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Headline Articles

Halofluorination of Alkenes Using Dilute Hydrofluoric Acid

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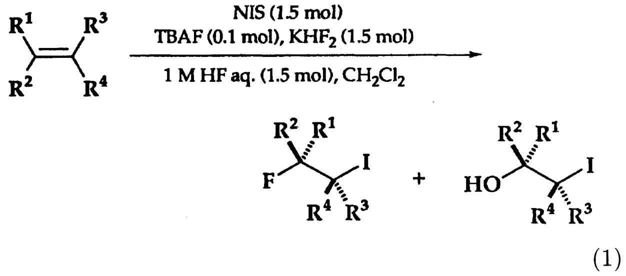
Iodofluorination of alkenes was achieved with *N*-iodosuccinimide, potassium hydrogendifluoride, and 1 M hydrofluoric acid using tetrabutylammonium fluoride as a phase-transfer catalyst. The active fluorinating reagent was shown to be tetrabutylammonium dihydrogentrifluoride by preparing the salt in a different way and by effecting the same transformation under anhydrous conditions. Bromofluorination of alkenes also was carried out using 1,3-dibromo-5,5-dimethylhydantoin. Treatment of the I–F adducts with DBU afforded fluoro olefins stereospecifically.

In view of increasing interest in fluroine-containing organic chemicals, exploratory research on new fluorination methods has been attracting much attention.[1—4] One basic and straightforward way is halofluorination of carbon–carbon unsaturated bonds. The resulting products, halofluoroalkanes, are useful synthetic intermediates of a variety of organofluorine compounds. For example, compounds containing ^{18}F, often used in positron-emission tomography (PET),[5] can be readily prepared by this particular reaction using H^{18}F.[6] Dehydrohalogenation of halofluoroalkanes gives monofluoro olefins, which can be used as enzyme inhibitors,[7] modified polypeptides,[8] or liquid crystals.[9]

Halofluorination of alkenes has usually been carried out with halogen fluorides.[10] Because halogen fluorides should be prepared before use from a halogen (Cl_2, Br_2 or I_2) and extremely reactive fluorine gas, an alternative reagent system is often applied consisting of a halonium ion-producing agent like *N*-halo imide (or amide) and a fluoride agent. Fluoride agents so far employed are hydrogen fluoride (HF),[11] HF-amine complex,[12—15] hexafluoropropene-diethylamine complex,[16] tetrabutylammonium fluoride[17] (or hydrogendifluoride)[18] ammonium hydrogendifluoride-aluminium fluoride,[19] silver(I) fluoride,[20] potassium fluoride[21] (or silver(I) fluoride)[22] on calcium fluoride, boron trifluoride,[23] and silicon tetrafluoride.[24] The halonium ion-producing agent may be replaced by halogen-silver nitrate,[25] $[I(collidine)_2]^+BF_4^-$,[26] $[Ipy_2]^+BF_4^-$,[27] ICl,[28] or CH_3IF_2.[29] In general, these reactions are performed under strictly anhydrous conditions to suppress halohydrin formation and with special care because, for example, anhydrous HF is a volatile corrosive liquid.[12]

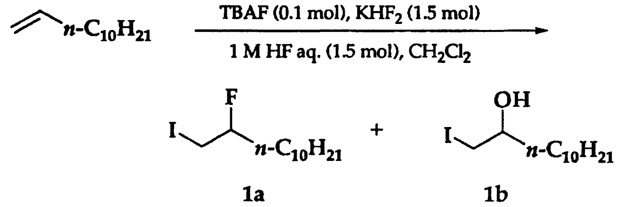
Although hydrogen fluoride is considered to be the cheapest fluorination reagent and widely used in industrial fluorination, this aqueous solution was rarely utilized for fluorination of organic substrates, probably due to competitive hydroxylation by water. For example, halohydrin is a serious by-product of halofluorination of alkenes. We herein report that iodofluorination of olefins can readily be carried out using dilute hydrofluoric acid and *N*-iodosuccinimide (NIS) in the presence of a phase-transfer catalyst (Eq. 1). As dilute hydrofluoric acid has been considered to be industrial waste, our findings should open a new area of fluorination reaction.



(1)

When we added 1-dodecene (1 mmol) to a mixture of 1 M hydrofluoric acid (1.5 mL, 1.5 mmol of F^-) (1 M=1 mol dm^{-3}), *N*-iodosuccinimide (NIS) (1.5 mmol), tetrabutylammonium fluoride trihydrate ($TBAF\cdot 3H_2O$, 0.1 mmol) and dichloromethane (1.5 mL) in a polypropylene reaction tube at 0 °C and stirred the resulting mixture for 9 h under gradually warming to room temperature, we could isolate 2-fluoro-1-iodododecane

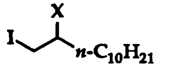
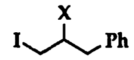
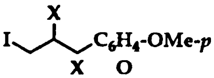
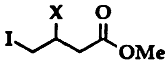
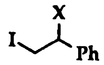
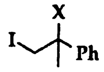
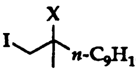
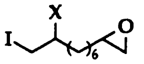
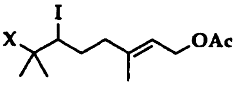
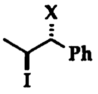
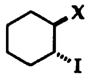
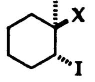
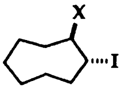
(**1a**) in 72% yield along with a by-product, 1-iodo-2-dodecanol (**1b**), in 4% yield. The same experiment carried out in the presence of potassium hydrogendifluoride (KHF_2) (1.5 mmol) increased the yield of **1a** up to 82% and suppressed the formation of **1b** in less than 0.2%. In the absence of TBAF, the reaction proceeded extremely slowly, and **1a** was obtained in only 40% yield. Thus, phase transfer conditions are essential to introduce fluorine effectively. When we used 48% (or 25 M) hydrofluoric acid, less amount (70%) of **1a** and more amount (14%) of **1b** were produced, in spite of the lower water content.[30] TBAF could be replaced by $(n\text{-Bu})_4N^+BF_4^-$, $(n\text{-Bu}_4)N^+OH^-$ or 18-crown-6, hereby **1a** being isolated in 80, 78 and 70% yields, respectively (Eq. 2). Use of acetonitrile in place of dichloromethane resulted in a homogeneous reaction mixture which gave only 5% of **1a** and 78% of **1b**.



(2)

The best reaction conditions were applied to various olefins; the results are summarized in Table 1. As is readily seen, the iodofluorination is applicable to olefins having alkyl and/or aryl substituent(s) and alicyclic olefins, and the corresponding F–I adducts were isolated in good to excellent yields with very small amounts of iodohydrins. Please note that oxirane ring and ester functional group are tolerant of the reaction conditions (Entries 4, 8, and 10). This is remarkable, because both anhydrous hydrogen fluoride and 48% hydrofluoric acid do react with epoxides to give fluorohydrins. Terminal alkenes gave Markovnikov adducts exclusively. Namely, fluorine was always introduced at the olefin carbon that was the more stabilized cationic center of an intermediate carbenium ion. The stereochemistry of the addition of fluorine and iodine is strictly *anti* (Entries 11—14),[35] as is often the case. The stereochemical assignment is based on ^{1}H NMR. For example, 1-fluoro-2-iodocyclohexane (**11a**) exhibited a trans coupling constant, $J_{1,2}=9$ Hz. When geranyl acetate was used as the substrate, only the double bond at 6-position was iodofluorinated (Entry 10). Alkynes could not be halofluorinated.

Table 1. Synthesis of Iodofluorohydrocarbon Using Dilute Hydrofluoric Acid[a)]

Entry	Product	X=F[b)] (%)	X=OH[b)] (%)
1		**1a**, 82	**1b**, 0.2
2		**2a**, 78	**2b**, 5
3		**3a**, 73	**3b**, 5
4		**4a**, 77	**4b**, 5
5		**5a**, 59	**5b**, 6
6		**6a**, 91	**6b**, 4
7		**7a**, 79	c)
8		**8a**, 63	**8b**, 17
9[d)]		**8a**, 78	**8b**, 9
10		**9a**, 86	c)
11		**10a**, 70	c)
12		**11a**, 75	c)
13		**12a**, 78	c)
14		**13a**, 77	c)

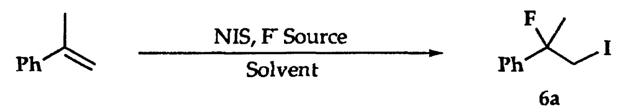
a) An alkene was allowed to react with NIS (1.5 mmol), 1 M hydrofluoric acid (1.5 mL, 1.5 mmol), KHF_2 (1.5 mmol) in CH_2Cl_2 (1.5 mL) in the presence of $TBAF{\cdot}3H_2O$ (0.1 mmol) at 0 °C to room temperature for 9 h. b) Isolated yields are given. c) Only a trace amount. d) Chloroform was employed as the solvent.

As a possible active fluorination species of the phase-transfer reaction, we considered TBAF, $TBA{\cdot}HF_2$,[18] and $TBA{\cdot}H_2F_3$.[31] Thus, we prepared the latter two according to the literature methods and studied the reaction of 2-phenylpropene in dichloromethane. Fluorinating reagent, reaction time, and yield of product **6a** were $TBA{\cdot}H_2F_3$, 1 h, 92%; $TBA{\cdot}HF_2$, 18 h, 83%; and TBAF, 18 h, 11%, respectively. As the two-phase reaction was actually completed in 1 h at 0 °C giving **6a** in 87% yield with 5% of the iodohydrin, we may conclude that the active fluorinating species is $H_2F_3^-$ rather than HF_2^- or F^-. This conclusion is consistent with experiments of Coussau[31] et al. who reported that $TBA{\cdot}H_2F_3$ was more nucleophilic than F^- or HF_2^-.

Since we have demonstrated that $TBA{\cdot}H_2F_3$ is an active nucleophilic fluorinating species of halofluorination, we studied reaction conditions using 2-phenylpropene as a substrate. The results summarized in Table 2 show that the reaction in chlorohydrocarbon completed within 2 h (Entries 1—3). $TBA{\cdot}H_2F_3$ was a better fluorination agent than $TBA{\cdot}HF_2$ or TBAF (Entries 2, 6, and 7, vide supra). Acetonitrile or 1,2-dimethoxyethane required slightly longer reaction time (Entries 4 and 5). What we should emphasize is that all these reactions could be carried out in glassware.

The best reaction conditions were applied to various

Table 2. Iodofluorination of 2-Phenylpropene Under Anhydrous Conditions[a)]

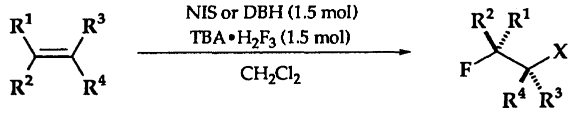


6a

Entry	F^-Source	Solvent	Conditions	Yield/%
1	TBA·H_2F_3	CH_2Cl_2	0 °C, 1 h	92
2	TBA·H_2F_3	$(CH_2Cl)_2$	0 °C, 1 h	90
3	TBA·H_2F_3	$CHCl_3$	0 °C, 1.5 h	90
4	TBA·H_2F_3	CH_3CN	0 °C, 5 h	87
5	TBA·H_2F_3	$(MeOCH_2)_2$	0 °C, 5 h	83
6	TBA·HF_2	$(CH_2Cl)_2$	0 °C, 5 h; r.t., 13 h	83
7	TBA·F	$(CH_2Cl)_2$	0 °C, 5 h; r.t., 13 h	11

a) A solution of 2-phenylpropene (1 mmol), NIS (1.5 mmol) and a fluoride ion source (1.5 mmol) in the solvent (1.5 mL) was stirred under the conditions specified.

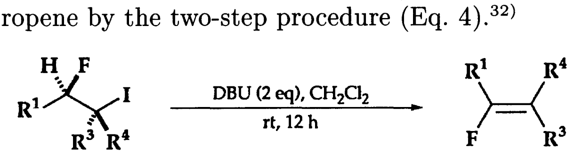
olefins, as summarized in Table 3. The iodofluorination products of various kinds of olefins could be isolated in good to excellent yields. Again, oxirane ring was found to tolerate the reaction conditions (Entry 11); Markovnikov products were obtained exclusively; The stereochemistry of the addition of F and I was *anti* (Entries 14, 17, 18, and 19) for all the olefins tested (Eq. 3).



(X = I or Br) (3)

Bromofluorination of alkenes could also be done under the similar conditions using 1.5 mol equivalents of 1,3-dibromo-5,5-dimethylhydantoin (DBH) (Entries 2, 6, and 8). Chlorofluorination with *N*-chlorosuccinimide as a chlorinating reagent, however, did not occur at all, and starting alkenes were recovered unchanged.

The F–I adducts obtained above are readily transformed to monofluoro olefins with a base. When we treated the F–I adducts with 1,8-diazabicyclo[5.4.0]-undec-7-ene (DBU) in dichloromethane at room temperature, dehydroiodination readily occurred to give fluoro olefins in a stereospecific manner[14e)] in excellent yields. Since both F–I addition and H–I elimination proceed in *anti*-manner, (*E*)-1-phenylpropene could be stereospecifically transformed to (*E*)-1-fluoro-1-phenylpropene by the two-step procedure (Eq. 4).[32)]



20: R^1 = *n*-$C_{10}H_{21}$, R^3 = R^4 = H, 92%
21: R^1 = Ph, R^3 = H, R^4 = Me, 93%
22: R^1 = *p*-$MeOC_6H_4CH_2$, R^3 = R^4 = H, 88%

(4)

In summary, we have demonstrated that dilute hydrofluoric acid can be utilized as a fluorination reagent of olefins and that $H_2F_3^-$ is the species responsible for success of the reaction. This new synthetic technology allows us to introduce fluorine and a halogen into olefins without using anhydrous hydrogen fluoride. In addition, this procedure should have economical advantages over previously known procedures.

Experimental

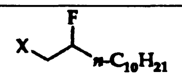
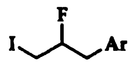
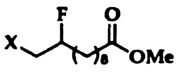
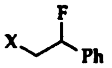
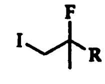
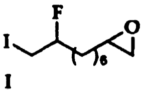
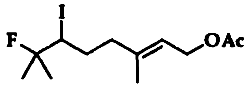
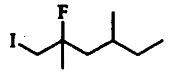
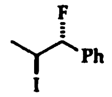
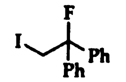
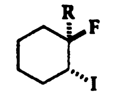
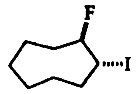
IR spectra were recorded on a JASCO A-202 spectrometer. ^{1}H and ^{19}F NMR spectra were obtained in $CDCl_3$ on a Bruker AC-200 spectrometer operating at 200 or 188 MHz, using tetramethylsilane and trichlorofluoromethane as an internal standard, respectively. Mass spectra were recorded with a Hitachi RMU-6MG spectrometer.

Alkenes used were purchased and distilled before use. Dichloromethane was distilled from CaH_2. TBAF trihydrate, KHF_2, and hydrofluoric acid (48%) were purchased and used without further purification. TBA·H_2F_3 was prepared as reported.[27)] NIS was recrystallyzed from dioxane. DBH was purchased and used without further purification. Wakogel C-200 or Merck Kieselgel 60 PF_{254} was used for the silica-gel column chromatography or the silica-gel preparative thin-layer chromatography (TLC), respectively. TLC analyses were performed on commercial glass plates bearing a 0.25-mm layer of Merck Kieselgel 60 F_{254}. The polypropylene reaction tube used was a round-bottom tube with a screw cap (14 mL–17×100 mm); it is commercially available as FALCON®.

Iodofluorination of Alkenes Using Dilute Hydrofluoric Acid and *N*-Iodosuccinimide. A Typical Procedure for Preparation of 2-Fluoro-1-iododecane (1a): To a mixture of 1 M hydrofluoric acid (1.5 mL, 1.5 mmol of fluoride), KHF_2 (0.117 g, 1.5 mmol), NIS (0.34 g, 1.5 mmol), a catalytic amount of TBAF trihydrate (0.031 g, 0.1 mmol) and dichloromethane (1.5 mL), all placed in a polypropylene tube, was added 1-dodecene (0.168 g, 1 mmol) at 0 °C. The resulting mixture was stirred and gradually warmed to room temperature over 9 h. The resultant mixture was poured into an aq solution of sodium hydrogencarbonate and sodium hydrogensulfite and extracted with Et_2O (20 mL×3). The organic layer was dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by preparative TLC to give **1a** (0.26 g, 0.82 mmol, 82%) along with **1b** (0.6 mg, 0.002 mmol, 0.2%). R_f 0.49 (hexane). IR (neat) 2955, 2925, 2850, 1462, 1425, 1410, 1388, 1350, 1332, 1182, 1123, 1102, 1080, 982, 943, 873, 788, 716 cm^{-1}; ^{1}H NMR δ=4.44 (double quintet, J=48, 6 Hz, 1H), 3.30 (dd, J=20, 6 Hz, 2H), 1.8—1.6 (m, 2H), 1.4—1.2 (m, 16H), 0.88 (t, J=7 Hz, 3H); ^{19}F NMR δ=−171.2 (dm, J=48 Hz); MS m/z (rel intensity) 314 (M$^+$; 4), 173 (3), 155 (3), 153 (1), 131 (5), 125 (4), 111 (20), 97 (35), 85 (26), 83 (34), 71 (37), 69 (64), 57 (88), 55 (66), 43 (100), 41 (60). Calcd for $C_{12}H_{24}FI$: C, 45.87; H, 7.70%. Found: C, 46.03; H, 7.87%.

1-Iodo-2-dodecanol (1b): R_f 0.08 (hexane). IR (neat) 3360, 2942, 2903, 2815, 1715, 1705, 1458, 1400, 1362, 1163, 1110, 1068, 1000, 710 cm^{-1}. ^{1}H NMR δ=3.7—3.6 (m, 1H), 3.42 (dd, J=10, 4 Hz, 1H), 3.22 (dd, J=10, 7 Hz, 1H), 2.0—1.8 (br s, 1H), 1.7—1.2 (m, 18H), 0.87 (t, J=5 Hz, 3H). MS

Table 3. Halofluorination of Alkenes Using Tetrabutylammonium Dihydrogentrifluoride[a)]

Entry	Product		Conditions	Yield/%[b)]
1		**1a** (X=I)	0 °C, 1 h	87
2		**14a** (X=Br)	0 °C, 5 h; r.t., 13 h	82
3		**2a** (Ar=Ph)	0 °C, 2 h	83
4		**3a** (Ar=C_6H_4OMe-*p*)	0 °C, 2 h	83
5		**4a** (X=I)	0 °C, 1 h	83
6		**15a** (X=Br)	0 °C, 5 h; r.t., 13 h	85
7		**5a** (X=I)	0 °C, 1 h	86
8		**16a** (X=Br)	0 °C, 5 h; r.t., 13 h	85
9		**6a** (R=Ph)	0 °C, 1 h	92
10		**7a** (R=*n*-C_9H_{19})	0 °C, 1.5 h	94
11		**8a**	0 °C, 2 h	64[c)]
12		**9a**	0 °C, 1 h	88
13		**17a**	0 °C, 1 h	87
14		**10a**	0 °C, 2 h	82
15		**18a**	0 °C, 2 h	67
16		**19a**	0 °C, 1 h	76
17		**11a** (R=H)	0 °C, 2 h	60
18		**12a** (R=Me)	0 °C, 1.5 h	85
19		**13a**	0 °C, 1 h	78

a) An alkene was allowed to react with NIS or DBH (1.5 mmol) and TBA·H_2F_3 (1.5 mmol) in CH_2Cl_2 (1.5 mL). b) Isolated yields are given. c) The starting material (21%) was recovered.

m/*z* (rel intensity) 312 (M^+; 0.3), 295 (0.3), 185 (39), 171 (29), 111 (30), 97 (69), 85 (16), 83 (75), 71 (23), 69 (100).

Iodofluorination of Alkenes Using TBA·H_2F_3 and NIS. A Typical Procedure for Preparation of 2-Fluoro-1-iodo-2-phenylpropane (6a): To a solution of TBA·H_2F_3 (0.45 g, 1.5 mmol) and NIS (0.34 g, 1.5 mmol) in dichloromethane (1.5 mL) was added 2-phenylpropene (0.118 g, 1 mmol) at 0 °C. The reaction mixture was stirred for 1 h, then poured into an aqueous solution of sodium hydrogencarbonate and sodium hydrogensulfite and extracted with Et_2O (20 mL×3). The organic layer was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography to give **6a** (0.24 g, 0.92 mmol, 92%). R_f 0.27 (hexane). IR (neat) 3052, 3023, 2980, 2920, 1600, 1492, 1440, 1408, 1376, 1283, 1196, 1162, 1135, 1062, 1045, 1022, 928, 902, 895, 863, 800, 759, 718, 695 cm^{-1}; ^{1}H NMR δ=7.5—7.4 (m, 5H), 3.60 (d, J=21 Hz, 2H), 1.78 (d, J=21 Hz, 3H); ^{19}F NMR δ=−142.43 (qt, J=21, 21 Hz). MS *m*/*z* (rel intensity) 264 (M^+; 0.6), 263 (M^+−1; 6), 137 (100), 123 (54), 122 (16), 177 (42), 115

(26), 109 (13), 103 (18), 91 (26), 77 (15). Calcd for $C_9H_{10}FI$: C, 40.93; H, 3.82%. Found: C, 40.92; H, 3.76%.

2-Fluoro-1-iodo-3-phenylpropane (2a): R_f 0.28 (hexane). IR (neat) 3075, 3050, 2950, 1605, 1500, 1453, 1429, 1416, 1383, 1359, 1339, 1280, 1224, 1182, 1080, 1029, 992, 968, 914, 876, 848, 796, 746, 702 cm^{-1}; ^{1}H NMR δ= 7.4—7.2 (m, 5H), 4.64 (double quintet, J=47, 6 Hz, 1H), 3.29 (ddd, J=18, 11, 6 Hz, 1H), 3.24 (ddd, J=21, 11, 6 Hz, 1H), 3.07 (dd, J=21, 6 Hz, 1H); ^{19}F NMR δ=−168.82 (double quintet, J=47, 21 Hz); MS m/z (rel intensity) 265 (M^++1; 1.4), 264 (M^+; 14), 137 (2), 127 (4), 117 (11), 91 (100). Calcd for $C_9H_{10}FI$: C, 40.93; H, 3.82%. Found: C, 40.83; H, 3.72 %.

2-Fluoro-1-iodo-3-(4-methoxyphenyl)propane (3a): R_f 0.46 (hexane–Et_2O=10 : 1). IR (neat) 3015, 2975, 2950, 2850, 1615, 1587, 1519, 1468, 1440, 1302, 1250, 1180, 1108, 1034, 992, 820, 758 cm^{-1}; ^{1}H NMR δ=7.23 (d, J=9 Hz, 2H), 6.92 (d, J=9 Hz, 2H), 4.69 (double quintet, J=47, 6 Hz, 1H), 3.86 (s, 3H), 3.35 (dd, J=19, 6 Hz, 2H), 3.11 (dd, J=21, 6 Hz, 2H); ^{19}F NMR δ=−169.57 (double quintet, J=47, 21 Hz); MS m/z (rel intensity) 295 (M^++1; 2), 294 (M^+; 21), 167 (5), 121 (100). Calcd for $C_{10}H_{12}FIO$: C, 40.84; H, 4.11%. Found: C, 40.93; H, 4.11%.

Methyl 10-Fluoro-11-iodoundecanoate (4a): R_f 0.30 (hexane–Et_2O=10 : 1). IR (KBr) 2950, 2880, 1742, 1471, 1436, 1418, 1383, 1364, 1344, 1319, 1281, 1250, 1219, 1176, 1120, 1073, 1041, 1020, 1000, 941, 893, 840, 798, 752, 723 cm^{-1}; ^{1}H NMR δ=4.44 (double quintet, J=48, 5 Hz, 1H), 3.64 (s, 3H), 3.28 (dd, J=20, 5 Hz, 2H), 2.28 (t, J=8 Hz, 2H), 1.8—1.7 (m, 2H), 1.7—1.6 (m, 2H), 1.5—1.3 (m, 10H); ^{19}F NMR δ=−171.3 (m); MS m/z (rel intensity) 313 (M^+-CH_3O; 2), 217 (2), 197 (2), 165 (8), 95 (10), 81 (32), 74 (52), 59 (35), 55 (70), 43 (33), 41 (100), 39 (35). Calcd for $C_{12}H_{22}FIO_2$: C, 41.87; H, 6.44%. Found: C, 41.75; H, 6.45%.

1-Fluoro-2-iodo-1-phenylethane (5a): R_f 0.34 (hexane). IR (KBr) 3080, 3051, 2978, 2950, 1955, 1882, 1730, 1500, 1452, 1413, 1383, 1352, 1308, 1212, 1179, 1058, 960, 918, 875, 841, 763, 750, 700, 643 cm^{-1}; ^{1}H NMR δ= 7.00—6.99 (m, 3H), 6.92—6.90 (m, 2H), 5.07 (ddd, J=47, 8, 4 Hz, 1H), 2.97 (ddd, J=18, 11, 8 Hz, 1H), 2.86 (ddd, J=24, 11, 4 Hz, 1H); ^{19}F NMR δ=−167.00 (ddd, J=47, 24, 18 Hz); MS m/z (rel intensity) 250 (M^+; 4), 123 (100), 109 (24), 103 (40). Calcd for C_8H_8FI: C, 38.43; H, 3.22%. Found: C, 38.49; H, 3.20%.

2-Fluoro-1-iodo-2-methylundecane (7a): R_f 0.45 (hexane). IR (neat) 2950, 2880, 1732, 1470, 1382, 1258, 1148, 1134, 1080, 1018, 910, 768, 720 cm^{-1}; ^{1}H NMR δ=3.32 (d, J=17 Hz, 2H), 1.8—1.7 (m, 2H), 1.49 (d, J=21 Hz, 3H), 1.4—1.2 (m, 14H), 0.89 (t, J=7 Hz, 3H); ^{19}F NMR δ=−140.45 (octet, J=17 Hz); MS m/z (rel intensity) 314 (M^+; 0.5), 125 (5), 111 (29), 97 (49), 83 (49), 69 (92), 57 (53), 55 (97), 43 (100), 41 (82). Calcd for $C_{12}H_{24}FI$: C, 45.87; H, 7.70%. Found: C, 46.07; H, 7.85%.

9-Fluoro-10-iodo-1,2-epoxydodecane (8a): R_f 0.23 (hexane–Et_2O=10 : 1). IR (neat) 3100, 3035, 2980, 2900, 1493, 1476, 1439, 1421, 1372, 1340, 1269, 1258, 1220, 1198, 1082, 1063, 994, 936, 910, 857, 803, 738, 620 cm^{-1}; ^{1}H NMR δ=4.43 (double quintet, J=48, 5 Hz, 1H), 3.30 (ddd, J= 20, 11 Hz, 1H), 3.29 (ddd J=20, 11, 6 Hz, 1H), 2.91 (m, 1H), 2.74 (dd, J=5, 4 Hz, 1H), 2.45 (dd, J=5, 3 Hz, 1H), 1.8—1.2 (m, 2H), 1.7—1.3 (m, 10H); ^{19}F NMR δ=−171.68 (double quintet, J=48, 20 Hz); MS m/z (rel intensity) 257 (M^+-CH_2CHO; 0.1), 95 (34), 81 (46), 71 (91), 63 (53), 58 (37), 55 (86), 41 (100). Calcd for $C_{10}H_{18}FI$: C, 40.02; H, 6.05%. Found: C, 40.03; H, 6.01%.

7-Fluoro-6-iodo-3,7-dimethyl-2-octenyl Acetate (9a): R_f 0.26 (hexane–Et_2O=5 : 1). IR (neat) 3000, 2948, 2850, 1736, 1662, 1460, 1440, 1381, 1370, 1236, 1170, 1143, 1112, 1099, 1020, 956, 880, 860, 800, 764, 600 cm^{-1}; ^{1}H NMR δ=5.43 (t, J=8 Hz, 1H), 4.60 (d, J=8 Hz, 2H), 3.98 (dt, J=4, 10 Hz, 1H), 2.4—1.5 (m, 4H), 2.3 (s, 3H), 1.7 (s, 3H), 1.54 (d, J=21 Hz, 3H), 1.53 (d, J=21 Hz, 3H). ^{19}F NMR δ=−132.0 (m); MS m/z (rel intensity) 342 (M^+; 0.06), 341 (M^+-1; 0.41), 195 (11), 153 (14), 135 (82), 107 (14), 99 (10), 95 (28), 93 (28), 87 (19), 85 (12), 81 (34), 79 (10), 73 (13), 69 (45), 68 (20), 67 (23), 61 (27), 59 (16), 55 (18), 53 (16), 43 (100), 41 (40). Calcd for $C_{12}H_{20}FIO_2$: C, 42.12; H, 5.89%. Found: C, 41.85; H, 6.01%.

***erythro*-1-Fluoro-2-iodo-1-phenylpropane (10a):**[33,34] R_f 0.42 (hexane). IR (neat) 3080, 3050, 2995, 2948, 1500, 1451, 1380, 1305, 1265, 1208, 1163, 1159, 1146, 1065, 1003, 962, 758, 700 cm^{-1}; ^{1}H NMR δ=7.4—7.3 (m, 5H), 5.51 (dd, J=46, 6 Hz, 1H), 4.40 (ddq, J=17, 7, 6 Hz, 1H), 1.90 (d, J=7 Hz, 3H); ^{19}F NMR δ=−172.25 (dd, J=46, 17 Hz); MS m/z (rel intensity) 264 (M^+; 4), 137 (100), 127 (14), 117 (58), 115 (37), 109 (66), 91 (51). Calcd for $C_9H_{10}FI$: C, 40.93; H, 3.82%. Found: C, 40.86; H, 3.77%.

***trans*-1-Fluoro-2-iodocyclohexane (11a):** R_f 0.45 (hexane). IR (neat) 2960, 2880, 1448, 1434, 1385, 1368, 1352, 1338, 1285, 1270, 1253, 1208, 1171, 1123, 1093, 1059, 1044, 1032, 1001, 954, 894, 860, 840, 794, 737 cm^{-1}; ^{1}H NMR[11] δ=4.55 (dddd, J=48, 9, 9, 4 Hz, 1H), 4.2—4.1 (m, 1H), 2.4—2.3 (m, 1H), 2.3—2.2 (m, 1H), 2.0—1.9 (m, 1H), 1.9—1.8 (m, 1H), 1.6—1.5 (m, 2H), 1.5—1.4 (m, 1H), 1.4—1.3 (m, 1H); ^{19}F NMR δ=−160.0 (dm, J=48 Hz); MS m/z (rel intensity) 229 (M^++1; 0.5), 228 (M^+; 5), 127 (11), 101 (17), 81 (100), 59 (36), 55 (30), 53 (22), 41 (59), 39 (49). Calcd for $C_6H_{10}FI$: C, 31.60; H, 4.42%. Found: C, 31.62; H, 4.35%.

***r*-1-Fluoro-*t*-2-iodo-1-methylcyclohexane (12a):** R_f 0.53 (hexane). IR (neat) 2960, 2885, 1730, 1448, 1435, 1383, 1337, 1310, 1293, 1241, 1200, 1162, 1150, 1114, 1080, 1022, 980, 962, 903, 880, 864, 800, 729, 661, 642 cm^{-1}; ^{1}H NMR δ=4.36 (dt, J=8, 4 Hz, 1H), 2.3—2.2 (m, 1H), 2.2—2.1 (m, 1H), 2.0—1.9 (m, 1H), 1.8—1.7 (m, 2H), 1.7—1.6 (m, 1H), 1.56 (d, J=22 Hz, 3H), 1.5—1.4 (m, 2H). ^{19}F NMR δ=−132.4 (m); MS m/z (rel intensity) 242 (M^+; 2), 128 (1), 127 (5), 115 (23), 95 (100), 73 (38), 67 (20). Calcd for $C_7H_{12}FI$: C, 34.73; H, 5.00%. Found C, 34.93; H, 5.08%.

***trans*-1-Fluoro-2-iodocyclooctane (13a):**[35] R_f 0.37 (hexane). IR (neat) 2950, 2880, 1462, 1442, 1220, 1157, 1040, 981, 958, 854, 822, 740, 642 cm^{-1}; ^{1}H NMR δ=4.82 (ddd, J=46, 9, 2 Hz, 1H), 4.34 (ddd, J=15, 9, 7 Hz, 1H), 2.2—2.1 (m, 1H), 2.1—1.9 (m, 2H), 1.5—1.2 (m, 9H); ^{19}F NMR δ=−147.0 (m); MS m/z (rel intensity) 256 (M^+; 0.3), 127 (6), 109 (100), 67 (77), 55 (49), 41 (73). Calcd for $C_8H_{14}FI$: C, 37.52; H, 5.51%. Found: C, 37.53; H, 5.41%.

2-Fluoro-1-bromodecane (14a): R_f 0.69 (hexane). IR (neat) 2952, 2880, 1468, 1460, 1420, 1380, 1264, 1120, 1090, 1008, 962, 940, 820 cm^{-1}; ^{1}H NMR δ=4.62 (dddt, J=47, 7, 5, 5 Hz, 1H), 3.49 (ddd, J=20, 11, 5 Hz, 1H), 3.45 (ddd, J=20, 11, 6 Hz, 1H), 1.9—1.7 (m, 2H), 1.6—1.3 (m, 16H), 0.88 (t, J=7 Hz, 3H); ^{19}F NMR δ=−178.07 (dddt, J=48, 26, 20, 20 Hz); MS m/z (rel intensity) 127 (1), 111 (65), 97 (13), 83 (15), 69 (16), 57 (40), 55 (42), 43 (100), 41 (91). Calcd for $C_{12}H_{24}BrF$: C, 53.94; H, 9.05%. Found: C, 54.09; H, 9.33%.

Methyl 10-Fluoro-11-bromoundecanoate (15a): R_f 0.40 (hexane–Et_2O=10:1). IR (neat) 2950, 2870, 1741, 1462, 1457, 1436, 1382, 1360, 1250, 1200, 1171, 1110, 1000, 820, 724 cm^{-1}; ^{1}H NMR δ=4.60 (double quintet, J=48, 6 Hz, 1H), 3.64 (s, 3H), 3.45 (dd, J=21, 6 Hz, 2H), 2.28 (t, J=7 Hz, 2H), 1.8—1.7 (m, 2H), 1.7—1.5 (m, 2H), 1.5—1.3 (m, 10H); ^{19}F NMR δ=−178.20 (dddt, J=49, 26, 20, 20 Hz); MS m/z (rel intensity) 279 (M^++2−F; 2), 277 (M^+−F; 2), 267 (2), 265 (2), 87 (22), 74 (100), 59 (31), 55 (46), 43 (34), 41 (85), 39 (31). Calcd for $C_{12}H_{22}BrFO_2$: C, 48.50; H, 7.46%. Found: C, 48.74; H, 7.73%.

1-Fluoro-2-bromo-1-phenylethane (16a): R_f 0.38 (hexane). IR (neat) 3095, 3052, 2985, 2950, 1959, 1890, 1816, 1730, 1500, 1455, 1420, 1383, 1355, 1316, 1290, 1241, 1214, 1158, 1062, 1043, 990, 920, 859, 814, 760, 704, 670, 598 cm^{-1}; ^{1}H NMR δ=7.5—7.3 (m, 5H), 5.64 (ddd, J=47, 8, 4 Hz, 1H), 3.71 (ddd, J=15, 11, 8 Hz, 1H), 3.62 (ddd, J=26, 11, 4 Hz, 1H); ^{19}F NMR δ=−174.44 (ddd, J=47, 26, 15 Hz); MS m/z (rel intensity) 204 (M^++2; 8), 202 (M^+; 8), 109 (100). Calcd for C_8H_8BrF: C, 47.32; H, 3.97%. Found: C, 47.36; H, 3.93%.

2-Fluoro-1-iodo-2,4-dimethylhexane (17a): R_f 0.44 (hexane). IR (neat) 2980, 2950, 2900, 1462, 1383, 1280, 1260, 1180, 1145, 1080, 1034, 930, 902, 850, 812, 762, 632 cm^{-1}; ^{1}H NMR δ=3.38 (d, J=16 Hz, 2H), 1.7—1.5 (m, 2H), 1.51 (d, J=21 Hz, 3H), 1.5—1.4 (m, 1H), 1.3—1.2 (m, 1H), 0.96 (d, J=6 Hz, 3H), 0.89 (t, J=7 Hz, 3H); ^{19}F NMR δ=−139.48 (m); MS m/z (rel intensity) 258 (M^+; 2), 127 (3), 111 (32), 69 (100), 57 (94), 55 (69). Calcd for $C_8H_{16}FI$: C, 37.23; H, 6.25%. Found: C, 37.52; H, 6.31%.

1-Fluoro-2-iodo-1,1-diphenylethane (18a): R_f 0.25 (hexane). IR (KBr) 3195, 3052, 3025, 1492, 1441, 1417, 1338, 1260, 1210, 1180, 1160, 1058, 1022, 996, 960, 924, 894, 882, 762, 750, 694, 642, 588 cm^{-1}; ^{1}H NMR δ=7.5—7.2 (m, 10H), 4.01 (d, J=22 Hz, 1H), 4.03 (s, 1H); ^{19}F NMR δ=−142.18 (t, J=22 Hz); MS m/z (rel intensity) 326 (M^+; 1), 307 (2), 306 (1), 199 (100). Calcd for $C_{14}H_{12}FI$: C, 51.56; H, 3.71%. Found: C, 51.80; H, 3.78%.

2-Fluoro-3-iodo-2,3-dimethylbutane (19a): R_f 0.28 (hexane). IR (neat) 3000, 2972, 2930, 2871, 1726, 1458, 1379, 1258, 1160, 1138, 1100, 890, 850, 820, 706 cm^{-1}; ^{1}H NMR δ=2.00 (s, 6H), 1.59 (d, J=21 Hz, 6H); ^{19}F NMR δ=−138.78 (br s); MS m/z (rel intensity) 231 (M^++1; 0.05), 230 (M^+; 0.76), 127 (8), 104 (9), 103 (100), 88 (12), 83 (19), 73 (11). Calcd for $C_6H_{12}FI$: C, 31.32; H, 5.26%. Found: C, 31.49; H, 5.08%.

2-Fluoro-1-dodecene (20):$^{10)}$ To a solution of 2-fluoro-1-iodododecane (0.31 g, 1 mmol) in CH_2Cl_2 (1 mL) was added DBU (0.30 g, 2 mmol) at 0 °C. The resulting mixture was stirred for 12 h at room temperature, then poured into sat NH_4Cl aq solution, and extracted with Et_2O (20 mL×3). The combined ethereal layer was dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by column chromatography to give **20** (0.171 g, 0.92 mmol, 92%). IR (neat) 2980, 2951, 2880, 1676, 1472, 1431, 1385, 1250, 1181, 1104, 936, 844, 725 cm^{-1}; ^{1}H NMR δ=4.48 (dd, J=18, 3 Hz, 1H), 4.19 (dd, J=50, 3 Hz, 1H), 2.17 (dt, J=16, 7 Hz, 2H), 1.50 (quintet, J=7 Hz, 2H), 1.4—1.2 (m, 14H), 0.89 (t, J=7 Hz, 3H); ^{19}F NMR δ=−95.2 (m); MS m/z (rel intensity) 166 (M^+−HF; 0.5), 124 (5), 110 (6), 96 (13), 82 (26), 69 (29), 68 (13), 55 (53), 43 (100), 41 (82).

(*E*)-1-Fluoro-1-phenyl-1-propene (21):$^{36)}$ IR (neat) 3080, 2965, 2948, 2895, 1685, 1500, 1445, 1388, 1356, 1203, 1091, 1068, 951, 920, 829, 774, 728, 701 cm^{-1}; ^{1}H NMR δ=7.51—7.46 (m, 2H), 7.44—7.36 (m, 3H), 5.47 (dq, J=22, 8 Hz, 1H), 1.80 (dd, J=8, 2 Hz); ^{19}F NMR δ=−102.62 (dq, J=22, 2 Hz); MS m/z (rel intensity) 137 (M^++1; 9), 136 (M^+; 90), 135 (100), 116 (17), 115 (63), 109 (40).

2-Fluoro-3-(4-methoxyphenyl)-1-propene (22): IR (neat) 3030, 2980, 2950, 2930, 2852, 1680, 1618, 1591, 1518, 1470, 1440, 1428, 1382, 1306, 1250, 1180, 1109, 1039, 943, 920, 854, 811, 765 cm^{-1}; ^{1}H NMR δ=7.18 (d, J=9 Hz, 2H), 6.87 (d, J=9 Hz, 2H), 4.59 (dd, J=17, 3 Hz, 1H), 4.22 (dd, J=49, 3 Hz, 1H), 3.81 (s, 3H), 3.45 (d, J=15 Hz, 2H); ^{19}F NMR δ=−95.04 (ddt, J=49, 17, 15 Hz); MS m/z (rel intensity) 167 (M^++1; 11), 166 (M^+; 100), 151 (22), 121 (33), 103 (20). Calcd for $C_{10}H_{11}FO$ C, 72.27; H, 6.67%. Found: C, 72.06; H, 6.72%.

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34) Dehydroiodation of **11a** gave *E*-1-fluoro-1-phenyl-1-propene (**21**). Therefore, the stereochemistry of **11a** was assigned to be *erythro*. See Ref. 36.

35) One of the referees pointed out that the stereochemistry of **13a** was ambiguous. Because *trans* addition of FX occurred with both cyclohexenes (cyclic system) and 1-phenyl-1-propene (acyclic system), we assigned tentatively the stereochemistry of **13a** as *trans*.

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