12. *The Mechanism of the Oxidation of Oleic and Elaidic Acids and their Methyl Esters by Hydrogen Peroxide in Acetic Acid. Further Observations on the Configurations of the* 9 : 10-*Dihydroxystearic Acids.*

By George King.

The oxidation of oleic acid by hydrogen peroxide in acetic acid at room temperature affords mainly a mixture of monoacetyl derivatives of the dihydroxystearic acid, m. p. 95°. Elaidic acid, however, furnishes an appreciable yield of oxidostearic acid, m. p. 55·5°, in addition to monoacetyl derivatives of the dihydroxystearic acid, m. p. 132°. The methyl esters of oleic and elaidic acids behave similarly, and in all cases small amounts of peroxides, probably of the type $\mathrm{CHR(OH)\cdot O\cdot O\cdot CHR\cdot OH}$, are formed.

r-Oxidostearic acid, m. p. 59·5° (oleic acid epoxide), unites with acetic acid during a few days at room temperature to give the same mixture of 9 : 10-hydroxyacetoxystearic acids (m. p. 81° after purification) as that obtained by oxidation of oleic acid in acetic acid solution. Under similar conditions *r*-oxidostearic acid, m. p. 55·5° (elaidic acid epoxide), is only partly transformed by acetic acid into monoacetyl derivatives of the dihydroxystearic acid, m. p. 132°, nearly 50% remaining unchanged after 11 days.

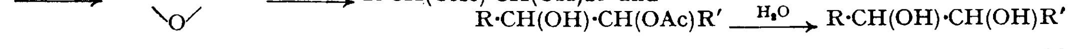
The oxidostearic acids are considered to be primary products in the oxidation of oleic and elaidic acids by "peracetic acid," and the ultimate formation of the dihydroxystearic acids, m. p.'s 95° and 132° respectively, or their derivatives is ascribed to inversion on fission of the oxide ring.

It was shown by Hilditch (J., 1926, 1829) that oleic and elaidic acids and their methyl esters are oxidised by hydrogen peroxide in the presence of acetic acid to products which, on saponification, furnish the 9 : 10-dihydroxystearic acids, m. p.'s 95° and 132° respectively, in good yields. The same dihydroxy-acids result from the action of perbenzoic acid, which is known to oxidise oleic and elaidic acids in ethereal solution at 0° primarily to the 9 : 10-oxidostearic acids melting respectively at 59·5° and 55·5° (Pigulevski and Petrova, *J. Russ. Phys. Chem. Soc.*, 1926, **58**, 1062; Böeseken and Belinfante, *Rec. Trav. chim.*, 1926, **45**, 918). Conversely, the oxidation of oleic and elaidic acids by potassium permanganate in cold alkaline solution furnishes the isomeric dihydroxy-acids, m. p.'s 132° and 95° respectively (Saytzeff, *J. pr. Chem.*, 1886, **33**, 300; Robinson and Robinson, J., 1925, **127**, 175; Lapworth and Mottram, *ibid.*, p. 1628).

The inversion of configuration which necessarily occurs during one or other of these processes has given rise to some conflict of opinion (Hilditch, *loc. cit.*; Hilditch and Lea, J., 1928, 1576; Pigulevski and Petrova, *loc. cit.*; Böeseken and Belinfante, *loc. cit.*, p. 917). Evidence has been adduced in support of the hypothesis that inversion occurs during hydrolysis of the oxide ring (Esafov, *J. Gen. Chem. Russia*, 1937, **7**, 1403; King, J., 1942, 387), similar examples of which are to be found in the alicyclic series (van Loon, *Chem. Zentr.*, 1920, **I**, 332; Farmer and Sundralingam, J., 1942, 135). Hilditch and Lea (*loc. cit.*) investigated the action of hydrogen peroxide on the methyl esters of oleic and elaidic acids in acetic acid solution, but were unable to obtain any evidence of the formation of intermediate oxido-compounds. On the other hand, Arbusov and Michailov (*J. pr. Chem.*, 1930, **127**, 1, 92), working more particularly on olefinic compounds of the alicyclic and terpene series, have since shown that peracetic acid resembles perbenzoic in forming cyclic oxides primarily at low temperatures (see also Böeseken and Schneider, *J. pr. Chem.*, 1931, **131**, 285; cf. Böeseken, *Rec. Trav. chim.*, 1927, **46**, 622).

It appeared desirable therefore to make a further study of the mode of action of hydrogen peroxide in acetic acid solution on oleic and elaidic acids and their methyl esters. Under conditions similar to those described by Hilditch (*loc. cit.*), but with a smaller excess of hydrogen peroxide, there were readily isolated elaidic acid epoxide, m. p. 55·5° (in 25—30% yield from the products of oxidation of elaidic acid), 10—15% of free dihydroxystearic acid, m. p. 132°, and about 50% of its monoacetyl derivatives. Oleic acid, however, afforded no epoxide, the main product being a mixture of monoacetyl derivatives of the dihydroxy-acid, m. p. 95°. Small amounts (not exceeding 2%) of peroxides, probably of the bis-type, $\mathrm{CHR(OH)\cdot O\cdot O\cdot CHR\cdot OH}$ (King, J., 1942, 218), were also formed. Similar results were obtained with the methyl esters of oleic and elaidic acids.

Oleic acid epoxide, m. p. 59·5°, united relatively easily with acetic acid, yielding a mixture of monoacetyl derivatives of the dihydroxystearic acid, m. p. 95°, but elaidic acid epoxide was transformed much more slowly into the monoacetyl derivatives of the dihydroxy-acid, m. p. 132°, about 50% remaining unchanged after 11 days at room temperature. It seems reasonable to suppose, therefore, that the reactions take the following course (cf. Böeseken, *loc. cit.*; Böeseken and Elsen, *Rec. Trav. chim.*, 1929, **48**, 363):



$$\mathrm{R\cdot CH{:}CHR' \xrightarrow{AcO_2H} R\cdot \underset{\diagdown O \diagup}{CH—CHR'} \xrightarrow{AcOH} \begin{array}{l} \mathrm{R\cdot CH(OAc)\cdot CH(OH)R'\ and} \\ \mathrm{R\cdot CH(OH)\cdot CH(OAc)R'} \end{array} \xrightarrow{H_2O} R\cdot CH(OH)\cdot CH(OH)R'}$$

Dorée and Pepper (J., 1942, 478) have shown that, when oxidised at 60° by hydrogen peroxide in acetic acid solution in the presence of osmium tetroxide, oleic acid gives the dihydroxy-acid of higher m. p., and elaidic that of lower m. p., but no epoxides were isolated. This accords with the mechanism suggested by Böeseken (*ibid.*, 1922, **41**, 199), postulating the formation of intermediate cyclic osmium compounds (to the exclusion of the usual epoxides) which oppose inversion. The balance of evidence, therefore, contributes further support for the configurational relationships between the unsaturated acids, the oxido- and dihydroxy-stearic acids suggested in a previous communication (J., 1942, 388), and leads with moderate certainty to the following conclusions: (1) Fission of the oxide ring, whether effected by hydrolysis or by union with an acid, is accompanied by an inversion of configuration. (2) The conversion of oleic acid by means of cold alkaline permanganate into the dihydroxy-acid of higher m. p. (and of elaidic acid into the dihydroxy-acid of lower m. p.) represents the normal *cis*-addition of two hydroxyl groups to the double bond.

EXPERIMENTAL.

Oxidation of Oleic Acid by Hydrogen Peroxide in Acetic Acid.—A 7% solution of crude oleic acid in acetone deposited saturated acids at −25° and oleic acid at −60° (cf. Brown and Shinowara, *J. Amer. Chem. Soc.*, 1937, **59**, 6). After recrystallisation, saturated acids were removed from a 10% solution at −30°. A solution of hydrogen peroxide (8 ml. of 100-vol.) and oleic acid (10 g., m. p. 7°. Found : I val., 86·6; equiv., 278. Calc. for $C_{18}H_{34}O_2$: I val., 90·1; equiv., 282) in acetic acid (200 ml.) was kept at room temperature for 12 days and then for 48 hours at 0° after addition of water. The dried, sticky product was dissolved in warm benzene (50 ml.), filtered from traces of dihydroxystearic acid, and cooled to 6°. The 9 : 10-hydroxyacetoxystearic acids deposited (5·5 g.) crystallised from acetone in colourless needles, m. p. 81° [Found : C, 66·5; H, 10·7; equiv., 360; sap. val. (excluding acid val.), 156. Calc. for $C_{20}H_{38}O_5$: C, 67·0; H, 10·7%; equiv., 358; sap. val., 156], sparingly soluble in light petroleum, but readily in 2N-sodium hydroxide (distinction from oxidostearic acids). Saponification of this product afforded dihydroxystearic acid, m. p. 94° alone or mixed with an authentic specimen. The benzene mother-liquor contained a small amount of peroxides, and no oxidostearic acid could be isolated.

Oxidation of Elaidic Acid.—A solution of elaidic acid (20 g., m. p. 44·5°. Found : I val., 88; equiv., 281) and hydrogen peroxide (16 ml. of 100 vol.) in acetic acid (400 ml.) was kept for 6 days at room temperature, and water then added. Extraction of the dried product with warm light petroleum (150 ml.) left an insoluble residue of dihydroxystearic acid, which crystallised from alcohol in rhombic plates (2·35 g.), m. p. 131° (Found : C, 68·5; H, 11·6; equiv., 312. Calc. for $C_{18}H_{36}O_4$: C, 68·3; H, 11·4%; equiv., 316). The petroleum extract, concentrated and cooled to 0°, deposited 9 : 10-oxidostearic acid, which separated from acetone in typical rhombic plates (5·5 g.), m. p. 55·5°, alone or mixed with an authentic specimen prepared from dihydroxystearic acid, m. p. 95°, *via* the chlorohydrins (J., 1942, 390) (Found : C, 72·3; H, 11·4; equiv., 296. Calc. for $C_{18}H_{34}O_3$: C, 72·4; H, 11·5%; equiv., 298).

The mother-liquors from the epoxide yielded a clear, viscous oil (7·9 g.), sparingly soluble in light petroleum, consisting of 9 : 10-hydroxyacetoxystearic acids (with a small quantity of peroxides), which slowly set to a crystalline mass, m. p. 40—42°, when kept in a refrigerator [Found : C, 67·4; H, 10·7%; equiv., 359; *M* (Rast), 384; sap. val. (excluding acid val.), 137; active oxygen (Lea, " Rancidity in Edible Fats," 1938, p. 107), 0·124%]. On saponification this furnished a nearly theoretical yield of dihydroxystearic acid, m. p. and mixed m. p. 131°.

Oxidation of Methyl Oleate.—A solution of hydrogen peroxide (6 ml. of 100-vol.) and methyl oleate (10 g., b. p. 226—227°/31 mm. Found : sap. val., 189; I val., 86. Calc. for $C_{19}H_{36}O_2$: sap. val., 189; I val., 86) in acetic acid (100 ml.) was kept for 6 days at room temperature, and then diluted with water. The oil was saponified with 0·6N-alcoholic potassium hydroxide (150 ml.) (19 hours at room temperature), and the solid product obtained on acidification was dried, and extracted with warm light petroleum (180 ml.), leaving an insoluble residue of dihydroxystearic acid (5·7 g.), m. p. 94° alone or mixed with an authentic specimen (Found : C, 68·4; H, 11·4%; equiv., 315).

The petroleum extract left on evaporation a pale yellow oil (1·87 g.), gradually becoming semi-crystalline, and corresponding closely to oxidostearic acid in composition [Found : C, 72·45; H, 11·5%; equiv., 312·5; *M* (Rast), 307; I val., 13·2; active oxygen, 0·02%]. No oleic acid epoxide could, however, be isolated, and no dihydroxystearic acid was obtained after saponification.

Oxidation of Methyl Elaidate.—Methyl elaidate (10 g., b. p. 218—220°/24 mm. Found : I val., 84·5; sap. val., 187) was oxidised for 6 days as described for the oleate. The acids obtained after cold saponification of the product were resolved by extraction with warm light petroleum into an insoluble fraction (7·2 g.), consisting of dihydroxystearic acid, m. p. and mixed m. p. 131° (Found : C, 68·5; H, 11·6%), and a more soluble fraction (2·2 g.) of 9 : 10-oxidostearic acid, m. p. 55·5° alone or mixed with authentic elaidic acid epoxide (Found : equiv., 298·5).

r-9 : 10-*Oxidostearic Acid, m. p.* 59·5° (*Oleic Acid Epoxide*).—Oleic acid epoxide was prepared from dihydroxystearic acid, m. p. 132°, *via* the chlorohydrins (King, *loc. cit.*), and also by the following methods.

(*a*) From oleic acid *via* the chlorohydrins (cf. Ellis, *Biochem. J.*, 1936, **30**, 757). A solution of oleic acid (10 g.) in 1·2N-Liquor Sodæ Chlorinatæ (60 ml.) and water (300 ml.) was made faintly turbid with hydrochloric acid, and then saturated with carbon dioxide. After 18 hours, acidification of the mixture and extraction with ether furnished the chlorohydrins as a clear viscous oil. This was refluxed for 2 hours with 2N-alcoholic potassium hydroxide (200 ml.), and the diluted and acidified solution was cooled in the refrigerator. The dried product was crystallised successively from light petroleum and acetone, yielding oxidostearic acid (3·0 g.) in long, slender laminæ, m. p. alone or mixed with a specimen prepared as above 59·5° (Found : C, 72·5; H, 11·5%; equiv., 298).

(*b*) From oleic acid *via* the bromohydrins. Bromine (1·8 ml.) in 10% aqueous potassium bromide (100 ml.) was added slowly and with vigorous shaking to oleic acid (10 g.) emulsified with water (500 ml.), any excess of halogen being finally removed with aqueous sodium hydrogen sulphite (Read and Reid, J., 1928, 749, 1487). Ether extraction yielded an oily mixture of bromohydrins, which after saponification gave oxidostearic acid (1·4 g.), m. p. and mixed m. p. 59·5°.

Action of Acetic Acid on the Oxidostearic Acids.—(*a*) A solution of oleic acid epoxide (1 g., m. p. 59·5°) in acetic acid (25 ml.) was kept for 7 days at room temperature, then diluted with water and cooled at 0° for 24 hours. The hydroxyacetoxystearic acids crystallised from benzene–alcohol in colourless needles (0·7 g.), m. p. 80·5° alone or mixed with a specimen prepared from oleic acid as above [Found : equiv., 357; sap. val. (excluding acid val.), 157·5]. Saponification afforded dihydroxystearic acid, m. p. 95°, in nearly theoretical yield. No unchanged epoxide was isolated.

(*b*) A solution of elaidic acid epoxide (1 g., m. p. 55·5°) in acetic acid (15 ml.), after 11 days at room temperature, gave unchanged epoxide (0·48 g.) and a colourless oil (0·57 g.). The latter gradually set to a crystalline mass, m. p. 37—39°, sparingly soluble in light petroleum, consisting of crude hydroxyacetoxystearic acids (Found : equiv., 379; sap. val., 149). It afforded a good yield of dihydroxystearic acid, m. p. 131°, on saponification, but could not be purified.

Action of Acetic Acid on the Dihydroxystearic Acids, m. p.'s 95° *and* 132°.—Solutions of the dihydroxy-acids in cold acetic acid were set aside for 14 days. More than 97% of the acids were recovered unchanged, and there was no evidence of epoxide formation.

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