



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.

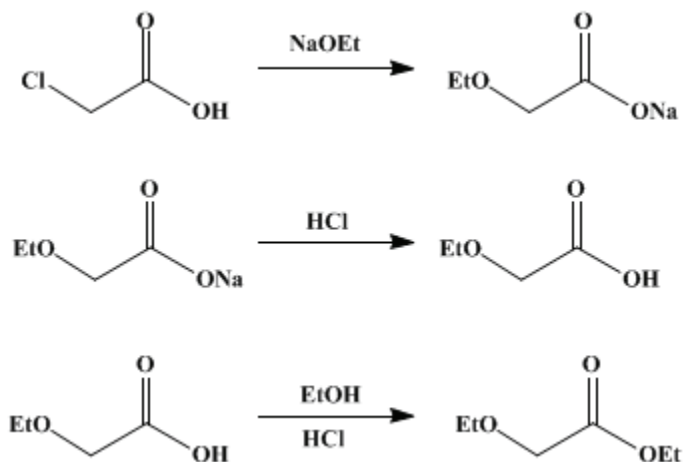
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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

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ETHOXYACETIC ACID AND ETHYL ETHOXYACETATE

[Acetic acid, ethoxy-, and ethyl ester]



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1. Procedure

(A) *Ethoxyacetic Acid*.—In a 2-l. round-bottomed flask, provided with a reflux condenser 70 to 80 cm. long, is placed 1250 cc. of absolute ethyl alcohol (Note 1). Through the condenser tube 69 g. (3 gram atoms) of metallic sodium is added rapidly enough to keep the alcohol refluxing gently. When the sodium has completely dissolved, a solution of 142 g. (1.5 moles) of chloroacetic acid in 180 cc. of absolute alcohol is added slowly in 20-cc. portions to the sodium ethoxide solution (Note 2). After all the acid has been added, the mixture is heated gently for ten minutes. The excess alcohol is removed as completely as possible by distilling from a steam bath and finally by passing steam into the residue. The aqueous solution is cooled, and 140 cc. (1.7 moles) of concentrated hydrochloric acid (sp. gr. 1.19) is added. The sodium chloride is removed by filtration with suction and is washed with two 50-cc. portions of ether. The original filtrate is saturated with dry sodium sulfate (30–35 g.) and is then extracted with the ether which was used for washing the precipitate, together with an additional 100 cc. of ether. The ether is separated from the aqueous layer, and the latter is extracted four times with 100-cc. portions of fresh ether. The ether is removed by distillation from a steam bath, and the residue is distilled under reduced pressure, using a 500-cc. Claisen flask equipped with a 500-cc. receiver. The acid boils at 109–111°/17–18 mm. and weighs 115–116 g. (74 per cent of the theoretical amount). By redistilling the low-boiling fraction and collecting the portion boiling at 150–210°, there is obtained an additional 7–10 g. of material which is chiefly ethoxyacetic acid and may be combined with the main fraction for conversion to the ester.

(B) *Ethyl Ethoxyacetate*.—The ethoxyacetic acid, which should amount to about 125 g. (1.2 moles), is placed in a 750-cc. Erlenmeyer flask containing 230 cc. (3.9 moles) of absolute ethyl alcohol. The flask is set in a pan filled with cold water (Note 3), and dry hydrogen chloride is passed into the mixture. After the mixture becomes saturated (Note 4) it is allowed to stand twenty-four hours to ensure the completion of the reaction at room temperature (Note 5). The solution is cooled, and a saturated solution of sodium carbonate is added cautiously and with stirring to avoid excessive foaming. The addition is continued until the mixture is faintly alkaline to litmus; an excess of sodium carbonate lowers the yield and should be avoided. The ester is extracted with four 100-cc. portions of ether; the extract is dried with 25 g. of anhydrous potassium carbonate, and the ether is distilled from a steam bath. The residue is distilled at ordinary pressure. The yield of ester boiling at 153–155° is 110–115 g. (55–58 per cent of the theoretical amount based on the chloroacetic acid, or 69–72 per cent based on the ethoxyacetic acid).

2. Notes

1. Alcohol dried over quicklime is satisfactory.
2. The chloroacetic acid should be added fast enough to keep the solution boiling.
3. Heat is evolved during the reaction, and, unless the flask is kept in cold water, an insufficient amount of hydrogen chloride will be absorbed. This lowers the yield.
4. A considerable quantity of dry hydrogen chloride is required. The gas should be allowed to bubble through the mixture for at least five hours.
5. The yield seems to be limited by the equilibrium between the acid and ester. At least twenty-four hours is required to reach this equilibrium.

3. Discussion

Ethoxyacetic acid was first prepared by Heintz¹ by the reaction of chloroacetic acid with sodium ethoxide. The procedure described above is essentially that of Sommelet.² Ethoxyacetic acid has also been prepared by hydrolysis of ethoxyacetoneitrile with concentrated hydrochloric acid³ and by the action of excess sodium ethoxide on 1,1,1,2-tetrachlorethane and on α,β -dichlorovinyl ethyl ether.⁴ A patent reports the synthesis from diethyl ether and carbon dioxide⁵ at high pressure.

Ethyl ethoxyacetate has been prepared by the action of ethyl iodide on sodium ethoxyacetate,⁶ of sodium ethoxide on ethyl chloroacetate,⁷ of alcohol on crude diazoacetic ester,⁸ and by the alcoholysis of ethoxyacetoneitrile using alcoholic hydrogen chloride.^{3, 9}

References and Notes

1. Heintz, Ann. Physik **109**, 331 (1860); **111**, 555 (1860); Rothstein, Bull. soc. chim. (4) **51**, 838 (1932).
2. Sommelet, Ann. chim. phys. (8) **9**, 489 (1906).
3. Gauthier, ibid. (8) **16**, 304 (1909).
4. Geuther and Brockhoff, J. prakt. Chem. (2) **7**, 113 (1873).
5. Dreyfus, Fr. pat. 671,103 [C. A. **24**, 1867 (1930)].
6. Heintz, Ann. **129**, 40 (1864).
7. Henry, Ber. **4**, 706 (1871).
8. Curtius, J. prakt. Chem. (2) **38**, 424 (1888).
9. Sommelet, Ann. chim. phys. (8) **9**, 501 (1906).

Appendix

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

quicklime

Acetic acid, ethoxy-, and ethyl ester

ethyl alcohol,
alcohol (64-17-5)

potassium carbonate (584-08-7)

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

ether,
diethyl ether (60-29-7)

sodium chloride (7647-14-5)

sodium carbonate (497-19-8)

sodium sulfate (7757-82-6)

carbon dioxide (124-38-9)

chloroacetic acid (79-11-8)

sodium,
metallic sodium (13966-32-0)

sodium ethoxide (141-52-6)

Ethyl chloroacetate (105-39-5)

1,1,1,2-tetrachlorethane (630-20-6)

Ethyl iodide (75-03-6)

Ethoxyacetic acid (627-03-2)

Ethyl ethoxyacetate (817-95-8)

ethoxyacetonitrile (62957-60-2)

α,β -dichlorovinyl ethyl ether

sodium ethoxyacetate