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.

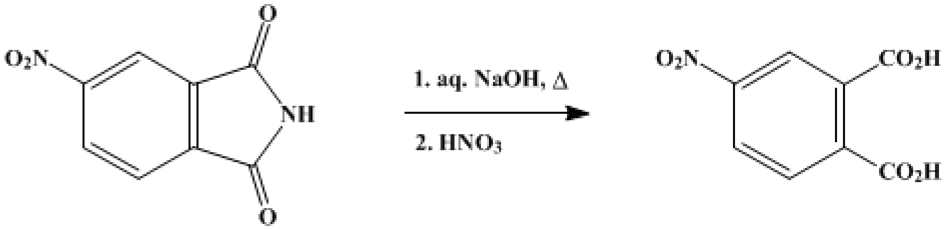
These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

DOI:10.15227/orgsyn.016.0056

Organic Syntheses, Coll. Vol. 2, p.457 (1943); Vol. 16, p.56 (1936).

4-NITROPHTHALIC ACID

[Phthalic acid, 4-nitro-]



Submitted by E. H. Huntress, E. L. Shloss, Jr, and P. Ehrlich.
Checked by W. W. Hartman and G. W. Sawdey.

1. Procedure

To a solution of 26.6 g. (0.66 mole) of sodium hydroxide in 240 cc. of water is added 80 g. (0.416 mole) of 4-nitrophthalimide (p. 459) (Note 1). The mixture is heated rapidly to boiling and boiled gently for ten minutes. The solution is made barely acid to litmus with concentrated nitric acid (sp. gr. 1.42); after the neutral point is reached, an additional 70 cc. (100 g., 1.1 moles) of nitric acid is added (Note 2). The solution is again boiled for three minutes, then cooled below room temperature, transferred to a 1-l. separatory funnel, and extracted with two 300-cc. portions of alcohol-free ether (Note 3). Care is taken to ensure thorough mixing before separation of the layers. After the extract is dried over anhydrous sodium sulfate, the ether is distilled until solid begins to separate. The concentrated ether solution is poured into a porcelain dish and the residual solvent allowed to evaporate in a hood (Note 4). The practically white crystals of 4-nitrophthalic acid which separate melt at 163–164° and have a neutralization equivalent of 105.5 (theoretical, 105.5). The yield is 85–87 g. (96–99 per cent of the theoretical quantity).

2. Notes

1. If a large amount of 4-nitrophthalimide is to be hydrolyzed, it will generally be found convenient to carry out a series of small runs of the size given here.
2. The quantity of alkali used at the start is sufficient to neutralize the nitroimide and leave the resulting alkaline solution approximately 1 *N*. When the solution is neutralized the red color changes to a dirty brown, which turns to a pale yellow on acidification. The 70-cc. portion of concentrated nitric acid suffices to set free all the 4-nitrophthalic acid but avoids the presence of a large excess during the ether extraction.
Nitric acid appears to be preferable to hydrochloric or sulfuric acid. The yields are similar, but the product obtained using nitric acid is pure white and in better physical condition.
3. The simultaneous presence of nitric acid and alcohol in the ether extract must be avoided as explosive oxidation might occur during evaporation of the ether. Furthermore, the presence of alcohol may lead to contamination of the product with traces of the acid ester.
4. Evaporation of the last portion of ether proceeds slowly; the rather soft, fluffy crystals of acid which separate at first gradually become hard and dense. No trouble was experienced from nitric acid remaining with the ether extract, if the ether was free from alcohol and the specified amount of nitric acid was used.

3. Discussion

4-Nitrophthalic acid has usually been prepared by nitration of phthalic acid[1] or phthalic anhydride,[2], [3] followed by separation from the accompanying 3-nitrophthalic acid.[4], [5], [6] It has also been prepared from 6-nitro-2-naphthol-4-sulfonic acid (obtained from the technical diazoanhydride of 6-nitro-1-amino-2-naphthol-4-sulfonic acid).[7] The present procedure is more convenient than any of the earlier methods.

References and Notes

1. Miller, Ann. **208**, 223 (1881); Huisinga, Rec. trav. chim. **27**, 261 (1908).
2. Levy and Stephen, J. Chem. Soc. **1931**, 79.
3. Culhane and Woodward, Org. Syn. Coll. Vol. I, **1941**, 408.
4. Bogert and Boroschek, J. Am. Chem. Soc. **23**, 752 (1901).
5. Cohen, Woodroffe, and Anderson, J. Chem. Soc. **109**, 232 (1916).
6. Lawrance, J. Am. Chem. Soc. **42**, 1872 (1920).
7. Ruggli, Knapp, Merz, and Zimmerman, Helv. Chim. Acta **12**, 1043 (1929).

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

alcohol-free ether

hydrochloric or sulfuric acid

diazoanhydride of 6-nitro-1-amino-2-naphthol-4-sulfonic acid

ether (60-29-7)

sodium hydroxide (1310-73-2)

nitric acid (7697-37-2)

sodium sulfate (7757-82-6)

3-Nitrophthalic acid (603-11-2)

phthalic anhydride (85-44-9)

4-nitrophthalic acid,
Phthalic acid, 4-nitro- (610-27-5)

phthalic acid (88-99-3)

4-Nitrophthalimide (89-40-7)

6-nitro-2-naphthol-4-sulfonic acid