

67. *The Dihydroxystearic Acid of Castor Oil: its Constitution and Structural Relationship to the 9:10-Dihydroxystearic Acids, m. p.'s 132° and 95°.*

By GEORGE KING.

Oxidation of the naturally occurring dihydroxystearic acid of castor oil, m. p. 141°, with periodic acid has been shown to afford η -aldehydo-octoic acid and nonaldehyde, thus confirming its constitution as a 9:10-dihydroxystearic acid.

Hydrogen chloride, or concentrated hydrochloric acid, at 160° converts it into an oily mixture of chlorohydroxystearic acids, which yields an optically active *oxidostearic acid*, m. p. 59·5°, when boiled with dilute aqueous or alcoholic alkali. This on hydrolysis with concentrated alkali affords *r*-dihydroxystearic acid, m. p. 95°. Similarly, *r*-dihydroxystearic acid, m. p. 132°, is converted *via* the chlorohydrins successively into *r*-oxidostearic acid, m. p. 59·5°, and *r*-dihydroxystearic acid, m. p. 95°, and under the same conditions the dihydroxy-acid, m. p. 95°, furnishes *r*-oxidostearic acid, m. p. 55·5°, and finally the dihydroxy-acid, m. p. 132°.

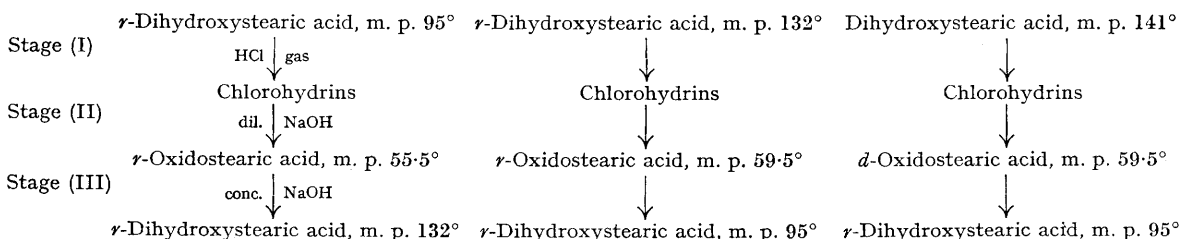
The optical inversion involved in these transformations almost certainly occurs during hydration of the oxide ring, and the conclusion is drawn that the dihydroxy-acid from castor oil is an active component of *r*-dihydroxystearic acid, m. p. 132°. It is, however, virtually internally compensated, its activity being too feeble for accurate measurement.

Configurational formulæ have been provisionally assigned to these acids.

It has long been known that a dihydroxystearic acid, m. p. 141°, occurs amongst the products of hydrolysis of castor oil. As a deposit from crude ricinoleic acid obtained from the oil, it was mentioned by Juillard (*Bull. Soc. chim.*, 1895, **13**, 246) and subsequently by Meyer (*Arch. Pharm.*, 1897, **235**, 185), Mühle (*Ber.*, 1913, **46**, 2095), and Fahrion (*Chem. Zentr.*, 1916, **II**, 580), but its constitution remained uncertain. More recently, Toyama and Ishikawa (*Bull. Soc. Chem. Japan*, 1936, **11**, 735) showed that the hydroxyl groups occupy the 9:10-positions by chromic acid oxidation to nonoic and azelaic acids, and by conversion of the methyl ester, m. p. 111°, into a mixture of oleic and elaidic acids *via* methyl dibromostearate. Polarimetric examination by these authors of the free acid and of its methyl ester revealed too feeble an optical activity to be measured with certainty, but it was considered that both were slightly dextrorotatory in methyl-alcoholic solution. In any case, the acid must be a component of one or other of the two racemic dihydroxystearic acids, m. p.'s 95° and 132°, or, much less probably, a mixture of diastereoisomerides.

Resolution of the racemic acids through their strychnine salts was claimed by Freundler (*Bull. Soc. chim.*, 1895, **13**, 1053) and by Inoue and Suzuki (*Proc. Imp. Acad. Tokyo*, 1931, **7**, 261), but unfortunately the melting points of the optically active isomerides were not recorded. According to Freundler, the rotatory power of the optically active acids was so small as to render an absolute differentiation almost impossible, whereas the latter workers recorded $[\alpha]_D + 23\cdot2^\circ$ and $- 23\cdot6^\circ$ for the *d*- and the *l*-isomeride of the dihydroxy-acid, m. p. 132°; $[\alpha]_D + 27\cdot6^\circ$ and $- 27\cdot45^\circ$ for those of the acid, m. p. 95°. Toyama and Ishikawa (*loc. cit.*), on the other hand, were unable to resolve the racemic acids by means of the strychnine salts.

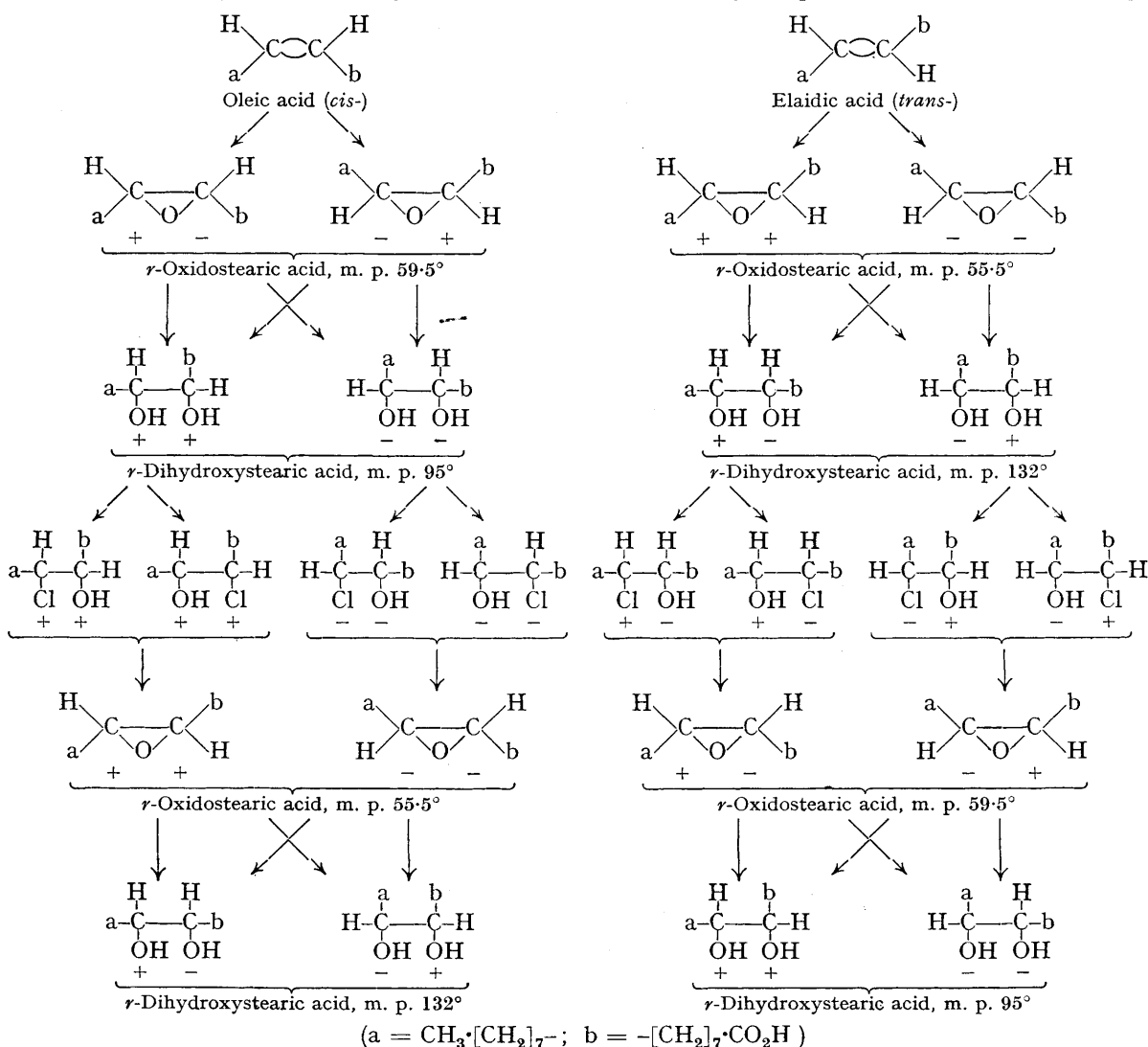
The purpose of the present investigation was to establish the constitution of the dihydroxystearic acid from castor oil, and to determine its relationship to the racemic acids. As a result, unequivocal evidence has now been obtained that the hydroxyl groups occupy the 9:10-positions, since oxidation with periodic acid has been shown to afford nonaldehyde and η -aldehydo-octoic acid (cf. King, J., 1938, 1826), and it is reasonably certain that the acid is an active component of the racemic acid, m. p. 132°. Although attempts to resolve the racemic acids through their strychnine salts were unsuccessful, evidence of the stereochemical relationships of all three acids was obtained by their interconversion through the corresponding chlorohydroxy- and oxido-stearic acids, as summarised below:



From stereochemical considerations, it is clear that complete inversion of one of the two asymmetric groups occurring at either stage (I) or stage (III) of the transformation, *i.e.*, during the replacement of hydroxyl by chlorine, or on fission of the oxide ring, would satisfactorily account for the mutual conversion

of the two racemic dihydroxy-acids. According to Böeseken and Belinfante (*Rec. Trav. chim.*, 1926, **45**, 917), inversion occurs during the hydration of the oxide ring in an acid medium, and Esafov (*J. Gen. Chem. Russ.*, 1937, **7**, 1403) suggested that isomerisation always takes place when α -oxides are hydrated. Esafov found that iodohydroxystearic acid from oleic acid gives dihydroxystearic acid, m. p. 132°, on treatment with dilute alkali, presumably by direct substitution of hydroxyl for halogen, whereas with concentrated alkali an oxidostearic acid is formed as an intermediate product, affording on hydrolysis the dihydroxy-acid, m. p. 95°. In the absence of any certain knowledge concerning the relative configurations of the iodohydroxy- and dihydroxy-stearic acids, however, similar results might be anticipated if a Walden inversion occurred instead during the replacement of halogen by hydroxyl.

Each of the two *r*-dihydroxystearic acids may give two pairs of antimeric chlorohydroxystearic acids with hydrogen chloride under controlled conditions. These in turn, by removal of hydrogen chloride in the presence of alkali, will afford one pair of enantiomorphously related oxidostearic acids, but the identity of the externally compensated oxido-acid so formed will depend on whether or not inversion has occurred during stage (I). The scheme below has been drawn up on the assumption that inversion occurs only during fission of the oxide ring [stage (III)]. Under these conditions any one of the four optically active dihydroxy-acids may furnish an active oxido-acid, whereas if inversion occurred during replacement of $-OH$ by $-Cl$ [stage (I)], the resulting oxido-acid would be externally compensated. The further assump-



tion has been made that the rotations contributed by the two asymmetric groups in *r*-oxidostearic acid, m. p. 55.5° [formed also by autoxidation of elaidic acid (Ellis, *Biochem. J.*, 1936, **30**, 756)], are of the same

sign, which finds a parallel in the oxidation of fumaric to racemic acid, and is in harmony with the extraordinarily feeble rotation exhibited by the dihydroxy-acid, m. p. 141° , in which it is reasonable to suppose the two asymmetric groups have opposing influences. The dihydroxy-acid from castor oil does, in fact, yield an optically active (*d*-)oxidostearic acid, m. p. 59.5° (via the chlorohydrins), which, although not identical with *r*-oxidostearic acid, m. p. 59.5° , gives the same dihydroxy-acid, m. p. 95° , on hydrolysis. The conclusion may be drawn that the active oxido-acid is a component of *r*-oxidostearic acid, m. p. 59.5° , and that the dihydroxy-acid from castor oil is itself an active component of the acid, m. p. 132° . These results lend strong support to the view that isomerisation occurs on hydration of the oxide ring. Further, it is clear that the dihydroxy-acid from castor oil cannot be a mixture of diastereo-isomerides such as $dA dB + dA lB$, where A and B represent the two asymmetric groups in the molecule, since this would lead to the production of a *mixture* of (diastereo-)isomeric oxido-acids, which in turn would furnish a *mixture* of the two racemic dihydroxy-acids, contrary to the observed facts.

Dihydroxystearic acid, m. p. 141° , was found by the author to be virtually internally compensated, its extremely feeble optical activity, combined with its low solubility in the usual solvents, making an accurate determination of its rotatory power practically impossible, although the polarimeter used was capable of detecting an angular rotation of $1'$ or more [the instrument used by Toyama and Ishikawa (*loc. cit.*) could not detect with certainty a rotation of less than $15'$].

Oleic and elaidic acids have been included in the scheme not only for the sake of completeness, but also because they contribute materially to a full appreciation of the stereochemical relationships existing between the oxidised acids. It may be relevant to point out that the oxidation of oleic and elaidic acids by alkaline permanganate to the dihydroxystearic acids, m. p.'s 132° and 95° respectively, appears to involve normal *cis*-addition of two hydroxyl groups, if the proposed configurational formulæ are correct (cf. Hilditch, J., 1926, 1828; Hilditch and Lea, J., 1928, 1576). At the same time a rational explanation is offered of the formation of the dihydroxy-acid, m. p. 95° , from oleic acid with the aid of perbenzoic acid (Pigulevski and Petrova, *J. Russ. Phys. Chem. Soc.*, 1926, 58, 1062; Böeseken and Belinfante, *loc. cit.*; Nicolet and Poulter, *J. Amer. Chem. Soc.*, 1930, 52, 1189), where an intermediate oxido-compound is known to be formed. It is still uncertain, however, whether a similar explanation may be applied to the use of Caro's acid (Albitski, *J. Russ. Phys. Chem. Soc.*, 1902, 34, 810), and of hydrogen peroxide in neutral or acid solution (Hilditch, *loc. cit.*), since in these cases, so far as is known, no intermediate oxidostearic acid has as yet been isolated (see, e.g., Hilditch and Lea, *loc. cit.*). However this may be, the configurations here assigned must be regarded as tentative only, and further evidence in this connexion is being sought.

The mutual transformation of the two *r*-dihydroxystearic acids was accomplished by Albitski (*loc. cit.*, p. 788) through the intermediate formation of bromoacetoxy- or diacetoxy-stearic acid, but from the latter mixtures usually resulted, and in the present investigation isomerism appears to have been complete.

The melting points obtained for the *r*-oxidostearic acids fully confirm those recorded by Ellis (*loc. cit.*) (cf. Pigulevski and Petrova, *loc. cit.*; Böeseken and Belinfante, *loc. cit.*; Nicolet and Poulter, *loc. cit.*; Hashi, *J. Soc. Chem. Ind. Japan*, 1936, 39, 162B).

EXPERIMENTAL.

Isolation and Physical Properties of 9 : 10-Dihydroxystearic Acid, m. p. 141° .—The source of the acid was the sludge deposited on long standing from technical ricinoleic acid. This was filtered with suction, and the finely crystalline residue washed with light petroleum. After several crystallisations from alcohol, the acid separated in small, colourless, hexagonal plates, m. p. 141° (Found : C, 68.3; H, 11.2; equiv., 316. Calc. for $C_{18}H_{36}O_4$: C, 68.3; H, 11.4%; equiv. 316). In solubility, the product closely resembled the synthetic 9 : 10-dihydroxystearic acid, m. p. 132° , being very sparingly soluble in light petroleum, cold chloroform and benzene, and only slightly soluble in cold alcohol and ether. The saturated solution in alcohol at 20° contained 0.82 g. per 100 ml., and the solubility of the acid, m. p. 132° , was 0.68 g., and that of a mixture of the acids, 0.89 g. per 100 ml. of solution at the same temperature. It was inferred that the acid, m. p. 132° , was a true racemic compound rather than a *dl*-conglomerate, assuming the acid from castor oil to be one of its optically active components.

Polarisation of a warm alcoholic solution of the acid, m. p. 141° , gave as a result of numerous readings $[\alpha]_D^{50} - 0.15^\circ$ ($l = 2$, $c = 3.8$), but the rotation observed ($0.7'$) was probably within the limits of experimental error. The addition of 5% of boric acid to the solution had no measurable effect on the rotation.

Oxidation with Periodic Acid.—Dihydroxystearic acid, m. p. 141° , (6 g.) in alcohol (300 ml.) was oxidised at 40° with periodic acid as previously described for the acid, m. p. 132° (King, *loc. cit.*, p. 1827), yielding nonaldehyde (2.74 g.), b. p. $185-190^\circ$ (Found : C, 75.7; H, 12.9. Calc. for $C_9H_{18}O$: C, 76.0; H, 12.8%) [2 : 4-dinitrophenylhydrazones, m. p. and mixed m. p. with an authentic specimen 106.5° (Found : C, 56.0; H, 7.2; N, 16.9. Calc. for $C_{15}H_{22}O_4N_4$: C, 55.9; H, 6.9; N, 17.4%); semicarbazone, slender rhombic and hexagonal plates from dilute alcohol, m. p. and mixed m. p. with an authentic specimen 101.5°], and η -aldehydo-octic acid (2.1 g.), m. p. 38° (Found : equiv., 173. Calc. for $C_8H_{16}O_3$: equiv., 172) [semicarbazone, m. p. 166.5°

(Found: C, 52.3; H, 8.6; N, 18.0; equiv., 229. Calc. for $C_{10}H_{19}O_3N_3$: C, 52.4; H, 8.3; N, 18.3%; equiv., 229); 2: 4-dinitrophenylhydrazone, orange prisms or blades from methyl alcohol, m. p. and mixed m. p. with an authentic specimen 122.5°].

Special care had to be taken in the extraction of these products to use ether free from peroxides, as otherwise the semialdehyde was more or less oxidised to bis- α -hydroxy- ω -carboxyoctyl peroxide, m. p. 112.5° (this vol., p. 219).

Conversion of Dihydroxystearic Acid, m. p. 141°, into d-9: 10-Oxidostearic Acid, m. p. 59.5°, and Dihydroxystearic Acid, m. p. 95°.—Attempts to racemise the acid from castor oil by heating with water or 0.4N-sulphuric acid in a sealed tube at 160° for 1 hour, by boiling with N/2-alcoholic potassium hydroxide, or by heating with N/4-aqueous sodium hydroxide in a sealed tube at 165° for 8 hours were ineffectual, the acid in each case being recovered substantially unchanged (Inoue and Suzuki, *loc. cit.*, reported that the optical isomerides of the dihydroxy-acids, m. p.'s 132° and 95°, were readily racemised during the formation of their potassium salts, or on boiling in alcohol for 30 minutes).

Dry hydrogen chloride was passed at a moderate rate through the dihydroxy-acid (2.85 g.), heated in an open tube in a glycerol bath at 160° for 4 hours. The viscous oily product, consisting of a mixture of chlorohydroxystearic acids, was washed by decantation, and boiled (without further purification) with 2N-sodium hydroxide (75 ml.) for 7 hours (or with 2N-alcoholic potassium hydroxide for 2 hours). The solid product obtained on acidification was collected, dried, and extracted with warm light petroleum (30–40 ml.). A small insoluble fraction was removed by filtration, and crystallised successively from benzene and methyl alcohol, separating from the latter in rectangular plates (0.26 g.), m. p. 94°, not depressed by admixture with authentic dihydroxystearic acid, m. p. 95°, prepared by oxidising elaidic acid with permanganate in alkaline solution (Found: C, 68.0; H, 11.1%; equiv., 317).

When the light petroleum filtrate was concentrated and cooled in ice, a deposit of *d-oxidostearic acid* (1.6 g.) was obtained. This crystallised from methyl alcohol and acetone in truncated triangular plates, m. p. 59.5°, usually separating in six- or eight-sided forms, $[\alpha]_D^{20}$ in alcohol + 0.29° ($l = 2$, $c = 8.54$) (Found: C, 72.3; H, 11.2; equiv., 298. $C_{18}H_{34}O_3$ requires C, 72.4; H, 11.5%; equiv., 298), readily soluble in most organic solvents other than light petroleum.

Hydrolysis of the oxidostearic acid (0.52 g.) was best effected by heating with 7N-potassium hydroxide (6 ml.) in a sealed tube at 170° for 5 hours. The product was dissolved in sufficient hot water, filtered from silica, and acidified with hydrochloric acid. After cooling, the precipitated acid was collected, and crystallised successively from benzene (*ca.* 30 ml.) and methyl alcohol, separating from the latter in rectangular plates (0.34 g.), m. p. 94.5°, not depressed by admixture with authentic dihydroxystearic acid, m. p. 95°.

As an alternative to hydrogen chloride, concentrated hydrochloric acid was sometimes used for the preparation of chlorohydroxystearic acids. For this purpose the dihydroxy-acid (2 g.), m. p. 141°, was heated with concentrated hydrochloric acid (5 ml.) in a sealed tube at 160° for 4 hours. Subsequent hydrolysis of the chlorohydrins afforded a yield of oxidostearic acid comparable with that obtained with the aid of hydrogen chloride, but the product was usually associated with varying amounts of an impurity, from which the more soluble oxido-acid was separated by fractional crystallisation from 80% alcohol. This substance furnished rhombic plates, m. p. 73.5°, and was possibly a mixture of 9- and 10-ketostearic acids, although its identity was not definitely established [Found: C, 72.4; H, 11.3; equiv., 301; *M* (Rast), 328. Calc. for $C_{18}H_{34}O_3$: C, 72.4; H, 11.5%; equiv., 298]. It was readily soluble in ether, benzene, and warm light petroleum, but sparingly soluble in the last at 20°, and differed sharply from oxidostearic acid in being resistant to hydrolysis and unaffected by periodic acid (the oxido-acids appeared to be oxidised by periodic acid in much the same way as the dihydroxy-acids, the characteristic odour of nonaldehyde being at once apparent).

Conversion of Dihydroxystearic Acid, m. p. 132°, into r-Oxidostearic Acid, m. p. 59.5°, and Dihydroxystearic Acid, m. p. 95°.—Dihydroxystearic acid (3.9 g.), m. p. 132°, was treated with hydrogen chloride at 160°, and the product boiled with 2N-alkali in the manner described above. Fractionation from light petroleum then afforded dihydroxystearic acid (0.9 g.), m. p. and mixed m. p. with an authentic specimen 94°, and *r*-oxidostearic acid (1.97 g.), crystallising from acetone in long slender laminae, m. p. 59.5°, not depressed by admixture with a specimen of oxidostearic acid of the same m. p. kindly supplied by Dr. G. W. Ellis, and prepared from oleic acid by treatment with hypochlorous acid, followed by alcoholic sodium ethoxide (Ellis, *loc. cit.*, p. 757) (Found: C, 72.5; H, 11.5%; equiv., 298). When mixed with an equal quantity of *d*-oxidostearic acid of the preceding experiment (which is one of its active components, and, although having the same m. p., differs markedly from it in crystalline form), the m. p. was depressed by a small but definite amount to 56°.

Hydrolysis of the racemic oxidostearic acid furnished a good yield of dihydroxystearic acid, m. p. and mixed m. p. with an authentic specimen, 94.5°, separating from methyl alcohol in characteristic rectangular plates. No trace of the dihydroxy-acid, m. p. 132°, as a result of hydrolysis was found either in this or in the preceding experiment.

Conversion of Dihydroxystearic Acid, m. p. 95°, into r-Oxidostearic Acid, m. p. 55.5°, and Dihydroxystearic Acid, m. p. 132°.—By the procedure described above, dihydroxystearic acid (1.20 g.), m. p. 95°, gave dihydroxystearic acid (0.05 g.), m. p. and mixed m. p. with an authentic specimen prepared by oxidising oleic acid with alkaline permanganate 131.5°, separating from alcohol in rhombic and hexagonal plates, and *r*-oxidostearic acid (0.77 g.), which crystallised from methyl alcohol in small rhombic plates, m. p. 55.5° (Found: C, 72.5; H, 11.6%; equiv., 299). The m. p. of the latter was not depressed by admixture with a specimen of oxidostearic acid, m. p.

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55·5°, kindly supplied by Dr. G. W. Ellis and prepared by autoxidation of elaidic acid. Mixed with *r*-oxido-stearic acid, m. p. 59·5°, or *d*-oxidostearic acid, m. p. 59·5°, the m. p. was depressed to 48—49°.

Hydrolysis of this oxido-acid afforded a good yield of dihydroxystearic acid, m. p. and mixed m. p. with an authentic specimen 132° (Found : equiv., 315). No trace of the dihydroxy-acid, m. p. 95°, was found as a result of hydrolysis.

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