dissociation in extreme dilution, then rather suddenly lose much of their conductivity through association of ion-pairs and ions to form colloidal particles of low conductivity, but after a well-defined minimum in moderately dilute solution, regain some of their conductivity through increasing formation of better conducting or ionic micelles.

2. This interpretation is in agreement with exact freezing point and diffusion data for dodecylsulfonic acid.

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF HARVARD UNIVERSITY]

# Naphthoquinones of the Vitamin K₁ Type of Structure[1]

BY LOUIS F. FIESER, WILLIAM P. CAMPBELL, EDWARD M. FRY[2] AND MARSHALL D. GATES, JR.

The synthesis of various allyl derivatives of α-naphthoquinone[3,4] by utilization of the Claisen rearrangement reaction was undertaken to provide model substances of the structural types postulated for vitamins K₁ and K₂. It was recognized that methods involving use of this reaction probably would not be applicable to the synthesis of the vitamins themselves, and the present paper reports attempts to develop methods suitable for accomplishing this second objective.

One scheme tried without success consisted in the attempted addition of a Grignard reagent to a naphthoquinone oxide. The reaction between allylmagnesium bromide and 2,6-dimethyl-1,4-naphthoquinone oxide (I) was studied because addition in the desired direction would lead to 2,6-dimethyl-3-allyl-1,4-naphthoquinone,[3] which was already characterized. The chief product isolated, however, proved to be the bromohydrin II, the structure following from the analysis of the colorless product and from its conversion to

a yellow bromodimethylnaphthoquinone of the composition of III. That cleavage of the oxide ring is due, as in comparable cases,[5] to interaction of the oxide with magnesium bromide present in the Grignard solution was established by the observation that the bromohydrin can be obtained in 73% yield from the oxide and magnesium bromide in ether. On attempted coupling of the MgBr derivative of II with allylmagnesium bromide there was isolated a small amount of the oxide, indicating that the cleavage reaction is reversible. When 2-methyl-1,4-naphthoquinone oxide was treated with methylmagnesium chloride and the oily product refluxed with alcoholic hydrochloric acid, a colorless substance resulted which appears to be formed by the addition of the elements of methane and of hydrogen chloride. The investigation was not pursued beyond these unpromising observations. A useful outcome of the brief study is the development of a method of preparing 1,4-naphthoquinone oxides which is much more convenient than Zincke's[6] hypochlorite procedure.

A few trials were made of the method of introducing a β-unsaturated group by direct C-alkylation of a phenolic salt, and it was observed that a small amount of 2-methyl-3-benzyl-1,4-naphthoquinone can be isolated from the very dark mixture produced by refluxing of 2-methyl-1,4-naphthohydroquinone with benzyl bromide and potassium carbonate in acetone. When the reaction was conducted at room temperature with two equivalents of benzyl bromide the mixture remained light in color and the sole crystalline product was methylnaphthohydroquinone dibenzyl ether (73% yield). With one equivalent
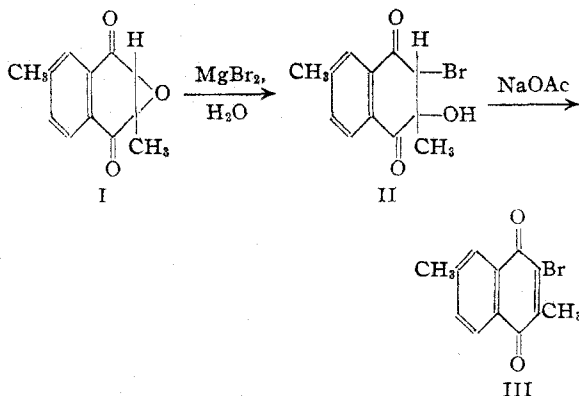
(1) For a preliminary account of a part of this work see Fieser, Campbell, Fry and Gates, THIS JOURNAL, 61, 2559 (1939).

(2) Du Pont Research Fellow.

(3) Fieser, Campbell and Fry, THIS JOURNAL, 61, 2206 (1939).

(4) Fieser, Bowen, Campbell, M. Fieser, Fry, Jones, Riegel, Schweitzer and Smith, ibid., 61, 1925 (1939).

(5) Gilman, "Organic Chemistry," Vol. I, John Wiley and Sons, Inc., New York, N. Y., pp. 428–429, 1938.

(6) Zincke, Ber., 25, 3602 (1892).

of the halide at room temperature a part of the starting material remained unchanged and both the mono and dibenzyl ethers were formed, but there was no indication of C-benzylation.
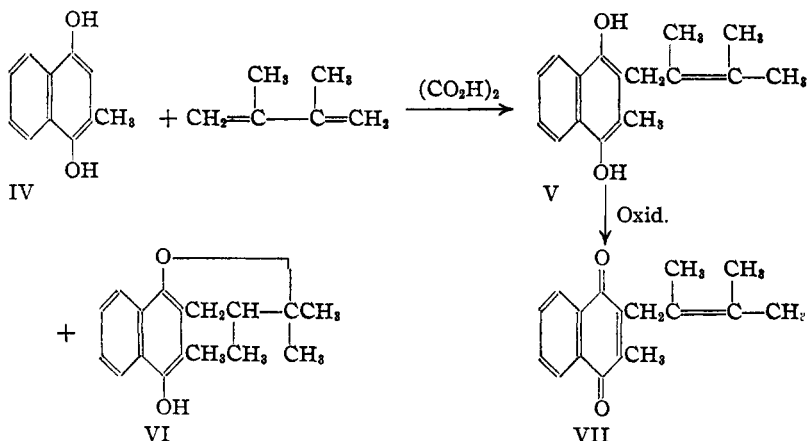
On the basis of the postulated[3] origin of vitamin K_1 in nature it seemed likely that this substance might be obtainable by the direct condensation of phytol with a 2-alkyl-1,4-naphthoquinone in either the oxidized or the reduced form. Trials with 2-methyl-1,4-naphthoquinone were invariably unpromising and attention was directed to use of the hydroquinone. From the investigations of Karrer, L. I. Smith, Todd, and others it is known that alkylated benzohydroquinones having a free nuclear position condense readily with β-unsaturated alcohols or with dienes in the presence of a mineral acid or a zinc halide, or under conditions where a mineral acid is liberated in the course of the initial condensation. The reported condensations invariably are attended by cyclization to compounds of the tocopherol type.[7] For the most direct approach to a substance of the desired vitamin K_1 type, it would appear necessary to avoid the natural disposition for the formation of a structure characteristic of vitamin E. The naphthalene derivatives, moreover, show a high sensitivity to mineral acids not encountered in the benzene series. It seemed desirable to seek a milder and less destructive condensing agent less prone to promote cyclization and other side reactions. Anhydrous oxalic acid fulfils the requirements, and dioxane is a suitable solvent. In isolated experiments successful use was made of trichloroacetic acid as the catalyst and ethylene glycol monomethyl ether as solvent.

On refluxing methylnaphthohydroquinone (IV) with excess 2,3-dimethylbutadiene in dioxane solution in the presence of anhydrous oxalic acid, the starting material was completely consumed in twenty-four hours, and in this time there was no appreciable discoloration or decomposition. The reaction mixture contained both the substituted hydroquinone V and an isomeric substance which probably is a naphthotocopherol of the structure VI, although this product has not been studied in

detail. The hydroquinone V can be separated from the mixture by virtue of its sparing solubility in petroleum ether, or it can be extracted with a liberal amount of strong alkali containing sodium hydrosulfite. The naphthotocopherol is considerably more soluble in the hydrocarbon solvent and shows even feebler acidic properties than the hydroquinone. The latter substance, which forms a diacetate, was oxidized in good yield to 2-methyl-3-(β,γ,γ-trimethylallyl)-1,4-naphthoquinone (VII). The spectrum of this crystalline yellow compound in absolute alcohol, kindly determined by Mr. D. M. Bowen, is very similar to that of vitamin K_1 as reported by Dam, Karrer, et al.,[8] and shows the following maxima (log E values in parenthesis): 243 mμ (4.23), 249, 264, 270.5 mμ (4.27), 329 mμ (3.43).

Reductive acetylation of the quinone VII under mild conditions gave the above diacetate, but when the temperature was not suitably controlled a part of the material was converted into a substance of the composition of the naphthotocopherol acetate. A new procedure for the reductive acetylation of quinones which avoids secondary reactions consists in the use of zinc dust, acetic anhydride, and a small amount of pyridine as catalyst. The reaction proceeds rapidly at 0°. In trials with 2-methyl- and 2-ethyl-1,4-naphthoquinone, it was found that reductive benzoylation can be accomplished readily by treating the quinone with zinc dust, pyridine and benzoyl chloride; this constitutes a useful method of preparing crystalline derivatives of low melting quinones.

Under the conditions indicated, the substituted hydroquinone V was obtained in 29% yield and

(7) Professor Lee I. Smith has kindly informed us that the isolation of hydroquinones is reported in papers from his Laboratory which are now in press.

(8) Dam, Geiger, Glavind, P. Karrer, W. Karrer, Rothschild and Solomon, Helv. Chim. Acta, 22, 310 (1939).

the naphthotocopherol VI in 15% yield. Using isoprene as the second component, no condensation was observed at the reflux temperature, but a small amount of product was formed at 180°. Piperylene likewise reacted less readily than 2,3-dimethylbutadiene, but there were indications of condensation at a temperature of 120°. Cinnamyl alcohol reacted rather readily at the reflux temperature with methylnaphthohydroquinone (22% yield), and somewhat less readily with ethylnaphthohydroquinone (9.4% yield). In each case some starting material was recovered by extraction with 1–2% alkali containing hydrosulfite, and the substituted hydroquinone was then separated most conveniently by repeated extraction with 10% alkali-hydrosulfite. The reaction products were readily converted into crystalline quinones of the type VIII. Benzyl
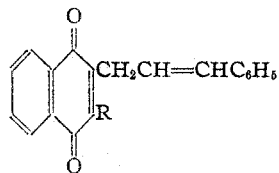
VIII (R = CH₃, C₂H₅)

alcohol combined with methylnaphthohydroquinone only to a minor extent at the boiling point, giving after oxidation 2-methyl-3-benzyl-1,4-naphthoquinone. With allyl alcohol no reaction occurred at 180°. It appears, therefore, that in the presence of anhydrous oxalic acid in dioxane solution certain highly reactive dienes, β-unsaturated alcohols, and aryl carbinols condense to a greater or less extent with alkylnaphthohydroquinones, but that the reaction has distinct limitations. It is significant, however, that with a compound of suitable reactivity, condensation to a hydroquinone with a β-unsaturated side chain can be accomplished without undue cyclization of the primary product.

In the Dam–Karrer[8] test with alcoholic alkali 2-methyl and 2-ethyl-3-cinnamyl-1,4-naphthoquinone give intense blue colors which persist somewhat longer than observed with corresponding allyl compounds.[3] The 3-benzyl compound gives a light purple color, but no purple or blue phase was observed with 2-methyl-3-trimethylallyl-1,4-naphthoquinone (VII). The presence of a substituent on the β-unsaturated carbon atom apparently interferes with the color reaction.

In bio-assays kindly conducted by Dr. W. L. Sampson, 2-methyl-3-benzyl-1,4-naphthoquinone

was inactive at a dosage level of 100 γ and the corresponding 3-trimethylallyl compound was inactive at a level of 200 γ. From carefully repeated assays of the compounds described in the early reports from our Laboratory[3,4,9] it is concluded that the only substance in the group previously considered which has appreciable antihemorrhagic activity is 2,3-dimethyl-1,4-naphthoquinone.[3] In addition, 2-methyl-3-cinnamyl-1,4-naphthoquinone has been found active at a dosage of 100 γ but not at 10 γ.

Experimental Part[10]

Preparation of Starting Materials

2-Methylnaphthoquinone (M. D. G.).—Satisfactory results were obtained by a procedure considerably shorter than that of Anderson and Newman.[11] (The yield was much lower when the oxidation was conducted at the reflux temperature as in the preparation of certain dimethylnaphthoquinones.[12]) A solution of 200 g. of β-methylnaphthalene in 2 liters of glacial acetic acid was added in the course of two hours to a well-stirred solution of 800 g. of chromic anhydride in 1.5 liters of 80% acetic acid, cooling the mixture in an ice-bath and keeping the temperature from rising above 20°. At the end of the addition the temperature was allowed to rise slowly; after a few hours cooling was again required to moderate the reaction and keep the temperature from rising above 50–60°. After .a total period of thirty-six hours, the solution was poured into water and the precipitated quinone collected and washed and obtained as a good yellow solid (100 g.). This was crystallized directly from methanol (Norite), giving in all 70 g. (29%) of yellow prismatic needles, m. p. 105–106°.

2-Ethyl-1,4-naphthoquinone.—In the preparation of β-ethylnaphthalene the best results were obtained (W. P. C.) using 50 g. of β-acetonaphthalene, 150 cc. of benzene, 300 cc. of methanol, 200 cc. of concentrated hydrochloric acid, and 155 g. of zinc amalgamated with 10 g. of mercuric chloride. The mixture was refluxed vigorously for twenty-four hours with the addition of three 20-cc. portions of fresh acid. About 1.5 liters of water was then added and a little ether was used to facilitate separation of the benzene layer. The latter, combined with an ether extract of the aqueous layer, was dried and the product distilled, giving 29 g. (63%) of colorless β-ethylnaphthalene, b. p. 127–129° at 14 mm. When the reflux period was extended to forty-seven hours the yield was 57%. The yield by the Martin procedure (M. D. G., 57%) was essentially the same as previously reported.[13]

The following oxidation procedure (W. P. C.) is regarded as more convenient than that described for the lower homolog or that of the literature.[14] A solution of

(9) Fieser, Bowen, Campbell, Fry and Gates, THIS JOURNAL, 61, 1926 (1939).

(10) Microanalyses by Lyon Southworth and Herbert S. Wight.

(11) Anderson and Newman, J. Biol. Chem., 103, 405 (1933).

(12) Fieser, "Experiments in Organic Chemistry," D. C. Heath and Co., Boston, Mass., 1935, p. 230.

(13) Martin, THIS JOURNAL, 58, 1438 (1936).

(14) Kruber and Schade, Ber., 69, 1722 (1936).

<div align="center">

TABLE I

ALKYL-1,4-NAPHTHOQUINONE OXIDES

</div>

Alkyl substituents	M. p., °C.	Properties Cryst. form	Analyses, % Carbon Found	Calcd.	Hydrogen Found	Calcd.
None	134.5–135.5	Prism. needles	...	...	..	..
2-Methyl	95.5– 96.5	Long needles	70.38	70.20	4.36	4.29
2,6-Dimethyl	97– 98	Prisms	71.23	71.27	5.07	4.99
2,7-Dimethyl	91– 92	Slender needles	71.29	71.27	5.09	4.99

70 g. of chromic anhydride in 30 cc. of water, diluted with 150 cc. of acetic acid, was added in one hour to a stirred solution of 29 g. of β-ethylnaphthalene in 200 cc. of acetic acid while maintaining the temperature at 45–50° by suitable cooling. The exothermic reaction was soon over, and after standing for fifteen hours the mixture was stirred at 60° for one hour and poured into 2 liters of water. The quinone separated as a light yellow solid and crystallization from methanol gave 12.6 g. (39%) of satisfactory material, m. p. 86–87°, in two crops.

2-Methyl-1,4-naphthohydroquinone (L. F. F., M. D. G.) (a) with Stannous Chloride.—A solution of 10 g. of 2-methyl-1,4-naphthoquinone in 100 cc. of hot alcohol was cooled rapidly to room temperature and the resulting paste treated with 40 g. of stannous chloride in 40 cc. of concentrated hydrochloric acid. The quinone dissolved at once giving a transient deep brown color (quinhydrone) rapidly fading to light yellow, and the solution became hot. Water (165 cc.) was added and the hydroquinone which precipitated was brought into solution at the boiling point. The solution was clarified with norite, filtered, diluted with an equal volume of water at the boiling point and set aside to crystallize. The hydroquinone separated as colorless needles and after thorough washing with cold water was dried at 50–60° either in the air or at 20 mm.; yield 9.2–9.5 g. When obtained by this procedure in an initially colorless condition, the material keeps for several days without deterioration.

(b) With Sodium Hydrosulfite.—A solution of 10 g. of the quinone in 50 cc. of hot alcohol was treated with a solution of hydrosulfite (about 30 g.) in water until the color (yellow, then brown) was discharged and the cooled mixture was diluted and the product extracted with ether. The dried, nearly colorless ethereal solution was evaporated nearly to dryness and the residual solid was triturated with petroleum ether and collected. The hydroquinone was obtained as a white powder (9.7 g.). This method is rapid and the product entirely suitable for immediate use, but the material darkens more rapidly on storage than the crystalline product of (a).

The diacetate[11] of 2-methyl-1,4-naphthohydroquinone, prepared by reductive acetylation of the quinone using either sodium acetate or pyridine, formed colorless prisms from ether–petroleum ether or ether, m. p. 112.5–113°. The dibenzoate was prepared by adding 1 cc. of benzoyl chloride by drops to a mixture of 0.5 g. of methylnaphthoquinone, 0.5 g. of zinc dust, and 3 cc. of pyridine, while cooling with ice. Reaction occurred at once and after standing at room temperature for ten minutes the pale yellow mixture was heated to boiling, cooled, and the product extracted with ether–alcohol. After washing with dilute acid and with soda solution and concentrating the dried solution to a small volume, the dibenzoate sepa-

rated as colorless needles (0.6 g.), m. p. 178.5–179.5°. Two crystallizations from alcohol (35 cc.) raised the m. p. to 180–180.5°.

Anal. Calcd. for C₂₈H₁₈O₄: C, 78.53; H, 4.75. Found: C, 78.71; H, 4.80.

2-Ethyl-1,4-naphthohydroquinone was prepared by the second procedure described above (b) with similar results; the material softened at 140° and melted at 144–145°, dec. The diacetate was obtained by adding 2 drops of pyridine to a suspension of 0.2 g. each of ethylnaphthoquinone and zinc dust in 2 cc. of acetic anhydride. Heat was evolved and the mixture became colorless; acetic acid was added and the mixture filtered at the boiling point, using more acetic acid and water in subsequent extractions of the residue. (A yellow color not connected with the acetylative reduction becomes quite pronounced if the reaction mixture is allowed to stand for some time but the color is easily eliminated in the purification process.) After suitable dilution at the boiling point the product separated in a good condition, m. p. 104–105° (0.20 g.). It forms prism clusters of the same m. p. from ether–petroleum ether or ligroin. The dibenzoate, prepared by reductive benzoylation as above, formed short needles from alcohol, m. p. 164–165°.

Alkylnaphthoquinone Oxides (L. F. F.)

In a typical experiment 5 g. of 2-methyl-1,4-naphthoquinone was dissolved in 15 cc. of alcohol and the solution was cooled to 45° and treated with 10 cc. of 30% hydrogen peroxide followed by a solution of 2.5 g. of sodium carbonate in 10 cc. of water. Heat was evolved, the yellow color was discharged, and inorganic salts separated. After five minutes the mixture was diluted well with water, whereupon 2-methyl-1,4-naphthoquinone oxide separated in the form of long colorless needles. One crystallization from dilute alcohol gave 3.6 g. of satisfactory product, m. p. 94.5–95.5°. The properties and analyses of purified samples of this and other oxides are recorded in Table I. The preparations were conducted as described, using sufficient alcohol to keep the quinone in solution at about 45°, and the yields were as reported in the example. The parent substance corresponds to the description of Zincke[6] (m. p. 136°); the 2-methyl derivative had the properties noted by Madinaveitia[15] except that the m. p. is considerably lower (M., 102°). The oxides crystallize well from alcohol, dilute alcohol, or ligroin.

Grignard Reactions with Alkylnaphthoquinone Oxides (E. M. F.)

2,6-Dimethyl-1,4-naphthoquinone Bromohydrin (II), (a) Grignard Reaction of Oxide.—The Grignard reagent obtained from 1.5 cc. of allyl bromide, added in 80 cc. of

(15) Madinaveitia, *Rev. acad. cienc. Madrid*, **31**, 617 (1934).

3220 L. F. Fieser, W. P. Campbell, E. M. Fry and M. D. Gates, Jr. Vol. 61

ether during one and one-half hours to a stirred suspension of 1.4 g. of magnesium in 20 cc. of ether, was added slowly to a solution of 3.16 g. of 2,6-dimethyl-1,4-naphthoquinone oxide in 50 cc. of ether. A white complex separated at once and on displacing most of the ether with benzene and refluxing for one-half hour it turned somewhat red. Decomposition was effected with dilute acetic acid (yellow color), and extraction of an ethereal solution of the reaction product with sodium carbonate (red solution) gave 0.1 g. of 2,6-dimethyl-3-hydroxy-1,4-naphthoquinone,[16] m. p. 192–194.5°, mixed m. p. 193–194.5°. The residual oil when treated with dilute alcohol afforded 0.38 g. of a crystalline product identified as the unchanged oxide and 1.25 g. of 2,6-dimethyl-1,4-naphthoquinone bromohydrin. This crystallized from dilute alcohol in colorless, rectangular plates, m. p. 146–148°.

Anal. Calcd. for $C_{12}H_{11}O_3Br$: C, 50.90; H, 3.92; Br, 28.23. Found: C, 51.05, 51.05; H, 4.24, 4.18; Br, 28.33.

(b) **With Magnesium Bromide.**—A solution prepared from 5.32 g. of bromine and 150 cc. of dry ether was added slowly to a stirred suspension of 0.81 g. of magnesium in ether. A vigorous reaction took place with the separation of a yellow oil turning dark purple at the end. After stirring for twenty minutes, 3 g. of 2,6-dimethyl-1,4-naphthoquinone oxide was added slowly in ether solution. A complex soon formed and eventually separated as a white solid mixed with a little of the dark oil. After stirring for fifteen minutes water was added and the yellowish ether layer was washed, dried, and evaporated. The crystalline residue, washed free of oil with a little ether, amounted to 3.07 g. (73%) and consisted of nearly pure bromohydrin. Recrystallized from dilute alcohol the substance melted at 147–148.5° and showed the properties of the sample obtained in (a).

In a further experiment 3 g. of the bromohydrin was treated in ether with two equivalents of allylmagnesium bromide (2 cc. of the halide). A complex formed at once with evolution of heat; after refluxing for seventeen hours and decomposing with dilute acetic acid, a small amount of acidic material was removed by extraction with 1 *N* alkali and the residual oil afforded 0.4 g. of 2,6-dimethyl-1,4-naphthoquinone oxide (m. p. 96.5–97.5°; no depression on mixing). No other pure product was isolated.

3-Bromo-2,6-dimethyl-1,4-naphthoquinone.—A solution of 0.1 g. of the bromohydrin II and 0.1 g. of sodium acetate in 2 cc. of acetic acid was refluxed for one-half hour, when it had become red, and diluted with water. The precipitated material on crystallization from alcohol gave 0.03 g. of yellow needles, m. p. 114–114.5°. The substance gives a positive Beilstein test and is not soluble in alkali.

Anal. Calcd. for $C_{12}H_9O_2Br$: C, 54.36; H, 3.42. Found: C, 54.64; H, 3.61.

Action of Methylmagnesium Chloride on Methylnaphthoquinone Oxide.—The reagent from 0.51 g. of magnesium was added to a solution of 3.35 g. of 2-methyl-1,4-naphthoquinone oxide in 75 cc. of ether. A complex separated at once and did not appear to undergo change on refluxing for two hours and allowing the mixture to

(16) Fieser and Seligman, THIS JOURNAL, **56**, 2690 (1934).

stand overnight. After decomposition with acetic acid and washing the ethereal solution with soda, 0.38 g. of starting material was collected on crystallization from dilute alcohol. The residual oil yielded a solid product only on being refluxed for a few minutes with two volumes of alcohol and 0.5 cc. of concentrated hydrochloric acid. The dark red solution was evaporated in vacuum, and the oil then crystallized from ether–petroleum ether. A total of 1 g. of crude brown product was collected, and crystallization from ether using Norite afforded 0.7 g. of colorless material in the form of parallelograms. The substance decomposes when heated slowly; when immersed in a bath just below the m. p. it melts at 141.5–142° to a colorless liquid which rapidly darkens with gas evolution.

Anal. Calcd. for $C_{12}H_{13}O_2Cl$: C, 59.88; H, 5.45; Cl, 14.73. Found: C, 60.05, 60.16; H, 5.75, 5.67; Cl, 14.99.

Benzylation of Methylnaphthohydroquinone (L. F. F.)

In the most successful preparation of 2-methyl-1,4-naphthohydroquinone dibenzyl ether a mixture of 2 g. of the hydroquinone, 4 g. of benzyl bromide and 20 cc. of acetone was flushed out with nitrogen, 4 g. of finely powdered potassium carbonate was added, and the vessel was stoppered and shaken at room temperature for twenty-five hours. The solution was orange-red at the start but became light yellow. The mixture was poured into water, extracted with ether, and the extract washed twice with 10% potassium hydroxide, which removed only a trace of phenolic material. Evaporation of the dried ether solution left a yellow oil which went solid on rubbing. Crystallization from 35 cc. of alcohol gave 2.91 g. (72%) of slightly yellow product, m. p. 72–3°. On further purification by crystallization from ligroin (b. p. 60–90°) the ether formed colorless needles, m. p. 74.5–75°.

Anal. Calcd. for $C_{25}H_{22}O_2$: C, 84.71; H, 6.26. Found: C, 84.93; H, 6.33.

The **monobenzyl ether** was isolated along with the diether in an experiment conducted as above but using only one equivalent of benzyl bromide (1 g. of hydroquinone, 1 g. of bromide, 1.5 g. of potassium carbonate, 10 cc. of acetone). The mixture was poured into aqueous sodium hydrosulfite solution, extracted with ether, and the light yellow ethereal solution extracted three times with 2% potassium hydroxide containing hydrosulfite, which removed about 0.2 g. of impure starting material (yellow alkaline liquor). Eight extractions with 10% alkali containing hydrosulfite (total, 200 cc.) then extracted the monobenzyl ether; after acidification this was taken into ether and the solution dried and evaporated. The oily residue yielded a solid on treatment with ether–petroleum ether, and after two recrystallizations from ligroin the substance formed small, colorless plates, m. p. 159–160°, with some previous darkening; yield 3 mg.

Anal. Calcd. for $C_{18}H_{16}O_2$: C, 81.79; H, 6.10. Found: C, 81.81; H, 6.25.

From the neutral fraction there was obtained 0.34 g. of the dibenzyl ether in a crystalline condition. In a qualitative trial the reaction seemed to proceed about the same in boiling ethylene glycol dimethyl ether as in cold acetone.

2-Methyl-3-benzyl-1,4-naphthoquinone was isolated in an exploratory experiment in which 2 g. of the hydroqui-

none was refluxed for fifteen and one-half hours with 4 g. of benzyl bromide, 4 g. of potassium carbonate, and 20 cc. of acetone. The very dark reaction mixture was diluted with water and extracted with ether and the extract shaken with dilute alkali-hydrosulfite. The ethereal solution remained very dark brown throughout this and other washings and the residue on evaporation was a dark resin. On distillation in vacuum the bulk of the material came over without decomposition and a part of the distillate solidified. Using this seed and employing ether–petroleum ether as solvent, a crystalline crust was obtained yielding on one crystallization from alcohol 0.3 g. of yellow crystals of the quinone, m. p. 107–108°. After two more crystallizations the substance formed ball-like clusters of bright yellow needles, m. p. 107.5–108°.

Anal. Calcd. for $C_{18}H_{14}O_2$: C, 82.41; H, 5.38. Found: C, 82.50; H, 5.42.

The substance gives a large depression when mixed with methylnaphthoquinone. It yields a colorless hydroquinone on reduction with aqueous hydrosulfite in alcoholic solution, and with 5% alcoholic potassium hydroxide in the cold it gives a light purple color changing through brown to greenish-yellow.

Condensation of Methylnaphthohydroquinone with 2,3-Dimethylbutadiene (L. F. F.)

A solution of 3 g. of 2-methyl-1,4-naphthohydroquinone, 3 g. of anhydrous oxalic acid (prepared by heating the hydrate at 140°), and 10 cc. of 2,3-dimethylbutadiene in 30 cc. of dioxane (purified with sodium) was refluxed for twenty-four hours and the pale orange solution was poured into water and extracted with ether. After washing with water the solution was extracted three times with 1% alkali containing hydrosulfite, each extract being weakly yellow. The alkaline liquor was washed with ether, acidified, and the precipitated solid dissolved in alcohol and treated with ferric chloride solution. This afforded 0.11 g. (m. p. 94–95°) of the quinone VII described below, showing that the starting material had been completely consumed. The ethereal solution was washed, dried, and evaporated to a small volume, and on displacing the ether with petroleum ether and cooling there was obtained 1.18 g. of a nearly colorless crystal powder which proved to be the hydroquinone of VII in an essentially pure condition (total yield, 29%).

On allowing the petroleum ether mother liquor to stand overnight, a few large prisms of the naphthotocopherol VI separated on the walls (0.08 g., m. p. 71.5–72°). To isolate the bulk of this the dark mother liquor was extracted with 4% alkali until this was colorless (five times) to remove traces of the substituted hydroquinone and the light yellow organic layer was dried and evaporated. A rather mobile yellow oil resulted, and when seeded with the above prisms gave a crystalline paste. After rubbing with methanol and cooling well there was collected 0.59 g. of colorless naphthotocopherol, m. p. 71.5–72°; total yield 15%.

When the refluxing time in the preparation was decreased to sixteen hours a significant amount of starting material was unconsumed (removed in one extraction with 1% alkali). In one experiment ethylene glycol monomethyl ether was used as solvent and the reaction was

conducted at 70°. Three extractions from ether with 1% alkali-hydrosulfite removed 38% of recovered starting material, identified by conversion to methylnaphthoquinone (m. p. 103–104°), and the yield of substituted hydroquinone based on material not recovered was 15%; some naphthotocopherol was also formed.

2 - Methyl - 3 - (β,γ,γ - trimethylallyl) - 1,4 - naphthoquinone (VII).—On adding a solution of 0.49 g. of ferric chloride crystals in dilute hydrochloric acid to a solution of 0.23 g. of the crude hydroquinone in 2 cc. of alcohol and gradually adding water, the quinone separated in yellow blades, m. p. 94–95° (0.22 g.). Lead tetraacetate gave nearly as good results (0.18 g., m. p. 93–94.5°). A sample for analysis was sublimed at 130–150° (2 mm.) and crystallized twice from methanol, forming bright yellow blades, m. p. 95–95.5°.

Anal. Calcd. for $C_{17}H_{18}O_2$: C, 80.28; H, 7.14. Found: C, 80.33; H, 7.25.

On treating a cold alcoholic solution of the quinone with an equal volume of 10% alcoholic potassium hydroxide, the original yellow color gives place to a faint pinkish coloration changing to dull red when heated. No blue or purple phase has been observed.

2 - Methyl - 3 - (β,γ,γ - trimethylallyl) - 1,4 - naphthohydroquinone Diacetate.—The crude hydroquinone separated from the reaction mixture as described above underwent oxidation on attempted crystallization from ligroin or dilute alcohol and was not obtained pure; the best material was pale rose colored and turned yellow on standing. For characterization the substance was therefore acetylated by warming with acetic anhydride–sodium acetate for a few minutes. The crude product was an oil, but after washing in ether with soda solution, drying, and replacing the solvent with petroleum ether, it was obtained as a white powder. The diacetate then crystallized from ligroin (b. p. 60–90°) in colorless cubes, m. p. (constant) 119–120°.

Anal. Calcd. for $C_{21}H_{24}O_4$: C, 74.09; H, 7.11. Found: C, 74.04; H, 7.23.

A product of the same m. p. and mixed m. p. was obtained by reductive acetylation of the quinone by the pyridine method without application of heat. In an earlier experiment the reaction was conducted with zinc dust, acetic anhydride, and sodium acetate and the mixture was boiled for a few minutes. In this case, after extraction with ether and crystallization from petroleum ether and then twice from ligroin there was obtained, in very poor yield, a substance having the composition of the acetate of the naphthotocopherol VI. The substance forms large, colorless, transparent prisms, m. p. 128.5–129°.

Anal. Calcd. for $C_{19}H_{22}O_3$: C, 76.48; H, 7.43. Found: C, 76.36; H, 7.54.

Naphthotocopherol of Probable Structure VI.—The material separated with methanol as described crystallized most satisfactorily from petroleum ether, in which it is quite soluble, but less so than in methanol. The substance forms large, transparent prisms, m. p. 73–73.5°.

Anal. Calcd. for $C_{19}H_{20}O_3$: C, 79.65; H, 7.87. Found: C, 79.95; H, 7.63.

The substance forms no picrate or trinitrobenzene derivative from alcohol. It is not extracted from ether by 10%

alkali but dissolves in alcoholic alkali with a deep yellow color and precipitates on dilution. No reaction was observed on treating the substance with silver nitrate in methanol, with ferric chloride in alcohol, or with lead tetraacetate in acetic acid.

Other Condensations of Methyl and Ethylnaphthohydroquinone (W. P. C.)

2-Methyl-3-cinnamyl-1,4-naphthoquinone.—A solution of 3 g. of methylnaphthohydroquinone, 1.54 g. of cinnamyl alcohol, and 2 g. of anhydrous oxalic acid in 20 cc. of dioxane was refluxed for twenty-two hours, poured into water and extracted with ether. Starting material was extracted with a total of 150 cc. of 1% sodium hydroxide-hydrosulfite and collected in the form of the quinone, m. p. 100–103° (1.0 g.). The ethereal solution was dried and evaporated and the oily product digested with three 80-cc. portions of petroleum ether. The solution each time was decanted and eventually left 1.55 g. of solid consisting largely of methylcinnamylnaphthohydroquinone. This was dissolved in ether, shaken with 5 g. of silver oxide and anhydrous sodium sulfate (twenty minutes) and the material left on filtering and evaporating the yellow solution was crystallized from ether–petroleum ether and gave 0.8 g. of the quinone, m. p. 124–126° (yield, allowing for recovered material, 22%). Purified by further crystallizations from alcohol the substance formed bright yellow blades, m. p. 127–127.5°. In the test with alcoholic alkali in the cold it gives an intense indigo blue which persists for about fifteen minutes and fades to brown.

Anal. Calcd. for $C_{20}H_{16}O_2$: C, 83.31; H, 5.59. Found: C, 83.63; H, 5.71.

In other runs the methylcinnamylnaphthohydroquinone was separated from the ethereal solution by repeated extraction with 10% alkali containing hydrosulfite, and this seemed more convenient than the above procedure. The extraction method was employed in an experiment paralleling that above but employing trichloroacetic acid (2 g.) in place of oxalic acid as the condensing agent (3 g. of the hydroquinone, twenty-three hours). There was obtained 0.7 g. of quinone, m. p. 126.5–127°, and 0.15 g., m. p. 125–126°; the yield is thus the same as in the above preparation.

The **hydroquinone diacetate** was obtained both from the crude hydroquinone with acetic anhydride and pyridine in the cold and from the quinone, zinc dust, acetic anhydride and pyridine. It crystallized from ether–petroleum ether in fine, silky needles, m. p. 167.5–168°.

Anal. Calcd. for $C_{24}H_{22}O_4$: C, 76.98; H, 5.92. Found: C, 77.17; H, 6.09.

2 - Ethyl - 3 - cinnamyl - 1,4 - naphthoquinone.—2-Ethyl-1,4-naphthohydroquinone (3 g.) was condensed with cinnamyl alcohol (1.54) exactly as described for the lower homolog (twenty-two hours) and unchanged starting material (1.68 g.) was extracted with three portions of 2% alkali-hydrosulfite. The substituted hydroquinone was then extracted with 10% alkali (five portions) and the yellow liquor washed with ether and acidified. The product was taken into ether and oxidized with silver oxide and the crude quinone (0.38 g.) crystallized three times from alcohol; yield, 0.2 g. (9.4%, based on material

consumed). The quinone forms flat needles, m. p. 118–118.5°; the behavior in the test with alcoholic alkali is like that of the methyl compound.

Anal. Calcd. for $C_{21}H_{18}O_2$: C, 83.41; H, 6.00. Found: C, 83.29; H, 6.10.

The **hydroquinone diacetate**, prepared as above by the pyridine method, was obtained from ether–petroleum ether as elongated prisms, m. p. 123.5–124.5°. Recrystallization from methanol did not change the m. p.

Anal. Calcd. for $C_{25}H_{24}O_4$: C, 77.30; H, 6.23. Found: C, 77.23; H, 6.34.

Condensation with Isoprene.—A solution of 2 g. each of methylnaphthohydroquinone, isoprene, and anhydrous oxalic acid in 20 cc. of dioxane was heated in a sealed tube at 180° for fifteen hours. Unchanged hydroquinone was extracted with 1% alkali-hydrosulfite (75 cc.) and yielded 0.6 g. of pure methylnaphthoquinone. Extraction with 100 cc. of 10% alkali-hydrosulfite in four portions and acidification with acetic acid gave 0.3 g. of white solid. This was oxidized with ferric chloride giving the quinone as a yellow oil which failed to crystallize and which was therefore converted by reductive acetylation (sodium acetate) to **2-methyl-3-(γ,γ-dimethylallyl)-1,4-naphthohydroquinone diacetate.** On purification this crystallized from ether–hexane as colorless prisms, m. p. 104.5–105.5°.

Anal. Calcd. for $C_{20}H_{22}O_4$: C, 73.60; H, 6.80. Found: C, 73.52; H, 6.79.

Condensation with Benzyl Alcohol.—The reaction was conducted with methylnaphthohydroquinone (2 g.), benzyl alcohol (1.24 g.), oxalic acid (2 g.), and dioxane (20 cc.) at the reflux temperature (twenty-five hours) and worked up as in the reaction with isoprene. The recovered starting material isolated as the quinone (m. p. 105–106°) amounted to 1.5 g., and oxidation of the product extracted with 10% alkali (75 cc.) afforded a few milligrams of **2-methyl-3-benzyl-1,4-naphthoquinone.** After two crystallizations from ether–petroleum ether this melted at 105–107.5°; a mixture with the sample described above melted at 107–108°, and the m. p. of methylnaphthoquinone was depressed to 73°.

Other Trials.—The starting material was largely recovered (1.4 g., as quinone) on attempted condensation of allyl alcohol (0.8 g.) with methylnaphthohydroquinone (2 g.) at 180° for twenty-four hours under the above conditions. Piperylene did not react readily, but there were indications of partial condensation at 120°. No reaction occurred on refluxing either the diacetate (thirty-six hours) or the dibenzyl ether (twenty-eight hours) of methylnaphthohydroquinone with dimethylbutadiene and oxalic acid in dioxane, the starting materials being recovered unchanged.

Summary

By using a mild condensing agent such as anhydrous oxalic acid in dioxane solution, 2-alkyl-1,4-naphthohydroquinones can be condensed with sufficiently reactive β-unsaturated alcohols, dienes or aryl carbinols, and under these conditions the substituted hydroquinones first formed are only partially cyclized and can be isolated and con-

verted into quinones of the structural type of vitamin K₁.

Another observation of this work is that a typical 2-alkyl-1,4-naphthoquinone oxide is converted into a bromohydrin by the action of mag-

nesium bromide in ether. New methods are described for the preparation of such oxides and for carrying out the reductive acetylation of quinones.

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Quantum Yields and Kinetics of a Photosensitized Production of Reducing Sugars from Sucrose in Aqueous Solutions of Uranyl Sulfate by Visible and Ultraviolet Light

BY LAWRENCE J. HEIDT

Aqueous solutions of sucrose are about as transparent as water in the visible and near ultraviolet to 200 mμ, so light in this region has not been found to produce any measurable effect upon the stability of sucrose dissolved in water. When uranyl ions are added to these solutions, they absorb visible and ultraviolet light; but their extinction coefficients between 470 and 208 mμ are the same as if no sucrose was present. Neither does the uranyl sulfate greatly affect the specific rotation of sucrose, which remains within 0.2% of 66.5° for the D lines of sodium.

Illumination of these sucrose–uranyl solutions with light absorbed by the uranyl ion causes a decrease in their optical activity and the formation of products which reduce the alkaline cupric solutions of Shaffer, Hartmann and Somogyi.[1]

Materials.—The sucrose was U. S. Bureau of Standards sample 17, lot 3650, and the fructose and glucose were recrystallized specimens with the correct rotations.[2] They were stored in vacuum over "Anhydrone" and were kept in the dark as much as possible.

The uranyl salts, oxalic acid, and permanganate were recrystallized and centrifuged specimens like those used previously.[3]

The sodium oxalate used to standardize the permanganate solutions was U. S. Bureau of Standards sample 40c.

All the other chemicals were reagent quality.

Apparatus and Procedure.—Monochromatic light was obtained by means of a prism monochromator using crystal quartz lenses. The 60° cornu prism was 6.5 cm. high and had faces 8 cm. long. It was purchased with a grant from the Warren Fund of the American Academy of Arts and Sciences. The monochromator transmitted in air the

185 mμ line of aluminum and separated the 578 and 546 mμ lines of mercury. In combination with a zinc spark, the energies at 208, 254 and 280 mμ transmitted by the exit slit were about the same as those obtained elsewhere with similar apparatus.[4]

Two reaction cells were used with the monochromator ensemble. One was rectangular, 20 mm. wide and 40 mm. high and held 5 cc. of solution in a 5-mm. layer. The other cell was trapezoidal and held 12 cc. of solution in a 30-mm. layer between the parallel windows. The front window was 10 mm. wide and 20 mm. high and the back window, 20 mm. wide and 40 mm. high. The transparency of the windows of both cells agreed within 2% at 208 mμ.

The source of light at 366 and 436 mμ was an inverted "U" type mercury vapor arc lamp.[5] Its intensity at these wave lengths was increased by reducing to 5 mm. the internal diameter of the quartz tubing containing the arc. This made available behind the exit slit (1 mm. wide × 10 mm. high) 7 × 10¹⁷ photons per minute at 366 mμ and 4 × 10¹⁷ at 436 mμ, varying less than 1% in twenty hours when the lamp was properly operated.

The amount of monochromatic light at 254 mμ was increased over 200-fold, to 5 × 10¹⁹ photons per minute, as described elsewhere.[6] Duplicate cells and stirrers used with this apparatus were made from the same pieces of transparent quartz. Quantum yields were the same whether obtained with this set-up or with the monochromator (see Table I, Expts. 12 and 13). The effectiveness of the light-proof aluminum tube that acted as a shutter was demonstrated in Expt. 9d, Table I, where the values in parentheses are directly proportional to the light flux which would have been incident on the sugar solution had the shutter been removed.

Analytical.—The light flux entering the actinic systems was measured with the uranyl oxalate solutions recommended for use as actinometers.[3,7] The oxalate content of the solutions was determined by electrometric titration with permanganate after proof that the method gave the same values of φ as titration to a color end-point. The

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(1) Heidt and Purves, THIS JOURNAL, **60**, 1206 (1938), give data when this reagent is used to follow the hydrolysis of sugars.

(2) I am indebted to Professor C. B. Purves for supplying these sugars and to Drs. F. B. Cramer and D. H. Grangaard for recrystallizing the fructose and glucose.

(3) Forbes and Heidt, THIS JOURNAL, **56**, 2363 (1934), and research referred to therein.

(4) Forbes and Brackett, ibid., **53**, 3973 (1931).

(5) Forbes and Heidt, ibid., **53**, 4349 (1931).

(6) Heidt, Science, forthcoming publication.

(7) Daniels, J. Phys. Chem., **42**, 701 (1938).