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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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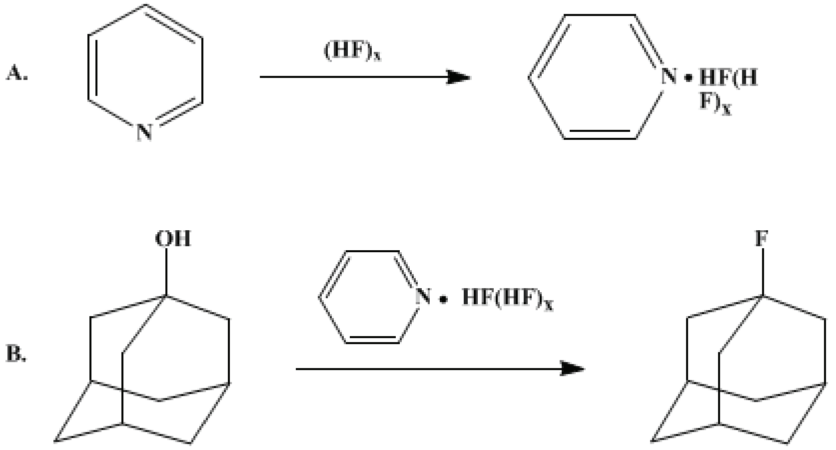
Organic Syntheses, Coll. Vol. 6, p.628 (1988); Vol. 58, p.75 (1978).

FLUORINATIONS WITH PYRIDINIUM POLYHYDROGEN FLUORIDE REAGENT: 1-FLUOROADAMANTANE

[Tricyclo[3.3.1.1^{3,7}]decane, 1-fluoro-]



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1. Procedure

> *Caution! Proper precautions must be used when handling anhydrous hydrogen fluoride and pyridinium polyhydrogen fluoride. Hydrogen fluoride is extremely corrosive to human tissue, contact resulting in painful, slow-healing burns. Laboratory work with HF should be conducted only in an efficient hood, with the operator wearing a full-face shield and protective clothing (Note 1).*

A. *Pyridinium polyhydrogen fluoride* (**1**). A tared, 250-ml., polyolefin bottle is equipped with a polyolefin gas-inlet and drying tube inserted through holes in the cap and sealed with Teflon tape. The bottle is charged with 37.5 g. (0.475 mole) of pyridine (Note 2) and cooled in an acetone–dry ice bath. After the pyridine has solidified, 87.5 g. (4.37 moles) of anhydrous hydrogen fluoride (Note 3) is condensed from a cylinder into the bottle through the inlet tube. The amount of hydrogen fluoride is determined by weighing the bottle. After the hydrogen fluoride has cooled, the bottle is cautiously swirled with cooling until the solid dissolves (Note 4). The solution can now be safely allowed to warm to room temperature.

B. *1-Fluoroadamantane* (**2**). A 250-ml., polyolefin bottle is equipped with a Teflon-coated magnetic stirring bar and a polyolefin drying tube inserted through a hole in the cap and sealed with Teflon tape. The bottle is charged with 5.0 g. (0.033 mole) of 1-adamantanol (Note 5) and 50 ml. of pyridinium polyhydrogen fluoride (**1**). The solution is allowed to stir for 3 hours at ambient temperature, after which 150 ml. of petroleum ether is added, and stirring is continued for another 15 minutes. The resulting two-phase solution is transferred to a 250-ml., polyolefin separatory funnel, and the bottom layer is discarded (Note 6). The organic layer is washed successively with 50 ml. of water, 50 ml. of a saturated sodium hydrogen carbonate solution and 50 ml. of water, then dried over magnesium sulfate. After the organic layer is filtered, the solvent is removed under reduced pressure (Note 7), yielding 4.5–4.6 g. (88–90%) of adamantane **2** as a white powder, m.p. 225–227° (sublimes in a sealed capillary) (Note 8), which can be purified by vacuum sublimation or by recrystallization from methanol-carbon tetrachloride.

2. Notes

1. The recommended first-aid for a hydrogen fluoride burn is to flood with water, pack with ice, and get medical attention as quickly as possible. Local medical personnel should be alerted and prepared when work with hydrogen fluoride is planned. Directions for proper medical treatment[2] are given in *Org. Synth.*, **Coll. Vol. 5**, 66 (1973).
2. The submitters used A.C.S. certified reagent grade pyridine from Fisher Scientific Company which was distilled from potassium hydroxide prior to use.
3. The submitters obtained anhydrous hydrogen fluoride from Harshaw Chemical Company, and the checkers purchased this reagent from Matheson Gas Products.
4. The dissolution is an extremely exothermic process that can be violent if the bath temperature is not carefully controlled at −78°. A preferred procedure developed by Dr. A. E. Feiring, Central Research and Development Department, Du Pont Experimental Station, involves keeping the pyridine as cold as possible without freezing (*ca.* −40°), then slowly condensing the hydrogen fluoride into the vessel so that the entire mixture remains liquid during the preparation. Stirring is also helpful.
5. This was obtained from Aldrich Chemical Company, Inc., and used without further purification.
6. The inorganic layer can be safely disposed by slow addition to large amounts of ice-cold water.
7. Since 1-fluoroadamantane sublimes easily, the water bath should be controlled at about 32°, and the vacuum evaporation of the solvent limited to as short a time as possible.
8. GC and IR analysis indicate no detectable amount of starting alcohol. ^{1}H NMR of adamantane **2** ($CDCl_3$) yields a series of multiplets centered at δ 1.62, 1.86, and 2.18.

3. Discussion

1-Fluoroadamantane can also be prepared by halogen exchange of the bromide with silver fluoride[3] or zinc fluoride.[4] The procedure described is more convenient and economical than the halogen exchanges, and has found successful application in the preparation of a wide variety of secondary and tertiary fluorides from the corresponding alcohols, with yields generally within the range of 70–90%[5] (Table I).

TABLE I

PREPARATION OF TERTIARY- AND SECONDARY-ALKYL FLUORIDES FROM ALCOHOLS WITH HYDROGEN FLUORIDE–PYRIDINE REAGENT

Alcohol	Temperature	Reaction Time (hours)	Alkyl Fluoride	b.p.(m.p.)	Yield (%)
Isopropyl	50	3.0	Isopropyl	−9 to −7	30
sec-Butyl	20	3.0	*sec*-Butyl	25–26	70
tert-Butyl	0	1.0	*tert*-Butyl	12	50
3-Ethyl-3-pentyl	0	0.5	3-Ethyl-3-fluoropentane	30–33 (60 mm.)	95
3-Methyl-3-heptyl	−70	0.5	3-Fluoro-3-methylheptane	35 (40 mm.)	85
3-Methyl-4-heptyl	0	2.0	4-Fluoro-3-methylheptane		35
Cyclohexyl	20	2.0	Cyclohexyl fluoride	100–102	99
2-Norbornyl	20	1.0	2-Fluoronorbornane	(56–59)	95
2-Adamantyl	20	0.5	2-Fluoroadamantane	(254–255)	98
α-Phenylethyl	20	0.5	1-Fluoro-1-phenylethane	46 (15 mm.)	65

The hydrogen fluoride–pyridine reagent is an effective complement to the dimethylaminosulfur trifluoride (DAST) reagent[6] in the preparation of alkyl fluorides from alcohols. DAST is also useful for the conversion of carbonyl groups to difluoromethylene functions. The hydrogen fluoride–pyridine reagent, however, can also be used for the hydrofluorination of alkenes,[7] alkynes,[7] cyclopropanes,[7] and diazo compounds,[8] the halofluorination of alkenes,[9] the preparation of fluoroformates from carbamates,[10] the preparation of α-fluorocarboxylic acids from α-amino acids,[11] and as a deprotecting reagent in peptide chemistry.[12] Examples of the hydrofluorination of alkenes with hydrogen fluoride–pyridine are given in Table II.

TABLE II

HYDROFLUORINATION OF ALKENES WITH HYDROGEN FLUORIDE-PYRIDINE REAGENT

Alkene	Reaction Temperature	Product	b.p.(m.p.)	Yield (%)
Propene	20	Isopropyl fluoride	−11 to −9	35
Cyclopropane	20	*n*-Propyl fluoride	−3 to −1	75
2-Butene	0	*sec*-Butyl fluoride	24–25	40
2-Methylpropene	0	*tert*-Butyl fluoride	11–13	60
Cyclopentene	0	Cyclopentyl fluoride	51–52 (200 mm.)	65
Cyclohexene	0	Cyclohexyl fluoride	102–104	80
Cycloheptene	0	Cycloheptyl fluoride	70–71 (200 mm.)	90
Norbornene	0	2-Fluoronorbornane	(56–59)	65
1-Hexyne	0	2,2-Difluorohexane	85–87	70
3-Hexyne	0	3,3-Difluorohexane	84–86	75

References and Notes

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

petroleum ether

PYRIDINIUM POLYHYDROGEN FLUORIDE

alcohol (64-17-5)

sodium hydrogen carbonate (144-55-8)

Propene (115-07-1)

Cyclohexene (110-83-8)

hydrogen fluoride (7664-39-3)

pyridine (110-86-1)

potassium hydroxide (1310-58-3)

cyclopropane (75-19-4)

magnesium sulfate (7487-88-9)

Cyclopentene (142-29-0)

Cyclohexyl (3170-58-9)

isopropyl (2025-55-0)

2-Methylpropene (9003-27-4)

1-Hexyne (693-02-7)

difluoromethylene

Cyclohexyl fluoride (372-46-3)

silver fluoride (7775-41-9)

α-Phenylethyl (2348-51-8)

Norbornene

Adamantane (281-23-2)

1-Adamantanol (768-95-6)

tert-BUTYL (1605-73-8)

cycloheptene

2-butene

1-Fluoroadamantane,
Tricyclo[3.3.1.1^{3,7}]decane, 1-fluoro- (768-92-3)

methanol-carbon tetrachloride

zinc fluoride (7783-49-5)

dimethylaminosulfur trifluoride (3880-03-3)

3-Ethyl-3-pentyl

3-Ethyl-3-fluoropentane

3-Methyl-3-heptyl

3-Fluoro-3-methylheptane

3-Methyl-4-heptyl

4-Fluoro-3-methylheptane

2-Norbornyl (30967-37-4)

2-Fluoronorbornane

2-Adamantyl (21517-94-2)

2-Fluoroadamantane (16668-83-0)

1-Fluoro-1-phenylethane

Isopropyl fluoride (420-26-8)

Cyclopentyl fluoride (1481-36-3)

Cycloheptyl fluoride

2,2-Difluorohexane

3-Hexyne (928-49-4)

3,3-Difluorohexane

sec-butyl (2348-55-2)

n-Propyl fluoride (460-13-9)

sec-Butyl fluoride

tert-Butyl fluoride