



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](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.

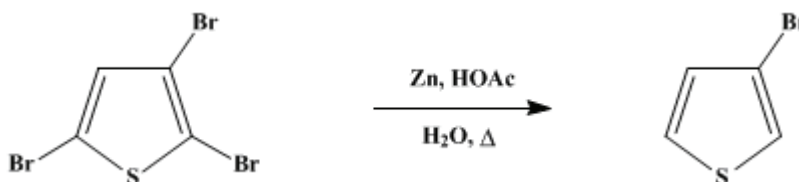
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*These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.*

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## 3-BROMOTHIOPHENE

[Thiophene, 3-bromo-]



Submitted by S. Gronowitz and T. Raznikiewicz<sup>1</sup>.

Checked by Max Tishler, Arthur J. Zambito, and Ronald B. Jobson.

### 1. Procedure

A 5-l., three-necked, round-bottomed flask is equipped with an efficient stirrer (Note 1), a reflux condenser, and a dropping funnel. Water (1850 ml.) is added, stirring is begun and continued throughout the procedure, and 783 g. (12.0 moles) of zinc dust (Note 2) and 700 ml. of acetic acid are added. The mixture is heated to reflux, the heating mantle is removed, and 1283 g. (4.00 moles) of 2,3,5-tribromothiophene (Note 3) is added dropwise at such a rate that the mixture continues to reflux. The addition is complete in about 70 minutes. Heat is applied, and the mixture is refluxed for 3 hours. A condenser is arranged for downward distillation, and the mixture is distilled until no more organic substance distills with the water (Note 4). The heavier organic layer is separated, washed successively with 50 ml. of 10% sodium carbonate solution and 100 ml. of water, dried over calcium chloride (Note 5), and fractionated through a vacuummantled Dufton column (Note 6). A 19-g. fore-run, b.p. 78–159°, consists mainly of thiophene and 3-bromothiophene. 3-Bromothiophene is collected at 159–160°;  $n^{20}_D$  1.5919–1.5928; weight 580–585 g. (89–90%) (Note 7) and (Note 8).

### 2. Notes

- The submitters used a Teflon<sup>®</sup> paddle-type stirrer sealed with rubber tubing lubricated by glycerol and driven by a powerful motor. The checkers used a Trubore<sup>®</sup> stirrer.
- Mallinckrodt zinc powder (analytical reagent grade) is used.
- 2,3,5-Tribromothiophene is conveniently prepared by the method of Troyanowsky.<sup>2</sup> Thiophene (1125 g., 13.4 moles) and 450 ml. of chloroform are charged into a 5-l. three-necked flask equipped with a stirrer, a dropping funnel, and an outlet for the hydrogen bromide evolved. The flask is in a deep pan through which cold tap water passes. Bromine (6480 g., 40.6 moles) is added dropwise to the stirred mixture over a period of 10 hours. After the mixture has stood overnight, it is heated at 50° for several hours, washed with 2*N* sodium hydroxide solution, refluxed for 7 hours with a solution of 800 g. of potassium hydroxide in 1.5 l. of 95% ethanol, and poured into water. The organic layer is separated, washed with water, dried over calcium chloride, and fractionated to give 3200–3650 g. (75–85%) of 2,3,5-tribromothiophene; b.p. 123–124° (9 mm.); m.p. 25–27°.
- About half of the volume is distilled over. The temperature of the vapor rises during the distillation from 95° to 101°.
- The checkers washed the drying agent with ether and combined the wash with the filtrate.
- A Dufton column was not available to the checkers. In its place a 2.5-cm. × 38-cm. column packed with glass helices was used. This column was heated by a 4.5-cm. concentric glass jacket wrapped with Nichrome ribbon. A 6.5-cm. concentric glass jacket surrounded the whole column and served to insulate it.
- In several experiments on one-fifth the scale, the yields were 89–92%.
- Infrared analysis shows that the 3-bromothiophene contains about 0.5% of 2-bromothiophene, as measured by 2-bromothiophene's characteristic absorption peak at 10.26  $\mu$ . The traces of this lower-boiling isomer can easily be removed by fractionation through a more efficient column.

### 3. Discussion

The procedure described is a modification of that described by Gronowitz.<sup>3</sup> 3-Bromothiophene has been obtained more tediously and in lower yields by removal of the  $\alpha$ -bromines of 2,3,5-tribromothiophene through the Grignard entrainment method<sup>4</sup> with ethyl bromide as the auxiliary halide, or by halogen-metal interconversion with *n*-butyllithium<sup>5</sup> followed by hydrolysis of the organometallic compounds. It has also been obtained from 4,5-dibromo-2-thiophenecarboxylic acid through simultaneous debromination and decarboxylation.<sup>6</sup>

### 4. Merits of the Preparation

3-Bromothiophene is a key intermediate for the synthesis of 3-substituted thiophenes.<sup>7</sup>

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### References and Notes

1. Department of Organic Chemistry, Chemical Institute, University of Uppsala, Sweden.
  2. C. Troyanowsky, *Bull. Soc. Chim. France*, 1424 (1955).
  3. S. Gronowitz, *Acta Chem. Scand.*, **13**, 1045 (1959).
  4. S. Gronowitz, *Arkiv Kemi*, **7**, 267 (1955).
  5. S. O. Lawesson, *Arkiv Kemi*, **11**, 373 (1957).
  6. R. Motoyama, S. Nishimura, E. Imoto, Y. Murakami, K. Hari, and J. Ogawa, *Nippon Kagaku Zasshi*, **78**, 950 (1957).
  7. S. Gronowitz, *Arkiv Kemi*, **13**, 295 (1959).
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### Appendix

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

ethanol (64-17-5)

calcium chloride (10043-52-4)

acetic acid (64-19-7)

ether (60-29-7)

sodium hydroxide (1310-73-2)

chloroform (67-66-3)

glycerol (56-81-5)

hydrogen bromide (10035-10-6)

sodium carbonate (497-19-8)

bromine (7726-95-6)

Ethyl bromide (74-96-4)

potassium hydroxide (1310-58-3)

zinc,  
zinc powder (7440-66-6)

Thiophene (110-02-1)

n-butyllithium (109-72-8)

2-Bromothiophene (1003-09-4)

3-Bromothiophene,  
Thiophene, 3-bromo- (872-31-1)

2,3,5-tribromothiophene

4,5-dibromo-2-thiophenecarboxylic acid (7311-68-4)