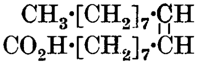
CCXLII.—*The Isomerism of the Dihydroxystearic Acids produced by Oxidation of Acids of the Oleic and Elaidic Series.*

By Thomas Percy Hilditch.

The 9 : 10-dihydroxystearic acid, m. p. 132°, which is produced when the sodium salt of oleic acid is oxidised in cold dilute alkaline solution by potassium permanganate, has come to be regarded as a convenient means of identifying oleic acid and directions for its improved preparation have recently been given by Robinson and Robinson (J., 1925, **127**, 177) and by Lapworth and Mottram (*ibid.*, p. 1628). The sodium salt of the geometrically isomeric elaidic acid yields under similar conditions an isomeric dihydroxy-acid, m. p. 95° (Saytzew, *J. pr. Chem.*, 1886, **34**, 315). Albitski (*J. Russ. Phys. Chem. Soc.*, 1899, **31**, 76; 1902, **34**, 788, 810) observed that, under other conditions, oleic acid gave the acid of lower melting point whilst elaidic acid furnished that melting at 132°, and, further, that it was possible mutually to transform the two dihydroxy-acids in certain circumstances.

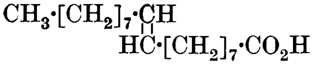
Experimental evidence has recently been obtained which points, especially when considered in conjunction with Albitski's data, to the conclusion that the dihydroxystearic acid of lower melting point is in fact most closely connected with oleic acid, and *vice versa.* Consequently, in view of the use of the acid of higher melting point as a criterion of the presence of ordinary oleic acid, it is well to reconsider the relations between the geometrical isomerides, oleic and elaidic acid, and the two 9 : 10-dihydroxystearic acids.

Whilst Albitski's explanation of the isomeric changes involved was based upon the assumption, accepted at the time, that oleic acid was the *trans*-isomeride, the present argument is developed upon the primary hypothesis that oleic and elaidic acids possess the following structures:



$$\begin{array}{r}CH_3\cdot[CH_2]_7\cdot CH\\ \|\\ CO_2H\cdot[CH_2]_7\cdot CH\end{array}$$

Oleic-*cis*-acid.



$$\begin{array}{l}CH_3\cdot[CH_2]_7\cdot CH\\ \qquad\qquad\quad\;\|\\ \qquad\qquad\quad HC\cdot[CH_2]_7\cdot CO_2H\end{array}$$

Elaidic-*trans*-acid.

Extensive search of the older literature has not revealed the reasons which originally led to the adoption of the alternative view.

On the other hand, Müller and Shearer (J., 1923, **123**, 3156) submitted oleic and elaidic acids, $C_{18}H_{34}O_2$, and also erucic and brassidic acids, $C_{22}H_{42}O_2$, to examination by the *X*-ray method and deduced that elaidic and brassidic acids were respectively the *trans*-forms of the respective pairs.

Again, Armstrong and Allan (*J. Soc. Chem. Ind.*, 1924, **43**, 207T) state: "It is customary to describe oleic acid as the *trans*-acid for reasons of which we must plead ignorance, though it is usual in other cases of geometrical isomerism, in the absence of any definite evidence, to regard the more stable higher-melting form as the *trans*-isomeride, which would therefore lead us to assign this structure to elaidic acid." These authors also point out that the absence of elaidic acid in nature is consistent with the latter view, since chemical changes induced by enzyme action in the living cell do not lead in general to the production of compounds in a form of maximum chemical stability.

G. M. and R. Robinson (*loc. cit.*) point out that the production of oleic acid from stearolic acid by reduction by zinc and hydrochloric acid in presence of titanous chloride indicates that oleic acid has the *cis*-configuration.

It has now been found that oleic and elaidic acids, when treated in glacial acetic acid or acetone solution in the cold, or more rapidly at about 60°, with moderately concentrated (30—35%) hydrogen peroxide, pass smoothly and almost quantitatively into the dihydroxystearic acids which melt, respectively, at 95° and 132°. Further, the methyl esters of these acids yield, by the same procedure, methyl 9 : 10-dihydroxystearates, m. p. 71° and 105° respectively, which, when hydrolysed by aqueous or alcoholic alkali, pass into the dihydroxystearic acids melting, respectively, at 95° and 132° without formation of any of the isomeric dihydroxy-acid; indeed, the sodium salts of the latter acids can be boiled with excess of aqueous caustic soda for some hours without any appreciable action taking place.

It is unlikely that the action of hydrogen peroxide in cold acetic acid solution should induce any isomeric change, and, bearing in mind the application of the method both to the free acids and to the esters, and also the high yields of individual products which result, it may well be inferred that the dihydroxy-acid, m. p. 95°, corresponds structurally with oleic acid, whilst that of m. p. 132° corresponds with elaidic acid.

However this may be, it is necessary to inquire why oxidation in an alkaline aqueous solution by means of potassium permanganate causes the production of the opposite, higher-melting acid from oleic acid, and *vice versa*. As Robinson and also Lapworth (*loc. cit.*) have pointed out, oxidation of oleic acid under the latter conditions leads to a high yield of dihydroxystearic acid only when definite precautions are taken, and, similarly, Saytzew apparently found difficulty in obtaining the lower-melting dihydroxystearic acid in quantity from alkaline elaidate solutions. At the same time, no evidence is apparent, either in the earlier or the present work, that any mixture of both acids is produced during the oxidation of either acid by alkaline permanganate; and it therefore appears that under the latter conditions the opposite acid to that normally produced is the only dihydroxystearic derivative formed. Further, the action of concentrated hydrogen peroxide in alkaline solutions of sodium oleate has also been examined, and, whilst under these conditions the oxidation proceeds with greater difficulty and oily products are also produced, there is formed a small proportion of the dihydroxystearic acid of m. p. 132°. Thus the nature of the dihydroxystearic acid formed when oleic acid is oxidised by hydrogen peroxide is conditioned by whether the medium is alkaline or not.

It is therefore believed, on the evidence at present available, that in an alkaline medium a change closely related to a Walden inversion takes place at the moment of transformation of the ethylenic linking, and that this offers the simplest and also the most complete explanation of the inter-relationships between the respective ethylenic and dihydroxystearic acids. Any "inversion" or isomerisation must occur in the actual formation of dihydroxy-acid from unsaturated acid, since, as already stated, each dihydroxystearic acid is perfectly stable in hot or even in boiling alkaline solution.

This explanation harmonises with many known instances of Walden inversion which take place during replacement of groups by hydroxyl by means of alkali and with well-known cases of racemisation of carbohydrates where the configuration of a –CH(OH)– group is reversed in presence of alkali, for example, the transformation of glucose into mannose.

Although not so closely comparable, it may also be recalled that Le Sueur (J., 1914, **105**, 2800) observed a very curious intramolecular rearrangement when 2 : 3-dihydroxystearic acid was fused with caustic potash at about 200° :

$$C_{15}H_{31}\cdot CH(OH)\cdot CH(OH)\cdot CO_2H \longrightarrow CH_2(OH)\cdot C(OH)(C_{15}H_{31})\cdot CO_2H$$

We may now consider how far this explanation accords with the earlier observations of Albitski (*loc. cit.*), who obtained the dihydroxystearic acid (m. p. 95°) from oleic acid, and also the acid (m. p. 132°) from elaidic acid, as follows :

(i) Addition of chlorine or bromine to the ethylenic acid, followed by treatment of the product with aqueous or alcoholic alkali.

(ii) Addition of hypochlorous acid to the ethylenic acid, when a chlorohydroxystearic acid was produced : (*a*) treatment of the latter acid with aqueous or alcoholic potash or baryta gave the dihydroxystearic acid as stated; although when silver oxide was used the opposite acid (*i.e.*, that which results by the action of alkaline permanganate) was produced; (*b*) treatment with baryta also gave a glycidic acid (an oil from oleic acid and crystalline, m. p. 60°, from elaidic acid); the glycidic acids gave the respective dihydroxystearic acids on treatment with alkali or with dilute sulphuric acid.

(iii) Oxidation of the unsaturated acids by Caro's acid.

Albitski assumed that, as in some other cases of Walden inversion, rearrangement occurred during the addition of halogen, which implies a similar rearrangement during the action of hypochlorous acid; whilst he was also forced to assume that some similar effect, ascribed to the influence of a sulphonated hydroxyl group, accounted for the results with Caro's acid. It is difficult to understand, nevertheless, how hydrogen peroxide alone (*i.e.*, except for acetone or acetic acid) should induce the same rearrangement.

Reviewing the whole of the reactions which have been employed in the transformation of oleic or elaidic acids into dihydroxystearic acids, the higher-melting dihydroxy-acid has been produced from oleic acid, and the lower-melting acid from elaidic acid, only when oxidation has proceeded in presence of aqueous alkali, whereas the opposite acids are consistently obtained by such diverse methods as those enumerated above. It seems reasonable to conclude that the acid so produced by a variety of means is that most closely connected with the corresponding ethylenic acid.

At the same time, further changes in configuration may take place during the replacement of hydroxyl groups, for example, in the dihydroxy-acids by means of halogen, since Albitski was able to convert the higher-melting into the lower-melting acid by intermediate production of a bromoacetylstearic acid, and also to show that two dibromostearic acids, which gave a mixture of oleic and elaidic acids on reduction, resulted when the acid of higher melting point interacted with hydrogen bromide.

As is well known, the experimental evidence on changes connected with the Walden inversion is in many cases apparently contradictory; it is not impossible that investigations on the lines indicated in this communication may assist to some extent in the elucidation of this complicated problem.

Further examination of the 9 : 10-dihydroxystearic acids is in progress, especially with reference to the possibility of their resolution into optically active forms. Freundler (*Bull. Soc. chim.*, 1895, **13**, 1052) showed that the acid of m. p. 132° was a racemic form, but it would appear uncertain whether complete resolution was effected.

The action of hydrogen peroxide in organic solvents upon simpler ethylenic derivatives is also being studied from a similar point of view.

The behaviour of oleic and elaidic acids on gentle oxidation in acidic or alkaline solution is exactly parallel with that of the other pairs of geometrically isomeric higher ethylenic acids which have so far been examined, as is illustrated in the following table :

	" Oleic " form.		" Elaidic " form.	
Dihydroxy-acids from	Acid. M. p.	Alkaline $KMnO_4$. M. p.	Acid. M. p.	Alkaline $KMnO_4$. M. p.
Oleic and elaidic acids, $C_{18}H_{34}O_2$	95° [1, 5]	132° [2]	132° [1, 5]	95° [2]
Petroselinic acid, $C_{18}H_{34}O_2$	96—99 [3]	122 [3]	120—123 [3]	96—99 [3]
Erucic and brassidic acids, $C_{22}H_{42}O_2$	100 [1]	133 [4]	133 [1]	100 [4]
Palmitoleic acid of whale oil, $C_{16}H_{30}O_2$	87 [5]	125 [5]		
2 : 3-Palmitoleic acid, $C_{16}H_{30}O_2$	105—106·5 [6]	125—127 [6]		

[1] Albitski, *loc. cit.* (Caro's acid, dihalogen additive products).

[2] Saytzew, *loc. cit.*

[3] Afanesievski, *J. Russ. Phys. Chem. Soc.*, 1915, **47**, 2124 (Caro's acid).

[4] Saytzew, *J. pr. Chem.*, 1894, **50**, 82.

[5] Present communication (hydrogen peroxide in acetic acid).

[6] Zimovski, *J. Russ. Phys. Chem. Soc.*, 1915, **47**, 2121 (Caro's acid).

In conclusion, it may be pointed out that, if the dihydroxystearic acid of m. p. 132° be not directly connected stereochemically with ordinary oleic acid, its use as an indication of the presence of the latter is not necessarily invalid on this ground, since under controlled conditions of experiment it is the exclusive product of oxidation. A more serious objection to its employment for purposes of identification lies in the fact that the melting points of most of the higher-melting forms of these dihydroxy-acids lie within a narrow range and, moreover, the data given in the experimental part of this paper show that mixtures of dissimilar dihydroxy-acids may exhibit unusually small depression of melting point.

EXPERIMENTAL.

Oxidation of Oleic Acid or Methyl Oleate.—Oleic acid was prepared from the fatty acids of pure olive oil, which were treated with 15% of their weight of lead acetate in a solution of four times their weight of alcohol (compare Twitchell, *J. Ind. Eng. Chem.*, 1921, **13**, 806). The insoluble lead salts having been removed, the fatty acids (iodine absorption 97·4%) were recovered from the dissolved lead salts and converted into lithium salts, which were crystallised twice from alcohol. The acid from the recrystallised lithium oleate was converted into methyl ester, which was fractionally distilled under reduced pressure; the main fraction then consisted of pure methyl oleate. Pure oleic acid was prepared from this ester by saponification.

The hydrogen peroxide which was mainly used in these experiments was of " 120 volumes " or 36% strength.

Oleic Acid and Hydrogen Peroxide in Cold Acetic Acid.—A solution of 12 g. of oleic acid in 80 c.c. of glacial acetic acid to which 20 g. of the concentrated hydrogen peroxide had been added was left at room temperature for 9 days, with occasional agitation until the mixture became homogeneous. The acetic acid was then distilled in steam, and the residual solid acid extracted with ether and boiled under reflux with excess of *N*-sodium hydroxide for 6 hours. The acid was recovered (11·0 g.) and recrystallised twice from ethyl acetate, in which it was somewhat soluble in the cold: 6·1 g. of dihydroxystearic acid, m. p. 95°, were thus obtained (Equiv., found, 312·9; required, 316).

Sodium Oleate and Hydrogen Peroxide in Aqueous Alkali.—Oleic acid (10 g.) was neutralised with *N*-sodium hydroxide in presence of 250 c.c. of water, a further 5 c.c. of the alkali were added followed by 20 g. of concentrated hydrogen peroxide, and the solution was heated for 5 hours at such a temperature that gaseous oxygen was not freely evolved. After 12 hours, a further 10 g. of peroxide were added and gentle heating was resumed on the steam-bath for several hours. The solution was then acidified and the fatty acids were extracted; the small deposit of crystalline acid obtained on standing, after twice crystallising from ethyl acetate, melted at 130—131°, alone or mixed with an equal amount of dihydroxystearic acid (m. p. 132°) prepared by alkaline permanganate oxidation of sodium oleate.

Methyl Oleate and Hydrogen Peroxide in Cold Acetic Acid.—12 G. of methyl oleate were dissolved in 80 c.c. of glacial acetic acid and 20 g. of concentrated hydrogen peroxide were added to the solution, which was left at room temperature for 5 days with occasional shaking. After the acetic acid had been removed by distillation in steam, the product was extracted with ether and the ethereal solution washed with aqueous sodium carbonate. The neutral ethereal solution yielded a crystalline ester which was purified by crystallisation from methyl alcohol (in which it was very soluble) and then melted at 70—71°.

The methyl alcohol mother-liquor was refluxed with sufficient solid caustic soda to ensure saponification, and the resulting acid was crystallised twice from ethyl acetate; it then melted at 93—95°, alone or mixed with the acid obtained by the action of hydrogen peroxide upon oleic acid.

Methyl Oleate and Hydrogen Peroxide in Hot Acetic Acid.—10 G. of methyl oleate were dissolved in 70 c.c. of glacial acetic acid and heated at 70—80° for several hours after addition of 20 g. of concentrated hydrogen peroxide. The product was worked up as in the preceding case and furnished 8·4 g. of solid esters (together with 1·2 g. of dihydroxystearic acid produced by hydrolysis during the process). Crystallisation of the ester from light petroleum (b. p. below 60°) yielded fine needles, m. p. 71° (Found : C, 68·9; H, 11·5. $C_{19}H_{38}O_4$ requires C, 69·1; H, 11·5%).

A specimen of the acid prepared by saponification of the ester crystallised from ethyl acetate in small, thin, waxy prisms, m. p. 95°, somewhat soluble in cold ethyl acetate, more soluble in cold ethyl alcohol (Found : C, 68·1; H, 11·5. $C_{18}H_{36}O_4$ requires C, 68·4; H, 11·4%).

Methyl Oleate and Hydrogen Peroxide in Boiling Acetone.—A solution of 5 g. of methyl oleate in 50 c.c. of acetone to which 10 g. of concentrated hydrogen peroxide had been added was heated under reflux for 8 hours and left over-night. After removal of the acetone the product was saponified with alcoholic soda and the resulting acids were treated in alcoholic solution with one-third of their equivalent weight of lead acetate. The acids recovered from the deposited lead salts were crystallised from ethyl acetate and then melted at 92—93°. The conversion into dihydroxystearic acid was by no means so complete as in acetic acid solution, but the acid produced was evidently the lower-melting form.

Oxidation of Elaidic Acid or Methyl Elaidate.—Crude elaidic acid (containing oleic and palmitic acids as impurities) was purified by fractional precipitation of its lead salt from alcohol by the Twitchell method, the least soluble fraction (containing small quantities of saturated acids) being rejected. The lead salts from succeeding selected fractions were recrystallised from alcohol and converted into the free acid, which then melted at 42—43°. This was esterified with methyl alcohol, and the neutral ester fractionally distilled under 3 mm. pressure: pure methyl elaidate was then obtained (saponification equivalent, found : 295·3, calc. : 296; iodine absorption, found: 82·0, calc.: 85·8%). The elaidic acid prepared from this ester melted without further purification at 44—44·5°.

Elaidic Acid and Hydrogen Peroxide in Cold Acetic Acid.—This oxidation was carried out as in the case of the corresponding experiment with oleic acid (p. 1833): from 12 g. of elaidic acid there were obtained, after two recrystallisations from ethyl acetate, 9·7 g. of dihydroxystearic acid, m. p. 131—132°. This melting point was not affected by admixture with dihydroxystearic acid prepared by oxidation of sodium oleate with alkaline permanganate.

Elaidic Acid and Aqueous Alkaline Permanganate.—2 G. of elaidic acid were dissolved in 2000 c.c. of ice-cold water after addition of 2 g. of solid caustic soda, and to the solution were added with agitation 3 g. of potassium permanganate dissolved in 500 c.c. of ice-cold water; the procedure recommended for the alkaline oxidation of oleic acid by Lapworth and Mottram (J., 1925, **127**, 1628) was closely followed and 1·6 g. of dry solid oxidised acid were obtained. After crystallisation three times from ethyl acetate the acid melted at 93—95° alone, and also when mixed with some of the pure acid prepared by oxidation of oleic acid with hydrogen peroxide in acetic acid solution.

Methyl Elaidate and Hydrogen Peroxide in Cold Acetic Acid.—6 G. of methyl elaidate were dissolved in 40 c.c. of glacial acetic acid, mixed with 10 g. of concentrated hydrogen peroxide, and left for 4 days at room temperature. The solution was then worked up as in the foregoing cases of methyl oleate, and 5·4 g. of solid ester were obtained in addition to a little free dihydroxy-acid. The purified ester melted sharply at 105° (Spiridonow, *J. pr. Chem.*, 1889, **40**, 244, states that the dihydroxystearic acid of m. p. 132° yields a methyl ester which melts at 105—106°), and the corresponding acid at 131—132°.

Oxidation of methyl elaidate by hydrogen peroxide in *warm* (70—80°) *acetic acid* produced a still greater yield of the higher-melting methyl dihydroxystearate. This ester is somewhat readily soluble in cold methyl alcohol, less soluble in ethyl acetate, and crystallises readily in small, waxy needles from light petroleum (b. p. below 60°). After several crystallisations from the latter solvent it still melted sharply at 105° (Found: C, 69·0; H, 11·4. Calc.: C, 69·1; H, 11·5%).

The free acid, m. p. 131—132°, was found by the mixed melting-point method to be identical with that obtained by alkaline oxidation of oleic acid (Found: C, 68·0; H, 10·9. Calc.: C, 68·4; H, 11·4%).

Oxidation of Palmitoleic Acid and Methyl Palmitoleate.—The methyl palmitoleate was prepared from the palmitoleic acid of whale oil (compare Armstrong and Hilditch, *J. Soc. Chem. Ind.*, 1925, **44**, 186T).

Oxidation of sodium palmitoleate by alkaline permanganate. It was stated in the paper referred to (p. 181) that under these conditions a dihydroxypalmitic acid which melts at 125° is formed. The following table illustrates the melting points of mixtures of this acid with the dihydroxystearic acid (m. p. 132°) in varying proportions :

% Dihydroxypalmitic acid.	% Dihydroxystearic acid.	M. p.
100	—	125°
75	25	124—125
50	50	124—125
25	75	125—126
—	100	132

The depression in melting point is thus of an abnormally small order.

Methyl palmitoleate and hydrogen peroxide in acetic acid. 10 G. of methyl palmitoleate were dissolved in 80 c.c. of glacial acetic acid and left with 20 g. of concentrated hydrogen peroxide at room temperature for several days. The product was treated as in previous cases and yielded the ester, methyl 9 : 10-dihydroxypalmitate, which was very soluble in light petroleum or ethyl acetate; it crystallised in soft, waxy leaflets, m. p. 65°.

The corresponding 9 : 10-dihydroxypalmitic acid was prepared by hydrolysis of the ester : this also was somewhat readily soluble in ethyl acetate, from which it separated in waxy crystals, m. p. 86—87° (Found : C, 66·4; H, 11·0. $C_{16}H_{32}O_4$ requires C, 66·7; H, 11·1%).

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