



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.

Organic Syntheses, Coll. Vol. 6, p.556 (1988); Vol. 50, p.72 (1970).

1,3-DITHIANE



Submitted by E. J. Corey¹ and D. Seebach².

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1. Procedure

A 1-l., three-necked, round-bottomed flask with ground-glass fittings is charged with a mixture of 36 ml. of boron trifluoride diethyl etherate, 72 ml. of glacial acetic acid, and 120 ml. of chloroform (Note 1). The flask is equipped with a spiral reflux condenser, an efficient mechanical stirrer, and a dropping funnel (Note 2). The chloroform solution is heated and maintained at reflux with vigorous stirring, and a solution of 32 g. (30 ml., 0.30 mole) of 1,3-propanedithiol and 25 g. (29 ml., 0.33 mole) of methylal (dimethoxymethane) in 450 ml. of chloroform (Note 1) is added at a constant rate over 8 hours. The mixture is allowed to cool to room temperature, washed successively with four 80-ml. portions of water, twice with 120 ml. of 10% aqueous potassium hydroxide, and twice with 80-ml. portions of water. The chloroform solution obtained is dried over potassium carbonate and concentrated in a 500-ml., round-bottomed flask under reduced pressure with a rotating flask evaporator (Note 3). The residue, which crystallizes on cooling to room temperature, is dissolved in 60 ml. of methanol by heating to the boiling point. The hot solution is filtered rapidly through a prewarmed funnel, allowed to cool slowly to room temperature, then kept overnight at -20° . The colorless crystals are collected by filtration through a prechilled Büchner funnel, washed with cold methanol (-20°), and dried under reduced pressure (Note 3) and (Note 4), yielding 28–29 g. of product, m.p. $53\text{--}54^{\circ}$. Solvent is removed from the mother liquor, and the residue is recrystallized as described, giving an additional 1.5–2.0 g.; the total yield of recrystallized 1,3-dithiane is 29.5–31.0 g. (82–86% based on propane-1,3-dithiol). A purer sample (Note 5) can be prepared by subsequent sublimation of the recrystallized product at 0.1–0.5 mm. ($45\text{--}48^{\circ}$ bath temp.) (Note 6). The yield of pure product is 28–30 g. (78–84%), m.p. $53\text{--}54^{\circ}$. The residue from the sublimation is a brown syrup weighing less than 1 g.

2. Notes

1. The following components were used as supplied: boron trifluoride etherate, Eastman white label; chloroform and methylal, Fischer reagent; glacial acetic acid, du Pont reagent; 1,3-propanedithiol, Aldrich Chemical Co. The submitters have scaled up this preparation by a factor of 5 without difficulty.
2. Neither the boron trifluoride etherate nor the acetic acid should be added through the dropping funnel, since the presence of even small amounts of acid in the funnel would catalyze undesired condensation of the reagents to be added later. Furthermore the reagents added from the dropping funnel should fall directly into the boiling liquid.
3. Owing to the volatility of 1,3-dithiane, the pressure should be above 30 mm., and the operation should not be prolonged.
4. The crude product can also be distilled; b.p. 95° (20 mm).
5. This additional purification is recommended if the 1,3-dithiane is to be used in organometallic reactions.³
6. Using a sublimator large enough to contain all the recrystallized product obtained, the sublimation can be completed in *ca.* 2 hours at 0.1 mm.

3. Discussion

Although many workers have reported studies with 1,3-dithiane,^{4,5,6,7,8} no satisfactory description of its preparation has been published. Generally, 1,3-propanedithiol and formaldehyde^{4,6,8} have been used

as components; in one instance, 1,3-dibromopropane was treated with sodium thiosulfate to form a precursor of the dithiol which was used as such with formalin.⁵ The formation of linear condensation products is a serious side reaction under such conditions.

The procedure given here is a simple and efficient method for producing 1,3-dithiane, a valuable intermediate in the synthesis *via* lithio derivatives of a wide variety of compounds, including aldehydes, ketones, α -hydroxyketones, 1,2-diketones, and α -keto acid derivatives.³

This preparation is referenced from:

- Org. Syn. Coll. Vol. 6, 109
- Org. Syn. Coll. Vol. 6, 316
- Org. Syn. Coll. Vol. 7, 114

References and Notes

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 3. E. J. Corey and D. Seebach, *Angew. Chem.*, **77**, 1134, 1135 (1965) [*Angew. Chem., Int. Ed. Engl.*, **4**, 1075, 1077 (1965)].
 4. W. Autenrieth and K. Wolff, *Ber. Dtsch. Chem. Ges.*, **32**, 1375 (1899).
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 6. E. E. Campaigne and G. F. Schaefer, *Bol. Col. Quim. P. R.*, **9**, 25 (1952) [*Chem. Abstr.*, **46**, 1088d (1952)].
 7. H. Friebolin, S. Kabuss, W. Maier, and A. Lüttringhaus, *Tetrahedron Lett.*, 683 (1962).
 8. S. Oae, W. Togaki, and A. Ohno, *Tetrahedron*, **20**, 427 (1964).
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Appendix

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

potassium carbonate (584-08-7)

acetic acid (64-19-7)

methanol (67-56-1)

formaldehyde,
formalin (50-00-0)

chloroform (67-66-3)

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

sodium thiosulfate (7772-98-7)

potassium hydroxide (1310-58-3)

methylal,

Dimethoxymethane (109-87-5)

boron trifluoride etherate,
boron trifluoride diethyl etherate (109-63-7)

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

1,3-Dithiane (505-23-7)