



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.

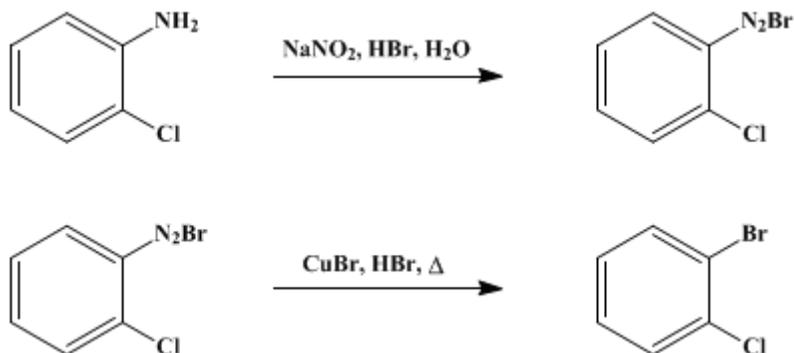
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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

Organic Syntheses, Coll. Vol. 3, p.185 (1955); Vol. 24, p.22 (1944).

***o*-CHLOROBROMOBENZENE**

[Benzene, 1-bromo-2-chloro-]



Submitted by Jonathan L. Hartwell
Checked by H. R. Snyder and Zeno Wicks, Jr..

1. Procedure

A mixture of 127.5 g. (1 mole) of a good commercial grade of *o*-chloroaniline and 300 ml. (2.5 moles) of 48% hydrobromic acid (Note 1) in a 2-l. flask set in an ice bath is cooled to 0° by the addition of ice. A solution of 70 g. (1 mole) of sodium nitrite in 125 ml. of water is added rapidly, with stirring, the temperature being kept below 10° by the addition of small pieces of ice. When only about 5 ml. of the sodium nitrite solution remains, further additions are made cautiously until an excess of nitrous acid remains after the last addition (Note 2).

In the meantime, a mixture of 79 g. (0.55 mole) of cuprous bromide (Note 3) and 80 ml. (0.6 mole) of 48% hydrobromic acid (Note 1) is heated to boiling in a 5-l. round-bottomed three-necked flask, equipped with a condenser set for distillation and provided with a 2-l. receiving flask, a steam inlet tube closed by a screw clamp, and a separatory funnel. About one-fourth of the diazonium solution is transferred to the separatory funnel, without filtration, and immediately run into the cuprous bromide-hydrobromic acid solution, which is kept boiling over a free flame, at such a rate that boiling is continuous. When the separatory funnel is nearly empty a further portion of the cold diazonium solution is transferred to it without interrupting the addition. All the diazonium solution is added in this way over a period of about 30 minutes, during which time much of the product steam-distills. When the addition is complete, the stopcock in the separatory funnel is closed, the screw clamp in the steam line is opened, and a vigorous current of steam is passed through the mixture until no more organic material distills. About 1–1.5 l. of distillate is collected.

The heavy organic layer is separated from the distillate and washed with 10-ml. portions of concentrated sulfuric acid until the acid becomes only slightly colored during the washings; four washings usually suffice. The oil is then washed with one 100-ml. portion of water, two 50-ml. portions of 5% aqueous sodium hydroxide, and finally with one 100-ml. portion of water. The product is dried over about 3 g. of calcium chloride and distilled from a 250-ml. distilling flask. The yield of pure, colorless *o*-chlorobromobenzene, boiling at 199–201°/742 mm., is 170–183 g. (89–95%) (Note 4) and (Note 5).

2. Notes

1. When 40% hydrobromic acid is used in both the diazotization and Sandmeyer reaction the yield is only about 75%.
2. Free nitrous acid causes an immediate blue color at the point of contact with starch-iodide test paper. A delayed color or a color around the periphery of the wetted area is of no significance. At all times

there must be an excess of mineral acid (blue color on Congo paper).

3. The submitter used commercial [cuprous bromide](#). The checkers prepared [cuprous bromide](#) by dissolving 600 g. (2.4 moles) of commercial [copper sulfate](#) crystals and 350 g. (3.4 moles) of [sodium bromide](#) in 2 l. of warm water; the solution was stirred while 151 g. (1.2 moles) of solid [sodium sulfite](#) was added over a period of 10 minutes. Occasionally a little more [sodium sulfite](#) was required to discharge the blue color. The mixture was cooled, and the solid collected on an 8-in. Büchner funnel, washed once with water, pressed nearly dry, and then dried in the air overnight. The yield of [cuprous bromide](#) was 320 g. (93%).

4. Runs 3 times this size give proportional yields.

5. The checkers have prepared the following bromides by the same procedure: [m-chlorobromobenzene](#) (b.p. 191–194°) from [m-chloroaniline](#) in 91–94% yields; [m-dibromobenzene](#) (b.p. 215–217°) from [m-bromoaniline](#) in 80–87% yields; and [o-bromoanisole](#) (b.p. 114–116°/29 mm.) from [o-anisidine](#) in 88–93% yields. In the preparation of [o-bromoanisole](#) the washing with [sulfuric acid](#) was omitted.

3. Discussion

[o-Chlorobromobenzene](#) has been prepared by the diazotization of [o-bromoaniline](#) followed by replacement of the diazonium group by [chlorine](#);¹ by the elimination of the amino group from [3-chloro-4-bromoaniline](#);² by the chlorination of [bromobenzene](#) in the presence of [thallous chloride](#),³ [aluminum chloride](#),⁴ or [ferric chloride](#);⁴ by the bromination of [chlorobenzene](#) without a catalyst⁵ or in the presence of [aluminum](#),⁴ [iron](#),⁴ [ferric bromide](#),⁴ or [aluminum-mercury couple](#);⁶ by the diazotization of [o-chloroaniline](#) followed by replacement of the diazonium group with [bromine](#);^{4,7} from [o-chlorophenylmercuric chloride](#) by the action of [bromine](#);⁸ and by treatment of [silver o-chlorobenzoate](#) with [bromine](#).⁹

This preparation is referenced from:

- [Org. Syn. Coll. Vol. 3, 200](#)
- [Org. Syn. Coll. Vol. 6, 36](#)

References and Notes

1. Dobbie and Marsden, *J. Chem. Soc.*, **73**, 254 (1898).
2. Wheeler and Valentine, *Am. Chem. J.*, **22**, 266 (1899).
3. Thomas, *Compt. rend.*, **144**, 33 (1907).
4. Vander Linden, *Rec. trav. chim.*, **30**, 305 (1911).
5. Van Loon and Wibaut, *Rec. trav. chim.*, **56**, 815 (1937).
6. Sen and Bhargava, *J. Indian Chem. Soc.*, **25**, 277 (1948).
7. Narbutt, *Ber.*, **52**, 1028 (1919).
8. Hanke, *J. Am. Chem. Soc.*, **45**, 1321 (1923).
9. Dauben and Tilles, *J. Am. Chem. Soc.*, **72**, 3185 (1950).

Appendix

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

[cuprous bromide-hydrobromic acid](#)

[calcium chloride](#) (10043-52-4)

[sulfuric acid](#) (7664-93-9)

sodium sulfite (7757-83-7)

sodium hydroxide (1310-73-2)

iron (7439-89-6)

HYDROBROMIC ACID (10035-10-6)

bromine (7726-95-6)

sodium bromide (7647-15-6)

copper sulfate (7758-98-7)

sodium nitrite (7632-00-0)

nitrous acid (7782-77-6)

aluminum (7429-90-5)

chlorobenzene (108-90-7)

aluminum chloride (3495-54-3)

chlorine (7782-50-5)

bromobenzene (108-86-1)

cuprous bromide (7787-70-4)

ferric chloride (7705-08-0)

Benzene, 1-bromo-2-chloro-,
o-Chlorobromobenzene (694-80-4)

3-chloro-4-bromoaniline (21402-26-6)

thallous chloride

ferric bromide (10031-26-2)

aluminum-mercury

m-chloroaniline (108-42-9)

o-chloroaniline (95-51-2)

o-bromoaniline (615-36-1)

m-bromoaniline (591-19-5)

[o-bromoanisole \(578-57-4\)](#)

[m-chlorobromobenzene \(108-37-2\)](#)

[m-dibromobenzene \(108-36-1\)](#)

[o-anisidine \(90-04-0\)](#)

[o-chlorophenylmercuric chloride](#)

[silver o-chlorobenzoate](#)