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.

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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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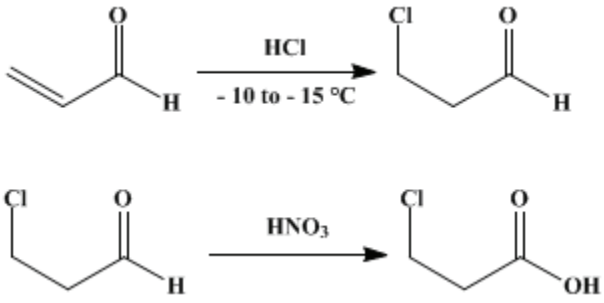
β-CHLOROPROPIONIC ACID

[Propionic acid, β-chloro-]

[(*A*) (*from Acrolein*)]



Submitted by C. Moureu and R. Chaux.
Checked by C. S. Marvel and L. F. Martin.

1. Procedure

In a tared Erlenmeyer flask surrounded by an ice-salt bath is placed 100 g. (119 cc., 1.78 moles) of acrolein (p. 15) (Note 1). When the temperature has dropped to −10 to −15° a current of dry hydrogen chloride (p. 293) is passed into the acrolein until it shows a gain in weight of 65 g.(1.78 moles). This requires about two hours. The product thus obtained is a clear, viscous, slightly yellow liquid which becomes very turbid and dark colored on standing one or two days (Note 2).

The oxidation of the crude β-chloropropionaldehyde is carried out in a 200-cc. flask fitted with a cork stopper held about 2 cm. above the opening of the neck by means of a clamp. The stopper carries a mechanical stirrer, a separatory funnel, a thermometer, and a glass delivery tube about 10 mm. in diameter which is connected to a water pump. The space between the stopper and the flask is closed by winding a strip of asbestos paper around it (Note 3).

In the flask is placed 64 g. (43 cc., 0.9 mole) of fuming nitric acid (sp. gr. 1.49) (Note 4), the stirrer is started, and about one-sixth (Note 5) of the crude β-chloropropionaldehyde is added (Note 6) very slowly through the separatory funnel. About 1 cc. of the aldehyde is added to the acid. The temperature remains constant for one or two minutes and then slowly rises. As the oxidation begins, oxides of nitrogen are evolved and are drawn off by means of the water pump. When the temperature of the reaction mixture reaches about 30° (Note 7), the flask is immersed in a water bath (at 15–20°) and the rate of addition of the aldehyde is regulated so that the temperature of the reaction mixture is 30–35°. After the addition of the last portion of the aldehyde, stirring is continued until the temperature drops below 25°. This oxidation requires about twenty-five minutes.

The products of six successive oxidations are combined in a 1-l. long-necked flask. Oxides of nitrogen are evolved but there is no danger of a violent reaction. The entire quantity of liquid is heated gradually on a water bath until the bath is boiling. This should be done under a hood as large quantities of oxides of nitrogen are evolved (Note 8). After about one and one-half hours the oxidation is complete and a yellow-brown liquid remains.

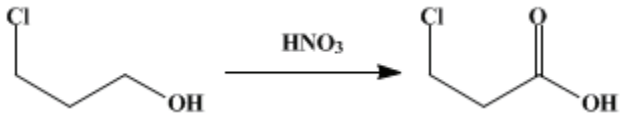
The liquid is placed in a modified Claisen flask (p. 130) and distilled (Note 9) from an oil bath with a water pump, care being taken to protect the manometer (placed in shunt in order to avoid the passage of a current of vapors) by a tube containing solid sodium hydroxide. A water condenser 40–50 cm. long should be used. At first oxides of nitrogen are evolved and it is difficult to obtain a low pressure. Then the pressure drops (to about 20–25 mm.) and nitric acid distils at 40–70°. When the distillation has nearly stopped, the temperature of the bath is raised until the boiling point of the distilling vapors

reaches 100°. This fraction weighs 160–170 g. and is nitric acid having a specific gravity of 1.25–1.30. It may contain a small amount of acrylic acid. The condenser is now removed from the apparatus, a distilling flask attached as receiver, and the residue is fractionated at 20 mm., collecting about 4–5 g. boiling up to 105°, and 116–125 g. of β-chloropropionic acid boiling at 105–107° (60–65 per cent of the theoretical amount). The product melts at 35–40° (purest acid melts at 42°). The fraction boiling below 105° contains a large proportion of β-chloropropionic acid and should be redistilled with a subsequent run.

2. Notes

1. The acrolein used by the checker was obtained by distilling the commercial material (stabilized by hydroquinone) purchased from Poulenc Frères. Acrolein has pronounced lachrymatory properties and is also highly toxic.
2. β-Chloropropionaldehyde is a very unstable substance which polymerizes rapidly, especially in the presence of traces of hydrochloric acid. The crude material must be oxidized without delay as standing before oxidation will cause a lowering of the yield.
3. This constitutes a safety device, since it prevents diffusion of the oxides of nitrogen, but in case the reaction becomes violent it permits a free expansion of a sudden surge of gases.
4. The concentration and purity of the fuming nitric acid are of considerable importance. It should have a specific gravity of not less than 1.49 and should leave no residue on distillation.
5. It is not advantageous to work with larger quantities as an explosive reaction is likely to occur if stirring is stopped.
6. It is absolutely necessary to introduce the aldehyde into the nitric acid. When the reverse is attempted the reaction starts slowly but soon becomes explosive.
7. The temperature interval most favorable for the reaction is 30–35°.
8. A gas-absorption trap (Fig. 7, p. 97) may also be used.
9. The reaction mixture may also be worked up by pouring it into water and extracting the β-chloropropionic acid with ether. This is less satisfactory as the nitric acid is lost and some of the β-chloropropionic acid remains in the water.

[(*B*) (*from Trimethylene Chlorohydrin*)]



Submitted by S. G. Powell, E. H. Huntress, and E. B. Hershberg.
Checked by L. F. Fieser and A. M. Seligman.

1. Procedure

A 3-l. long-necked Pyrex flask containing 880 g. (620 cc., 10 moles) of concentrated nitric acid (sp. gr. 1.42) is supported in an ice bath in a hood and supplied with a mechanical stirrer and a thermometer suspended in the liquid. While the temperature is kept between 25° and 30° by means of the ice bath, 200 g. (2.12 moles) of trimethylene chlorohydrin (p. 533) is run in from a dropping funnel (Note 1). The addition takes two to three hours. Stirring is continued for a half hour longer.

The reaction mixture is allowed to stand overnight and is then heated for one hour on the steam bath. It is transferred to a modified Claisen flask (p. 130), and the β-chloropropionic acid is isolated by distillation under reduced pressure, employing a water pump. Nitric acid is collected up to 100°/20 mm., using a water condenser (Note 2). The condenser is replaced by a distilling flask, and the residual material is fractionated. The yield of β-chloropropionic acid boiling at 107–109°/20 mm. and freezing at 39° is 179–181 g. (78–79 per cent of the theoretical amount).

2. Notes

1. There is sometimes difficulty in starting the reaction using pure nitric acid. Once started, the

oxidation proceeds rapidly under the catalytic influence of the oxides of nitrogen formed. The checkers found it convenient, in order to start the reaction, to oxidize a few drops of the chlorohydrin with nitric acid by heating in a test tube and to add this to the nitric acid in the flask without stirring. A small portion of the chlorohydrin is then added and allowed to react for a few minutes before starting the stirrer and continuing the oxidation of the main lot.
2. About 500 cc. of nitric acid (sp. gr. 1.27) is obtained. If desired the oxidation mixture may be diluted with water and the β-chloropropionic acid extracted with ether and distilled. Some material is lost in the water by this procedure.

3. Discussion

β-Chloropropionic acid can be prepared by the hydrolysis of ethylene cyanohydrin with hydrochloric acid;[1] by the oxidation of β-chloropropionaldehyde with nitric acid;[2] by the oxidation of trimethylenechlorohydrin with nitric acid[3] or permanganate;[4] and by hydrolysis of the condensation product of phosgene and ethylene.[5]

References and Notes

1. Jacobs and Heidelberger, J. Am. Chem. Soc. **39**, 1466 (1917).
2. Krestownikow, Ber. **12**, 1487 (1879); Moureu, Bull. soc. chim. (3) **9**, 388 (1893); Ann. chim. phys. (7) **2**, 157 (1894); Moureu and Chaux, Bull. soc. chim. (4) **35**, 1360 (1924).
3. Rojahn, Ber. **54**, 3116 (1921); Adams and Marvel, Organic Chemical Reagents, Univ. of Ill. Bulletin, 20, No. 8, 14 (1922); Powell, J. Am. Chem. Soc. **46**, 2879 (1924).
4. I. G. Farbenind. A.-G., Fr. pat. 824,489 [C. A. **32**, 5857 (1938)].
5. Klebanskii and Chevychalova, Trans. State Inst. Applied Chem. **1937**, No. 31, 46; Khim. Referat. Zhur. **1938**, No. 6, 92 [C. A. **34**, 6222 (1940)].

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

oxides of nitrogen

aldehyde

chlorohydrin

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

ether (60-29-7)

sodium hydroxide (1310-73-2)

Acrolein (107-02-8)

hydroquinone (123-31-9)

nitric acid (7697-37-2)

nitrogen (7727-37-9)

phosgene (75-44-5)

ethylene (9002-88-4)

Ethylene cyanohydrin (109-78-4)

Acrylic acid (9003-01-4)

Trimethylene chlorohydrin,
trimethylenechlorohydrin (627-30-5)

β-Chloropropionic acid,
Propionic acid, β-chloro- (107-94-8)

β-chloropropionaldehyde

permanganate