



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.

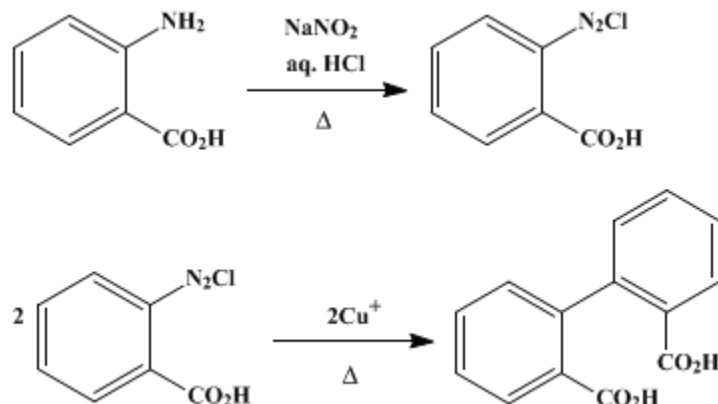
In some articles in *Organic Syntheses*, chemical-specific hazards are highlighted in red "Caution Notes" within a procedure. It is important to recognize that the absence of a caution note does not imply that no significant hazards are associated with the chemicals involved in that procedure. Prior 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.

Organic Syntheses, Coll. Vol. 1, p.222 (1941); Vol. 7, p.30 (1927).

DIPHENIC ACID



Submitted by E. R. Atkinson and H. J. Lawler.
Checked by R. L. Shriner and Roy D. Johnson.

1. Procedure

(A) *Diazotization of Anthranilic Acid.*—Fifty grams (0.365 mole) of **anthranilic acid** (m.p. 143–144°) is ground in a mortar with 150 cc. of water and 92 cc. of concentrated **hydrochloric acid** (sp. gr. 1.19). The suspension is transferred to a 1-l. round-bottomed flask which is equipped with a mechanical stirrer. The flask is surrounded by an ice bath. When the contents have cooled to 0–5°, a solution of 26.3 g. (0.38 mole) of **sodium nitrite** in 350 cc. of water is added from a dropping funnel during thirty minutes. The resulting diazonium solution is kept at a temperature below 5° and, unless it is entirely clear, is filtered by suction through a chilled Büchner funnel immediately before use.

(B) *Preparation of the Reducing Agent.*—One hundred and twenty-six grams (0.505 mole) of hydrated **cupric sulfate** is dissolved in 500 cc. of water in a 2-l. beaker and 210 cc. of concentrated **ammonium hydroxide** (sp. gr. 0.90) is added. The solution is then cooled to 10°. A solution of 42 g. (0.256 mole) of commercial **hydroxylammonium sulfate** (Note 1) in 120 cc. of water is prepared and cooled to 10°; to this latter solution there is added 85 cc. of 6 *N* **sodium hydroxide** solution, and the resulting solution of hydroxylamine is then filtered by suction if not clear. The hydroxylamine solution is immediately added to the ammoniacal cupric sulfate solution with hand stirring. Reduction occurs at once; a gas is evolved during the process, and the solution becomes pale blue in color. If this solution is not to be used at once it should be protected from the air.

(C) *Synthesis of Diphenic Acid.*—The reducing solution in the 2-l. beaker is surrounded by an ice bath so that the temperature of the solution is kept at about 10°. The beaker is fitted with a mechanical stirrer. The stem of a 100-cc. cylindrical dropping funnel is fitted with a glass tube which dips well below the surface of the solution and is bent upward at the end and constricted so that the opening is about 2 mm. (Note 2). An 80- to 90-cc. portion of the diazonium solution is placed in the dropping funnel and added at the rate of about 10 cc. per minute (Note 3). The remainder of the diazonium solution is added at the same rate and stirring is continued for five minutes longer.

The solution is then rapidly heated to boiling and carefully acidified with 250 cc. of concentrated **hydrochloric acid** (Note 4). Diphenic acid precipitates as light brown crystals. After the solution has stood overnight the solid is removed by filtration and washed free of mother liquor while on the filter with about 50 cc. of cold water. When dried, the product melts at 222–227° (corr.) and weighs 39–40 g. (88–91 per cent of the theoretical amount).

The crude product is suspended in 200 cc. of water, and 40 g. of solid **sodium bicarbonate** is added. The resulting solution is filtered by gravity, then boiled with 0.1 g. of **Norite**. The mixture is filtered and the yellowish-brown filtrate is acidified while still hot with an excess of 6 *N* **hydrochloric acid**. The

precipitated diphenic acid is collected on a filter and washed with 40 cc. of cold water. When dried at 100° the product melts at 225–228° and weighs 32–37 g. (72–84 per cent of the theoretical amount). It is a light cream color (Note 5).

2. Notes

1. This material may be purchased from the Commercial Solvents Corporation, New York City. It may be replaced by 35.6 g. (0.512 mole) of [hydroxylamine hydrochloride](#).
2. This trap arrangement prevents premature reaction of the entering diazonium solution with [ammonia](#) which otherwise would be carried up the stem by ascending bubbles of [nitrogen](#).
3. It is advisable to calibrate the dropping funnel so that the proper rate of addition may be used.
4. Rapid addition of acid near the neutral point (about 160 cc. of acid) causes the formation of small lumps of copper compounds which then contaminate the product. These are easily removed during the purification.
5. This color may be removed by further leachings with hot water. It is characteristic of the product formed when reducing agents containing hydroxylamine are used. If a colorless product is desired the use of a cupro-ammonia-sulfite reducing agent is preferable.¹

3. Discussion

This procedure is based on a detailed study¹ of the preparation of symmetrical biaryls by the action of reducing agents on diazotized amines. The reducing agent used above was introduced by Vorländer and Meyer.² Although the yield of diphenic acid is not appreciably greater than that obtained with two other reducing agents,¹ there are economies of time and materials which recommend it.

Diphenic acid can be prepared by oxidizing [phenanthrenequinone](#) with [chromic acid](#);³ and by heating [potassium *o*-bromobenzoate](#) with [copper powder](#).⁴

This preparation is referenced from:

- [Org. Syn. Coll. Vol. 4, 872](#)
- [Org. Syn. Coll. Vol. 5, 493](#)

References and Notes

1. Atkinson, Lawler, Heath, Kimball, and Read, *J. Am. Chem. Soc.* **63**, 730 (1941).
 2. Vorländer and Meyer, *Ann.* **320**, 122 (1902).
 3. Roberts and Johnson, *J. Am. Chem. Soc.* **47**, 1399 (1925).
 4. Hurtley, *J. Chem. Soc.* 1870 (1929).
-

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

Diphenic acid

ammoniacal cupric sulfate

copper compounds

cupro-ammonia-sulfite

hydrochloric acid (7647-01-0)

ammonia (7664-41-7)

sodium hydroxide (1310-73-2)

sodium bicarbonate (144-55-8)

nitrogen (7727-37-9)

cupric sulfate (7758-98-7)

sodium nitrite (7632-00-0)

copper powder (7440-50-8)

Norite (7782-42-5)

chromic acid (7738-94-5)

ammonium hydroxide (1336-21-6)

Anthranilic Acid (118-92-3)

hydroxylammonium sulfate

Hydroxylamine hydrochloride (5470-11-1)

phenanthrenequinone (84-11-7)

potassium o-bromobenzoate