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Articles

Generation of Interhalogen Fluorides under Mild Conditions: A Comparison of Sluggish and Reactive Interhalogen Fluorides‡

Dale F. Shellhamer,* Mark J. Horney, Benjamin J. Pettus, Tobiah L. Pettus,
Joy Merry Stringer, and Victor L. Heasley

Department of Chemistry, Point Loma Nazarene University, San Diego, California 92106-2899

Robert G. Syvret and John M. Dobrolsky, Jr.

Fluorine Technology Center, Air Products and Chemicals, Inc., Allentown, Pennsylvania 18195-1501

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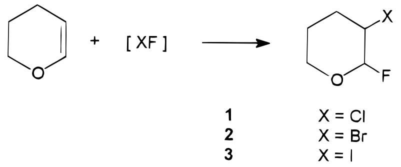
Interhalogen fluorides (XF; X = I, Br, or Cl) generated from xenon difluoride (XeF_2) or triethylamine trihydrofluoride (TREAT HF) with iodine (I_2), *N*-halosuccinimides (NXS; X = I, Br, or Cl), or alkylhypohalites (ROX; R = CH_3 or *t*-Bu, X = Br or Cl) with alkenes and aromatics are reported. A comparison of the above reactions with other methods reported in the literature to generate interhalogen fluorides is made. Interhalogens generated from direct action of elemental fluorine (F_2) or XF_3 (X = I, Br, or Cl) with chlorine (Cl_2), bromine (Br_2), or iodine (I_2) give a species that can react with electron-deficient alkenes or aromatics. These reagents are too reactive for electron-rich substrates. Interhalogen fluorides from reagents like NXS or ROX with XeF_2 or amine HF are much less reactive and give good yields with electron-rich akenes or aromatics.

Halofluorination of alkenes is an extremely useful method for incorporating fluorine into organic molecules.[1] The importance of organofluorides both biologically and medicinally is well recognized.[2] Recently, we reported on the reaction of xenon difluoride (XeF_2) with iodine (I_2) or *N*-iodosuccinimide (NIS) in the presence of alkenes and/or aromatics, and demonstrated that iodofluorination of the alkenes and iodination of the aromatics occurred in good yield.[3] This procedure was not applicable to the reaction of XeF_2 with Br_2 or Cl_2 because these halogens reacted too rapidly with the alkenes. We also reported in an earlier paper that XeF_2 reacts with *tert*-butyl hypochlorite (*t*-BuOCl) in the presence of cyclohexene to give a good yield of *trans*-1-chloro-2-fluorocyclohexane.[4] In both papers, we suggest a complex that delivers a "sluggish electrophile" XF (X = I or Cl) to the unsaturated hydrocarbon.

In this paper, we report on a new, mild reaction for generating chloro- and bromomonofluorides (ClF, BrF) from hypohalites (MeOX and *t*-BuOX; X = Cl or Br) and XeF_2 or triethylamine trihydrofluoride [$(Et)_3N{\cdot}3HF$]. We also compare the reactivities and synthetic utility of "sluggish" interhalogen fluorides prepared from amine hydrogen fluorides, fluoride salts, and XeF_2 with "reactive" interhalogen fluorides generated from fluorine gas or halogen trifluoride (XF_3, X = I, Br, or Cl).

Results

Data for the reaction of hypohalites with triethylamine trihydrofluoride in the presence of alkenes are given in Table 1. Reactions were carried out in both methylene chloride and hexane to show that these reactions can be accomplished in nonpolar and polar aprotic solvents. The yield is poor with the alkyne 3-hexyne because it is an unreactive substrate. Excellent yields are obtained with more reactive alkenes and these sluggish interhalogen fluorides. Yields are excellent even with the very reactive substrate 3,4-dihydro-2*H*-pyran (Table 2). Compound **1** was isolated by bulb-to-bulb distillation. Compounds **2** and **3** decomposed during bulb-to-bulb distillation at room temperature and were characterized by GC−MS and NMR data from their crude reaction mixtures.



Reactions of *t*-BuOX (X = Cl or Br) and triethylamine trihydrofluoride or XeF_2 with an electron-rich aromatic such as anisole give a moderate yield of aromatic halogen

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* To whom correspondence should be addressed: Ph: (619) 849-2207. Fax: (619) 849-2598. E-mail: dshellha@ptloma.edu.

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(3) Shellhamer, D. F.; Jones, B. C.; Pettus, B. J.; Pettus, T. L.; Stringer, J. M.; Heasley, V. L. *J. Fluorine Chem.* **1998**, *88*, 37. A minimum amount of nonpolar solvent must be used such that a two-phase system (solid−liquid) is formed for the reaction of I_2 or NIS with XeF_2. No products are formed in a homogeneous solution with this reaction or in a polar solvent such as acetonitrile.

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Table 1. Reactions of Hypohalites with Triethylamine Trihydrofluoride

alkene	solvent	yield[a] (%) t-BuOCl	 CH_3OCl	 t-BuOBr
cyclohexene[b]	CH_2Cl_2	90	100	95
cyclohexene[b]	hexane	65	40	20
methylenecyclohexane[c]	CH_2Cl_2	55[d]	80[d]	45[d]
methylenecyclohexane[c]	hexane	45[d]		
3-hexene[e]	CH_2Cl_2	90	90	85
3-hexene[e]	hexane	55	25	45
1-hexene[f]	CH_2Cl_2	40	25	50
1-hexene[f]	hexane	45	20	20
styrene[g]	CH_2Cl_2	70[d]	90[d]	80[d]
3-hexyne[h]	CH_2Cl_2	15	15	20
3-hexyne[h]	hexane	15	15	10

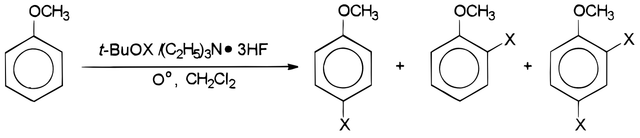
[a] Percent yield by GC with chlorobenzene as internal standard corrected for flame response, except where noted. [b] Product *trans*-1-halo-2-fluorocyclohexane. [c] Product 1-fluoro-1-halomethylcyclohexane. [d] Percent yield by NMR with ethylene chloride or benzene as internal standard. [e] Product 3-fluoro-4-halohexane. [f] Major regioisomer 1-halo-2-fluorohexane (~87%). [g] Product 2-fluoro-1-halo-2-phenylethane. [h] Product *trans*-3-fluoro-4-halohex-3-ene.

Table 2. Halofluorination of 3,4-Dihydro-2*H*-pyran

reagents	product[a]	ratio[b] *trans*:*cis*	yield[c] (%)
t-BuOCl/$(C_2H_5)_3N{\cdot}3HF$	**1**	79:21	70
t-BuOCl/XeF_2	**1**	51:49	10
NCS/$(C_2H_5)_3N{\cdot}3HF$[d]	**1**	79:21	80
NBS/$(C_2H_5)_3N{\cdot}3HF$[d]	**2**	97:3	85
NIS/$(C_2H_5)_3N{\cdot}3HF$[d]	**3**	98:2	85

[a] Products are 1-fluoro-2-halotetrahydropyran. [b] Ratio by GC with F. I. D. detector. [c] By NMR on crude reaction mixture with benzene as internal standard. [d] Data obtained from reaction procedures described in the literature. See ref 12c.

Table 3. Electrophilic Aromatic Substitution with Anisole



reagents	yield (%) A	 B	 C
t-BuOBr/$(C_2H_5)_3N{\cdot}3HF$; 0°	45	25	5
t-BuOCl/$(C_2H_5)_3N{\cdot}3HF$; 0°	65	4	
t-BuOBr/XeF_2; 25°	40	5	
t-BuOCl; dark/XeF_2; 25°	46	7	1−2

substitution products (Table 3). Less reactive aromatics gave poor yields or did not give products with these reagents.

Discussion

Interhalogen fluorides (XF; X = Cl or Br) generated from hypohalites and triethylamine trihydrofluoride or hypohalites and XeF_2[4,5] are sluggish electrophiles, and they are even less reactive than Cl_2 or bromine monochloride (BrCl).[6] For example, ClF from ROCl (R = Me or *t*-Bu) and triethylamine trihydorfluoride or XeF_2 does not react with alkenes that have electron-deficient π-bonds, such as methyl methacrylate. However, BrCl[6a] and ClF generated from elemental fluorine[7] readily react with methyl methacrylate and other electron-deficient alkenes via an ionic pathway in aprotic solvent. This low reactivity and the *unusual minor products* from the reaction of XeF_2 and *t*-BuOX (X = Cl or Br) with cyclohexene led us to propose a complex that delivers ClF to the unsaturated hydrocarbon.[4,5] A sluggish electrophile was also found for reaction of IF with alkenes or aromatics from XeF_2 and I_2 or NIS.[3] The heterogeneous phase (solid−liquid) requirement for the formation of iodofluorination products with XeF_2 also seems to suggest a complex that delivers IF to the substrate,[3] because IF generated from iodine and fluorine[8] gas or iodine trifluoride[9c] is a very reactive species.

Reactions of XF with aromatics also show this difference in reactivity. Electrophilic substitution products are produced in moderate yield from amine hydrogen fluorides or XeF_2 and hypohalites with anisole (Table 3) and in good yield from XeF_2/I_2 or NIS with anisole.[3] In contrast, reaction of anisole and IF generated from iodine and fluorine gas gives only tar even at −78°.[8e] Also, substitution of bromine occurs readily without a catalyst with *m*-dinitrobenzene and BrF generated from bromine and fluorine gas.[10] *m*-Dinitrobenzene does not react with the sluggish BrF generated from amine hydrogen fluorides or XeF and alkyl hypohalites or *N*-halosuccinimides, as demonstrated for anisole in Table 3.

Relative rate studies also suggest there is a difference between XF generated from fluorine gas or halogen trifluorides compared with other methods. For example, 2-methyl-2-pentene reacts ca. 1.7−3.8 (see Experimental Section) times faster than 1-hexene for reaction of XF generated from fluorine gas. Reactions to generate XF from hypohalites or *N*-halosuccinimides show that 2-methyl-2-pentene reacts 10−33 times faster than 1-hexene except for reactions of *t*-BuOCl and NCS with triethylamine trihydrofluoride, which show rate enhancements of only 4 and 3, respectively. Although these data support our claim of a complex that delivers XF as a sluggish electrophile, they are not definitive because some reactions do not follow the reactivity−selectivity principle.[11] This may account for the low selectivity (4, 3) for reactions of *t*-BuOCl and NCS with $(C_2H_5)_3{\cdot}3HF$.

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(5) Reaction of *t*-BuOBr with XeF_2 and cyclohexene was carried out (90% yield) as described for *t*-BuOCl.[4] Products were *trans*-1-bromo-2-fluorocyclohexane, *trans*-2-bromocyclohexanol, *trans*-1-bromo-2-*tert*-butoxy cyclohexane, *trans*-1-bromo-2-methoxy cyclohexane, and allylic halides in a ratio of 5:3:2:1:1, respectively.

(6) These electrophiles (BrCl and Cl_2) readily react with unreactive substrates. See: (a) Heasley, V. L.; Spaite, D. W.; Shellhamer, D. F.; Heasley, G. E. *J. Org. Chem.* **1979**, *44*, 2608. (b) Shellhamer, D. F.; Heasley, V. L.; Foster, J. E.; Luttrull, J. K.; Heasley, G. E. *J. Org. Chem.* **1977**, *42*, 2141.

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Comparison of Halofluorination Reactions

Literature methods to generate XF (X = Cl, Br, or I) include:

(a) Reaction of *N*-halosuccinimides (NXS; X = Cl, Br, or I) with hydrogen fluoride−pyridine ($(Py(HF)_x)$),[12a] anhydrous hydrogen fluoride,[12b] or triethylamine trihydrofluoride $[(C_2H_5)_3N{\cdot}3HF]$.[12c]

(b) Reaction of alkyl hypohalites (ROX; R = *t*-Bu or CH_3; X = Cl or Br) with boron trifluoride etherate[13a] or anhydrous hydrogen fluoride.[13b]

(c) Reaction of xenon difluoride (XeF_2) with iodine[3] or alkyl hypohalites.[4,5]

(d) Reaction of metal fluorides or ammonium fluorides with iodine, bromine, or *N*-halosuccinimides.[14]

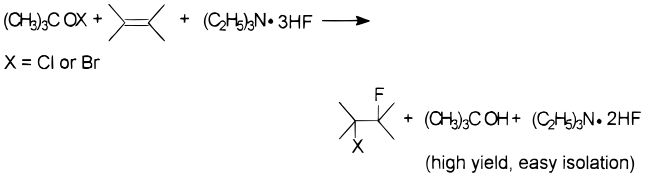
(e) Direct action of elemental fluorine with chlorine, bromine, or iodine.[8]

(f) Reaction of halogen trifluorides (XF_3; X = Cl, Br, or I) with Cl_2,[9a] Br_2,[9b] or I_2.[9c]

We found that XF generated from methods a−d above produce a sluggish electrophile. Reaction of alkyl hypohalites with boron trifluoride etherate gave the most reactive species in this group as products were obtained with less reactive substrates such as *trans*-1,2-dichloroethylene and methyl acrylate.[13a] Reactions of 3,4-dihydro-2*H*-pyran with some of these less reactive reagents are given in Table 2. The good yields of products **1**−**3** confirm the mild nature of these reagents, because a more reactive reagent would have led to decomposition.

Tables 4−6 (see Supporting Information) compare various methods for the reaction of XF with cyclohexene and terminal alkenes. Data are listed in order of the highest to lowest yields for these reactions. Xenon difluoride (Table 4), with I_2 or NIS is a good reaction for iodofluorination. We found that nonpolar solvents such as hexane work well in many cases.[3]

Bromine and chlorine do not give interhalogens with XeF_2, because molecular chlorine or bromine react rapidly with the alkene. Our experience has demonstrated that the best synthetic reaction for bromofluorination of ordinary or reactive substrates is with triethylamine trihydrofluoride and *tert*-butylhypobromite or N-bromosuccinimide[12c] (Table 5). *tert*-Butyl hypobromite is not readily available and, therefore, not as convient as NBS in reactions where the byproduct succinimide is not a problem. Triethylamine trihydrofluoride plus *tert*-butyl hypochlorite (as shown below) is the best reaction to generate ClF, unless you have an unreactive substrate (Table 6). Alkyl hypochlorites are easy to prepare from bleach,[13a] and *t*-BuOCl can be prepared neat in large quantities.[15] Table 1 presents our data with hypohalites and triethylamine trihydrofluoride in methylene chloride and hexane as solvent. Yields are good except for 3-hexyne, which is an unreactive substrate. The reaction is



Conclusion

We have demonstrated that interhalogen monofluorides prepared from *N*-halosuccinimides, hypohalites, and amine hydrogen fluorides or from xenon difluoride and hypohalites or iodine are a species different from reactive interhalogen fluorides generated from fluorine gas or halogen trifluorides. Halogen monofluorides from hypohalites, *N*-halosuccinimides, and xenon difluoride are less reactive than the interhalogen bromine monochloride (BrCl), which seems consistent for delivery of XF from a complex, as indicated by our earlier studies.[3,4] Both reactive and sluggish halogen monofluorides may work for substrates of intermediate reactivity such as 1-hexene or toluene. These milder reagents are required to carry out reactions with electron-rich substrates such as 3,4-dihydro-2*H*-pyran, whereas reactive interhalogen monofluorides are needed for reaction with unreactive substrates.

Experimental Section

Xenon difluoride was purchased from PCR, Inc. Triethylamine trihydrofluoride was a gift from FAR Research, Inc. or was purchased from the Aldrich Chemical Co. Methyl- and *tert*-butyl hypohalites were prepared as described in the literature.[12a,15] ***Caution***: We prepared CH_3OCl in CH_2Cl_2 because neat CH_3OCl is unstable. Solvents were dried over sieves. NMR data were obtained on a Varian Unity 300 (University of San Diego) in $CDCl_3$ and are relative to Me_4Si or $CFCl_3$. Mass spectral analyses were obtained at 70 eV on a Hewlett-Packard 5890 GC interfaced with an HP 5970B mass selective detector. Gas chromatography analyses were accomplished on an HP 5890 (F. I. D. detector) interfaced to a 3396A integrator. The GC and GC−MS analyses were done with a 25-m Hewlett-Packard ultraperformance column of internal diameter 0.20 mm with a methyl silicone stationary phase of 0.33 μm film thickness. A 50-m ultraperformance methyl silicone column was required for GC analyses of 2-methyl-2-pentene and 1-hexene used in the relative rate studies. All products (except those from 2-methyl-2-pentene, 3,4-dihydro-2*H*-pyran, or ClF addition to methylenecyclohexane) were identified by comparison with spectral data in the literature[14a,e] or their GC−MS data from independent synthesis[12a] or commercial samples.

Halofluorination Products from 2-Methyl-2-pentene. The following procedure for reaction with 2-methyl-2-pentene is also representative for the other substrates from our work listed in Tables 1 through 6.

Halofluorination with XeF_2 and *tert*-Butyl Hypohalites (*t*-BuOX; X = Cl or Br) or *N*-Iodosuccinimide (NIS) or I_2. To a 0.45 mL soluton of 0.40 M (0.18 mmol) *t*-BuOBr,[13a] or a 0.25 mL solution of 0.73 M (0.18 mmol) *t*-BuOCl, or a source of iodine [41 mg (0.18 mmol) of NIS or 46 mg of (0.18 mmol) I_2] in 0.25 mL of solvent[3] was added 24 μL (16.8 mg, 0.20 mmol) of 2-methyl-2-pentene followed by the addition of 15 mg (0.083 mmol) of solid XeF_2. The mixture was

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(14) (a) Hall, L. D.; Jones, D. L. *Can. J. Chem.* **1973**, *51*, 2902. Variations of the reaction in (a) include: (b) AgF supported on CaF_2 (Ando, T.; Jujita, J.; Kimura, T.; Tatauno, T. *Chem. Lett.* **1988**, 1877); (c) ammonium fluoride supported on AlF_3 (Ichihara, J.; Funabiki, K.; Hanfusa, T. *Tetrahedron Lett.* **1990**, *31*, 3167); (d) Tetrabutyl phosphate and H_2F_3 (Uchibori, Y.; Umeno, M.; Seto, H.; Yoshioka, H. *Chem. Lett.* **1993**, 673); (e) Tetrabutylammonium and $H_2F_3^-$ (Kuroboshi, M.; Hiyama, T. *Tetrahedron Lett.* **1991**, 1215); (f) Tetrabutylammonium and $H_2F_3^-$ (Camps, F.; Chamarro, E.; Gasol, V.; and Guerreo, A. *J. Org. Chem.* **1989**, *54*, 4294; (g) Metal hydrogen fluoride salts (Tamura, M.; Shibakami, M.; Sekiya, A. *Synthesis* **1995**, 515).

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stirred for 1.5 h. Workup was with 0.2−0.3 mL of 5% aqueous sodium bicarbonate followed by 20 μL of 1.0 M chlorobenzene in carbon tetrachloride as internal standard. The aqueous layer was extracted with methylene chloride. The combined organic layers were dried over anhydrous magnesium sulfate, and the mixture was analyzed by GC.

Halofluorination with Triethylamine Trihydrofluoride and Alkyl Hypohalites (ROX; R = *t*-Bu, X = Cl or Br; R = CH_3, X = Cl; or NIS). To a round-bottom flask at 0 °C was added with stirring 0.011 mol hypohalite (25 mL of 0.44 M *t*-BuOBr[13a] in methylene chloride or hexane; or 20 mL of solvent (Table 1) followed by 7.8 mL of 1.4 M *t*-BuOCl in methylene chloride or hexane)[13a,15] or 2.48 g of NIS in 20 mL methylene chloride, was added 0.863 g (0.010 mol) 2-methyl-2-pentene and 1.612 g (0.010 mol) $(C_2H_5)_3N{\cdot}3HF$. The mixture was stirred for 30 min at 0 °C and then worked up as described above. Analysis by GC gave yields (85% from *t*-BuOBr; 50% from *t*-BuOCl) with chlorobenzene as internal standard corrected for flame response. Solvent was removed under vacuum, and bulb-to-bulb distillation at 6−10 Torr, oil bath at 50−70 °C, gave 3-bromo-2-fluoro-2-methylpentane or 3-chloro-2-fluoro-2-methylpentane that was greater than 90% pure by GC. Iodofluorination of 2-methyl-2-pentene was carried out with $(C_2H_5)_3N{\cdot}3HF$ and NIS[12c] in 85% yield, greater than 95% pure by GC. Analysis by ^{19}F NMR showed that the minor isomers (3-fluoro-2-halo-2-methylpentanes) were less than 1% for each reaction. The following data were obtained.

3-Chloro-2-fluoro-2-methylpentane: GC−MS (*m*/*z*) 138 (M^+, 0.03), 103 (M − Cl, 0.2), 102 (M − HCl, 0.5), 87 (6), 61 (M − C_3H_6F, 100), 60 (27), 59 (10), 41 (33), 39 (14). ^1H NMR δ 0.96 (t, J = 7.6 Hz, 3H), 1.76 (d, J = 22.3 Hz, 6H), 1.90 (m, 2H), 4.28 (m, 1H). ^{19}F NMR (282 MHz) δ −139.5 (hept. d, J = 22 and 10 Hz).

3-Bromo-2-fluoro-2-methylpentane: GC−MS (*m*/*z*) 184 and 182 (M^+, 0.1), 103 (M − Br, 17), 83 (21), 61 (M − C_3H_6F, 100), 60 (47), 59 (24), 41 (85), 39 (44). ^1H NMR δ 1.11 (t, J = 7.0 Hz, 3H), 1.48 (d, J = 22 Hz, 3H), 1.54 (d, J = 22 Hz, 3H), 1.59−1.74 (m, 2H), 3.86 (ddd, J = 11.2, 9.0 and 2.4 Hz, 1H). ^{19}F NMR (282 MHz) δ −136.2 (hept. d, J = 22 and 9 Hz).

2-Fluoro-3-iodo-2-methylpentane: GC−MS (*m*/*z*) 230 (M^+, 2), 186 (0.3), 155 (1), 127 (5), 83 (34), 61 (M − C_3H_6F, 100), 59 (11), 43 (24), 41 (44), 39 (21). ^1H NMR δ 1.06 (t, J = 7.2 Hz, 3H), 1.53 (d, J = 21.5 Hz, 3H), 1.56 (d, J = 21.5 Hz, 3H), 1.61−1.88 (m, 2H), 3.98 (ddd, J = 11.3, 8.5 and 2.3 Hz, 1H). ^{19}F NMR (282 MHz) δ −131.3 (hept. d, J = 21.5 and 8.5 Hz).

From methylenecyclohexane, 1-Chloromethyl-1-fluorocyclohexane was isolated by preparative GC with a Hewlett-Packard 700 (TC) gas chromatograph with a 6′ × $^3/_8$″ stainless steel column of 10% Carbowax 20 M on 80/100 Chromosorb W−H. P. The product was >90% pure by analytical GC analysis, and the following data were obtained: GC−MS (*m*/*z*) 150 (M^+, 0.1), 101 (78), 81 (100), 41 (30), 39 (28), 27 (24). HRMS MNH_4^+ calcd for $C_7H_{12}ClFNH_4$ 168.0955; found 168.0957. ^1H NMR (60 MHz) δ 1.00−2.20 (m, 10H), 3.58 (d, J = 18.0 Hz, 2H). ^{13}C (75.4 MHz) δ 21.7, 25.1, 32.9 (d, J = 22 Hz), 50.7 (d, J = 29 Hz), 117.3 (d, J = 337 Hz). ^{19}F NMR (282 MHz) δ −159.3 (m).

Halofluorination of 3,4-Dihydro-2*H*-Pyran with Triethylamine Trihydrofluoride. To 500 mg (5.94 mmol) of 3,4-dihydro-2*H*-pyran in 75 mL of dry methylene chloride at 0 °C was added with stirring 6.54 mmol of NXS (X = Cl, Br, or I), followed by the dropwise addition of 2.39 g (14.8 mmol) of $(C_2H_5)_3N{\cdot}3HF$. The reaction was stirred for 30 min at 0° and then poured into ice-cold aqueous 2% sodium bicarbonate. The organic layer was washed several times with cold 2% sodium bicarbonate until the aqueous layer was basic. The organic layer was dried over anhydrous $MgSO_4$ and filtered, and the solvent was removed on a rotary evaporator at room temperature. Bulb-to-bulb distillation at room temperature (20−0.1 Torr) gave **1** (*trans*/*cis* 80:20), which was greater than 95% pure by GC (major contaminant was unreacted 3,4-dihydro-2*H*-pyran). Products **2** and **3** decomposed during bulb-to-bulb distillation but did survive solvent removal at room temperature. Products **2** and **3** contained succinimide (singlets at 2.72 and 5.29 ppm). The iodofluoroproduct **3** did survive GC, GC−MS, and ^1H and ^{19}F NMR analysis but decomposed during ^{13}C data collection. The following data were obtained.

2-Chloro-1-fluorotetrahydropyran (1). *trans*: GC−MS (*m*/*z*) 140 (M^+, 0.8), 138 (M^+, 0.2), 92 (7), 90 (21), 75 (12), 64 (16), 63 (52), 55 (100), 54 (23), 53 (13). HRMS MH^+ calcd for C_5H_9OFCl 139.0326; found 139.0321. ^1H NMR δ 1.48 (dm, J = 16.2 Hz, 1H), 1.99 (dm, J = 16.2 Hz, 1H), 2.09−2.24 (m, 1H), 2.27−2.40 (m, 1H), 3.80 (dm, J = 11.5 Hz, 1H), 3.95 (dd, J = 11.5 and 2.8 Hz, 1H), 4.08 (m, 1H), 5.51 (d, J = 51.0 Hz, 1H). ^{19}F δ −127.3 (d, J = 51.0 Hz). ^{13}C δ 18.9 (s), 25.8 (s), 53.5 (d, J = 39 Hz), 62.1 (s), 106.6 (d, J = 220 Hz). *cis*: GC−MS 140 (M^+, 1), 138 (M^+, 0.3), 92 (6), 90 (20), 75 (12), 64 (15), 55 (100), 55 (22), 53 (15). ^1H NMR δ 5.56 (dd, J = 53.2 and 2.0 Hz) other protons covered by *trans*. ^{19}F δ −152.5 (dd, J = 53.2 and 24.3 Hz).

2-Bromo-1-fluorotetrahydropyran (2). *trans*:[16] GC−MS (*m*/*z*) 184 (M^+, 3), 182 (M^+, 3), 136 (28), 134 (29), 108 (31), 106 (30), 55 (100), 53 (18), 51 (9). ^1H NMR δ 1.47 (dm, J = 16.2 Hz, 1H), 1.99 (dm, J = 16.2 Hz, 1H), 2.08−2.25 (m, 1H), 2.29−2.44 (m, 1H), 3.78 (dm, J = 11.5 Hz, 1H), 3.97 (ddd, J = 12.0, 11.5 and 2.5 Hz, 1H), 4.15 (m, 1H), 5.57 (brd.d, J = 52.0 Hz, 1H). ^{19}F δ −123.0 (brdd, J = 52.0 Hz). ^{13}C δ 19.7 (s), 26.2 (s), 48.8 (d, J = 37 Hz), 62.1 (s), 106.6 (d, J = 220 Hz). cis: GC−MS (*m*/*z*) 184 (M^+, 0.6), 182 (M^+, 0.6), 136 (29), 134 (30), 108 (28), 106 (29), 55 (100), 53 (21), 51 (7). ^{19}F NMR δ −149.3 (dd, J = 52.6 and 25.8 Hz).

2-Iodo-1-fluorotetrahydropyran (3). *trans*: GC−MS (*m*/*z*) 230 (M^+, 21), 154 (26), 127 (20), 103 (89), 84 (6), 83 (17), 73 (11), 59 (12), 56 (7), 55 (100), 53 (28), 47 (16). ^1H NMR δ 1.52 (dm, J = 13.0 Hz, 1H), 1.91 (qt, J = 13.0 and 4.1 Hz, 1H), 2.19 (qd, J = 13.0 and 3.9 Hz, 1H), 2.66 (dm, J = 13.0 Hz, 1H), 3.69 (ddd, J = 12.4, 12.2 and 1.9 Hz, 1H), 4.18 (dd, J = 12.4 and 5.0 Hz, 1H), 5.11−5.26 (m, 2H). ^{19}F δ −122.9 (dd, J = 51.4 and 4.7 Hz). *cis*: GC−MS (*m*/*z*) 230 (M^+, 60), 154 (26), 127 (22), 103 (90), 84 (13), 83 (41), 73 (12), 56 (17), 55 (100), 53 (33), 47 (16). ^{19}F δ −143.4 (dd, J = 51.0 and 28.0 Hz).

Relative Rates. Method A (for generating XF from $(C_2H_5)_3N{\cdot}3HF$ or XeF_2). A stock solution of 0.0780 M 2-methyl-2-pentene, 0.0780 M 1-hexene, and 0.0390 M *n*-heptane as internal standard was prepared in methylene chloride. One milliliter of this stock solution was placed in a 3 mL dry plastic vial with stirring bar at 0°. To this stirred mixture were added 0.060 mmol of the halogen and the interhalogen or 0.060 mmol of each reagent needed to generate the interhalogen (Table 1). The reaction was stirred at 0° for 30 min, and then 1.0 mL of 5% aqueous sodium bicarbonate solution was added to quench the reaction. The organic layer was separated and dried with anhydrous $MgSO_4$. Relative concentrations of the unreacted alkenes were determined by GC analysis corrected for flame response.[17] The following data were obtained. Halogen source (rel rate 2-methyl-2-pentene/1-hexene): Br_2 (20 ± 4), Cl_2 (1.6 ± 0.2), NIS−$(C_2H_5)_3N{\cdot}3HF$ (16 ± 3), NBS−$(C_2H_5)_3N{\cdot}3HF$ (33 ± 4), *t*-BuOBr−$(C_2H_5)_3N{\cdot}3HF$ (10 ± 4), *t*-BuOBr−XeF_2 (16 ± 3), *t*-BuOCl−XeF_2 (60 ± 10), *t*-BuOCl−$(C_2H_5)_3N{\cdot}3HF$ (4 ± 1), NCS−$(C_2H_5)_3N{\cdot}3HF$ (3 ± 1).

Method B (for F_2 and ClF from F_2). In a typical experiment, 200 mL of the stock solution was transferred to a 300-cc 316-ss Parr Instrument Co. magnetically stirred reactor. A sample of the stock solution was analyzed in triplicate. The reactor was cooled to −2 or −3 °C under a nitrogen atmosphere. A mixture of the gas [ClF in N_2 (ca. 6% v/v), F_2 in N_2 (ca. 5% v/v)] was then added to the reaction mixture with vigorous stirring while the reaction temperature was maintained at −3 °C for reaction with F_2 and at −2 °C for reaction with ClF. The mole ratio of ClF or F_2 to alkenes was 0.71:1.

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(16) Mass spectral and NMR data are similar to ours.[14f] 2-Bromo-1-fluorotetrahydropyran could not be purified by our attempted distillation or column chromatography.[14f]

(17) Relative rate calculated as described in our earlier study. Heasley, V. L.; Louie, T. J.; Luttrull, D. K.; Millar, M. D.; Moore, H. B.; Nogales, D. F.; Sauerbrey, A. M.; Shevel, A. B.; Shibuya, T. Y.; Stanley, M. S.; Shellhamer, D. F.; Heasley, G. E. *J. Org. Chem.* **1988**, *53*, 2199.

After the reaction was complete, the reactor and contents were purged with N_2 for 5 min and then analyzed in triplicate by GC (corrected for flame response).[17] Halogen (rel rate): F_2 (3.0 ± 0.2), ClF (1.7 ± 0.2).

Method C (for BrF and IF from F_2). Bromine fluoride (8.5 mmol) and iodine fluoride (8.7 mmol) were prepared at −78° in 250 mL of $CFCl_3$ according to the method of Rozen and Brand.[9c] The solution (250 mL of BrF or 250 mL of IF) was added in one portion to the stock solution (155 mL for BrF, 246 mL for IF) at −78 °C. The resulting mixture was allowed to warm to room temperature with stirring. Ratio of BrF:alkenes = 0.71:1; IF:alkenes = 0.91:1. The stock solution and final reaction mixtures were analyzed in triplicate by GC (corrected for flame response).[17] Halogen (rel rate): BrF (1.8 ± 0.1), IF (3.8 ± 0.2).

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Supporting Information Available: A comparison of the various methods to generate interhalogen fluorides. This material is available free of charge via the Internet at http://pubs.acs.org.

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