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

The Reaction between Quinones and Metallic Enolates. XXIV.[1] Synthesis and Reactions of Bis-(2,4,5-trimethylquinonyl)-methane

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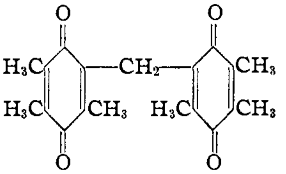
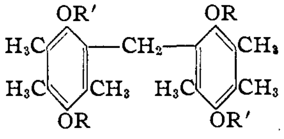
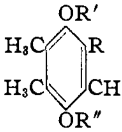
Studies described in the previous papers of this series have shown that a completely substituted *p*-benzoquinone may react with metallic enolates in one of three possible ways, depending largely upon the nature and relative positions of the substituents attached to the quinone nucleus. Thus, attack of the enolate may occur at a methyl group, resulting in formation of a coumarin[4]; at a halogen atom, resulting in replacement[5]; or at a conjugated system of the quinone, resulting in addition.[6]

If two independent quinone systems, differently substituted, could be combined in the same molecule, the behavior of a series of such substances toward metallic enolates could possibly be made the basis for an evaluation of the relative effects of different substituents in promoting these three types of reactions. It was decided to start with a compound containing two otherwise fully substituted *p*-benzoquinone rings joined by a single carbon atom. Accordingly, bis-(2,4,5-trimethylquinonyl)-methane, I, has been synthesized and studied. The substance I is the first representative of its class to be prepared, although not the only known compound containing two independent quinone systems. Thus, Dalgliesh[7] has prepared a compound containing two naphthoquinone nuclei joined by a single carbon atom, and Euler, Adler and Caspersson[8] have prepared a compound formulated as containing two *p*-benzoquinone nuclei, but joined by a chain of two carbon atoms.


I


II, R' = H; R = Ac
V, R' = R = Ac
VI, R' = R = H


III, R = H; R' = R" = Ac
IV, R = CH₂Cl; R' = H; R" = Ac

Smith and Carlin,[9] who studied the chloromethylation of trimethylhydroquinone diacetate (III), reported that the product, IV, was accompanied by a high melting, dinuclear substance (m. p. 229°). The latter substance was not investigated in detail by Smith and Carlin, but it was later shown[3] that this substance, upon oxidation, gave a diquinone, presumably I. To this high melting product, structure II was assigned, and in a study of the reaction, Sogn found that II was formed when III and IV were refluxed in dilute acetic acid. The substance gave analytical values for carbon, hydrogen, and acetyl groups consistent with those required by structure II; on oxidation, it was converted into a yellow diquinone I; and it gave a tetraacetate V when subjected to the action of acetyl chloride and pyridine.

In the present work, it was found that action of dilute acetic acid alone upon IV converted it into II in nearly quantitative yields, a result in accordance with the findings of Fries[10] and of Buehler[11] that certain *p*-hydroxybenzyl halides, when heated in polar solvents, give the corresponding diphenylmethanes with elimination of a methyl halide. This observation led to a very convenient synthesis of I in three steps from trimethylquinone, *via* trimethylhydroquinone and action of formaldehyde and a small amount of hydrochloric acid upon the hydroquinone. The product of this reaction was the di-hydroquinone VI; oxidation of VI by action of ferric chloride in dilute ethanol upon VI produced I. The over-all yield of I from trimethylquinone was 89%. This synthesis of I *via* the dihydroquinone VI is much better than the original synthesis of I *via* the diacetate II.

Both II and VI gave the same tetraacetate V; VI was also converted into the tetrapropionate. When the dihydroquinone was dissolved in warm ethanol, a molecule of water was eliminated and the hexamethyldihydroxyxanthene VII was formed. The yield of VII was never better than 75%, and varying amounts of the diquinone I could be isolated from the mother liquors. The xanthene formed a diacetate VIII.

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[1] Paper XXIII, *J. Org. Chem.*, **14**, 740 (1949).

[2] Abstracted from a thesis by Horace R. Davis, Jr., presented to the Graduate Faculty of the University of Minnesota, in partial fulfillment of the requirements for the Ph.D. degree, July, 1949. National Research Council Predoctoral Fellow, 1946–1949.

[3] Many preliminary experiments, incidental to this work, are described in the M.S. thesis of A. Walter Sogn, University of Minnesota, 1942.

[4] THIS JOURNAL, **48**, 1693 (1926); **59**, 662 (1937); **63**, 612 (1941); **68**, 887 (1946); also Ref. 1.

[5] *Ibid.*, **64**, 528 (1942); **65**, 1739 (1943).

[6] *J. Org. Chem.*, **14**, 732 (1949).

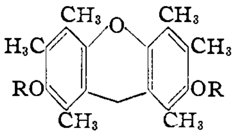
[7] Dalgliesh, THIS JOURNAL, **71**, 1697 (1949).

[8] Euler, Adler and Caspersson, *Arkiv. Kemi. Mineral. Geol.*, **16A**, No. 11, 1 (1943).

[9] Smith and Carlin, THIS JOURNAL, **64**, 524 (1942).

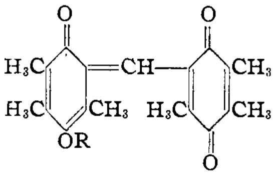
[10] Fries, *Ber.*, **36**, 3037 (1903).

[11] Buehler, *J. Tennessee Acad. Sci.*, **22**, 303 (1947); *Chem. Abs.*, **42**, 2244^d (1948).



VII R = H

VIII R = Ac



IX R = H
X R = Ac
XI R = C_6H_5CO—
XII R = CH_3

The diacetate II, as well as the hydroxy compounds VI and VII, were converted into I by oxidation; oxidation of II always produced some of the xanthene diacetate VIII along with I. When a solution of I was shaken with aqueous sodium hydrosulfite, the hydroquinone VI was produced. These reactions, together with the analytical data, serve to fix the structures of I, V, VI, VII and VIII and they show that VII exhibits the typical chemical behavior of a *p*-hydroxychroman.

The absorption spectrum of I in the ultraviolet is very similar to that of duroquinone: the position of the maxima are nearly coincident at 260 mμ, but the molar extinction coefficient of I is about twice that of duroquinone. Reduction of I at the dropping mercury electrode gave a half-wave potential of −0.200 volt and from this it was calculated that the oxidation–reduction potential of II is 0.457 volt. This value is very close to that of duroquinone, 0.471 volt.[12,13] Attempts to titrate I potentiometrically with standard titanous chloride failed because I was not sufficiently soluble in ethanol (50% or 95%) to give convenient concentrations.

Under a variety of conditions successful in bringing about such condensation reactions of quinones, the diquinone I failed to react with the sodio derivative of malonic ester. In every experiment, the only isolable product was a red, amorphous, infusible powder. This same material was formed when the enolate was omitted; it therefore resulted from the action of sodium ethoxide alone upon I. Since the only structural detail, present in I but not present in duroquinone, is the methylene bridge, it appeared that a different reaction of I, induced by bases, might be responsible for the failure of I to condense with enolates, and that a base weaker than sodio malonic ester or sodium ethoxide might be capable of initiating a reaction leading to a crystalline product. When I was dissolved in pyridine at room temperature, the yellow solution became red, and, after several days, deposited a red, crystalline material. The maximum yield of this material was 65%; bases other than pyridine also brought about the same reaction, but the yields were always much lower. The new substance (IX) was isomeric with I; it formed a yellow mono acetate (X), a mono benzoate (XI), and a mono methyl ether (XII). The substance was not affected by action of sodium hydrosulfite, but catalytic reduction over Raney nickel produced the xanthene VII. The mono acetate of the red compound, when reduced catalytically, produced a mono acetate of VII, identified by conversion to the known diacetate VIII.

These properties of the red compound showed that, in its formation from I, no basic change in the carbon skeleton of I had occurred and with this limitation, the only possible structures for an isomer of I containing a single hydroxyl group are the various "pentad-enols" of I involving one of the methyl groups, or the methylene bridge. Since the "enol" did not react with sodio malonic ester, structure IX involving the methylene bridge, was assigned to it. Had a methyl group been involved in the isomerization, there could have been no apparent reason for the failure of the substance to react with sodio malonic ester. Structure IX is supported by the chemical evidence obtained by oxidative degradation. Most oxidizing agents—alkaline hydrogen peroxide in aqueous dioxane,[14] permanganate in pyridine[15] either did not attack IX or its methyl ether XII, or else converted the molecule completely into water soluble products. However, action of a mixture of nitric and sulfuric acids upon IX or the acetate X produced a small yield (16%) of nitrotrimethylquinone. The enol IX was recovered unchanged when acidic solutions of it were refluxed; the only way found for conversion of IX to I involved reduction of IX to the xanthene VII and oxidation of the latter. The ultraviolet absorption spectrum of IX shows a considerable shift of the bands toward the red as compared with the spectrum of I, which is in accord with the greater continuous conjugation in IX. The infrared spectra of I and IX are in agreement with the structures assigned.[16] Structure IX allows for the possibility of *cis–trans* isomerism about the double bond between the two rings. However, only one form of IX was ever isolated, but since the yield of IX never exceeded 65%, it is possible that a stereoisomer escaped isolation even though a careful examination of the mother liquors

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(12) The authors wish to thank Dr. Ralph A. Johnson for assistance and advice in connection with the polarographic work.

(13) For results on duroquinone, see Smith, Kolthoff, Wawzonek and Ruoff, THIS JOURNAL, **63**, 1018 (1941). Conant and Fieser, *ibid.*, **45**, 2194 (1923), found 0.466 volt for duroquinone.

(14) Fieser and Fieser, *ibid.*, **70**, 3215 (1948).

(15) Smith and Spoehr, *J. Biol. Chem.*, **86**, 87 (1930); Bucher, THIS JOURNAL, **32**, 374 (1910).

(16) The authors wish to thank Dr. B. L. Crawford, Jr., and Mr. J. E. Lancaster, for measuring and interpreting the infrared spectra of I and IX. A saturated solution of I in carbon tetrachloride shows a peak in the proper position (1440 cm.$^{-1}$) and of the expected breadth for a methylene group; there is also a strong peak at 1380 cm.$^{-1}$ indicating the presence of methyl groups. Unfortunately, IX is not coefficiently soluble in carbon tetrachloride, carbon bisulfide, or pyridine to measure the spectrum in these solvents. A suspension of IX in Nujol gave a very satisfactory spectrum even though some of the expected bands were covered by the bands of the medium. A peak at 3500 cm.$^{-1}$ shows the presence of a hydroxyl group; a band at 680 cm.$^{-1}$ probably arises from the methinyl group, although this is not certain. A peak at 1710 cm.$^{-1}$ arises from the carbonyl groups and the peak at 1560 cm.$^{-1}$ probably arises from the conjugated system of double bonds. Bands in the region of 1600 cm.$^{-1}$ are consistent with the structure IX although they do not prove this structure.

from IX was made. Unsuccessful attempts were made to isomerize IX, as well as its acetate and methyl ether, to stereoisomers by action of ultraviolet light, but chromatography of the resulting solutions failed to reveal, in significant amounts, anything but unchanged starting materials.

Since the enol IX was more acidic than malonic ester, condensation with the free enol was not attempted. The acetyl derivative X did not react at room temperature with sodio malonic ester in dioxane; when the solution was refluxed, the only result was hydrolysis of the acetate to IX. The methyl ether XII likewise failed to react with sodio malonic ester at room temperature in dioxane; when this solution was refluxed, the product was a brown, amorphous powder which could not be purified by any method tried, including chromatography. Similar results were obtained when attempts were made to condense the methyl ether XII with sodio cyanoacetic ester. That the lateral conjugated system in IX is hindered is shown by the fact that IX failed to give an oxime with hydroxylamine, and the failure of IX to react with sodio malonic ester is in itself evidence in favor of structure IX for this enolate, rather than one of the possible structures involving a methyl group of I.

The enol IX is unique in that it is a stable "pentad-enol" of the type postulated by Fuson[17] as a transient intermediate in the condensation of duroquinone with metallic enolates. Smith and Horner[18] obtained definite evidence for the transient existence of such a methylene quinone in a condensation with sodio malonic ester, but IX is the first pentad-enol reported that is stable enough for isolation.

Experimental Part[19]

2,5,2',5'-Tetrahydroxy-3,4,6,3',4',6'-hexamethyldiphenylmethane (VI).—A warm solution of trimethylhydroquinone (30 g., 0.2 mole) in acetic acid (400 cc.) was diluted with water (800 cc.). Hydrochloric acid (60 cc.) was added, the solution was heated to the boiling point, and formalin (40%, 12 g., 0.16 mole) was added with shaking. Solid was deposited within thirty seconds, and within two minutes the mixture was nearly solid. The solid was removed from the cooled (5°) mixture, washed with three 200-cc. portions of cold water, and dried in vacuum over potassium hydroxide for twenty-four hours. The material (30.9 g., 99%) did not have a sharp melting point, and it was not readily purified by crystallization from any of the common solvents. The analytical sample, precipitated from acetone solution by addition of petroleum ether (b. p., 60–68°) and dried in vacuum for eighteen hours, melted at 222–227°. The dried substance easily acquired an electrostatic charge which made it impossible to handle for microanalysis; the charge was completely removed by exposing the substance for a few minutes to the rays of an X-ray tube.

Anal. Calcd. for $C_{19}H_{24}O_4$: C, 72.12; H, 7.65. Found: C, 72.12; H, 7.97.

2,5,2',5'-Tetraacetoxyhexamethyldiphenylmethane (V).—Sulfuric acid (1 drop) was added to a solution of VI (1 g.) in acetic anhydride (10 cc.), the solution was heated to the boiling point for five minutes, poured into ice water (100 cc.), and allowed to stand for three hours. The solid was removed, washed with cold water, and dissolved in hot ethanol (300 cc., 95%). The hot solution was filtered, the filtrate was concentrated to 150 cc. and allowed to stand overnight. The solid was removed and dried in vacuum over potassium hydroxide, when it weighed 1.39 g. (91%) and melted at 237–238°.

Anal. Calcd. for $C_{27}H_{32}O_8$: C, 66.92; H, 6.66; acetoxy (four), 35.53. Found: C, 67.07; H, 6.56; acetoxy, 34.9, 35.5, 35.0.[20]

2,5,2',5'-Tetrapropionoxyhexamethyldiphenylmethane (1.64 g., 96%) was prepared from VI (1 g.) and propionic anhydride (10 cc.) as described above for the tetraacetate except that the reaction mixture was decomposed by pouring it into aqueous ethanol (50%, 100 cc.). The solid, crystallized twice from ethanol, melted at 199–200°.

Anal. Calcd. for $C_{31}H_{40}O_8$: C, 68.86; H, 7.46. Found: C, 68.95; H, 7.56.

2-Hydroxy-5-acetoxy-3,4,6-trimethylbenzyl Chloride (IV).—Trimethylhydroquinone diacetate (III) (5 g.) was added to a mixture of hydrochloric acid (20 cc.), formalin (40%, 15 cc.) which had been saturated with hydrogen chloride at 5°. The mixture was stirred for two hours while hydrogen chloride was passed in; the temperature was allowed to rise to 30° during this operation. The mixture was poured into ice water (100 cc.), the solid (3.7 g., 75%, m. p., 137–141°) was removed, washed with water and dried in vacuum over potassium hydroxide. After crystallization from ether–petroleum ether, the substance melted at 146–148°.[21]

2,2'-Dihydroxy-5,5'-diacetoxyhexamethyldiphenylmethane (II) A: From the Diacetate III.—The above procedure for chloromethylation of III was repeated, except that the reaction mixture was maintained at 0–5° throughout. The washed and dried product was extracted with ether; the insoluble portion weighed 1.8 g. (42%) and melted at 221–227°. Crystallization from chloroform–petroleum ether (b. p. 60–68°) gave material melting at 227–229°.

Anal. Calcd. for $C_{23}H_{28}O_6$: C, 68.98; H, 7.05. Found: C, 69.35; H, 6.97.

This material was halogen free, gave a positive Folin test, and was converted, by action of acetic anhydride, into the tetraacetate V, m. p., and mixed m. p., 237–238°.

B. From the Benzyl Chloride IV.—A solution of IV (0.5 g.) in aqueous acetic acid (60%, 15 cc.) was refluxed for five minutes. The solution was diluted with water (15 cc.), the solid (0.31 g., 76%, m. p., 219–224°) was removed, dried in vacuum over potassium hydroxide, and crystallized from chloroform–petroleum ether (b. p. 60–68°). It then melted at 226–228°. Action of acetic anhydride upon this material give the tetraacetate V, m. p., and mixed m. p., 237–238°.

Bis-(2,4,5-trimethylquinonyl)-methane (I): (A) From the Tetrahydroxy Compound VI.—A slurry of VI (30 g., 0.95 mole) in ethanol (95%, 750 cc.) was refluxed while a solution of ferric chloride hexahydrate (240 g.) in water (900 cc.) and hydrochloric acid (20 cc.) was added. The mixture became red, then black, and complete solution occurred in a few minutes. Refluxing was continued for twenty minutes, then the solution was rapidly cooled (ice-bath), and diluted with water (200 cc.). The yellow solid was removed, washed with three 50-cc. portions of cold water, and dried in vacuum over potassium hydroxide for twenty-four hours. The product melted at 124–125° and weighed 29 g. (98%). The analytical sample, crystallized twice from ethanol, melted at 127–127.5°.

Anal. Calcd. for $C_{19}H_{20}O_4$: C, 73.06; H, 6.45. Found: C, 73.09; H, 6.41.

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[17] Fuson, *Chem. Rev.*, **16**, 1 (1935).

[18] Smith and Horner, THIS JOURNAL, **60**, 676 (1938).

[19] Microanalyses by R. W. Amidon, J. S. Buckley, William Cummings, W. H. Hunter, and S. A. Sundet.

[20] The determination of acetyl groups was carried out using a modification of the method of Pregl and Soltys, *Microchem.*, **7**, 1 (1929). The details of the method are described in the Ph.D. thesis of Horace R. Davis, Jr., University of Minnesota, pp. 55-61, 1949.

[21] Smith and Carlin, ref. 9, p. 526, give 150-151° as the m. p. of the pure substance.

The above directions must be followed carefully; in several runs in which the procedure was varied, the product was not entirely a bright yellow crystalline solid, but was contaminated with a dark amorphous powder; when the relative amounts of materials specified above were used, this contaminant never appeared. The quinone could be completely removed from this dark material by extraction with petroleum ether (b. p., 60–68°).

(B) **From the Dihydroxy-diacetoxy Compound II.**—A solution of potassium dichromate (5 g.) in water (50 cc.) and sulfuric acid (10 cc.) was added to a solution of II (2 g.) in acetic acid (30 cc.). The mixture was warmed for thirty minutes on the steam-bath, then filtered, and the filtrate was diluted with water (100 cc.) and cooled. The yellow solid was removed, washed with water, and refluxed with methanol for fifteen minutes. The insoluble material (VIII, 0.6 g., m. p. 239–242°) was removed; the filtrate, when cooled deposited I (0.58 g., 37%) melting at 123–126°. The high melting material obtained from this reaction was not investigated further.

Malonic ester (1 cc.) in dry ethanol (3 cc.) was added to a solution of sodium (115 mg.) in dry ethanol (5 cc.). To this solution of sodio malonic ester was added slowly (two hours), and with stirring, a solution of the diquinone I (1.56 g.) in dry ethanol (75 cc.). The mixture acquired a blue green color, which later became an opaque dark brown. Stirring was continued overnight; the mixture was then poured over ice (300 g.) and hydrochloric acid (3 cc.). The brick red precipitate was removed and washed with water. Attempts to crystallize this material from several solvents resulted only in dark, amorphous materials. The material decomposed without melting, but left no residue when it was burned. Essentially the same results were obtained when the reaction was carried out in benzene, or when the diquinone I was refluxed in benzene with sodium alone.

Reduction of the diquinone I (0.5 g.) in methanol (20 cc.) by action of sodium hydrosulfite (3 g.) in water (10 cc.) was rapid, and led, after dilution of the reaction mixture with water, to the dihydroquinone VI (0.49 g., 97%, m. p. 222–227°).

3,6-Dihydroxy-1,2,4,5,7,8-hexamethylxanthene (VII).—The dihydroquinone VI (1 g.) was dissolved in warm ethanol (25 cc.). The warm solution was filtered, and the filtrate was cooled. The solid (0.7 g., 75%) melted at 260–268°, and formed long white needles which became tan on drying.

Anal. Calcd. for $C_{19}H_{22}O_3$: C, 76.48; H, 7.43. Found: C, 76.78; H, 7.75.

The filtrate from the xanthene, when concentrated to a volume of 5 cc., cooled, and seeded with a crystal of the diquinone I, deposited 0.1 g. of I, m. p. and mixed m. p., 123–127°. Oxidation of the xanthene VII (127 mg.) in ethanol (30 cc.) by action of ferric chloride (3 g.) in water (15 cc.) and hydrochloric acid (1 cc.) gave the diquinone I (108 mg.).

3,6-Diacetoxy-1,2,4,5,7,8-hexamethylxanthene (VIII).—A solution of the xanthene VI (75 mg.) in acetic anhydride (5 cc.) and sulfuric acid (1 drop), was refluxed for three minutes and then poured into water (40 cc.). The white solid was removed and dried in vacuum over potassium hydroxide, when it weighed 94 mg. (97%) and melted at 218–230°. After crystallization twice from methanol and once from petroleum ether (b. p. 75–115°) the substance melted at 243.5–245.5°. A mixture of VIII and the tetraacetoxy compound V (m. p., 237–238°) melted at 218–226°.

Anal. Calcd. for $C_{23}H_{26}O_5$: C, 72.23; H, 6.85. Found: C, 72.45; H, 6.77.

Pentad-enol (IX) of I.—The diquinone I (10 g.) was dissolved in dry pyridine (50 cc.). The solution became orange within one minute, and deep red within ten minutes. Granular, red crystals were deposited after two days; the mixture was allowed to stand for seven days at room temperature. The solid was removed; the filtrate was diluted with water (30 cc.) and a second crop of crystals was collected. The combined solids were washed with petroleum ether (b. p. 60–68°) and dried. The material then weighed 6.5 g. (65%) and melted at 250–254° (dec.). The analytical sample, crystallized from benzene and petroleum ether (b. p. 60–68°), melted at 253–255° (dec.).

Anal. Calcd. for $C_{19}H_{20}O_4$: C, 73.06; H, 6.45; mol. wt., *312*. *Found:* C, 73.27; H, 6.57; mol. wt. (Rast), 317, 326.

When the reaction time was less than seven days, the yield of IX was lower, but increasing the reaction time beyond seven days did not result in a better yield.

The enol IX (1.5 g.) in ethanol (100 cc.) was subjected to the action of hydrogen under a pressure of 1100 lb. and at 170° for five hours in the presence of Raney nickel catalyst. The product was dark and oily, but from it was isolated, by repeated crystallization from ethanol, 153 mg. of the xanthene VII, m. p. 262–268°; acetate VIII, m. p., 242–244°.

The enol IX (0.32 g.) and hydroxylamine hydrochloride (0.2 g.) in ethanol (20 cc.) were refluxed for forty hours with a solution of sodium ethoxide (sodium, 0.06 g., ethanol, 4 cc.). The only product was material with a wide melting point range similar to that obtained by action of alkali alone upon IX.

Acetate (X).—The enol IX (1.2 g.) was dissolved in acetic anhydride (10 cc.) containing sulfuric acid (1 drop). The solution was refluxed for three minutes and then poured into water (100 cc.). The yellow solid was washed with water and dried in vacuum over potassium hydroxide. It then weighed 1.33 g. (98%) and melted at 186–193°. The analytical sample, crystallized first from ethanol and then from benzene–petroleum ether, melted at 194–195°.

Anal. Calcd. for $C_{21}H_{22}O_5$: C, 71.17; H, 6.26. Found: C, 71.48; H, 6.35.

The acetate X (1 g.) in ethanol (100 cc.) was subjected to the action of hydrogen for two and one-half hours at 150° under a pressure of 1200 lb. The product was oily, but from it was isolated a crystalline material (78 mg.) melting at 279–282°. This was the monoacetate of the xanthene VII. The substance could not be obtained analytically pure but, when acetylated, it gave the xanthene diacetate VIII, m. p. and mixed m. p., 243–245°.

Anal. Calcd. for $C_{21}H_{24}O_4$: C, 74.09; H, 7.11. Found: C, 73.39; H, 7.26.

Benzoate (XI).—The enol IX (0.3 g.) was dissolved in pyridine (5 cc.); benzoyl chloride (2 cc.) was added, the solution was gently warmed for one minute and poured into water (30 cc.). Sodium carbonate (2 g.) was added, the mixture was stirred, and the yellow oil was rubbed with a rod. Crystallization usually occurred at once; if not, the mixture was allowed to stand overnight. The solid (0.38 g., 91%, m. p., 209–215°) was removed, washed with water, dried and recrystallized from ethanol, when it melted at 217.5–218.5°.

Anal. Calcd. for $C_{26}H_{24}O_5$: C, 74.98; H, 5.81. Found: C, 74.76; H, 5.95.

Methyl Ether (XII).—A solution of methyl sulfate (32 g., freshly distilled) in methanol (100 cc.) was added to a warm solution of the enol IX (10 g.) in dioxane (250 cc.). The mixture was refluxed and stirred while a solution of potassium hydroxide (25 g.) in methanol (200 cc.) was added dropwise over a period of thirty minutes. The mixture was poured into water (1.5 l.), stirred for an hour, and the solid was removed, washed with water, crystallized from ethanol, and dried in vacuum over potassium hydroxide. It weighed 8.2 g. (79%), and melted at 179–185°, but it could not be purified by crystallization from any of the common solvents because the principal impurity, the enol IX, was less soluble than XII. The crude product was dissolved in benzene (100 cc.) and the solution was passed through a column of alumina (15 × 180 mm.). The red band at the top of the column was cut out, and the rest of the column was eluted with a mixture of benzene and ether (3:1). The solvent was removed and the residue was crystallized from ethanol (60 cc.). The product weighed 6.7 g. (65%) and melted at 189–190°.

Anal. Calcd. for $C_{20}H_{22}O_4$: C, 73.59; H, 6.80. Found: C, 73.77; H, 6.98.

Oxidation of the Enol IX.—The enol (1 g.) was added to a mixture of sulfuric acid (4 cc.) and nitric acid (12 cc.) at room temperature. Heat was evolved and brown oxides of nitrogen were given off; the solid dissolved completely within twenty seconds. The solution was warmed (60–70°) for one hour and then poured into water (50 cc.). The yellow solid was removed, washed with water and dried in vacuum over potassium hydroxide. It weighed 0.48 g. and melted at 88–94°. The material was extracted several times with warm petroleum ether (b. p. 60–68°); the combined extracts were evaporated and the residue was crystallized, first from petroleum ether and then from aqueous ethanol (50%). The material then weighed 97 mg. (16%) and melted at 109–111°, alone or when mixed with an authentic sample of nitrotrimethylquinone. The acetate X (1 g.) subjected to the above procedure, gave 72 mg. (13%) of nitrotrimethylquinone.

Action of Sodiomalonic Ester upon the Acetate X.—A solution of X (1.06 g., 0.003 mole) in dioxane (50 cc.) was slowly (ten minutes) added dropwise to a cooled solution of sodio malonic ester in dioxane (from sodium, 0.21 g., dimethyl malonate 1.33 g., and dioxane, 20 cc.). The solution was stirred for six hours at room temperature and allowed to stand thereafter for fifteen hours. There was no apparent reaction; when the mixture was poured into water (200 cc.) and hydrochloric acid (10 cc.), the precipitate (0.9 g.) consisted of unchanged X, which, after crystallization from ethanol, melted at 193–194°, alone or when mixed with authentic X. The experiment was repeated, except that the solution was refluxed for two hours and then allowed to stand at room temperature for eighteen hours before pouring it into water (500 cc.) and hydrochloric acid (10 cc.). The orange brown product weighed 0.96 g. and melted at 160–210°. It was extracted twice with petroleum ether (100 cc., b. p. 60–68°); this removed 0.19 g. of material (X) which melted at 192–194° after crystallization from methanol. The residue was extracted exhaustively (10 times) with petroleum ether, leaving a red material (0.11 g.) which, after crystallization from methanol, melted at 253–255° (dec.) alone or when mixed with IX.

Action of Sodiomalonic Ester upon the Methyl Ether XII.—A solution of the methyl ether XII in dioxane (100 cc.) was added to a solution of sodiomalonic ester (from sodium, 0.46 g., methyl malonate, 2.9 g., and dioxane, 20 cc.). The mixture was stirred for three hours; there was no apparent reaction. The mixture was then refluxed and stirred for three hours; the color became red within a few minutes, and a dark red solid separated. The solid was removed, washed with dioxane, triturated with acetone (50 cc.) and then suspended in acetone. Hydrochloric acid (1 cc.) and then water (100 cc.) were added; the tan amorphous material was removed in vacuum over potassium hydroxide. It weighed 1.25 g., and melted at 147–195°. The filtrate from this material was acidified with hydrochloric acid (15 cc.) and diluted with water (1.5 l.). The yellow, amorphous solid was removed; it weighed 2.4 g. and melted at 110–145°. Neither solid could be resolved into any pure materials by crystallization from any of the common solvents or mixtures of solvents, nor was any resolution into pure materials achieved by chromatographic adsorption on alumina. Essentially, the same results were obtained when cyanoacetic ester was substituted for malonic ester; from 2.16 g. of XII, the only pure material obtained was a small amount of unchanged XII.

Summary

1. A new and efficient synthesis for bis-(2,4,5-trimethylquinonyl)-methane (I) has been devised, and the transformations of this substance have been studied.

2. The bis-quinone has been converted, by action of pyridine, into a stable isomer IX, and evidence has been accumulated to show that this isomer is a stable pentad-enol of an alkylated quinone, the first of its class to be prepared.

3. The diquinone I, as well as two derivatives of the isomeric enol, all failed to add sodio malonic ester.

4. The structure of the high melting by-product obtained from chloromethylation of trimethylhydroquinone diacetate has been established as 2,2'-dihydroxy-5,5'-diacetoxyhexamethyldiphenylmethane, II.

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The Rearrangement of α,α,α'-Tribromoketones

BY R. B. WAGNER AND JAMES A. MOORE

In the course of studies of steroidal bromoketones, these compounds have been found to be generally very susceptible to rearrangements when subjected to basic reagents. The α-bromo-*s*-alkyl ketones when treated with mild base undergo a rearrangement to esters of tertiary acids, *e. g.*, 17-bromopregnane-3(β)-ol-20-one to methyl 3(β)-hydroxy-17-methyl-*etio*-cholanate. This reaction is analogous to the Favorski rearrangement in which α-chlorocyclohexanones are converted by alkali into cyclopentanecarboxylic acids[1,2,3] (Eqn. 1). The rearrangement of α,α'-dibromoketones under similar conditions gives esters of α,β-unsaturated acids, *e. g.*, 17,21-dibromopregnane-3(β)-ol-20-one to methyl 17-pregnene-3(β)-ol-21-oate; a reaction first discovered by Favorski and recently extended to simple aliphatic and alicylic α,α'-dibromoketones (Eqn. 2).[4,5,6] The rearrangement of a steroidal α,β-dibromoketone, namely, 16,17-dibromopregnene-3(β)-ol-20-one, gave this same pregnenoic ester. On the other hand, extension of this rearrangement to simpler alicylic and aliphatic α,β-dibromoketones showed that β,γ-unsaturated

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