



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.

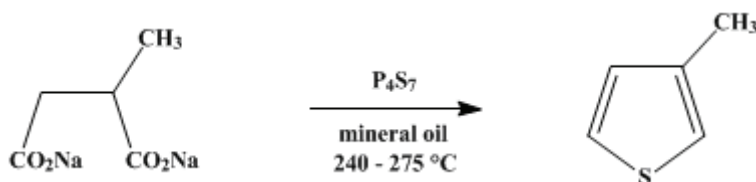
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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

Organic Syntheses, Coll. Vol. 4, p.671 (1963); Vol. 34, p.73 (1954).

3-METHYLTHIOPHENE

[Thiophene, 3-methyl-]



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1. Procedure

Caution! This preparation should be conducted in a well-ventilated hood to avoid exposure to hydrogen sulfide.

A 1-l. three-necked round-bottomed flask is fitted with a ground-glass-sealed stirrer, an immersed thermometer, a gas inlet tube, an addition funnel (Note 1), and a distilling head, wrapped with asbestos cloth, connected to a condenser arranged for distillation. The flask is charged with 150 ml. of mineral oil (Note 2), and the system is thoroughly swept out with a slow stream of carbon dioxide admitted through the gas inlet tube while the flask is heated with an electric heating mantle. When the temperature of the oil reaches 240–250°, a slurry of 90 g. (0.51 mole) of powdered anhydrous disodium methylsuccinate (Note 3) and 100 g. (0.287 mole) of phosphorus heptasulfide (Note 4) in 250 ml. of mineral oil is placed in the addition funnel. With efficient stirring and a slow continuous stream of carbon dioxide passing through the system, the slurry is added to the hot mineral oil at such a rate as to effect fairly rapid distillation of 3-methylthiophene accompanied by considerable gas evolution (mostly hydrogen sulfide). During the addition, which requires about 1 hour, the temperature is maintained at 240–250° (Note 5). The temperature is then raised to 275° and stirring continued in the inert atmosphere for an additional hour or until distillation ceases. The total distillate, amounting to 33–38 ml., is washed with two 50-ml. portions of 5% sodium hydroxide solution and finally with 50 ml. of water (Note 6). The crude 3-methylthiophene is then distilled (Note 7). A small fore-run is discarded, and the fraction boiling between 112° and 115° is collected. The yield is 26–30 g. (52–60%), n_D^{25} 1.5170 ± 0.0005 (Note 8), (Note 9), and (Note 10).

2. Notes

1. A gravity funnel fitted with a glass rod of suitable diameter is satisfactory for regulating the addition of the slurry.
2. Dowtherm A may also be used as a solvent for this reaction. However, because the boiling point (about 265°) is close to the reaction temperature, considerable quantities of Dowtherm distil along with the 3-methylthiophene. The total distillate amounts to 60–75 ml., which after washing and fractionally distilling gives the same yield as with mineral oil. Dowtherm gives a more fluid slurry and final residue and can be easily recovered by distillation at reduced pressure.
3. Disodium methylsuccinate was made by hydrogenating a concentrated solution of itaconic acid supplied by Chas. Pfizer and Company in aqueous sodium hydroxide (pH 8.7) over Raney nickel catalyst at 50 p.s.i. and 80–100°. After the catalyst was removed by filtration, the product was isolated by evaporation of the water and the residue was dried in a vacuum oven at 70–80°.
4. Phosphorous heptasulfide was obtained from the Oldbury Electrochemical Company. It has been shown² that the 'phosphorus trisulfide' used by earlier workers for such fusions was actually somewhat impure phosphorus heptasulfide.
5. The rate of addition of the slurry and the reaction temperature should be carefully controlled. About

two-thirds of the crude 3-methylthiophene distillate is collected during the addition of the slurry. Further heating at 260–275° gives the remainder of the material.

6. An emulsion may be obtained on further washing with water. A small amount of sodium chloride (2–3 g.) dissolved in the wash water assists in breaking such emulsions.

7. Rather violent foaming may occur during this distillation but is easily controlled in a 250-ml. flask. The distilling head and flask may be wrapped in asbestos cloth in order to increase the speed of distillation.

8. When fresh mineral oil was used (first run), a yield of 52–54% was obtained. However, when the recovered mineral oil (Note 9) was used, the yield increased to 60%.

9. The reaction residue is allowed to cool to room temperature and is filtered by suction. The dark mineral oil filtrate may be reused in the process. The malodorous filter cake is not pyrophoric and is almost completely soluble in water or dilute alkali with liberation of hydrogen sulfide.

10. The submitters obtained comparable yields on twice the scale described. They also applied the same procedure to disodium succinate to give a 25% yield of thiophene comparable to the yield obtained by dry fusion.³

3. Discussion

3-Methylthiophene has been prepared by the dry fusion of a salt of methylsuccinic acid and phosphorus trisulfide.⁴ This reaction was later investigated quite completely in respect to ratio of reactants, rate of heating, carbon dioxide atmosphere, and dilution of reactants with sand.⁵ An excellent technical method for preparing methylthiophenes has been described which involves a vapor-phase reaction of preheated sulfur with pentanes.⁶ 3-Methylthiophene has also been prepared by adding 50% crude isoprene (amylenes) to molten sulfur at 350°,⁷ and by passing a mixture of 2-methyl-2-butene and sulfur dioxide over a chromium oxide-aluminum oxide catalyst at 450°.⁸

References and Notes

1. Sterling-Winthrop Research Institute, Rensselaer, New York.
2. Pernert and Brown, *Chem. Eng. News*, **27**, 2143 (1949).
3. *Org. Syntheses Coll. Vol. 2*, 578 (1943).
4. Volhard and Erdmann, *Ber.*, **18**, 454 (1885).
5. Linstead, Noble, and Wright, *J. Chem. Soc.*, **1937**, 915.
6. Rasmussen and Hansford, U. S. pat. 2,450,686 [*C. A.*, **43**, 1067 (1949)].
7. Shepard, Henne, and Midgley, Jr., *J. Am. Chem. Soc.*, **56**, 1355 (1934).
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Appendix

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

phosphorus trisulfide

phosphorus heptasulfide

Phosphorous heptasulfide

phosphorus 'trisulfide.'

chromium oxide-aluminum oxide

sodium hydroxide (1310-73-2)

sodium chloride (7647-14-5)

hydrogen sulfide (7783-06-4)

sulfur dioxide (7446-09-5)

sulfur (7704-34-9)

carbon dioxide (124-38-9)

nickel (7440-02-0)

Thiophene (110-02-1)

Itaconic acid (97-65-4)

2-methyl-2-butene (513-35-9)

disodium succinate (150-90-3)

ISOPRENE (78-79-5)

Methylsuccinic acid (498-21-5)

3-Methylthiophene,
Thiophene, 3-methyl- (616-44-4)

disodium methylsuccinate