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.

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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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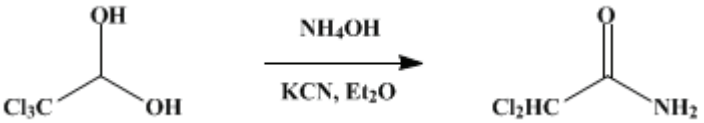
α,α-DICHLOROACETAMIDE

[Acetamide, α,α-dichloro-]



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1. Procedure

A solution of 134 g. (0.81 mole) of chloral hydrate (Note 1) in 400 ml. of ether (Note 2) is placed in a 2-l. round-bottomed three-necked flask equipped with a dropping funnel, a reflux condenser, and an efficient mercury-sealed stirrer (Note 3). A solution of 12 g. of potassium cyanide (Note 4) in 220 ml. of concentrated ammonium hydroxide (sp. gr. 0.9) is added through the dropping funnel over the course of 15 minutes at a rate sufficient to cause the ether to reflux vigorously. Stirring is continued for an additional 20 minutes (Note 5). The layers are separated, and the ether layer is washed once with 75 ml. of water and once with 75 ml. of 10% aqueous sulfuric acid solution (Note 6). (These washings are retained and used again later.) The aqueous layer from the reaction mixture is extracted with three 75-ml. portions of ether, and each ether extract is washed successively with the same water and sulfuric acid solutions used previously. The combined ether extracts are dried with 40 g. of sodium sulfate, the ether is removed by distillation, and the residue is recrystallized from 200 ml. of benzene. The solid is removed by filtration with suction and washed with two 25-ml. portions of cold benzene. The yield is 66–76 g. melting at 97.5–99.5° (cor.). Concentration of the filtrate gives 1–5 g. of material with a slightly lower (96–97° cor.) melting point, making the total yield 67–81 g. (65–78%).

2. Notes

1. The chloral hydrate was of U.S.P. XI quality.
2. Ether decreases the amount of charring, presumably by controlling the temperature of the reaction mixture.
3. It is very difficult to prevent the escape of ammonia and ether. The reaction should be carried out in a hood.
4. Baker's potassium cyanide, 94–96%, was used.
5. A decided increase in reaction time will cause charring and give a product that is difficult to purify. The reaction should not be interrupted until the ethereal extracts have been washed as described.
6. The ethereal extracts of the reaction mixture contain impurities that cause charring when the solvent is removed. The water and acid treatments remove these impurities. Equally good yields may be obtained by omitting these washings, but then it is necessary to decolorize with Norit in the recrystallization from benzene, and a second recrystallization may be necessary to obtain a white product.

3. Discussion

Dichloroacetamide has been prepared from ethyl dichloroacetate with alcoholic ammonia[1] or aqueous ammonium hydroxide;[2] from ethyl dichloromalonate and ethanolic ammonia;[3] by the action of ammonia on pentachloroacetone,[4] chloral cyanohydrin,[5] and hexachloro-1,3,5-cyclohexanetrione;[6] from chloral ammonia and potassium cyanide;[7] by the action of hydrogen chloride on dichloroacetonitrile;[8] from the reaction of asparagine with the sodium salt of N-chloro-*p*-toluenesulfonamide;[9] and by the action of an alkali cyanide and ammonia on chloral hydrate.[10]

References and Notes

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2. d'Ouville and Connor, *J. Am. Chem. Soc.*, **60**, 33 (1938).
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Appendix
Chemical Abstracts Nomenclature (Collective Index Number); (Registry Number)

sodium salt of N-chloro-p-toluenesulfonamide

sulfuric acid (7664-93-9)

hydrogen chloride (7647-01-0)

ammonia (7664-41-7)

Benzene (71-43-2)

ether (60-29-7)

sodium sulfate (7757-82-6)

potassium cyanide (151-50-8)

ammonium hydroxide (1336-21-6)

chloral hydrate (302-17-0)

pentachloroacetone (1768-31-6)

α,α-DICHLOROACETAMIDE,
Dichloroacetamide,
Acetamide, α,α-dichloro- (683-72-7)

ethyl dichloroacetate (535-15-9)

ethyl dichloromalonate

chloral cyanohydrin

hexachloro-1,3,5-cyclohexanetrione

chloral ammonia (594-65-0)

dichloroacetonitrile (3018-12-0)

asparagine (70-47-3)