Organic Syntheses

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.

In some articles in *Organic Syntheses*, chemical-specific hazards are highlighted in red "Caution Notes" within a procedure. It is important to recognize that the absence of a caution note does not imply that no significant hazards are associated with the chemicals involved in that procedure. Prior to performing a reaction, a thorough risk assessment should be carried out that includes a review of the potential hazards associated with each chemical and experimental operation on the scale that is planned for the procedure. Guidelines for carrying out a risk assessment and for analyzing the hazards associated with chemicals can be found in Chapter 4 of Prudent Practices.

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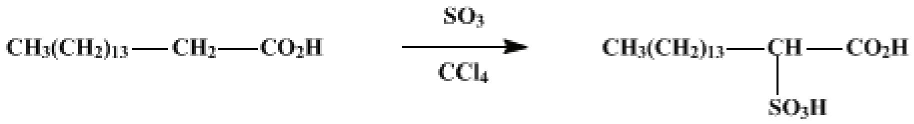
These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

DOI:10.15227/orgsyn.036.0083

Organic Syntheses, Coll. Vol. 4, p.862 (1963); Vol. 36, p.83 (1956).

α-SULFOPALMITIC ACID

[Hexadecanoic acid, 2-sulfo-]



$$CH_3(CH_2)_{13}—CH_2—CO_2H \xrightarrow[CCl_4]{SO_3} CH_3(CH_2)_{13}—\underset{SO_3H}{CH}—CO_2H$$

Submitted by J. K. Weil, R. G. Bistline, Jr., and A. J. Stirton[1].
Checked by James Cason and Gerhard J. Fonken.

1. Procedure

Caution! Rubber gloves and a protective face shield should be worn while handling liquid sulfur trioxide, and the reaction should be carried out in a hood.

A 2-l. three-necked round-bottomed flask, with standard-taper ground-glass joints, is equipped for heating with an electric mantle or an oil bath, and fitted with a ball joint-sealed mechanical stirrer, a thermometer well, a graduated, pressure-equalizing dropping funnel, and a small vent. The dropping funnel, which should have a close-fitting stopcock well lubricated with heavy silicone grease, is placed so as to discharge sulfur trioxide well above the surface of the reaction mixture. Palmitic acid (200 g., 0.78 mole) (Note 1) and 600 ml. of carbon tetrachloride (Note 2) are added to the flask. Solution of the palmitic acid is endothermic and causes the temperature of the mixture to fall 5 to 10° below room temperature (Note 3). Stabilized liquid sulfur trioxide, 53 ml. (100 g., 1.25 moles) (Note 4), is added dropwise from the dropping funnel to the stirred mixture. Solution of palmitic acid becomes complete, the solution darkens, and the temperature rises to 45° as the sulfur trioxide is added over a 30-minute period. The reaction mixture is finally heated for 1 hour at 50–65° with continued stirring and is then chilled in an ice bath before the accessories are removed from the flask. The necks are closed with glass stoppers, and the reaction mixture is refrigerated at about −15° overnight (Note 5).

Crystallized solids are filtered by suction (Note 6), washed with cold carbon tetrachloride, and dried at room temperature in a vacuum desiccator to constant weight (1 to 2 days). The crude dark product weighs 197–223 g. (75–85%), and is usually satisfactory for the preparation of derivatives such as salts (Note 7) and esters.[2] One crystallization from acetone (7 ml./g.) at −20° yields a light gray solid, with neutralization equivalent within 1–2% of the theoretical value of 168, in a yield of 178–197 g. (68–75%). Two or three additional crystallizations (leaving a yield of only 25–30%) are required to give an almost colorless crystalline solid, m.p. 90–91° (Note 8). Once crystallized material is moderately stable to storage in a container protected from moisture, but slow darkening occurs, especially in presence of sunlight.

2. Notes

1. A purified fatty acid is recommended for the preparation of a pure α-sulfo acid. Purified palmitic acid (m.p. 60.8–61.4°, neutralization equivalent 256.2) is prepared by twice recrystallizing a good commercial grade of palmitic acid from acetone at 0°, using a solvent ratio of 10 ml. to 1 g. However, the reaction may be applied to commercial saturated higher fatty acids, if the iodine number is sufficiently low. The checkers obtained similar results with recrystallized Neo-Fat 1-56 (Armour and Company, Chicago, Ill.) or Eastman white label grade palmitic acid.
2. Other chlorinated solvents such as tetrachloroethylene or chloroform may be used in place of carbon tetrachloride. *Caution! The reaction of sulfur trioxide with chlorinated solvents has been reported[3] to give phosgene and other toxic products. Adequate venting of all by-product gases is essential.*
3. The mixture which is a slurry at 15° may be used or it may be warmed to about 30° to give a clear solution. If the slurry is warmed before sulfur trioxide addition, it is usually not necessary to heat after

all of the sulfur trioxide has been added.

4. Liquid sulfur trioxide may be purchased in stabilized form as Sulfan B,[4] m.p. 17°, b.p. about 45°. Caution must be exercised in handling sulfur trioxide. The liquid is highly corrosive to the skin and the vapor may cause injury if inhaled. The powerful oxidizing and dehydrating effects of sulfur trioxide should not be underestimated. The liquid may be stored in a glass-stoppered bottle if the stopper is lubricated with a heavy silicone grease. Because the liquid reacts violently with water the bottle lip should be wiped free of any moisture to avoid spattering when the liquid is poured. If solidification of sulfur trioxide should occur as the result of hydration, the vented (*Hood!*) solid may be liquefied by gentle application of heat from an infrared lamp.

5. Shorter refrigerating periods at temperatures up to +5° give slightly lower yields.

6. Since the mixture filters rather slowly, even after storage overnight, a Büchner funnel of at least 20 cm. diameter should be used, and a hard grade of filter paper (such as Whatman No. 50) is recommended. Use of a rubber dam helps to express solvent and exclude moisture from the hygroscopic product.

7. The monosodium salt $CH_3(CH_2)_{13}CH(SO_3Na)CO_2H$ may be prepared by neutralizing only the sulfonic acid group or by adding aqueous sodium sulfate to a hot aqueous solution of the crude α-sulfo acid and cooling to room temperature. The monosodium salt crystallizes in white plates, leaving most of the color in the filtrate. The disodium salt is formed by further neutralization with sodium hydroxide.

8. α-Sulfolauric, α-sulfomyristic, α-sulfostearic, and α-sulfobehenic acids have been prepared by this procedure. The table shows the melting point and neutralization equivalent after at least four recrystallizations and a 12-hour drying period at 76° under 1 mm. pressure. There is some uncertainty in the melting points because of the hygroscopic character of the α-sulfo acids.

	Neutralization Equivalent		
	Found	Theoretical	M.P.
α-Sulfolauric acid	142	140.4	86.5–88°
α-Sulfomyristic acid	154	154.2	85–86.5°
α-Sulfopalmitic acid	171	168.2	90–91°
α-Sulfostearic acid	182	182.2	96–97°
α-Sulfobehenic acid	212	210.3	95–97°

3. Discussion

Other direct methods for the sulfonation of the higher fatty acids are by the use of sulfur trioxide vapor[5] or by the use of chlorosulfonic acid.[6] Indirect methods are also available for the preparation of α-sulfo fatty acids and their salts from an α-bromo fatty acid made by the Hell-Volhard-Zelinsky reaction. The bromo compound may be converted directly to the sodium salt of a sulfonic acid through the Strecker reaction[7] or may be converted to the mercaptan and oxidized to the sulfonate.[8] Sulfonation of the lower fatty acids has been studied by Backer and co-workers.[9]

α-Sulfonation with sulfur trioxide appears to be generally applicable to carboxylic acids having an α-methylene group.

References and Notes

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2. Weil, Bistline, and Stirton, *J. Am. Chem. Soc.*, **75**, 4859 (1953).
3. "Reactions of SO_3," Tech. Service Bull. SF-2, General Chemical Division, Allied Chemical and Dye Corporation, 40 Rector Street, New York 6, N. Y.
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5. Günther (1932), PB30081, Office of Tech. Services, U. S. Department of Commerce; *Bibliography of Scientific and Industrial Reports*, **4**, 662 (1947).
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7. Mehta and Trivedi, *Melliand Textilber.*, **21**, 117, 288 (1940) [*C. A.*, **34**, 6087 (1940)].
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9. For example, de Boer, *Rec. trav. chim.*, **71** 814 (1952).

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

monosodium salt $CH_3(CH_2)_{13}CH(SO_3Na)CO_2H$

sodium hydroxide (1310-73-2)

chlorosulfonic acid (7790-94-5)

sulfur trioxide (7446-11-9)

chloroform (67-66-3)

sodium sulfate (7757-82-6)

carbon tetrachloride (56-23-5)

acetone (67-64-1)

phosgene (75-44-5)

tetrachloroethylene (127-18-4)

palmitic acid (57-10-3)

α-Sulfopalmitic acid,
Hexadecanoic acid, 2-sulfo- (1782-10-1)

α-Sulfolauric acid

α-Sulfomyristic acid

α-Sulfostearic acid

α-Sulfobehenic acid