# CLXXXVI.—*The Constitution of Linolic Acid.*

By ROBERT DOWNS HAWORTH.

THE structures of the polyethylenic acids, which occur abundantly in the fats, are still very uncertain. In most cases, oxidation with potassium permanganate or ozone has been employed in structural determinations and the assumption has been made that oxidation occurs at the double bond. This assumption is justified when the esters of the ethylenic acids are oxidised with ozone, or with potassium permanganate in acetone solution (Armstrong and Hilditch, *J. Soc. Chem. Ind.*, 1925, **44**, 43T, 180T), but the work of Lapworth and Mottram (J., 1925, **127**, 1628, 1987) on the dihydroxystearic acid obtained from oleic acid shows that, in cold dilute alkaline solution, potassium permanganate attacks the molecule between the secondary alcoholic group and the adjacent methylene group, and in view of this much of the earlier work requires verification before the suggested structures for the polyethylenic acids can be accepted.

It would appear from the literature that at least two linolic acids are known. One of these, isolated from poppy-seed oil, is converted into sativic acid (tetrahydroxystearic acid) by the action of potassium permanganate in dilute alkaline solution. Goldsobel (*J. Russ. Phys. Soc.*, 1906, **38**, 904) obtained a mixture of *n*-hexoic, oxalic and azelaic acids by oxidising sativic acid with potassium permanganate in alkaline solution, and concluded that linolic acid was octadeca-$\Delta^{9:10,\ 12:13}$-dienoic acid (I). Goldsobel assumed that the oxalic acid was produced by oxidation of malonic acid, and later (*ibid.*, 1910, **42**, 55) he showed that the optical constants for linolic acid were in better agreement with formula (I) than with a structure containing conjugated double bonds. This structure has been confirmed by Reinger (*Ber. deut. Pharm. Ges.*, 1928, **32**, 124) by a method based on the progressive dehydration of sativic acid.

Takahashi (*J. Tokyo Chem. Soc.*, 1919, **40**, 233; *J. Chem. Soc. Japan*, 1921, **42**, 130) claims to have isolated a second linolic acid from soya-bean and rice-bran oils. This yielded tetrabromo- and tetrahydroxy-stearic acids which were identical in melting point with the corresponding derivatives of linolic acid obtained from poppy-seed oil. However, oxidation of this second linolic acid by means of 4% potassium permanganate or ozone afforded *n*-butyric, glutaric, and azelaic acids or the corresponding aldehydes, and Takahashi concluded that linolic acid was octadeca-$\Delta^{9:10,\ 14:15}$ dienoic acid (II).

$$CH_3\cdot[CH_2]_4\cdot CH\colon CH\cdot CH_2\cdot CH\colon CH\cdot[CH_2]_7\cdot CO_2H \quad \text{(I.)}$$

$$CH_3\cdot[CH_2]_2\cdot CH\colon CH\cdot[CH_2]_3\cdot CH\colon CH\cdot[CH_2]_7\cdot CO_2H \quad \text{(II.)}$$

The structures of the linolic acids derived from poppy-seed and from soya-bean oil have been reinvestigated. The acids were obtained from the oils by hydrolysis with methyl-alcoholic potassium hydroxide and purified by conversion into the tetrabromostearic acids (Rollett, *Z. physiol. Chem.*, 1909, **62**, 410). The tetrabromo-acid obtained from poppy-seed oil was identical with that obtained from soya-bean oil, and the identity of the two specimens was confirmed by comparing the methyl esters of the tetrabromo-acids. The methyl linolates, obtained by reducing the tetrabromostearic acids by Rollett's method (*loc. cit.*), were identical in boiling point, and *n*-hexoic, azelaic, and oxalic acids were isolated, in yields approximating to 80% of those calculated from structure (I), after the ester derived from either poppy-seed or soya-bean oil had been oxidised with potassium permanganate in cold acetone solution. In a few experiments, the presence of malonic acid was detected by the isolation of hydrogen formazyl (von Pechmann, *Ber.*, 1892, **25**, 3175). The majority of the malonic acid, however, was converted into oxalic acid, and a control experiment showed that malonic acid was slowly oxidised to oxalic acid under the conditions employed in the oxidation of methyl linolate. These oxidation experiments indicate that linolic acid obtained from poppy-seed or soya-bean oil has the formula (I), and this has been confirmed by oxidation with potassium permanganate in dilute alkaline solution. The method which Lapworth and Mottram (*loc. cit.*, p. 1628) employed in the conversion of oleic acid into dihydroxystearic acid applies equally well to the preparation of sativic acid from linolic acid, and the sativic acid, prepared from poppy-seed oil, showed no depression in melting point when mixed with a specimen obtained from soya-bean oil. The sativic acid was oxidised with ice-cold potassium permanganate in alkaline solution and a mixture, consisting mainly of suberic, *n*-valeric, and oxalic acids, together with smaller quantities of azelaic and *n*-hexoic acids, was isolated. When the oxidation was carried out in hot alkaline solution, the products isolated were *n*-hexoic and azelaic acids and a smaller quantity of suberic acid, and the presence of *n*-valeric acid was indicated by the low equivalent of the volatile acids. These observations are in agreement with those of Lapworth and Mottram (*loc. cit.*, p. 1987) on the oxidation of dihydroxystearic acid.

Doubts have been cast on the homogeneity of the linolic acid obtained by Rollett's method, mainly on account of the numerous tetrabromo- and tetrahydroxy-addition products which can be prepared (see Lewkowitsch, " Chemical Technology and Analysis of Oils, Fats and Waxes," 6th ed., 1921, vol. I, p. 237; Bedford, *Dissertation*, Halle, 1908; Rollett, *loc. cit.*; Takahashi, *loc. cit.*; Nicolet, *J. Amer. Chem. Soc.*, 1922, **44**, 144; Smith and West, *Philippine J. Sci.*, 1927, **32**, 297). These derivatives can be explained on stereochemical grounds, and the yields of oxidation products isolated in this work would suggest that linolic acid is almost entirely composed of octadeca-$\Delta^{9:10,\ 12:13}$-dienoic acid, although the presence of geometrical isomerides is not excluded.

## EXPERIMENTAL.

Poppy-seed or soya-bean oil (200 c.c.) was hydrolysed by boiling with 10% methyl-alcoholic potassium hydroxide (800 c.c.) for 2 hours, and the acids, liberated by the addition of 10% sulphuric acid, were extracted with light petroleum (b. p. 60—80°), washed with water, and dried with anhydrous sodium sulphate. The crude acids were converted by Rollett's method (*loc. cit.*) into 9 : 10 : 12 : 13-tetrabromostearic acid, which was obtained pure, m. p. 113—114°, after two recrystallisations from light petroleum (b. p. 60—80°) (Found : Br, 53·0. Calc. : Br, 53·3%). No depression in m. p. was observed when the bromo-acids obtained from the two different sources were mixed. The yields of pure tetrabromo-acid from 200 c.c. of oil were * (*a*) 100 g., (*b*) 60 g. Methyl 9 : 10 : 12 : 13-tetrabromostearate (compare Santos and West, *Philippine J. Sci.*, 1927, **34**, 199) was prepared by refluxing the tetrabromo-acid with methyl alcohol containing a little hydrogen bromide for 1 hour. The ester, from both sources, crystallised from methyl alcohol in colourless plates, m. p. 56°, and no depression in m. p. was observed with a mixture of the two specimens [Found : Br, (*a*) 52·0, (*b*) 52·2. Calc. : Br, 52·1%]. Methyl linolate, b. p. 168—170°/1 mm. (iodine number, 170. Calc., 172), was obtained by reducing the tetrabromostearic acid by Rollett's method.

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* The figures recorded after (*a*) and (*b*) refer to material obtained from poppy-seed and soya-bean oil, respectively.

*Oxidation of Methyl Linolate with Potassium Permanganate in Acetone Solution.*—A suspension of sodium bicarbonate (2 g.) in a solution of methyl linolate (10 g.) in acetone (150 c.c.) was stirred at – 5° to 0° during the gradual addition of finely powdered potassium permanganate (40—45 g.) until a permanent pink coloration was produced. The acetone was removed by distillation, and the residue extracted several times with hot dilute sodium hydroxide solution. The combined alkaline extracts were concentrated to about 150 c.c., acidified with concentrated hydrochloric acid, and extracted with ether.

*Isolation of oxalic acid and detection of malonic acid.* The aqueous layer from the ether extraction described above was made alkaline with ammonia and boiled, a solution of calcium chloride added, and the calcium oxalate * collected, washed with hot dilute acetic acid and estimated by titration with potassium permanganate [Found : (*a*) 1·7 g., (*b*) 2·0 g. Calc., 3·1 g.]. In a few experiments, malonic acid was detected as follows : the filtrate, after removal of the calcium oxalate, was acidified with dilute hydrochloric acid, cooled to 0°, and mixed with a well-cooled solution of benzenediazonium chloride (from 2 g. of aniline), and excess potassium acetate added. After 24 hours, the red solid (0·2 g.) was collected, washed with water, dried, and crystallised twice from benzene–light petroleum (b. p. 40—60°); red needles, m. p. 118°, which gave no depression in m. p. with an authentic specimen of hydrogen formazyl, were obtained.

*Isolation of azelaic acid.* The dried ethereal extract was evaporated, and the residue distilled in steam for 2 hours. The hot non-volatile residue was treated with charcoal, filtered from a little tar, and cooled, and azelaic acid collected. A small impure crop, m. p. 98—101°, obtained by concentrating the mother-liquors, was recrystallised from water. The total yield of azelaic acid, m. p. 104—105°, was (*a*) 5·2 g., (*b*) 5·0 g. (calc., 6·4 g.) (Found : equiv., 94·1. Calc., 94·0). No suberic acid was isolated, but a very small amount of oxalic acid (less than 0·1 g.) was precipitated as calcium salt from the final mother-liquors.

*Isolation of* n-*hexoic acid.* The volatile distillate was extracted three times with light petroleum (b. p. 40—60°), the extract dried with anhydrous sodium sulphate, the solvent removed through a short fractionating column, and the residue distilled. It boiled steadily at 202—205°; the yield of *n*-hexoic acid was (*a*) 2·9 g., (*b*) 3·1 g. (calc., 3·9 g.) (Found : equiv., 117. Calc., 116). The acid was exactly neutralised with sodium hydroxide, the sodium

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* In some cases the oxalic acid was isolated by decomposing the calcium salt with dilute sulphuric acid.

salt dissolved in a little water, and the calculated amount of zinc sulphate crystals added. The mixture was evaporated to dryness and extracted with boiling absolute alcohol. *Zinc hexoate* crystallised from alcohol in colourless plates, m. p. 142° (Found in salt dried at 100°: C, 48·5; H, 7·6. $C_{12}H_{22}O_4Zn$ requires C, 48·7; H, 7·4%) and was identical with the zinc salt prepared from an authentic specimen of *n*-hexoic acid. *n*-Hexoyl chloride was prepared by refluxing the acid with an excess of thionyl chloride for 2 hours and distilling the mixture. The chloride, b. p. 153—156°, was poured into a well-cooled solution of concentrated ammonia and the amide was collected and crystallised from aqueous alcohol, giving colourless prisms which melted, either alone or when mixed with an authentic specimen of *n*-hexoamide, at 99°.

A similar oxidation of methyl linolate (10 g.) in boiling acetone solution afforded oxalic acid (*a*) 0·08 g., (*b*) 0·05 g., azelaic acid (*a*) 5·0 g., (*b*) 5·3 g., and *n*-hexoic acid (*a*) 2·7 g., (*b*) 2·7 g.

Sativic acid was prepared very conveniently by the following method. Methyl linolate (10 g.) was hydrolysed by the action of 5% methyl-alcoholic potassium hydroxide (140 c.c.) for 12 hours at the ordinary temperature. The mixture was diluted with water, acidified with dilute sulphuric acid, and extracted with light petroleum (b. p. 40—60°); the extract was washed with water and dried, and the solvent removed. The residual linolic acid was dissolved in 1% potassium hydroxide solution (1000 c.c.), mixed with an equal volume of ice-cold water, and 1% potassium permanganate solution (800 c.c.) rapidly added. After being shaken for 5 minutes, the mixture was decolorised with sulphur dioxide, concentrated hydrochloric acid (150 c.c.) added, and the sativic acid collected and washed with a little ether. The dried residue (11·5 g.), m. p. 145—165°, crystallised from 30% acetic acid in small needles (10·4 g.), m. p. 171—172°. The sativic acid prepared from poppy-seed oil was identical with that prepared from soya-bean oil and no depression in mixed m. p. was observed.

*Oxidation of Sativic Acid with Potassium Permanganate in Cold Alkaline Solution.*—Sativic acid (10 g.), dissolved in 1% potassium hydroxide solution (1000 c.c.), was mixed with ice-cold water (2000 c.c.), and 2% potassium permanganate solution (2000 c.c.) rapidly added with shaking. After 4 hours, the mixture was heated to 80° and the manganese dioxide was collected and thoroughly washed with hot dilute sodium hydroxide solution. The combined washings and filtrate were concentrated to 500 c.c., acidified with concentrated hydrochloric acid, and extracted with ether, and the oxidation products were separated as described on p. 1459. The calcium oxalate was estimated and the yield of oxalic acid was (*a*) 3·2 g., (*b*) 3·0 g.

*Isolation of suberic and azelaic acids.* The non-volatile dibasic acids from the ether extract deposited azelaic acid, (*a*) 0·6 g., (*b*) 0·9 g., on cooling, and concentration of the mother-liquors afforded crude suberic acid, m. p. 115—125°, which recrystallised from ether in needles, (*a*) 5·0 g., (*b*) 4·7 g., m. p. 136—138° (Found : equiv., 86·4. Calc., 87·0).

*Isolation of* n-*valeric and* n-*hexoic acids.* The volatile acids were extracted with light petroleum (b. p. 40—60°) and dried; the residue distilled completely between 180° and 198°. The yield was (*a*) 3·0 g., (*b*) 3·2 g. and the equivalent found was 107, the high value being due to the presence of *n*-hexoic acid. A larger quantity (15 g.) of mixed volatile acids was collected and fractionated systematically and two fairly pure fractions were isolated. The first (8·0 g.), b. p. 180—184°, had an equivalent of 103 (Calc. for *n*-valeric acid, 102). The acid was converted into the amide, m. p. 102—104°, by the method described on p. 1460, and the amide was identified as *n*-valeramide by comparison with a specimen of the latter prepared from an authentic specimen of *n*-valeric acid. A second fraction (1·5 g.), b. p. 198—202°, was collected and converted into zinc salt, m. p. 142°. The acid liberated from the zinc salt by treatment with dilute sulphuric acid had b. p. 203—205° and equivalent 115·5; it was converted into the amide, m. p. 99°, which was identical with *n*-hexoamide.

*Oxidation of Sativic Acid with Potassium Permanganate in Hot Alkaline Solution.*—A 4% solution of potassium permanganate (1000 c.c.) was gradually added to a hot solution of sativic acid (10 g.) in 1% potassium hydroxide solution (300 c.c.), and the heating on the water-bath continued until the green colour was destroyed. The mixture was treated as described in the previous experiment and no oxalic was isolated. The volatile acids, (*a*) 2·7 g., (*b*) 2·9 g., b. p. 197—202°, composed mainly of *n*-hexoic acid, had an equivalent of 112. The low value is probably due to traces of *n*-valeric acid, but it has not been possible to isolate this acid. The non-volatile acids afforded (*a*) 3·8 g., (*b*) 4·0 g. of azelaic acid, m. p. 103—105° (Found : equiv., 93·5), and suberic acid, (*a*) 0·6 g., (*b*) 0·9 g., m. p. 135—137° (Found : equiv., 87·4).

UNIVERSITY OF DURHAM, ARMSTRONG COLLEGE,
NEWCASTLE-ON-TYNE.

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