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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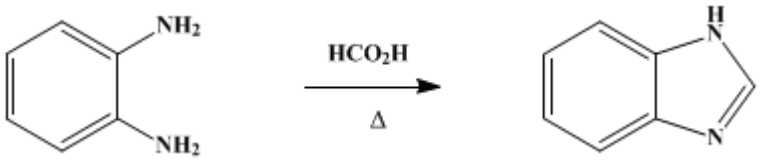
BENZIMIDAZOLE



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1. Procedure

In a 500-cc. round-bottomed flask 54 g. (0.5 mole) of *o*-phenylenediamine (Note 1) is treated with 32 cc. (34.6 g.) of 90 per cent formic acid (0.75 mole) (Note 2). The mixture is heated in a water bath at 100° for two hours. After cooling, 10 per cent sodium hydroxide solution is added slowly, with thorough mixing by rotation of the flask, until the mixture is just alkaline to litmus. The crude benzimidazole is collected with suction in a 75-mm. Büchner funnel; ice-cold water is used to rinse all solid out of the reaction flask. The crude product is pressed thoroughly on the filter, washed with about 50 cc. of cold water, and then purified without previous drying (Note 3).

The benzimidazole is dissolved in 750 cc. of boiling water in a 1.5-l. beaker. The solution is digested for fifteen minutes with about 2 g. of Norite and filtered rapidly through a well-heated filter (Note 4). The filtrate is cooled to 10–15°, and the benzimidazole is filtered and washed with 50 cc. of cold water. The white (Note 5) product is dried at 100°. The melting point is 170–172°, and the yield is 49–50.5 g. (83–85 per cent of the theoretical amount) (Note 6) and (Note 7).

2. Notes

1. The *o*-phenylenediamine used was a good grade of commercial material, m.p. 99–101°. The hydrochloride can be used with or without addition of sodium formate. Directions for preparing *o*-phenylenediamine are given on p. 501.
2. The yield is not greatly affected if the amount of formic acid is decreased almost to the theoretical, but a safe excess is recommended to ensure utilization of the *o*-phenylenediamine. Formic acid of considerably less than 90 per cent concentration will form benzimidazole; good yields were obtained with 40 per cent acid.
3. The crude benzimidazole, if dried at 100°, weighs 57.5–59 g. (97–99 per cent of the theoretical amount), melts at 167–168°, and is yellow tinged. This discoloration is difficult to remove and persists after two crystallizations (Note 5).
4. The solution is almost saturated when boiling, and crystallization begins at once on cooling. The filter must be thoroughly heated and filtration must be rapid, or crystallization will occur in the filter.
5. If the crystallized benzimidazole is discolored, the following treatment will yield a good product. The benzimidazole is dissolved in boiling water (13 cc. per gram), and a strong solution of potassium permanganate is added until the liquid becomes opaque owing to the precipitated brown oxide of manganese. To the hot mixture solid sodium bisulfite is added until clarification results. Decolorizing carbon is introduced, and the mixture is digested for fifteen minutes and filtered hot. The recovery is 90–92 per cent.
6. A small additional amount (2–2.5 g.) can be obtained by evaporation of the mother liquor to about 30 cc.
7. This is a general method of preparing benzimidazoles. Using an equivalent of acetic acid (45 g.) in place of formic acid, 2-methyl-benzimidazole, m.p. 172–174°, can be prepared in 68 per cent yield.

3. Discussion

Benzimidazole has been prepared from *o*-phenylenediamine by the action of chloroform and

alcoholic potassium hydroxide[1] and of formic acid,[2] and by the reduction of *o*-nitroformanilide.[3] Less serviceable methods include the interaction of *o*-phenylenediamine and dichloromethylformamidine,[4] or diphenylformamidine,[5] or formoacetic anhydride,[6] and the thermal decarboxylation of benzimidazole-2-carboxylic acid.[7] The procedure described was developed[8] from that of Wundt.[2]

The conversion of aliphatic acids to 2-alkylbenzimidazoles, by heating with *o*-phenylenediamine, has been proposed as a general method for preparing solid derivatives for identification.[9]

This preparation is referenced from:

- Org. Syn. Coll. Vol. 2, 501

References and Notes

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8. Wagner and Simons, J. Chem. Education **13**, 267 (1936).
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Appendix
Chemical Abstracts Nomenclature (Collective Index Number); (Registry Number)

oxide of manganese

formoacetic anhydride

acetic acid (64-19-7)

sodium hydroxide (1310-73-2)

chloroform (67-66-3)

potassium permanganate (7722-64-7)

formic acid (64-18-6)

sodium bisulfite (7631-90-5)

decolorizing carbon,
Norite (7782-42-5)

potassium hydroxide (1310-58-3)

sodium formate

Benzimidazole (51-17-2)

dichloromethylformamidine

diphenylformamidine

benzimidazole-2-carboxylic acid

o-Phenylenediamine (95-54-5)

2-methyl-benzimidazole (615-15-6)

o-nitroformanilide