



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.

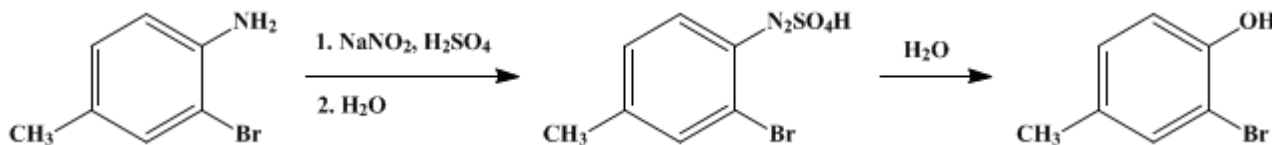
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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

Organic Syntheses, Coll. Vol. 3, p.130 (1955); Vol. 23, p.11 (1943).

3-BROMO-4-HYDROXYTOLUENE

[*p*-Cresol, 2-bromo-]



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1. Procedure

In a 2-l. beaker is placed 75 g. (0.4 mole) of 3-bromo-4-aminotoluene (Note 1), and to it is added the hot diluted acid obtained by adding 72 ml. of concentrated sulfuric acid to 200 ml. of water. The clear solution is stirred and cooled to about 15°, after which 180 g. of ice is added; the amine sulfate usually separates. As soon as the temperature has dropped below +5°, a solution of 32.2 g. (0.47 mole) of sodium nitrite in 88 ml. of water is added from a dropping funnel, the stem of which extends below the surface of the liquid. The temperature of the solution is kept below +5° during the addition, which requires about 15 minutes. The solution is stirred for 5 minutes after the addition of all the sodium nitrite, and 300 g. of cold water, 3 g. of urea, and 300 g. of cracked ice are then added successively. The solution is kept in an ice bath until used.

A 1-l. Claisen flask fitted with a dropping funnel and a thermometer dipping into the liquid is attached to a condenser set for downward distillation. In the flask are placed 150 g. of anhydrous sodium sulfate, 200 g. (108 ml.) of concentrated sulfuric acid, and 100 ml. of water. The flask is heated over a wire gauze, and while the internal temperature is maintained at 130–135°, the diazonium solution, in 25-ml. portions, is added at the same rate as the distillate is collected (Note 2). When this operation has been completed, 200 ml. of water, in 25-ml. portions, is introduced and the distillation is continued until an additional 200 ml. of distillate has been collected. The complete distillation requires 3–3.5 hours.

The distillate is extracted with two 150-ml. portions of ether, and the combined extracts are washed successively with 100 ml. of water and 150 ml. of 10% sodium bicarbonate solution. The phenol is then extracted from the ether layer by use of one 200-ml. and two 50-ml. portions of 10% sodium hydroxide solution. The combined alkaline solutions are acidified, with cooling, by the addition of 100 ml. of concentrated hydrochloric acid. The phenol is extracted with one 200-ml. and two 100-ml. portions of ether, and the combined extracts are washed with 100 ml. of water and dried over 50 g. of anhydrous sodium sulfate. The mixture is filtered, and the ether is removed from the filtrate by distillation on a water bath. The residue, 65–72 g. of a brown oil (Note 3), is then distilled from a Claisen flask with modified side arm; b.p. 102–104°/20 mm. The yield is 60–69 g. (80–92%) (Note 4).

2. Notes

1. The 3-bromo-4-aminotoluene may be purchased, or prepared according to *Org. Syntheses Coll. Vol. 1*, 111 (1941). The material used melted at 12–13°.
2. If the diazonium solution is added too rapidly, and the temperature of the liquid falls, the addition is interrupted until the temperature again exceeds 130°.
3. This crude product serves for most purposes, e.g., conversion to *o*-bromo-*p*-methylanisole.
4. The procedure has been used by the submitters for the conversion of *m*-bromoaniline into *m*-bromophenol, b.p. 234–237°/742 mm.; 105–107°/11 mm. The yield was 66%.

3. Discussion

o-Bromo-*p*-cresol has been prepared by the direct bromination of *p*-cresol in chloroform solution;^{1,2} by bromination of dry sodium *p*-cresoxide;³ and by decomposition of the diazonium sulfate of 3-bromo-4-aminotoluene;⁴ the last is a general method.^{5,6}

References and Notes

1. Vogt and Henninger, *Ber.*, **15**, 1081 (1882).
 2. Zincke and Wiederhold, *Ann.*, **320**, 202 (1902).
 3. Schall and Dralle, *Ber.*, **17**, 2530 (1894).
 4. Cain and Norman, *J. Chem. Soc.*, **89**, 24 (1906).
 5. Kalle and Company, Ger. pat. 95,339 [*Frdl.*, **4**, 124 (1894–1897)].
 6. Niemann, Mead, and Benson, *J. Am. Chem. Soc.*, **63**, 609 (1941).
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Appendix Chemical Abstracts Nomenclature (Collective Index Number); (Registry Number)

sodium *p*-cresoxide

sulfuric acid (7664-93-9)

hydrochloric acid (7647-01-0)

ether (60-29-7)

sodium hydroxide (1310-73-2)

chloroform (67-66-3)

sodium bicarbonate (144-55-8)

sodium sulfate (7757-82-6)

sodium nitrite (7632-00-0)

3-Bromo-4-aminotoluene (583-68-6)

urea (57-13-6)

3-Bromo-4-hydroxytoluene,
o-Bromo-*p*-cresol,
p-Cresol, 2-bromo- (6627-55-0)

o-bromo-*p*-methylanisole (22002-45-5)

m-bromoaniline (591-19-5)

p-CRESOL (106-44-5)

m-bromophenol (591-20-8)

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