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.

The procedures described in *Organic Syntheses* are provided as published and are conducted at one's own risk. *Organic Syntheses, Inc.*, its Editors, and its Board of Directors do not warrant or guarantee the safety of individuals using these procedures and hereby disclaim any liability for any injuries or damages claimed to have resulted from or related in any way to the procedures herein.

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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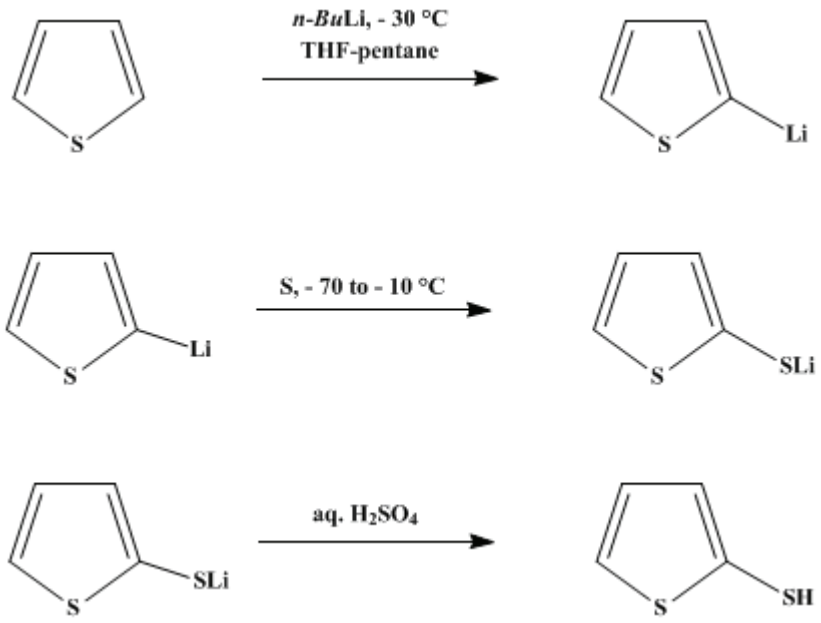
2-THIOPHENETHIOL



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1. Procedure

A 3-l. three-necked flask fitted with a mechanical stirrer, a 600-ml. dropping funnel, and filled with dry nitrogen is charged with 500 ml. of tetrahydrofuran (distilled from lithium aluminum hydride; see *Org. Synth.*, **Coll. Vol. 5**, 976 (1973) for warning concerning the purification of tetrahydrofuran) and 56 g. (53 ml., 0.67 mole) of thiophene. This mixture is stirred under nitrogen and cooled to −40° with an acetone–dry ice bath while 490 ml. (0.662 mole) of 1.35 *M* *n*-butyllithium in pentane (Note 1) and (Note 2) is added over a 5-minute period *via* the dropping funnel. The temperature of the mixture is held between −30° and −20° for 1 hour, then lowered to −70° by the addition of dry ice to the bath. Powdered sulfur crystals (20.4 g., 0.638 g.-atom) are added in one aliquot to the stirred mixture. After 30 minutes the temperature is allowed to rise to −10°, whereupon the yellow solution is carefully poured into 1 l. of rapidly stirred ice water, dissolving the lithium thiolate and destroying any unreacted 2-thienyllithium. The pentane layer is extracted with three 100-ml. portions of water. These aqueous extracts are combined with the aqueous layer, and the whole is chilled and carefully acidified with 4 *N* sulfuric acid (Note 3). This aqueous phase is immediately extracted with three 200-ml. portions of diethyl ether (Note 4). The combined ether extracts are washed twice with 100-ml. portions of water to remove acid and remaining tetrahydrofuran and dried over anhydrous sodium sulfate. After removal of ether, the residual, golden-brown oil is purified by distillation at reduced pressure. The portion boiling at 53–56° (5 mm.) is collected, yielding 49.5–53.5 g. (65–70%) of 2-thiophenethiol as a yellow oil, n_D^{25} 1.6110.

2. Notes

1. The checkers obtained *n*-butyllithium from the Foote Mineral Co., Exton, Pennsylvania. The concentration of *n*-butyllithium was determined by the method of Gilman and Haubein.[2] This reagent is conveniently transferred to a precalibrated addition funnel under nitrogen pressure, through a short length of inert (*e.g.*, Teflon) tubing.
2. The submitters employed *n*-butyllithium prepared by the method of Jones and Gilman.[3] The *n*-butyllithium solution so prepared was filtered to remove finely divided lithium, using an apparatus

previously described.[4]
3. The general procedure is similar to that described by Gronowitz[5] in the preparation of 3-thiophenethiol, the principal differences being the use of tetrahydrofuran–pentane solvent and the omission of a 10% potassium hydroxide extraction before acidification with sulfuric acid. This omission leads to higher yields of thiol.
4. Undue delay in the ether extraction of the thiol has been found to result in reduced yields.

3. Discussion

Houff and Schuetz[6] have prepared 2-thiophenethiol by two different routes. One involves the sulfurization of 2-thienylmagnesium bromide followed by acidification, giving the thiol; the other method is an *in situ* reduction of 2-thienylsulfonyl chloride with zinc dust and sulfuric acid. Gronowitz[5] has prepared the isomeric 3-thiophenethiol by sulfurization of 3-thienyllithium, which was obtained by metalation of 3-bromothiophene with *n*-butyllithium.

This method is based on the known reactivity of the 2-position of thiophene; the desired 2-thiophenethiol may be prepared in good yield by direct substitution of thiophene. 2-Chloro-5-thiophenethiol may also be prepared by this method in 59% yield from 2-chlorothiophene.[7]

Direct substitution in the 3-position of the thiophene ring is difficult and can be achieved only by activation of this reaction site. Thus, the isomeric 3-thiophenethiol may be prepared by this general method starting with a 3-halogenothiophene. For example, 3-thiophenethiol may be obtained from 3-bromothiophene in 63% yield.[5]

The procedure outlined above also offers a general method for the synthesis of alkyl and aryl thiols starting from the appropriate halides. Thus, thiophenol may be obtained in 62% yield by lithiation and sulfurization of bromobenzene.[8]

This preparation is referenced from:

- Org. Syn. Coll. Vol. 6, 109
- Org. Syn. Coll. Vol. 6, 558

References and Notes

1. Work done at the former Arthur D. Little Research Inst., Inveresk Gate, Musselburgh, Midlothian, Scotland.
2. H. Gilman and A. H. Haubein, *J. Am. Chem. Soc.*, **66**, 1515 (1944).
3. R. G. Jones and H. Gilman, *Org. React.*, **6**, 339–366 (1951).
4. H. Gilman, W. Langham, and F. W. Moore, *J. Am. Chem. Soc.*, **62**, 2327 (1940).
5. S. Gronowitz and R. Hakansson, *Ark. Kemi*, **16**, 309 (1960).
6. W. H. Houff and R. D. Schuetz, *J. Am. Chem. Soc.*, **75**, 6316 (1953).
7. E. Jones and I. M. Moodie, *Tetrahedron*, **21**, 2413 (1965).
8. H. Gilman and L. Fullhart, *J. Am. Chem. Soc.*, **71**, 1478 (1949).

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

sulfuric acid (7664-93-9)

ether,

diethyl ether (60-29-7)

sodium sulfate (7757-82-6)

nitrogen (7727-37-9)

sulfur (7704-34-9)

potassium hydroxide (1310-58-3)

zinc (7440-66-6)

bromobenzene (108-86-1)

Pentane (109-66-0)

Thiophenol (108-98-5)

Thiophene (110-02-1)

lithium (7439-93-2)

butyllithium,
n-butyllithium (109-72-8)

Tetrahydrofuran (109-99-9)

lithium aluminum hydride (16853-85-3)

2-thiophenethiol (7774-74-5)

2-thienylmagnesium bromide

3-Bromothiophene (872-31-1)

2-thienyllithium

2-thienylsulfonyl chloride (16629-19-9)

3-thienyllithium

2-Chloro-5-thiophenethiol

2-chlorothiophene (96-43-5)

3-thiophenethiol