(XXII)



(XXIII)



(XXIV), R = H
(XXV), R = Br

2-ethyl-dihydropyran in the reaction between 1,3-dibenzoyl-2,2-diphenylpropane and ethylmagnesium bromide.

With ammonia, ammonia derivatives and reducing agents, the behavior of the diketone (VII) was similar to that of open chained 1,5-diketones in that substituted tetrahydropyridines and glycols, respectively, were formed. The product, (XV) obtained from ammonia, was soluble in dilute hydrochloric acid, and could be converted either by nitrous acid or by melting into the diketone (VII). The compound (XVI) obtained from semicarbazide, upon heating alone or in the presence of powdered potassium hydroxide, gave a mixture of diphensuccindene-10 (VI) and diphensuccindane (XVII). Because of stereochemical reasons, the characteristic loss of water to form pyridines observed with ammonia addition products of open chained 1,5-diketones is impossible with ammonia derivatives of *sym*-dibenzocycloöctanedione-5,11. The glycol (XVIII), formed by the reduction of the diketone (VII) with either amalgamated zinc and hydrochloric acid or zinc and alkali, could be cleaved with lead tetraacetate to the diketone (VII). Treatment of the glycol (XVIII) with either sulfuric or hydriodic acid in acetic acid solution gave a highly insoluble polymer melting above 350°.

That enolic forms were possible was shown in the formation of a mono- and a diacetate by refluxing the diketone (VII) with acetic anhydride in the presence of anhydrous potassium acetate and sulfuric acid, respectively.

The structure of the monoacetate (XIX) was demonstrated by hydrolysis with alkali to the diketone (VII), and oxidation with chromic anhydride to *o,o'*-desoxybenzoindicarboxylic acid (XX). Treatment with bromine in acetic acid caused substitution and the formation of a monobromomonoacetate of structure (XXI), since the product failed to react on refluxing with anhydrous potassium acetate in acetic acid. Further treatment of the monobromomonoacetate (XXI) with bromine in chloroform gave a compound which was not obtained in a pure state, but which contained a smaller percentage of carbon than the starting material. Hydrolysis of the impure product with aqueous alcoholic ammonia gave an orange colored compound which was probably the *sym*-dibenzo-cycloöctanetrione-5,6,11 (XXII), since it formed a bright red hydrated phenazine (XXIII). No reaction could be brought about between the triketone (XXII) and either hydrogen peroxide in alkaline solution, or acetic anhydride in the presence of sulfuric acid or potassium acetate.

The diacetate (XXIV) could be obtained from the monoacetate (XIX) and was hydrolyzed to the cyclic diketone (VII) by alkali. Treatment with bromine in acetic acid gave a monobromodiacetate (XXV), which likewise could be obtained by acetylating the monobromomonoacetate (XXI). No reaction took place between the monobromodiacetate (XXV) and bromine or potassium acetate in acetic acid.

Experimental[7]

α,β-Diphenylsuccinic Acid (II).—The following procedure is a modification of Lapworth and McRae's[8] original directions. A suspension of α,β-diphenylsuccinonitrile (I) (117 g.) in a mixture of concentrated sulfuric acid (333 ml.), water (333 ml.) and glacial acetic acid (166 ml.) was refluxed for eleven hours. The resulting gray suspension was diluted with water, filtered and the acid thus obtained was purified through its potassium salt; yield, 116 g. The product, which was used as such in the next step, melted at 220° when crystallized from acetic acid.

9,12-Dichlorodiphensuccindadiene-9,11 (IV) and 9,9,12,12-Tetrachlorodiphensuccindene-10 (V).—Brand's original directions[5] were changed in the following manner. Diphensuccindanedione-9,12[9] (III) (24 g.) was heated slowly with phosphorus pentachloride (48 g.) until a clear solution was obtained. The resulting red liquid after cooling was treated with glacial acetic acid (400 ml.) and allowed to stand for twenty-six days. Attempts to accelerate the loss of hydrogen chloride by heating or other means gave less clean-cut reactions. The 9,12-dichlorodiphensuccindadiene-9,11 (IV) that separated out during this time was filtered; yield, 19 g. The filtrate, on pouring into water and extracting with ether, gave a mixture of the red dichlorodiene (IV) and a yellow compound, which, from its analysis and reaction, was 9,9,12,12-tetrachlorodiphensuccindene-10 (V). The red dichlorodiene (IV) obtained in the first step was contaminated by this yellow compound. One gram of starting material (III) was also recovered. 9,9,12,12-Tetrachlorodiphensuccindene-10 (V) crystallized once from a (60–68°) petroleum ether–benzene mixture and once from acetic acid formed yellow prisms melting at 178–179°.

Anal. Calcd. for $C_{16}H_8Cl_4$: C, 56.14; H, 2.34. Found: C, 55.79; H, 2.40.

Diphensuccindene-10 (VI).—9,9,12,12-Tetrachlorodiphensuccindene-10 (V) (0.2 g.) in boiling acetic acid (10 ml.) was treated with zinc dust until the solution became colorless. Upon pouring into water and extracting with ether a white solid (0.08 g.) was obtained melting at 197–204°. When crystallized from ethyl acetate, the solid melted at 204–208° and gave no depression when mixed with diphensuccindene-10 (VI) obtained from 9,12-dichlorodiphensuccindadiene-9,11 (IV).[4]

***sym*-Dibenzocycloöctanedione-5,11 (VII).**—Crude diphensuccindene-10 (VI) (6.06 g.) suspended in pure ethyl acetate (210 ml.) was treated with 12% ozone at −40° until all the diphensuccindene-10 (VI) had gone into solution. Warming to room temperature precipitated the white ozonide (VIa) melting at 191–193° with decomposition but exploding when heated rapidly. The suspension of the ozonide was mixed with 5% Pd·$BaSO_4$ catalyst (0.3 g.) and ethyl acetate (50 ml.) and reduced at room temperature with hydrogen at thirty-five pounds (2.3 atm.) pressure for twenty-four hours. From the resulting solution, after removing the catalyst and unreacted ozonide by centrifuging, and then removing the solvent, there was obtained the white crystalline *sym*-dibenzocycloöctanedione-5,11 (VII) (1.95 g.) melting at 202–204°. The unreacted ozonide and catalyst obtained by centrifuging gave upon further treatment in ethyl acetate (100 ml.) with hydrogen at 1000 pounds pressure and 120° for three hours, an oil from which more of the diketone (VII) (0.29 g.) was isolated. The residual oil, taken up in ether and washed with sodium carbonate, gave upon vacuum distillation an additional 0.35 g. of the diketone (VII); total yield, 2.5 g. The acidic by-products were not investigated further. *sym*-Dibenzocycloöctanedione-5,11 (VII), after four crystallizations from benzene, gave white needles melting at 203.5–204.5°.

Anal. Calcd. for $C_{16}H_{12}O_2$: C, 81.36; H, 5.08. Found: C, 81.30; H, 5.02.

The cyclic diketone (VII) is difficultly soluble in aqueous alkali but easily in alcoholic aqueous alkali to give a pale yellow solution. The yellow solution upon heating turns orange. Upon cooling the original hue returns. Acidification of the solution gives the diketone (VII) back unchanged.

No color change was observed when the diketone (VII) was treated in alcoholic alkali with benzenediazonium sulfate.

The dioxime (XII), obtained by refluxing the diketone (VII) in alcohol for four hours with an excess of hydroxylamine hydrochloride neutralized by sodium carbonate, was crystallized twice from ethanol. It formed white needles melting at 240–243° with decomposition.

Anal. Calcd. for $C_{16}H_{14}O_2N_2$: C, 72.18; H, 5.26; N, 10.53. Found: C, 71.96; H, 5.43; N, 10.50.

Methylation of the Diketone.—The diketone (VII) (0.25 g.) in methanol (4 ml.) was treated alternately with 20% potassium hydroxide and dimethyl sulfate until the solution when basic showed no yellow color. Ether extraction gave a white solid (VIII) (0.25 g.) which, after two crystallizations from ethanol, formed prisms, m. p. 143–144°.

Anal. Calcd. for $C_{16}H_{12}O(OCH_3)_2$: C, 76.60; H, 6.38; OCH_3, 21.67. Found: C, 76.16; H, 6.32; OCH_3, 21.32, 21.29.

The dimethyl ether (VIII) would not brominate but could be cleaved by hydrobromic acid in acetic acid to the diketone (VII).

Dibenzal Derivative of the Diketone (X).—A solution of the diketone (VII) (0.1 g.) in a mixture of ethanol (5 ml.), benzaldehyde (0.5 ml.) and saturated alcoholic potassium hydroxide solution (0.5 ml.) was allowed to stand at room temperature for eight days and then poured into water. Acidification followed by extraction with

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(7) Microanalyses by J. W. Opie, C. O. Guss and H. H. Hoehn.

(8) Lapworth and McRae, *J. Chem. Soc.*, **121**, 1699 (1922).

(9) Roser, *Ann.*, **247**, 153 (1888).

ether gave a white solid (X) (0.035 g.) which melted at 244–246° after two crystallizations from toluene.

Anal. Calcd. for $C_{30}H_{20}O_2$: C, 87.37; H, 4.85. Found: C, 86.86; H, 4.23.

Reaction of the Diketone with Isatin.—A mixture of the cyclic diketone (VII) (0.24 g.) and isatin (0.29 g.) in 20% potassium hydroxide solution (5 ml.) was heated for forty-eight hours and the resulting solution then cooled to 0°. Acidification with acetic acid of the insoluble potassium salt formed followed by extraction with ether gave a white solid (XI) (0.115 g.) soluble in both acids and bases. Crystallization twice from ethanol and once from ethyl acetate gave very fine, white crystals which melted at 297° with gas evolution.

Anal. Calcd. for $C_{24}H_{15}O_3N$: C, 78.90; H, 4.10; neut. eq., 365. Found: C, 78.29; H, 4.69; neut. eq., 351, 349.

Reaction of the Diketone with Phosphorus Pentachloride.—A mixture of the diketone (VII) (0.24 g.) and phosphorus pentachloride (1 g.) was heated until completely liquid, cooled and then poured into water. Extraction with ether gave a white solid (XIII) (0.277 g.) which contained both phosphorus and chlorine and melted at 123–126° with gas evolution. Three crystallizations from (60–68°) petroleum ether gave white needles which melted at 123–126° with gas evolution. The residue from melting no longer contained chlorine.

Anal. Calcd. for $C_{16}H_{16}Cl_2P_2O_6$: C, 43.93; H, 3.66. Found: C, 44.14; H, 3.23.

Reaction of the Diketone with Methylmagnesium Iodide.—A solution of the diketone (VII) (0.47 g.) and excess methylmagnesium iodide in ether (10 ml.) and benzene (10 ml.) was refluxed for two hours. Decomposition with ammonium chloride followed by extraction with ether gave the tetrahydropyran (XIV) (0.35 g.) which formed white cubes after two crystallizations from benzene. It melted at 213–215°.

Anal. Calcd. for $C_{17}H_{16}O_2$: C, 80.95; H, 6.35. Found: C, 81.24; H, 6.06.

In the Grignard machine the diketone (VII) showed only one carbonyl group.

The Grignard product (XIV) in the Grignard machine liberated only one mole of gas. No dehydration of the Grignard product was observed after six hours of refluxing with a few drops of concentrated sulfuric acid in acetic acid.

Reaction of the Diketone with Ammonia.—A solution of the diketone (VII) (0.12 g.) in concentrated ammonium hydroxide (5 ml.) and ethanol (5 ml.) was refluxed for thirty minutes and poured into water. Extraction with ether gave a white solid (XV) (0.06 g.) soluble in dilute hydrochloric acid. After two crystallizations from benzene and one from a (60–68°) petroleum ether–ether mixture the substituted tetrahydropyridine (XV) melted, if heated rapidly, at 167° with gas evolution, then solidified and melted again at 202–203.5°.

Anal. Calcd. for $C_{16}H_{15}O_2N$: C, 75.88; H, 5.93. Found: C, 75.39; H, 5.55.

The ammonia addition product (XV) when treated with nitrous acid or when heated above its melting point, gave the diketone (VII).

Reaction of the Diketone with Semicarbazide.—A solution of the diketone (VII) (0.12 g.), semicarbazide hydrochloride (0.25 g.) and sodium carbonate (0.06 g.) in ethanol (5 ml.) and water (1 ml.) was refluxed for two hours and the crystalline precipitate (XVI) formed, filtered; yield, 0.105 g., m. p. 207–208° with decomposition. A sample recrystallized twice from methyl cellosolve melted at 210° with decomposition.

Anal. Calcd. for $C_{17}H_{17}O_3N_3$: C, 65.60; H, 5.47. Found: C, 65.50; H, 5.69.

Decomposition of the Semicarbazide Addition Product.—A mixture of the semicarbazide addition product (XVI) (0.35 g.) and powdered potassium hydroxide (0.04 g.) upon heating in a sublimer at atmospheric pressure gave a mixture (0.11 g.) separable by fractional crystallization into diphensuccindene-10 (VI) and diphensuccindane[5] (XVII). A similar behavior was observed when the addition product was heated without potassium hydroxide.

Reduction of the Diketone.—The diketone (VII) (0.24 g.) was refluxed with amalgamated zinc (5 g.) in a mixture of water (5 ml.), concentrated hydrochloric acid (5 ml.) and acetic acid (10 ml.) for seven hours. The glycol (XVIII) (0.125 g.) obtained, after two crystallizations from benzene and one from (60–68°) petroleum ether, gave fine, white needles which melted at 148.5–149°.

Anal. Calcd. for $C_{16}H_{14}O_2$: C, 80.67; H, 5.88. Found: C, 80.99; H, 6.00.

A similar result was obtained by refluxing the diketone (VII) (0.12 g.) in 20% potassium hydroxide (14 ml.) and ethanol (4 ml.) with excess zinc dust until the solution was colorless. Acidification followed by extraction with ether gave the glycol (XVIII) (0.082 g.).

The glycol (XVII) when treated with either sulfuric or hydriodic acid in acetic acid gave a very insoluble yellow compound melting above 350°.

Cleavage of the Glycol.—A mixture of the glycol (XVIII) (0.23 g.) and lead tetraacetate (0.5 g.) in dry benzene (10 ml.) was allowed to stand for six hours at 50° and poured into dilute hydrochloric acid. Extraction with ether gave the cyclic diketone (VII) (0.14 g.).

Monoacetate of the Diketone.—A solution of the diketone (VII) (1.17 g.) in acetic anhydride (15 ml.) was refluxed with anhydrous potassium acetate (0.25 g.) for thirty minutes and then poured into water. Extraction with ether gave a white solid (XIX) (0.85 g.), m. p. 137–140°. Crystallization from ethanol gave white plates melting at 138–139°.

Anal. Calcd. for $C_{18}H_{14}O_3$: C, 77.69; H, 5.04. Found: C, 77.78; H, 5.08.

Alkaline hydrolysis of the monoacetate (XIX) gave the diketone (VII).

Oxidation of the Monoacetate.—A solution of the monoacetate (XIX) (0.14 g.) in acetic acid (10 ml.) was heated with chromic anhydride (0.16 g.) in water (0.2 ml.) at 50–60° for one hour, then poured into water and extracted with ether. A carbonate extraction of the ether layer gave a white solid (0.035 g.) which after crystallization from acetic acid first softened at 180° then melted at 215–220° with all the solid phase disappearing at 245°. This behavior was similar to that of *o,o'*-desoxybenzoindicarboxylic acid (XX) prepared according to the directions of Ephraim.[10]

Bromination of the Monoacetate.—A solution of the monoacetate (XIX) (0.28 g.) in glacial acetic acid (10 ml.) was treated with bromine (0.3 g.) in acetic acid (3 ml.) and allowed to stand at room temperature for twelve hours. The white crystals (XXI) (0.2 g.) formed were filtered and recrystallized twice from benzene, m. p. 219–223° with gas evolution. An additional 0.065 g. of the monobromomonoacetate (XXI) could be obtained from the filtrate.

Anal. Calcd. for $C_{18}H_{13}O_3Br$: C, 60.50; H, 3.65. Found: C, 60,10; H, 3.62.

The monobromomonoacetate (XXI) was not affected by refluxing in acetic acid with anhydrous potassium acetate.

Further treatment of the monobromomonoacetate (XXI) (0.25 g.) with bromine (0.5 ml.) in chloroform (10 ml.) at room temperature for thirty-six hours gave a white compound (0.12 g.) that melted at 173–178° with gas evolution. This compound could not be purified.

Anal. Calcd. for $C_{18}H_{13}O_3Br$ (XXI): C, 60.50; H, 3.65. Calcd. for $C_{16}H_{10}O_2Br_2$: C, 48.73; H, 2.54. Found: C, 52.63; H, 3.46.

***sym*-Dibenzocycloöctanetrione-5,6,11.**—The above impure bromo compound (m. p. 173–8°) (0.244 g.) was refluxed with concentrated ammonium hydroxide (2 ml.) and ethanol (7 ml.) for ten minutes and then poured into water. Extraction with ether and chloroform gave an orange solid (XXII) which was purified by sublimation under reduced pressure; yield 0.033 g., m. p. 245–250°. Two crystallizations from ethyl acetate followed by a sublimation at atmospheric pressure gave orange needles melting at 254–256°.

Anal. Calcd. for $C_{16}H_{10}O_3$: C, 76.80; H, 4.00. Found: C, 76.88; H, 3.47.

The triketone (XXII) was not affected by refluxing in acetic anhydride with potassium acetate or sulfuric acid and was stable toward alkaline peroxide.

The hydrated phenazine (XXIII) was obtained by refluxing the triketone (XXII) in absolute ethanol with phenylenediamine and a few drops of acetic acid for five hours. Two crystallizations from ethyl acetate gave bright red needles melting at 283–285°.

Anal. Calcd. for $C_{22}H_{16}O_2N_2$: C, 77.64; H, 4.71. Found: C, 77.16; H, 4.57.

Diacetate of the Diketone.—A solution of the diketone (VII) (0.708 g.) in acetic anhydride (10 ml.) was refluxed with one drop of concentrated sulfuric acid for thirty minutes and then poured into water. Extraction with ether gave the diacetate (XXIV) (0.525 g.) melting at 145–148°. Three crystallizations from ethanol gave white plates melting at 150–151°.

Anal. Calcd. for $C_{20}H_{16}O_7$: C, 75.00; H, 5.00. Found: C, 74.98; H, 4.97.

The diacetate (XXIV) could also be obtained from the monoacetate (XIX). Alkaline hydrolysis of the diacetate (XXIV) gave the diketone (VII).

Bromination of the Diacetate.—A solution of the diacetate (XXIV) (0.32 g.) in acetic acid (10 ml.) was treated with bromine (0.4 g.) in acetic acid (4 ml.) and allowed to stand at room temperature for five hours. The crystalline plates (XXV) (0.24 g.) formed were filtered, m. p. 225–229°. An additional 0.055 g. was obtained from the filtrate. Two crystallizations did not change the melting point. A mixture with the monobromomonoacetate (XXI) showed a depression in melting point.

Anal. Calcd. for $C_{20}H_{15}O_4Br$: C, 60.76; H, 3.79. Found: C, 60.66; H, 3.92.

The same monobromodiacetate (XXV) was obtained by refluxing the monobromomonoacetate (XXI) in acetic anhydride with a drop of sulfuric acid.

The monobromodiacetate (XXV) was not affected by refluxing in acetic acid with either anhydrous potassium acetate or excess bromine.

Acknowledgment.—The author wishes to thank Professor C. F. Koelsch for his advice and interest during the course of this research.

Summary

1. The preparation of *sym*-dibenzocycloöctanedione-5,11 from diphensuccindene-10 is described.

2. The properties and reactions of *sym*-dibenzocycloöctanedione-5,11 resemble those of open chained 1,5-diketones.

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[10] Ephraim, *Ber.*, **24**, 2820 (1891).