109.5–110°; mixed melting point with ethyl 3,4-dihydro-5,6-benzocoumarin-3-carboxylate 89–100°. The compound crystallized from ligroin (90–120°) in the form of beautiful white needles. It was immediately soluble in cold 1% sodium hydroxide solution; ultraviolet spectrum in 95% ethanol (log ϵ); 270 mμ (3.61), 280 mμ (3.73), 292 mμ (3.65), 325 mμ (3.39), and 337 mμ (3.45).

Anal. Calcd. for $C_{18}H_{20}O_5$: C, 68.34; H, 6.37. Found: C, 68.77; H, 6.13.

2-(2-Hydroxy-5,6,7,8-tetrahydro-1-naphthylmethyl)propane-1,3-diol (III). Ethyl 5,6-benzocoumarin-3-carboxylate (10.73 g., 0.04 mole), in 450 ml. of absolute ethanol, with 24.7 g. of freshly prepared W-1 Raney nickel, was hydrogenated at 90° and 1520 p.s.i. of hydrogen. The reaction time was 24 hr. After removal of the catalyst and solvent, the crude reaction product was obtained as a viscous oil. The oil was first triturated with ligroin (30–60°), and then with ether to yield white crystals which were filtered, washed with ligroin, and then with a little dry ether. The yield was 1.03 g. (11%), m.p. 149–151°. After three recrystallizations from water-ethanol, the white crystals melted at 153–154°; ultraviolet spectrum in 95% ethanol (log ϵ): 284 mμ (3.29).

Anal.[10] Calcd. for $C_{14}H_{20}O_3$: C, 71.16; H, 8.53. Found: C, 70.93; H, 8.73.

The compound was immediately soluble in 8% sodium hydroxide solution, from which it reprecipitated unchanged by the addition of excess acid. An ethanolic solution gave a green color with ferric chloride solution. Attempts to prepare a crystalline acetate or 3,5-dinitrobenzoate derivative failed.

1-Isobutyl-2-decalol (IV). A suspension of ethyl 5,6-benzocoumarin-3-carboxylate (13.41 g., 0.05 mole) in 450 ml. of absolute ethanol was hydrogenated at a hydrogen pressure of 1850 p.s.i. and at 140°, using 20.9 g. of W-1 Raney nickel as the catalyst. The total reaction time was 29 hr. The oil (8.93 g.) which remained after removal of the catalyst and solvent was refluxed with 30 ml. of 10% sodium hydroxide for 3 hr. The remaining oil was separated and fractionated to give 2.27 g. of a mobile, colorless oil, b.p. 66–98° (0.06 mm.). This liquid was redistilled and the fraction having a boiling point of 66–68° (0.055 mm.) was collected, n_D^{25} 1.4980.

Anal.[10] Calcd. for $C_{14}H_{26}O$: C, 79.93; H, 12.46. Found: C, 79.91; H, 11.71.

Repeated attempts to prepare a crystalline 3,5-dinitrobenzoate or phenylurethane failed.

5,6-Benzocoumarin-3-carboxamide. Fifteen milliliters of a 6% solution of ammonia in absolute ethanol and 1.0 g. (.373 mole) of ethyl 5,6-benzocoumarin-3-carboxylate were placed in a 50-ml. flask, and the flask was stoppered. Immediate solution occurred when the flask was swirled. After standing at room temperature for 64 hrs. the flask was chilled in an ice bath and the resulting precipitate collected by filtration, washed with ethanol, and recrystallized from glacial acetic acid. Light yellow needles were obtained, m.p. 297–298°; the yield was 0.83 g. (93%).

Anal. Calcd. for $C_{14}H_9NO_3$: N, 5.86. Found: N, 5.81.

Ethanol and glacial acetic acid solutions of the carboxamide exhibited a very intense blue fluorescence. Hydrolysis of the carboxamide, followed by acidification, yielded an acidic compound which melted at 236–237° (dec.). Sachs and Brigl[11] reported a melting point of 234–235° for 5,6-benzocoumarin-3-carboxylic acid.

(2-Hydroxy-1-naphthylmethyl)malonamide. Ethyl 3,4-dihydro-5,6-benzocoumarin-3-carboxylate (2.75 g., 0.0102 mole) dissolved instantly in 30 ml. of 6% alcoholic ammonia solution. The stoppered reaction vessel was allowed to stand at room temperature for 60 hr. The crystals which resulted were collected by filtration and washed with 10 ml. of ethanol. There was obtained 2.47 g. (94.0%) of product, m.p. 213–214° (with copious evolution of ammonia). λ_{max} (95% ethanol): 270 mμ (log ϵ 3.60), 280 (3.73), 292 (3.65), 326 (3.36), 335 (3.40).

Anal. Calcd. for $C_{14}H_{14}N_2O_3$: C, 65.10; H, 5.46; N, 10.84. Found: C, 65.27; H, 5.64; N, 10.97.

The compound was soluble in 2*N* sodium hydroxide solution, from which it was recovered unchanged by the addition of excess acid. A warmed suspension of the compound in ethanol did not give a color with ferric chloride solution.

(2-Hydroxy-5,6,7,8-tetrahydro-1-naphthylmethyl)malonamide. Ethyl 2,3,7,8,9,10-hexahydro-3-keto-1*H*-naphtho[2,1-*b*]pyran-2-carboxylate (1.0 g., 3.64 millimoles) was dissolved in 5.4 ml. of 6% alcoholic ammonia solution. The stoppered reaction vessel containing the solution was allowed to stand for 2 hr. and the white precipitate which had formed was collected by filtration. After one recrystallization from a large volume of absolute ethanol-acetone (1:1), there was obtained 0.66 g. (69.1%) of white crystals, m.p. 198.5–199.5° (with evolution of gas); ultraviolet spectrum in 95% ethanol (log ϵ) 285 mμ (3.40).

Anal. Calcd. for $C_{14}H_{18}N_2O_3$: N, 10.68. Found: N, 10.56.

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[CONTRIBUTION FROM THE FOREST PRODUCTS LABORATORY UNIVERSITY OF CALIFORNIA, RICHMOND, CALIF.]

On the Structure of the Photodimer of Thymoquinone

EUGENE ZAVARIN

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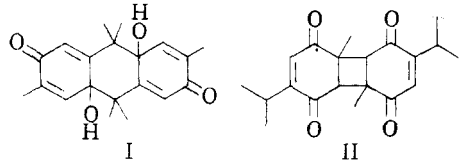
It has been demonstrated that the photodimerization of thymoquinone takes place along the less hindered 3,4-double bond with the formation of the corresponding cyclobutane derivative. The proposed analogous formula for the 2-methylnaphthoquinone photodimer has been spectroscopically substantiated.

The chemistry of the dimer of thymoquinone formed by irradiating the quinone in thin crystalline layers with daylight has been the subject of several papers. The material consists of pale yellow crystals that melt at 200–201° and on further heating, dissociate to give thymoquinone. On reduction by a variety of reagents, hydrothymoquinone is formed. With hydroxylamine di- or tetraoxime is

obtained, depending upon the conditions used. Reduction converts the first into *p*-aminothymol and the second into 2,5-diamino-*p*-cymene, respectively. The material reacts with bromine but does not react with either acetyl chloride or acetic anhydride. With methyl magnesium iodide 1.84 equivalents of gas are formed. In 1944 Smith and Tess, on the basis of their own experiments and the evidence presented by earlier workers, discarded some of the older unsatisfactory formulations for the dimer and proposed two new structure types.[1]



I II

The first type could arise through the double aldol condensation of thymoquinone and the second through the photodimerization similar to the formation of truxillic and truxinic acids from cinnamic acids[2] or dimerization of the various coumarins.[3] Smith and Tess could not definitely decide between the two structures, but they favored structure II. The chief argument against structure I was that it did not explain satisfactorily the formation of the tetraoxime. In their opinion, the results of the active hydrogen analysis, on the other hand, contradicted the second formulation, although they realized the possibility that the reagent might attack the enolizable hydrogens of the keto groups. In view of the many known examples where the latter actually takes place,[4] the present author feels that the results of the active hydrogen analysis can not constitute an argument against structure II. For example, it has been established that 3,9-diphenyl-5,8,9,10-tetrahydro-1,4-naphthoquinone and similar compounds with structures related to II, react with methyl magnesium iodide to give one equivalent of gas.[5] It seemed desirable, therefore, to try to obtain additional evidence that would definitely determine the cyclobutane structure type II proposed for dithymoquinone.

In the ultraviolet and the visible, the dimer exhibited two peaks with maxima at 238–239 and 385 mμ, the second band being responsible for the yellow color of the compound. It is known that unsaturated 1,4-diketones, such as obtained by Diels-Alder 1:1 addition of dienes to quinones, together with benzo-

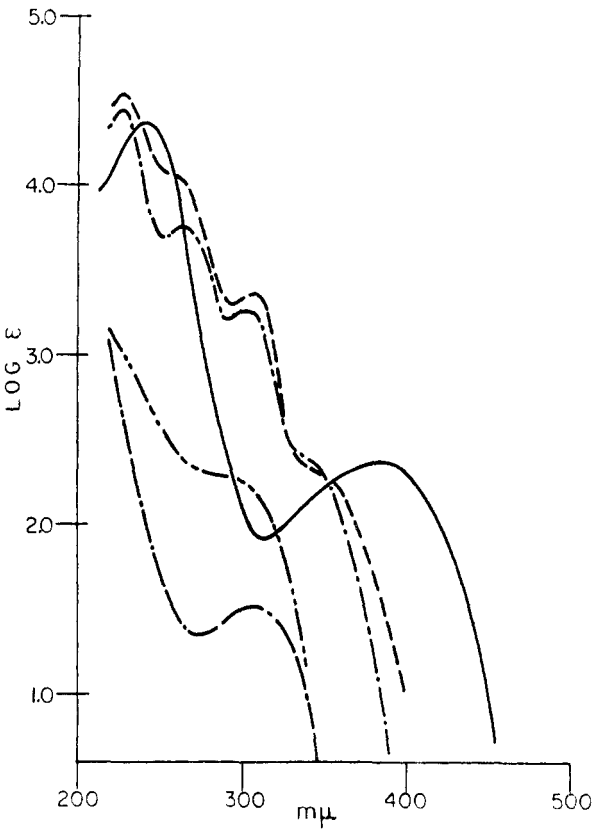


FIG. 1. ULTRAVIOLET ABSORPTION SPECTRA of dithymoquinone ———, diepoxythymoquinone ·—·—·—, diepoxydithymoquinone —·—·—, di-2-methylnaphthoquinone – – –, epoxy-2-methyl-naphthoquinone —·—·—.

quinones and α diketones are yellow colored[5,6]; on the other hand, αβ, α′β′, unsaturated ketones, such as quinols and similar compounds, are colorless and absorb at the lower wave length.[7,8]

In the infrared the dimer did not exhibit any band due to the hydroxyl stretching; it showed, however, an unsaturated carbonyl maximum at 1665 cm.$^{-1}$ and a conjugated double bond maximum at 1610 cm.$^{-1}$

Treatment of the dimer with alkaline hydrogen peroxide resulted in the formation of the diepoxide. In the ultraviolet the latter showed a weak ketonic band at 290 mμ; in the infrared it did not exhibit any hydroxyl or conjugated double bond band and the carbonyl maximum was shifted to 1715 cm.$^{-1}$ The ultraviolet spectrum and the infrared spectrum in the 1550–1800 cm.$^{-1}$ region were similar to the spectra of thymoquinone diepoxide, prepared by the same reaction, that absorbed at 307 mμ in the ultraviolet and showed a carbonyl band at 1720–25 cm.$^{-1}$ but no hydroxyl or conjugated double bond band in the infrared. The above evidence seems to eliminate structure I, and to be in complete agreement with structure II.

Formulation II is subject to isomerism. Struc-

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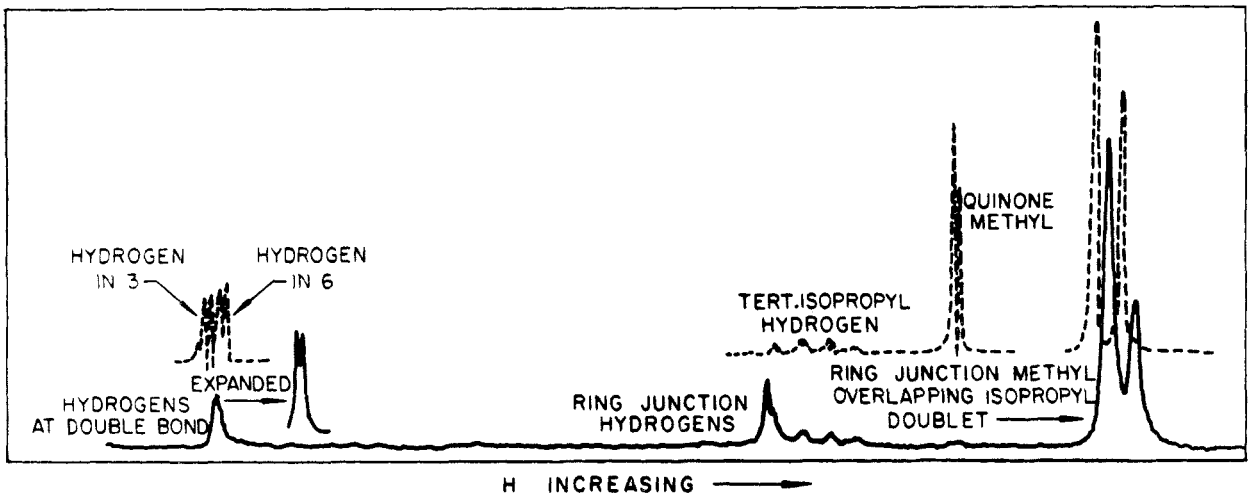

FIG. 2. NMR SPECTRA of dithymoquinone ———, and thymoquinone - - - - - -.

tures are possible with the isopropyl or methyl groups being attached to the ring junctions, the six membered rings could be in *cis* or *trans* positions to each other and also joining of the two thymoquinone units could take place with the alkyl substituents either in 1,2 or 1,3 positions on the cyclobutane ring. Nuclear magnetic resonance methods were applied to settle the first of these questions. The spectrum (Fig. 2) was run using a deuterated chloroform solution and exhibited a band in the aromatic region of the spectrum arising from the hydrogens on the double bond. The split into the doublet resulted from the spin-spin coupling of the above hydrogens with the tertiary isopropyl hydrogens. The 1:3:3:1 quadruplet present in the thymoquinone arising from the quinoid hydrogen in the 3 position coupled with the hydrogens of the attached methyl group was not present.[9] Instead, the band corresponding to the above proton in thymoquinone moved into the region of tertiary aliphatic hydrogen absorption. The band arising from the methyl group attached to the quinoid nucleus in thymoquinone also moved to the aliphatic methyl region and overlapped the first peak of the isopropyl doublet. The evidence obtained indicates that the dimerization takes place along the less hindered, methyl substituted double bond of thymoquinone. The nature of the NMR spectrum thus substantiates the general structure proposed for the dimer.

At present no clear decision can be made between the other possible isomers. The examination of the molecular models revealed that there is not much difference in steric hindrance between the structures with methyls in 1,2 or 1,3 positions, but the *trans*-orientation of the rings seems to be definitely favored. The assumption that steric hindrance is the decisive factor[1] however, may be seriously questioned. There are strong indications that in the case of the photodimerization of the cinnamic acid, the type of structure formed is more influenced by the orientation of the cinnamic acid molecules in the crystal than by other effects,[2] and so, since the dimerization of thymoquinone also takes place in the crystalline state, steric hindrance would not necessarily be the decisive factor.

The other quinone known to dimerize under influence of daylight is 2-methylnaphthoquinone.[10] We examined the ultraviolet spectrum of this dimer. It exhibited four bands at 227, 254–256, 303, and 340–350 mμ; the spectrum was strikingly similar to that of 2-methylnaphthoquinone epoxide, prepared by the alkaline epoxidation of the parent quinone.[11] The infrared spectrum of the dimer exhibited a carbonyl maximum at 1690 cm.$^{-1}$ and an aromatic double bond band at 1595 cm.$^{-1}$ but no hydroxyl or conjugated double bond band. The spectrum was again very similar to that of the epoxide in the 1550–1800 cm.$^{-1}$ region. The evidence is in complete agreement with the dimeric structure analogous to that of dithymoquinone and proposed by Madinaveitia[10] on the basis of his experiments.

It would seem that the quinone photodimerization reaction leading to dithymoquinone type of compounds is more common than usually anticipated. Thus Zincke *et al.* report the formation of a nearly colorless polymeric substance upon exposure of the 2-phenylnaphthoquinone to daylight.[12] Upon heating, the polymer dissociated into the original quinone. From the foregoing it seems highly probable that the structure of the reported substance parallels that of the other two dimers.

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EXPERIMENTAL[13]

Preparation of the diepoxydithymoquinone. A 413 mg. portion of the dithymoquinone, m.p. 198–200°, was dissolved in 10 ml. of pyridine to which 1.0 g. of sodium carbonate was added. To the mixture obtained 5 ml. of 30% hydrogen peroxide in 1 ml. portions was added gradually under stirring. The temperature of the reaction mixture rose to 40° and the liquid slowly became colorless. The solution was allowed to stand at that temperature for several minutes, diluted with 75 ml. of water and the colorless crystals that separated at this point were filtered off and washed with water to give 430 mg. of material m.p. 213–214°. Crystallization from chloroform/acetone mixture yielded colorless long plates weighing 378 mg., m.p. 217.7–218.5° (83%).

Anal. Calcd. for $C_{20}H_{24}O_6$: C, 66.65; H, 6.71; mol. wt., 360. Found: C, 66.42; H, 6.64; mol. weight (camphor), 370.

Ultraviolet absorption spectrum: Inflection point at λ 290 mμ, log ε 2.28 (alcohol). Infrared absorption spectrum: ν_{max} 1715 cm.$^{-1}$ (carbonyl, KBr pellet); no OH band (Nujol).

Preparation of diepoxythymoquinone. A 1.148 g. portion of thymoquinone m.p. 44–44.5° was dissolved in 10 ml. of acetone. To the resulting solution 0.5 g. of sodium carbonate, followed by 3 ml. of 30% hydrogen peroxide solution was added and the liquid heated on a steam bath to the complete discoloration point. The mixture obtained was diluted to 125 ml. with water and acidified with 10% hydrochloric acid. Saturation of the solution with sodium sulfate and scratching induced the separation of diepoxide. The mixture was allowed to stand overnight to complete the crystallization. The separated crystalline material was filtered off to give 720 mg. of a colorless solid, m.p. 85–89° (53%). Further purification was achieved by crystallizations from methanol/water and iso-octane that raised the melting point of the material to 89.6–90.4°.

Anal. Calcd. for $C_{10}H_{12}O_4$: C, 61.21; H, 6.17. Found: C, 61.34; H, 6.24.

(13) All melting points are corrected; microanalysis by Microchemical Laboratory, University of California, Berkeley. Ultraviolet and infrared spectra were run on Beckman DK II and Perkin Elmer Model 21 recording spectrophotometers, respectively, and the NMR spectra on Varian Associates high resolution NMR spectrometer.

Ultraviolet absorption spectrum: λ_{max} 307 mμ, log ε 1.54; λ_{min} 271 mμ, log ε 1.37 (alcohol). Infrared absorption spectrum: ν_{max} 1720–5 cm.$^{-1}$ (carbonyl) (KBr pellet); no OH band (Nujol).

Dithymoquinone was prepared according to Liebermann and Ilinski[14] and was purified by recrystallization from iso-octane chloroform, m.p. 198–200°. Ultraviolet absorption spectrum: λ_{max} 238–239 mμ, log ε 4.39; 385 mμ, log ε 2.37; λ_{min} 310–312 mμ, log ε 1.90 (alcohol). Infrared absorption spectrum: ν_{max} 1665 cm.$^{-1}$ (carbonyl), 1610–1615 cm.$^{-1}$ (conj. double bond) (KBr pellet); no OH band ($CHCl_3$ solution).

Di-2-methylnaphthoquinone was prepared according to Madinaveitia,[10] and crystallized from ethanol/dimethylformamide, m.p. 234–236°. Ultraviolet absorption spectrum: λ_{max} 227 mμ, log ε 4.56, infl. point at 254–256 mμ, log ε 4.08; λ_{max} 303 mμ, log ε 3.37, infl. point at 340–350 mμ, log ε 2.34–2.28 (alcohol). Infrared absorption spectrum: ν_{max} 1690 cm.$^{-1}$ (carbonyl), 1595 cm.$^{-1}$ (aromatic) (KBr pellet); no OH band (Nujol).

Epoxy-2-methylnaphthoquinone was prepared according to Fieser *et al.*,[11] m.p. 94–95°.

Ultraviolet absorption spectrum: λ_{max} 227 mμ, log ε 4.47; 265–266 mμ, log ε 3.76; 303 mμ, log ε 3.28; infl. point at 340 mμ, log ε 2.41 (alcohol). Infrared absorption spectrum: ν_{max} 1695 cm.$^{-1}$ (carbonyl), 1595 cm.$^{-1}$, (aromatic) (KBr pellet).

Nuclear Magnetic Resonance spectra (Fig. 2) were obtained at 40 mc. frequency using carbon disulfide as the solvent in case of thymoquinone and deuterated chloroform in case of dithymoquinone.

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[CONTRIBUTION OF CENTRAL EXPERIMENT STATION, U. S. DEPARTMENT OF THE INTERIOR, BUREAU OF MINES]

Preparation and Properties of Trimethylsilyl Ethers and Related Compounds

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Preparative methods for trimethylsilyl ethers have been investigated. Hexamethyldisilazane (III) has been found to be a convenient reagent for converting alcohols and primary amines to their trimethylsilyl derivatives. The reaction is apparently acid catalyzed. The trimethylsilyl ethers of less reactive alcohols may be prepared from the reaction of equivalent amounts of trimethylchlorosilane and hexamethyldisilazane with the alcohol. The preparation and properties of 22 new trimethylsilyl derivatives of alcohols, phenols, and amines are reported. Trimethylbutylmercaptosilane has also been prepared.

The potential usefulness of trimethylsilyl ethers in separation procedures was strikingly demonstrated by Martin[1] through the isolation of trimethylolphenol as its trimethylsilyl derivative. More recently, a number of other investigators[2–4] have pointed out the utility of trimethylsilyl derivatives for isolation purposes. These derivatives

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