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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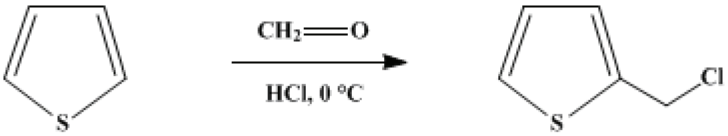
2-CHLOROMETHYLTHIOPHENE

[Thiophene, 2-chloromethyl-]



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1. Procedure

Caution! Suitable precautions should be observed in the preparation, purification, and storage of 2-chloromethylthiophene. The product is lachrymatory, and the procedure should be carried out in an efficient hood. The distillation and storage of the material are described in (Note 6) and (Note 7).

In a 2-l. beaker surrounded by an ice-salt bath (Note 1), and fitted with a mechanical stirrer and a thermometer, are placed 420 g. (392 ml., 5 moles) of thiophene (Note 2) and 200 ml. of concentrated hydrochloric acid. A rapid stream of hydrogen chloride (Note 3) is passed continuously into the mixture with vigorous stirring. When the temperature reaches 0°, 500 ml. of 37% formaldehyde solution (Note 4) is added at a rate that will permit the temperature to remain below 5°. The addition requires about 4 hours. When all the formaldehyde solution has been added, the mixture is extracted with three 500-ml. portions of ether. The ether extracts are combined, washed successively with water and saturated sodium bicarbonate solution, and then dried over anhydrous calcium chloride. The solvent is removed by distillation, and the product is distilled under reduced pressure through a 50-cm. fractionating column (Note 5). The product boiling at 73–75°/17 mm. is collected. The yield is 257–267 g. (40–41%) of a colorless oily liquid (Note 6) and (Note 7).

2. Notes

1. The checkers preferred to use a Dry Ice bath or to add Dry Ice to the reaction mixture as needed.
2. The thiophene used by the submitters was that supplied by the Socony-Vacuum Oil Company. It was used without any additional purification.
3. A satisfactory hydrogen chloride generator has been described earlier.[1]
4. The apparatus should be set up in a hood, for, although nearly all the hydrogen chloride is absorbed, a small amount does escape. The rate of addition of hydrogen chloride should be such that nearly complete absorption is maintained at all times.

According to the submitters, paraformaldehyde (165 g., 5.5 moles) may be substituted for the formaldehyde solution. This modification affords an easier control of the temperature. However, paraformaldehyde does not react to any appreciable extent below 0°, and so the temperature should be kept between 0° and 5°. The reaction time is 6–8 hours, and the yield is unchanged.

5. A Vigreux column was used by both the submitters and checkers.
6. Some *bis*-(2-thienyl) methane may be obtained from the residue at 125–126°/9 mm. When recrystallized from methanol it melts at 46–47°.
7. It is advisable not to store chloromethylthiophene for any length of time or in sealed containers, since it has a tendency to decompose, often with explosive violence, even when kept cold and in the dark. If the product is to be used for the preparation of 2-thiophenaldehyde it is convenient to convert it to the more stable hexamethylenetetrammonium salt, for storage.

Instances of explosion of the product on storage have been reported; these are apparently due to generation of hydrogen chloride within a closed container. The following procedure for distillation and storage is recomended (F. C. Myer, private communication). The crude product is stabilized by the addition of 2% by weight of dicyclohexylamine and purified by rapid distillation under reduced pressure. The pot temperature should not rise above 100° during the main part of the distillation, or above 125° at the end of the distillation. The distillate is stabilized immediately with 1–2% by weight of dicyclohexylamine and stored in a glass bottle plugged loosely with a stopper wrapped with glass wool. The bottle is placed in a large beaker and stored in a refrigerator. A small amount of gelatinous salt separates on standing; this has no deleterious effect.

When stabilized properly and stored in the cold, decomposition is slow. The material should be inspected regularly to observe excessive darkening and liberation of hydrogen chloride. Restabilization and distillation may permit recovery of pure material if the decomposition is not too far advanced. Complete decomposition results in frothing, resinification, and liberation of hydrogen chloride.

3. Discussion

2-Chloromethylthiophene has been prepared by the action of hydrogen chloride on 2-thienylcarbinol[2] and by the action of hydrogen chloride and formaldehyde on thiophene.[3] The above procedure is essentially that of Blicke and Burckhalter.[3]

This preparation is referenced from:

- Org. Syn. Coll. Vol. 3, 811

References and Notes

1. *Org. Syntheses* Coll. Vol. **1**, 534 (1941).
2. Biedermann, *Ber.*, **19**, 636 (1886).
3. Blicke and Burckhalter, *J. Am. Chem. Soc.*, **64**, 477 (1942).

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

calcium chloride (10043-52-4)

hydrogen chloride,
hydrochloric acid (7647-01-0)

methanol (67-56-1)

ether (60-29-7)

formaldehyde (50-00-0)

sodium bicarbonate (144-55-8)

Thiophene (110-02-1)

2-Chloromethylthiophene,
Thiophene, 2-chloromethyl-,
chloromethylthiophene (765-50-4)

2-thiophenaldehyde

dicyclohexylamine (101-83-7)

2-thienylcarbinol (636-72-6)

bis-(2-thienyl) methane (4341-34-8)

paraformaldehyde (30525-89-4)