A Publication
of Reliable Methods
for the Preparation
of Organic Compounds

Working with Hazardous Chemicals

The procedures in *Organic Syntheses* are intended for use only by persons with proper training in experimental organic chemistry. All hazardous materials should be handled using the standard procedures for work with chemicals described in references such as "Prudent Practices in the Laboratory" (The National Academies Press, Washington, D.C., 2011; the full text can be accessed free of charge at http://www.nap.edu/catalog.php?record_id=12654). All chemical waste should be disposed of in accordance with local regulations. For general guidelines for the management of chemical waste, see Chapter 8 of Prudent Practices.

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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

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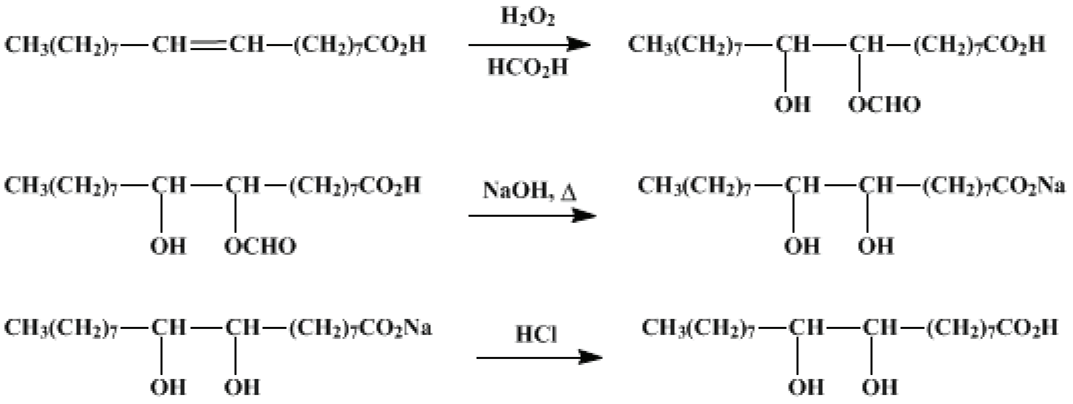
9,10-DIHYDROXYSTEARIC ACID

[low-melting isomer]

[Octadecanoic acid, 9,10-dihydroxy-]



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1. Procedure

To a well-stirred mixture of 141 g. (0.5 mole) of oleic acid (Note 1) and 425 ml. of formic acid (Note 2) in a 1-l. three-necked flask at 25° is added the appropriate amount (Note 3) of 30% (100 volume) hydrogen peroxide (approximately 60 g.) over a 15-minute period (Note 4). The reaction becomes mildly exothermic after a lag of about 5–10 minutes, and homogeneous after about 20–30 minutes. The temperature is maintained at 40° with a cold water bath at the beginning, and with a warm water bath or heating mantle toward the end, of the reaction. After about 3 hours or after analysis has indicated that the peroxide has been consumed (Note 5), the formic acid is removed by distillation under reduced pressure (b.p. 50°/125 mm.) in a stream of gas (carbon dioxide or nitrogen) to prevent bumping (Note 6). The residue in the flask, which consists of hydroxyformoxystearic acids, is heated for 1 hour at 100° with an excess of 3*N* aqueous sodium hydroxide, and the hot, amber-colored soap solution is cautiously poured into an excess of 3*N* hydrochloric acid with stirring. The oil which separates is allowed to solidify, and the aqueous layer is discarded. The tan-colored solid is remelted on the steam bath by addition of hot water and stirred well to remove residual salts and water-soluble acids (Note 7). When the oil has solidified, the aqueous layer is discarded, and the solid is broken into small pieces and dissolved in 400 ml. of 95% ethanol by heating on the steam bath. After crystallization at 0° for several hours, the product is collected on a filter and dried under vacuum. The yield of crude 9,10-dihydroxystearic acid is 75–80 g., m.p. 85–90°. After a second recrystallization from 250 ml. of 95% ethanol, the product weighs about 60–65 g. and melts at about 90–92°. A third recrystallization may be necessary to produce a pure product melting at 94–95°. The over-all yield is 55–60 g. (50–55%, based on the available oleic acid) (Note 8).

2. Notes

1. The checkers used commercial U.S.P. oleic acid, which has an iodine number of about 60–70 and contains 65–75% oleic acid. The submitters report that, if highly purified oleic acid is used, the yield of fairly pure 9,10-dihydroxystearic acid is almost quantitative, but the purification procedure for oleic acid [*Biochem. Preparations*, **2**, 100 (1952)] is more lengthy and inconvenient than the purification of the hydroxylation product. The over-all yield is approximately the same in either case.
2. The formic acid employed is the 98–100% grade. The submitters report that the 90% grade of acid is satisfactory, but the reaction mixture remains heterogeneous throughout. They also state that, instead of

formic acid, an equal volume of glacial acetic acid containing 2.5% by weight of concentrated sulfuric acid may be employed. With acetic acid-sulfuric acid, a 6-hour reaction time is required. However, the yield of 9,10-dihydroxystearic acid is slightly lower than the yield obtained when formic acid is employed and the iodine number of the crude reaction product is about 6–9.

3. If commercial oleic acid is used, the iodine number should be determined beforehand and the quantity of hydrogen peroxide adjusted accordingly. The hydrogen peroxide should be assayed immediately before use; "100 volume peroxide" usually contains about 30% hydrogen peroxide by weight. This determination is conveniently carried out by weighing 0.2–0.3 g. of the hydrogen peroxide solution into an Erlenmeyer flask with a ground-glass stopper and adding 20 ml. of a glacial acetic acid-chloroform solution (3:2 by volume). Two milliliters of saturated aqueous potassium iodide solution is added, and the mixture is allowed to stand for 5 minutes. Distilled water (75 ml.) is added and the liberated iodine titrated with 0.1*N* sodium thiosulfate solution to a starch end point. This procedure is also satisfactory for determining the peroxide content of the oxidation mixture, except that 1–2 g. samples are taken [cf. Wheeler, *Oil & Soap*, **9**, 89 (1932)].

4. The submitters state that in one-tenth scale preparations the hydrogen peroxide solution can be added in 1 portion. In larger runs the addition may require 30 minutes to 1 hour.

5. The reaction time ranges from 1.5 to about 4 hours. Progress of the reaction should be followed by determining the peroxide content of the oxidation mixture at half-hour intervals after all the hydrogen peroxide has been added. Approximately all the peroxide should be consumed before distillation is attempted.

6. Instead of removing the formic acid by distillation, the reaction mixture may be poured into a large quantity of water and the oily layer dissolved in ether. The ether solution is washed free of formic acid and then subjected to distillation to remove the ether; hydroxyformoxystearic acids are left as a residue. The submitters found that, in larger-scale operations (five or more times the size of the run described), no ether was required and the oily layer was washed with water until free of formic acid. When acetic acid containing sulfuric acid was employed as the solvent, the reaction mixture was poured into hot water, and the oil which formed was separated mechanically or by extraction with ether.

7. The pH of the wash water should be below 6 in order to be certain that all soap in the product has been converted to free acid. If the pH is above 6, a small quantity of 3*N* hydrochloric acid should be added and the stirring continued for several minutes.

8. The submitters report that the high-melting isomer of 9,10-dihydroxystearic acid can be prepared from elaidic acid [*Biochem. Preparations*, **3**, 118 (1953)] by essentially the procedure described for oleic acid. With elaidic acid, instead of removing the formic acid by distillation, the reaction mixture may be poured into hot water and the oil which forms separated mechanically. The product is not readily soluble in ether. When acetic acid containing sulfuric acid is employed as the solvent, the reaction mixture is poured into *hot* water with thorough mixing, allowed to cool to room temperature, and filtered. The subsequent procedure (saponification and acidification) is the same as that described for the hydroxylation of oleic acid except that the crude dihydroxystearic acid, obtained after acidification of the soap, cannot be melted with hot water during the washing but is merely stirred well at 95–100° on the steam bath with a large quantity of hot water (Note 7). About 5 ml. of ethanol per gram of solute should be used in the recrystallization. The pure product melts at 130–131°. The yield depends on the purity of the starting material; if highly purified elaidic acid is used, the yield is about 80% after one recrystallization.

3. Discussion

The procedures described have been published.[2] Other procedures, which are not so satisfactory as the ones described, have also been published.[3,4]

References and Notes

1. U. S. Dept. of Agriculture, Eastern Utilization Research and Development Division, Philadelphia 18, Pennsylvania.
2. Swern, Billen, Findley, and Scanlan, *J. Am. Chem. Soc.*, **67**, 1786 (1945).
3. Hilditch, *J. Chem. Soc.*, **1926**, 1828; Hilditch and Lea, *ibid.*, **1928**, 1576.

4. Scanlan and Swern, *J. Am. Chem. Soc.*, **62**, 2305 (1940).

Appendix
Chemical Abstracts Nomenclature (Collective Index Number);
(Registry Number)

acetic acid-chloroform

ethanol (64-17-5)

sulfuric acid (7664-93-9)

hydrochloric acid (7647-01-0)

acetic acid (64-19-7)

ether (60-29-7)

sodium hydroxide (1310-73-2)

formic acid (64-18-6)

potassium iodide (7681-11-0)

sodium thiosulfate (7772-98-7)

nitrogen (7727-37-9)

carbon dioxide (124-38-9)

iodine (7553-56-2)

hydrogen peroxide (7722-84-1)

oleic acid (112-80-1)

dihydroxystearic acid

9,10-Dihydroxystearic acid,
Octadecanoic acid, 9,10-dihydroxy- (120-87-6)

acetic acid-sulfuric acid

elaidic acid (112-79-8)