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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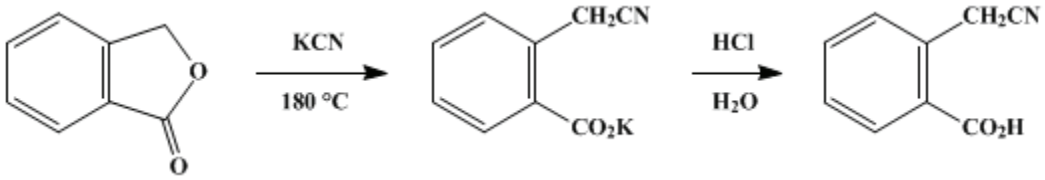
o-CARBOXYPHENYLACETONITRILE

[*o*-Toluic acid, α-cyano-]



Submitted by Charles C. Price and Richard G. Rogers.
Checked by W. E. Bachmann and Richard D. Morin.

1. Procedure

A mixture of 100 g. of phthalide (Note 1) and 100 g. of powdered potassium cyanide is placed in a 2-l. round-bottomed flask fitted with a stirrer and a thermometer. The stirred mixture is heated to 180–190° (internal temperature) for 4–5 hours in an oil bath (Note 2). One liter of water is added to the cooled mass, and the mixture is stirred until the solid salts are dissolved (Note 3). Any insoluble material that separates is removed by filtration (Note 4). Under a hood, 6 *N* hydrochloric acid (20–60 ml.) is added to the dark aqueous solution until it becomes turbid (Note 5). The solution is carefully neutralized with sodium bicarbonate (Note 6), a few grams of Norit is added, and the mixture is stirred for several minutes and filtered. The nearly colorless filtrate is acidified with 40–50 ml. of concentrated hydrochloric acid and, after cooling in an ice bath, is filtered with suction. The yield is 80–100 g. (67–83%) of white crystals which melt at 113–115° (Note 7).

2. Notes

1. The submitters used phthalide obtained from E. I. du Pont de Nemours and Company, Wilmington, Delaware. The checkers prepared it according to *Org. Syntheses* Coll. Vol. **2**, 526 (1943).
2. At the end of the reaction, the mixture should be dark brown and nearly solid. The temperature must not rise above 200°; the checkers kept it at 180°.
3. About 1 hour is required to disintegrate the mass.
4. In some runs 5–15 g. of phthalide is recovered at this point.
5. Occasionally a small amount of crystalline homophthalimide separated from the alkaline solution at this point; m.p. 235°.[1]
6. The checkers found it advisable to acidify the solution slightly at this stage in order to precipitate dark impurities.
7. This material is satisfactory for most purposes. It can be purified by recrystallization from benzene or acetic acid, though with considerable loss.

3. Discussion

o-Carboxyphenylacetonitrile has been prepared by the reaction of phthalide with potassium cyanide.[2,3,4] The above procedure is essentially that of Wislicenus.[2,3]

References and Notes

1. Gabriel, *Ber.*, **19**, 1655 (1886).
2. Wislicenus, *Ann.*, **233**, 102 (1886).
3. Price, Lewis, and Meister, *J. Am. Chem. Soc.*, **61**, 2760 (1939).
4. Johnston, Kaslow, Langsjoen, and Shriner, *J. Org. Chem.*, **13**, 477 (1948).

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

hydrochloric acid (7647-01-0)

acetic acid (64-19-7)

Benzene (71-43-2)

sodium bicarbonate (144-55-8)

potassium cyanide (151-50-8)

Norit (7782-42-5)

Phthalide (87-41-2)

homophthalimide

o-CARBOXYPHENYLACETONITRILE,
o-Toluic acid, α-cyano- (6627-91-4)