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.

The procedures described in *Organic Syntheses* are provided as published and are conducted at one's own risk. *Organic Syntheses, Inc.*, its Editors, and its Board of Directors do not warrant or guarantee the safety of individuals using these procedures and hereby disclaim any liability for any injuries or damages claimed to have resulted from or related in any way to the procedures herein.

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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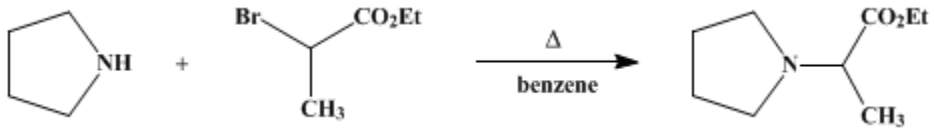
ETHYL α-(1-PYRROLIDYL)PROPIONATE

[1-Pyrrolidineacetic acid, α-methyl-, ethyl ester]



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1. Procedure

A 1-l. three-necked round-bottomed flask is placed on a steam bath and fitted with a stirrer, reflux condenser, and dropping funnel. A solution of 181 g. (1 mole) of ethyl α-bromopropionate in 200 ml. of benzene is placed in the flask (Note 1), and 148 g. (2.1 moles) of pyrrolidine (Note 2) is added slowly with stirring at such a rate that the solvent refluxes gently. When the addition is complete (about 1 hour is required), the mixture is heated under reflux for 1 hour. After being cooled, the mixture is poured into about 500 ml. of ice water and acidified with dilute hydrochloric acid. The aqueous layer is separated, washed once with ether, and made strongly basic with cold 40% sodium hydroxide solution. The basic ester is extracted with four 200-ml. portions of ether. The ether extracts are combined, washed with 100 ml. of water, and dried over anhydrous potassium carbonate. The drying agent is removed by filtration and the ether by distillation. The residue is distilled under reduced pressure through a short fractionating column; b.p. 84°/12 mm. (95–96°/19 mm., 99.5–100.5°/23 mm., 104–105°/30 mm.); n_D^{20} 1.4478, n_D^{25} 1.4450; d_4^{25} 0.9724. The yield is 137–156 g. (80–91%).

2. Notes

1. The yield of product is lowered appreciably if the solution is preheated before addition of the pyrrolidine.
2. Pyrrolidine is obtainable from E. I. du Pont de Nemours and Company, Electrochemicals Division, Niagara Falls, New York.

3. Discussion

Ethyl α-(1-pyrrolidyl)propionate has been prepared by the reaction of pyrrolidine with ethyl α-bromopropionate.[2]

References and Notes

1. The Upjohn Company, Kalamazoo, Michigan.
2. Moffett, *J. Org. Chem.*, **14**, 862 (1949).

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

potassium carbonate (584-08-7)

hydrochloric acid (7647-01-0)

Benzene (71-43-2)

ether (60-29-7)

sodium hydroxide (1310-73-2)

ethyl α-bromopropionate (535-11-5)

pyrrolidine (123-75-1)

Ethyl α-(1-pyrrolidyl)propionate,
1-Pyrrolidineacetic acid, α-methyl-, ethyl ester (26846-86-6)