



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.

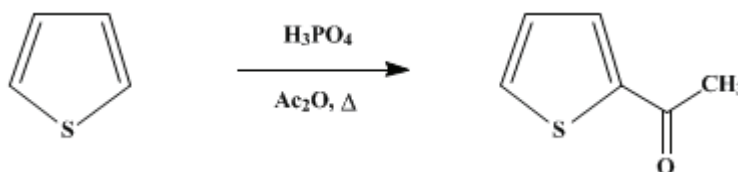
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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

Organic Syntheses, Coll. Vol. 3, p.14 (1955); Vol. 28, p.1 (1948).

2-ACETOTHIENONE

[Ketone, methyl 2-thienyl]



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1. Procedure

In a 1-l. three-necked flask fitted with a mechanical stirrer, a thermometer, and a reflux condenser are placed 168 g. (2 moles) (Note 1) of thiophene (Note 2) and 107 g. (1 mole) of 95% acetic anhydride (Note 3). The solution is heated to 70–75°, the source of heat is removed, and 10 g. (6 ml.) of 85% phosphoric acid is added with stirring. After 2–3 minutes an exothermic reaction occurs, and it is necessary to immerse the flask in a cold water bath to control the reaction. The boiling subsides in a few minutes; heat is again applied, and the mixture is refluxed for a total of 2 hours. The cooled mixture is washed successively with one 250-ml. portion of water and two 100-ml. portions of 5% sodium carbonate and is dried over anhydrous sodium sulfate. The orange-red liquid is distilled through a short fractionating column. After the removal of 76–80 g. of unchanged thiophene (b.p. 83–84°) by distillation at atmospheric pressure the residue is distilled under reduced pressure. The yield of 2-acetothiophene, b.p. 89–90°/10 mm. (m.p. 9.2–10.5°; n_D^{20} 1.5662), is 93–100 g. (74–79%).

2. Notes

1. Acetic anhydride rather than thiophene may be used in excess, but the unchanged reagent cannot be recovered by the procedure given. With a 3:1 mole ratio of thiophene to anhydride the yield is of the order of 85%.
2. Commercial 99+% thiophene was employed.
3. The use of an equivalent amount of freshly distilled 100% acetic anhydride does not improve the yield.

3. Discussion

In addition to the methods of preparation given in connection with the procedure¹ for the acetylation of thiophene with acetyl chloride in the presence of stannic chloride, 2-acetothiophene has been prepared from thiophene and either acetyl chloride or acetic anhydride in the presence of iodine,² hydriodic acid,² silica-metal oxides,³ zinc chloride,⁴ inorganic oxyacids,^{5,6} and boron trifluoride.^{7,8,9} It has also been prepared from thiophene and acetic acid in the presence of hydrogen fluoride⁵ or phosphorus pentoxide.¹⁰ The acylation in the presence of phosphorus pentoxide is particularly useful with higher aliphatic acids.¹⁰

Procedures using acetic anhydride and stannic chloride or ferric chloride have been described.¹¹

References and Notes

1. *Org. Syntheses Coll. Vol. 2*, 8 (1943).
2. Hartough and Kosak, *J. Am. Chem. Soc.*, **68**, 2639 (1946).
3. Hartough, Kosak, and Sardella, *J. Am. Chem. Soc.*, **69**, 1014 (1947).

4. Hartough and Kosak, *J. Am. Chem. Soc.*, **69**, 1012 (1947).
 5. Hartough and Kosak, *J. Am. Chem. Soc.*, **69**, 3093 (1947).
 6. U. S. pat. 2,496,786 [*C. A.*, **44**, 4930 (1950)].
 7. Heid and Levine, *J. Org. Chem.*, **13**, 409 (1948).
 8. Hartough and Kosak, *J. Am. Chem. Soc.*, **70**, 867 (1948).
 9. Levine, Heid, and Farrar, *J. Am. Chem. Soc.*, **71**, 1207 (1949).
 10. Hartough and Kosak, *J. Am. Chem. Soc.*, **69**, 3098 (1947).
 11. Farrar and Levine, *J. Am. Chem. Soc.*, **72**, 4433 (1950).
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Appendix
Chemical Abstracts Nomenclature (Collective Index Number);
(Registry Number)

silica-metal oxides

acetic acid (64-19-7)

acetic anhydride (108-24-7)

acetyl chloride (75-36-5)

sodium carbonate (497-19-8)

sodium sulfate (7757-82-6)

hydrogen fluoride (7664-39-3)

iodine (7553-56-2)

phosphoric acid (7664-38-2)

zinc chloride (7646-85-7)

hydriodic acid (10034-85-2)

ferric chloride (7705-08-0)

Ketone, methyl 2-thienyl (88-15-3)

Thiophene (110-02-1)

stannic chloride (7646-78-8)

boron trifluoride (7637-07-2)

phosphorus pentoxide (1314-56-3)

2-Acethienone (88-15-3)

