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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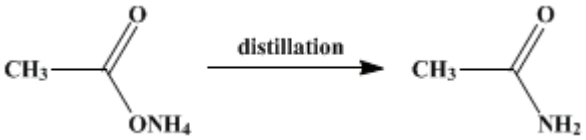
ACETAMIDE



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1. Procedure

In a 5-l. flask is placed 3 kg. (2860 cc., 50.0 moles) of glacial acetic acid and to this is added a weight of ammonium carbonate corresponding to 400 g. (23.5 moles) of ammonia (Note 1). The flask is fitted with a one-hole stopper holding an efficient fractionating column 90 cm. long with condenser and receiver. An air condenser 150–200 cm. long may be employed. The mixture in the flask is heated to gentle boiling and the flame so regulated that the rate of distillation does not exceed 180 cc. per hour. The distillation is continued in this way for eight to ten hours, until the temperature at the head of the column reaches 110°. The distillate, which is a mixture of water and acetic acid, amounts to 1400–1500 cc. The receiver is changed, the flame under the flask is gradually increased, and the distillation is continued at about the same rate until the temperature at the head of the column rises to 140°. The distillate, which amounts to 500–700 cc., is largely acetic acid and may be used in the next run.

The contents of the flask are transferred to a 2-l. flask for fractional distillation (p. 130), having a column 40–50 cm. long, and distilled under atmospheric pressure, using an air condenser. The fraction boiling below 210°, amounting to 250–300 cc., is collected separately. The material remaining in the flask is nearly pure acetamide and may all be distilled, 1150–1200 g. passing over at 210–216°. By redistilling the fraction boiling below 210°, the yield may be increased to 1200–1250 g. (87–90 per cent of the theoretical amount). The acetamide thus obtained is pure enough for most purposes, but if a purer product is desired it may be recrystallized from a mixture of benzene and ethyl acetate; 1 l. of benzene and 300 cc. of ethyl acetate are used for 1 kg. of acetamide (Note 2). Colorless needles melting at 81° are thus obtained (Note 3). The solvent and the acetamide it contains may be recovered by distillation.

2. Notes

1. Ammonium carbonate of commerce is often extremely impure, and care must be taken to obtain a representative sample for the determination of the ammonia content by titration with standard acid. The ammonium carbonate used in this preparation contained 27.2 per cent of ammonia, and 1470 g. was used in each run.
2. Crystallization of acetamide, by solution in hot methyl alcohol (0.8 cc. per g.) and dilution with ether (8–10 cc. per g.), has been recommended as the best method of purification.[1]
3. As acetamide is somewhat hygroscopic, it cannot be exposed to the air unless precautions are taken to have the air dry.

3. Discussion

Acetamide can be prepared by the rapid distillation of ammonium acetate;[2] by heating ammonium acetate in a sealed tube and distilling the product;[3] by treating acetic anhydride with ammonia;[4] by heating a mixture of ammonium chloride and sodium acetate to 240°;[5] by the action of cold aqueous ammonia on ethyl acetate;[6] by boiling a mixture of glacial acetic acid and ammonium thiocyanate for four days;[7] by saturating glacial acetic acid with dry ammonia and then refluxing;[8] by distillation of ammonium acetate through a reflux condenser filled first with glacial acetic acid and then with aniline until the temperature of the mixture reaches 220°;[9] by passing a stream of ammonia through heated acetic acid;[10] and from formamide and hydrogen at 200–500°.[11]

The procedure described is based on the method of Noyes and Goebel,[12] in which equimolecular proportions of ammonium acetate and acetic acid are heated together, the acetic acid having been shown to accelerate both the dehydration of ammonium acetate and the hydrolysis of acetamide.

References and Notes

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

Acetamide (60-35-5)

acetic acid (64-19-7)

ammonium carbonate (506-87-6)

ammonia (7664-41-7)

Benzene (71-43-2)

ethyl acetate (141-78-6)

methyl alcohol (67-56-1)

ether (60-29-7)

ammonium acetate (631-61-8)

acetic anhydride (108-24-7)

ammonium chloride (12125-02-9)

sodium acetate (127-09-3)

ammonium thiocyanate (1762-95-4)

aniline (62-53-3)

formamide (75-12-7)

hydrogen (1333-74-0)