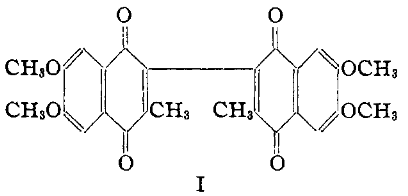
[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

Structure of Gossypol. XXIII. Attempts to Prepare Desapogossypolone Tetramethyl Ether. Condensation of Hexadiene-2,4 with Dibenzoylethylene[1]

BY ROGER ADAMS AND T. A. GEISSMAN

The completion of the verification of the postulated structure for gossypol is dependent either on the degradation of gossypol to a substance of known structure which will establish the positions of the methyl groups and the linkage between the naphthalene nuclei or on the synthesis of one of the supposed β,β-binaphthyl degradation products of gossypol. The former procedure has thus far met with failure. Attempts are now being made to synthesize desapogossypolone tetramethyl ether (I) and the initial series of reactions studied is described in this communication.

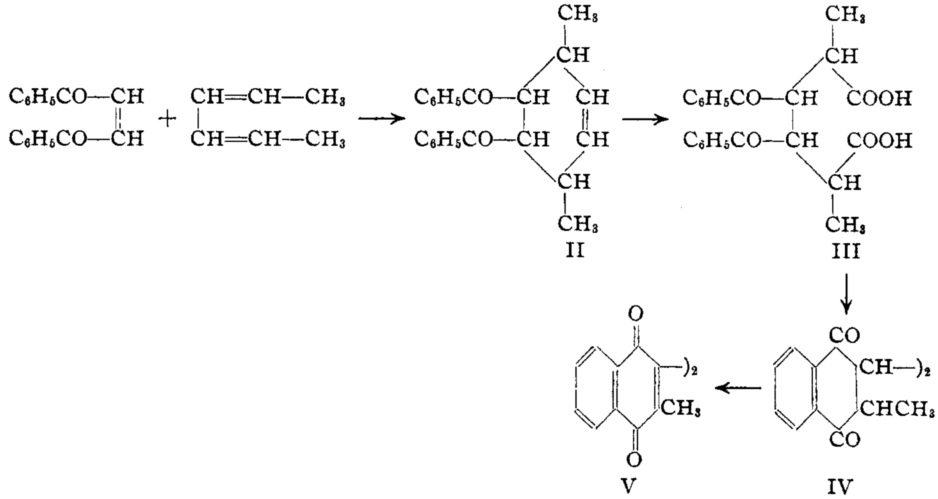


I

In order to test the feasibility of the method, the synthesis of the methoxyl-free analog of desapogossypolone tetramethyl ether was undertaken. *trans*-Dibenzoylethylene and hexadiene-2,4 were condensed to give product II. It was planned to oxidize the double bond in II to give the dibasic acid (III). This, in turn, was to be cyclicized either directly or indirectly to IV which should oxidize to the desired compound (V).

The initial reaction of the dibenzoylethylene and the diene proceeded without difficulty but all the oxidation reactions of II resulted in complete degradation of the molecule or in substances different from the dibasic acid (III) desired. A description of the results actually obtained is given here, along with a description of studies made on the conversion of the adduct (II) by methods which appear to be general for compounds of this type into the fully aromatic derivative (XIX) and the benzofuran (XVI).

The Diels–Alder reaction between hexadiene-2,4 and dibenzoylethylene results in a good yield of a mixture of two products in a ratio of 10:1. These are unquestionably *cis–trans* isomers and each was converted into a dibromide. Merely the higher melting compound, obtained in larger amounts, was further studied. It was oxidized by means of (a) ozone, (b) potassium permanganate, (c) osmium tetroxide and chlorates, and (d) by other specific reagents, such as Prévost's reagent and the action of acetates on the dibromide (XIII), but in no case were satisfactory results obtained. The conclusion drawn from these experiments was that the reactivity of the hydrogen atoms on the carbons *alpha* to the carbonyl groups was so great that these reagents did not confine their action to the double bond.



Upon oxidation of the adduct with monoperphthalic acid in an ether–chloroform solution,

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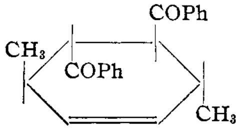
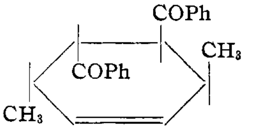
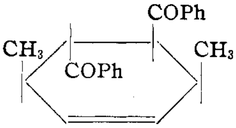
[1] For previous paper in this series see Adams and Dial, THIS JOURNAL, 61, 2077 (1939).

a smooth consumption of one atom of oxygen was observed and the product was a fairly good yield of a mixture of two isomeric oxido compounds. Of the two oxido compounds, one could be separated easily in a pure state by virtue of its extreme insolubility in methanol, while the other was contaminated with what appeared to be a third substance and was difficult to purify.

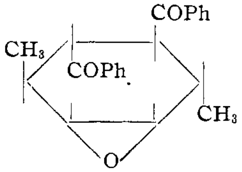
The stereochemical possibilities in these compounds may be deduced with reasonable certainty on the following considerations. Assuming that the benzoyl groups are *trans* in the adducts, the following configurations are to be expected (VI, VII, VIII).

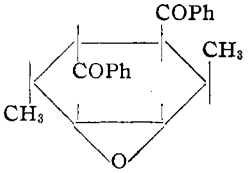

VI

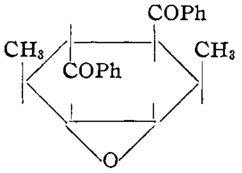

VII

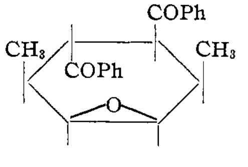

VIII

The oxido compounds derived from these three adducts would be


VIa

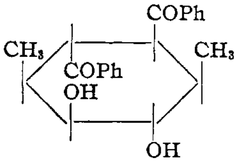

VIIa

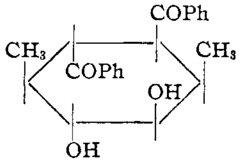

VIIIa


VIIIb

The symmetry of VI or VII precludes the formation of more than one oxido compound from each. These are represented by VIa and VIIa which obviously are different from each other. As the structure VIII is the only one which can give two different oxido compounds, it is assumed that this represents the more abundant higher-melting isomer in the original adduct mixture (II). The lower-melting compound must then have structure VI or VII. The lower-melting oxido compound may be assigned structure VIIIb and the higher-melting VIIIa on the basis of the relationship of the oxido group to the two methyls.

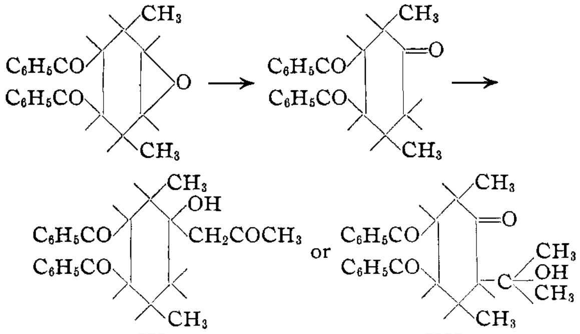
Since the formation of a glycol from an oxide leads to the *trans*-glycol, it would be expected that both VIIIa and VIIIb would give a mixture of the same two glycols (IX and X).


IX


X

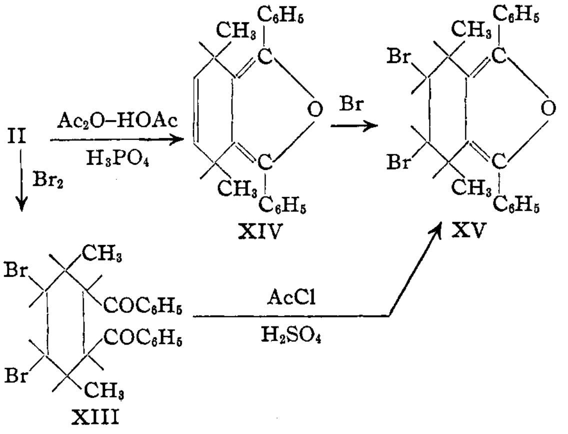
Upon hydrolysis of the oxides in acetone solution this was found to be the case, but different proportions of the glycols were obtained from each oxide. From the lower-melting oxide, the higher-melting glycol and from the higher-melting oxide, the lower-melting glycol predominated. The glycols had similar solubility characteristics and were difficult to separate.

In the preparation of glycol from a low-melting fraction of oxide a third substance was isolated in one run which appeared to be an addition product of one molecule of acetone to the oxide. The structure was not determined but it may possibly be one of the following two, XI and XII, on the assumption that the glycol has rearranged to a ketone and then condensed with acetone. The structure XII is preferred since the compound does not give ketone derivatives (the benzoyl groups in other compounds of the series do not form ketone derivatives) and gives no iodoform on treatment with sodium hypobromite in dioxane solution.

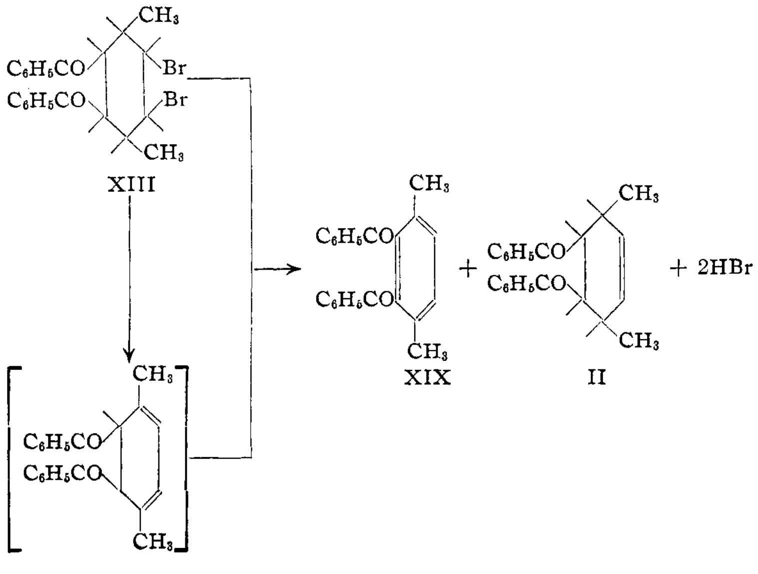

XI XII

The dibromide (XIII) of the higher-melting adduct of hexadiene-2,4 and dibenzoylethylene upon treatment with sodium acetate rearranged to an isomeric dibromide, probably a stereoisomer of the original compound.

The conversion of the adduct (II) and its dibromide (XIII) into derivatives of isobenzofuran can be accomplished readily by treatment with dehydrating agents under the proper conditions. When the adduct (II) is treated with a mixture of acetic acid, acetic anhydride and a trace of phosphoric acid it is converted smoothly into the dihydrobenzofuran derivative (XIV). The adduct dibromide (XIII) when treated with acetyl chloride containing sulfuric acid is dehydrated in good yield to the corresponding dibromo derivative (XV). Bromination of XIV under suitable conditions also yields XV.

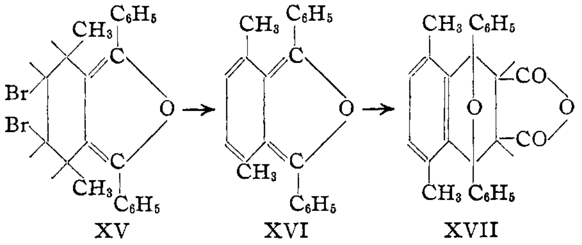


Attempts to convert the adduct (II) into the fully aromatic compound (XIX) by treatment of the dibromide (XIII) with pyridine led to the formation of a mixture of the desired benzene derivative (XIX) and the original adduct. Apparently the dihydrobenzene formed as a direct result of the removal of two molecules of hydrogen bromide from the dibromide (XIII) reacts as shown below to debrominate a molecule of the dibromide and becomes aromatized

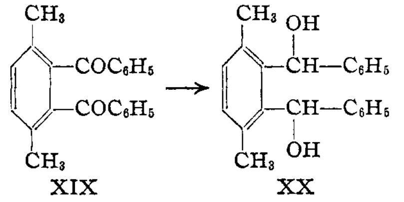


The formation of the benzene derivative (XIX) was accomplished in good yield by treatment of the dihydrobenzofuran (XIV) with two moles of bromine in the presence of sodium acetate.

The dibromotetrahydrobenzofuran (XV) was unchanged by boiling with sodium acetate in acetic acid, but on treatment with dry pyridine it was converted smoothly into the benzofuran (XVI). The latter compound reacted with maleic anhydride instantly in the cold to give the addition product (XVII).



Since other studies in this Laboratory have indicated that certain benzofurans of the type of compound XVI can be obtained by reduction of the dibenzoylbenzenes corresponding to XIX with zinc dust in alcoholic alkali, an attempt was made to form XVI from XIX in this way. None of the benzofuran (XVI) was produced, however, the product being a colorless compound which may be the *o*-*bis*-(α-oxybenzyl) derivative (XX)



A further study of diene additions to diaroylethylenes and their reaction products is under way.

Experimental

Preparation of Hexene-2-ol-4.—The Grignard reagent prepared from 305 g. of ethyl bromide and 64 g. of magnesium in 1500 cc. of dry ether was cooled in an ice-bath, and 160 g. of crotonaldehyde (in a little ether) was added dropwise with vigorous stirring at such a rate as to keep the solution at 15–20°. After the aldehyde was added stirring was continued for one-half hour while the solution was allowed to come to room temperature. The mixture was decomposed with iced ammonium chloride solution, the ether layer separated, and worked up in the usual manner. There was obtained 188 g. (83%) of hexene-2-ol-4, b. p. 55° (15 mm.). Reiff[2] reports 85–87° (120 mm.) and 133–134° (760 mm.).

Hexadiene-2,4.—A mixture of 75 g. of hexene-2-ol-4 and 5 cc. of 48% hydrobromic acid was distilled slowly through a short column, the outlet temperature of which was maintained by controlling the rate of distillation at 85–95°. The distillate was separated from the water formed and dried over calcium chloride. It boiled at 79–83°; yield, 41 g. (67%).

This method is faster and more convenient than that described by Kyriakides.[3]

3,6-Dimethyl-4,5-dibenzoylcyclohexene-1,2 (II).—A mixture of 60 g. of dibenzoylethylene, 56 cc. (41 g.) of hexadiene-2,4 and 75 cc. of toluene was heated on the steam-bath for eighteen hours (under reflux). The solvent was evaporated in a stream of air and to the residual sirup while still hot was added 150 cc. of methanol. On cooling, the solution set to a crystalline mass. The product was collected by suction and washed with methanol. The crude product was a cream-colored crystalline material weighing 63 g. Recrystallized from acetone–methanol, it formed stout, colorless needles, weighing 53 g., m. p. 136–137°.

Anal. Calcd. for $C_{22}H_{22}O_2$: C, 82.97; H, 6.97. Found: C, 82.66, 83.09; H, 7.00, 6.83.

From the methanol mother liquors from two preparations with a total of 90 g. of dibenzoylethylene there was obtained by concentration 10.5 g. of a low-melting crystalline compound. After repeated recrystallization from methanol there was obtained 6.5 g. of white needles, m. p. 86–88°. This is an isomeric adduct.

Anal. Calcd. for $C_{22}H_{22}O_2$: C, 82.97; H, 6.97. Found: C, 82.73; H, 7.09.

Dibromides of Addition Products

(1) **Of High-Melting Adduct (XIII).**—To a solution of 3.18 g. of adduct (m. p. 136°) in 25 cc. of glacial acetic acid, was added dropwise with cooling a solution of 1.60 g. of bromine in 16 cc. of acetic acid. The bromine was decolorized instantly. The solution was poured into water, the dibromide extracted with chloroform, the chloroform solution concentrated to a small volume, diluted with ethanol, and concentrated again until crystallization began: white crystals, m. p. 169–170°; yield 3.94 g.

Anal. Calcd. for $C_{22}H_{22}O_2Br_2$: C, 55.23; H, 4.60. Found: C, 55.52; H, 4.64.

This dibromide is converted by means of sodium acetate to another dibromide, presumably stereoisomeric with the first. A mixture of 2 g. of the dibromide, 2 g. of anhydrous sodium acetate, 15 cc. of acetic acid, 1 cc. of acetic anhydride was refluxed for five hours. The solution was poured into water. The product crystallized from methanol as white needles, m. p. 202.5–203°, with decomposition; yield, 0.6 g.

Anal. Calcd. for $C_{22}H_{22}O_2Br_2$: C, 55.23; H, 4.65; Br, 33.43. Found: C, 55.66; H, 4.98; Br, 33.15.

(2) **Of Low-Melting Adduct.**—The bromination was carried out essentially as described for the high-melting adduct. The dibromide forms pearly-white leaflets from chloroform–ethanol, m. p. 152°, with decomposition.

Anal. Calcd. for $C_{22}H_{22}O_2Br_2$: Br, 33.43. Found: Br, 33.41.

3,6-Dimethyl-4,5-dibenzoylcyclohexene Oxide-1,2 (VIIIa and VIIIb).—Phthalmonoperacid was prepared according to the directions of Böhme.[4]

To a cold (0°) solution of 31.8 g. of adduct in 100 cc. of chloroform was added a liter of phthalmonoperacid (0.32–0.34 molar in available oxygen), and the solution stored at 0°.

After the oxidation was complete (about five days), as shown by no further drop in titer, a deposit of white prisms was present in the solution. The solution was decanted from this material which was collected, washed with ether, and dried. The oxide (VIIIa) weighed 7.0 g., and after recrystallization from acetone–methanol formed white needles, m. p. 187.5–188°.

Anal. Calcd. for $C_{22}H_{22}O_3$: C, 79.04; H, 6.59. Found: C, 79.28; H, 6.79.

The ether solution was washed with aqueous sodium bisulfite to remove excess oxidizing agent, then with aqueous sodium hydroxide to remove phthalic acid. The solution was dried over sodium sulfate and evaporated under diminished pressure.

The residual solid was recrystallized from methanol and by successive concentrations and removal of the fractions which were, in turn, recrystallized there was obtained the following: 6.6 g., m. p. 148–150°, and 9.7 g., m. p. 146–149°. The first crop after several crystallizations from methanol gave colorless prisms, m. p. 154–155°.

Anal. Calcd. for $C_{22}H_{22}O_3$: C, 79.04; H, 6.59. Found: C, 78.81; H, 6.58.

3,6-Dimethyl-4,5-dibenzoylcyclohexanediol-1,2 (IX and X) from High-melting Oxide.—A solution of 1 g. of the higher melting oxide (m. p. 187°) in 20 cc. of acetone and 5 cc. of 25% sulfuric acid was refluxed for thirty minutes. The solution was poured into water and extracted with chloroform. The oil obtained on evaporation of the chloroform solidified on triturating with ether and petroleum ether; yield 0.62 g.; m. p. about 160°. On crystallization from a mixture of ether–petroleum ether (b. p. 30–60°) first a small amount of product was obtained which separated in colorless prisms. These were recrystallized from dilute methanol, white needles, m. p. 212–213°.

Anal. Calcd. for $C_{22}H_{24}O_4$: C, 74.96; H, 6.87. Found: C, 74.91; H, 6.94.

The filtrates from the ether–petroleum ether crystallization deposited a second product in colorless rosets which, after purification from ethyl acetate–petroleum ether (b. p. 30–60°), melted at 173–175°.

Anal. Calcd. for $C_{22}H_{24}O_4$: C, 74.96; H, 6.87. Found: C, 75.20; H, 6.99.

From Low-Melting Oxide.—In place of pure low-melting oxide, either of the two low-melting fractions, m. p. 148–150° or 146–149°, described under the preparation of the oxides, was used. The procedure followed for hydrolysis was identical with that for the high-melting oxide. From 3.1 g. was obtained as a main product 1.7 g. of high-melting glycol which was purified to its proper melting point of 212–213° with dilute methanol. From the ether–petro-

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(2) Reiff, *Ber.*, **39**, 1603 (1906); **41**, 2739 (1908).

(3) Kyriakides, THIS JOURNAL, **36**, 987 (1914).

(4) Böhme, *Ber.*, **70**, 379 (1937).

leum ether filtrates was obtained 0.35 g. of low-melting glycol which on crystallization from the same mixed solvent melted at 173–175°.

From one run of oxide purification was not carried to the extent previously described but merely three fractions were separated, one of high-melting oxide, a second primarily of low-melting, and a third fraction presumably chiefly low-melting oxide. When the last fraction and the mother liquors were hydrolyzed together with sulfuric acid in acetone, a new product (XII) was obtained. It was purified with methanol, white prisms, m. p. 187–188°. A mixed melting point showed it to be different from the high-melting or low-melting oxide.

Anal. Calcd. for $C_{25}H_{28}O_4$: C, 76.53; H, 7.14. Found: C, 76.12; H, 7.19.

The cause of the difference of results in the run just described and the others that were made may be due to the fact that the peracid ether solution was less dry in this experiment. The composition corresponds to a compound from one molecule of oxide and one of acetone.

1 - Hydroxy - 2 - acetoxy - 3,6 - dimethyl - 4,5 - dibenzoylcyclohexane.—In an attempt to cleave the glycol by means of periodic acid, four 1-g. runs of the low-melting oxide were allowed to stand for three hours with various concentrations of one molar periodic acid (1–10 equivalents) in 20 cc. of glacial acetic acid. After pouring into water, extracting with ether, washing, and evaporating the solvent, an oil resulted which crystallized on scratching. It was purified from ether–petroleum ether (b. p. 30–60°), then from dilute methanol; yield, 0.77 g. from the four runs, flat leaflike needles, m. p. 207°.

Anal. Calcd. for $C_{24}H_{26}O_5$: C, 73.06; H, 6.65. Found: C, 72.92; H, 6.58.

Apparently any oxidation products of the oxide or glycol produced from it could not be isolated and merely the monoacetate of the glycol resulted.

The same product could be obtained merely by heating 1 g. of the low-melting oxide, 15 g. of acetic acid and 5 cc. of 25% sulfuric acid on a steam cone for fifteen minutes. Dilution to cloudiness and cooling caused the product to separate. By boiling the compound with 15 cc. of methanol and 15–20 mg. of sodium for fifteen minutes, there was obtained from the reaction mixture 0.2 g. of solid which on purification from dilute methanol melted at 212–213° and proved to be identical with the higher-melting glycol.

Oxidation of Lower-Melting Oxide with Periodic Acid in Acetone Solution.—A solution of 1.0 g. of oxide (low-melting form) in a mixture of 20 cc. of acetone and 5 cc. of 1 *M* periodic acid was refluxed for thirty minutes. The solution was poured into water, extracted with chloroform and the solvent removed under reduced pressure. The residual sirup crystallized on scratching with ethyl acetate–ligroin, and yielded 0.82 g. of crystalline material. After several recrystallizations from benzene, in which the compound is difficultly soluble, the product melted at 177–178° with decomposition.

Anal. Calcd. for $C_{24}H_{26}O_5$: C, 73.06; H, 6.65. Found, C, 73.88, 73.27; H, 6.91, 6.97.

It may also be recrystallized from dilute acetone.

The same product is obtained by oxidizing the glycol with periodic acid in acetone.

Oxidation of the Glycol (M. p. 212°) with Lead Tetraacetate.—A suspension of 1.35 g. of lead tetraacetate in a solution of 1.05 g. of glycol in 10 cc. of acetic acid was shaken at room temperature for four hours and allowed to stand for two days. A crystalline precipitate formed, weight 0.63 g. Upon recrystallization from benzene it formed white needles, m. p. 170–170.5°, with decomposition.

Anal. Found: C, 69.93, 70.69, 69.96; H, 6.42, 6.41, 6.41.

α,α' - Diphenyl - β,β' - (3,6 - dihydro - 3,6 - dimethylbenzo)-furan (XIV).—A solution of 10 g. of the adduct (II) in a mixture of 80 cc. of glacial acetic acid, 40 cc. of acetic anhydride and 0.5 cc. of sirupy (85%) phosphoric acid was refluxed for twenty minutes. The solution was poured into water, extracted with chloroform and the solvent removed under reduced pressure. The residue crystallized on triturating with warm methanol. It weighed 9.0 g. and melted at 100–107°. Recrystallized from methanol it formed silky white needles or stout prisms melting at 114–115°. Occasionally the needle form separated first and changed into the prism form on standing in the solution.

Anal. Calcd. for $C_{22}H_{20}O$: C, 87.95; H, 6.70. Found: (prisms): C, 88.16; H, 6.94; (needles): C, 88.29; H, 6.92.

α,α' - Diphenyl - β,β' - (3,4,5,6 - tetrahydro - 4,5 - dibromo-3,6-dimethylbenzo)-furan (XV).—This compound can be obtained in either of two ways: (a) by bromination of the dihydrobenzofuran (XIV) or (b) by dehydration of the adduct dibromide (XIII).

(a) **Bromination of the Dihydrobenzofuran (XIV).**—To a cold solution of 2.0 g. of the dihydrobenzofuran in 15 cc. of glacial acetic acid was added, slowly and with cooling, a solution of 1.07 g. (1 mol) of bromine in 10 cc. of acetic acid. The bromine was decolorized instantly, and before all was added the addition compound began to separate. After precipitation was complete the product was collected, washed with acetic acid and water and dried. It weighed 2.10 g. and melted at about 165°, with decomposition. Recrystallized from *n*-butanol it formed pale yellow needles, m. p. 168–170°, with decomposition.

Anal. Calcd. for $C_{22}H_{20}OBr_2$: C, 57.39; H, 4.35. Found: C, 57.01; H, 4.50.

(b) **Dehydration of Adduct Dibromide.**—The dibromotetrahydrobenzofuran is most conveniently prepared by this procedure. After preliminary experiments on the pure adduct dibromide, it was found unnecessary to isolate and purify the adduct dibromide and that good results were obtained by dehydration of the crude product obtained by bromination of the adduct.

A solution of 5.0 g. of bromine in 50 cc. of acetic acid was added slowly to a well-cooled solution of 10 g. of the adduct (II) in 50 cc. of acetic acid. The faintly yellow solution was poured into water containing a little sodium bisulfite, extracted with chloroform and the solvent removed under reduced pressure. To the crystalline residue was added 50 cc. of acetyl chloride and five drops of concentrated sulfuric acid and the mixture heated under reflux. The dibromide went into solution rapidly and the solution assumed a brown-red color. After about ten minutes of refluxing, yellow crystals began to separate and soon a heavy crystalline precipitate filled the liquid. The color of the solution slowly faded and at the end of thirty minutes had become a pale greenish-yellow. The mixture was cooled and filtered and the product washed with acetic acid and with water. There was obtained 11.4 g. of faintly yellow crystals, m. p. about 165°, with decomposition. Recrystallized from *n*-butanol it formed tiny, pale yellow needles, m. p. 168–170°, with decomposition, identical with the material obtained in (a).

α,α'-Diphenyl-β,β'-(3,6-dimethylbenzo)-furan (XVI).—A solution of 2.0 g. of the dibromotetrahydrobenzofuran in 10 cc. of dry pyridine was refluxed for thirty minutes. The solution, almost colorless at the start, became a bright yellow and after ten to fifteen minutes crystals of pyridine hydrobromide separated from solution. The solution was poured into water and the oil which separated soon crystallized. The crude product, which contained a trace of bromine, weighed 1.46 g. and melted at about 115–120°. The benzofuran was separated from unchanged dibromo compound by virtue of its ready solubility in cold ether, in which the dibromo compound is practically insoluble. Removal of the ether and recrystallization of the bright yellow crystalline residue from methanol gave bright yellow needles, m. p. 129–131°.

Anal. Calcd. for $C_{22}H_{18}O$: C, 88.53; H, 6.10. Found: C, 88.26; H, 6.27.

The benzofuran appeared to be somewhat unstable, considerable loss occurring on recrystallization. In the reaction with maleic anhydride described below the first ether extract of the crude product was used, giving a good yield of the addition product based on the original dibromotetrahydrobenzofuran.

1,4 - Endoxo - 1,4 - diphenyl - 5,8 - dimethyl - 1,2,3,4-tetrahydronaphthalene - 2,3 - dicarboxylic Anhydride (XVII).—Treatment of a solution of the benzofuran (XVI) in ether or benzene with a solution of maleic anhydride caused immediate precipitation of the addition product as fine white needles. The compound was best prepared by treating 2.0 g. of the dibromotetrahydrobenzofuran with pyridine as described above, and extracting the crude, dried product with ether. An ether solution containing an excess of the calculated amount of maleic anhydride was added and the addition product began to crystallize immediately. After cooling the solution in ice, the product was collected and washed thoroughly with fresh ether. It formed tiny white needles weighing 1.10 g. (70% over both steps). After recrystallization from glacial acetic acid from which it formed tiny white plates the compound melted at 310–312° with some decomposition.

Anal. Calcd. for $C_{26}H_{20}O_4$: C, 78.79; H, 5.05. Found: C, 78.85; H, 5.04.

The compound dissolves readily in methyl alcoholic potassium hydroxide but only with difficulty in aqueous alkali.

1,2-Dibenzoyl-3,6-dimethylbenzene (XIX).—This compound was obtained (a) by treatment of the adduct dibromide (XIII) with pyridine, (b) by treatment of the adduct (II) with bromine in pyridine solution, (c) by treatment of the dibromotetrahydrofuran (XV) with one mole of bromine in acetic acid containing sodium acetate, and (d) by treatment of the dihydrobenzofuran (XIV) with two moles of bromine in acetic acid containing sodium acetate. Only method (d) gave satisfactory results but method (a) is also described since it involved the unusual reaction mentioned previously which led to the formation of some of the original adduct (II).

(a) A solution of 2.0 g. of the high-melting adduct dibromide (XIII) in 10 cc. of dry pyridine was heated for twenty hours on the steam-bath. Crystalline pyridine hydrobromide separated during the heating. The solution was poured into water and extracted with ether. After washing the ether solution with dilute hydrochloric acid and water and drying, it was evaporated under reduced pressure. The oily residue crystallized on triturating with an ether–petroleum ether mixture and the solid was collected; yield 0.30 g. Upon recrystallization from methanol it formed white, flat prisms, m. p. 144–145°.

Anal. Calcd. for $C_{20}H_{18}O_2$: C, 84.08; H, 5.74. Found: C, 83.82; H, 5.82.

The ether–petroleum ether filtrate yielded on evaporation 0.40 g. of the original adduct (II), bromine-free.

(d) To a solution of 1.0 g. of the dihydrobenzofuran (XIV) and 1.5 g. of anhydrous sodium acetate in 5 cc. of hot acetic acid was added a solution of 1.0 g. of bromine in 10 cc. of acetic acid. The bromine was absorbed instantly and sodium bromide separated. The solution was refluxed for thirty minutes and diluted to cloudiness with water. The product separated on cooling. It weighed 0.83 g., melted at 140–143°, and contained no bromine (Beilstein test). Recrystallized from methanol it formed white prisms, m. p. 143–145°, shown by mixed melting point to be identical with the compound obtained by method (a).

Methods (b) and (c) gave inferior yields of the same compound.

1,2-*bis*-(α-Oxybenzyl)-3,6-dimethylbenzene (XX).—A solution of 1 g. of the benzene derivative (XIX) in a solution of 2 g. of sodium hydroxide in 20 cc. of alcohol was boiled until a deep yellow-brown color appeared. About 0.5 g. of zinc dust was added in portions to the boiling solution and heating was continued for fifteen minutes on the steam-bath.

The nearly colorless solution was poured into water and the gummy precipitate crystallized from dilute methanol. After several recrystallizations from 50% methanol the compound was obtained as tiny white prisms melting at 149–151°. The substance was somewhat unstable and showed a tendency to decompose when dried at 100°.

Anal. Calcd. for $C_{22}H_{22}O_2$: C, 82.97; H, 6.97. Found: C, 83.74; H, 6.68.

Summary

1. The addition of hexadiene-2,4 to *trans*-dibenzoylethylene has been described.

2. An unsuccessful attempt has been made to convert the cyclohexene derivative so obtained into an analog of one of the degradation products of gossypol, namely, desapogossypolone tetramethyl ether.

3. The oxidation of the cyclohexene derivative with perphthalic acid to the corresponding cyclo-

hexene oxides, and the stereochemistry of these oxides and certain of their derivatives, are described.

4. Various transformation products of the cyclohexene derivative have been described, among them the corresponding dibenzoylxylene and α,α'-diphenyl-β,β'-(3,6-dimethylbenzo)-furan. It is believed that the methods described are general for the preparation of compounds of these types.

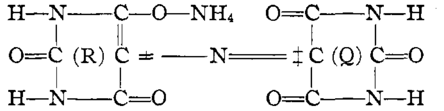
URBANA, ILLINOIS RECEIVED MAY 31, 1939

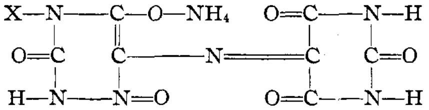
[CONTRIBUTION FROM JONES CHEMICAL LABORATORY, UNIVERSITY OF CHICAGO]

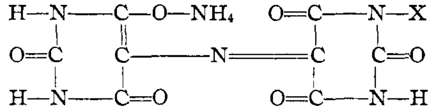
Structure of the Murexides and the Alloxantines[1]

BY N. M. WINSLOW[2]

The structure of the dye murexide (I) was established independently by Stieglitz,[3] Moehlau,[4] and Piloty.[5] Acid hydrolysis of the dye gives uramil and alloxan in semiquantitative yields. Hydrolysis should, therefore, provide a means of distinguishing isomeric N-substituted murexides of general structures II and III.[6] Hydrolysis of II should give N-substituted uramil and alloxan, while similar treatment of III should give uramil and N-substituted alloxan. However, if II and III exist in tautomeric equilibrium, or if resonance occurs between the two forms, then any preparative procedure calculated to yield either II or III would give the same mixture of the two, and hydrolysis of the product would yield four products: N-substituted uramil, N-substituted alloxan, uramil, and alloxan. The present investigation is concerned with the two isomeric N-phenylmurexides, 1-phenylmurexide (II, X = C_6H_5) and 1'-phenylmurexide (III, X = C_6H_5).


I

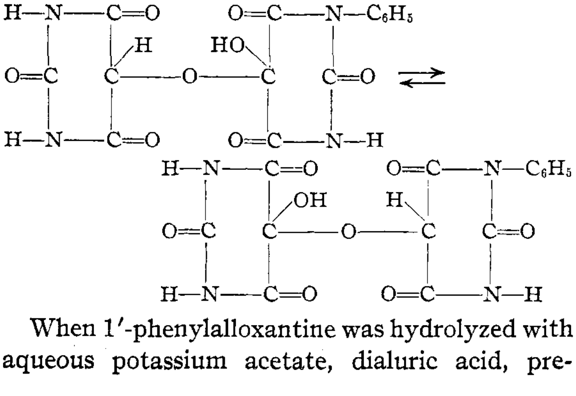

II


III

1-Phenylmurexide was prepared readily from 1-phenyluramil and alloxan in ammonium carbonate solution. When the dye was hydrolyzed within forty-eight hours of its preparation, 1-phenyluramil and alloxan, the latter determined as alloxantine, were recovered in yields representing 70 and 56%, respectively, of the theoretical.

The synthesis of 1'-phenylmurexide in a manner analogous to the method used for the preparation of 1-phenylmurexide was attempted without success, due to the relative insolubility of uramil in ammonium carbonate solution and the instability of the murexide in alkali sufficiently strong to dissolve uramil. There remained the alternative method of preparing the corresponding 1'-phenylalloxantine and treating this compound with ammonia.

Pure 1'-phenylalloxantine was prepared by the condensation of N-phenylalloxan with dialuric acid in hot aqueous solution. But chemical purity, as established by elementary analysis, was not the only requirement of 1'-phenylalloxantine intended for use in the preparation of 1'-phenylmurexide; it must also maintain its tautomeric identity. Quite obviously if a tautomeric equilibrium existed, treatment of the alloxantine with ammonia would give only a mixture of 1-phenylmurexide and 1'-phenylmurexide.



When 1'-phenylalloxantine was hydrolyzed with aqueous potassium acetate, dialuric acid, pre-

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[1] A part of a dissertation submitted by the author in partial fulfilment of the requirements for the degree of Doctor of Philosophy at the University of Chicago in 1936. The investigation was carried out under the direction of the late Professor Julius Stieglitz.

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[3] Stieglitz, *Am. Chem. J.*, **31**, 661 (1904).

[4] Moehlau, *Ber.*, **37**, 2686 (1904).

[5] Piloty, *Ann.*, **333**, 22 (1904).

[6] The murexides decompose without melting. A study of absorption spectra should furnish confirmatory evidence.