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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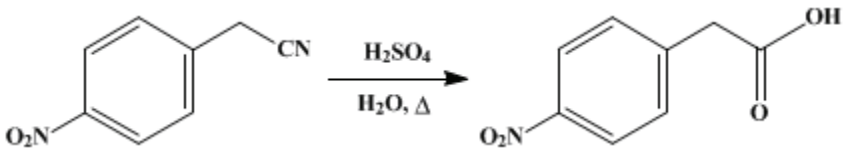
Organic Syntheses, Coll. Vol. 1, p.406 (1941); Vol. 2, p.59 (1922).

p-NITROPHENYLACETIC ACID

[α-Toluic acid, *p*-nitro-]



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1. Procedure

In a 1-l. round-bottomed flask is placed 100 g. (0.62 mole) of *p*-nitrobenzyl cyanide (p. 396). A solution of 300 cc. (5.4 moles) of concentrated sulfuric acid (sp. gr. 1.84) in 280 cc. of water is prepared, and two-thirds of this solution is poured onto the *p*-nitrobenzyl cyanide. The mixture is shaken well, until the solid is all moistened with the acid. Any solid material adhering to the walls of the vessel is now washed down into the liquid with the remainder of the acid; the flask is attached to a reflux condenser, then set, without shaking, over a 10-cm. hole in a large sheet of asbestos board which rests on a tripod, and heated until the mixture boils (Note 1). The boiling is continued for fifteen minutes (Note 2).

The reaction mixture, which becomes rather dark, is diluted with an equal volume of cold water and cooled to 0° or below. The solution is filtered; the precipitate is washed several times with ice water and then dissolved in 1600 cc. of boiling water (Note 3). This solution is filtered as rapidly as possible through a large folded filter, preferably with a steam funnel (Note 4). In spite of all precautions, however, some solid usually separates on the filter. This must be redissolved in a minimum quantity of boiling water, and this solution then filtered into the main solution. The *p*-nitrophenylacetic acid separates in long, pale yellow needles, which melt at 151–152°. The yield is 103–106 g. (92–95 per cent of the theoretical amount).

2. Notes

1. If the flask is not protected with an asbestos board or the equivalent, decomposition occurs where the substance is superheated on the side walls of the flask. If crystals of the cyanide are allowed to remain on the upper walls of the flask, they are not easily washed down and so are not hydrolyzed.
2. In making experiments with 500 g. of *p*-nitrobenzyl cyanide, it was found that the time for hydrolysis was about the same as when smaller amounts were used.
3. If a good grade of cyanide is used, it is not necessary to add animal charcoal in order to obtain the acid in a pure state. With technical *p*-nitrobenzyl cyanide, a few grams of animal charcoal are added in dissolving the precipitate.
4. The solubility curve of *p*-nitrophenylacetic acid is very steep at temperatures near 100°, so that the filtering of the boiling solution should be rapid.

3. Discussion

p-Nitrophenylacetic acid can be prepared by the nitration of phenylacetic acid[1] and by the hydrolysis of its nitrile with hydrochloric acid.[2]

This preparation is referenced from:

- Org. Syn. Coll. Vol. 1, 52
- Org. Syn. Coll. Vol. 1, 396

- Org. Syn. Coll. Vol. 3, 444

References and Notes

1. Maxwell, Ber. **12**, 1765 (1879); Borsche, Ber. **42**, 3596 (1909).
2. Gabriel, Ber. **15**, 834 (1882).

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

sulfuric acid (7664-93-9)

hydrochloric acid (7647-01-0)

Phenylacetic acid (103-82-2)

p-Nitrophenylacetic acid (104-03-0)

p-Nitrobenzyl cyanide (555-21-5)

α-Toluic acid, p-nitro-