



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.109 (1941); Vol. 5, p.17 (1925).

***p*-BROMOACETOPHENONE**

[Acetophenone, *p*-bromo-]



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1. Procedure

In a 5-l. round-bottomed, three-necked flask, fitted with a mechanical stirrer, separatory funnel, and reflux condenser connected with a gas absorption trap (Fig. 7 on p. 97) for disposing of the evolved hydrogen chloride, is placed 392 g. (2.5 moles) of bromobenzene in 1-l. of dry carbon disulfide (Note 1). To this is added 750 g. (5.6 moles) (Note 2) of anhydrous aluminum chloride. The mixture is heated on a steam bath until gentle refluxing starts, and then 204 g. (2 moles) of acetic anhydride (Note 3) is added slowly through the dropping funnel. The time of addition is about one hour. Gentle refluxing should be continued throughout the time of addition of the anhydride and for one hour afterward. The reaction is accompanied by a copious evolution of hydrogen chloride which does not entirely cease even after this subsequent heating.

A condenser is attached to one of the side necks, and the carbon disulfide is distilled without removing the flask from the steam bath. After the removal of the solvent (Note 4), the reaction mixture is allowed to cool somewhat (Note 5); but while it is still warm, it is poured slowly with stirring over cracked ice to which hydrochloric acid has been added. In this way only a small amount of the aluminum chloride addition product remains in the flask. This is decomposed with ice and hydrochloric acid and added to the main product. The volume is now about 5 l. Each 2-l. portion is extracted twice with 300-cc. and 200-cc. portions of benzene or ether. The extracts are combined and washed twice with water, once with 10 per cent sodium hydroxide solution, and twice more with water. The final water washings should be practically colorless and the separation sharp, any precipitate being allowed to separate with the water.

The extract is dried for one hour with about 30 g. of calcium chloride and filtered, and the solvent is distilled from a steam bath. The residue is distilled under reduced pressure with a short column (p. 130). Some low-boiling material comes over first, and then the temperature rises rapidly. If care has been taken in the water decomposition to remove all the aluminum salts (Note 6), the product comes over water-white and crystallizes to a white solid melting at 49–50.5°. The yield is 340–395 g. (69–79 per cent of the theoretical amount) of a product boiling over a 3° range (Note 7) and (Note 8). On redistillation the boiling point is 117°/7 mm.; 129–130°/15 mm.; and 255.5°/736 mm.

2. Notes

1. If the carbon disulfide-bromobenzene solution is not clear it should be dried over calcium chloride and filtered before the aluminum chloride is added. In using such large amounts of carbon disulfide, particular precautions must be taken to prevent fires.
2. The aluminum chloride should be added in about this excess. When the excess is larger the yield does not seem to be increased, and when only 2 equivalents are used it is diminished by 10 to 15 per cent.
3. The acetic anhydride should boil at 136–139°. Some commercial grades are satisfactory, whereas others have been found to contain almost 50 per cent of acetic acid.
4. About 600–800 cc. of carbon disulfide is recovered and may be used in the next run.

5. If the product is allowed to come to room temperature before decomposition with water, it becomes semi-solid and is not easily removed from the flask.
6. If the [aluminum chloride](#) double compound is not entirely decomposed by water and the [aluminum](#) salts thus removed, the distillate comes over slightly red and does not crystallize well on cooling. Redistillation, however, gives a pure product.
7. This method is an improvement over the older methods for the preparation of substituted acetophenone derivatives. The yields obtained by the use of [acetyl chloride](#) in place of [acetic anhydride](#) in the preparation of [p-bromoacetophenone](#) were invariably lower. The yield is based on the [bromobenzene](#), because a side reaction between the [acetic acid](#), [aluminum chloride](#), and [bromobenzene](#) also produces some ketone.
8. Under the same general conditions, satisfactory yields of other acetophenones may be obtained. Thus, from 281 g. of [chlorobenzene](#), 750 g. of [aluminum chloride](#), and 205 g. of [acetic anhydride](#), a consistent yield of 285–300 g. (74–78 per cent of the theoretical amount) of [p-chloroacetophenone](#), boiling at 124–126° /24 mm. and melting at 20–21°, is obtained. Similarly, [acetophenone](#) may be obtained in 76–83 per cent yields, [p-methylacetophenone](#) in 85–89 per cent yields, and [p-methoxyacetophenone](#) in 90–94 per cent yields.

3. Discussion

[p-Bromoacetophenone](#) can be prepared by the action of [acetyl chloride](#) in [carbon disulfide](#) on [bromobenzene](#) in the presence of anhydrous [aluminum chloride](#),¹ and by the use of [acetic anhydride](#) in place of the [acetyl chloride](#).²

This preparation is referenced from:

- [Org. Syn. Coll. Vol. 1, 127](#)
- [Org. Syn. Coll. Vol. 2, 503](#)
- [Org. Syn. Coll. Vol. 4, 110](#)

References and Notes

1. Schweitzer, *Ber.* **24**, 550, 3766 (1891); Hale and Thorp, *J. Am. Chem. Soc.* **35**, 266 (1913).
 2. Noller and Adams, *ibid.* **46**, 1892 (1924).
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Appendix

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

carbon disulfide-bromobenzene

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

[hydrogen chloride](#),
[hydrochloric acid](#) (7647-01-0)

[acetic acid](#) (64-19-7)

[Benzene](#) (71-43-2)

[ether](#) (60-29-7)

acetic anhydride (108-24-7)
sodium hydroxide (1310-73-2)
acetyl chloride (75-36-5)
aluminum (7429-90-5)
Acetophenone (98-86-2)
chlorobenzene (108-90-7)
aluminum chloride (3495-54-3)
bromobenzene (108-86-1)
carbon disulfide (75-15-0)
p-Bromoacetophenone,
Acetophenone, p-bromo- (99-90-1)
p-Chloroacetophenone (99-91-2)
p-Methylacetophenone (122-00-9)
p-Methoxyacetophenone (100-06-1)