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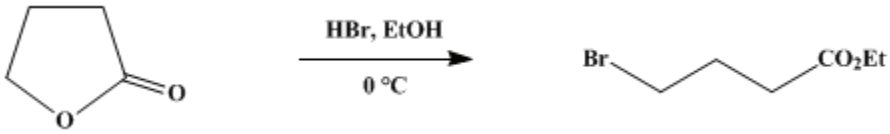
These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

DOI:10.15227/orgsyn.045.0042

Organic Syntheses, Coll. Vol. 5, p.545 (1973); Vol. 45, p.42 (1965).

ETHYL γ-BROMOBUTYRATE

[Butyric acid, γ-bromo-, ethyl ester]



Submitted by J. Lavety and G. R. Proctor[1].
Checked by Ian Morrison and Virgil Boekelheide.

1. Procedure

A solution of 200 g. (2.33 moles) of γ-butyrolactone (Note 1) in 375 ml. of absolute ethanol is cooled to 0° in an ice bath while a stream of dry hydrogen bromide (Note 2) is introduced. The passage of gas is discontinued 1 hour after hydrogen bromide is seen to pass through the reaction mixture unchanged (Note 3).

The alcoholic solution of the product is kept for 24 hours at 0° and then poured into 1 l. of ice-cold water. The oily layer is separated, and the aqueous layer is extracted with two 100-ml. portions of ethyl bromide (Note 4). The combined oil and extracts is washed with ice-cold 2% potassium hydroxide solution, then with very dilute hydrochloric acid, and finally with water. The organic layer is dried over sodium sulfate, the solvent is removed under reduced pressure, and the residual crude ester is purified by distillation. The yield of ethyl γ-bromobutyrate, obtained as a colorless oil, b.p. 97–99° (25 mm.), n^{25}D 1.4543, is 350–380 g. (77–84%) (Note 5) and (Note 6).

2. Notes

1. Technical grade γ-butyrolactone was employed.
2. The hydrogen bromide is made by burning together hydrogen and bromine. The apparatus is essentially that described previously.[2,3] The submitters found that standard ground-glass fittings can be used throughout, connected where necessary by Neoprene® tubing. The combustion tube is made by "butt-joining" two ground-glass sockets. The checkers used commercial hydrogen bromide from a cylinder which was connected to the reaction flask through a safety trap.
3. The time varies from 6 to 8 hours, and the increase in weight from 450 g. to 480 g. Using the commercial hydrogen bromide, the checkers found the time for saturation to be 3.5–4 hours.
4. The aqueous layer may be kept and used again in repeating the reaction.
5. In smaller runs, yields as high as 95% have been obtained.[4]
6. The product is best stored in dark bottles at 0°.

3. Discussion

The ester has been made from the corresponding acid which was obtained from the nitrile,[5] but the present method is the more practicable.[4,6] This procedure is an adaptation of the method used for the preparation of ethyl 2-bromocyclopentaneacetate.[7]

4. Merits of the Preparation

This is a procedure for preparing ethyl γ-bromobutyrate in good yield. Ethyl γ-bromobutyrate is used for adding chains of four carbons and has been particularly useful in syntheses of benzazepines.[3,6,8,9]

References and Notes

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

ethanol (64-17-5)

hydrochloric acid (7647-01-0)

hydrogen (1333-74-0)

hydrogen bromide (10035-10-6)

bromine (7726-95-6)

Ethyl bromide (74-96-4)

sodium sulfate (7757-82-6)

potassium hydroxide (1310-58-3)

γ-butyrolactone (96-48-0)

Ethyl γ-bromobutyrate,
Butyric acid, γ-bromo-, ethyl ester (2969-81-5)

ethyl 2-bromocyclopentaneacetate

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