



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.

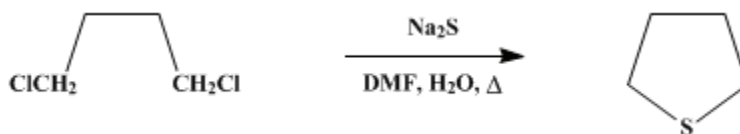
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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

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TETRAHYDROTHIOPHENE

[Thiophene, tetrahydro-]



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Checked by William S. Johnson and W. David Wood.

1. Procedure

A 5-l. round-bottomed three-necked flask equipped with a mechanical stirrer, a reflux condenser (Note 1), and two 250-ml. dropping funnels (mounted with the aid of a Y-tube) is charged with 1.7 l. of dimethylformamide (Note 2). The flask is heated until the dimethylformamide is almost refluxing. Then, with stirring, 280 ml. (318 g., 2.5 moles) of 1,4-dichlorobutane and a solution of 359 g. (2.75 moles) of 60% sodium sulfide (Note 2) in 1 l. of hot water are added simultaneously from the dropping funnels at such a rate that the mixture refluxes without application of heat (Note 3). After the addition is complete (about 1.5 hours), the mixture is heated at reflux with stirring for an additional 2 hours. The condenser is arranged for distillation, and 600 ml. of distillate is collected (Note 4). The distillate is made alkaline by adding 20 g. of sodium hydroxide, and sodium chloride is added to the saturation point. The aqueous layer is separated and discarded, and the crude tetrahydrothiophene layer is dried over solid potassium hydroxide. Distillation through a 30-cm. Vigreux column gives, after a small fore-run (Note 5), 160–172 g. (73–78%) of colorless tetrahydrothiophene, b.p. 119–121°, n_D^{25} 1.5000–1.5014 (Note 6) and (Note 7).

2. Notes

1. The reaction should be carried out in a hood, or the outlet of the condenser should be connected to a fume trap.
2. Technical grade DMF is available from the Grasselli Chemicals Department of E.I. duPont de Nemours and Company. The 1,4-dichlorobutane was obtained from the Electrochemicals Department, E. I. duPont de Nemours and Company. Technical Baker and Adamson fused chip sodium sulfide assaying 60% sodium sulfide was used. The checkers obtained somewhat lower yields when the appropriate amount of reagent grade $\text{Na}_2\text{S}\cdot 9\text{H}_2\text{O}$ was employed instead of the technical material.
3. The addition of the reactants takes approximately 1.3 hours and should be carried out so that the addition of both reactants is completed at approximately the same time.
4. The dimethylformamide solution may be used repeatedly if each time the volume is reduced by the distillation of the remaining water. After two runs the accumulated sodium chloride should be removed by filtration.
5. A small amount of dimethylamine is always present in the crude product. This is removed before collection of the product by operating the column under total reflux for 1–2 hours. The vent of the still head should be connected to a hood during this operation. If foaming does not subside after this treatment the use of a 1-l. still pot is indicated.
6. When several runs are made, an additional amount of the product can be obtained by redrying and redistilling the foreruns. The submitters have obtained yields as high as 90% on a larger-scale operation.
7. The reaction may also be carried out in aqueous medium with an increase in the time of reaction to 4 hours. By this method the submitters obtained a 78% yield on a large-scale run. When only a single run is to be made, this procedure may be preferred as a matter of economy.

3. Discussion

Tetrahydrothiophene has been prepared by the reaction of 1,4-diiodobutane and potassium sulfide;²

by the reaction of 1,4-dibromobutane^{3,4} or 1,4-dichlorobutane^{5,6,7} and sodium sulfide; by the reaction of tetramethylene glycol and hydrogen sulfide in the presence of alumina at high temperature;⁸ by the reaction of tetrahydrofuran and hydrogen sulfide in the presence of alumina at high temperature;^{9,10,11,12} by the hydrogenation of thiophene with molybdenum disulfide¹³ or palladium on charcoal¹⁴ as catalyst; and by treatment of S-(4-hydroxybutyl)isothiourea chloride hydrochloride with base.¹⁵

References and Notes

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Appendix

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

alumina

sodium hydroxide (1310-73-2)

sodium chloride (7647-14-5)

hydrogen sulfide (7783-06-4)

potassium hydroxide (1310-58-3)

palladium (7440-05-3)

sodium sulfide (1313-82-2)

potassium sulfide (1312-73-8)

dimethylamine (124-40-3)

Thiophene (110-02-1)

Tetrahydrofuran (109-99-9)

tetramethylene glycol

1,4-dichlorobutane (110-56-5)

dimethylformamide,
DMF (68-12-2)

1,4-Diiodobutane (628-21-7)

Tetrahydrothiophene,
Thiophene, tetrahydro- (110-01-0)

1,4-dibromobutane (110-52-1)

molybdenum disulfide

S-(4-hydroxybutyl)isothiourea chloride hydrochloride