



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.

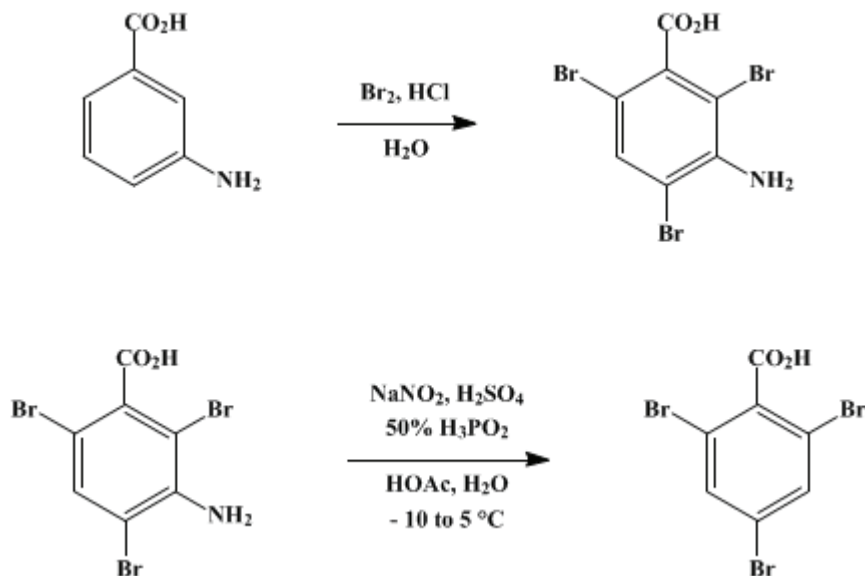
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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

Organic Syntheses, Coll. Vol. 4, p.947 (1963); Vol. 36, p.94 (1956).

2,4,6-TRIBROMOBENZOIC ACID

[Benzoic acid, 2,4,6-tribromo-]

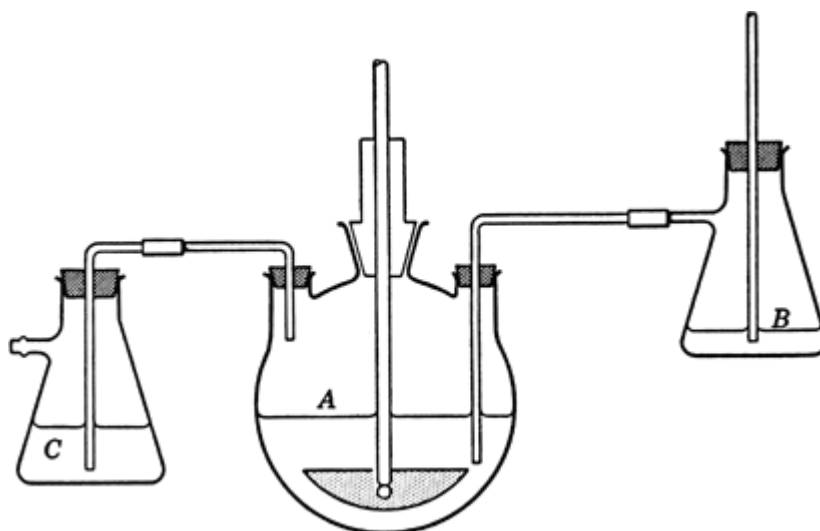


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1. Procedure

A. *3-Amino-2,4,6-tribromobenzoic acid*. The bromination apparatus consists of a 2-l. three-necked standard-taper flask *A*, equipped with a "Trubore" stirrer and attached by rubber stoppers and glass tubing to two filter flasks, *B* and *C*, as shown in Fig. 17. The 250-ml. flask *C*, which serves as a bubbler and trap, is half-filled with water, and its side arm is connected to a water pump. The reaction flask *A* is charged with 27.4 g. (0.2 mole) of *m*-aminobenzoic acid (Note 1), 165 ml. of concentrated hydrochloric acid, and 780 ml. of water, after which it is surrounded by an ice bath, and the stirrer is started. One hundred and forty grams (45 ml., 0.88 mole) of bromine is placed in the vaporization flask *B*, which is then surrounded by a water bath heated to 40–50°. Bromine vapor is drawn through the reaction mixture at a moderate rate by applying suction at the water pump. Stirring and cooling of the mixture are continued throughout the reaction period, during which time the product precipitates (Note 2). The bromination requires about 3 hours and is complete when the slurry assumes a distinct yellow color.²

Fig. 17.



The cream-colored solid is separated at once by filtration and washed thoroughly with water to remove excess bromine water and acids. It is used in the next step without drying. The melting range of the crude product is usually 170–172°.

B. *2,4,6-Tribromobenzoic acid*. A 5-l. three-necked flask, equipped with a mechanical stirrer and thermometer and surrounded by an ice-salt bath, is charged with a precooled mixture of 1.02 l. of concentrated sulfuric acid and 500 ml. of water. Cooling during the reaction period is assisted by the ice-salt bath, but is effected chiefly by periodic additions of large amounts of crushed Dry Ice directly to the reaction mixture. The temperature of the stirred mixture is lowered to -5° to -10° and 37 g. (0.54 mole) of sodium nitrite is added in small portions over a period of about 15 minutes. Cold 50% hypophosphorous acid (193 ml., 1.86 moles) (Note 3) is then added over a period of 10–15 minutes, the temperature still being maintained below -5° . A solution of the bromination product in 1.85 l. of glacial acetic acid is then added to the stirred diazotizing solution from a dropping funnel. During the 1–1.25 hours required to complete this addition the temperature is held between -10° and -15° (Note 4). Stirring of the slurry is continued for approximately 2 hours longer, and during this period the temperature is allowed to rise gradually to $+5^{\circ}$. The loosely stoppered flask is kept in a refrigerator for 36 hours (Note 5), during which time nitrogen and some oxides of nitrogen are evolved (Caution!). Most of the acetic acid is then removed by volatilization in a current of steam, 3 l. of distillate being collected. During the steam distillation the product starts to precipitate from the clear solution, and nitrogen dioxide and some hydrogen sulfide are given off. The residual liquid is cooled, and the product is collected on a sintered-glass funnel and washed with water. It is next suspended in 800 ml. of water, and approximately 9 g. of anhydrous sodium carbonate is added with shaking to bring it into solution. The yellow liquid is filtered to remove small quantities of insoluble impurities, and the acid is reprecipitated by acidification to pH 1–2 with 5% hydrochloric acid, while swirling vigorously. The cream-colored precipitate is separated by filtration, washed with water, and dried. The yield of *2,4,6-tribromobenzoic acid*, sufficiently pure for preparative purposes, is 50–57.5 g. (70–80%), m.p. 192.5–194.5° (Note 6).

2. Notes

1. Matheson Company *m*-aminobenzoic acid was used without further purification.
2. Efficient stirring and cooling are necessary at this stage to obtain a final product that is not colored.
3. Baker "purified" hypophosphorous acid was used.
4. Near the end of the addition of the acetic acid solution it is usually desirable to raise the stirrer temporarily to break up the lumps which form at the surface of the solution.
5. The temperature of the refrigerator was approximately 6° .
6. The product may be recrystallized from 1:2 acetic acid-water (about 8 ml./g.), but this process effects little improvement in melting point or color, even when activated carbon is used.

3. Discussion

2,4,6-Tribromobenzoic acid has been prepared by the deamination of 2,4,6-tribromo-3-aminobenzoic acid (reagents not specified),³ by hydrolysis of 2,4,6-tribromobenzonitrile,^{4,5,6,7} and by oxidation of the tribromotoluene,^{8,9} the benzyl chloride,¹⁰ the aldehyde,¹¹ and the glyoxylic acid.¹² The present method is a modification of that of Bunnett, Robison, and Pennington.¹³

References and Notes

1. Amherst College, Amherst, Massachusetts.
2. This is the method of Coleman and Talbot, *Org. Syntheses Coll. Vol. 2*, 592 (1943), for 2,4,6-tribromoaniline.
3. Hübner, *Ber.*, **10**, 1708 (1877).
4. Sudborough, *Ber.*, **27**, 512 (1894).
5. Wegscheider, *Monatsh.*, **18**, 218 (1897).
6. Sudborough, Jackson, and Lloyd, *J. Chem. Soc.*, **71**, 230 (1897).
7. Montagne, *Rec. trav. chim.*, **27**, 351 (1908).
8. Asinger, *J. prakt. Chem.*, **142**, 291 (1935).
9. Cohen and Dutt, *J. Chem. Soc.*, **105**, 516 (1914).
10. Henraut, *Bull. soc. chim. Belges*, **33**, 132 (1924).
11. Blanksma, *Chem. Weekblad*, **9**, 865 (1912) [*Chem. Zentr.*, **1912 II**, 1965].
12. Fuchs, *Monatsh.*, **36**, 137 (1915).
13. Bunnett, Robison, and Pennington, *J. Am. Chem. Soc.*, **72**, 2378 (1950).

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

oxides of nitrogen

hypophosphorous acid

sulfuric acid (7664-93-9)

hydrochloric acid (7647-01-0)

acetic acid (64-19-7)

hydrogen sulfide (7783-06-4)

sodium carbonate (497-19-8)

bromine (7726-95-6)

nitrogen (7727-37-9)

sodium nitrite (7632-00-0)

carbon (7782-42-5)

benzyl chloride (100-44-7)

nitrogen dioxide (10102-44-0)

glyoxylic acid (298-12-4)

2,4,6-tribromobenzonitrile

2,4,6-Tribromobenzoic acid,
Benzoic acid, 2,4,6-tribromo- (633-12-5)

2,4,6-tribromo-3-aminobenzoic acid,
3-Amino-2,4,6-tribromobenzoic acid (6628-84-8)

tribromotoluene (6320-40-7)

m-aminobenzoic acid (99-05-8)