

[CONTRIBUTION FROM THE CHEMICAL LABORATORY, GENERAL MILLS, INC.]

Hydroxylated Stearic Acids. II. The Periodate Oxidation of the 9,10-Dihydroxystearic Acids and the 1,9,10-Trihydroxyoctadecanes^{1a}

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The quantitative oxidative cleavage of vicinal hydroxyl groups by the action of periodic acid to yield two carbonyl compounds was first demonstrated by Malaprade,^{1b} and it was later postulated by Criegee² and co-workers that the reaction proceeded through an acidic cyclic ester which decomposed with water to yield the observed products.

That a cyclic diester is an intermediate in this reaction has likewise been postulated by Price and co-workers³ who further pointed out that if ring formation is the rate-controlling factor then so-called *cis* glycols would be expected to oxidize faster than the corresponding *trans* isomers. This follows since the requisite double inversion which must necessarily occur in cyclic ester formation does not change the relative positions in space of the *cis* and *trans* hydroxyl pairs.

Criegee² had previously shown this to be so in compounds in which the space relationships of the adjacent hydroxyl groups were determined and rigidly maintained by the cyclic nature of the compounds. Price and co-workers³ extended the work to the open chain compounds, ethylene glycol and pinacol, and showed that the hydroxyl groups are on the average more proximal in acidic than in basic medium probably because of association with a proton at a lower *pH*. Furthermore, this difference in space relationship was readily detectable by the difference in rate of oxidation by periodate.

Thus previous work has shown that periodate oxidation is a valuable tool for the determination of configuration of glycols when the configuration depends either on a cyclic structure or on the *pH* of the medium. It was postulated, therefore, that this reagent would be valuable, likewise, in indicating the proximity of the hydroxyl groups in the diastereoisomeric open chain glycol pairs. That lead tetraacetate was an adequate reagent for this purpose had previously been reported by Hilditch and Jasperson^{4a} and Dorée and Pepper^{4b} who had shown respectively that the low-melting forms of 9,10-dihydroxystearic acid and 13,14-dihydroxybehenic acid are oxidized more rapidly than the high-melting forms.

In the case of alicyclic glycols the so-called *cis*

(1a) Paper No. 83, Journal Series, Research Laboratories, General Mills, Inc.

(1b) L. Malaprade, *Bull. soc. chim.*, [4] **43**, 683 (1928); [5] **1**, 833 (1934); [5] **4**, 906 (1937).

(2) R. Criegee, *Sitzber. Ges. Beförder. ges. Naturw. Marburg*, **69**, 25 (1934).

(3) (a) C. C. Price and H. Kroll, *THIS JOURNAL*, **60**, 2726 (1938);

(b) C. C. Price and M. Knell, *ibid.*, **64**, 552 (1942).

(4) (a) T. P. Hilditch and H. Jasperson, *Nature*, **147**, 327 (1941);

(b) C. Dorée and A. C. Pepper, *J. Chem. Soc.*, 447 (1942).

and *trans* relationship arises from a combination of the repulsive effects of the hydroxyl groups and of the groups attached to the hydroxyl-bearing carbon atoms. In such instances it is interesting to note that free rotation is probably reduced to what may be regarded as a sort of oscillation within a restricted area.

Accordingly, periodate oxidation was applied to each of the forms of the 9,10-dihydroxystearic acids and the 1,9,10-trihydroxyoctadecanes in the hope that there would be a detectable difference in the rate of oxidation which in turn would provide additional evidence for the configuration of these compounds.

King⁵ had previously oxidized with periodate both forms of the 9,10-dihydroxystearic acids in order to obtain the expected scission products without, however, noting a difference in the rates of oxidation. In the present investigation it was observed that low-melting 9,10-dihydroxystearic acid (95°) consumed periodate at a much more rapid rate than did the high-melting form (132°) when the oxidations were carried out in aqueous media in the presence of an emulsifying agent consisting of sodium β -alkylaminopropionate in which the alkyl moiety was derived from soybean oil fatty acids. This is indicated in Table I.

TABLE I
OXIDATION OF THE 9,10-DIHYDROXYSTEARIC ACIDS IN AQUEOUS MEDIA AT 24°

Time, min.	Moles of acid oxidized	
	Low-melting form	High-melting form
5	0.29	..
15	.60	..
30	.91	0.02
45	.94	..
60	1.04	.10
90	1.05	.30
105	..	.42
120	1.03	.54
180	..	.74
240	..	.89
300	..	.95

Since there was a possibility that the results might have been influenced by a difference in the solubilities of the two forms, the oxidations were carried out in the homogeneous medium provided by 75 volume per cent. aqueous ethanol. Although homogeneity greatly accelerated the reaction rates, a very marked difference in behavior was still demonstrated by the two forms.

Similarly the low melting form of 1,9,10-trihydroxyoctadecane was oxidized at a more rapid rate

(5) G. King, *ibid.*, 1826 (1938).

than the high melting form in 75 volume per cent. aqueous ethanol. These results are indicated in Table II.

TABLE II

OXIDATION OF THE 9,10-DIHYDROXYSTEARIC ACIDS AND THE 1,9,10-TRIHYROXYOCTADECANES IN 75 VOLUME PER CENT. ETHANOL-WATER AT 24°

Time, min.	Moles acid oxidized in—			
	9,10-Dihydroxy-stearic acids		1,9,10-Trihydroxy-octadecanes	
	Low melting	High melting	Low melting	High melting
2	0.8	0.37
5	.9	.47	0.78	0.47
10	.9	.63	.87	.61
1574	.96	.80

From the scission products of the low melting form of 1,9,10-trihydroxyoctadecane, pelargonic aldehyde was isolated as the 2,4-dinitrophenylhydrazone, indicating that the desired reaction had taken place.

The structural feature responsible for these results also comes into play when one determines which form is capable of yielding an acidic cyclic complex with boric acid by the classical procedure. Boësen and Couvert⁶ had shown that *cis* glycols of rigid systems form a complex possessing an acidic hydrogen atom which is readily demonstrable by conductivity measurements.

This technique was shown to be applicable to diastereoisomeric open chain glycols by Lees and co-workers⁷ and by Knowlton and co-workers⁸ who showed that the *dl* form of 2,3-butanediol formed a borate complex whereas the *meso* form did not. With the 9,10-dihydroxystearic acids conductivity measurements in absolute ethanol indicated that the low melting form was amenable to complex formation with boric acid since the specific conductivity increased with increasing concentration of the acid. On the other hand, successive increase of the concentration of the high melting form had no effect on the specific conductivity of the borate mixture. The data are presented in Table III.

TABLE III

SPECIFIC CONDUCTIVITY MEASUREMENTS FOR THE 9,10-DIHYDROXYSTEARIC ACIDS AT 25° IN ABSOLUTE ETHANOL

Low-melting form—		High-melting form—	
Moles of acid/liter of 1 N H ₃ BO ₃	Specific conductivity	Moles of acid/liter of 1 N H ₃ BO ₃	Specific conductivity
0	8.37×10^{-5}	0	8.37×10^{-5}
0.0106	1.58×10^{-4}	0.0112	1.04×10^{-4}
.0269	1.88×10^{-4}	.0275	1.03×10^{-4}
.0446	2.09×10^{-4}	.0510	1.02×10^{-4}
.0936	2.97×10^{-4}	.0989 ^a	1.04×10^{-4}

^a This was a supersaturated solution which started to crystallize as the reading was taken.

- (6) J. Boësen and H. Couvert, *Rec. trav. chim.*, **40**, 354 (1921).
 (7) T. M. Lees, E. I. Fulmer and L. A. Underkofer, *Iowa State Coll. J. Sci.*, **18**, 359 (1944).
 (8) J. W. Knowlton, N. C. Schieltz and D. MacMillan, *THIS JOURNAL*, **68**, 208 (1946).

All of these data, then, indicate that the vicinal hydroxyl groups in the low-melting forms of 9,10-dihydroxystearic acid and 1,9,10-trihydroxyoctadecane possess a closer spatial relationship than those in the high-melting form. Accordingly it follows that the normal hydroxylation products of oleic acid and oleyl alcohol (*cis* double bond) are the high-melting forms of 9,10-dihydroxystearic acid and 1,9,10-trihydroxyoctadecane, whereas the normal hydroxylation products of elaidic acid and elaidyl alcohol (*trans* double bond) are the low-melting forms. These conclusions are in accord with those of Esafov,⁹ King¹⁰ and Wittcoff and Miller¹¹ but are at variance with those of Atherton and Hilditch.¹²

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Experimental

Materials.

The low-melting form of 9,10-dihydroxystearic acid was prepared by the hydroxylation of U. S. P. oleic acid as described by Scanlan and Swern.¹³ After numerous crystallizations from ethyl acetate it melted sharply at 94–95°.¹⁴

The high-melting form of 9,10-dihydroxystearic acid was prepared by the hydroxylation of U. S. P. oleic acid by action of permanganate as described by Lapworth and Mottram¹⁵ save that considerably less water was used. Thus a solution of oleic acid (20 g.) and potassium hydroxide (10 g.) in water (3 l.) reacted at 0–5° with a solution (400 ml., 2%) of potassium permanganate. The product was isolated as indicated by the previous workers. During crystallization from ethyl acetate, however, an insoluble crystalline material separated. This was shown by melting point, neutral equivalent and elementary analysis to be one of the high melting forms of 9,10,12,13-tetrahydroxystearic (sativic) acid.¹⁶ Thus from three runs there was obtained, in addition to 13 g. of 9,10-dihydroxystearic acid (m. p., 129–30°), 2.0 g. of sativic acid melting at 172–173°.

Anal. Calcd. for C₁₈H₃₆O₄: C, 62.07; H, 10.44; neut. eq., 348.5. Found: C, 61.89; H, 10.44; neut. eq., 345.

The low-melting form of 1,9,10-trihydroxyoctadecane was prepared according to the procedure of Scanlan and Swern,¹³ employing commercial oleyl alcohol from which all of the C₁₄ and C₁₆ compounds had been removed by stripping through a Podbielniak column. The product was crystallized successively from absolute ethanol, ethyl acetate and isopropyl ether and melted at 75–76°.

The high-melting form of 1,9,10-trihydroxyoctadecane was prepared by hydroxylating with permanganate the half acid phthalate of oleyl alcohol and saponifying the resultant product as described by Collin and Hilditch.¹⁷ Pure oleyl alcohol¹⁸ was used and the crude hydroxylation

- (9) (a) V. I. Esafov, *J. Gen. Chem. (U. S. S. R.)*, **6**, 1818 (1936);
 (b) V. I. Esafov, *ibid.*, **7**, 1403 (1937).
 (10) G. King, *J. Chem. Soc.*, 37 (1943).
 (11) H. Wittcoff and S. E. Miller, *THIS JOURNAL*, **69**, 3138 (1947).
 (12) D. Atherton and T. P. Hilditch, *J. Chem. Soc.*, 204 (1943); *cf. ref. 11* for a discussion of Hilditch's conclusions.
 (13) J. T. Scanlan and D. Swern, *THIS JOURNAL*, **62**, 2305 (1940).
 (14) Melting points are uncorrected.
 (15) A. Lapworth and E. N. Mottram, *J. Chem. Soc.*, 1628 (1925).
 (16) R. W. Riemenschneider, D. H. Wheeler and C. E. Sando, *J. Biol. Chem.*, **127**, 391 (1939).
 (17) G. Collin and T. P. Hilditch, *J. Chem. Soc.*, 246 (1933).
 (18) D. Swern, H. B. Knight and T. W. Findley, *Oil and Soap*, **21**, 133 (1944). The authors are indebted to Mr. David E. Terry for the preparation of the pure alcohol.

product was saponified by refluxing it (5.5 g.) with a solution of potassium hydroxide (3.0 g.) in ethanol (50 ml.) for two hours. The potassium phthalate was filtered from the cooled mixture, and the filtrate was made exactly neutral by addition of dilute hydrochloric acid. Evaporation to dryness *in vacuo* yielded a residue which was taken up in ethyl acetate and was filtered to remove inorganic salt. From the filtrate there resulted on standing 2.5 g. of product which, when crystallized from the same solvent, melted at 125–126°.

The Periodate Oxidation of the 9,10-Dihydroxystearic Acids in Aqueous Suspension.—All of the oxidations by periodate were performed at 24° using aqueous 0.05 *M* periodate (buffered, pH 4.2) prepared from trisodium paraperiodate and acetic acid.¹⁹ The periodate oxidations of both forms of 9,10-dihydroxystearic acid were carried out in aqueous suspension in the presence of a known quantity of sodium β -alkylaminopropionate in which the alkyl moiety was derived from soybean oil fatty acids. The titrations of the aliquot portions of the reaction mixtures were carried out according to the method of Fleury and Lange²⁰ as modified by Grangaard, Gladding and Purves.²¹ Corrections were made for blanks. The results of the periodate oxidation in aqueous suspension are given in Table I.

The Periodate Oxidation of the 9,10-Dihydroxystearic Acids and the 1,9,10-Trihydroxyoctadecanes in Ethanol-Water.—Since ethanol proved to be a suitable solvent for all of the glycols under investigation, the oxidations by periodate in homogeneous medium were carried out at 24° in the following manner: The compounds (0.0200 g.) were dissolved in absolute ethanol (15 ml.); a solution of periodate (0.05 *M*, 5 ml.) was added and the oxidations were permitted to continue for the periods of time indicated in Table II. The titrations were performed as previously described and corrections were made for blanks.

(19) (a) D. H. Grangaard, J. H. Michell and C. B. Purves, *THIS JOURNAL*, **61**, 1290 (1939); (b) O. A. Moe, S. E. Miller and M. H. Iwen, *ibid.*, **69**, 2621 (1947).

(20) P. Fleury and J. Lange, *J. pharm. chim.*, [8] **17**, 107, 196 (1933).

(21) D. H. Grangaard, E. K. Gladding and C. B. Purves, *Paper Trade J.*, **115**, no. 7, 41 (1942).

Perfectly clear reaction mixtures resulted in all oxidations of this type. The results obtained are given in Table II.

Identification of Pelargonic Aldehyde among the Scission Products of 1,9,10-Trihydroxyoctadecane.—1,9,10-Trihydroxyoctadecane (5.0 g., m. p. 75–76°) was dissolved in absolute ethanol (100 ml.), and 0.5 *M* periodate (50 ml.) was added. After one hour at room temperature the reaction mixture was poured into water and was extracted with ether. From the ether solution there resulted an oil (4.8 g.) which was converted, during refrigeration, to a pasty solid. This crude product was dissolved in warm Skellysolve B. Cooling yielded a small amount of solid which was probably unreacted glycol. From the filtrate there was obtained an oil which was treated with 2,4-dinitrophenylhydrazine in the conventional manner. The crude dinitrophenylhydrazone first obtained melted at 91–96°. After three recrystallizations from ethanol the product melted at 104–5° (uncor., lit. 100°).²²

Anal. Calcd. for C₁₅H₂₂O₄N₄: C, 55.9; H, 6.8; N, 17.4. Found: C, 55.8; H, 6.9; N, 17.7.

Conductivity of the Borate Complexes of the 9,10-Dihydroxystearic Acids.—The conductivity measurements were carried out in a one normal solution of boric acid in absolute ethanol with the aid of an alternating current, 1000 cycle, conductivity Wheatstone bridge. The results are contained in Table III.

Summary

The results of periodate oxidation have been used to show that the hydroxyl groups are more proximal in the low-melting forms of the 9,10-dihydroxystearic acids and the 1,9,10-trihydroxyoctadecanes than in the high-melting forms.

The low-melting form of 9,10-dihydroxystearic acid has been shown to form a cyclic, acidic complex with boric acid, whereas the high-melting form does not.

(22) H. H. Strain, *THIS JOURNAL*, **57**, 758 (1935).

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The Reaction of Amines with Phosphorus Pentasulfide; Thiophosphoric Amides

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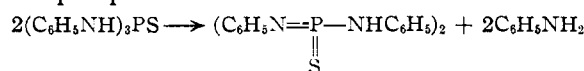
Previous investigations of products obtained by the action of amines on phosphorus pentasulfide have been limited to a single reaction. Knop^{1c} observed that six moles of aniline and one mole of phosphorus pentasulfide heated at a temperature not exceeding 150° evolved hydrogen sulfide and gave a pungent smelling product in the form of monoclinic crystals which melted at 153°. Rudert² prepared the same product from aniline and thiophosphoryl chloride and showed it to be thiophosphoric trianilide, (C₆H₅NH)₃PS.

Knop's results were repeated in this Laboratory. A 50% yield of thiophosphoric trianilide melting at 153–154° was obtained. This product did not

depress the melting point of thiophosphoric trianilide prepared from aniline and thiophosphoryl chloride. Although Knop regarded temperatures in excess of 150° to be detrimental, we obtained the maximum yield at a reaction temperature of 180°.

The anilide was not hydrolyzed upon refluxing with dilute acid or with aqueous or alcoholic potassium hydroxide, but was by heating with concentrated phosphoric acid at 130°, for two hours, and with glacial acetic acid for twenty hours.

When thiophosphoric trianilide was heated at 225° *in vacuo*, it lost aniline and formed dimeric thiophosphoric anil anilide:



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(1b) Standard Oil Co., Cleveland, Ohio.

(1c) Knop, *Ber.*, **20**, 3352 (1887).

(2) Rudert, *ibid.*, **26**, 565 (1893).

Upon refluxing the anil anilide in aniline the reaction was reversed. This reaction will be discussed in a future paper.