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.

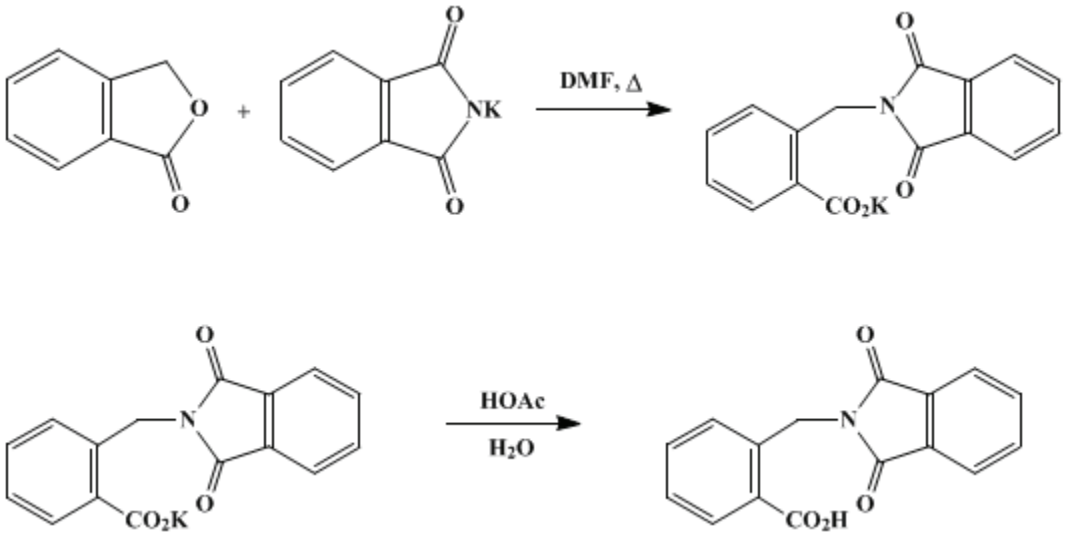
These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

DOI:10.15227/orgsyn.038.0081

Organic Syntheses, Coll. Vol. 4, p.810 (1963); Vol. 38, p.81 (1958).

α-PHTHALIMIDO-*o*-TOLUIC ACID

[*o*-Toluic acid, α-phthalimido-]



Submitted by J. Bornstein, P. E. Drummond, and S. F. Bedell[1].
Checked by John C. Sheehan and Y. L. Yeh.

1. Procedure

A 2-l. three-necked round-bottomed flask, fitted with a sealed stirrer and a reflux condenser carrying a drying tube, is charged with 100 g. (0.75 mole) of phthalide (Note 1), 150 g. (0.81 mole) of potassium phthalimide (Note 2), and 500 ml. of dimethylformamide (Note 3). The stirred suspension is heated under reflux by means of an electric mantle for 5 hours; the deep blue solution is then cooled to room temperature (Note 4). A solution of 300 ml. of glacial acetic acid in 500 ml. of water is added in one portion to the stirred reaction mixture, and the resulting yellow suspension, which becomes slightly warm, is stirred for an additional 30 minutes.

The precipitate is separated by suction filtration, pressed on the funnel, and washed successively with three 100-ml. portions of water and two 100-ml. portions of 95% ethanol. The product is transferred to a 1-l. Erlenmeyer flask, boiled for 10 minutes with 400 ml. of 60% ethanol with occasional stirring, filtered hot, washed twice with 50-ml. portions of 95% ethanol, and then dried in an oven at 90–100° for 6–12 hours. The crude α-phthalimido-*o*-toluic acid, which weights 140–155 g., is divided into two equal portions, and each portion is dissolved in boiling propionic acid (Note 5). Each solution is treated with 1 tablespoon of Norit and filtered through an electrically heated gravity funnel. The filtrates are allowed to cool slowly to room temperature and are then refrigerated overnight. The crystals from the two portions are collected by suction filtration in one funnel and washed on the funnel with 400 ml. of 95% ethanol. The product is dried over potassium hydroxide in a vacuum desiccator. The yield of nearly white crystals of α-phthalimido-*o*-toluic acid is 126–141 g. (60–67% based on phthalide), m.p. 265.0–266.5°.

2. Notes

1. The phthalide was prepared according to *Organic Syntheses*[2] and was also purchased from Aldrich Chemical Company. The commercial product (200 g.) was recrystallized in 50-g. portions from 1.5 l. of water, the mother liquor from the first crop being employed for recrystallization of the subsequent portions. Each portion was treated with 2 tablespoons of Norit, filtered hot, allowed to cool to room temperature with occasional stirring, and then cooled to 5° before collecting the crystals which were

washed on the funnel with small quantities of cold water. Final drying was effected in a vacuum desiccator containing phosphorus pentoxide.
2. Eastman Kodak Company potassium phthalimide (200 g.) was digested with 450 ml. of boiling acetone for 15 minutes, filtered hot, washed on the funnel with 100 ml. of acetone, and dried at 100° for 6 hours.
3. The dimethylformamide was obtained from Eastman Kodak Company and was used without further purification.
4. The reaction mixture is most conveniently cooled by allowing it to stand at room temperature overnight. Occasionally the potassium salt of α-phthalimido-*o*-toluic acid precipitates at this point, but this does not interfere with the subsequent operations.
5. Approximately 1.33 l. of propionic acid is required for 78 g. of the crude α-phthalimido-*o*-toluic acid. Glacial acetic acid may be used as the solvent, but considerably larger volumes are required than when propionic acid is employed. This step should be carried out in a hood, since hot propionic acid vapors are very irritating.

3. Discussion

The present procedure is that described by the submitters.[3] α-Phthalimido-*o*-toluic acid has also been prepared by the acidolysis of the corresponding ethyl ester, obtained from the reaction of ethyl α-bromo-*o*-toluate with potassium phthalimide.[3]

This preparation is referenced from:

- Org. Syn. Coll. Vol. 6, 951

References and Notes

1. Boston College, Chestnut Hill, Massachusetts.
2. *Org. Syntheses Coll. Vol.* **2**, 526 (1943).
3. Bornstein, Bedell, Drummond, and Kosloski, *J. Am. Chem. Soc.*, **78**, 83 (1956).

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

ethanol (64-17-5)

acetic acid (64-19-7)

propionic acid (79-09-4)

acetone (67-64-1)

Norit (7782-42-5)

potassium hydroxide (1310-58-3)

Potassium Phthalimide (1074-82-4)

Phthalide (87-41-2)

dimethylformamide (68-12-2)

phosphorus pentoxide (1314-56-3)

α-Phthalimido-o-toluic acid,
o-Toluic acid, α-phthalimido- (53663-18-6)

ethyl α-bromo-o-toluate

potassium salt of α-phthalimido-o-toluic acid