



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.

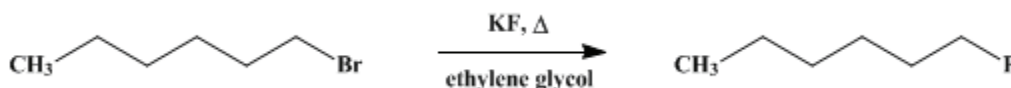
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These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

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***n*-HEXYL FLUORIDE**

[Hexane, 1-fluoro-]



Submitted by Arthur I. Vogel, James Leicester, and William A. T. Macey¹.
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1. Procedure

The 1-fluoroalkanes are the most toxic of the fluoro compounds. This fact, together with their relatively high volatility, emphasizes the need for care in handling these materials. This preparation should be carried out in a good hood and the operator should wear rubber gloves (Note 1).

In a thoroughly dry 500-ml. three-necked round-bottomed flask, equipped with a mercury-sealed stirrer, a 100-ml. dropping funnel and a short fractionating column (Note 2), is placed a mixture of 116 g. (2.0 moles) of anhydrous finely powdered potassium fluoride (Note 3) and 200 g. of dry ethylene glycol (Note 4). The fractionating column carries a thermometer and is connected to a downward double-surface condenser with a filter flask as receiver. The round flask is heated at a bath temperature of 160–170°, and 165 g. (1.0 mole) of *n*-hexyl bromide, b.p. 154–156° (Note 5), is added dropwise during 5 hours; liquid passes over intermittently at 60–90° (temperature at the top of the fractionating column). The bath temperature is allowed to fall to 110–120°, and a slow stream of air is drawn through the apparatus by attaching the side arm of the filter flask to a water pump and replacing the dropping funnel by a narrow-bore tube dipping just below the surface of the liquid; stirring is maintained during this operation. It is advisable to interpose a U-tube cooled in ice between the water pump and the receiver in order to recover any uncondensed liquid. The combined distillates are then distilled at atmospheric pressure through an efficient fractionating column; after a small fore-run (up to 10 g.) of 1-hexene, the crude *n*-hexyl fluoride is collected at 89–92° (46–48 g.). The crude product is purified by cooling in ice and adding 1-ml. portions of a solution containing 9.0 g. of bromine and 6.0 g. of potassium bromide in 50 ml. of water until the organic layer acquires an orange color; after each addition the mixture is shaken vigorously for a minute or so. The volume of bromine-potassium bromide solution required is usually less than 5 ml. The aqueous layer is separated, the organic layer is washed with saturated aqueous potassium bromide solution until color-less and finally with water. The liquid is dried with anhydrous magnesium sulfate and distilled through an efficient fractionating column; the *n*-hexyl fluoride is collected at 91–92°. This procedure yields 42–47 g. (40–45% over-all yield based on the bromide employed) of a water-white product, n_D^{20} 1.375, n_D^{25} 1.372–1.373, d_4^{20} 0.8011. It has been kept for 1 year without change of physical properties and therefore appears to be stable (Note 6).

2. Notes

1. Data giving lethal doses of the 1-fluoroalkanes in mice may be found in Pattison's *Toxic Aliphatic Fluorine Compounds*, Elsevier Publishing Company, 1959, and in Pattison, *J. Am. Chem. Soc.*, **79**, 2311 (1957). It has been estimated that 0.1–0.2 g. of *n*-hexyl fluoride would be a fatal dose for a human being.²
2. Any fractionating column of moderate efficiency is satisfactory. The submitters employed a 20-cm. Dufton column containing a spiral 10 cm. in length, 2 cm. in diameter, with 8 turns of the helix. A 20–25 cm. Vigreux column may also be used.
3. Pure laboratory grade anhydrous potassium fluoride is finely ground and kept for 48 hours in an oven at 180–210°; it is stored in a desiccator. Before use, the powdered salt is dried for 3 hours at 180° and ground again in a warm (50°) glass mortar.

4. Laboratory grade ethylene glycol is redistilled under diminished pressure, and the fraction boiling at 85–90°/7 mm. is used as the solvent for the potassium fluoride.
5. The *n*-hexyl bromide may be prepared from redistilled *n*-hexyl alcohol by the red phosphorus-bromine procedure or may be purchased from Eastman Kodak Company.
6. The procedure described has been employed by the submitters for the preparation of the alkyl fluorides listed below. Due regard must be paid to the boiling point of the alkyl bromide; as a general rule the bath temperature is maintained at about the boiling point of the alkyl bromide, with a minimum value (for *n*-amyl fluoride) of about 140–150°. For bromides of higher boiling point, the bath temperature is held at about 190°. In all cases, after the alkyl bromide has been added, the bath is allowed to cool 10–20° below the original reaction temperature, and a slow stream of air is drawn through the apparatus; the alkyl fluoride and ethylene glycol which pass over are collected, and the latter is removed by washing with water.

Alkyl fluoride	B.P.	d_4^{20}	n_D^{20}	n_D^{25}	Yield, %
<i>n</i> -Amyl	63.5–65°	0.79171	1.35971	1.3562	27
<i>n</i> -Heptyl	119–121°	0.80601	1.38611	1.3833	35
<i>n</i> -Octyl	144–146°	0.81371	1.39551	1.3927	34
<i>n</i> -Nonyl	166–169°	0.81591	1.40331	1.4002	46
<i>n</i> -Decyl	186–188°	0.81971	1.40951	1.4068	37
<i>n</i> -Undecyl	70–71.5°/3 mm.	0.82391	1.41511	1.4122	45
<i>n</i> -Dodecyl	93–95°/3 mm.	0.82571	1.41921	1.4162	34
<i>n</i> -Tetradecyl	119–121°/3 mm., m.p. 8°	0.82771	1.42661	1.4236	43
<i>n</i> -Hexadecyl	150–152°/2 mm., m.p. 19°	0.83131	1.43221	1.4295	27

3. Discussion

Alkyl fluorides have been prepared by reaction between elementary fluorine and the paraffins,³ by the addition of hydrogen fluoride to olefins,⁴ by the reaction of alkyl halides with mercurous fluoride,⁵ with mercuric fluoride,⁶ with silver fluoride,⁷ or with potassium fluoride under pressure,⁸ and by the reaction of potassium fluoride with *n*-hexyl methanesulfonate⁹ or *n*-hexyl *p*-toluenesulfonate.¹⁰ The procedure used is based on that of Hoffmann¹¹ involving interaction at atmospheric pressure of anhydrous potassium fluoride with an alkyl halide in the presence of ethylene glycol as a solvent for the inorganic halide; a small amount of olefin accompanies the alkyl fluoride produced and is readily removed by treatment with bromine-potassium bromide solution.

The reaction of *n*-hexyl bromide with potassium fluoride in several glycols has been studied,¹² and the methods for the preparation of alkyl monofluorides have been reviewed.¹³

References and Notes

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

red phosphorus

bromide (24959-67-9)

bromine (7726-95-6)

hydrogen fluoride (7664-39-3)

ethylene glycol (107-21-1)

potassium bromide (7758-02-3)

n-HEXYL ALCOHOL (111-27-3)

magnesium sulfate (7487-88-9)

potassium fluoride (7789-23-3)

1-hexene (592-41-6)

Hexane, 1-fluoro-,
n-HEXYL FLUORIDE,
n-hexyl fluoride (373-14-8)

bromine-potassium bromide

Fluorine (7782-41-4)

mercurous fluoride (13967-25-4)

mercuric fluoride (7783-39-3)

silver fluoride (7775-41-9)

n-Nonyl fluoride (463-18-3)

n-hexyl bromide (111-25-1)

n-amyl fluoride (592-50-7)

n-hexyl methanesulfonate

n-hexyl p-toluenesulfonate (3839-35-8)

n-Heptyl fluoride

n-Octyl fluoride

n-Decyl fluoride

n-Undecyl fluoride

n-Dodecyl fluoride

n-Tetradecyl fluoride

n-Hexadecyl fluoride