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.

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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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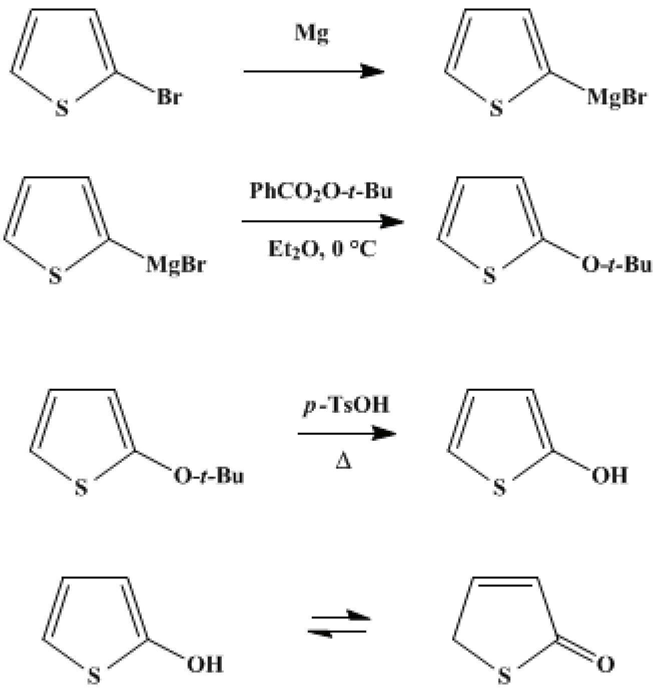
2-HYDROXYTHIOPHENE

[Thiophene-2-ol and 2(5H)-thiophenone]



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1. Procedure

A. *2-t-Butoxythiophene*. A dry 1-l. three-necked flask is fitted with a mechanical stirrer (Note 1), a reflux condenser having a take-off attachment, and a 250-ml. dropping funnel with a pressure-equalizing side tube.[2] A nitrogen-inlet tube is connected to the top of the condenser, and a T-tube branch of this is led to a mercury valve. The latter consists of a U-tube the bend of which is just filled with mercury.

Ten grams (0.41 g. atom) of magnesium turnings (Note 2) is placed in the flask and covered with 200 ml. of dry ether. Ten milliliters of a solution of 65.2 g. (0.40 mole) of 2-bromothiophene in 60 ml. of dry ether is added, the Grignard reaction is started by gently warming the reaction flask, and the remainder of the solution is added dropwise during 45 minutes. The mixture is stirred for 3.5 hours, the last 15 minutes under reflux. The Grignard reagent is cooled to 0–5° by immersing the flask in ice water. *t*-Butyl perbenzoate (62 g., 56 ml., 0.32 mole) (Note 3) in 100 ml. of dry ether is added dropwise during 45 minutes to the stirred ice-cooled mixture. The reaction mixture is stirred overnight, poured into ice water, and acidified with concentrated hydrochloric acid. The two phases are separated, and the water phase is twice extracted with ether. The combined ether solutions are extracted with three 60-ml. portions of 2*N* sodium hydroxide solution (Note 4), washed until neutral with water, dried over anhydrous sodium sulfate, and transferred to a distillation flask equipped with a Vigreux column. *Caution! The ether extract should not be distilled unless a test shows that peroxides are absent (Note 5).* The ether is distilled off at atmospheric pressure, and the residual oil is distilled under reduced pressure to give 35–38 g. (70–76%) of 2-*t*-butoxythiophene, b.p. 64–66°/13 mm., n_D^{20} 1.4991.

B. *2-Hydroxythiophene*. The 2-*t*-butoxythiophene obtained in Step A is placed in a distillation flask equipped with a short Vigreux column and a capillary inlet for nitrogen, and 0.1 g. of *p*-toluenesulfonic acid is added. The apparatus is placed in an oil bath at 155°. Decomposition begins immediately. After

5–10 minutes the oil bath is removed, and the distillation assembly is connected to a water pump (Note 6). 2-Hydroxythiophene is distilled under reduced pressure, nitrogen gas being drawn through the capillary during the whole procedure (Note 7). 2-Hydroxythiophene is collected at 91–93°/13 mm.; yield 20–23 g. (89–94%); n_D^{20} 1.5613 (Note 8).

2. Notes

1. Although a mercury seal is preferable, a rubber tube lubricated with glycerol is an adequate seal.
2. Common laboratory magnesium is as satisfactory as extremely pure sublimed magnesium.
3. *t*-Butyl perbenzoate is supplied by Lucidol Division, Wallace and Tiernan, Inc., Buffalo, New York, and Light and Co., Colnbrook, Bucks, England.
4. Acidification of the basic solution gives 29–32 g. (80–88%) of benzoic acid if the reaction has proceeded properly.
5. To make a peroxide test, place a few milligrams of sodium iodide, a trace of ferric chloride, and 2–3 ml. of glacial acetic acid in a test tube and carefully add 1–2 ml. of the ether solution. When unconsumed perbenzoate is present, a yellow ring is immediately formed between the two phases. *If this test indicates the presence of peroxide, the extract should not be concentrated and distilled until it has been extracted first with a solution of potassium iodide in acetic acid to remove peroxide and then with aqueous sodium thiosulfate to remove iodine.*
6. The decomposition is considered to be complete when the pressure is constant.
7. 2-Hydroxythiophene resinifies on prolonged exposure to air.
8. It has recently been shown that 2-hydroxythiophene exists mainly as 2(5H)-thiophenone at room temperature.[3]

3. Discussion

The procedure described is essentially that of Lawesson and Frisell.[4] 2-Hydroxythiophene has been prepared in low yields by Hurd and Kreuz[5] from 2-thienylmagnesium bromide and oxygen in the presence of excess isopropylmagnesium bromide.

4. Merits of the Preparation

The first step of the procedure illustrates a general way of preparing aryl *t*-butyl ethers.[4,6] The second step is the best way to prepare 2-hydroxythiophene, inasmuch as the yield is good and *t*-butyl perbenzoate is a readily available perester that is relatively stable. The same procedure has been used to convert several other haloaromatic compounds to hydroxyaromatic compounds in good yield[4] and is probably quite general.

References and Notes

1. Department of Chemistry, University of Aarhus, 8000 Aarhus C, Denmark.
2. K. B. Wiberg, "Laboratory Technique in Organic Chemistry," McGraw-Hill Book Company, Inc., New York, 1960, p. 207.
3. S. Gronowitz and R. A. Hoffman, *Arkiv Kemi*, **15**, 499 (1960).
4. S.-O. Lawesson and C. Frisell, *Arkiv Kemi*, **17**, 393 (1961).
5. C. D. Hurd and K. L. Kreuz, *J. Am. Chem. Soc.*, **72**, 5543 (1950).
6. C. Frisell and S.-O. Lawesson, this volume, p. 549.

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

t-butyl perbenzoate

hydrochloric acid (7647-01-0)

acetic acid (64-19-7)

ether (60-29-7)

sodium hydroxide (1310-73-2)

glycerol (56-81-5)

magnesium,
magnesium turnings (7439-95-4)

sodium sulfate (7757-82-6)

oxygen (7782-44-7)

potassium iodide (7681-11-0)

sodium thiosulfate (7772-98-7)

nitrogen (7727-37-9)

Benzoic acid (65-85-0)

mercury (7439-97-6)

iodine (7553-56-2)

ferric chloride (7705-08-0)

sodium iodide (7681-82-5)

isopropylmagnesium bromide (920-39-8)

2-Bromothiophene (1003-09-4)

2-thienylmagnesium bromide

t-Butyl (1605-73-8)

2-Hydroxythiophene,
Thiophene-2-ol (17236-58-7)

2(5H)-thiophenone

p-toluenesulfonic acid (104-15-4)

2-t-butoxythiophene (23290-55-3)