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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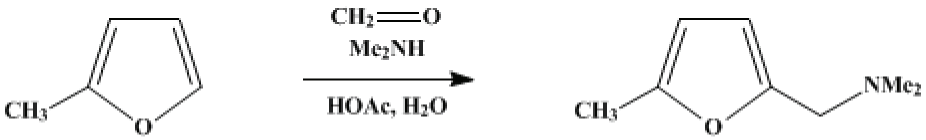
5-METHYLFURFURYLDIMETHYLAMINE

[Furfurylamine, N,N,5-trimethyl-]



Submitted by Ernest L. Eliel and Milton T. Fisk[1].
Checked by James Cason, Mary S. Nakata, and William G. Dauben.

1. Procedure

To 200 ml. of glacial acetic acid in a 1-l. round-bottomed flask is added slowly, with cooling in an ice bath, 151 ml. (54 g. of dimethylamine, 1.2 moles) of 40% aqueous dimethylamine solution, followed by 90 ml. (36 g. of formaldehyde, 1.2 mole) of 37% aqueous formaldehyde (formalin) solution. The flask is removed from the ice bath and equipped with a reflux condenser, through which 82 g. (90 ml., 1 mole) of 2-methylfuran (Note 1) is added all at once. Upon gentle swirling of the flask, an exothermic reaction may set in spontaneously; if it does not, the flask is heated on a steam bath until reaction commences. In any event, the spontaneous reaction is allowed to proceed without further external heating. When it ceases, the reaction mixture is heated on a steam bath for another 20 minutes, cooled, and without delay poured into a cold solution of 250 g. of sodium hydroxide (Note 2) in 800 ml. of water.

The reaction mixture is steam-distilled until the distillate is only faintly alkaline (Note 3). To the distillate is added sodium hydroxide (Note 2) to the extent of 10 g. for each 100 ml. of distillate. The strongly alkaline solution is cooled and extracted with two 300-ml. portions of ether. The combined ether layers are dried over 25 g. of solid potassium hydroxide (Note 4), decanted, and concentrated. The residue is distilled under reduced pressure; the yield of 5-methylfurfuryldimethylamine boiling at 62–63°/13 mm. is 96–106 g. (69–76%), n_D^{25} 1.4616–1.4620.

2. Notes

1. The submitters used du Pont 2-methylfuran. Since the stabilizer contained in this material inhibits the reaction, it should be removed before use. The liquid is stored over solid potassium hydroxide (10 g. for each 100 ml. of 2-methylfuran) for 24 hours, decanted, and stored over the same amount of fresh potassium hydroxide at least overnight. A more rapid but less convenient method of removing the stabilizer is to extract the liquid with 10% aqueous potassium hydroxide until the extracts are only faintly colored.
2. The submitters used commercial sodium hydroxide flakes.
3. The steam distillate amounts to 2–3 l.
4. If a large aqueous phase appears, the amine should be decanted and dried further over a fresh portion of potassium hydroxide pellets.

3. Discussion

The first preparation of 5-methylfurfurylamines by the Mannich reaction was by Holdren and Hixon.[2] The present modification has been published[3] without the stem-distillation step, which facilitates separation of the product.

References and Notes

1. University of Notre Dame, Notre Dame, Indiana.

2. Holdren and Hixon, *J. Am. Chem. Soc.*, **68**, 1198 (1946).
3. Eliel and Peckham, *J. Am. Chem. Soc.*, **72**, 1210 (1950).

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

acetic acid (64-19-7)

ether (60-29-7)

sodium hydroxide (1310-73-2)

formaldehyde,
formalin (50-00-0)

potassium hydroxide,
potassium hydroxide pellets (1310-58-3)

dimethylamine (124-40-3)

2-methylfuran (534-22-5)

5-Methylfurfuryldimethylamine,
Furfurylamine, N,N,5-trimethyl- (14496-35-6)