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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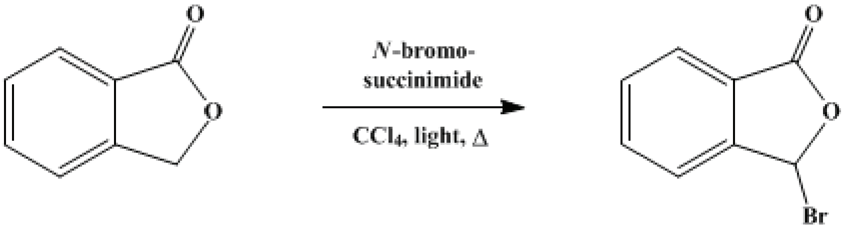
3-BROMOPHTHALIDE

[1(3H)-Isobenzofuranone, 3-bromo-]



Submitted by I. A. Koten and Robert J. Sauer[1].
Checked by R. C. Juola, Marjorie C. Caserio, and John D. Roberts.

1. Procedure

Ten grams (0.075 mole) of phthalide (Note 1), 13.3 g. (0.075 mole) of N-bromosuccinimide (Note 1), and 200 ml. of dry carbon tetrachloride (Note 1) are refluxed for 30 minutes in a 500-ml. flask carrying a reflux condenser equipped with a drying tube containing Drierite. The reaction mixture is exposed to the light of an ordinary 100-watt unfrosted light bulb placed 6–8 in. from the flask. The end of the reaction is indicated by the disappearance of N-bromosuccinimide from the bottom of the flask and accumulation of succinimide at the top of the reaction mixture. The succinimide is removed by filtration and the filtrate concentrated under atmospheric pressure to 15–20 ml. Cooling of this concentrate followed by filtration gives 12–13 g. (75–81%) of crude 3-bromophthalide, m.p. 74–80°. The crude material, when recrystallized from cyclohexane, gives colorless plates, m.p. 78–80° (Note 2), (Note 3),(Note 4).

2. Notes

1. The phthalide used was obtained from Aldrich Chemical Co. It was also prepared by the method of Gardner and Naylor, *Org. Syntheses Coll. Vol.* **2**, 526 (1943). The N-bromosuccinimide was obtained from Arapahoe Chemicals, Inc.
The carbon tetrachloride used is dried over Drierite and filtered or distilled.
2. About 150 ml. of cyclohexane is necessary to recrystallize 12–13 g. of product, and the temperature of the solvent should be kept below 70° to avoid oiling of undissolved material. The recovery is 11–12 g.
3. When pure 3-bromophthalide is allowed to stand, its melting point is depressed, owing apparently to some decomposition. It may, therefore, be desirable to prepare the compound in smaller quantities than specified here. A sample of 3-bromophthalide, prepared by using 20 g. of phthalide and 26.6 g. of N-bromosuccinimide, amounted to 29.8 g. (93.4%) of crude product. Hydrolysis of the crude material[2] gave phthalaldehydic acid, m.p. 96–98°.
4. Since one of the checkers developed a serious allergy to 3-bromophthalide, suitable precautions should be taken to avoid its inhalation and contact with the skin.

3. Discussion

3-Bromophthalide has previously been prepared by direct bromination of phthalide over a period of 10–13 hours in yields of 82–83%.[2] The procedure above, a modification of the Wohl-Ziegler method, appears to be preferable since it may be completed in 3–4 hours, is applicable to the preparation of small samples, and gives comparable yields.

References and Notes

1. Department of Chemistry, North Central College, Naperville, Ill. This work was supported by a grant from Research Corporation of New York City.
2. R. L. Shriner and F. J. Wolf, *Org. Syntheses*, Coll. Vol. **3**, 737 (1955).

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

Drierite

carbon tetrachloride (56-23-5)

cyclohexane (110-82-7)

Succinimide (123-56-8)

Phthalaldehydic acid (119-67-5)

Phthalide (87-41-2)

N-bromosuccinimide (128-08-5)

3-BROMOPHTHALIDE,
1(3H)-Isobenzofuranone, 3-bromo- (6940-49-4)