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.

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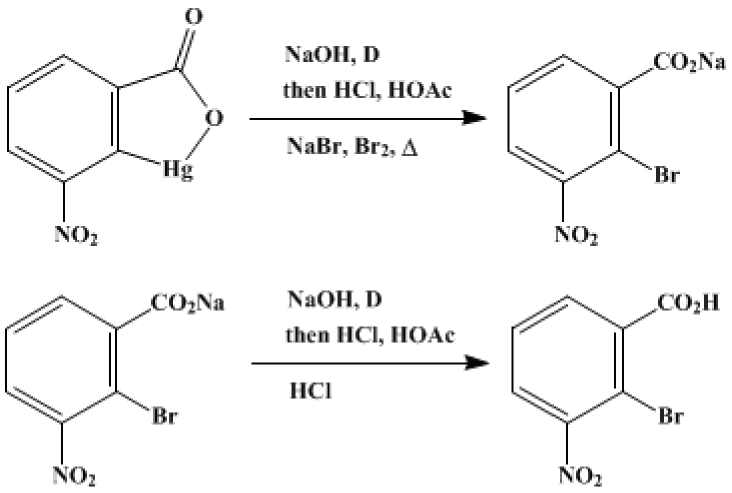
Organic Syntheses, Coll. Vol. 1, p.125 (1941); Vol. 7, p.12 (1927).

2-BROMO-3-NITROBENZOIC ACID

[Benzoic acid, 2-bromo-3-nitro-]



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1. Procedure

A solution of 50 g. (1.25 moles) of sodium hydroxide in 1.5 l. of water is prepared in a 5-l. flask, and the solution is heated to gentle boiling. To the hot solution is added, in small quantities, 330 g. (0.9 mole) of anhydro-2-hydroxymercuri-3-nitrobenzoic acid (p. 56) (Note 1). The mixture is stirred after the addition of each portion of about 50 g. until the material has gone into solution except for a small residue. The flask is then fitted with a stirrer and addition tube (Note 2) and with a connection to a reflux condenser. The material is heated to boiling and stirred vigorously. There is slowly added, with continuous stirring, 101 g. (85 cc., 0.95 mole) (Note 3) of concentrated hydrochloric acid (sp. gr. 1.19). Heating is discontinued at this point, and 31.5 g. (30 cc., 0.5 mole) of glacial acetic acid (sp. gr. 1.05) (Note 3) is added slowly. A curdy precipitate forms.

A solution of bromine is prepared by dissolving 103 g. (1 mole) of sodium bromide and 160 g. (50.2 cc., 1 mole) of bromine in 150 cc. of water (Note 4). The mixture is stirred, and the bromine solution is added as rapidly as possible through the shaft of the stirrer. The precipitate dissolves. The solution is heated to boiling for five minutes after the last of the bromine has been added. The solution is then made slightly alkaline by the addition of 20 g. (0.5 mole) of solid sodium hydroxide and filtered through a fluted filter. The filtrate is then made acid to Congo red, using about 150 cc. of concentrated hydrochloric acid. The precipitated 2-bromo-3-nitrobenzoic acid is filtered with suction and sucked as dry as possible. It is then crystallized from 1 l. of hot 30 per cent alcohol. The yield of product melting at 185–187° is 130–150 g. (53–61 per cent of the theoretical amount, based on the 3-nitrophthalic acid used). About 25 g. of material melting at about 175° can be recovered from the mother liquor.

2. Notes

1. The reaction product from the mercuration of 3-nitrophthalic acid (1 mole) is used. The mercury compound can be used without drying if desired. If this is done, solution takes place much more readily.
2. A rapid distribution of the added material is necessary to prevent a local excess of the reagent added. This is very important when hydrochloric acid is added, as this tends to decompose the mercury compound. A convenient arrangement consists of a three-way tube of about 15-mm. bore. The stirrer operates through the center tube. The other arms are used for the condenser and for the addition of material. A three-necked flask provided with a long-stemmed separatory funnel reaching below the

stirrer may be used.
3. The addition of one mole of hydrochloric acid allows the formation of one mole of sodium chloride, which is of advantage in the subsequent addition of halogen, owing to the formation of a sodium salt of the chloromercuric acid, this being more soluble and hence more reactive than the anhydro compound. Acetic acid is used for the final acidification because it does not decompose the mercury compound. The replacement by bromine takes place best in a slightly acid medium.
4. The mercury can be replaced by iodine in a similar manner. An iodine solution is made by dissolving 166 g. (1 mole) of potassium iodide and 255 g. (1 mole) of iodine in 250 cc. of water. This is used instead of the bromine solution. The mixture is filtered from the mercuric iodide and the filtrate acidified with 200 cc. of concentrated hydrochloric acid. The precipitate is filtered and then stirred with a solution of 10 g. of potassium iodide in 250 cc. of water to remove mercuric iodide. The mixture is filtered with suction and the precipitate crystallized from 1 l. of 50 per cent alcohol. The yield is 180 g. of 2-iodo-3-nitrobenzoic acid melting at 204–205.5° (61 per cent of the theoretical amount, based on the 3-nitrophthalic acid used).

3. Discussion

2-Bromo-3-nitrobenzoic acid can be prepared by the nitration of 2-bromobenzoic acid, the 2,3 acid being separated from the 2,5 acid, which is the principal product of the nitration, by fractional crystallization of the potassium salts from water.[1]

2-Iodo-3-nitrobenzoic acid can be prepared by the diazotization of 3-nitroanthranilic acid.[2]

This preparation is referenced from:

- Org. Syn. Coll. Vol. 1, 56

References and Notes

1. Holleman and de Bruyn, Rec. trav. chim. **20**, 211 (1901).
2. James, Kenner and Stubbings, J. Chem. Soc. **117**, 776 (1920).

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

Anhydro-2-hydroxymercuri-3-nitrobenzoic acid

sodium salt of the chloromercuric acid

alcohol (64-17-5)

hydrochloric acid (7647-01-0)

acetic acid (64-19-7)

sodium hydroxide (1310-73-2)

sodium chloride (7647-14-5)

bromine (7726-95-6)

sodium bromide (7647-15-6)

potassium iodide (7681-11-0)

3-Nitrophthalic acid (603-11-2)

mercury (7439-97-6)

2-Bromo-3-nitrobenzoic acid,
Benzoic acid, 2-bromo-3-nitro- (573-54-6)

iodine (7553-56-2)

mercuric iodide (7774-29-0)

2-iodo-3-nitrobenzoic acid (5398-69-6)

2-bromobenzoic acid (88-65-3)

3-nitroanthranilic acid