Organic Syntheses

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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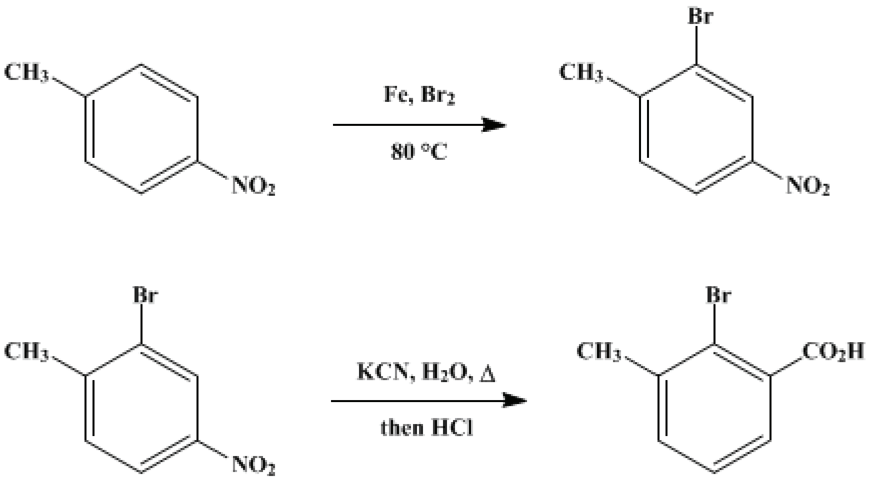
# 2-BROMO-3-METHYLBENZOIC ACID

## [*m*-Toluic acid, 2-bromo-]



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## 1. Procedure

A. *2-Bromo-4-nitrotoluene*. In a 200-ml. three-necked, round-bottomed flask provided with an efficient reflux condenser bearing a suitable trap for absorbing hydrogen bromide, a 100-ml. separatory funnel, and a ball-joint or mercury-sealed mechanical stirrer are placed 68.5 g. (0.5 mole) of *p*-nitrotoluene (Note 1) and 1.0 g. of iron powder. The mixture is heated to 75–80° by means of a water bath, vigorous stirring is begun, and 30.5 ml. (94.8 g., 0.59 mole) of bromine is added over the course of 30 minutes. After the addition of bromine is complete, the reaction mixture is maintained at 75–80° with continuation of stirring for an additional 1.5 hours.

The reaction mixture is poured with vigorous stirring into 750 ml. of ice-cold 10% sodium hydroxide solution, the solid is allowed to settle, and the supernatant liquid is decanted. To the residue is added 250 ml. of glacial acetic acid, and the mixture is heated until the solid is completely melted. The two liquid phases are thoroughly mixed by stirring, the mixture is cooled to 5° in an ice bath, and the supernatant liquid is decanted. The product is then heated with 500 ml. of 10% acetic acid until molten, stirred thoroughly, and cooled to room temperature. The aqueous liquor is decanted, and the cycle is repeated with 500 ml. of 1% sodium hydroxide solution (Note 2). The solid 2-bromo-4-nitrotoluene is collected on a Büchner funnel and thoroughly washed with water. The moist product may be used directly in the next stage of the synthesis. It can be dried to yield 93–97 g. (86–90%) of light-brown material melting at 75–76°.

B. *2-Bromo-3-methylbenzoic acid*. *Caution! This procedure must be carried out in a hood with a good draft, because poisonous hydrogen cyanide is evolved.* In a 5-l. round-bottomed flask are placed 90 g. of potassium cyanide, 900 ml. of 2-ethoxyethanol (Note 3), 850 ml. of water, and the moist 2-bromo-4-nitrotoluene obtained above. A reflux condenser is attached, and the mixture is boiled for 16 hours (Note 4). To the hot, dark-red solution is then added 1.5 l. of water, and the mixture is acidified with concentrated hydrochloric acid. (*Caution! Hydrogen cyanide is evolved.*) The acidified mixture is boiled for 15 minutes to expel hydrogen cyanide and then allowed to cool to 35–40°. Five grams of diatomaceous earth is stirred in, and the mixture is filtered through a Büchner funnel precoated with a little diatomaceous earth. The solid is discarded, and the filtrate is extracted three times with 200-ml. portions of chloroform. The chloroform extracts are combined and extracted with three 100-ml. portions of 5% ammonium carbonate solution. The basic extracts are combined, acidified with concentrated hydrochloric acid, and cooled in an ice bath. The oil which first forms soon crystallizes.

The tarry solid is collected on a Büchner funnel, washed with 50 ml. of water, and dried. The dried solid is pulverized and boiled under reflux for 3 hours with 500 ml. of petroleum ether (b.p. 90–100°). The hot mixture is then filtered (fluted filter paper), and the solid is discarded. The filtrate is allowed to cool to room temperature, and the 2-bromo-3-methylbenzoic acid is collected by filtration. The white acid when dry weighs 7.5–8.5 g. (7–8%, based on the *p*-nitrotoluene) and melts at 134–136° (Note 5).

## 2. Notes

1. Eastman Kodak Company practical grade *p*-nitrotoluene was used.
2. The hot mixture of 2-bromo-4-nitrotoluene and 1% sodium hydroxide solution should be stirred vigorously during cooling in order to avoid obtaining the product as a solid cake. If stirring is omitted, subsequent treatment is less convenient.
3. Commercial Cellosolve was used.
4. An electric heating mantle is a convenient heat source.
5. The submitters report 11–14 g. (10–13%) of material having m.p. 132–135°, which yields, after crystallization from benzene, 9–13 g. product having m.p. 135–137°.

## 3. Discussion

Although 2-bromo-4-nitrotoluene has been obtained by several routes, it is most easily prepared by bromination of *p*-nitrotoluene.[2] The procedure given is adapted from that described by Cavill.[3] 2-Bromo-3-methylbenzoic acid has not been prepared by any other means; evidence for its structure is presented elsewhere.[4]

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## References and Notes

1. University of North Carolina, Chapel Hill, North Carolina.
2. Scheufelen, *Ann.*, **231**, 152 (1885); Lucas and Scudder, *J. Am. Chem. Soc.*, **50**, 244 (1928); Frejka and Vitha, *Publs. fac. sci. univ. Masaryk*, **20** (1925) [*Chem. Zentr.*, **96**, II, 1153 (1925)]; Higginbottom, Hill, and Short, *J. Chem. Soc.*, **1937**, 263; Truce and Amos, *J. Am. Chem. Soc.*, **73**, 3013 (1951).
3. Cavill, *J. Soc. Chem. Ind. (London)*, **65**, 124 (1926).
4. Bunnett and Rauhut, *J. Org. Chem.*, **21**, 934 (1956).

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

petroleum ether

hydrochloric acid (7647-01-0)

acetic acid (64-19-7)

ammonium carbonate (506-87-6)

Benzene (71-43-2)

sodium hydroxide (1310-73-2)

chloroform (67-66-3)

iron powder (7439-89-6)

hydrogen cyanide (74-90-8)

hydrogen bromide (10035-10-6)

bromine (7726-95-6)

potassium cyanide (151-50-8)

cellosolve (107-21-1)

2-ethoxyethanol (110-80-5)

2-Bromo-3-methylbenzoic acid,
m-Toluic acid, 2-bromo- (53663-39-1)

2-Bromo-4-nitrotoluene (7745-93-9)

p-nitrotoluene (99-99-0)