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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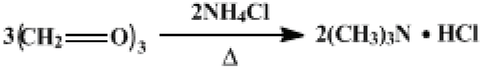
Organic Syntheses, Coll. Vol. 1, p.531 (1941); Vol. 1, p.79 (1921).

TRIMETHYLAMINE HYDROCHLORIDE



$$3(CH_2{=}O)_3 \xrightarrow[\Delta]{2NH_4Cl} 2(CH_3)_3N \cdot HCl$$

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1. Procedure

Five hundred grams (9.35 moles) of technical ammonium chloride and 1330 g. (14.8 moles) of paraformaldehyde are thoroughly mixed and placed in a 5-l. round-bottomed flask fitted with a long reflux condenser (a jacket of about 100-cm. length and an inner tube of about 2-cm. diameter) (Note 1). By means of an oil bath, the temperature of the reaction mixture is gradually raised. Between 85° and 105° liquefaction begins to take place at the bottom of the flask, and at the same time a very vigorous evolution of carbon dioxide starts. The heat is at once withdrawn, and if the reaction is too violent, the oil bath should be removed. The reaction is allowed to continue without further heating until the gas evolution is less vigorous. This requires about one and one-half hours. Heat is again applied and the temperature of the bath raised to about 160°, where it is held until there is practically no more evolution of carbon dioxide. This takes two and one-half to three and one-half hours, after which time the reaction is complete.

To obtain the trimethylamine hydrochloride, it is now merely necessary to treat the mixture with sodium hydroxide, and to distil the free amine into hydrochloric acid. A separatory funnel is therefore inserted through the stopper of the flask and the reflux condenser is changed to a downward position for distillation. The open end of the condenser is fitted tightly into the neck of a distilling flask or suction flask, to the outside arm of which is attached, by means of rubber tubing, a glass tube which leads under hydrochloric acid in a receiver. Care must be taken to have all the joints in the apparatus tight as the trimethylamine is very volatile and can easily be lost. The object of the intermediate boiling or suction flask is to catch any water which may distil with the trimethylamine during the treatment with the sodium hydroxide. This water is often colored yellow, and if allowed to go directly into the hydrochloric acid in the receiver contaminates the trimethylamine hydrochloride.

A solution of 1100 g. of sodium hydroxide (two and one-half to three times the amount theoretically necessary to liberate the free amine) in 2 l. of water is allowed to drop through the separatory funnel into the reaction mixture, which has cooled somewhat during the change of apparatus. The amine distils, passes through the condenser, through the intermediate bottle, and into the receiver, in which is placed an amount of concentrated hydrochloric acid (930 cc. of sp. gr. 1.19) slightly more than enough to neutralize the weight of amine which should theoretically be formed. To be certain that all the amine has been driven from the reaction flask, heat is finally applied for ten or fifteen minutes to the mixture. The whole procedure, from the beginning of the first reaction until a solution of trimethylamine hydrochloride is obtained, requires not more than six to seven hours.

To obtain the trimethylamine hydrochloride, the hydrochloric acid solution is evaporated, first over a free flame, and later, when the crystals start to form, on a steam bath. As the solution gets more and more concentrated, the trimethylamine hydrochloride crystallizes out and is filtered from time to time, dried for a few minutes in an air bath (temperature 100–110°), and then kept in a tightly closed bottle. If the trimethylamine hydrochloride as it crystallizes is centrifuged, the product is obtained pure and dry at once. The average yield from four runs is 710 g. of pure trimethylamine hydrochloride and 82 g. of product which is tinged slightly yellow (a total of 89 per cent of the theoretical amount based on the ammonium chloride) (Note 2). The coloration results from the evaporation to dryness of the very last portion of solution.

2. Notes

1. The reaction takes place with the evolution of a considerable amount of heat, and consequently a condenser as efficient as that mentioned is necessary in order to avoid loss. The wide inner tube is used to avoid any possibility of paraformaldehyde subliming and clogging the condenser.
2. The complete solubility of the product in chloroform[1] shows the trimethylamine hydrochloride to be free from ammonium chloride and methylamine hydrochloride, and the fact that no precipitate is obtained when the trimethylamine hydrochloride in aqueous solution is treated with sodium hydroxide and benzenesulfonyl chloride shows that dimethylamine hydrochloride is absent.

3. Discussion

Methods for the preparation of trimethylamine hydrochloride are essentially like those given at the end of the preceding preparation (p. 530) of trimethylamine.

This preparation is referenced from:

- Org. Syn. Coll. Vol. 1, 528

References and Notes

1. Bertheaume, Compt. rend. **150**, 1251 (1910).

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

hydrochloric acid (7647-01-0)

ammonium chloride (12125-02-9)

sodium hydroxide (1310-73-2)

chloroform (67-66-3)

carbon dioxide (124-38-9)

Benzenesulfonyl chloride (98-09-9)

Methylamine hydrochloride (593-51-1)

dimethylamine hydrochloride (506-59-2)

Trimethylamine (75-50-3)

Trimethylamine hydrochloride (593-81-7)

paraformaldehyde (30525-89-4)