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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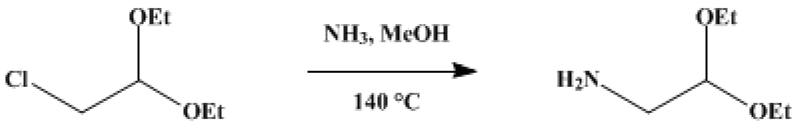
AMINOACETAL

[Acetaldehyde, amino-, diethyl acetal]



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1. Procedure

To a solution of 38.2 g. (0.25 mole) of chloroacetal (b.p. 62–64°/20 mm.) in 800 ml. of absolute methanol, cooled in a hydrogenation bomb of about 1.1-l. capacity to the temperature of a Dry Ice-acetone bath, is added approximately 300 g. (290 ml.; about 18 moles) of liquid ammonia (Note 1). The bomb is closed, connected with a pressure gauge, and heated at 140° with shaking for 10 hours.

After the bomb has cooled, the ammonia is allowed to escape (Note 2) and the solution is poured out. The bomb is rinsed with two 200-ml. portions of dry methanol (Note 3), and the combined solution and washings are filtered. The colored solution is concentrated on the steam bath to about 500 ml., 100 ml. of 5% aqueous potassium hydroxide is added, and concentration is continued until the vapors no longer burn (about 2 hours). The solution is saturated with salt (Note 4) and placed in the bulb of an automatic extractor (Note 5); 100 ml. of 50% aqueous potassium hydroxide is added, and the solution is extracted continuously with 350 ml. of ether overnight. The oil that remains after concentration of the ether extract gives on fractionation under reduced pressure (Note 6) 23–24 g. (71–74%) of aminoacetal, b.p. 99–103°/100 mm. (Note 7), (Note 8), and (Note 9).

2. Notes

1. The bomb is cooled by placing it in an iron pot of about two-thirds the height of the bomb. The pot is half filled with acetone, and pieces of Dry Ice are added until the vigorous evolution of carbon dioxide accompanying the addition of each new piece is no longer observed. If liquid ammonia is added to an insufficiently cooled solution of chloroacetal and alcohol, the ammonia is volatilized so vigorously that much of the starting material is lost. It is possible to force the ammonia from a small bomb into the bomb containing the alcohol and chloroacetal, at room temperature, by the aid of compressed hydrogen.[1]
2. Some of the reaction mixture may be carried from the bomb by the escaping ammonia. If the ammonia is allowed to escape through a tube leading into a beaker or flask, this material can be collected.
3. An appreciable amount of a slimy solid collects on the walls of the bomb. It appears to consist of ammonium chloride together with a small amount of iron salts dissolved from the walls of the bomb by the action of the ammonia. The amount of product recovered by careful working of this material is less than 2 g.
4. About 70 g. is required.
5. An automatic extraction apparatus supplied by Ace Glass, Inc., Vineland, New Jersey, was used; see their catalog 40, p. 90, No. 6835 (500-ml. extraction chamber).
6. An ordinary Claisen flask having a modified side arm was used.
7. Yields of 56–70% were obtained by using larger quantities (76–100 g.) of chloroacetal but the same amounts of methanol and ammonia.
8. The residue contains diacetalylamine (b.p. 124–127°/7 mm.; 189°/100 mm.). It can be isolated by combining the residues from several runs and fractionating through an efficient column. The residues from 14 runs of double the size given above gave 83 g. of diacetalylamine.
9. The main difference between this procedure and the one published earlier[2] is that a much smaller

amount of haloacetal is used in the same total volume.

3. Discussion

The most useful and general method for preparing aminoacetal consists of the action of ammonia upon the haloacetals.[3,4,5,6,7,8,9,10] It has also been prepared by the reduction of nitroacetal using sodium in alcohol,[11] and by the reduction of glycine ester hydrochloride with sodium amalgam.[12] The haloacetal-ammonia reaction has been patented.[13]

References and Notes

1. *Org. Syntheses*, **23**, 69 (1943).
2. *Org. Syntheses*, **24**, 4 (1944).
3. Cass, *J. Am. Chem. Soc.*, **64**, 785 (1942).
4. Wohl, *Ber.*, **21**, 617 (1888); **39**, 1953 (1906).
5. Wolff, *Ber.*, **21**, 1482 (1888); **26**, 1832 (1893).
6. Wolff and Marburg, *Ann.*, **363**, 179 (1908).
7. Marckwald, *Ber.*, **25**, 2355 (1892).
8. Hartung and Adkins, *J. Am. Chem. Soc.*, **49**, 2521 (1927).
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10. Woodward and Doering, *J. Am. Chem. Soc.*, **67**, 860 (1945).
11. Losanitsch, *Ber.*, **42**, 4049 (1909).
12. Fischer, *Ber.*, **41**, 1021 (1908).
13. U. S. pat. 2,490,385 [*C. A.*, **44**, 6426 (1950)].

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

glycine ester hydrochloride

Aminoacetal

chloroacetal

iron pot

iron salts

diacetalylamine

nitroacetal

ammonia (7664-41-7)

methanol (67-56-1)

ether (60-29-7)

ammonium chloride (12125-02-9)

hydrogen (1333-74-0)

carbon dioxide (124-38-9)

acetone (67-64-1)

potassium hydroxide (1310-58-3)

sodium (13966-32-0)

Acetaldehyde, amino-, diethyl acetal