

This would also be true if, in the partial hydrolysis from cellulose triacetate, the loss of acetyl from either one of the two positions tended to stabilize the adjacent group in the same anhydroglucose residue.

### Experimental

**Materials.**—The acetone soluble cellulose acetate was from the batch previously studied<sup>3</sup> and the triacetate was made from it by careful acetylation with pyridine and acetic anhydride. Both were dried over phosphorus pentoxide in a vacuum at 55°.

The chloroform was washed with water and distilled from phosphorus pentoxide while the glacial acetic acid was distilled from chromic anhydride to free it from any aldehyde.

**Oxidation with Lead Tetraacetate.**—The cellulose acetate, 2.6 g. or 0.01 mole, was dissolved completely in 25 cc. of glacial acetic acid contained in a 100-cc., glass-stoppered volumetric flask. An approximately decinormal solution of lead tetraacetate in the same solvent, 25 cc., was then added at 25° and the volume made up to the mark. The viscid solution required prompt and thorough mixing, after which it was kept at 25 ± 0.5° in the dark. Samples were withdrawn at intervals in a 10-cc. pipet and discharged into 20 cc. of an aqueous solution containing 20 g. of potassium iodide and 250 g. of sodium acetate per liter. The pipet was rinsed well with 5 cc. of the acetic acid and after the addition of the rinsings the liberated

iodine was titrated with *N*/100 sodium thiosulfate.<sup>5</sup> Vigorous shaking of the heterogeneous mixtures was necessary during the titrations, which took about five minutes each to complete. The blank on the reagents remained constant at 37.5 cc. of thiosulfate throughout the experiment. Differences from the blank are plotted as the right-hand ordinate in Fig. 1 and at the break in the curve (eighty hours) the 1 millimole sample of cellulose acetate utilized about 2 cc. of *N*/100 sodium thiosulfate. This corresponded to 10<sup>-5</sup> mole of lead tetraacetate or of glycol. The results of precisely similar experiments, carried out in chloroform-acetic acid solution, are mentioned in the Introduction.

### Summary

A commercial acetone soluble cellulose acetate had an average of 0.35 to 0.45 mole of unesterified hydroxyl distributed between the second and third positions of the anhydroglucose units. The unsubstituted —CHOH—CHOH— or glycol groupings it contained were estimated, by means of lead tetraacetate, to occur not more frequently than once in a hundred glucose residues. A significantly greater frequency of once in twenty to thirty was calculated by assuming a purely random distribution of hydroxyl between the two positions.

CAMBRIDGE, MASS.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF FISK UNIVERSITY]

## Ricinus communis. I. Oxidation of Ricinoleic Acid

BY ST. ELMO BRADY

The oxidation of ricinoleic acid, its ethyl ester and its isomer, ricinelaic acid, as well as some of their oxidation products, the trihydroxystearic acids and the *n*-aldehydo-octanoic acid has been studied and the experimental results obtained in these studies are presented in this communication.

### Experimental Part

(a) **Preparation and Purification of Ricinoleic Acid and Derivatives.**—The castor oil was saponified with alcoholic potassium hydroxide, the excess alcohol removed, the potassium salt dissolved in water and the solution exhausted with ether to remove the unsaponifiable materials. These will be the subject of a future investigation. The free fatty acids were liberated with dilute hydrochloric acid, collected and allowed to stand for two days during which time the insoluble acids separated and were removed. The free fatty acids were mixed with an equal volume of alcohol and cooled below zero for several days, when another small portion of insoluble acids separated. The free fatty acids were again converted into the sodium salts using approximately the calculated weight of pure

sodium hydroxide dissolved in alcohol. After the removal of the solvent and dilution with water a practically clear solution remained. The barium salt was precipitated from this solution, filtered, dried and refluxed with ether to remove any soluble barium salt present. Several recrystallizations of the barium ricinoleate from alcohol finally gave a white crystalline product that analyzed pure.

The dry salt was suspended in ether and carefully decomposed with dilute hydrochloric acid. After washing thoroughly and drying the ethereal solution over anhydrous sodium sulfate, the solvent was removed in a vacuum desiccator by the aid of the pump. Especial care was exercised not to heat the acid since it polymerizes very easily even at a temperature of 40°. The acid so prepared was of a very slight yellowish tinge, somewhat viscous and perfectly clear. It solidified in the refrigerator at 3–4° to a white waxy solid which melted approximately at 5°.

*Anal.* Calcd. for C<sub>18</sub>H<sub>34</sub>O<sub>3</sub>: iodine no., 85.1. Found: iodine no., 85.0, 85.1.

**Preparation of the Ethyl Ester of Ricinoleic Acid.**—The pure ricinoleic acid was dissolved in twice the volume

of absolute alcohol and the temperature reduced to near  $0^{\circ}$  in a freezing mixture. A stream of dry hydrogen chloride was introduced slowly until the solution was saturated. The solution was then allowed to stand overnight at room temperature. The alcohol was washed out of the solution and the residue taken up with ether. The ethereal solution was shaken several times with a dilute solution of potassium hydroxide, washed with water and dried over anhydrous sodium sulfate. After the removal of the solvent, the ethyl ricinoleate was distilled under reduced pressure and collected at  $193\text{--}194^{\circ}$  (1–2 mm.) or  $206^{\circ}$  (3–4 mm.). The ester so prepared is water clear.

*Anal.* Calcd. for  $C_{20}H_{38}O_2$ : iodine no., 77.91. Found: iodine no. (Hanus), 77.92, 77.93. Refractive index,  $n_D^{20}$  1.4595,  $n_D^{25}$  1.4590. Specific gravity  $20^{\circ}/20^{\circ}$ , 0.9182.

**Preparation of the Ethyl Acetylricinoleate.**—The ethyl ricinoleate (50 g.) as described above was dissolved in 70 cc. of chloroform, 30 cc. of pyridine added and the solution cooled to  $0^{\circ}$  in a salt-ice-bath. A slight excess of acetyl chloride was introduced carefully and the solution allowed to remain at the temperature of the bath for two hours and then overnight at room temperature. The excess acid chloride and pyridine were washed out with water, the residue taken up in ether, dried over anhydrous sodium sulfate and the solvent removed. The acetyl derivative was distilled under reduced pressure and collected at  $196^{\circ}$  (2–3 mm.); refractive index,  $n_D^{20}$  1.452; iodine no., 69.1; theoretical, 69.02.

(b) **Oxidations.** (1) **Ethyl Ricinoleate: with Neutral Potassium Permanganate.**—Fifty grams of the ester was dissolved in 350 cc. of dry acetone and 200 g. of finely powdered potassium permanganate added during the course of an hour, the solution being refluxed gently during the addition and finally for fifteen hours.

The solvent was then removed, the residue mixed with water and the precipitated oxides of manganese brought into solution by the action of sulfuric acid and sodium bisulfite. After cooling, the acid solution was exhaustively extracted with ether.

The ethereal extract was washed, then repeatedly extracted with sodium carbonate solution (20%) and the combined alkaline extracts shaken with ether to remove any suspended neutral products.

The ethereal solution from the alkaline extract was washed with water, dried, the solvent removed and the resulting oil cooled. The neutral substances amounted to 7.1 g. The odor was somewhat aromatic and pleasant.

**Separation of the Acid Products.**—The sodium carbonate extract was treated with solid sodium hydroxide dissolved in a little water and heated under the reflux for an hour. This ensured the conversion of any esters into the sodium salts. The cooled solution was acidified and extracted with ether several times. After the removal of the solvent, the residue partially solidified on cooling and amounted to 40.7 g.

The mixture of solid acids was refluxed with five successive portions of petroleum ether (b. p.  $40\text{--}60^{\circ}$ ), employing 150 cc. of solvent each time, for one-half hour. The undissolved acids were of a light yellow color and amounted to 22.0 g. About 0.4 g. of solid acid was deposited from the light petroleum which was filtered before the removal of the solvent.

There were 17.1 g. of liquid acids remaining after the evaporation of the petroleum ether. This material was fractionated under reduced pressure several times and the following fractions finally obtained. Fraction 1, b. p.  $84\text{--}85^{\circ}$  (3 mm.), was a colorless, limpid liquid. Calcd. for  $C_9H_{18}O_2$ : Ag, 48.40; mol. wt., 116. Found: Ag, 48.23; neut. equiv., 128; caproic acid. Fraction 2, b. p.  $90\text{--}95^{\circ}$  (3 mm.), was a colorless liquid, slightly viscous. Calcd. for  $C_7H_{14}O_2$ : Ag, 45.54; mol. wt., 130. Found: Ag, 45.37; neut. equiv., 128; heptylic acid. Fraction 3, b. p.  $95\text{--}100^{\circ}$  (3 mm.), colorless liquid. Calcd. for  $C_8H_{16}O_2$ : Ag, 43.00; mol. wt., 147. Found: Ag, 42.87; neut. equiv., 146.8, 146; caprylic acid. Fraction 4, b. p.  $159\text{--}160^{\circ}$  (3 mm.), was a colorless liquid which solidified to a white solid at room temperature. It was recrystallized from petroleum ether and separated in large glistening plates, m. p.  $49\text{--}50^{\circ}$ . Calcd. for  $C_9H_{18}O_2$ : C, 62.06; H, 10.34; mol. wt., 174. Found: C, 62.15; H, 10.40; mol. wt. (Rast), 176;  $\beta$ -hydroxypelargonic acid.

**Purification of the Insoluble Acids.**—The crude product insoluble in petroleum ether was dissolved in hot water, filtered from a small quantity of impurities and then heated with decolorizing charcoal. The final filtrate was water-clear and deposited, on cooling, fine needles of m. p.  $95^{\circ}$ . The crystals had the odor of one of the liquid acids which seemed to persist after several recrystallizations, even though the melting point increased to  $104^{\circ}$ . To remove this persistent odor, the crystals were refluxed with petroleum ether and filtered hot. The large glistening crystals now had no odor and melted at  $106\text{--}107^{\circ}$ . Further recrystallization did not raise the melting point.

*Anal.* Calcd. for  $C_9H_{16}O_4$ : Ag, 53.70; mol. wt., 188. Found: Ag, 53.82; neut. equiv., 94; mol. wt. (Rast), 190; azelaic acid.

The dianilide of azelaic acid was prepared and melted at  $186.5\text{--}187^{\circ}$ .

The aqueous filtrate from the above crystallization was evaporated to a small bulk and cooled. A white amorphous solid separated which was removed and dried. This was recrystallized from hot water when small granular crystals separated, m. p.  $125\text{--}126^{\circ}$ . These crystals were thought to contain possibly a small amount of stearic acid and were therefore refluxed with benzene, in which the latter is soluble. On filtering and drying the crystals no increase was noted in the melting point. Because of the variation in the analytical data, the product was recrystallized several times from hot water without any change in the melting point. The crystals were then dissolved in a sufficient volume of ether for the solution and cooled in the refrigerator at  $3\text{--}4^{\circ}$  when a separation of crystals took place. These were filtered off and the solution again cooled for twelve hours when a second crop of crystals was obtained. The solution was then concentrated on the bath and allowed to cool and a third crop of crystals was obtained. The three fractions showed the same melting point,  $141^{\circ}$ .

*Anal.* Calcd. for  $C_8H_{12}O_4$ : Ag, 55.64; mol. wt., 174. Found: Ag, 55.52; neut. equiv., 86.4; mol. wt. (Rast), 175; suberic acid.

The ethereal solution from the suberic acid failed to produce additional crystals after standing in the refrigerator for forty-eight hours. The solution was concentrated to a

small bulk and crystals separated which were filtered and dried. These amounted to almost the same weight of the suberic acid and of m. p. 96°. These crystals were not further examined at this time but will be the subject of future investigation as will be true of the neutral products obtained in the oxidation.

(2) **Ricinoleic Acid: with Alkaline Potassium Permanganate.**—Five grams of ricinoleic acid was dissolved in an alkaline solution containing 1.6 g. of potassium hydroxide and made up to 2500 cc. of solution. Ice was then added until the temperature was around 0°. A solution of potassium permanganate (5.3 g. in 250 cc. water) was added hurriedly and the solution stirred for ten minutes, after which time a solution of bisulfite (30 g. in 150 cc. of water) was added and then 70 cc. of 5 *N* hydrochloric acid. During this time ice remained and the stirring was continued until it had melted. The solution amounted to approximately 3000 cc., and was allowed to stand overnight, when a white flocculent precipitate settled. This was collected and dried. The yield of the crude product was practically quantitative.

The crude product was refluxed with petroleum ether (b. p. 40–60°) and the insoluble portion removed. The latter was refluxed with chloroform and the insoluble portion filtered. On cooling the chloroform solution deposited crystals which were filtered and recrystallized from alcohol. On standing, white needle-like crystals separated, m. p. 110°.

*Anal.* Calcd. for trihydroxystearic acid, C<sub>18</sub>H<sub>36</sub>O<sub>3</sub>: C, 65.06; H, 10.84. Found: C, 65.12; H, 10.90.

The solid insoluble in chloroform was recrystallized from alcohol and white crystals were obtained, m. p. 141°. Recrystallization did not alter the melting point.

*Anal.* Calcd. for trihydroxystearic acid: mol. wt., 332. Found: neut. equiv., 337, 334; mol. wt. (Rast), 335.

Five grams of ricinoleic acid gave under the conditions of the experiment: 1.80 g. of acid, m. p. 141°; 1.70 g. of acid, m. p. 110°; 1.50 g. of oily product of pleasant odor.

(3) **Ricinelaic Acid: with Alkaline Potassium Permanganate.**—The ricinelaic acid was prepared by the action of nitric acid and potassium nitrite on ricinoleic acid. Crystallization from petroleum ether gave a white product, m. p. 51°. The same procedure was used in the oxidation of this acid as with the ricinoleic acid. The product, however, was the acid of m. p. 110° with a very small amount of the acid with m. p. 141°.

(4) **Trihydroxystearic Acid: with Periodic Acid.**—Potassium periodate (6 g.) was dissolved in 200 cc. of *N* sulfuric acid at 20° and was added rapidly to a solution of trihydroxystearic acid, 6 g. in 400 cc. of alcohol at 40°. After ten minutes the clear solution was cooled to 15°, diluted with water to dissolve any potassium sulfate precipitating, and extracted with ether. The ethereal solution, on the removal of the solvent, gave an oily product which was submitted to steam distillation. The aqueous distillate was extracted with ether, the ethereal solution dried over anhydrous sodium sulfate, and the solvent removed. The  $\beta$ -hydroxypelargonic aldehyde gave a semicarbazone, crystallized from alcohol, m. p. 151°. The bisulfite compound crystallized in thin plates, from which the aldehyde was regenerated easily.

The acetyl derivative is a colorless oil, b. p. 61–62°,

while the semicarbazone of the  $\beta$ -acetylpergonic aldehyde forms shining plates from water, m. p. 171°.

Attempted purification of the aldehyde by distillation under reduced pressure resulted in the elimination of water and the formation of an unsaturated aldehyde. This decomposition took place around 100° (3 mm.).

The aqueous solution of the non-volatile product, after the steam distillation, was filtered from a small amount of material and reduced to a small volume. On cooling, an oily product separated which finally solidified on cooling. This was extracted with ether, the ethereal solution dried and the solvent removed. The product was a light yellow solid. The impure *n*-aldehydo-octanoic acid was extracted with boiling petroleum ether (b. p. 40–60°) in which most of the product dissolved. Cooling of the petroleum ether solution in the refrigerator over a long period of time gave small plates which were recrystallized from water and separated in glistening plates, m. p. 40°. The 2,4-dinitrophenylhydrazone crystallized from methyl alcohol in orange prisms, m. p. 121° (King<sup>1</sup> gave 122.5°). The semicarbazone separated immediately in the cold, was recrystallized from alcohol in small, colorless crystals, m. p. 166°, insoluble in light petroleum (Harries and Thieme,<sup>2</sup> gave 166°; King<sup>1</sup> 166.5°).

The oxidation of the trihydroxystearic acid, m. p. 110°, with periodic acid gave the same products and yields equally as good as those obtained from the acid, m. p. 141°.

(5) ***n*-Aldehydo-octanoic Acid: with Acid Permanganate.**—A solution of potassium permanganate containing 2 g. in 100 cc. of water at 50°, was added slowly to a solution of the semialdehyde in 100 cc. of water acidified with sulfuric acid (3.5 g.), until the color of the permanganate persists for several minutes. After decolorizing with a solution of sodium bisulfite, the clear solution was cooled. The deposit of azelaic acid was recrystallized from hot water and gave the characteristic rectangular plates, m. p. 107°, which was unchanged when mixed with an authentic specimen.

### Summary

1. Ricinoleic acid and its ethyl ester with theoretical iodine numbers have been prepared.
2. The oxidation of ethyl ricinoleate in dry acetone yields the liquid acids, caproic, heptylic and caprylic; and the solid acids,  $\beta$ -hydroxypelargonic acid, azelaic, suberic, and an acid of m. p. 96°.
3. The oxidation of ricinoleic acid in alkaline permanganate solution at 0° gave two trihydroxystearic acids already known, m. p. 110° and 141°, respectively, in approximately equal amounts. The oxidation of ricinelaic acid, on the other hand, gave a large percentage of the acid, m. p. 110°, and a small amount of the acid, m. p. 141°.
4. The oxidation of both the trihydroxystearic acids obtained from ricinoleic and ricine-

(1) King, *J. Chem. Soc.*, 1826 (1938).

(2) Harries and Thieme, *Ann.*, **343**, 454 (1905).

laidic acids, respectively, with periodic acid, pelargonic aldehyde and aldehydo-azelaic acid. resulted in the same products,  $\beta$ -hydroxy-

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## Synthesis of Vitamin K<sub>1</sub><sup>1</sup>

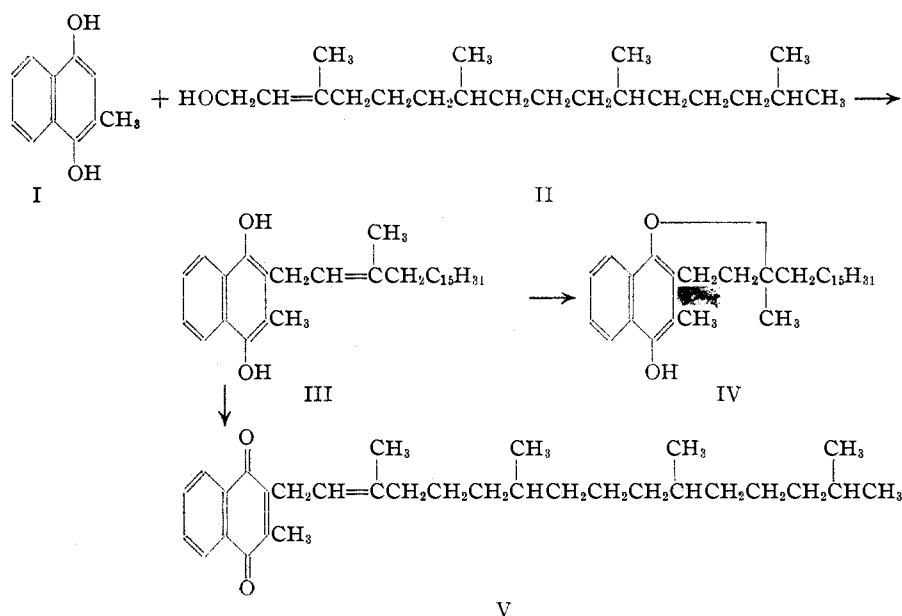
BY LOUIS F. FIESER

In seeking to apply to the synthesis of vitamin K<sub>1</sub> the method of condensation employed successfully<sup>2</sup> for the synthesis of simple quinones of the structural type postulated<sup>3</sup> for the natural substance, trial was first made<sup>2</sup> of the condensation of 2-methyl-1,4-naphthohydroquinone with an equivalent amount of phytol in molten oxalic acid dihydrate at 140°. A smooth reaction ensued but the product had the properties of the naphthotocopherol IV, rather than of the desired substituted hydroquinone III. The result was

provement consisted in using a large excess of methyl-naphthohydroquinone (up to 5.7 equivalents) in order to accelerate the bimolecular condensation reaction and thus give it precedence over the monomolecular cyclization. The tabulation of results given in the Experimental Part shows that this definitely increases the yield based upon phytol. The best results were obtained with a reaction time of thirty-six hours; the yield falls off on more prolonged heating, evidently because of cyclization to the naphtho-

tocopherol. The proportion of oxalic acid can be varied considerably without change in the results and this reagent can be replaced by trichloroacetic acid.

The problem of separating the primary product III from the reaction mixture was solved very simply by working with the material in the reduced condition. The unchanged methyl-naphthohydroquinone can be separated completely and recovered in a usable condition



much the same on conducting the reaction in the presence of anhydrous oxalic acid in dioxane solution at the reflux temperature.<sup>2</sup> On attempting to avoid the cyclization step by further moderating the conditions, it was found that reaction occurs at a reasonable rate at 75° and there were indications of the formation of 2-methyl-3-phytyl-1,4-naphthohydroquinone (III). A further im-

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by extraction of an ethereal solution of the mixture with 1-2% alkali containing sodium hydrosulfite to prevent oxidation, the yellow vat color providing a convenient index of the course of the extraction. The more highly substituted naphthohydroquinone is not extracted from ether even with 25% aqueous alkali, and the separation of the two dihydroxy compounds is therefore very sharp. The impurities retained in the ether, including the naphthotocopherol, phytol, and possibly phytadiene, are all very soluble in petroleum ether whereas methylphytylnaphtho-

(1) See preliminary communications, *THIS JOURNAL*, **61**, 2559, 2561 (1939).

(2) Fieser, Campbell, Fry and Gates, *ibid.*, **61**, 2559, 3216 (1939).

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