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Hydrogenation of Methyl β -Eleostearate

BY MARY LOUISE WOLTEMATE AND B. F. DAUBERT

Introduction

The process of hydrogenation of fatty acids or glycerides containing them does not usually involve merely the simple addition of hydrogen to a double bond, as isomerization and dehydrogenation also are reported to occur.¹ The simultaneous occurrence of these processes results usually in an increase in the number of products obtained by partial hydrogenation, *e. g.*, in the case of oleic acid, both positional and geometric isomers have been observed.² As the number of double bonds in the molecule increases there are more positions at which the hydrogen can attack, thus resulting in the formation of a greater number of isomers.

Instead of hydrogen adding to all of the double bonds at once, the hydrogenation may be selective in that one bond is attacked preferentially. There has been much experimental evidence to indicate that in a poly-unsaturated fatty acid the double bond farthest from the carboxyl group is hydrogenated first.¹ Recently, however, Lemon³ has reported the preferential hydrogenation of the 12,13 or middle double bond in linolenic acid. In the selective hydrogenation of a poly-unsaturated acid the hydrogenation occurs in a progressive or stepwise manner. This was first pointed out by Moore, Richter and Van Arsdel⁴ and has been confirmed by many others.^{5,6}

Two conjugated double bonds characteristically undergo 1,4-addition, and this type of addition is most likely to occur when the double bonds are hydrogenated. With three conjugated double bonds the possibilities are more numerous: 1,6-addition at the ends of the long conjugated system; 1,4-addition to either of the two conjugated diene systems, or 1,2-addition at each double bond. From a study of the hydrogenation of alpha and beta eleostearate esters, Böeseke⁷ concluded that the reduction occurred in such a way that a conjugated system still remained after one mole of hydrogen had been added. A 10,12-octadecadienoic acid was isolated and after two moles of hydrogen had been added, 11-octadecenoic or vaccenic acid was isolated. Böeseke's conclusion that a conjugated diene system was produced on the hydrogenation of the eleostearic

esters was substantiated by Moore,⁸ who found that the hydrogenation of tung oil or eleostearic acid resulted in a decrease of the conjugated triene absorption at 2700 Å. and a corresponding increase in the conjugated diene absorption at 2330 Å.

The purpose of the present work was to determine, if possible, the manner in which the hydrogenation of a conjugated triene system occurred by following the progressive solvent hydrogenation of methyl β -eleostearate and studying the characteristic ultraviolet and infrared absorption of the products.

Experimental

Preparation of Methyl β -Eleostearate.— β -Eleostearic acid was isolated from raw tung oil,⁹ isomerized by ultraviolet light, according to the method outlined by O'Connor, *et al.*¹⁰ The free acid, m. p. 71°, was converted to the methyl ester by slow addition of a cold solution of diazomethane in ethyl ether. The ether was removed under reduced pressure and the ester stored under nitrogen at approximately -20°.

The per cent. of triene conjugation in the ester was determined spectrophotometrically using a Beckman quartz spectrophotometer and 1-cm. absorption cells. The calculations proposed by Brice and Swain,¹¹ later adopted by the Spectroscopy Committee of the American Oil Chemists' Society, were used to determine the percentages of conjugated diene and triene. The calculated per cent. of conjugated triene in the methyl β -eleostearate was 98.

Hydrogenation of the Methyl β -Eleostearate.—Seven separate hydrogenations were carried out at room temperature and atmospheric pressure. For each, 4.18 g. of ester was dissolved in 30 ml. of purified ethyl acetate containing 4% by weight of Raney nickel catalyst. The catalyst was prepared from a commercial nickel-aluminum alloy by a simplification of the method described by Mozingo.¹² The absorption of hydrogen was measured by a gas buret with water as the leveling fluid and the mixture was stirred by a magnetic stirrer. The hydrogen was absorbed in increments of 100 ml., from 100 ml. for the first sample to 700 ml. for the seventh sample.

Isolation of *trans*-Monoethenoid Acid Produced on Hydrogenation of Methyl β -Eleostearate.—Twenty grams of methyl β -eleostearate, hydrogenated to an I. V. of 98, under the same conditions as sample 6, Table I, was saponified with alcoholic potassium hydroxide. The soaps were decomposed with 50% sulfuric acid under nitrogen and the free acids extracted with petroleum ether. In order to remove the saturated fatty acids, the acid product (14 g.) was converted to the mercury salts which were allowed to stand overnight in acetic acid solution. The soluble mercury salts, obtained by gravity filtration of the solution, were treated with 50% hydrochloric acid to give the fatty acids (8 g.). The product was recrystallized several times from cold acetone 20°, m. p. 40.0°, I. V. 88.7, yield 6 g. Mixed melting point with natural vaccenic acid isolated by Rao and Daubert¹³ gave no depression.

(1) K. Markley, "Fatty Acids," Interscience Publishers, Inc., 215 Fourth Avenue, New York, N. Y., 1947.

(2) T. P. Hilditch and N. L. Vidyarthi, *Proc. Roy. Soc. (London)* **A122**, 532-563 (1929).

(3) H. W. Lemon, *Can. J. Research*, **F22**, 191-198 (1944).

(4) H. K. Moore, G. A. Richter and W. B. Van Arsdel, *J. Ind. Eng. Chem.*, **9**, 451-462 (1917).

(5) A. S. Richardson and C. A. Knuth, *Ind. Eng. Chem.*, **16**, 519-522 (1924); **17**, 80-83 (1925).

(6) T. P. Hilditch and N. L. Vidyarthi, *Proc. Roy. Soc. (London)*, **A122**, 563-570 (1929).

(7) J. Böeseke, *Rec. trav. chim.*, **41**, 247-256 (1930).

(8) T. Moore, *Biochem. J.*, **33**, 1635-1638 (1939).

(9) Generously supplied by the Gulf Paint and Chemical Company, Gulfport, Mississippi.

(10) R. O'Connor, D. Heinzelman, R. McKinney and F. Pack, *J. Am. Oil Chem. Soc.*, **24**, 212 (1947).

(11) B. Brice and M. Swain, *ibid.*, **22**, 219 (1945).

(12) R. Mozingo, "Organic Syntheses," Vol. 21, John Wiley and Sons, Inc., New York, N. Y., 1941, p. 15.

(13) P. Rao and B. F. Daubert, *THIS JOURNAL*, **70**, 1102 (1948).

TABLE I

SPECTROPHOTOMETRIC DATA ON HYDROGENATED METHYL β -ELEOSTEARATE

| Sample | Hydrogen absorbed, ml. | Conjugated triene, % | Conjugated diene, % | Alkali conjugable diene, % |
|---------------------------|------------------------|----------------------|---------------------|----------------------------|
| Original methyl ester (E) | 0 | 98 | .. | .. |
| 1 | 100 | 77 | 18.5 | 5 |
| 2 | 200 | 61 | 16 | 2 |
| 3 | 300 | 43.5 | 17 | 0 |
| 4 | 400 | 36 | 14.5 | 0 |
| 5 | 500 | 20 | 13.7 | 0 |
| 6 | 600 | 7.5 | 11 | 0 |
| 7 | 700 | 0 | 1 | 0 |

Oxidation of the *trans*-Monoethenoid Acid.—The position of the double bond in the *trans*-monoethenoid acid was determined by potassium permanganate oxidation of the methyl ester in acetone solution. Twelve grams of powdered potassium permanganate was added to 3 g. of the ester over a period of two hours and the solution was refluxed for four hours more.

The mixture was filtered and the acetone solution containing free acids and unattacked ester was decolorized with sulfur dioxide water. After a second filtration this solution was evaporated to 20 ml., an equal volume of water was added, and the mixture extracted with ethyl ether. The ether extracts were evaporated to dryness and gave 0.7 g. of unoxidized material.

The residue from the filtration of the acetone solution contained oxides of manganese and potassium salts of acids produced during the oxidation. This residue was extracted with dilute sodium bicarbonate solution and then with three portions of hot water. These extracts were combined with the aqueous layer after the ether extraction, and concentrated to approximately 150 ml. This solution was then acidified with 50% sulfuric acid and steam distilled until the distillate was no longer acid to litmus paper.

The steam-volatile water-insoluble acids were separated, washed with a few drops of water, and dried over anhydrous sodium sulfate. They were transferred to a small distilling flask and fractionally distilled at atmospheric pressure (740 mm.), b. p. 222–225°.

Anal. Calcd. for *n*-heptoic acid, $C_7H_{14}O_2$: C, 64.57; H, 10.84. Found: C, 64.55; H, 10.85.

The amide of the monobasic acid was prepared from the acid chloride and liquid ammonia. The monobasic acid (0.07 g.) was refluxed with thionyl chloride (5 ml.) for twenty minutes. After the excess thionyl chloride was boiled off, the acid chloride was cooled below 0° in an ice-salt mixture and then added to approximately 3 ml. of liquid ammonia. When the reaction was completed, water was added and the precipitated amide removed by filtration. The product was recrystallized from water, filtered and dried. The amide melted at 93°; m. p. *n*-heptamide 94°.

Anal. Calcd. for $C_7H_{15}ON$: C, 65.06; H, 11.70; N, 10.84. Found: C, 64.92; H, 11.46; N, 11.01.

The aqueous solution of non-volatile products from the potassium permanganate oxidation was neutralized with 50% sulfuric acid and evaporated to dryness. The residue was extracted with ethyl ether, which after evaporation gave 1 g. of non-volatile material. The greater part of this product was a dibasic acid, soluble in warm benzene but insoluble in cold water and petroleum ether. By repeated fractional crystallization from benzene, a dibasic acid was obtained which had the following constants: m. p. 109°; neutralization equivalent 109 (m. p. and neutralization equivalent for undecanedioic acid, 110° and 108, respectively).

Anal. Calcd. for $C_{11}H_{20}O_4$: C, 61.07; H, 9.32. Found: C, 60.50; H, 9.49.

From the identification of *n*-heptoic and undecanedioic acids, it is concluded that the *trans*-monobasic acid obtained from the hydrogenated methyl β -eleostearate was an acid with the double bond in the 11,12-position.

Spectrophotometric Analysis.—The catalyst was removed from each hydrogenated sample by gravity filtration, using a very fine filter paper, and the solvent removed by distillation under reduced pressure with slight warming. Each sample of the partially hydrogenated methyl β -eleostearate was spectrophotometrically analyzed for conjugated (in isoctane) and alkali-isomerized triene and diene.¹¹

Infrared Analysis.—Infrared absorption curves of the methyl β -eleostearate and the seven hydrogenated samples were determined, using a Baird infrared spectrophotometer through the courtesy of Dr. Foil A. Miller of Mellon Institute.

Discussion of Results

The data in Table I show the percentages of conjugated and alkali-isomerized triene and diene calculated from the spectrophotometric analyses of the seven hydrogenated samples and the original ester.

The infrared absorption curves of the original methyl β -eleostearate and the seven hydrogenated samples are shown in Fig. 1. Curve 8 is the infrared curve for the vaccenic acid isolated from the hydrogenated sample 6. The significant regions of these curves are at 10 and 10.3 μ . The absorption at 10 μ has been shown by Gamble and Barnett¹⁴ to be due to conjugation, and Rao and Daubert¹³ showed that a *trans*-monoethenoid acid gives a strong absorption at 10.3 μ . The methyl β -eleostearate shows the absorption at 10 μ but none at 10.3 μ . β -Eleostearic acid is reported to be a *trans* acid.¹⁵ However, if this is true, it seems likely that methyl β -eleostearate should absorb in the region of 10.3 μ . Examination of curve E, Fig. 1, shows that the minimum typical of *trans* configuration was not obtained. As the hydrogenation continues, the strong absorption peak at 10 μ in the original ester becomes smaller and is not present in the curve of the most hydrogenated sample. This decrease in absorption at 10 μ coincides with the decrease and final disappearance of the conjugation as shown by ultraviolet absorption (Table I).

While the peak at 10 μ is decreasing, a new absorption peak at 10.3 μ appears. It becomes more pronounced than the absorption peak due to conjugation and remains after the conjugation has disappeared. Since absorption at 10.3 μ is due to *trans* configuration, the appearance of a peak at this wave length is evidence that a *trans* acid is being produced by hydrogenation. The fact that this peak still remains after conjugation has disappeared indicates that the *trans* acid is probably a monoethenoid acid. Böeseken¹⁶ has reported vaccenic or 11-octadecenoic acid as a product of the hydrogenation of both ethyl β - and α -eleostearate.

(14) D. L. Gamble and C. E. Barnett, *Ind. Eng. Chem.*, **32**, 375–378 (1940).

(15) A. W. Ralston, "Fatty Acids and Their Derivatives," John Wiley and Sons, Inc., New York, N. Y., 1948.

(16) J. Böeseken and J. Van Krimpen, *Rec. trav. chim.*, **49**, 247–256 (1930).

The nature of the products obtained by permanganate oxidation, together with a comparison of the infrared and X-ray data¹⁷ with natural vaccenic acid, indicate that the major acid produced on hydrogenation in sample 6 of methyl β -eleostearate in solvent is a 11,12-octadecenoic acid (vaccenic acid).

It may also be seen from the data in Fig. 1 that infrared absorption can conveniently be used to follow the formation of *trans* acids in a hydrogenation process.

The spectrophotometric data obtained from the hydrogenated samples show that the hydrogenation is fairly selective in the place of addition of the hydrogen. One definition of selectivity is that the addition takes place in one way, perhaps as a 1,6- or 1,4-addition, or that one particular double bond is preferentially hydrogenated. In the case of a conjugated triene system, only one type of diene structure would be obtained if the hydrogenation were entirely selective in this respect. The spectrophotometric analysis shows, however, that two diene structures are produced, at least in the early stages of the hydrogenation. The greater part of the triene system is changed to a conjugated diene system and a much smaller part to a "normal linoleic" type structure that appears as additional conjugated diene after alkali isomerization. When 23% of the starting material has been hydrogenated (Table I), the sum of the percentages of conjugated triene, conjugated diene, and "linoleic" diene total 100.5%. This seems to indicate that only diene structures are produced and eliminates as a possible method of addition an attack at the middle double bond of the conjugated triene system. Such an addition would produce an isolated double bond structure non-conjugable by alkali and had it occurred the observed percentages would not total 100. The methyl β -eleostearate is thus shown to produce two diene structures on solvent hydrogenation, one conjugated and one conjugable by alkali.

The methods of addition which possibly could produce these structures are numerous, and it is not possible on the basis of spectrophotometric analysis to state which has occurred. The conjugated diene could result from either a 1,6-addition at the ends of the triene system or hydrogenation of an end double bond of the same system. The hydrogenation of methyl β -eleostearate occurs predominantly by one of these methods, for when 23% of the ester has been hydrogenated, the ratio of conjugated diene to "linoleic" type diene is approximately 4 to 1. The "linoleic" structure could be produced by 1,4-addition at either of the conjugated double bonds or by isomerization of diene during hydrogenation. This method of addition is a

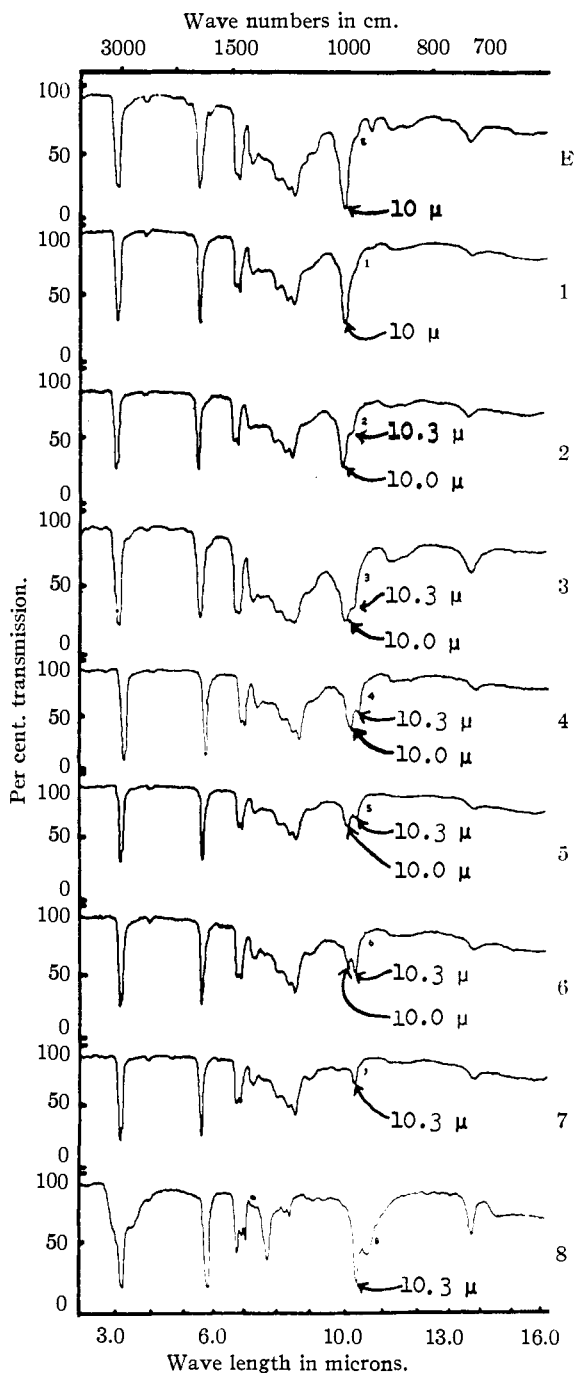
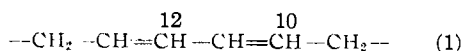


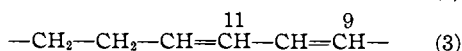
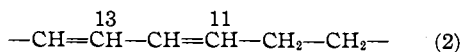
Fig. 1.—Infrared absorption curves for the progressive hydrogenation of methyl β -eleostearate.

secondary one for the percentage of "linoleic" diene was never more than 5.

The principal mono-unsaturated acid produced during the hydrogenation of methyl β -eleostearate has been shown to be 11-octadecenoic acid. Of the three possible diene structures



(17) J. Benedict and B. F. Daubert, *THIS JOURNAL*, **71**, 4113 (1949).



that result from either a 1,6-addition or hydrogenation of end double bond only (1) would produce 11-octadecenoic acid on the characteristic 1,4-addition to a conjugated diene. It is postulated that a 1,6-addition to the conjugated diene system is then the main course of hydrogenation.

In the selective hydrogenation of a poly-unsaturated compound, the addition occurs in a progressive or stepwise manner. The hydrogenation of methyl β -eleostearate would be selective in this respect if no monoethenoid compound were produced before all of the conjugated triene had been converted into the two diene structures. The analysis shows, however, that hydrogenation to a monoethenoid compound did occur before all of the triene system had disappeared. It has been shown that when 23% of the original ester had been reduced, the

percentages of triene and diene total 100, and it can be concluded that no monoethenoid compound had been produced to this point of hydrogenation. When 40% of the ester had been hydrogenated, the percentages of remaining triene and diene produced did not total 100 and it is therefore concluded that some monoethenoid and saturated material were formed.

The solvent hydrogenation of methyl β -eleostearate has been shown to be fairly selective in the manner of addition of hydrogen, occurring predominantly by a 1,6-addition. It is non-selective however, in the respect that it does not occur in a stepwise manner.

Summary

Data on the solvent hydrogenation of methyl β -eleostearate are reported. *trans*-11,12-Octadecenoic acid (vaccenic) was isolated from the products of hydrogenation and its structure and configuration confirmed.

PITTSBURGH, PA.

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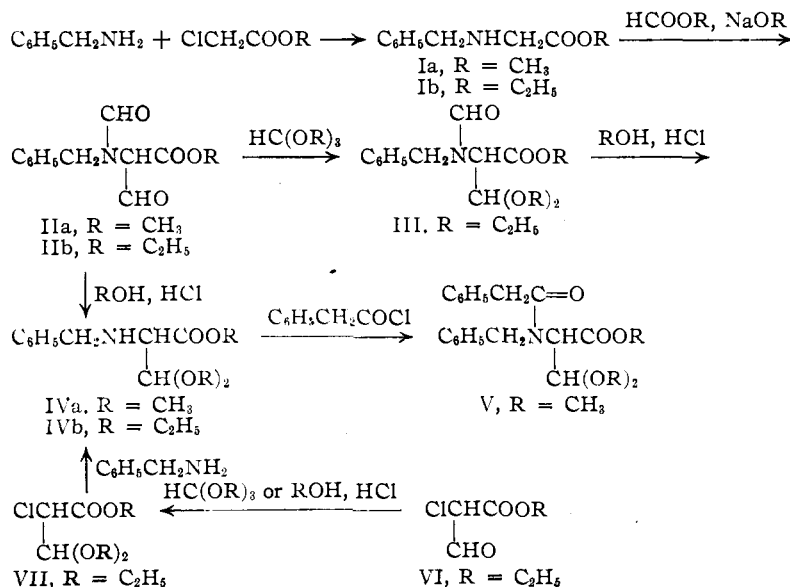
[CONTRIBUTION FROM THE RESEARCH LABORATORIES OF WINTHROP CHEMICAL COMPANY, INC.]

The Preparation of Some α -Benzylamino- β,β -dialkoxypropionic Acid Derivatives

BY JOHN A. KING¹ AND FREEMAN H. McMILLAN¹

As an intermediate in the synthesis of substances possibly related to penicillin it was desirable to use methyl α -(*N*-phenacetyl)-benzyl-

ethyl esters (b series of compounds) were used throughout the exploratory experiments; after suitable reaction conditions had been found the corresponding methyl esters (a series of compounds) were prepared.



amino- β,β -dimethoxypropionate (V). The present paper reports the preparation of this material.

Because they were more readily available, the

Benzylamine and ethyl chloroacetate condensed in benzene solution to give ethyl benzylaminoacetate (Ib). Treatment of this with ethyl formate and sodium ethoxide gave ethyl α,N -diformylbenzylaminoacetate (IIb). This was first acetalified to ethyl α -(*N*-formyl)-benzylamino- β,β -diethoxypropionate (III) by a modification of Claisen's^{1a} orthoformate method and (III) was then converted to ethyl α -benzylamino- β,β -diethoxypropionate (IVb) with ethanolic hydrogen chloride by Fischer's² method.

Compound IVb was also prepared by another method.

Ethyl chloroacetate was formylated by a modification of the method of Wislicenus³ to yield

(1a) Claisen, *Ber.*, **40**, 3903 (1907).

(2) Fischer and Giebe, *ibid.*, **31**, 545 (1898).

(3) Wislicenus, *ibid.*, **43**, 3528 (1910).

(1) Present address: Warner Institute for Therapeutic Research, New York, N. Y.