Organic Syntheses

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.

The procedures described in *Organic Syntheses* are provided as published and are conducted at one's own risk. *Organic Syntheses, Inc.*, its Editors, and its Board of Directors do not warrant or guarantee the safety of individuals using these procedures and hereby disclaim any liability for any injuries or damages claimed to have resulted from or related in any way to the procedures herein.

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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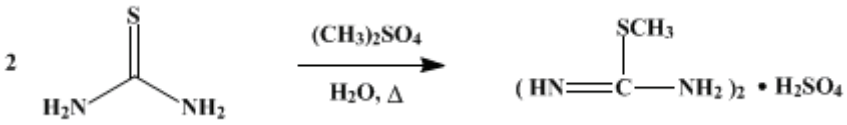
Organic Syntheses, Coll. Vol. 2, p.411 (1943); Vol. 12, p.52 (1932).

S-METHYL ISOTHIOUREA SULFATE

[Pseudourea, 2-methyl-2-thio-, sulfate]



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1. Procedure

In a 2-l. round-bottomed flask are mixed 152 g. (2 moles) of finely divided thiourea and 70 cc. of water. To this is added 138 g. (1.1 moles) of technical methyl sulfate (Note 1). The flask is immediately attached to a long reflux condenser carrying a trap. The reaction is allowed to progress spontaneously (Note 2), with occasional cooling as the reaction becomes more rapid and the flask becomes filled with vapor. After the initial vigorous reaction is completed, the mixture is refluxed for one hour, during which time crystallization takes place (Note 3). The mixture is then allowed to cool, the flask is removed, 200 cc. of 95 per cent ethyl alcohol is added, and the contents of the flask are then filtered with suction. The residue is washed twice with 100-cc. portions of 95 per cent alcohol and allowed to dry in air. The yield is 190 g. of a product which melts with decomposition at 235°. Another crop of crystals weighing 43 g. and melting at 230° can be obtained from the alcoholic filtrate by concentrating it to a paste to which, after cooling, is added 120 cc. of 95 per cent alcohol. The total yield is 220–233 g. (79–84 per cent of the theoretical amount).

2. Notes

1. Technical methyl sulfate, if it has not turned dark brown, need not be distilled before using.
2. If the mixture is cooled too much with ice water, the spontaneous reaction almost ceases and gentle heating is required to start the reaction again. If the mixture is not cooled, the initial vigorous reaction is so violent that material is likely to be lost through the condenser. Since methyl sulfate is poisonous, this must be avoided. Ammonia, which is a specific antidote for methyl sulfate, should be kept at hand.
The checkers observed no spontaneous reaction, and in order to initiate reaction the flask and contents were gently heated with a moving low flame. When reaction sets in, the flame is removed. A container with ice water is kept handy to moderate any unduly vigorous reaction, particularly if the water condenser is less than 125 cm. in length.
3. The completion of the vigorous reaction indicates that half of the thiourea is methylated and that the methyl sulfate has been converted to methylhydrogen sulfate. Vigorous heating is necessary to complete the methylation.

3. Discussion

The procedure described is essentially that of Arndt.[1]

This preparation is referenced from:

- Org. Syn. Coll. Vol. 2, 345
- Org. Syn. Coll. Vol. 3, 73

References and Notes

1. Arndt, Ber. **54**, 2236 (1921).

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

ethyl alcohol,
alcohol (64-17-5)

ammonia (7664-41-7)

methyl sulfate,
methylhydrogen sulfate (75-93-4)

thiourea (62-56-6)

S-Methyl isothiourea sulfate,
Pseudourea, 2-methyl-2-thio-, sulfate (867-44-7)