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.

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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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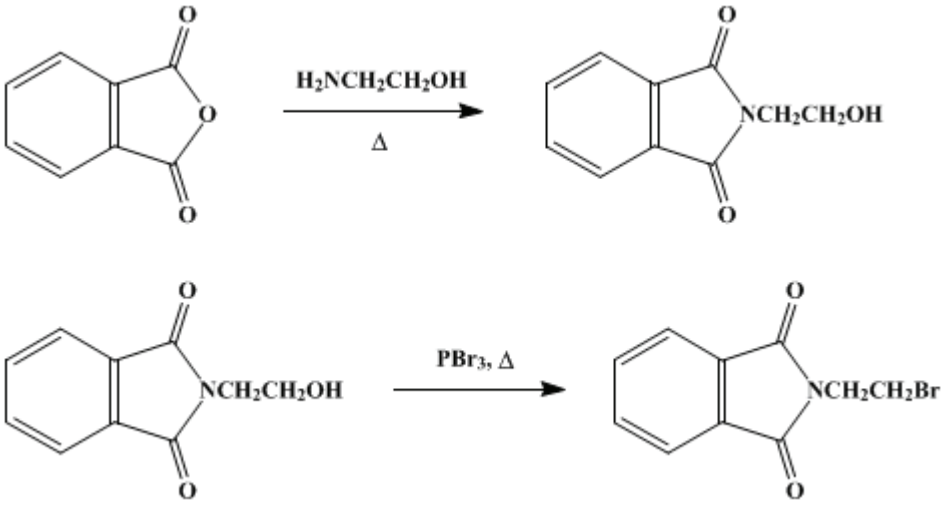
β-BROMOETHYLPHTHALIMIDE

[Phthalimide, N-2-bromoethyl-]



Submitted by T. O. Soine and M. R. Buchdahl[1].
Checked by Cliff S. Hamilton and John D. Sculley.

1. Procedure

Caution! This preparation should be carried out in a hood.

In a 1-l. round-bottomed flask are placed 74 g. (0.5 mole) of phthalic anhydride and 30 ml. (0.5 mole) of freshly distilled monoethanolamine. The mixture is heated on a steam bath for 30 minutes; the initial reaction is vigorous (Note 1). The reaction mixture is cooled to room temperature, and a reflux condenser is attached to the flask. To the cooled reaction mixture is added slowly, with shaking, 32 ml. (91.3 g., 0.34 mole) of freshly distilled phosphorus tribromide. The reaction flask is then placed on a steam bath and heated under reflux with occasional shaking for 1.25 hours (Note 2). The hot liquid reaction mixture is poured with stirring onto 750 g. of crushed ice. When the ice has melted completely, the crude β-bromoethylphthalimide is collected on a Büchner funnel, washed with cold water, and allowed to dry for a few minutes. The crude product (Note 3) is dissolved in 1.2 l. of aqueous ethanol (50% by volume) with the aid of heat. If necessary a small amount of 95% ethanol is added to effect complete solution. The hot solution is filtered and cooled in a refrigerator. A white crystalline product weighing 94–99 g. is obtained. Concentration of the mother liquor to 400 ml. yields an additional 1–3 g. of product. The total yield of product is 95–102 g. (75–80%); m.p. 80–82°.

2. Notes

1. It is not necessary to isolate the intermediate β-hydroxyethylphthalimide before going on to the next step. However, recrystallization of the product from 250 ml. of boiling water yields an initial crop of white crystals; m.p. 128°. The mother liquors will deposit further material until a yield of 95% may be obtained.
2. The final reaction mixture should contain no undissolved material.
3. This product weighs approximately 110 g. when dry.

3. Discussion

β-Bromoethylphthalimide has been prepared by the method of Gabriel[2] as recorded by Salzberg and

Supniewski.[3] Illg and Smolinski have carried out this reaction in a specially designed apparatus.[4] The procedure outlined above is a modification of the method given by Soine.[5]

References and Notes

1. University of Minnesota, Minneapolis, Minnesota.
2. Gabriel, *Ber.*, **20**, 2224 (1887); **21**, 566 (1888); **22**, 1137 (1889).
3. *Org. Syntheses Coll. Vol.* **1**, 119 (1941).
4. Illg and Smolinski, *Roczniki Chem.*, **23**, 426 (1949) [*C. A.*, **45**, 6173 (1951)].
5. Soine, *J. Am. Pharm. Assoc.*, **33**, 141 (1944).

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

ethanol (64-17-5)

phosphorus tribromide (7789-60-8)

phthalic anhydride (85-44-9)

β-Bromoethylphthalimide

Phthalimide, N-2-bromoethyl- (574-98-1)

monoethanolamine (141-43-5)

β-hydroxyethylphthalimide