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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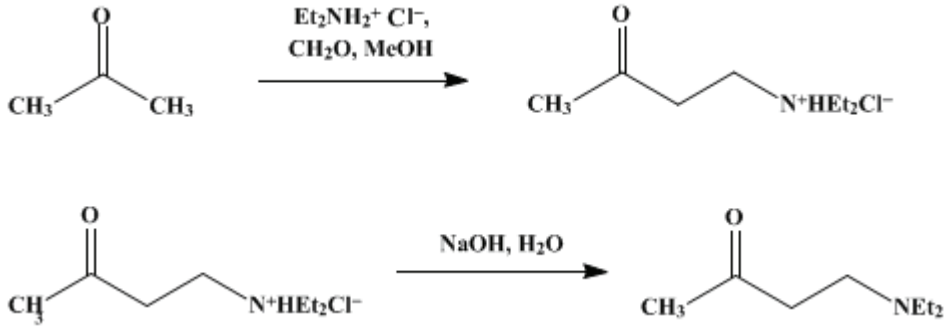
1-DIETHYLAMINO-3-BUTANONE

[2-Butanone, 4-diethylamino-]



Submitted by Alfred L. Wilds, Robert M. Nowak, and Kirtland E. McCaleb[1].
Checked by William S. Johnson and Duane Zinkel.

1. Procedure

In a 3-l. round-bottomed flask equipped with a reflux condenser (Note 1) are placed 176 g. (1.60 moles) of diethylamine hydrochloride (Note 2), 68 g. (2.26 moles) of paraformaldehyde, 600 ml. (8.2 moles) of acetone, 80 ml. of methanol, and 0.2 ml. of concentrated hydrochloric acid. The mixture is heated for 12 hours at a moderate to vigorous rate of reflux (Note 3). The light-yellow solution, in which a small amount of gelatinous solid remains, is cooled, and a cold solution of 65 g. of sodium hydroxide in 300 ml. of water is added. The mixture is extracted with three 200-ml. portions of ether, the combined extracts are washed with two 150-ml. portions of saturated sodium chloride solution, and the washes are re-extracted with two 150-ml. portions of ether.

The combined ether solutions are dried overnight with about 80 g. of anhydrous sodium sulfate, filtered, and then distilled under reduced pressure (5 to 12 mm.) (Note 4) through a 20-cm. asbestos-wrapped Vigreux distilling column, with an efficient water-cooled condenser (Note 5). After the solvent and a small fore-run have been distilled, 150–171 g. (66–75%) of 1-diethylamino-3-butanone is collected as a light-yellow to nearly colorless liquid, b.p. 63–67°/7mm. (75–77°/15mm.), n_D^{25} 1.4300–1.4310. The product may contain a small amount of 1,1-bis(diethylaminomethyl)acetone (the bis-Mannich base), which can interfere with some uses of this product. Refractionation gives relatively pure material, 142–161 g. (62–70%), b.p. 72–75°/10mm., n_D^{25} 1.4301–1.4307, d_4^{25} 0.8626, M_D (found) 43.2–43.3, M_D (calcd.) 43.1 (Note 6).

2. Notes

1. Ground-glass joints are desirable.
2. A good grade of commercial diethylamine hydrochloride (Eastman Kodak white label grade or Matheson, Coleman and Bell) is satisfactory without purification.
3. At first some bumping may occur if the heating is too vigorous; mechanical stirring may reduce this, but does not improve the yield. The submitters found an electrically heated oil bath or a steam bath to be satisfactory, but *not a heating mantle.*
4. If the temperature of distillation is too high, or if a heating mantle is used, decomposition to methyl vinyl ketone may occur. The submitters used an electrically heated oil bath and prefer pressures below 12 mm. to minimize decomposition. A more elaborate fractionating column necessitating a higher bath temperature or prolonged heating is also undesirable. If the material stands more than one or two days before distillation it may decompose.
5. Unless the condenser is efficient, some product will be lost; a Dry Ice-cooled trap located between the receiver and the pump is recommended.
6. This product gave satisfactory analytical values: Calcd. for $C_8H_{17}NO$: C, 67.1; H, 12.0. Found: C,

67.2; H, 11.9. The neutral equivalent of various samples, titrated potentiometrically with standard hydrochloric acid solutions, ranged between 144 and 145 (calcd. 143.2).

3. Discussion

1-Diethylamino-3-butanone has been prepared by the Mannich reaction,[2,3,4,5,6,7] and by the condensation of methyl vinyl ketone with diethylamine hydrochloride in the presence of acetic anhydride.[8] The present procedure is a modification of that described by Wilds and Shunk.[5]

References and Notes

1. University of Wisconsin, Madison, Wisconsin.
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3. du Feu, McQuillin, and Robinson, *J. Chem. Soc.*, **1937**, 53.
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5. Wilds and Shunk, *J. Am. Chem. Soc.*, **65**, 469 (1943).
6. Spaeth, Geissman, and Jacobs, *J. Org. Chem.*, **11**, 399 (1946).
7. Halsall and Thomas, *J. Chem. Soc.*, **1956**, 2431.
8. Swaminathan and Newman, *Tetrahedron*, **2**, 88 (1958).

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

hydrochloric acid (7647-01-0)

methanol (67-56-1)

ether (60-29-7)

acetic anhydride (108-24-7)

sodium hydroxide (1310-73-2)

sodium chloride (7647-14-5)

sodium sulfate (7757-82-6)

acetone (67-64-1)

1-Diethylamino-3-butanone,
2-Butanone, 4-diethylamino- (3299-38-5)

1,1-bis(diethylaminomethyl)acetone

diethylamine hydrochloride (660-68-4)

methyl vinyl ketone (78-94-4)

paraformaldehyde (30525-89-4)