



A Publication
of Reliable Methods
for the Preparation
of Organic Compounds

Working with Hazardous Chemicals

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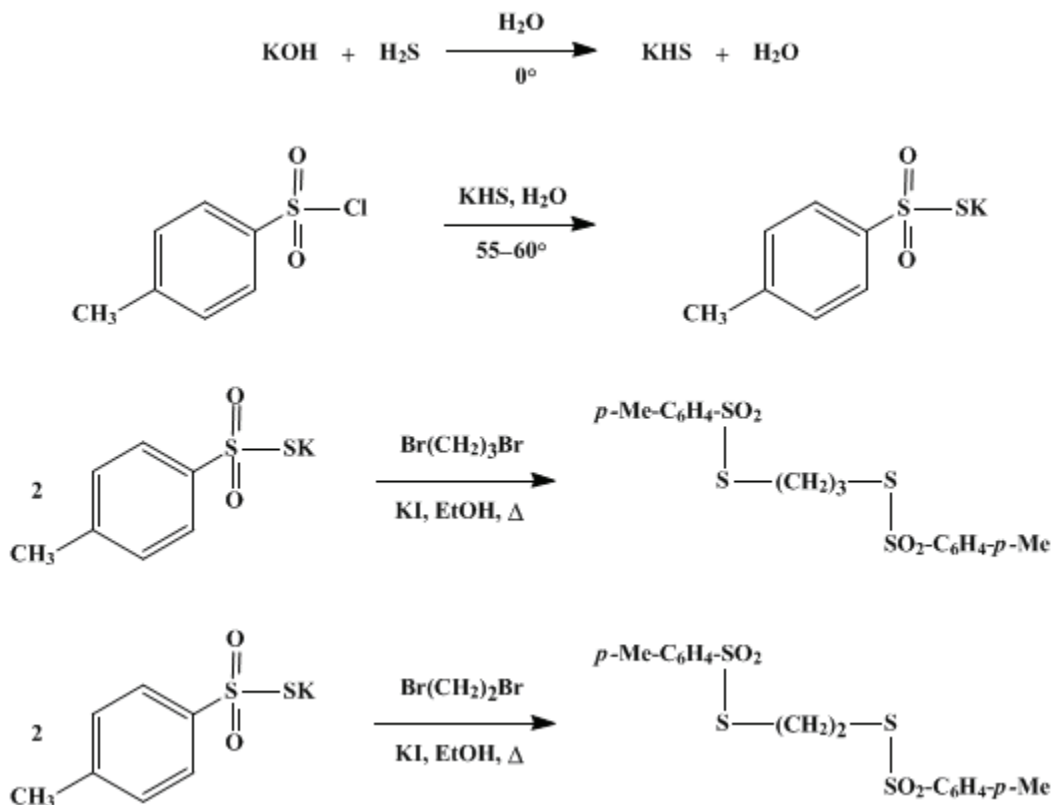
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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

Organic Syntheses, Coll. Vol. 6, p.1016 (1988); Vol. 54, p.33 (1974).

TRIMETHYLENE DITHIOTOSYLATE AND ETHYLENE DITHIOTOSYLATE

[Benzenesulfonyl chloride, 4-methyl-, *S,S'*-1,3-propanediyl and *S,S'*-1,2-ethanediyl esters]



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 Checked by P. A. Rossy and S. Masamune.

1. Procedure

Caution! This procedure should be carried out in a hood to avoid inhalation of hydrogen sulfide.

A. *Potassium thiothiosylate*. A solution of 64.9 g. (1.00 mole) of 86.5% potassium hydroxide (Note 1) in 28 ml. of water is cooled in an ice bath, saturated with hydrogen sulfide, and flushed with nitrogen to ensure complete removal of excess hydrogen sulfide (Note 2) and (Note 3). The freshly prepared potassium hydrosulfide solution is diluted with 117 ml. of water and stirred under nitrogen at 55–60° before 95.3 g. (0.500 mole) of finely ground *p*-toluenesulfonyl chloride (Note 3) is introduced in small portions at a uniform rate so that the reaction temperature is maintained at 55–60° (Note 2). A mildly exothermic reaction ensues, and the solution becomes intensely yellow. After about 90 g. of the tosyl chloride has been introduced, the yellow color disappears, and the dissolution of the chloride ceases. The reaction mixture is rapidly filtered with suction through a warmed funnel, and the filtrate is cooled several hours at 0–5°. The crystals of potassium thiothiosylate are filtered, dissolved in 200 ml. of hot 80% ethanol, filtered hot to remove traces of sulfur, and cooled several hours at 0–5°. The recrystallized salt is filtered and air-dried, providing 48–55 g. (42–49%) of white crystals.

B. *Trimethylene dithiotosylate*. To 150 ml. of 95% ethanol containing 10–20 mg. of potassium

iodide is added 40 g. (0.18 mole) of potassium thiosylate and 20 g. (0.10 mole) of 1,3-dibromopropane (trimethylene dibromide) (Note 4). The mixture is refluxed with stirring for 8 hours in the dark and under nitrogen. The reaction mixture is cooled to ambient temperature, diluted with an equal volume of cold water, and agitated. After decantation of the supernatant liquid, the residual honeylike layer of product is washed with three 200-ml. portions of cold water, once with 100 ml. of cold 95% ethanol, and once with 100 ml. of cold absolute ethanol. The crude product (Note 5) is dissolved in 10 ml. of acetone, diluted with 80 ml. of hot absolute ethanol, and stirred under nitrogen at 0°. The oil which separates is redissolved by the addition of a minimum amount (ca. 5 ml.) of acetone. Seed crystals are introduced (Note 6), and the mixture is stirred for 1 hour at 0° under nitrogen and stored at -30° for several hours. The microcrystalline product is collected by filtration and weighs 20.2 g., m.p. 63.5–65.0°. Three recrystallizations from nine parts (180 ml.) of ethanol give 17.2 g. (41%) of white needles, m.p. 66–67° (Note 7). During the recrystallizations some of the material oils out when the solution is cooled to room temperature. The supernatant liquid is decanted, seeded, and stored at -30° for several hours. The oil is not further purified. The recrystallized material is chemically pure for further use [*Org. Synth.*, Coll. Vol. 6, 590 (1988)].

C. *Ethylene dithiosylate*. To 200 ml. of ethanol containing 10–20 mg. of potassium iodide is added 45.3 g. (0.200 mole) of potassium thiosylate and 18.8 g. (0.100 mole) of 1,2-dibromopropane. The mixture is refluxed with stirring for 8 hours in the dark and under a nitrogen atmosphere. The solvent is removed, and the resulting white solid is washed with a mixture of 80 ml. of ethanol and 150 ml. of water. After decantation, the solid is washed three times with 50-ml. portions of water and recrystallized from approximately 150 ml. of ethanol, yielding 28.7 g. of crude product, m.p. 72–75°. Three recrystallizations from a mixture of ethyl acetate and ethanol afford 24 g. (60%) of white crystals, m.p. 75–76° (Note 8).

2. Notes

1. Potassium hydroxide pellets of reagent grade commonly available, such as that from Fisher Scientific Company, contain 10–15% water. The checkers used the amount calculated on the basis of 86.5%, as specified.
2. Hydrogen sulfide is undesirable because its presence can lead to the formation of potassium *p*-toluenesulfinate. The latter can be formed by the desulfurization of thiosylate by hydrogen sulfide generated in the reaction of potassium hydrosulfide with the tosyl chloride. Attention should be directed toward control of the reaction temperature so that hydrogen sulfide is rapidly removed, thereby ensuring survival of the S-S bond of the thiosylate. *p*-Toluenesulfinate ion can displace bromide to form stable sulfones which are less soluble in common solvents, such as benzene, than trimethylene dithiosylate. Therefore, purification of the dithiosylate contaminated with the sulfones is difficult to achieve by fractional recrystallization.
3. The *p*-toluenesulfonyl chloride should be free of *p*-toluenesulfonic acid, otherwise potassium *p*-toluenesulfonate will be formed and result in the formation of tosylates, rather than thiosylates. The reagent used by the checkers was obtained from British Drug Houses Ltd. and was purified by washing benzene solution of the tosyl chloride with 5% aqueous sodium hydroxide, drying with magnesium sulfate, and distilling under reduced pressure, b.p. 146° (15 mm.).⁴
4. Trimethylene dibromide, available from Eastman Organic Chemicals, was distilled prior to use (b.p. 167–168°).
5. The checkers found that the crude oily product crystallizes after storage for a few days under nitrogen at -30°. Some of this solid was saved and used as seed crystals.
6. The submitters reported that seed crystals were obtained by column chromatography, using 40 parts by weight of Woelm neutral alumina (activity grade one) and benzene elution. The center cuts of m.p. 65° or higher were combined and recrystallized from nine parts of ethanol to give white needles, m.p. 67°. Two recrystallizations of chromatographed gave trimethylene dithiosylate, m.p. 67.5°.
7. The purified trimethylene dithiosylate exhibits IR bands (CHCl₃) at 3030 (w), 2930 (w), 1590 (w), 1490 (w), 1440 (w), 1410 (w), 1325 (s), 1300 (m), 1180 (w), 1140 (s), 1075 (s), 1015 (w), and 810 (m) cm⁻¹. The ¹H NMR spectrum (CDCl₃) included signals at δ 1.98 (quinlet, *J* = 7 Hz., 2H, CH₂CH₂CH₂), 2.43 (s, 6H, 2 CH₃), 2.97 (t, *J* = 7 Hz., 4H, CH₂CH₂CH₂), 7.30 (d, *J* = 9 Hz., 4H), and 7.75 (d, *J* = 9 Hz., 4H). Analysis calculated for C₁₇H₂₀O₄S₄: C, 49.01; H, 4.84; S, 30.79. Found: C, 49.13; H, 4.81; S, 30.51 (submitters). Found: C, 48.71; H, 4.64; S, 30.45 (checkers). The checkers found that the product

exhibited a single peak on a 3 ft. \times 1/8 in. Waters Associates Analytical Liquid Chromatographic column, packed with Durapak-Carbowax 400/Poracil C. **Chloroform** was used as the eluting solvent.

8. The ^1H NMR spectrum (CDCl_3) has absorptions at δ 2.47 (s, 6H, 2CH_3), 3.31 (s, 4H, 2CH_2), 7.48 (complex in, $J = 9$ Hz., 4H) and 7.97 (d, $J = 9$ Hz., 4H). Analysis calculated for $\text{C}_{16}\text{H}_{18}\text{S}_4\text{O}_4$: C, 47.73; H, 4.51; S, 31.86. Found: C, 47.89; H, 4.44; S, 32.22.

3. Discussion

Although it has been long known that **trimethylene dithiosylate** can be prepared by the reaction of thiosylate ion with **trimethylene dibromide**,^{5, 6} various difficulties are associated with the preparation. These problems are to a considerable extent related to the mode of preparation and the resultant purity of **potassium thiosylate**. The thiosylate salt must be free of tosylate and *p*-toluenesulfinate impurities, otherwise side products such as tosylates or sulfones will form. One such by-product, **tosyltrimethylene thiosylate**, $\text{CH}_3\text{C}_6\text{H}_4\text{SO}_2(\text{CH}_2)_3\text{SSO}_2\text{C}_6\text{H}_4\text{CH}_3$, m.p. 92° , was isolated from contaminated samples of **trimethylene dithiosylate**. It is products such as these, that make crystallization of the dithiosylate difficult. The procedure described herein serves as a reliable technique for minimizing these experimental difficulties. More recently, it has been shown⁷ that **trimethylene dithiosylate** can be prepared easily by the reaction of **tosyl chloride** and **1,3-propanedithiol** in **pyridine**. This procedure, however, is unchecked.

Trimethylene dithiosylate can react with activated methylene groups, enamines, or hydroxyethylene derivatives of carbonyl compounds to form dithiane derivatives. In this context, **trimethylene dithiosylate** has been employed in the preparation⁸ and modification^{9, 10} of several steroids. It has also been used in the synthesis of alkaloids,^{11, 12, 13} 10-membered ring lactones,¹⁴ and vernolepin analogues.¹⁵ **Ethylene dithiosylate** undergoes similar reactions, forming dithiolanes.^{3, 16}

This preparation is referenced from:

- [Org. Syn. Coll. Vol. 6, 590](#)
- [Org. Syn. Coll. Vol. 6, 1014](#)

References and Notes

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

Benzenesulfonothioic acid, 4-methyl-, S,S'-1,3-propanediyl

S,S'-1,2-ethanediyl esters

ethanol (64-17-5)

Benzene (71-43-2)

ethyl acetate (141-78-6)

sodium hydroxide (1310-73-2)

chloroform (67-66-3)

hydrogen sulfide (7783-06-4)

1,2-dibromopropane (78-75-1)

trimethylene dibromide,
1,3-dibromopropane (109-64-8)

potassium iodide (7681-11-0)

nitrogen (7727-37-9)

sulfur (7704-34-9)

acetone (67-64-1)

pyridine (110-86-1)

potassium hydroxide (1310-58-3)

potassium hydrosulfide (1310-61-8)

magnesium sulfate (7487-88-9)

p-toluenesulfonic acid (104-15-4)

1,3-propanedithiol (109-80-8)

tosyl chloride,
p-Toluenesulfonyl chloride (98-59-9)

ethylene dithiotosylate

trimethylene dithiosylate (3866-79-3)

potassium thiosylate

tosyltrimethylene thiosylate

potassium p-toluenesulfonate

potassium p-toluenesulfinate

p-toluenesulfinate