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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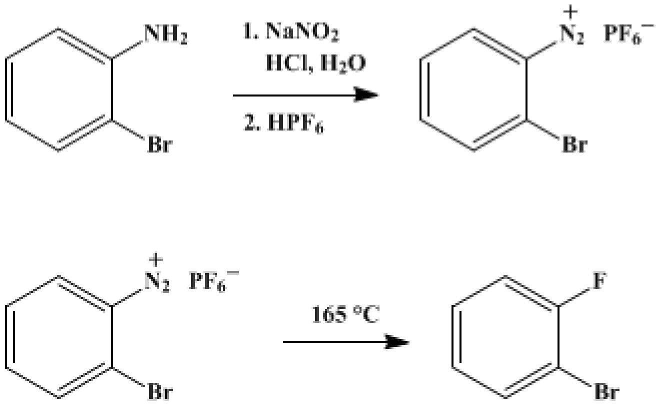
1-BROMO-2-FLUOROBENZENE

[Benzene, 1-bromo-2-fluoro-]



Submitted by K. G. Rutherford and W. Redmond[1].
Checked by M. Paulshock and B. C. McKusick.

1. Procedure

A. *o-Bromobenzenediazonium hexafluorophosphate*. A solution of 95 ml. of 12*N* hydrochloric acid in 650 ml. of water is added with stirring to 60 g. of *o*-bromoaniline (0.35 mole; (Note 1)) in a 2-l. three-necked flask equipped with stirrer and thermometer. Solution is effected by heating the mixture on a steam bath (Note 2). A solution of 29 g. (0.42 mole) of sodium nitrite in 75 ml. of water is added with stirring while the mixture is maintained at −5° to −10° by means of a bath of ice and salt or of dry ice and acetone. At the end of the addition there is an excess of nitrous acid, which can be detected with starch iodide paper. Seventy-four milliliters (134 g., 0.60 mole) of 65% hexafluorophosphoric acid (Note 3) is added in one portion, with vigorous stirring, to the cold solution of the diazonium salt. Cooling and slow stirring are continued for an additional 30 minutes, and the precipitated diazonium hexafluorophosphate is then collected on a Büchner funnel. The diazonium salt is washed on the funnel with 300 ml. of cold water and with a solution of 80 ml. of methanol in 320 ml. of ether (Note 4). The salt is partly dried by drawing air through the funnel for 2 hours. It is then transferred to a pile of several filter papers, powdered with a spatula, and dried at about 25°/1 mm. for at least 12 hours. The dried *o*-bromobenzenediazonium hexafluorophosphate is cream-colored; weight 108–111 g. (94–97%); m.p. 151–156° (dec.) (Note 5).

B. *1-Bromo-2-fluorobenzene*. *Caution! This step should be carried out in a hood because the* PF_5 *evolved on thermal decomposition of the diazonium salt is poisonous.* The apparatus consists of a 1-l., three-necked, round-bottomed flask equipped with a thermometer, a condenser, a magnetic stirrer (optional), and a 250-ml. Erlenmeyer flask that is attached by means of a short rubber Gooch connecting tube. The dry powdered hexafluorophosphate salt is placed in the Erlenmeyer flask, and 300 ml. of heavy mineral oil is placed in the round-bottomed flask. The mineral oil is heated to 165–170° by means of an oil bath or electric heating mantle and maintained at this temperature while the salt is added rapidly in portions over a period of 30 minutes. The flask is cooled rapidly to room temperature, the side flask is removed, and 400 ml. of 10% aqueous sodium carbonate is added slowly through the condenser. The mixture is steam-distilled until no more oil is visible in the distillate.

The oil, which is heavier than water, is separated, and the aqueous layer is extracted with three 50-ml. portions of methylene chloride. The oil and extracts are combined, dried over anhydrous sodium sulfate, and distilled from a Claisen flask with an indented neck. Colorless 1-bromo-2-fluorobenzene is collected at 58–59°/17 mm. or 156–157°/760 mm.; weight 45–47 g. (73–75% based on *o*-bromoaniline); n_{D}^{25} 1.5320–1.5325.

2. Notes

1. *o*-Bromoaniline obtained from Eastman Kodak and used without redistillation is satisfactory.
2. The amine is dissolved to ensure its complete conversion to the hydrochloride. The amine hydrochloride may partly crystallize as the solution is cooled, but it redissolves as diazotization proceeds.
3. The 65% hexafluorophosphoric acid (density 1.81) was obtained from the Ozark-Mahoning Company, Tulsa, Oklahoma. A graduated polypropylene (Nalgene®) cylinder was used to contain the measured quantity of the acid. Rubber gloves should be worn as a precautionary measure against burns. Working in a hood prevents any contact of exposed parts of the body with fumes. *In the event of accidental contact of the acid with the skin, the affected place should be immediately washed well with running water and then treated with a paste of magnesium oxide and glycerol*[2] *or soaked in ice water.*
4. The methanol-ether filtrate has a slight yellow color. It is not known what impurity is removed by this solvent pair. However, the submitters found that this treatment improved the yield of several aryl fluorides prepared according to the present procedure.
5. The checkers had *o*-bromobenzenediazonium hexafluoro-phosphate examined in laboratories of the Du Pont Co. Explosives Department to see if it could be detonated. It was found sensitive to neither shock nor static electricity, and to decompose but not detonate when rapidly heated to 250°. Hence it probably does not present an explosion hazard, but it should be kept away from heat, especially if in a closed container.

3. Discussion

1-Bromo-2-fluorobenzene has been prepared in 37% yield by the Schiemann reaction from *o*-bromoaniline, nitrous acid, and fluoboric acid.[3,4] The present procedure[5] is a modification of the Schiemann reaction.

4. Merits of the Preparation

This procedure is a general way of converting arylamines to aryl fluorides, for it has been used to make fifteen other aryl fluorides. It generally gives better yields than the Schiemann reaction.

1-Bromo-2-fluorobenzene is used to prepare the highly reactive intermediate, benzyne.[6]

References and Notes

1. Department of Chemistry, Essex College, Assumption University of Windsor, Windsor, Ontario, Canada.
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3. E. Bergmann, L. Engel, and S. Sandor, *Z. Physik. Chem. (Leipzig)*, **10B**, 117 (1930).
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Appendix
Chemical Abstracts Nomenclature (Collective Index Number);
(Registry Number)

fluoboric acid

hydrochloric acid (7647-01-0)

benzyne (71-43-2)

methanol (67-56-1)

ether (60-29-7)

glycerol (56-81-5)

sodium carbonate (497-19-8)

sodium sulfate (7757-82-6)

sodium nitrite (7632-00-0)

nitrous acid (7782-77-6)

methylene chloride (75-09-2)

magnesium oxide

1-Bromo-2-fluorobenzene,
Benzene, 1-bromo-2-fluoro- (1072-85-1)

hexafluorophosphoric acid (16940-81-1)

o-bromoaniline (615-36-1)

o-Bromobenzenediazonium hexafluorophosphate,
o-bromobenzenediazonium hexafluoro-phosphate