methyltin group as in 2, the remaining chlorine can be replaced by a second trimethyltin group about a thousand times as fast as the first. This accounts for the fact that 2 cannot be prepared from methylene chloride by reaction with 1 equiv of (trimethylstannyl)alkali.

It has been shown that vicinal dihalides react with $Me_3SnNa$ to form alkenes by dehalogenation.[10] Kinetic studies were conducted to determine whether the elimination occurred primarily due to a strong driving force for the $E_2$ process or to large deactivation of the $S_N2$ process. The rate for 1,2-dichloropropane in entry 15 is four times greater than that for 1-chlorobutane, showing that the dominant driving force is enhancement of the formal abstraction of a halogen cation by the stannyl anion in the $E_2$ dehalogenation mechanism. This is also evident for 2,3-dichloropropene (entry 15) which reacted with $Me_3SnLi$ at a rate too fast to measure. It was established that the only $C_3$ product was allene.

The foregoing results firmly establish the supernucleophilic behavior of silyl and stannyl anionoids.[12] They also reveal unexpectedly high selectivity toward typical organic chlorides, as well as the extremely high reactivity as $S_N2$ substrates of chlorides bearing a silyl or stannyl group on the carbinyl carbon. With these substrates, however, the selectivity is more nearly "normal" in that iodide reacts with 2 about 360 times as fast as with 1; the corresponding factor is 140 for $Me_3SnLi$ and 195 for $Vi_3SnLi$. Further study of the kinetics of these and other supernucleophiles with various substrates should contribute to our understanding of these and other structure/reactivity and reactivity/selectivity relationships.

## Experimental Section

**General.** Halides were commercial samples if available or were prepared by standard methods. They were carefully distilled, checked for purity (>99%), and stored under argon before use. THF was dried and purified by distillation from calcium hydride and then from $LiAlH_4$ through a 12-in. packed column under argon. All reactions were conducted under argon using apparatus dried in the oven at 110 °C overnight. Reaction products were checked for identity by a comparison with authentic samples. NMR spectra were taken on a Varian EM360 instrument. GC/MS spectra were obtained with a Finnigan GC/MS data system series 9500/1015D/6000 using a $^1/_4$ in. × 8 ft stainless steel column packed with 10% SE-30 on Anakrom ABS.

The stopped flow system consisted of two pneumatically driven drive syringes, an eight-jet mixing chamber, and a 1-cm viewing cell of Kellef with quartz windows enclosed in a chamber through which water at 20 °C was circulated from a constant temperature bath. A Beckmann DU monochromator was used and a Dumont 1P28 photomultiplier tube (PMT) was used to collect transmitted light. The output was digitalized and collected by using a Kim-1 microcomputer. A General Radio 1191-Z counter was used to determine rates of data acquisition, which could range up to 6100 $s^{-1}$. The raw data could be viewed on an oscilloscope and processed on a mainframe computer (Univac 1110). Data were collected at 360 nm on the tail of the (organostannyl)lithium absorption band, thus permitting maximum initial concentrations of about 0.007 M to be viewed by the instrument. Concentrations of halide were always at least 10 times that of the organotinlithium, so pseudo-first-order kinetics were observed. At infinite time 100% trasmittance was observed in all experiments. Data were processed by the normal method and the Guggenheim method. Satisfactory agreement in the values of the rate constants were observed; if not, the data were not used. The reliability of the system was checked by using the reaction of tris(*o*-phenanthroline)ferrous sulfate with ceric sulfate in 0.5 M $H_2SO_2$ at 20 °C studied earlier by Sutin and Dulz.[13] Their rate constant at 25 °C, along with an activation energy of 6.50 kcal/mol, yielded a value of $1.18 \times 10^{-5}$ $M^{-1}$ $s^{-1}$ at 20 °C compared with our measured value of 1.09 $M^{-1}$ $s^{-1}$.

**Preparation of (Trialkylstannyl)lithiums.** A Schlenk tube filled with argon was charged with 1.88 mL of 1.65 M *n*-butyllithium (3.10 mmol) in hexane. The solvent was removed by evacuation with a vacuum pump, leaving a yellow oil. It was cooled to 0 °C and 6.0 mL of THF containing 3.11 mmol of hexamethylditin was added, yielding a pale yellow-green solution of (trimethylstannyl)lithium. This stock solution (0.45 M) was then diluted appropriately for charging the syringe of the stopped flow system which was done without exposure to air. (Trivinylstannyl)lithium was prepared in the same way from hexavinylditin.[14]

**Reaction of 2,2-Dichloropropane with (Trimethylstannyl)lithium.** A reaction between 0.38 M dichloride and 0.31 M (trimethylstannyl)lithium was conducted in THF at 0 °C. GC/MS analysis of the product mixture revealed peaks assigned to 2-chloropropane, isopropenyltrimethyltin, isopropyltrimethyltin, 2,3-bis(trimethylstannyl)propane, and hexamethylditin. When the same reaction was conducted in the presence of 1.6 M dicyclohexylphosphine, the yield of 2-chloropropane increased from 8.2% to 32%, that of hexamethylditin increased from 52% to 84%, and the yields of the other three products dropped to zero.

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(10) Kuivila, H. G.; Choi, Y. M. *J. Org. Chem.* **1979**, *44*, 4774.
(11) Kuivila, H. G.; Reeves, W. G. *Bull. Soc. Chim. Belg.* **1980**, *89*, 801.
(12) Dessy has shown that $Ph_3S^-$-*n*-$Bu_4N^+$ reacts with a biomolecular rate constant of 22 $M^{-1}$ $s^{-1}$ with ethyl bromide: Dessy, R. E.; Pohl, R. L.; King, R. B. *J. Am. Chem. Soc.* **1966**, *88*, 5121.
(13) Sutin, W.; Dulz, G. *Inorg. Chem.* **1963**, *2*, 917.
(14) We thank Todd McComb for preparing this compound.

# Unusual β-Fluorination of Secondary Alkyl and Cycloalkyl Bromides in Their Reaction with $NO_2^+BF_4^-$ in $(HF)_n$-Pyridine Solution[1]

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## Introduction

Halogen exchange fluorination of aliphatic halides is a widely used synthetic reaction.[2] The majority of cyclic halides, however, undergo elimination under the reaction conditions to give olefins. Recently Yoneda and coworkers[3] have reported halogen exchange fluorination of cyclic and acyclic halides without concommitant elimination by using cuprous oxide in anhydrous HF/THF (or ether) solution. In our continued investigation of the utility of the pyridinium polyhydrogen fluoride reagent,[4] we reported that bridgehead adamantyl and diamantyl halides undergo halogen exchange fluorination in the

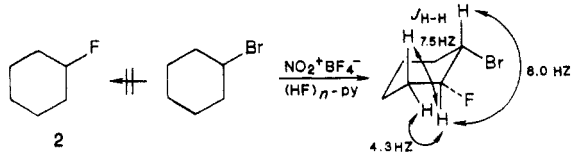
(1) Synthetic Methods and Reactions. 128. For part 127, see: Olah, G. A.; Ohannesian, L.; Arvanaghi, M. *Synthesis* **1986**, 868.
(2) Banks, R. E. *Organofluorine Chemicals and Their Industrial Applications*; Ellis Horwood Ltd: Chichester, 1979. Ishikawa, N. *Halogen Chemicals No Saisentan*; CMC: Tokyo, 1980. Gerstenberger, M. R. C.; Haas, A. *Angew. Chem., Int. Ed. Engl.* **1981**, *20*, 647.
(3) Yoneda, N.; Fukuhara, T.; Nagata, S.; Suzuki, A. *Chem. Lett.* **1985**, 1693.
(4) For a recent review, see: Olah, G. A.; Shih, J. G.; Prakash, G. K. S. *J. Fluorine Chem.* **1986**, *33*, 377.

0022-3263/87/1952-0931$01.50/0 

presence of $NO_2^+BF_4^-$ with $(HF)_n$–pyridine.[5,6] Under the same reaction conditions, however, secondary 2-haloadamantanes gave instead of halogen–fluorine exchange preferentially 2-adamantanone.[5] Prompted by this unusual reaction,[6] we now report that cyclic and acyclic bromides in the presence of $NO_2^+BF_4^-$ in $(HF)_n$–pyridine solution give unexpected β-fluorination.

## Results and Discussion

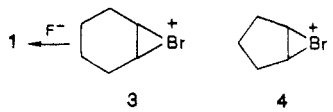
1-Bromocyclohexane, when treated with an equivalent of $NO_2^+BF_4^-$ in an excess of $(HF)_n$–pyridine at −5 °C for 15 h, gave, upon usual workup, *trans*-1-bromo-2-fluorocyclohexane (**1**) as the sole product in 69% isolated yield. None of the expected halogen exchange product, i.e., 1-fluorocyclohexane (**2**), was obtained.




2 1

The structure of **1** was confirmed by its $^{13}C$ NMR spectrum [$\delta(^{13}C)$ $C_2$ = 93.6, $J_{C-F}$ = 179.4 Hz; $C_1$ = 52.2 ($J_{C-C-F}$ = 19.5 Hz)]. Further confirmation of the trans geometry came from selective homonuclear decoupling experiments, providing $^1H$–$^1H$ coupling constants consistent with the proposed structure **1**. The same product **1** was obtained by using either $NO^+BF_4^-$ or $NaNO_3$ in $(HF)_n$–pyridine.

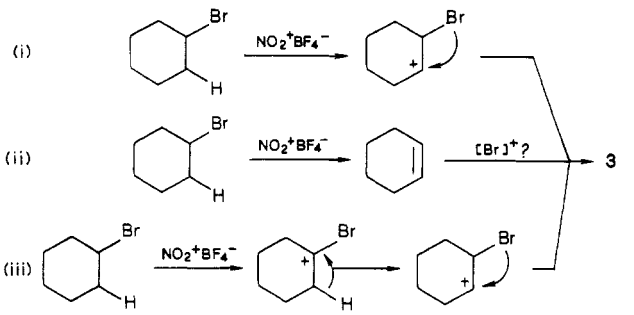
The unexpected formation of *trans*-1-bromo-2-fluorocyclohexane (**1**) is rather interesting. The trans stereochemistry suggests that a cyclic bromonium ion (**3**) may be involved as a reaction intermediate. Such a cyclic bromonium ion in a cyclopentane skeleton, i.e., the cyclopentene bromonium ion (**4**), has earlier been characterized by one of us[7] under stable ion conditions. The cyclic bromonium ion (**3**) could then react with $F^-$ ion to give the trans product **1**.

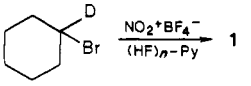



3 4

How can the cyclic bromonium ion (**3**) be formed under the reaction conditions? It is well-known that nitronium and nitrosonium ions are good hydride abstracting agents.[8,9] In fact, recently we used[9] such a hydride abstraction to prepare 1-fluoroadamantane and 1-fluorodiamantane from their hydrocarbon precursors in $(HF)_n$–pyridine. Based on these observations, one can suggest following three alternative mechanistic paths for the formation of the trans product **1** through the intermediacy of **3**: (i) β-hydride abstraction followed by cyclization, (ii) dehydrobromination to cyclohexene followed by $Br^+$ attack, (iii) α-hydride abstraction followed by 1,2-hydride shift and cyclization.

To distinguish the first two mechanisms [(i) and (ii)] from the third [(iii)] we prepared 1-bromo-1-deuteriocyclohexane (**5**) using standard procedures. Treatment of **5** with $NO_2^+BF_4^-$ in $(HF)_n$–pyridine under identical conditions gave product **1** with no deuterium in the product, clearly supporting mechanism iii. The other two alternative mechanistic paths should leave significant amount of deuterium in the product. Furthermore, the recovered starting material in an incomplete reaction (reaction mixture quenched after 3 h) contained all the deuterium at the α-position, clearly supporting mechanism iii. Also under the reaction conditions monodeuteriocyclohexane does not undergo deuterium–hydrogen exchange, clearly ruling out the other two mechanisms.




5

Attempted reaction with 1-chlorocyclohexane did not give any fluorinated product, and the starting chloro compound was recovered intact. However, 1-iodocyclohexane under similar conditions gave 1-fluorocyclohexane (**2**), the usual halogen exchange product, in about 30% yield. The discussed β-fluorination reaction seems to take place only with secondary bromides. Results of related reactions with other cyclic and acyclic secondary bromides are listed in Table I. The yields of the vicinal bromofluoro products are moderate to good. In the case of 2-bromobutane a diastereomeric pair of products was obtained in an approximately 2:1 ratio. 2-Bromohexane gives 2 sets of diastereomeric pairs, indicating a lack of regioselectivity in this reaction. No reaction takes place with primary bromides. For example, attempted reaction of 1-bromooctane led to the recovery of the starting compound.

In conclusion, secondary alkyl and cycloalkyl bromides give, unexpectedly, vicinal bromofluoro compounds when reacted with $NO_2^+BF_4^-$ in $(HF)_n$–pyridine. The reaction proceeds through the intermediacy of cyclic bromonium ions. The unusual keto product obtained earlier[5] in the reaction of 2-bromo(halo)adamantane can now be easily rationalized. The rigidity of the locked chair-cyclohexane rings in adamantane cage ensures an unfavorable dihedral angle between $C_1$ and $C_2$ positions, preventing a 1,2-hydrogen shift.

## Experimental Section

**Caution**: Extreme care should be exercised[10] while handling the $(HF)_n$–pyridine reagent. Hydrogen fluoride is extremely corrosive to human tissue.

The halides employed were commercially available from Aldrich and were used as received. $NO_2^+BF_4^-$ and $NO^+BF_4^-$ salts were also purchased from Aldrich. $(HF)_n$–pyridine (70:30) was prepared from anhydrous HF and pyridine as earlier reported.[11] The $^1H$, $^{19}F$, and $^{13}C$ NMR spectra were obtained on a Varian XL-200

(5) Olah, G. A.; Shih, J. G.; Singh, B. P.; Gupta, B. G. B. *Synthesis*, **1983**, 713.
(6) Krishnamurthy, V. V.; Shih, J. G.; Singh, B. P.; Olah, G. A. *J. Org. Chem.* **1986**, *51*, 1354.
(7) Olah, G. A.; Liang, G.; Staral, J. *J. Am. Chem. Soc.* **1974**, *96*, 8112.
(8) Olah, G. A.; Salem, G.; Staral, J.; Ho, T. L. *J. Org. Chem.* **1978**, *43*, 173.
(9) Olah, G. A.; Shih, J. G.; Singh, B. P.; Gupta, B. G. B. *J. Org. Chem.* **1983**, *48*, 3356.
(10) (a) Olah, G. A.; Watkins, M. *Org. Synth.* **1978**, *58*, 75. (b) Sharts, C. M.; Sheppard, W. A. *Org. React. (N.Y.)* **1974**, *21*, 192, 220–223.
(11) Olah, G. A.; Welch, J. T.; Vankar, Y. D.; Nojima, M.; Kerekes, I.; Olah, J. A. *J. Org. Chem.* **1979**, *44*, 3872.

Table I. Preparation of Trans Vicinal Fluoro-Bromo Compounds

| substrate | reactn conditions[f] | product | yield,[a] % | bp °C/mm (lit.) | δ(¹⁹F) NMR[d] | δ(¹³C) NMR[e] |
|---|---|---|---|---|---|---|
|  | 1, 0 |  | 35 | 41–44/21 | 160.6 (m) | $C_2$ = 100.2 ($J_{C-F}$ = 179.4 Hz), $C_1$ = 52.7 ($J_{C-C-F}$ = 27.7 Hz), $C_4$ or $C_5$ = 33.9, $C_4$ or $C_5$ = 21.2, $C_3$ = 29.7 ($J_{C-C-F}$ = 20.7 Hz) |
|  | 15, −5 |  | 69 | 75–77/11 (30/11)[12] | 169.3 (dd) | $C_2$ = 93.6 ($J_{C-F}$ = 179.4 Hz), $C_1$ = 52.2 ($J_{C-C-F}$ = 19.5 Hz), $C_6$ = 34.5 ($J_{C-C-C-F}$ = 3.7 Hz), $C_5$ = 24.6, $C_4$ = 22.4 ($J_{C-C-C-F}$ = 8.6 Hz), $C_3$ = 30.9 ($J_{C-C-F}$ = 19.1 Hz) |
|  | 20, −5 |  | 39 | 70–73/3.5 | 161.3 (m) | $C_2$ = 98.1 ($J_{C-F}$ = 175.1 Hz), $C_1$ = 56.1 ($J_{C-C-F}$ = 23.6 Hz), $C_7$ = 33.8 ($J_{C-C-C-F}$ = 5.6 Hz), $C_5$ or $C_6$ = 27.2, $C_5$ or $C_6$ = 24.6, $C_4$ = 20.7 ($J_{C-C-C-F}$ = 4.4 Hz), $C_3$ = 31.3 ($J_{C-C-F}$ = 22.0 Hz) |
|  | 5, 0 |  | 58[b] | | 171.6 (m), 175.6 (m) | $C_4$ = 19.5 ($J_{C-C-F}$ = 19.4 Hz), 19.4 ($J_{C-C-F}$ = 25.5 Hz), $C_3$ = 93.8 ($J_{C-F}$ = 174.5 Hz), 93.1 ($J_{C-F}$ = 175.5 Hz), $C_2$ = 52.4 ($J_{C-C-F}$ = 23.4 Hz), $C_1$ = 22.8 ($J_{C-C-C-F}$ = 3.0 Hz), 22.5 ($J_{C-C-C-F}$ = 5.7 Hz) |
|  | 15, −5 |  | 60[c] | | 169.6 (m), 176.1 (m), 181.6 (cm) | too complex to assign |
| $CH_3(CH_2)_6CH_2Br$ | no reaction | | 0 | | | |

[a] Isolated and purified product. [b] Mixture of diastereomers in 2:1 ratio. [c] Mixture of regioisomers with diastereomeric pairs. [d] In ppm (upfield) from external $CFCl_3$, dd = doublet of doublet, m = multiplet, cm = complex multiplet. [e] In ppm downfield from tetramethylsilane. [f] Time (h), temperature (°C).

NMR spectrometer. The boiling points reported are uncorrected. All manipulations were done in polyethylene ware since $(HF)_n$–pyridine is corrosive to glass.

**1-Bromo-2-fluorocyclohexane (1) from 1-Bromocyclohexane.** To a stirred solution of $NO_2^+BF_4^-$ (6.64 g, 50 mmol) in 30 mL of $(HF)_n$–pyridine (70:30) in a 200-mL polyethylene bottle at −5 °C under a dry nitrogen atmosphere was added dropwise 1-bromocyclohexane (6.52 g, 40 mmole) over a period of 10 min. The reaction mixture was stirred at −5 °C for 15 h and was then poured into ice–water (200 mL). The resulting mixture was extracted with ether (2 × 200 mL), and the combined ethereal extract was washed several times with 10% aqueous $NaHCO_3$ solution followed by brine solution until neutral. The neutral ether extract was dried over anhydrous $Na_2SO_4$ and concentrated in vacuo. The remaining residue was distilled under vacuum to provide pure *trans*-1-bromo-2-fluorocyclohexane (1), bp 75–77 °C/11 mmHg[12] (5.0 g, 69%).

**Preparation of 1-Bromo-1-deuteriocyclohexane (5). 1-Deuterio-1-cyclohexanol.** A solution of cyclohexanone (9.82 g, 0.01 mol) in ether (15 mL) was added slowly to a suspension of lithium aluminum deuteride (2.31 g, 0.055 mol) in ether (100 mL) so as to maintain a gentle reflux. The reaction mixture was refluxed for 0.5 h and then poured into aqueous 10% $H_2SO_4$ solution and extracted with ether (200 mL). The extract was washed with water, aqueous saturated $NaHCO_3$ solution, water, and brine, dried over $MgSO_4$, and evaporated in vacuo. The crude product was distilled under reduced pressure to give the deuterio alcohol as a colorless oil, bp 61–63 °C/7 mmHg (7.9 g, 78%).

**1-Deuterio-1-cyclohexyl *p*-Toluenesulfonate.** To a solution of 1-deuterio-1-cyclohexanol (1.85 g, 18.3 mmol) in pyridine (75 mL) was added *p*-toluenesulfonyl chloride (3.49 g, 18.3 mmol). The mixture was stirred at room temperature for 24 h, poured into ice–water, and extracted with ether. The extract was washed with aqueous 10% HCl solution and water, dried over $Na_2SO_4$, and concentrated to give the *p*-toluenesulfonate as an oil, which was used in the next step without further purification (3.7 g, 81%).

**1-Bromo-1-deuteriocyclohexane (5).** A mixture of dry LiBr (1.22 g, 14.1 mmol) and 1-deuterio-1-cyclohexyl *p*-toluenesulfonate (3.0 g, 14.1 mmol) in hexamethylphosphoramide (18 mL) was heated at 150 °C under vacuum (25 mmHg) and the volatile product was trapped in an acetone–dry ice bath. Purification by redistillation gave **5** (300 mg) as a colorless oil: bp 53–54 °C/20 mmHg; $^{13}C$ NMR ($CDCl_3$, ambient) δ 53.2 ($J_{C-D}$ = 23.1 Hz), 37.3, 25.8, and 25.0.

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(12) Bowers, A.; Ibanez, L. C.; Denot, E.; Becerra, R. *J. Am. Chem. Soc.* **1960**, *82*, 4001.

## Chemical Behavior of (+)-(1*R*,3*S*)-1,2,2-Trimethyl-1,3-bis(hydroxymethyl)cyclopentane upon Attempted Halogenation. Formation of (+)-(1*S*,3*S*)-1-Bromo-3-(bromomethyl)-1,2,2-trimethylcyclohexane

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In an earlier report,[1] we pointed out the desirability of finding a convenient synthesis of (+)-(1*R*,3*S*)-1,2,2-trimethyl-1,3-bis(bromomethyl)cyclopentane (1) from the readily available glycol (+)-(1*R*,3*S*)-1,2,2-trimethyl-1,3-

(1) Erickson, G. W.; Fry, J. L. *J. Org. Chem.* **1980**, *45*, 970–972.

0022-3263/87/1952-0933$01.50/0 