



A Publication
of Reliable Methods
for the Preparation
of Organic Compounds

Working with Hazardous Chemicals

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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.

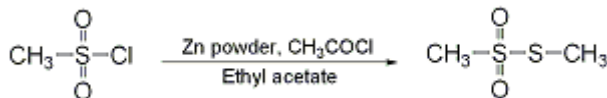
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September 2014: The paragraphs above replace the section "Handling and Disposal of Hazardous Chemicals" in the originally published version of this article. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

Organic Syntheses, Coll. Vol. 10, p.546 (2004); Vol. 78, p.99 (2002).

REDUCTION OF SULFONYL HALIDES WITH ZINC POWDER: S-METHYL METHANETHIOSULFONATE

[**Methanesulfonyl chloride, S-methyl ester**]



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Checked by Mitsuru Kitamura and Koichi Narasaka.

1. Procedure

CAUTION: The reaction must be performed in a well-ventilated hood.

A 1-L, three-necked, round-bottomed flask equipped with a large magnetic stirring bar, a thermometer, reflux condenser, and a 100-mL pressure-equalizing addition funnel with a rubber septum is charged with 49 g (0.75 mol) of **zinc** dust, 1.0 mL (0.012 mol) of **1,2-dibromoethane**, 2.0 mL (0.016 mol) of **chlorotrimethylsilane**, and 500 mL of **ethyl acetate** (Note 1). After the mixture is stirred for 15 min at room temperature, it is heated to reflux by means of an oil bath and 38.7 mL (0.500 mol) of **methanesulfonyl chloride** (Note 2) is added dropwise through the addition funnel. The reaction is highly exothermic. At the end of the addition (1 hr), a large part of the **zinc** is consumed. The resulting grey suspension is stirred for an additional 15 min. **Acetyl chloride**, 35.7 mL (0.502 mol), (Note 2) is then added dropwise (*CAUTION: Note 3*) through the addition funnel with care taken to maintain vigorous stirring of the reaction mixture. After completion of the addition, the resulting mixture becomes clear and no **zinc** remains. Heating is maintained for an additional 15 min, and the mixture is allowed to cool to room temperature. The resulting clear solution is poured into a 1 M aqueous **hydrochloric acid** solution (ca. 200 mL) and the phases are separated. The aqueous phase is extracted with **ethyl acetate** (ca. 200 mL) and the combined organic phases are washed with brine (ca. 200 mL) and dried over anhydrous **magnesium sulfate**. The solvent is removed under reduced pressure and the residual yellow oil is distilled under reduced pressure to give 24.1 g (76% yield) of **methyl methanethiosulfonate** (Note 4) as a colorless liquid, bp 80-83°C/0.5 mm.

2. Notes

- Zinc** dust (<10 micron) was purchased from Aldrich Chemical Company, Inc. **1,2-Dibromoethane** and **chlorotrimethylsilane** were purchased from Acros Chemicals or Tokyo Chemical Industry Co. and used as received. **Ethyl acetate** was purchased from Merck (HPLC grade) and used without any purification.
- Methanesulfonyl chloride** and **acetyl chloride** were purchased from Acros Chemicals, Tokyo Chemical Industry Co., and Wako Pure Chemical Industries, Ltd. and used as received.
- The reaction is highly exothermic. The addition rate is approximately one drop per two seconds, in order to achieve addition within approximately 1 hr. The reaction mixture must be well-stirred and maintained at reflux during this period to avoid any uncontrolled event.
- The product exhibits the following physical and spectral properties: ¹H NMR (CDCl₃, 400 MHz) δ: 2.70 (s, 3 H), 3.32 (s, 3 H); ¹³C NMR (CDCl₃, 126 MHz) δ: 18.2, 48.8; IR (film) cm⁻¹: 3030 (weak), 3010 (weak), 2930 (weak), 1430 (medium), 1410 (medium), 1330 (strong), 1300 (strong), 1130 (strong), 960 (strong), 750 (strong). Microanalysis: Calcd for C₂H₆O₂S₂: C, 19.04; H, 4.76. Found: C, 18.99; H, 4.91.

Waste Disposal Information

All toxic materials were disposed of in accordance with "Prudent Practices in the Laboratory"; National Academy Press; Washington, DC, 1995.

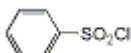
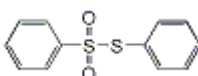

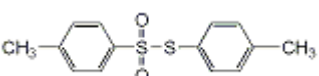
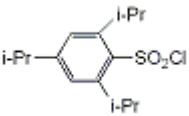
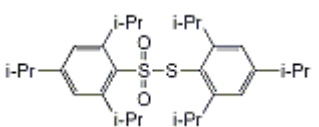

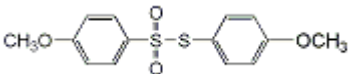

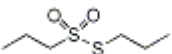
3. Discussion

Thiosulfonic S-esters³ are powerful sulfenylating reagents,⁴ more reactive than the commonly used disulfides, and more stable than the very reactive sulfenyl halides. In addition, they have found wide industrial applications as biologically active compounds or in polymer production.³ Their use, however, has been limited by the lack of easy and practical preparations.

S-Methyl methanethiosulfonate is commercially available, but is expensive. Other preparation methods involve oxidation of thiols or disulfides by halogens or peroxides,³ reduction of sulfinyl halides⁵ (which have to be prepared) or sulfonyl halides with potassium iodide⁶ or copper/bronze⁷ as well as thermolysis of sulfonylhydrazines.⁸ Finally, a two-day procedure for the preparation of methyl methanethiosulfonate has been reported from dimethyl sulfoxide.⁹

The reaction described above has been successfully applied to the preparation of various symmetrical thiosulfonic S-esters (Table).¹⁰ The procedure described here gives better and more reproducible results than the one reported before.¹⁰

TABLE¹⁰
PREPARATION OF SYMMETRICAL THIOSULFONATES
FROM SULFONYL CHLORIDES

	Starting Material	Product	Yield
1			90 %
2			90 %
3			44 %
4			65 %
5			60 %

References and Notes

1. Laboratoire de Chimie des OrganoEléments, Tour 44-45, Case 183, Université Pierre et Marie Curie, 4 place Jussieu, 75252 Paris Cedex 05, France.
2. Laboratoire de Chimie Organique Biologique, Tour 44-45, Case 182, Université Pierre et Marie Curie, 4 place Jussieu, 75252 Paris Cedex 05, France.
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Appendix
Chemical Abstracts Nomenclature (Collective Index Number);
(Registry Number)

Zinc (8,9); (7440-66-6)

S-Methyl methanethiosulfonate:
Methanesulfonic acid, thio-, S-methyl ester (8);
Methanesulfonyl chloride (8,9); (124-63-0)

1,2-Dibromoethane:
Ethane, 1,2-dibromo-, (8,9); (106-93-4)

Chlorotrimethylsilane:
Silane, chlorotrimethyl-, (8,9); (75-77-4)

Methanesulfonyl chloride (8,9); (124-63-0)

Acetyl chloride (8,9); (75-36-5)