



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.

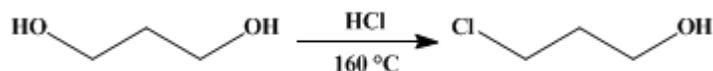
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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

Organic Syntheses, Coll. Vol. 1, p.533 (1941); Vol. 8, p.112 (1928).

TRIMETHYLENE CHLOROHYDRIN

[1-Propanol, 3-chloro-]



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1. Procedure

A 100-cc. round-bottomed, wide-mouthed flask (or a large test tube 18 cm. long and 4.5 cm. wide) is fitted with a rubber stopper carrying a separatory funnel, a thermometer, an inlet tube reaching almost to the bottom of the flask, and an outlet tube leading to a condenser set for downward distillation. A receiver consisting of a suction flask is attached tightly to the end of the condenser, and the side arm of the receiver is attached to a reflux condenser. A tube is led from the top of the condenser to the hood in order to take care of excess hydrogen chloride during the distillation, or a gas-absorption trap (Fig. 7, p. 97) can be used for this purpose. About 25–30 cc. of trimethylene glycol (b.p. 210–215°) is placed in the flask and heated by means of an oil or metal bath to 150–170°. A very rapid stream of dry hydrogen chloride (Note 1) is now led into the hot glycol through the inlet tube. A reddish distillate consisting of water, trimethylene chlorohydrin, hydrogen chloride, and some unchanged glycol begins to distil. As rapidly as the glycol is used up in the reaction flask, more is added from the separatory funnel. It is always advisable to keep the amount of material in the reaction flask as small as possible. The rate at which the hydrogen chloride is passed through the flask controls the reaction and also has a marked effect on the yield (Note 2). The best results are obtained by passing in the gas rapidly enough to use up 2–3 cc. of trimethylene glycol in one minute. The process is continuous and can be run indefinitely without changing the apparatus. The weight of crude distillate from 1800 g. of trimethylene glycol is usually 2300–2500 g.

To obtain the trimethylene chlorohydrin, the distillate from this operation is heated for about one hour on a steam bath in order to drive out most of the excess hydrogen chloride. The distillate is then fractionated under reduced pressure (Note 3) in a modified Claisen flask (p. 130). The fractionating side arm should be 25 cm. in length. The fractions collected under 10 mm. are: to 55°, 55–57°, 57–65°, 65–85°, 85–105°, residue.

Before a further fractionation is carried out, the residue is discarded; the portion boiling at 85–105°, consisting chiefly of unchanged trimethylene glycol, is set aside for use in a later preparation; the low-boiling portion up to 55°, consisting mainly of water and hydrogen chloride with some trimethylene chloride (Note 4) and trimethylene chlorohydrin, is neutralized carefully with powdered sodium carbonate. Two layers form, and the upper containing the chlorohydrin is separated, dried over anhydrous potassium carbonate, and again replaced as the portion boiling up to 55°. Another complete fractional distillation, carried out in the usual way, is now made except that the highest fraction boils at 65–85°/10 mm.

The material boiling above 65°/10 mm. is chiefly trimethylene glycol and is used in a succeeding experiment. The final yield of trimethylene chlorohydrin (Note 5) boiling at 60–64°/10 mm. is 835–1000 g. from 1800 g. of trimethylene glycol (50–60 per cent of the theoretical amount), and 400–450 g. of trimethylene glycol is recovered.

2. Notes

1. *Hydrogen Chloride*.—The hydrogen chloride may be generated by any method desired. Since a large quantity of gas is required, the first procedure described on p. 293 is rather expensive. A more satisfactory arrangement is to half fill a 12-l. flask with a paste of salt and concentrated hydrochloric

acid and run into this commercial sulfuric acid. The gas is dried by a single wash bottle of sulfuric acid. If sulfuric and hydrochloric acids are used, then, for the conversion of 1800 g. of trimethylene glycol, a 20-l. bottle half-filled with concentrated sulfuric acid is treated with concentrated hydrochloric acid introduced through a tube reaching to the bottom. The hydrochloric acid is added at the rate of 30–40 drops per minute. Two charges of sulfuric acid are needed and a total of about 24 kg. of hydrochloric acid.

2. The yield of chlorohydrin is largely determined by the rate at which the reaction is carried out. A very rapid stream of hydrogen chloride is absolutely essential for obtaining the yields mentioned. Moreover, it is very important to keep as small an amount of glycol as possible in the reaction flask. If larger amounts of glycol are present at any one time, the yield of product is lowered and considerable tar is produced.

3. Trimethylene chlorohydrin cannot be distilled under atmospheric pressure without some decomposition. The fractionation can be carried out at ordinary pressures when the fractions collected are up to 125°, 125–158°, 158–164°, 164–190°, 190–210° and residue. This procedure is less desirable as some hydrogen chloride is evolved and the product turns dark on standing.

4. The portion boiling up to 55°/10 mm., obtained after the second fractionation, was washed with concentrated sulfuric acid, then water, and finally dried and distilled. A certain amount of trimethylene chloride was sometimes obtained, boiling at 115–120° and amounting to about 30 per cent of the total fraction.

5. The chlorohydrin contains a very small amount (less than 0.5 per cent) of water-insoluble material, which is probably trimethylene chloride and di- γ -chloropropyl ether.

3. Discussion

Trimethylene chlorohydrin can be prepared from trimethylene glycol by the action of dry hydrogen chloride under various conditions;¹ by the action of aqueous hydrochloric acid;² and by the action of sulfur chloride.³ It can also be prepared from γ -chloropropyl acetate and methyl alcoholic hydrochloric acid.⁴

This preparation is referenced from:

- Org. Syn. Coll. Vol. 1, 156
- Org. Syn. Coll. Vol. 1, 166
- Org. Syn. Coll. Vol. 1, 292
- Org. Syn. Coll. Vol. 1, 294
- Org. Syn. Coll. Vol. 3, 197
- Org. Syn. Coll. Vol. 3, 203
- Org. Syn. Coll. Vol. 4, 238
- Org. Syn. Coll. Vol. 4, 605

References and Notes

1. Reboul, *Ann. chim. phys.* (5) **14**, 493 (1878); Malengreau and Lebailly, *Z. physiol. Chem.* **67**, 37 (1910); Karvonen, *Ann. acad. sci. Fennicae [A]*, **3**, 1 (1912) [*Chem. Zentr.* II, 1271 (1912)]; Derick and Bissell, *J. Am. Chem. Soc.* **38**, 2481 (1916); Karvonen, *Ann. acad. sci. Fennicae [A]*, **5**, 1 (1914) [*C. A.* **14**, 2176 (1920)].
 2. Norris and Mulliken, *J. Am. Chem. Soc.* **42**, 2095 (1920); Hultman, Davis, and Clarke, *ibid.* **43**, 369 (1921).
 3. Derick and Bissell, *ibid.* **38**, 2481 (1916).
 4. Henry, *Bull. Acad. roy. Belg. cl. sci.* **8**, 738 (1906).
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**Chemical Abstracts Nomenclature (Collective Index Number);
(Registry Number)**

sulfuric and hydrochloric acids

methyl alcoholic hydrochloric acid

potassium carbonate (584-08-7)

sulfuric acid (7664-93-9)

hydrogen chloride,
hydrochloric acid (7647-01-0)

sodium carbonate (497-19-8)

trimethylene glycol (504-63-2)

Trimethylene chlorohydrin,
1-Propanol, 3-chloro- (627-30-5)

sulfur chloride

trimethylene chloride (142-28-9)

di- γ -chloropropyl ether (629-36-7)

γ -Chloropropyl acetate (628-09-1)