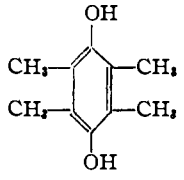
[CONTRIBUTION FROM THE RESEARCH LABORATORIES, MERCK & COMPANY, INC.]

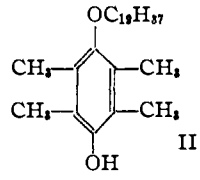
On the Constitution of α-Tocopherol

BY E. FERNHOLZ

Some time ago I was able to report[1] that durohydroquinone (I) is a characteristic pyrolytic decomposition product of α-tocopherol. α-Tocopherol is the most active compound of the



I



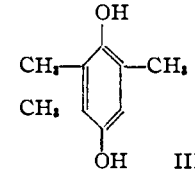
II

vitamin E group, and Evans, Emerson and Emerson[2] have demonstrated that it has the empirical formula $C_{29}H_{50}O_2$.[3]

When durohydroquinone, $C_{10}H_{14}O_2$, is subtracted from $C_{29}H_{50}O_2$ there remains a hydrocarbon residue $C_{19}H_{36}$. The thermal splitting is a comparatively smooth reaction and durohydroquinone was isolated in a yield of 67%. A hydrocarbon also was isolated and it had the expected properties. It did not react with perbenzoic acid, but added approximately one molecule of bromine. This result seemed to be best explained by giving α-tocopherol the structure of a mono-ether of durohydroquinone (II) with an alcohol which on account of a deficit of two hydrogen atoms would have to contain an isocyclic ring. This assumption had to be abandoned, however, as the investigation of α-tocopherol progressed.

Before entering into a discussion of these experiments, mention must be made of certain publications which, in the meantime have appeared from other laboratories. Independently, McArthur and Watson[4] made a very similar observation, when they noted the formation of duroquinone when α-tocopherol was subjected to treatment with selenium at high temperatures. The Canadian investigators have drawn conclusions from their observations which, in a very essential point, are at variance with my own explanation. They suggested that α-tocopherol is a cyclopentenophenanthrene derivative with a side-chain of two isoprene units which contain the two oxygen atoms. My interpretation of the result of the thermal decomposition definitely precludes the possibility, frequently discussed, that α-tocopherol is related to the sterols. These authors obviously neglected the fact that the selenium remains nearly unchanged during the experiment, and it is thus quite clearly a purely thermal reaction. In their hands the primarily formed durohydroquinone then suffered complete autoxidation.

The thermal decomposition was repeated successfully in other laboratories. Todd, Bergell, Waldmann and Work[5] repeated it on concentrates, and more recently an interesting contribution has appeared from Windaus' laboratory in Göttingen[6] which has a direct connection with the subject although it deals chiefly with another factor of the vitamin E group which was isolated from wheat germ oil by John. This new compound was named "cumo-"tocopherol because it gave "pseudocumo"-hydroquinone (III) on thermal decomposition. The analysis indicates an empirical formula $C_{28}H_{48}O_2$, and its close relationship to α-tocopherol is obvious. This substance is very probably identical with Karrer's[7] neo-tocopherol and β- or γ-tocopherol[8]



III

It appears from John's article that he accepts the assumption that α-tocopherol and, therefore, also cumo-tocopherol, are mono-ethers of durohydroquinone or trimethylhydroquinone, respectively. In his opinion, there is a close resemblance between these compounds and a mono-ether of durohydroquinone, particularly in their behavior toward oxidizing reagents.

In this Laboratory, J. Finkelstein has prepared the *s*-butyl, dodecyl, cetyl, octadecyl, 2-methyl-*n*-octadecyl-(1), and *n*-nonadecyl-(2) mono ethers

(1) Fernholz, THIS JOURNAL, **59**, 1154 (1937).
(2) Evans, Emerson and Emerson, *J. Biol. Chem.*, **113**, 319 (1936).
(3) This formula was misprinted in my previous article.[1]
(4) McArthur and Watson, *Science*, **86**, 35 (1937); *Can. Med. Assoc. J.*, **37**, 289 (1937); *Am. J. Pharm.*, **110**, 548 (1937).
(5) Todd, Bergel, Waldmann and Work, *Nature*, **140**, 361 (1937).
(6) W. John, *Z. physiol. Chem.*, **250**, 11 (1937).
(7) P. Karrer, H. Salomon and H. Fritzsche, *Helv. Chim. Acta*, **20**, 1422 (1937).
(8) O. H. Emerson, G. A. Emerson, A. Mohammad and H. M. Evans, *J. Biol. Chem.*, **122**, 99 (1937).

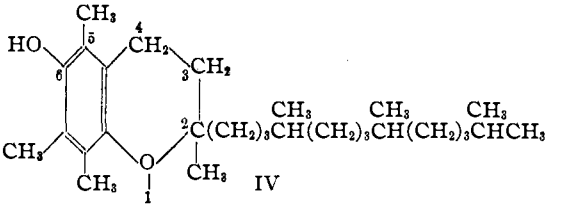
of durohydroquinone, melting points 85–86, 93–94, 101, 105, 94–95, 94–95°, respectively, with the object of finding substances which closely resembled the tocopherols in chemical behavior. Full details of the preparation of these ethers will be given in a succeeding paper. The spectrum of a typical representative, in comparison with that of α-tocopherol, is shown in Fig. 1.

The ethers all have in common a spectrum which is quite different from that of α-tocopherol. α-Tocopherol has its maximum of absorption at 2900–3000 Å., $E^{1\%}_{cm.}$ 73,[8] whereas the ethers of durohydroquinone of similar molecular weight have a maximum at 2800–2850 Å., $E^{1\%}_{cm.}$ 50. The absorption is in a region of shorter wave lengths and very much less in intensity.

The mono-ethers of durohydroquinone reduce a silver nitrate solution much more slowly than α-tocopherol, and they are oxidized to duroquinone. On the other hand, α-tocopherol gives a red oil with a very characteristic absorption spectrum with the same reagent[3] and this red compound seems to have approximately the same molecular weight as α-tocopherol. The fact that duroquinone is not split off during this oxidation suggests that the alkyl portion is connected with the aromatic ring not only by means of an ether bond, but also by a carbon bridge. α-Tocopherol would then be derived from chromane or coumarane. This hypothesis also was supported by the failure of all the more common ether splitting reagents to bring about the formation of durohydroquinone.

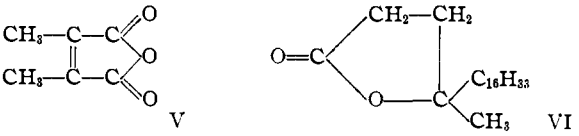
Only aluminum bromide gave traces of duroquinone, while hydriodic acid with which John obtained cleavage was quite unsuccessful in my hands. These observations are not in conformity with an ether structure for α-tocopherol, an assumption to which J. C. Drummond and A. A. Hoover[9] have taken objection, since they were unable to explain surface film measurements on that basis.

While all these observations hardly can be considered to be more than suggestive, oxidation experiments have led to results which gave definite evidence in favor of such a heterocyclic ring structure. The oxidation products, however, are not easily explained on the basis of a coumarane structure. They indicate a chromane structure, and it is believed that α-tocopherol can now be represented by formula IV.



IV

When α-tocopherol was oxidized with chromic acid under mild conditions the main products isolated were dimethylmaleic anhydride (V), and a lactone $C_{21}H_{40}O_2$ (VI). The dimethylmaleic anhydride is derived from the aromatic portion of the molecule, giving new support for its relation to durene. The lactone, $C_{21}H_{40}O_2$, is derived from the aliphatic part and its empirical composition was established with great care. It is a liquid, but the corresponding hydroxy acid forms a crystalline benzylthiuronium salt,[10] m. p. 120°, which can be purified easily. The free hydroxy acid relactonizes readily, thus indicating that the hydroxyl group is in either the γ- or δ-position. A δ-lactone is improbable, because the ring containing the original ether bridge would have to be seven-membered. A coumarane system, on the other hand would yield a β-hydroxy acid. The formation of a lactone with 21 carbon atoms could not be explained on the assumption that α-tocopherol is a mono-ether of durohydroquinone with an alcohol



V VI

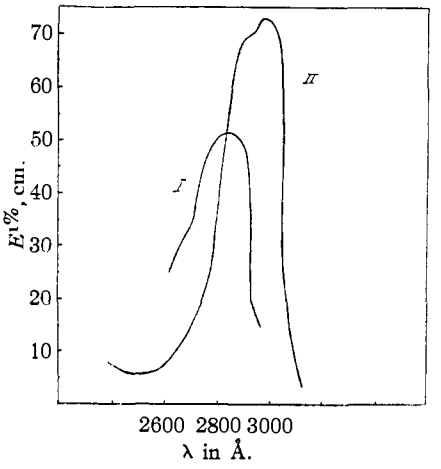


Fig. 1.—I Mono-*n*-nonadecyl-(2) ether of durohydroquinone (T. J. Webb); II, α-tocopherol (Emerson, *et al.*[8]).

(9) J. C. Drummond and A. A. Hoover, *Biochem. J.*, **31**, 1857 (1937).

(10) John J. Donleavy, THIS JOURNAL, **58**, 1004 (1936).

$C_{19}H_{38}O$, and it would even be difficult to explain the smooth formation of a lactone with nineteen carbon atoms or less. It also must be remembered that such a lactone should have an isocyclic ring while the lactone actually obtained is purely aliphatic. The values for the analysis do not agree with a formula having two hydrogens less. It is believed that the isolation of the lactone $C_{21}H_{40}O_2$ in good yields makes the ether theory quite untenable, while it strongly supports the assumption that α-tocopherol is a substituted chromane.

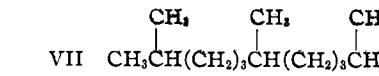
The lactone has one or more asymmetric centers since the thiuronium salt mentioned above is optically active. A methyl ester of the hydroxy acid can be prepared by refluxing a methanol solution of the lactone after the addition of sulfuric acid. This derivative was used to determine the nature of the hydroxyl group. It could not be esterified and proved to be fairly stable to chromic acid. By warming, oxidation could be enforced and with one available oxygen, a part of the material is broken up while a large portion remains unchanged. This indicates that the hydroxyl is tertiary.

The structure VI assigned to this lactone was derived from a study of other degradation products, which were obtained besides the lactone when the oxidation of α-tocopheryl acetate was carried out under somewhat more drastic conditions. The oxidation was carried out with a larger excess of chromic acid in boiling acetic acid solution. Among the volatile products, *diacetyl* and *acetone* were identified as *p*-nitrophenylhydrazones. While the former compound is derived from the aromatic ring, the latter comes from the aliphatic part, and proves the presence of an isopropyl residue.

From the acid fraction, an acid $C_{16}H_{32}O_2$ could be isolated by means of the *p*-phenylphenacyl ester,[11] m. p. 49°. The empirical formula was substantiated by the analysis of a benzyl-thiuronium salt of m. p. 146° and by titration.

C-Methyl determinations were carried out with the *p*-phenylphenacyl ester by Mr. Hayman of this Laboratory. Two molecules of acetic acid were obtained and since the theoretical yield is not obtained from saturated substances, the presence of at least three such groups seems to be assured. By applying the frequently successful isoprene scheme, formula VII is proposed for the acid $C_{16}H_{32}O_2$.

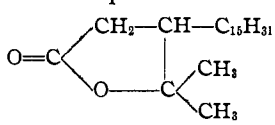
(11) N. L. Drake and J. Bronitsky, THIS JOURNAL, **52**, 3715 (1930).



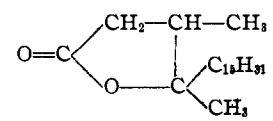
VII

Such an acid could be prepared from its homolog now available from ammoresinol.[12] Unfortunately the acid from α-tocopherol was found to be optically active, so that comparison can be made only after a successful resolution of the racemic form.

The formation of an acid with sixteen carbon atoms limits the number of possible structures for the lactone. To account for the formation of durohydroquinone, there can be no substituent on C_4 of α-tocopherol, and, since the γ-hydroxy acid has a tertiary hydroxyl group, three structures remain for discussion: VI, VIII, and IX. Formula IX is improbable since, because an acid $C_{15}H_{30}O_2$



VIII



IX

would be expected on degradation, and both VIII and IX are ruled out by the production of a neutral degradation product, a ketone $C_{18}H_{36}O$. Such a ketone could however, also be formed from α-tocopherol if there were were an ethyl group on C_2, but this possibility seems to be more remote. This ketone is formed in small amounts, as compared with the acid. It could not be isolated as such, since it did not react with ketone reagents. This is unexpected since an optically inactive ketone of the same structure has been described in the literature[12] and forms a semicarbazone. The presence of such a ketone among the neutral oxidation products was demonstrated by the formation of an alcohol on hydrogenation with sodium and alcohol. The alcohol was identified by a crystalline dinitrobenzoate, m. p. 103°. Formulas VIII and IX can explain the formation of a C-17 ketone, but the analyses are inconsistent with such a formula.

On the basis of the above evidence, structure VI is proposed for the lactone and structure IV for α-tocopherol, which is thus represented as a substituted 6-hydroxychromane.

It is hoped that the degradation products here described will be of use in establishing the relationship of the other tocopherols with α-tocopherol. A most important line of investigation is, however, the synthesis of such compounds, and a program along these lines has been in progress in this Laboratory for some time.

(12) E. Späth, A. F. J. Simon and J. Lintner, *Ber.*, **69**, 1668 (1936).

Experimental

Thermal Decomposition of α-Tocopherol.—The decomposition was carried out in a small retort, the neck of which was bent to serve as receiver of liquid products, and it had an inlet tube for carbon dioxide and was connected with an azotometer. The α-tocopherol (2.1 g.) was placed in the retort and the bulb immersed in a potassium–sodium nitrate bath as soon as the air was completely replaced. The temperature of the bath was kept at 355° for six hours; 15 cc. (0.33 mole) of a combustible gas collected in the azotometer in that time. A crystalline sublimate and a red liquid collected in the neck. There was some black tar left in the bulb of the retort.

The neck of the retort was cut off and the material washed off with petroleum ether; 0.257 g. (67%) of durohydroquinone was obtained.

Its identification by means of the diacetate and quinone and their analysis have been reported already.[1]

The liquid fraction, diluted with 100 cc. of petroleum ether, was passed through a column of activated aluminum oxide, 20 cm. long. It was washed thoroughly with the same solvent. The petroleum ether left on evaporation 1.17 g. of a colorless liquid, which was distilled at 0.02 mm. and a bath temperature of 110°. *Anal.* Calcd. for $C_{19}H_{36}$: C, 86.29; H, 13.72; mol. wt., 264.5. Calcd. for $C_{18}H_{36}$: C, 85.62; H, 14.37; mol. wt., 252.5. Found: C, 85.49, 85.47; H, 15.24, 14.20; mol. wt., 241, 263.

Titration with Perbenzoic Acid.—A sample of the hydrocarbon was kept with an excess of a chloroform solution of perbenzoic acid for two days, and another sample for five days. There was no measurable addition of oxygen in the first case and only 0.2 mole had been used up in the second experiment.

Titration with Bromine.—To 0.5743 g. of the hydrocarbon there was added 10 cc. of an approximately *N*/3 bromine solution in carbon tetrachloride. The sample and a blank were kept for twenty hours and then titrated with 0.1 *N* thiosulfate after addition of potassium iodide solution. A solution of potassium iodate was then added and the iodine liberated by hydrogen bromide titrated also.

Total consumption of bromine	0.358 g.
Substituted bromine	.044 g.
Additive bromine	0.314 g.

This amounts to 0.86 mole if the calculation is based on the formula $C_{19}H_{36}$ for the hydrocarbon, an assumption which may not be quite correct.

Oxidation of α-Tocopherol.—α-Tocopherol (4.3 g., 0.01 mole) was dissolved in 50 cc. of glacial acetic acid. To this solution was added in portions and at room temperature a solution of 7 g. of chromium trioxide in 10 cc. of water and 60 cc. of acetic acid. After the addition was completed the mixture was heated on the steam-bath for one-half hour.

The acetic acid solution was diluted with water and extracted with ether. The ether was washed several times with water to remove acetic acid as far as possible, and then washed with dilute sodium hydroxide to extract acidic substances. The alkali extract was acidified with hydrochloric acid and the organic acids taken up with ether. The ether left behind 1.0 g. of a crystalline residue. The crystalline material was separated from oily material by sublimation at 100° (0.02 mm.), the receiver being cooled with solid carbon dioxide; 0.33 g. (26%) of dimethylmaleic anhydride was thus isolated, m. p. 94° after recrystallization from petroleum ether. *Anal.* Calcd. for $C_6H_6O_3$: C, 57.14; H, 4.80. Found: C, 57.31; H, 4.79.

The fraction freed from acidic products was boiled for an hour with 25 cc. of *N* potassium hydroxide in alcohol. The mixture turned very dark. It was diluted with water and extracted with ether. The ether left 0.42 g. of a neutral residue. The alkali solution was acidified and extracted with ether, and 2.26 g. of lactonic fraction was obtained. The crude lactone was distilled at a bath temperature of 170–200°, 0.02 mm. About 0.5 g. of tar remained. The distillate was dissolved in 20 cc. of alcohol and *N* sodium hydroxide added until the solution stayed alkaline after heating on the steam-bath for an hour; 0.1 *N* hydrochloric acid was then added to discharge the color of phenolphthalein and 1.5 g. of benzyl-thiuronium chloride dissolved in hot alcohol was added. Water was added until the solution became cloudy. Crystals soon began to appear and they were filtered after the solution had been kept in an ice-box for an hour. The crude salt was dried in a desiccator and recrystallized from acetone and obtained as white needles, m. p. 120°. It is quite soluble in hot alcohol but less soluble in acetone; yield 1.6 g. (31.4%). *Anal.* Calcd. for $C_{27}H_{48}O_3N_2S$: C, 67.46; H, 10.06; N, 5.83. Calcd. for $C_{29}H_{52}O_3N_2S$: C, 68.45; H, 10.30; N, 5.50. Found: C, 68.61, 68.45; H, 10.26, 10.30; N, 5.30, 5.50. 0.1737 g. in 10 cc. of absolute alcoholic solution, α_D +0.08°, $[\alpha]^{22}D$ +4.6°.

The thiuronium salt was decomposed with hydrochloric acid, taken up with ether, and distilled at a bath temperature of 130° and 0.02 mm. pressure. *Anal.* Calcd. for $C_{20}H_{38}O_2$: C, 77.36; H, 12.33; equiv. wt., 310.5. Calcd. for $C_{21}H_{38}O_2$: C, 78.20; H, 11.88; equiv. wt., 322.5. Calcd. for $C_{21}H_{40}O_2$: C, 77.72; H, 12.42; equiv. wt., 324.5. Found: C, 77.56, 77.67; H, 12.37, 12.30; equiv. wt., 316.9. For the determination of the equivalent weight a sample of 0.5846 g. was refluxed for one hour in a Pyrex flask with 40 cc. of 0.0959 *N* alcoholic potassium hydroxide. The same amount of potassium hydroxide was refluxed in a similar flask, and the consumed alkali determined by difference.

To prepare the methyl ester of the hydroxy acid, 1.0 g. of the lactone was dissolved in 30 cc. of absolute methanol, 0.5 cc. of concd. sulfuric acid was added, and the mixture refluxed for two hours. The ester was isolated by means of ether extraction and distilled (140° at 0.02 mm.). *Anal.* Calcd. for $C_{21}H_{42}O_3$: OCH_3, 9.06. Calcd. for $C_{22}H_{44}O_3$: OCH_3, 8.70. Found: OCH_3, 8.86.

Oxidation of the Methyl Ester.—The methyl ester (0.79 g.) was dissolved in 30 cc. of acetic acid and a solution of 0.17 g. of CrO_3 (=1.10) was added at room temperature. The next day the color of the mixture still indicated a large excess of chromium trioxide. The solution was then heated on the steam-bath and after thirty minutes the reaction for chromic acid was very weak. The material was divided into neutral, acidic and lactonic fractions. The lactonic portion gave 0.6 g. of the thiuronium salt of the hydroxy acid. There were only traces of acidic degradation products.

Oxidation of α-Tocopheryl Acetate.—Twenty-five grams of α-tocopheryl allophanate was hydrolyzed with methyl alcoholic potassium hydroxide, and the tocopherol obtained was then acetylated by boiling it with 100 cc. of acetic anhydride for an hour. The acetic anhydride was decomposed with water, the acetate extracted with ether and dissolved in 250 cc. of acetic acid. This solution was heated to boiling in an oil-bath having a temperature of 140–150°. A solution of 75 g. of chromium trioxide in 250 cc. of water and 250 cc. of acetic acid was added slowly to the boiling solution and the volatile substances were distilled off simultaneously. After having completed the addition of chromic acid, 250 cc. of 2 *N* sulfuric acid was dropped into the mixture and the distillation continued. The whole procedure required four hours.

The distillate (500 cc.) was kept in a separatory funnel to allow separation of oily drops having an odor resembling that of methyl isohexyl ketone. The odor of this ketone disappeared on treatment with semicarbazide, but no solid derivative could be isolated.

A solution of 3 g. of *p*-nitrophenylhydrazine in acetic acid was then added to the distillate and a red precipitate appeared on short standing. It was filtered after an hour and recrystallized from pyridine, which seemed to be the only solvent in which the substance was sufficiently soluble: dark red needles, m. p. 330°, with decomposition; yield 0.36 g. This compound was expected to be the *di-p-nitrophenylhydrazone of diacetyl* which does not seem to be recorded in the literature. This derivative was therefore prepared from diacetyl and found to be identical. *Anal.* Calcd. for $C_{16}H_{16}N_6O_4$: N, 23.58. Authentic specimen, found: N, 23.59, 23.46. Unknown specimen, found: N, 23.40, 23.59.

The filtrate of the osazone of diacetyl was made strongly acidic with sulfuric acid and 150 cc. was distilled off. A solution of 1 g. of *p*-nitrophenylhydrazine in some acetic acid was added to the distillate and caused a voluminous, yellow precipitation. It was filtered after an hour; yield 0.5 g. The hydrazone was recrystallized from benzene–petroleum ether and obtained in the form of flat, yellow needles melting at 148°. It was found to be identical with *acetone p-nitrophenylhydrazone* by direct comparison. *Anal.* Calcd. for $C_9H_{11}O_2N_3$: C, 55.95; H, 5.74. Found: 56.00, 55.94; H, 5.44, 5.53.

The degradation products not volatile with steam were isolated with ether and divided into the three chief groups, acids (6.1 g.), lactone (5.1 g.) and neutral (2.1 g.), in the manner fully described above.

The Acid Fraction.—Six and one-tenth grams was dissolved in alcohol and neutralized with *N* sodium hydroxide. A solution of 4.5 g. of barium acetate in water was added and a barium soap came out. The supernatant liquid was decanted after a day of standing in the ice-box. The barium salt was dissolved in ether and decomposed with hydrochloric acid. The acid (4.8 g.) was then distilled at a bath temperature of 150° and 0.02 mm. pressure. The distillate weighed 4.4566 g. and was titrated with *N* sodium hydroxide, giving an equivalent weight 334. A solution of the calculated amount of *p*-phenylphenacyl bromide (3.69 g.) in alcohol was added, and the mixture refluxed for two hours. The ester was extracted with ether, and washed with sodium carbonate solution. The crude ester was dissolved in 50 cc. of alcohol and the solution cooled with solid carbon dioxide for a few days. The crystalline material was then filtered and recrystallized from the same solvent. After five crystallizations the ester was obtained pure; yield 1.53 g. It forms leaflets, m. p. 49°, fairly soluble in all organic solvents. 23.0 mg. in 2.5 cc. chloroform solution, α_D −0.05°, $[\alpha]^{24}D$ −8.7°. *Anal.* Calcd. for $C_{30}O_{40}O_3$: C, 80.31; H, 8.99. Calcd. for $C_{30}H_{42}O_3$: C, 79.95; H, 9.39. Found: C, 79.95, 79.98, 80.09, 80.12; H, 9.34, 9.36, 9.30,[13] 9.46.[13] C-Methyl determinations gave 6.55, 6.60% CH_3. Calcd. for $C_{30}H_{42}O_3$: 9.99% (3 CH_3), 6.66% (2 CH_3).

The acid is best prepared by first converting the *p*-phenylphenacyl ester into the methyl ester and saponifying the latter with alcoholic potassium hydroxide. To a solution of 0.5 g. of the *p*-phenylphenacyl ester in 30 cc. of methanol, 5 drops of concentrated sulfuric acid was added, and the mixture refluxed for one hour. The solution was diluted with water and extracted with ether. The ether residue was digested with 30 cc. of petroleum ether, which leaves *p*-phenylbenzoylcarbinol largely undissolved. The residue was removed by filtering the solution through a layer of charcoal: petroleum ether residue, 0.2895 g.; calculated 0.311 g. The methyl ester was then saponified with alcoholic potassium hydroxide in the usual way and 0.268 g. of an oily acid was obtained. This acid was distilled at a bath temperature of 140°, pressure 0.02 mm.: 97.8 mg. consumed 3.12 cc. of 0.121 *N* sodium hydroxide. Calcd. for $C_{16}H_{32}O_2$: 256.4. Found: 259.1.

The acid forms an unstable, insoluble silver salt. The amide could not be obtained in crystalline form, the *benzyl-thiuronium salt* was, however, obtained easily in crystalline form.

The solution of 0.2683 g. in 10 cc. of alcohol was neutralized with *N* sodium hydroxide and a solution of 0.22 g. of benzyl-thiuronium chloride in 2 cc. of hot alcohol added. The same volume of water was then added and the salt soon crystallized. It was recrystallized from aqueous alcohol, a procedure which causes some decomposition, and from acetone. It forms small leaflets, m. p. 146°, and is very soluble in absolute alcohol, methanol and dioxane. *Anal.* Calcd. for $C_{25}H_{44}O_2N_2S$: C, 68.76; H, 10.15; N, 6.41. Calcd. for $C_{25}H_{42}O_2N_2S$: C, 69.06; H, 9.74; N, 6.44. Calcd. for $C_{24}H_{42}O_2N_2S$: C, 68.20; H, 10.01; N, 6.53. Found: C, 68.30, 68.23; H, 10.04, 10.09; N, 6.32, 6.44.

The Neutral Oxidation Products.—The neutral oxidation products (2.1 g.) were distilled at a pressure of 0.02 mm. and a bath temperature of 110°. One gram of a colorless distillate was obtained. Experiments were made to obtain a nitrophenylurethan or an oxime, but with negative results. The recovered substance was dissolved in 20 cc. of absolute alcohol and hydrogenated with 2 g. of sodium, added in portions. The products isolated with ether were dissolved in 30 cc. of dry pyridine and treated on the steam-bath with 2 g. of *m*-dinitrobenzoyl chloride. The dinitrobenzoate, isolated by extraction with ether, was dissolved in a small amount of acetone and some methanol added to reduce the solubility. The flask was kept in dry-ice and crystallization set in after a few days.

(13) These analyses were carried out by Dr. C. Tiedcke, New York. All other determinations were made in this Laboratory by Messrs. Hayman and Reiss.

The dinitrobenzoate was purified by crystallization from alcohol and obtained as small leaflets, m. p. 101–103°; yield about 0.1 g. *Anal.* Calcd. for $C_{26}H_{42}O_6N_2$: C, 65.24; H, 8.85. Calcd. for $C_{26}H_{40}O_6N_2$: C, 65.52; H, 8.46. Calcd. for $C_{25}H_{40}O_6N_2$: C, 64.63; H, 8.68. Found: C, 64.74, 64.55; H, 8.77, 8.91.

Summary

1. The thermal decomposition of α-tocopherol, leading to the formation of durohydroquinone and an unsaturated, aliphatic hydrocarbon, has been described.

2. A study of the degradation products obtained by oxidation with chromic acid has been reported.

These degradation products, isolated as such or in form of derivatives, are: acetone, diacetyl, dimethylmaleic acid, an acid $C_{16}H_{32}O_2$, a lactone $C_{21}H_{40}O_2$, a ketone $C_{18}H_{36}O$.

3. A structural formula is proposed for α-tocopherol derived from these degradation experiments.

α-Tocopherol is regarded as a substituted 6-hydroxychromane with a long aliphatic side chain attached to the pyran ring.

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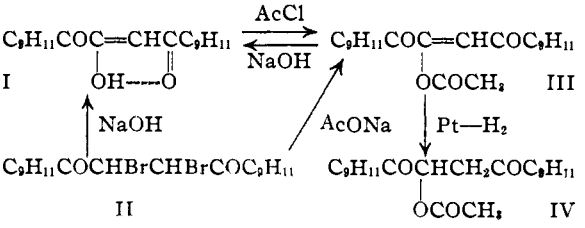
[CONTRIBUTION FROM THE COBB CHEMICAL LABORATORY OF THE UNIVERSITY OF VIRGINIA]

1,4-Dimesityl-1,2,4-butanetrione Enol and its Reduction Products

BY ROBERT E. LUTZ AND JOHN L. WOOD

In the light of recent work on the tautomerism of the 1,2,4-triketones and their reactions as open chain enols or as hydroxyfuranones, it seemed of interest to extend the studies on dimesitylbutanetrione enol, particularly because one would expect a marked influence of the mesityl groups not only on the reactivity of the systems involved but also on the tendency or ability to undergo cyclization.

Dimesitylbutanetrione enol, I, may be prepared either by the action of alcoholic alkali on di-(trimethylbenzoyl)-dibromoethane[1] (II) or by rearrangement of di-(trimethylbenzoyl)-ethylene oxide.[2] The ketonic form of this compound is at present unknown.[3] The enol reacts rapidly with bromine, diazomethane and ferric chloride, and is a relatively strong acid as shown by the fact that the sodium salt is precipitated when a petroleum ether solution is shaken with aqueous sodium carbonate. In contrast with the diphenyl analog it is not etherified with alcohol and acids, and there is at present no evidence to indicate that it can undergo cyclization to a hydroxyfuranone type. It does not undergo the quinoxaline reaction but it reacts readily with ketone reagents and gives a monoxime, a semicarbazone, and a 2,4-dinitrophenylhydrazone. The enol is converted by acetyl chloride and pyridine into an enol acetate in contrast with the diphenyl analog which gives the acetoxyfuranone under these conditions. The structure of the enol acetate is evident from analysis and acetyl determination, synthesis by the action of sodium acetate on di-(trimethylbenzoyl)-dibromoethane, II,[1a,3] and catalytic reduction to the acetate of di-(trimethylbenzoyl)-hydroxyethane, IV.



I $C_9H_{11}COC{=}CHCC_9H_{11}$ (OH---O)

III $C_9H_{11}COC{=}CHCOC_9H_{11}$ ($OCOCH_3$)

II $C_9H_{11}COCHBrCHBrCOC_9H_{11}$

IV $C_9H_{11}COCHCH_2COC_9H_{11}$ ($OCOCH_3$)

We have for convenience written the structure of the enol as I since reaction occurs largely in this sense upon acylation or on methylation with diazomethane. The latter reaction gives chiefly the yellow *trans*-di-(trimethylbenzoyl)-methoxyethylene, from which the colorless *cis* isomer has been made.[1b] However, on repetition of the experiments with diazomethane, two new yellow methyl ethers have been isolated in small amounts. These are evidently a stereoisomeric pair since the higher melting of the two (the labile and probably *cis* form) can be converted practically quantitatively into the lower melting, stable (and presumably *trans*) form by heating with alcoholic potassium hydroxide, exposing to sunlight in alcohol solution, or distilling *in vacuo*. The two new ethers are structurally isomeric with the two previously known ethers, and must be derivatives of the tautomeric enol form V. This was proved by

(1) Lutz, THIS JOURNAL, (a) **48**, 2905 (1926); (b) **56**, 1590 (1934).

(2) Lutz and Wood, *ibid.*, **60**, 229 (1938).

(3) The supposed keto form previously reported,[1a] prepared by the action of sodium acetate on di-(trimethylbenzoyl)-dibromoethane, is in reality the enol acetate III (see experimental part).