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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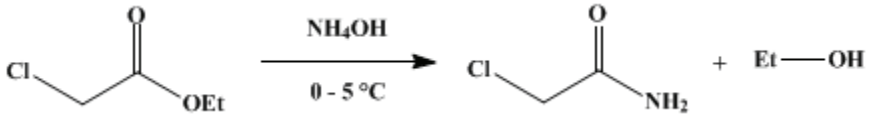
Organic Syntheses, Coll. Vol. 1, p.153 (1941); Vol. 7, p.16 (1927).

CHLOROACETAMIDE

[Acetamide, α-chloro-]



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1. Procedure

In a 2-l. round-bottomed flask fitted with a mechanical stirrer and surrounded by an ice-salt bath is placed 215 g. (1.75 moles) of ethyl chloroacetate (Note 1). Vigorous stirring is started, and to the cold ester (Note 2) 200 cc. of chilled aqueous ammonia (sp. gr. 0.9) is added. The solution is stirred in the cold for about fifteen minutes; then another 200-cc. portion of aqueous ammonia is added, and the stirring is continued for about fifteen minutes. The mixture is then allowed to stand for thirty minutes, filtered with suction, and washed with two 25-cc. portions of cold water to remove ammonium chloride. The yield of air-dried material melting at 118–119° (Note 3) is 128–138 g. (78–84 per cent of the theoretical amount).

This product contains traces of ammonium chloride which may be removed by crystallization from water. When 100 g. of crude product is recrystallized from 400 cc. of water, about 80 g. of product is obtained. The recrystallized product melts at 119–120°.

2. Notes

1. The ethyl chloroacetate used may be a commercial grade which boils at 141–146°. The ethyl chloroacetate and the chloroacetamide have the usual irritating effect of chloroacetyl compounds.
2. The temperature is best maintained at 0–5°. At higher temperatures there is more replacement of the chlorine and the yields are considerably lower.
3. Traces of moisture lower the melting point considerably.

3. Discussion

Chloroacetamide can be prepared from chloroacetyl chloride and dry ammonia gas,[1] and by the treatment of ethyl chloroacetate[2] or methyl chloroacetate[3] with cold aqueous ammonia solutions. The procedure described was developed from the methods of Scholl[2] and Tröger and Hille.[2]

This preparation is referenced from:

- Org. Syn. Coll. Vol. 1, 488
- Org. Syn. Coll. Vol. 4, 144

References and Notes

1. Willm, Ann. **102**, 110 (1857).
2. Willm, Ann. **102**, 110 (1857); Menschutkin and Jermolajev, Z. Chem. 5 (1871); Bauer, Ann. **229**, 165 (1885); Scholl, Ber. **29**, 2417 (1896); Tröger and Hille, J. prakt. Chem. (2) **71**, 204 (1905).
3. Henry, Rec. trav. chim. **24**, 165 (footnote 3) (1905).

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

chloroacetyl compounds

ammonia (7664-41-7)

ammonium chloride (12125-02-9)

chlorine (7782-50-5)

CHLOROACETAMIDE,
Acetamide, α-chloro- (79-07-2)

Ethyl chloroacetate (105-39-5)

chloroacetyl chloride (79-04-9)

methyl chloroacetate (96-34-4)