powder diffraction pattern as that for either the D- or L-mannoheptulose alone (Table I), thereby proving it to be a racemic mixture rather than a true racemic compound.

Summary

1. The synthesis of L-mannoheptulose from L-arabinose is described.

2. D,L-Mannoheptulose is prepared and demonstrated to be a racemic mixture.

3. Mannonamide is hydrolytically unstable in aqueous solution.

4. The following substances are also described in crystalline condition: ethyl L-mannonate; L-mannonamide (in pure form); D,L-mannonamide (shown to be a racemic compound); the O-pentaacetates of the L and D,L (shown to be a racemic compound) forms of mannonamide, of L-mannonic acid monohydrate and of methyl L-mannonate; 1-diazo-1-desoxy-*keto*-L-mannoheptulose pentaacetate; and *keto*-L-mannoheptulose hexaacetate.

COLUMBUS, OHIO RECEIVED AUGUST 22, 1950

[CONTRIBUTION FROM THE DIVISION OF AGRICULTURAL BIOCHEMISTRY, UNIVERSITY OF MINNESOTA]

The Preparation of a Reversible Oxidation Product of α-Tocopherol, α-Tocopheroxide and of Related Oxides[1]

BY PAUL D. BOYER

The oxidation of α-tocopherol (I) by ferric or auric chloride or by silver nitrate has been shown to give α-tocopherylquinone (IV),[2] which has hitherto been regarded as the first oxidation product stable enough to be isolated. This paper records the isolation and tentative characterization of an intermediate, biologically active,[3] reversible oxidation product of α-tocopherol which has been designated as "α-tocopheroxide." In addition there is reported herein the preparation of oxides of β-, γ- and δ-tocopherols, oxides of *p*-xylohydroquinone and durohydroquinone monoalkyl ethers and of duroquinone dioxide.

The initial observations which indicated that a well-defined intermediate product was formed in the conversion of α-tocopherol to α-tocopherylquinone were made during a study of the oxidation of α-tocopherol in 95% ethanol by ferric chloride in the presence of 2,2′-bipyridine. Addition of L-ascorbic acid to the reaction mixture immediately after oxidation of the α-tocopherol was found to yield a product which resembled α-tocopherol and not α-tocopherylhydroquinone or α-tocopherylquinone in its properties. As measured by the color of the ferrous iron-2,2′-bipyridine complex, the initial oxidation involved the transfer of two electrons per α-tocopherol molecule. It was therefore apparent that the observations were not due to the formation of a free radical of α-tocopherol, such as recently has been demonstrated by Michaelis and Wollman.[4]

Subsequent experiments led to the isolation of α-tocopheroxide as a labile colorless oil which under mildly acid conditions was readily converted irreversibly to α-tocopherylquinone or which could be reduced by ascorbic acid or sodium hydrosulfite to α-tocopherol. That the product obtained upon reduction of α-tocopheroxide with ascorbic acid was α-tocopherol was shown by the identity of the reduction product and of authentic α-tocopherol with respect to the ultraviolet absorption spectrum, total reducing potency, rate of reaction with ferric chloride and 2,2′-bipyridine, nature of the products formed by oxidation and the formation of the 3,5-dinitrophenylurethan derivative[5] which melted at 142–144° alone or when mixed with the derivative from an authentic sample of *d,l*-α-tocopherol.

Oxidation of α-tocopherol by ferric iron is known to be slow in the absence of 2,2′-bipyridine.[6] When tocopherol was oxidized by ferric iron without 2,2′-bipyridine present the chief product obtained was α-tocopherylquinone. If excessive amounts of 2,2′-bipyridine were used, the α-tocopheroxide contained more extraneous products other than α-tocopherylquinone. The 2,2′-bipyridine modifies the reaction probably through regulation of the acidity of the medium as well as by forming a complex with ferrous iron.

Characterization of the α-tocopheroxide was of interest both because of the possible biological importance of the compound and the lack of any readily apparent structure for an intermediate between α-tocopherol and α-tocopherylquinone.

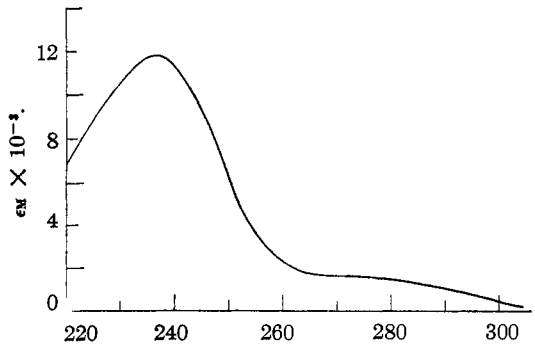


Fig. 1.—The ultraviolet absorption spectrum of α-tocopheroxide in isoöctane.

(1) Paper No. 2561, Scientific Journal Series, Minnesota Agricultural Experiment Station. Aided by a grant from the Nutrition Foundation, Inc., New York. Preliminary reports of part of the data presented herein have appeared in *Fed. Proc.*, **8**, 187 (1949), and the *Ann. N. Y. Acad. Sci.*, **52**, 188 (1949).

(2) (a) W. John, E. Dietzel and W. Emte, *J. Physiol. Chem.*, **257**, 173 (1939); (b) P. Karrer and A. Geiger, *Helv. Chim. Acta*, **23**, 455 (1940).

(3) Bioassay results will be reported elsewhere.

(4) L. Michaelis and S. H. Wollman, *Biochim. Biophys. Acta*, **4**, 156 (1950).

(5) L. I. Smith and J. A. Sprung, THIS JOURNAL, **64**, 433 (1942).

(6) C. Golumbic and H. A. Mattill, *J. Biol. Chem.*, **134**, 535 (1940).

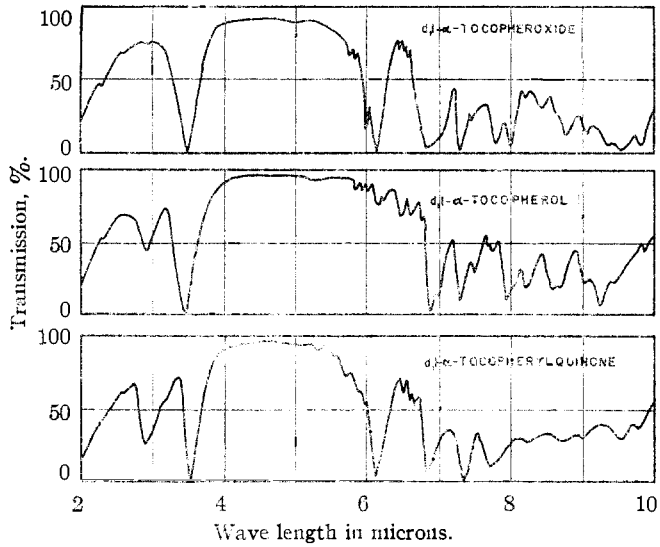
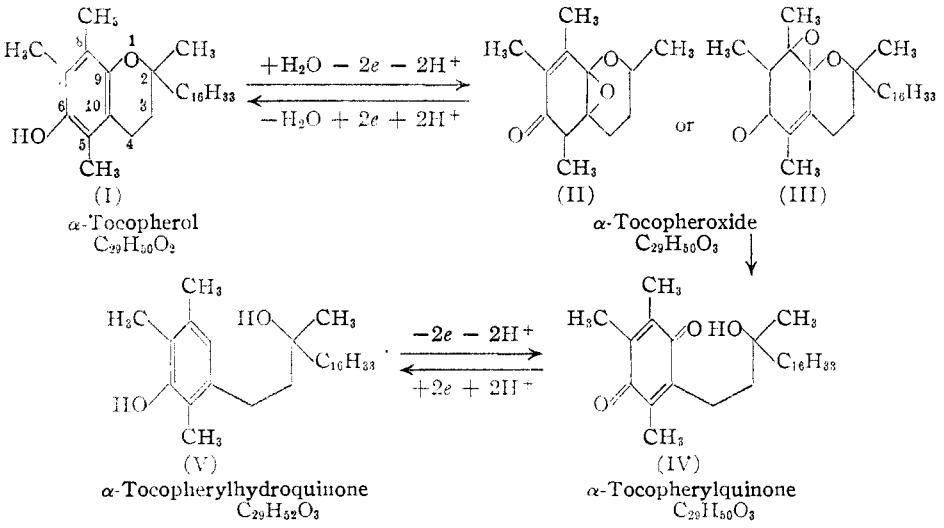


Fig. 2.—The infrared transmission of α-tocopherol, α-tocopherylquinone and α-tocopheroxide.

While the chemical reactions of α-tocopheroxide give useful information for characterization work, its instability has definitely limited the use of conventional organic procedures for structural studies. The use of ultraviolet and infrared absorption spectra, shown in Figs. 1 and 2, respectively, has thus been particularly helpful. The probable structures which have been assigned to α-tocopheroxide and the relationship of α-tocopheroxide to other products derived from α-tocopherol are



Elementary analyses and molecular weight determinations made on freshly prepared α-tocopheroxide show that it is a monomeric oxidation product which contains one more oxygen atom than α-tocopherol. α-Tocopheroxide is thus a structural isomer of α-tocopherylquinone. The mild oxidizing properties of α-tocopheroxide are shown by its slow liberation of iodine from sodium iodide in acetic anhydride and by its rapid oxidation of ascorbic acid. In the reaction with sodium iodide approximately 50% of the α-tocopheroxide loses oxygen to form α-tocopherol and the balance is converted principally to α-tocopherylquinone. With ascorbic acid the conversion to α-tocopherol is quantitative. That α-tocopheroxide is less polar than α-tocopherylquinone is shown by the observations that in phase separation between 90% ethanol and petroleum ether the α-tocopherylquinone may be preferentially extracted into the alcoholic phase and the α-tocopheroxide into the petroleum ether, and that on an activated alumina column α-tocopheroxide dissolved in petroleum ether migrates ahead of α-tocopherol and α-tocopherylquinone in the same solution.

The acetate and phosphate esters of α-tocopherol are not oxidized under the conditions used for the formation of α-tocopheroxide, which suggests that the hydroxyl group of α-tocopherol is oxidized in the formation of α-tocopheroxide. The absence of any hydroxyl groups in α-tocopheroxide is indicated by the negative results that were obtained with various hydroxyl-group reagents and further demonstrated by the infrared absorption spectra shown in Fig. 2. The very characteristic absorption of the hydroxyl group in the 3 micron region[7] present in the spectra of α-tocopherol and α-tocopherylquinone[8] (Fig. 2) is absent in the spectrum of α-tocopheroxide. The lack of a hydroxyl group in α-tocopheroxide rules out some possible structures, among which is the oxonium structure suggested for a reversible oxidation product formed from α-tocopherol at the dropping mercury electrode.[9] In addition to its hydroxyl group such an oxonium compound would be expected to have pronounced instability and an ultraviolet absorption maximum at considerably longer wave lengths than α-tocopheroxide. Nonetheless α-tocopheroxide may correspond to the reversible oxidation product noted in solution in the polarographic studies.

The preceding observations, the ease with which α-tocopheroxide may be reduced to α-tocopherol and the observation discussed below that oxidation products analogous to α-tocopheroxide may be formed from substituted hydroquinone monoalkyl ethers, allow the conclusions that the hetero ring present in α-tocopherol remains intact in the formation of α-tocopheroxide, and that in α-toco-

(7) (a) R. B. Barnes, R. C. Gore, R. W. Stafford and V. Z. Williams, *Anal. Chem.*, **20**, 402 (1948); (b) R. N. Jones and K. Dobriner, in R. S. Harris and K. V. Thimann, eds., "Vitamins and Hormones," Academic Press, New York, N. Y., Vol. 7, 1949, p. 293.

(8) R. Rosenkrantz, *J. Biol. Chem.*, **173**, 439 (1948).

(9) L. I. Smith, L. H. Spillane and I. M. Kolthoff, THIS JOURNAL, **64**, 447 (1942).

pheroxide there are two oxygen atoms associated with the carbocyclic ring. Both oxygens could not be present as separate ring oxygens since such a molecule would contain only one double bond and hence the ultraviolet absorption maximum would be expected to be below 200 mμ.[10] The presence of both oxygens in a peroxide grouping, similar to the transannular peroxide structures found in oxidation products of certain steroids and hydrocarbons,[11] would offer an attractive explanation for the liberation of iodine from sodium iodide, but does not satisfactorily account for the marked acid lability or the ultraviolet absorption spectrum. The peroxide group itself has only a very weak absorption in the ultraviolet region above 200 mμ. It is unlikely that a cyclic peroxide structure would be present with the peroxide attached to two adjacent carbon atoms. In addition, such a molecule would be a homoannular conjugated diene, and on the basis of the established absorption of dienes of this type[12] such a derivative formed from α-tocopherol would be expected to show an absorption maximum in the region of 270–280 mμ, considerably above the observed absorption maximum of α-tocopheroxide which in ethanol is at 241 mμ. The most plausible cyclic peroxide structure for α-tocopheroxide is one in which the peroxide is attached to carbons 6 and 9. In such a molecule the double bonds of the ring would be isolated and would not be expected to show absorption in the ultraviolet above 200 mμ unless the peroxide group caused a prominent shift in their absorption to longer wave lengths. This seems unlikely because previous measurements indicate that a peroxide group on a carbon atom adjacent to a double-bonded carbon on a conjugated diene does not affect the absorption of the diene,[13] and dehydro-ergosterol peroxide with a transannular peroxide one carbon removed from the double bond has been reported to show no selective absorption above 230 mμ. The possible effect of a peroxide group was further checked by measurement of the absorption of ascaridole, which showed only weak absorption at 210 mμ with a continued slow decrease in absorption as the wave length was increased. The molecular extinction coefficient at 240 mμ was only 200. This result is at variance with the report that ascaridole has an absorption maximum at 240 mμ with a molecular extinction coefficient of 3,600,[14] and makes untenable the suggestion that the absorption reported was due to the carbon–carbon double bond of ascaridole.

The elimination of the previously considered structures leads to the conclusion that α-tocopheroxide has a keto and a cyclic oxygen attached to the carbocyclic ring. Of the limited number of possible structures that which contains an α,β-unsaturated ketone grouping most satisfactorily accounts for the strong ultraviolet absorption in ethanol at 241 mμ. That α,β-unsaturated ketones show intense selective absorption in the region of 230 to 250 mμ has been recognized for some time,[15] and the relations between absorption spectra and structure of compounds of this type have been outlined in detail.[15b,11a] The predicted absorption maxima for α-tocopheroxide formulated as either (II) or (III) are 6 and 11 mμ higher, respectively, than the observed absorption maximum. Likewise the observed absorption maxima of the substituted hydroquinone monoalkyl ether oxides are 7 to 11 mμ less than the calculated maxima. The explanation of these small discrepancies may lie in other aspects of the structure of these compounds. Cyclic α-β-unsaturated ketones with five-membered rin s show absorption maxima at some 10 to 12 mμ shorter wave lengths than corresponding compounds with six-membered rings, and this shift in the absorption maxima has been attributed to the strain introduced by the five-membered ring.[16] The presence of a 3- to 5-membered oxide ring in α-tocopheroxide would likewise introduce a strain, and might be responsible for the hypsochromic effect.

Additional strong support for the presence of an α,β-unsaturated keto group may be drawn from the infrared spectra (Fig. 2). Conjugation of carbonyl groups with a $-\overset{|}{C}=\overset{|}{C}-$ bond results in a shift of the carbonyl stretching vibration to lower frequencies by about 30 to 40 cm.$^{-1}$.[17,7b] For example, Δ^4-3-ketosteroids absorb at 1674–1677 cm.$^{-1}$, while 3-ketosteroids without a double bond in a position of conjugation absorb at 1717–1719 cm.$^{-1}$.[17a] Further, a $-\overset{|}{C}=\overset{|}{C}-$ bond in conjugation with the carbonyl is associated with strong absorption in the region of 1580–1640 cm.$^{-1}$.[17a,b,c] In the Δ^4-3-ketosteroids this band appears at 1580–1615 cm.$^{-1}$. In isophorone and other α,β-unsaturated ketones, the band for the conjugated $-\overset{|}{C}=\overset{|}{C}-$ has been reported to be at 1621 to 1647 cm.$^{-1}$.[17c] The strong absorption band noted in α-tocopheroxide at 5.95 μ (1680 cm.$^{-1}$) is very probably due to the carbonyl group and the band at 6.10 μ (1639 cm.$^{-1}$) to the double bond in conjugation with the carbonyl group.

While the preceding considerations strongly support the conclusion that a ketone group is present in α-tocopheroxide, derivatives were not obtained with carbonyl reagents under various conditions. This may be attributed to the lability of the oxide to heat especially under alkaline conditions and in the presence of some group reagents and its marked lability to acids, to the readiness with which α-tocopheroxide will oxidize some carbonyl reagents, and to the expected inertness of the carbonyl with methyl groups adjacent. With

(10) S. R. Platt, H. B. Klevens and W. C. Price, *J. Chem. Phys.*, **17**, 466 (1949).

(11) W. Bergmann and M. J. McLean, *Chem. Revs.*, **28**, 367 (1941).

(12) (a) L. F. Fieser, M. Fieser, and S. Rajagopalan, *J. Org. Chem.*, **13**, 800 (1948); (b) R. B. Woodward, THIS JOURNAL, **64**, 72 (1942).

(13) J. L. Bolland and H. P. Koch, *J. Chem. Soc.*, 445 (1945); E. H. Farmer, H. P. Koch and D. A. Sutton, *ibid.*, 541 (1943).

(14) H. H. Szmant and A. Halpern, THIS JOURNAL, **71**, 1133 (1949).

(15) (a) W. Menschick, I. H. Page and K. Bossert, *Ann.*, **495**, 225 (1932); (b) R. B. Woodward, THIS JOURNAL, **63**, 1123 (1941).

(16) A. E. Gillam and T. F. West, *J. Chem. Soc.*, 486 (1942); A. L. Wilds, L. W. Beck, W. J. Close, C. Djerassi, J. A. Johnson, Jr., T. L. Johnson and C. H. Shunk, THIS JOURNAL, **69**, 1985 (1947).

(17) (a) R. N. Jones, V. Z. Williams, J. M. Whalen and K. Dobriner, *ibid.*, **70**, 2024 (1948); (b) N. H. Cromwell, F. A. Miller, A. R. Johnson, R. L. Frank and D. J. Wallace, *ibid.*, **71**, 3337 (1949); (c) R. L. Rasmussen, D. D. Tunnicliff and R. R. Brattain, *ibid.*, **71**, 1068 (1949); (d) H. W. Thompson and P. Torkington, *J. Chem. Soc.*, 640 (1945).

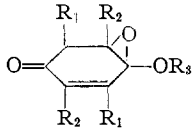
regard to the last factor, it has been established that the carbonyl groups of quinones with 2 adjacent substituents are hindered in their reaction with carbonyl reagents.[18]

Various properties of α-tocopheroxide point to the occurrence of the cyclic oxygen as an epoxy group. The instability of α-tocopheroxide makes it probable that the oxygen is not present in a four-membered or larger ring. The three-membered ring of epoxy compounds is readily split by dilute acids but is quite stable to alkali at room temperatures, in harmony with the properties of α-tocopheroxide. Likewise, the presence of an epoxy group offers an explanation for the liberation of iodine from sodium iodide by α-tocopheroxide. Although ethylene oxide and a number of simple epoxide derivatives show no oxidation properties, some unsymmetrically substituted epoxides are known to liberate iodine from iodides.[19] Further, carotinoids have been shown to form epoxides which readily lose their oxygen with formation of the parent carotinoid and which undergo rearrangement under the influence of dilute acid.[20] The location of the probable epoxide group in α-tocopheroxide is uncertain, but the ease with which the compound is converted to α-tocopherylquinone suggests that one point of attachment is at carbon 9 para to the keto group. Two such structures, represented by formulas II and III, are plausible. The conversion of α-tocopheroxide to α-tocopherylquinone, which is accelerated by water and dilute acids may be visualized as occurring by splitting of the epoxy ring through addition of water to give hydroxyl groups on carbons 9 and 10 (or 8 and 9), followed by opening of the hemi-ketal link to give a carbonyl on carbon 9 and a tertiary alcohol on the side chain, and by loss of water from carbons 5 and 10 (or 7 and 8) to form the stable quinone structure.

In addition to formation of α-tocopherylquinone, α-tocopheroxide when stored or when heated alone or in xylene solution undergoes partial conversion to a chemically inert product which is insoluble in absolute ethanol but readily soluble in petroleum ether. This conversion is hastened by the presence of alkali or of certain hydroxyl or ketone group reagents. When α-tocopheroxide was heated alone to 135–150°, the principal product isolated by chromatographic separation was a dimer which, on the basis of elementary analyses, had been formed from α-tocopheroxide by the loss of one oxygen atom and possibly one methyl group. The ultraviolet absorption spectrum of the product was similar to that of α-tocopherol and typical of substituted phenols and hydroquinones.

Oxidation products analogous to α-tocopheroxide were obtained from *d,l*-β-, *d*-γ-, and *d*-δ-tocopherols but only as impure preparations. The very limited amount of β-tocopherol available and the instability of the oxides from γ- and δ-tocopherols prevented the purification of the products. Nonetheless, products were obtained which shortly after isolation showed like α-tocopheroxide prominent, well-defined absorption peaks in the 230 to 240 mμ region. The β-tocopheroxide was readily reduced to β-tocopherol by ascorbic acid or converted to β-tocopherylquinone by exposure to 1:100 hydrochloric acid in 95% ethanol. The yields of the γ- and δ-tocopherol oxides were poor under conditions where α- and β-tocopherol gave good yields. This was due not only to incomplete oxidation, as might be anticipated from the known more rapid oxidation of β-tocopherol by ferric iron,[21] but also to the decreased stability of the oxides with resultant formation of extraneous products. The ease with which the various tocopherols form oxides and the stability of the oxides is roughly parallel to the respective biological activity of the tocopherols.

Because of their structural resemblance to the tocopherols, it was of interest to investigate the oxidation of monoethers of durohydroquinone and related compounds. The oxidation of the monoethers of durohydroquine by silver nitrate has previously been shown to form duroquinone.[22] However, under conditions similar to those used for the preparation of the tocopheroxides, the monolauryl and monocetyl ethers of durohydroquinone and *p*-xylohydroquinone formed oxides without cleavage of the ether linkage. These oxides were isolated as low-melting solids or colorless oils which, on the basis of elementary analysis, contained one more oxygen than the original ether. The oxides from durohydroquinone monoalkyl ethers showed a strong absorption maximum at 236 mμ in ethanol, which is 5 mμ lower than the maximum of α-tocopheroxide. On the basis of the known relationships between structure and absorption spectra for α-β-unsaturated ketones,[11a,15] this may be taken as an indication that the —C=C— bond in α-tocopheroxide is exocyclic to the hetero ring as in formula II. The oxides from the *p*-xylohydroquinone ethers had absorption maxima 8 to 9 mμ lower than those from the durohydroquinone ethers, in harmony with the known effect of depletion of methyl groups on the absorption of α-β-unsaturated ketones. Their composition, mode of formation, ultraviolet absorption spectra and chemical properties allow the probable structures VI and VII or VIII to be assigned to the durohydroquinone and *p*-xylohydroquinone monocetyl ether oxides, respectively.



VI, R_1 and R_2 = CH_3, R_2 = $C_{16}H_{33}$
VII, R_1 = CH_3, R_2 = H, R_3 = $C_{16}H_{33}$
VIII, R_1 = H, R_2 = CH_3, R_3 = $C_{16}H_{33}$

Although considerably more stable than the tocopheroxides, the monoether oxides were cleaved into the corresponding alcohols and quinones when warmed with dilute acid. In contrast to α-tocopheroxide, the ether oxides did not liberate iodine from sodium iodide nor were they reduced by ascorbic acid or sodium hydrosulfite. Exposure to

(18) L. I. Smith and W. B. Irwin, THIS JOURNAL, **63**, 1036 (1941); F. Kehrmann, F. Musemann and P. Facchinetti, *Ber.*, **48**, 2021, 2027 (1915).

(19) P. Karrer and E. Rodmann, *Helv. Chim. Acta*, **31**, 1074 (1948).

(20) P. Karrer and E. Jucker, "Carotinoide," Birkhauser, Basel, 1948, p. 66-71, and elsewhere.

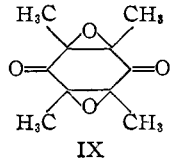
(21) M. H. Stern and J. G. Baxter, *Anal. Chem.*, **19**, 902 (1947).

(22) (a) E. Fernholz and J. Finkelstein, THIS JOURNAL, **60**, 2402 (1938); (b) E. Fernholz, *ibid.*, **60**, 700 (1938).

stannous chloride and strong hydrochloric acid effected reduction of the ether oxides to the original ethers. Apparently the epoxy group is cleaved by acid with the formation of an unstable intermediate which undergoes spontaneous decomposition to the quinone and alcohol or which, in the presence of a suitable reducing agent, may be reduced to the ether.

The resistance of the ether oxides to reduction gives additional evidence against a peroxide structure for the ether oxides or the tocopheroxides. Although some organic peroxides such as di-*t*-butyl peroxide are unreactive as contrasted to simpler dialkyl peroxides,[23] a peroxide grouping, if present in the ether oxides, would be expected to show stronger oxidizing properties than those observed.

The difference in stability and ease of reduction of the tocopheroxides and the monoether oxides is probably due to differences in the properties of the epoxide group. Epoxides are known to differ markedly in their ability to react with iodides, and this has been related to the asymmetry of the molecules.[19] The heterocyclic ring or the substituents in position-2 of the tocopheroxides may have a labilizing effect on the epoxide group. As a further example of the difference in the behavior of epoxides, duroquinone dioxide (IX), prepared in the course of this investigation, was found to be inert toward sodium iodide in acetic anhydride while 2-methyl-1,4-naphthoquinone oxide very readily liberated iodine.



IX

Attempts were made to prepare an oxide from the monoethyl ether of trimethylhydroquinone with the view that such an oxide without a long alkyl side chain would be more readily purified and crystallized. However, oxidation of the monoethyl ether of trimethylhydroquinone yielded only trimethylquinone. Similarly, the stability of α-tocopheroxide is apparently enhanced by the presence of the $C_{16}H_{33}$ side chain. While an oxide was formed from 2,2,5,7,8-pentamethyl-6-hydroxychroman, this oxide was considerably less stable than α-tocopheroxide.

The oxides from the monoethers when treated either with hydroxylamine or with semicarbazide hydrochloride under various conditions underwent decomposition and rearrangement, or else yielded derivatives of the corresponding quinones. Oxides from the *p*-xylohydroquinone ethers when treated with *p*-nitrophenylhydrazine gave mixtures of substances, some of which might correspond to carbonyl derivatives, but further work is necessary to define the nature of the products formed.

The duroquinone dioxide mentioned earlier was prepared by treatment of duroquinone with alkaline hydrogen peroxide. The well-defined crystalline product obtained had only very weak absorption in the ultraviolet above 210 mμ, as would be expected if both of the carbon double bonds of the original duroquinone had undergone addition. Reduction converted the product to durohydroquinone. These properties together with the elementary analysis and mode of preparation characterize the compound as the dioxide of duroquinone.

(23) N. A. Milas and D. M. Surgenor, THIS JOURNAL, **68**, 205 (1946).

Experimental Part[24]

Ultraviolet and Infrared Absorption Spectra.—Ultraviolet absorption measurements were made with a model DU Beckman spectrophotometer with isoöctane or ethanol as the solvent. The spectra presented in Fig. 2 were obtained through the courtesy of Dr. Bryce Crawford of the Physical Chemistry Division with a Perkin-Elmer infrared spectrometer. Measurements were made directly on the pure oils in a cell spaced at a width of 25 microns.

Molecular Weight Determinations.—Molecular weights were estimated by comparison of the melting depression of an approximately 10% solution of the test compound in camphor or camphene with the depression given by a similar quantity of *d*-α-tocopherol. The melting points were determined in sealed tubes essentially as outlined by Pregl and Grant.[25]

Determination of the Reducing Power of Various Preparations.—This was done by addition of 1.0 ml. of glacial acetic acid containing 50 mg. of $FeCl_3 \cdot 6H_2O$ and 100 mg. of 2,2′-bipyridine per ml. and 1 ml. of absolute ethanol to 5.0 ml. of a petroleum ether or isoöctane solution of the compound to be tested. The solutions were mixed and the color developed was read in a Coleman junior spectrophotometer at 510 mμ after 3–4 minutes. The use of the reagents in the portions specified obviates the necessity of evaporation of the hydrocarbon solvent and replacement by alcohol or acetic acid for the colorimetric determination.

Preparation of α-Tocopheroxide.—α-Tocopheroxide of 90% purity or better and in yields of 95% may be readily obtained by the following simple procedure. Two hundred mg. of *d,l*- or *d*-α-tocopherol and 0.9 g. of 2,2′-bipyridine are dissolved in about 150 ml. of absolute ethanol in a beaker and cooled in an ice-salt-bath to −5 to −10°. While the solution is rapidly stirred with an electric stirrer, 250 mg. of $FeCl_3 \cdot 6H_2O$ dissolved in 100 ml. of absolute ethanol is added slowly (40–60 minutes) from a buret with the tip immersed. Forty to fifty ml. of redistilled, low-boiling petroleum ether is then added, the solution mixed and transferred to a separatory funnel. About 100 ml. of cold water is added, the mixture gently shaken and, after separation, the lower layer is discarded. (Yields can be increased slightly by reëxtraction of this layer.) The petroleum ether solution is washed three times with 50% ethanol containing 10 mg. of sodium chloride per ml., and is then shaken with 10 ml. of ferrous sulfate solution containing 5 mg. of $FeSO_4 \cdot 7H_2O$ per ml., washed with 50% ethanol and finally with water. The petroleum ether solution is then dried over anhydrous sodium sulfate and the solvent removed under vacuum with warming in a water-bath to give the α-tocopheroxide as a pale yellow oil. Such preparations have been found to have a reducing power calculated as α-tocopherol equivalent to less than 1% of their weight. The chief contaminants are products resembling non-reducing dimers in properties together with smaller amounts of α-tocopherylquinone.

Removal of small amounts of contaminants from α-tocopheroxide prepared as described above was difficult and has been best achieved by a combination of chromatographic and phase separation procedure. For example, a sample for elementary analysis was obtained as follows: 400 mg. of crude α-tocopheroxide dissolved in petroleum ether were chromatographed on a column of Brockmann alumina (Merck and Co., Inc.) which had been previously activated by moistening with calcium hydroxide solution (1 g. per 500 ml.) and heating at 475° overnight. The column was developed with petroleum ether, and the α-tocopheroxide which migrated as a diffuse pale yellow band ahead of α-tocopherol and α-tocopherylquinone was collected in por-

(24) Melting points, other than those for the camphor and camphene melting point depressions, were measured with a Fisher-Johns melting point block. Microanalyses by H. W. Turner, R. W. Amidon and W. Cummings, of the School of Chemistry, University of Minnesota.

(25) F. Pregl and J. Grant, "Quantitative Organic Microanalysis," The Blakiston Co., Phila., Pa., 1945, p. 198.

tions as it passed through the column. The first portions of α-tocopheroxide which passed through had less color than later portions. Rechromatographing of the first portions yielded a colorless sample devoid of any reducing power. The best fraction from the chromatographic separation was dissolved in isoöctane and further purified by phase separation. Extraction of the isoöctane solution twice with aqueous ethanol (1 ml. water per 10 ml. of absolute ethanol) saturated with isoöctane removed some impurities along with a portion of the α-tocopheroxide. The remaining isoöctane solution was then extracted twice with more concentrated aqueous ethanol (1 ml. water per 15 ml. of absolute ethanol). This extraction removed considerable α-tocopheroxide and left behind impurities preferentially soluble in the isoöctane. The combined extracts from the last ethanol extraction were diluted with an equal volume of water and the α-tocopheroxide extracted into low-boiling petroleum ether. The solvent was removed under a vacuum of less than 1 mm. to give 35 mg. of purified α-tocopheroxide. Analyses were made within several hours after preparation to minimize changes.

Anal. Calcd. for $C_{29}H_{50}O_3$: C, 77.97; H, 11.28. Found: C, 77.92; H, 11.30.

The melting point depression obtained with α-tocopheroxide in camphene was 0.97 times as great on a weight basis as that obtained with α-tocopherol; the approximate molecular weight for α-tocopheroxide calculated from this value is 440.

Conversion of α-Tocopheroxide to α-Tocopherol and α-Tocopherylquinone.—To convert α-tocopheroxide to α-tocopherol an absolute ethanol solution containing 0.01 to 1.0 mg. of α-tocopheroxide per ml. was mixed with 1/4 volume of aqueous 10% ascorbic acid. To convert α-tocopheroxide to α-tocopherylquinone the tocopheroxide was dissolved in 95% ethanol containing 1 ml. of concd. hydrochloric acid per 100 ml. The respective solutions were allowed to stand for 15 minutes at room temperature, diluted with an equal volume of water and extracted with petroleum ether or isoöctane to separate the α-tocopherol or α-tocopherylquinone from the other reactants. The conversion of α-tocopheroxide to α-tocopherol was markedly accelerated by the presence of water. Spectrophotometric measurements showed that under conditions where conversion was complete in 5 minutes with 95% ethanol as a solvent, no conversion occurred with absolute ethanol as a solvent.

The shaking of a petroleum ether solution of α-tocopheroxide with 0.1 *M* acetate buffer, *p*H 3.8, for 10 minutes was sufficient to convert 75% to the α-tocopherylquinone as calculated from the ultraviolet absorption spectrum using the simple equations for a two-component system. In contrast, shaking of α-tocopheroxide in petroleum ether with 0.1 or 1.0 *N* sodium hydroxide did not change the ultraviolet absorption of the α-tocopheroxide.

Stability of α-Tocopheroxide During Storage.—As estimated from their ultraviolet absorption spectra, solutions of α-tocopheroxide in absolute ethanol or isoöctane showed a 10–20% decrease in α-tocopheroxide concentration in 3 days at room temperature, with appearance of α-tocopherylquinone and other products. A sample stored 3 weeks as an oil at −12° showed about 6% and a sample stored 7 weeks about 23% of α-tocopherylquinone and, in addition, considerable amounts of ethanol-insoluble materials similar in properties to the dimer obtained by the heating α-tocopheroxide.

Reaction of α-Tocopheroxide with Sodium Iodide.—Addition of a few mg. of α-tocopheroxide to acetic anhydride containing 1 g. of sodium iodide per 10 ml. at room temperature resulted in a slow liberation of iodine over a 20-minute period. In contrast under the same conditions the liberation of iodine by 2-methyl-1,4-naphthoquinone oxide was complete within 2 minutes and duroquinone dioxide caused no iodine liberation within the limits of experimental error in 30 minutes. That the liberation of iodine by α-tocopheroxide was not due to the formation of α-tocopherylquinone which then reacted with the iodide was shown by the very slow rate of iodine liberation by α-tocopherylquinone and by duroquinone.

Quantitative determination of iodine liberation was made by titration with 0.1 *N* thiosulfate with use of a special microburet of 0.2 ml. total volume. When 36.4 mg. of α-tocopheroxide was exposed to 1 ml. of the acetic anhydride–sodium iodide reagent for 30 minutes with occasional shaking only 57% of the theoretical amount of iodine was liberated. In contrast under comparable conditions, a 23.8-mg. sample of 2-methyl-1,4-naphthoquinone oxide liberated 93% of the theoretical amount of iodine. By measurement of the reducing potency and ultraviolet absorption of a suitable extract from the α-tocopheroxide sodium iodide reaction mixture, it was estimated that about 60% of the α-tocopheroxide had been converted to α-tocopherol and the balance principally to α-tocopherylquinone.

Exposure of α-Tocopheroxide to Various Group Reagents.—α-Tocopheroxide was recovered essentially unchanged after exposure to diazomethane in ether at room temperature or to ketene in toluene at 100°. With acetic anhydride and acetyl chloride under various conditions, α-tocopheroxide was not acetylated but was converted largely to α-tocopherylquinone or its chloro derivatives.[26] Hydroxyl group derivatives could not be isolated following treatment with 3,5-dinitrobenzoyl chloride, 3,5-dinitrobenzazide and α-naphthyl isocyanate under various conditions. Chromatographic separations of the reaction mixtures on alumina yielded fractions resembling in properties dimers obtained under other conditions.

Treatment of α-tocopheroxide with 2,4-dinitrophenylhydrazine, asymmetrical diphenylhydrazine, semicarbazide or hydroxylamine under as weakly acid conditions as feasible with these reagents led chiefly to the formation of α-tocopherol from reduction by the reagents and of α-tocopherylquinone. Hydroxylamine with strongly alkaline conditions did not yield an oxime.

Attempts to split the epoxy group with the formation of an ether and hydroxy group by the use of sulfuric acid in absolute ethanol as done with epoxides of fatty acids,[27] or with sodium methoxide, as done with the anhydro sugars,[28] were not successful. In the former instance the quinone was formed, in the latter a product similar to the dimer obtained by heating α-tocopheroxide alone.

The Effect of Heat on α-Tocopheroxide.—α-Tocopheroxide, 114 mg., was heated in a test-tube immersed in a wax-bath and the changes produced were followed by determining the qualitative absorption spectra of small samples removed at intervals. Slow heating to 135° produced pronounced changes which were accentuated by heating to 155°. Further elevation of the temperature to 175–180° produced only slight additional changes. When the samples were removed for ultraviolet absorption during and shortly after the heat treatment, it was noted that their ultraviolet absorption continued to change for about 0.5 hour after they were first dissolved in ethyl alcohol. This change was manifested by a general increase in absorption, particularly in the 210 to 230 mμ region where an 80% increase was noted. These results indicate that some intermediate product without strong absorption in the ultraviolet was rearranging to give absorption typical of compounds with a substituted benzene ring.

Extraction of the heated sample by mixing with several portions of absolute ethanol removed 23 mg. of material which was principally α-tocopherylquinone. The residual brown alcohol-insoluble material was dissolved in petroleum ether and passed through an activated alumina column. Three fractions were collected, a very pale yellow lower fraction (33 mg.) which passed through the column first, an intermediate fraction (11 mg.) and an upper yellow-brown (26 mg.) fraction. The lower and upper fractions showed similar absorption spectra, with a weak maximum at 293–295 mμ ($E^{1\%}_{1cm.}$ 55–58), a minimum in the region of 260–270 mμ, and a strong increase in absorption up to about 230 mμ with a continued but less pronounced increase to 220 mμ ($E^{1\%}_{1cm.}$ at 220 mμ 268–280). From camphor melting point depression the molecular weight of the lower fraction was estimated as 820–940.

Anal. Calcd. for $C_{58}H_{100}O_4$: C, 80.87; H, 11.84 for $C_{56}H_{96}O_4$: C, 81.10; H, 11.18. Found, lower fraction: C, 81.13; H, 11.44. Upper fraction: C, 81.08; H, 11.36.

Although these fractions had an elementary analysis closely corresponding to α-tocopherol and an ultraviolet absorption resembling that of α-tocopherol, they differed markedly from α-tocopherol in other properties. The

(26) M. Tishler and N. L. Wendler, THIS JOURNAL, **63**, 1532 (1941).
(27) D. Swern, G. N. Billen and J. T. Scanlan, *ibid.*, **70**, 1226 (1948).
(28) W. H. G. Lake and S. Peat, *J. Chem. Soc.*, 1417 (1938).

fractions were devoid of reducing action toward the ferric chloride-2,2'-bipyridine reagent, stable when heated with acid and alkali, practically insoluble in absolute ethanol but freely soluble in hydrocarbon solvents, and were not changed by exposure to ascorbic acid or hydrosulfite. They were inert to hydroxyl and ketone group reagents.

Oxides of β-, γ- and δ-Tocopherol and of 2,2,5,7,8-Pentamethyl-6-hydroxychroman.—When oxidized with ferric chloride and 2,2'-bipyridine under conditions similar to those used for the preparation of α-tocopheroxide, a 50-mg. sample of *d,l*-β-tocopherol readily formed an oxide which as first isolated had an absorption maximum at 235 mμ. Chromatographic purification on activated alumina resulted in separation of an impurity which migrated more rapidly than the β-tocopheroxide. The final product showed a well-defined absorption maximum at 234 mμ of intensity comparable to that of α-tocopheroxide, no reducing power, and, as measured by the ultraviolet absorption spectrum, was readily converted to β-tocopherol or β-tocopherylquinone under the same conditions as α-tocopheroxide.

Oxidation of *d*-γ-tocopherol under conditions similar to those used for the preparation of α-tocopheroxide gave initial preparations which showed only a very poorly defined maximum in the 230 mμ region. This was due partly to the presence of unoxidized γ-tocopherol. More complete oxidation was obtained with standing for 30 minutes following addition of the ferric chloride, but this also resulted in formation of more extraneous products. When crude preparations so obtained were chromatographed on activated alumina, a colorless fraction resembling in properties the non-reducing dimer obtained by heating α-tocopheroxide first passed through the column. This fraction was followed by material which on the basis of the well-defined ultraviolet absorption maximum at 232-234 mμ and changes when exposed to ascorbic acid or hydrochloric acid was principally γ-tocopheroxide. The γ-tocopheroxide was not readily further purified as it continued to change into more stable products during purification procedures.

The product first isolated from the oxidation of δ-tocopherol showed high absorption but no discernible maximum in the 230 mμ region. More unchanged tocopherol and extraneous reaction products were present than with the γ-tocopherol preparations. By chromatographic separation, a small amount of product with absorption at 230-232 mμ but which was even less stable than γ-tocopheroxide was isolated.

An oxide was readily formed when 30 mg. of 2,2,5,7,8-pentamethyl-6-hydroxychroman was treated with ferric chloride as described for the tocopheroxide preparation. The initially isolated product was a pale yellow oil which showed an ultraviolet absorption very similar to that of α-tocopheroxide, with a strong maximum (ϵ_M about 1.2×10^4) in isooctane at 236 mμ. When attempts were made to crystallize the oxide from ethyl alcohol-water mixtures with standing overnight only the oily quinone was isolated. Like α-tocopheroxide, the oxide from 2,2,5,7,8-pentamethyl-6-hydroxychroman did not yield derivatives with hydroxyl group reagents.

Durohydroquinone Monoethers.—The monolauryl and monocetyl ethers of durohydroquinone were prepared essentially as described by Fernholz and Finkelstein[22a] except that the products were isolated on the basis of the difference in solubility of the mono- and diethers in acetone or ethanol. After crystallization from glacial acetic acid plus a small amount of water the monocetyl ether melted sharply at 100.5-101.5°, reported 99-100.5°[22a] and 98°.[29] The monolauryl ether melted at 95-96°, reported 96-97°.[22a]

Anal. Calcd. for $C_{22}H_{38}O_2$: C, 78.98; H, 11.45. Found: C, 78.72; H, 11.59.

Duroquinone was prepared from durene[30] and durohydroquinone was prepared from duroquinone by reduction with hydrosulfite in aqueous ethanol as described below for *p*-xylohydroquinone.

***p*-Xylohydroquinone Monoethers.**—For the preparation of *p*-xylohydroquinone, 4 g. of *p*-xyloquinone (Eastman Kodak Co.) was dissolved in 30-50 ml. of absolute ethanol with warming. About 8 g. of sodium hydrosulfite was added, the solution heated on a steam-bath to near boiling, and water added slowly with stirring until the intense brown color of the free radical appeared. The color faded as the reduction proceeded to completion and more water was then added slowly until *p*-xylohydroquinone crystals just began to appear. The solution was cooled in the refrigerator, and the crystals collected and recrystallized from ethanol; yield 3.3 g.

For preparation of the monolauryl ether, 1.23 g. of *p*-xylohydroquinone, 2.26 g. of lauryl bromide (Eastman) and 75 ml. of absolute ethanol in a flask equipped with a dropping funnel were refluxed gently for 0.5 hour to remove air from the reaction mixture and flask. A solution of 600 mg. of potassium hydroxide in 25 ml. of absolute ethanol was then added from the dropping funnel over a 20-minute period and the straw-colored solution refluxed for an additional 20 minutes. The potassium hydroxide solution was prepared by grinding the hydroxide (assay, min. 85%) with the ethanol in a mortar, and heating to boiling on a steam-bath just before addition to the dropping funnel to reduce the concentration of dissolved oxygen. After several hours the solution was decanted from the insoluble residue containing potassium bromide and some of the dilauryl ether. The solution was then diluted with 2 volumes of water, extracted 3 times with diethyl ether, and the diethyl ether solution washed twice with dilute sodium carbonate and dried over anhydrous sodium sulfate. The solvent was removed on a steam-bath, the residue was dispersed in warm absolute ethanol and a small amount of insoluble material was removed by centrifugation and discarded. Addition of a small amount of water to the solution and storage for several hours in a refrigerator gave a crystalline product. This was dissolved in absolute methanol, a small amount of insoluble material discarded, and the monoether crystallized as fine needles (m.p. 60-64°) after addition of a small amount of water and storage overnight at 3°. Two subsequent crystallizations from glacial acetic acid plus a small amount of water gave the monoether as fine white needles which melted sharply at 67.0-67.5°; yield 400 mg.

Anal. Calcd. for $C_{20}H_{34}O_2$: C, 78.38; H, 11.18. Found: C, 78.37; H, 11.16.

The method of preparation, elementary analysis, reducing potency and ultraviolet absorption spectrum characterized the compound as the *p*-xylohydroquinone monolauryl ether.

The monocetyl ether of *p*-xylohydroquinone was prepared in a similar manner to the monolauryl ether from 1.5 g. of *p*-xylohydroquinone and 3.36 g. of cetyl bromide; yield 500 mg., m.p. 72.5-73°.

The color produced by reaction of the *p*-xylohydroquinone monocetyl and monolauryl ethers with ferric chloride and 2,2'-bipyridine in ethanol reached a maximum in 2 to 3 minutes. With the corresponding durohydroquinone ethers, the maximum was not reached for 6 to 7 minutes. With α-tocopherol maximum color developed within 1 minute.

2,3,6-Trimethyl-4-ethoxyphenol.—This ether was readily prepared by the action of sulfuric acid on trimethyl-*p*-hydroquinone and ethanol.[31] This procedure was not applicable to the preparation of the monoalkyl ethers of *p*-xylohydroquinone. Under conditions similar to those used with trimethyl-*p*-hydroquinone, *p*-xylohydroquinone remained largely unchanged.

Oxides from Hydroquinone Monoalkyl Ethers.—Oxides of monolauryl and monocetyl ethers of durohydroquinone were prepared in essentially the same manner as α-tocopheroxide, except that the ethers were oxidized at room temperature. After completion of the ferric chloride addition, the reaction mixtures were allowed to stand for 20 to 30 minutes at room temperature before extraction with petroleum ether. The desired products were separated from some unoxidized monoether and from by-products by chromatography on alumina; however, complete removal of impurities was difficult to achieve. The best preparation of the oxide from durohydroquinone monolauryl ether was isolated from ethanol-water at −12° as a white solid which melted at 21.5-22°, but was not yet analytically pure. The durohydroquinone monocetyl ether oxide preparation was a solid at room temperature, from which a sample for analysis was isolated by repeated crystallization from ethanol-water solution as white needles which melted at 40.5°. The product showed intense selective absorption in isooctane at 236 mμ in the ultraviolet, and the absorption spectrum was qualitatively nearly identical with that of α-tocopheroxide.

(29) F. Bergel, A. R. Todd and T. S. Work, *J. Chem. Soc.*, 253 (1938).

(30) L. I. Smith, in A. H. Blatt, editor, "Organic Syntheses," 2nd ed., Coll. Vol. II, p. 254 (1943).

(31) W. John and F. H. Rathman, *Ber.*, **73**, 995 (1940).

Anal. Calcd. for $C_{26}H_{46}O_3$: C, 76.79; H, 11.40. Found: C, 76.81; H, 11.70.

The durohydroquinone monocetyl ether oxide partially liquefied after standing at room temperature for 9 months; the remaining solid material melted at 28–36°.

The oxides of the *p*-xylohydroquinone monolauryl and monocetyl ethers were prepared in a manner analogous to the durohydroquinone ether oxides, except that the oxidation was carried out at 0°. These oxides were obtainable only as oils which showed intense selective absorption at 227–228 mμ. Except for the difference in the position of the maxima, the ultraviolet absorption was qualitatively closely analogous to that of the duroquinone ether oxides and α-tocopheroxide.

When *p*-xylohydroquinone monocetyl ether oxide was dissolved in 95% ethanol containing 1 ml. of concentrated hydrochloric acid per 100 ml., cleavage to the corresponding quinone and alcohol although slower than with α-tocopheroxide was complete within 15 minutes. With the oxides from the durohydroquinone monoethers, warming was necessary to effect cleavage under otherwise comparable conditions.

The durohydroquinone monocetyl ether oxide did not react with 10% sodium iodide in acetic anhydride during 0.5 hour at room temperature. Further, no iodine liberation as compared to controls was obtained when durohydroquinone monocetyl ether oxide samples were allowed to stand for 8 hours in 1 ml. of 10% sodium iodide in acetic anhydride containing one-third volume of ethanol. Durohydroquinone monocetyl ether oxide was not reduced by exposure to ascorbic acid overnight under conditions where α-tocopheroxide was reduced within 5 minutes. Likewise, the oxide was not reduced when refluxed for one-half hour in about 75% ethanol with added sodium hydrosulfite. When dissolved in 2 ml. of ethanol plus 0.5 ml. of 0.5 *M* stannous chloride in concentrated hydrochloric acid followed by heating on a steam-bath for 15 minutes, durohydroquinone monolauryl ether oxide was converted chiefly to durohydroquinone monolauryl ether, which was isolated and identified by its ultraviolet absorption spectrum and melting point (95°).

When 108 mg. of *p*-xylohydroquinone monocetyl ether oxide was refluxed with 19 mg. of hydroxylamine hydrochloride in 1 ml. of pyridine and 1 ml. of ethanol for about 0.5 hour, the chief product was the dioxime of *p*-xyloquinone, as established by the identity of the ultraviolet absorption maximum (315 mμ) and the decomposition temperature (255–260°) with that of an authentic specimen. Likewise, refluxing of 50 mg. of *p*-xylohydroquinone monocetyl ether oxide with 50 mg. of semicarbazide hydrochloride and 75 mg. of anhydrous sodium acetate in 0.5 ml. of ethanol plus sufficient water for initial turbidity yielded a product which on the basis of ultraviolet absorption spectrum was the same as that obtained with *p*-xylohydroquinone and semicarbazide. The durohydroquinone monocetyl ether oxide did not react with hydroxylamine or semicarbazide under the above conditions. With hydroxylamine under strongly alkaline conditions products other than an oxime were formed.

2-Methyl-1,4-naphthoquinone Oxide.—This was prepared according to Fieser, *et al.*, m.p. observed 95.5–96°, previously reported, 96°.[32]

Duroquinone Dioxide.—To 200 mg. of duroquinone in two ml. of 95% ethanol were added 1 ml. of 30% hydrogen peroxide and 0.5 ml. of sodium carbonate solution containing 250 mg. per ml. The mixture was heated under a reflux condenser at 50–60° for 110 minutes, in which time the duroquinone dissolved and a small amount of white crystals of the oxide appeared. The sample was then allowed to cool and the white crystalline product collected and washed with about 40% ethanol, then with water. The product was recrystallized from hot 95% ethanol by addition of water and slow cooling to give relatively large, flat needles which sublimed readily. Two recrystallizations yielded material of constant melting point at 111.5–112°; yield 90 mg. In aqueous ethanol the duroquinone dioxide showed only very weak absorption at 210 mμ with continued decrease in absorption as the wave length was increased.

Anal. Calcd. for $C_{10}H_{12}O_4$: C, 61.21; H, 6.18. Found: C, 61.27; H, 6.33.

Duroquinone dioxide when dissolved in 10% sodium iodide in acetic anhydride gave negligible iodine liberation in 15 minutes. When a small sample was treated with aqueous hydrosulfite the oxide was reduced with a transient appearance of a yellow color, probably duroquinone. From the reduction mixture, crystalline durohydroquinone was isolated with a melting point of 234–235° alone or when mixed with an authentic specimen.

Ascaridole.—This was obtained by distillation of chenopodium oil.[33] As measured by iodine liberation the ascaridole had a purity of 96%.

Acknowledgments.—I am indebted to Professor L. I. Smith of the Organic Chemistry Division for samples of 2,2,5,7,8-pentamethyl-6-hydroxychroman, durene, duroquinone and for making available a sample of *d,l*-β-tocopherol synthesized in the Merck and Co., Inc., Laboratories.

Summary

α-Tocopherol when oxidized by ferric chloride in the presence of 2,2′-bipyridine has been found to form an intermediate oxidation product, α-tocopheroxide, which may readily be reduced to α-tocopherol or converted irreversibly to α-tocopherylquinone. α-Tocopheroxide has been isolated as a colorless oil and on the basis of its ultraviolet and infrared absorption spectra and chemical properties has been assigned a probable structure as 2,5,7,8-tetramethyl-2(4,8,12-trimethyltridecyl)-8,9-epoxy-6(7H)-chromanone, or as the corresponding isomer with the epoxy group in the 9,10-position. Similar oxides have been prepared from β-, γ- and δ-tocopherols, 2,2,5,7,8-pentamethyl-6-hydroxychroman and from the monolauryl and monocetyl ethers of *p*-xylohydroquinone and durohydroquinone.

A dioxide of duroquinone has been prepared by the oxidation of duroquinone with alkaline hydrogen peroxide, and the preparation of the monolauryl and monocetyl ethers of *p*-xylohydroquinone is described.

ST. PAUL 1, MINNESOTA RECEIVED JULY 19, 1950

(32) L. F. Fieser, W. P. Campbell, E. M. Fry and M. D. Gates, Jr., THIS JOURNAL, **61**, 3216 (1939).

(33) H. Paget, *J. Chem. Soc.*, 829 (1938).