



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.

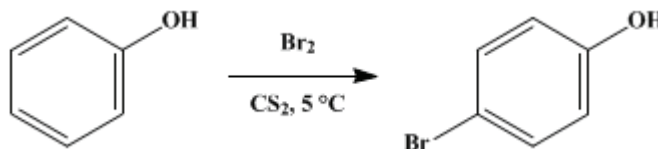
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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

Organic Syntheses, Coll. Vol. 1, p.128 (1941); Vol. 1, p.39 (1921).

***p*-BROMOPHENOL**

[Phenol, *p*-bromo-]



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1. Procedure

In a 5-l. round-bottomed flask fitted with a rubber stopper, holding a mechanical stirrer, reflux condenser and separatory funnel, is placed 1 kg. (10.6 moles) of phenol dissolved in 1 l. of carbon disulfide. To the top of the condenser is attached a calcium chloride tube (Note 1) and from this a glass tube leads into a beaker holding about 1200 cc. of cracked ice and water for the absorption of the hydrogen bromide evolved. In the separatory funnel is placed 1702 g. (546 cc., 10.7 moles) of bromine dissolved in 500 cc. of carbon disulfide. The flask is well cooled (below + 5°) in a salt and ice mixture (Note 2), stirring is started, and the bromine solution is allowed to run in. The addition requires about two hours. When this is completed, the flask is disconnected, and a condenser set for downward distillation is attached to it. By having a distilling flask as a receiver attached tightly to the lower end of the condenser, the dissolved hydrogen bromide which is evolved at the beginning of the heating may be led into the water used for collecting the first hydrogen bromide.

The carbon disulfide is distilled off; it amounts to about 1200 cc. (Note 3). The residual liquid is then slowly distilled under reduced pressure with a good fractionating column (Note 4) in a 1.5- or 2-l. Claisen flask which must be slightly modified (Fig. 9, p. 130) so that the *p*-bromophenol after coming in contact with cork or rubber will not be carried into the condenser (Note 5); if it does, it becomes pinkish. The yield is 1475–1550 g. (80–84 per cent of the theoretical amount) of *p*-bromophenol boiling at 145–150° /25–30 mm. In addition, there is obtained 250–350 g. of lower-boiling material consisting of a mixture of *o*-bromophenol and *p*-bromophenol from which it is very difficult to extract either constituent in pure form, and a small quantity of high-boiling material consisting chiefly of 2,4-dibromophenol. The *p*-bromophenol on cooling solidifies to a solid white mass containing practically no oil. By centrifuging the product, perfectly dry white crystals are obtained, m.p. 63°. There is also produced in this preparation about 1.5–1.6 l. of hydrobromic acid with a specific gravity of about 1.3 (Note 6).

2. Notes

1. Moisture prevents the *p*-bromophenol from crystallizing, so that particular care should be taken to keep it out of the reaction mixture.
2. Although it is not absolutely necessary that the reaction mixture be cooled with salt and ice, it is highly desirable, since this reduces the amount of *o*-bromophenol and hence the amount of low-boiling fraction; the recovery of carbon disulfide is also more satisfactory. A run of the same size as is described above was made, keeping the solution at room temperature, and under these conditions the yield of pure *p*-bromophenol was diminished.
3. The loss of carbon disulfide is due to its great volatility, the consequent passing off with the hydrogen bromide and the general loss during experimental manipulations. The experiments may be run with a larger amount of carbon disulfide with satisfactory results. This, however, involves a longer time for distillation and is therefore undesirable. More concentrated solutions were not tried.
4. The *p*-bromophenol if distilled without using a fractionating column and collected over a 5° range, as

already described, will generally amount to 1600–1660 g. (87–90 per cent of the theoretical amount). This material on cooling, however, never solidifies completely but always contains a certain amount of oil; it is satisfactory for most purposes, just as it is. Even though the once-distilled material may be freed from oil and then redistilled without special fractionation, some oil remains. To obtain a very pure product this material must be cooled to 10° and then centrifuged. In this way, hard white crystals which melt sharply at 63° result. During this process about 15–20 per cent of the product goes to the filtrate which, however, can be chilled again so that a certain amount of pure *p*-bromophenol may be obtained from it. Although a number of solvents were used in an attempt to crystallize *p*-bromophenol, none was found that was entirely satisfactory.

5. The flasks shown in Fig. 9 are particularly suited for distilling liquids which attack rubber or cork. Figure 9(a) illustrates a flask which is a modification of one already described in the literature;¹ the side arm outlet tube extends a short distance into the neck of the flask, thus preventing any vapor which has touched the cork or rubber

Fig. 9.



from condensing and flowing down the side arm into the condenser. Figure 9(b) shows a flask of the type used in the Eastman Kodak Company Laboratories. It has a longer column than the standard Claisen flask so that larger amounts of liquid can be distilled from it than from a standard Claisen flask of the same size and there is less danger from bumping. The upward angle on the first portion of the side arm outlet tube serves the same purpose as the inset side arm in the flask 9(a).

6. A complete run may be made in less than five hours.

3. Discussion

The methods for preparing *p*-bromophenol are: the action of bromine on phenol in carbon disulfide,² in glacial acetic acid,³ and in a mixture of sulfuric and acetic acids;⁴ and the diazotization of *p*-bromoaniline and subsequent heating with water.⁵ The relative yields of ortho and para derivatives have been studied⁶ in a miscellany of solvents, including water and carbon tetrachloride, and under varying temperatures.

In this investigation it was found that the diazo reaction did not give a good yield of pure compound. Bromination in glacial acetic acid is satisfactory except that the acetic acid cannot be recovered conveniently. The bromination in sulfuric acid (75 per cent) is unsatisfactory since the phenol does not dissolve readily at 0°, and, if a temperature high enough to dissolve it is used, a considerable amount of *o*-bromophenol is produced. Carbon tetrachloride might appear preferable to carbon disulfide on account of its non-inflammability; however, this advantage is offset because it must be used in much larger quantities to dissolve the phenol at 0°; it is much less easily removed, and the proportion of *o*-bromophenol is slightly greater.

This preparation is referenced from:

- Org. Syn. Coll. Vol. 1, 3
- Org. Syn. Coll. Vol. 1, 58
- Org. Syn. Coll. Vol. 1, 77
- Org. Syn. Coll. Vol. 1, 95

- Org. Syn. Coll. Vol. 1, 102
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- Org. Syn. Coll. Vol. 1, 323
- Org. Syn. Coll. Vol. 1, 435
- Org. Syn. Coll. Vol. 1, 494
- Org. Syn. Coll. Vol. 1, 524
- Org. Syn. Coll. Vol. 1, 533
- Org. Syn. Coll. Vol. 1, 544
- Org. Syn. Coll. Vol. 3, 28
- Org. Syn. Coll. Vol. 3, 444
- Org. Syn. Coll. Vol. 4, 771

References and Notes

1. Noyes and Skinner, J. Am. Chem. Soc. **39**, 2718 (1917).
 2. Körner, Ann. **137**, 200 (1866); Hantzsch and Mai, Ber. **28**, 978 (1895).
 3. Hübner and Brenken, Ber. **6**, 171 (1873); Hand, Ann. **234**, 136 (1886).
 4. Hewitt, Kenner and Silk, J. Chem. Soc. **85**, 1227 (1904).
 5. Fittig and Mager, Ber. **7**, 1176 (1874).
 6. Holleman and Rinke, Rec. trav. chim. **30**, 49 (1911).
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Appendix Chemical Abstracts Nomenclature (Collective Index Number); (Registry Number)

sulfuric and acetic acids

sulfuric acid (7664-93-9)

acetic acid (64-19-7)

phenol (108-95-2)

HYDROBROMIC ACID,
hydrogen bromide (10035-10-6)

bromine (7726-95-6)

carbon tetrachloride (56-23-5)

carbon disulfide (75-15-0)

2,4-dibromophenol (615-58-7)

o-Bromophenol (95-56-7)

p-bromoaniline (106-40-1)

p-Bromophenol,
Phenol, p-bromo- (106-41-2)