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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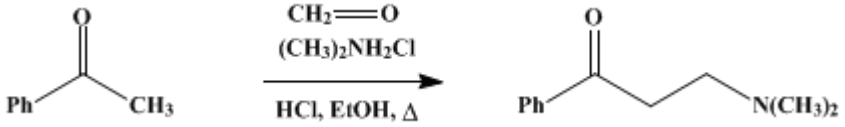
# β-DIMETHYLAMINOPROPIOPHENONE HYDROCHLORIDE

## [Propiophenone, β-dimethylamino-]

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## 1. Procedure

In a 500-ml. round-bottomed flask attached to a reflux condenser are placed 60 g. (58.5 ml., 0.5 mole) of acetophenone (Note 1), 52.7 g. (0.65 mole) of dimethylamine hydrochloride, and 19.8 g. (0.22 mole) of paraformaldehyde. After the addition of 1 ml. of concentrated hydrochloric acid (sp. gr. 1.19) in 80 ml. of 95% ethanol, the mixture is refluxed on a steam bath for 2 hours (Note 2). The yellowish solution is filtered, if it is not clear (Note 3) and (Note 4), and is transferred to a 1-l. wide-mouthed Erlenmeyer flask. While still warm, it is diluted by the addition of 400 ml. of acetone (Note 5), allowed to cool slowly to room temperature, and then chilled overnight in the refrigerator. The large crystals are filtered and washed with 25 ml. of acetone. After it has been dried for 2.5 hours at 40–50°, this crude product weighs 72–77 g. (68–72%) and melts at 138–141° (Note 6) and (Note 7); it is suitable for many reactions.

It may be recrystallized by dissolving it in 85–90 ml. of hot 95% ethanol and slowly adding 450 ml. of acetone to the solution. The recovery is about 90%. The purified material, dried at 70°, melts at 155–156° (Note 8) and (Note 9).

## 2. Notes

1. Acetophenone, m.p. 19–20°, and a practical grade of dimethylamine hydrochloride were used.
2. The reaction mixture, which at first forms two layers, soon becomes homogeneous, and the paraformaldehyde dissolves.
3. The filtration must be done rapidly, preferably through a preheated funnel. Any material that crystallizes in the receiver is brought into solution again by warming on the steam bath.
4. Alternatively, the reaction mixture may be cooled at once and the solid product removed. The filtrate is successively concentrated and chilled three times, each crop of crystals being rinsed with acetone. For example, in a run using 480 g. of acetophenone, the amounts obtained were 297, 92, 53, and 16 g. respectively, and 42 g. from the acetone washings, making a total of 500 g., or 66% of the theoretical amount.
5. The excess dimethylamine hydrochloride is held in solution by the acetone.
6. The material is somewhat hygroscopic and holds traces of water tenaciously. The melting point is lowered by the presence of moisture; a preliminary shrinking is usually observed.
7. After it has been dried for an additional 4 hours, the product melts at 152–153°. The product melts at this same temperature after it has been kept for 60 hours in a vacuum desiccator, except that then there is no preliminary shrinking.
8. These directions are applicable equally well for runs of larger size.
9. The diethylamino homolog results when diethylamine hydrochloride is used.

## 3. Discussion

The procedure described is an example of a general reaction,[1,2] the Mannich reaction, a review of which, from the experimental point of view, has been published.[3]

## References and Notes


1. Mannich and Heilner, *Ber.*, **55**, 359 (1922).
2. Blicke and Burckhalter, *J. Am. Chem. Soc.*, **64**, 453 (1942).
3. Blicke, *Org. Reactions*, **1**, 303 (1942), New York, John Wiley & Sons.


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

ethanol (64-17-5)

hydrochloric acid (7647-01-0)

acetone (67-64-1)

Acetophenone (98-86-2)

dimethylamine hydrochloride (506-59-2)

β-Dimethylaminopropiophenone hydrochloride (879-72-1)

Propiophenone, β-dimethylamino- (3506-36-3)

diethylamine hydrochloride (660-68-4)

paraformaldehyde (30525-89-4)