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Chromium-mediated fluoroalkenylation reactions of 1,1-dibromo-1-fluoroalkane and 1-bromo-1-fluoroalkene derivatives

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Abstract

$CrCl_2$- and $NiCl_2$-mediated coupling reactions of *E/Z* mixture of 1-bromo-1-fluoroalkenes with aldehydes proceeded in a high stereoselectivity to give the corresponding (*Z*)-2-fluoroallylic alcohol derivatives. On the other hand, in the reaction of 1,1-dibromo-1-fluoroalkane with $CrCl_2$, (*Z*)-fluoroalkene derivative was formed via α-elimination reaction of the chromium carbenoid intermediate accompanying the concomitant 1,2-shift of β-hydrogen.

Keywords: Chromium chloride; Fluoroalkenylation; 1-Bromo-1-fluoroalkene; 1,1-Dibromo-1-fluoroalkane; 2-Fluoroallylic alcohol

1. Introduction

Fluorinated olefins are an important class of compounds in the field of medicinal chemistry and material science, for example in medicinal chemistry area as potential enzyme inhibitors [1,2] or as an ideal mimic of amide bond [3–5]. Therefore, development of new and efficient synthetic methods for fluorinated olefins has been extensively investigated. The synthetic methods for fluorinated olefins can be classified into two types, which involve carbon–fluorine bond forming reactions and the use of the fluorinated compounds as building blocks. In the former case, fluorination of alkenyl anion with electrophilic fluorinating reagent, such as *N*-fluorosulfonamide [6] or fluoroolefin formation by the reaction of carbonyl compounds with diethylaminosulfur trifluoride (DAST) [7] are known, while there remains several problems in the stereoselectivity and the generality of these reactions. As typical building blocks for fluorinated olefin synthesis, fluorophosphonoacetate in the Horner–Emmons reaction [8], fluorosilylacetate in the Peterson olefination [9] and 1-fluoro-1-sulfonyl- or 1-fluoro-1-stannyl-alkenes in palladium-catalyzed coupling reactions [10] are providing highly useful positions.

It would be expected that like non-fluorinated vinyl metal chemistry [11], if fluorovinyl metal species were readily generated by hydrometalation or carbometalation reaction with fluoroacetylene derivatives, such reactive organometallics should open convenient accesses to a variety type of fluorinated olefins. However, it is known that fluoroacetylenes oligomerize very easily [12], that is, fluoroacetylenes are too unstable to handle as synthetic intermediates (Scheme 1).

Therefore, development of an efficient method for the stereo- and chemo-selective generation of reactive fluorovinyl metal species should be challenging subject. Among such studies, Burton et al. have reported the kinetic separation of the (*E*)- and (*Z*)-isomers of 1-bromo-1-fluoroalkenes using Pd-catalyzed carbonylation and hydrogenolysis reactions, in which the (*E*)-isomer shows remarkably higher reactivity than the (*Z*)-isomer [13]. Related to this, very recently, Pannecoucke and co-workers reported the stereoselective dehydrobromination of 1-bromo-1-fluoroalkenes with DBU or LiHMDS obtaining the (*E*)-isomer unchanged [14].

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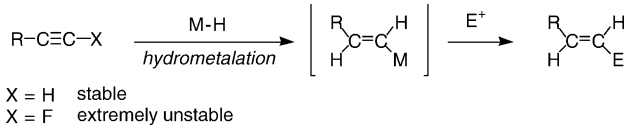


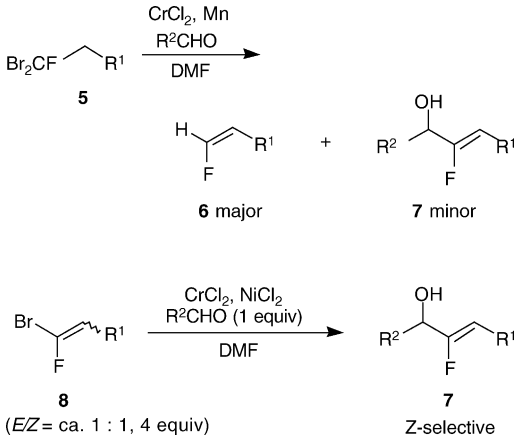
Scheme 1.

Accumulated synthetically useful methods for the preparation of alkenylated compounds employing chromium chemistry [15] prompted us to examine the generation of fluoroalkenyl chromium species from 1,1-dihalo-1-fluoroalkane or 1-bromo-1-fluoroalkene. Falck et al. demonstrated that 1,1,1-trichloroalkane **1** reacts with chromium(II) chloride to generate (*E*)-chloroalkenyl chromium(III) species **3** stereoselectively via *gem*-bischromium(III) carbenoid intermediate **2** and this chloroalkenyl chromium species **3** can serve in carbon–carbon bond forming reactions such as addition to aldehyde and Pd-catalyzed arylation reaction [16] (Scheme 2). As one of the most useful chromium-mediated reactions, a highly chemo-selective addition reaction of alkenylchromium(III) generated from alkenyl iodide and $CrCl_2/NiCl_2$ with aldehyde, so-called Nozaki–Hiyama–Kishi (N–H–K) reaction, has been well documented with many applications to the key steps in the total synthesis of structurally complicated natural products [15,17].

Contrary to the hydrocarbon chemistry area, however, when we started the chromium chemistry, there had been no report on the reaction of 1,1-dihalo-1-fluoroalkane or 1-bromo-1-fluoroalkene with $CrCl_2$ [18], while very recently, Pannecoucke et al. reported the stereoselective fluoroalkenylation of aldehydes employing N–H–K reaction of 1-bromo-1-fluoroalkene [19]. In this paper, we report our collective results obtained from the reactions of 1,1-dibromo-1-fluoroalkane and 1-bromo-1-fluoroalkene derivatives with $CrCl_2$, in particular, the former shows a different reactivity as compared with that of trichloroalkanes and the latter provides *Z*-selective formation of 1-substituted 2-fluoroallylic alcohols using the *E/Z* mixture (Scheme 3).

2. Results and discussion

Initially, reaction of TBDPS ether of 3,3-dibromo-3-fluoropropanol **5** with $CrCl_2$ was conducted under various conditions to see the possibility for the generation of fluoroalkenyl chromium species, similar to trichloro derivative (Table 1). Dibromofluoro compound **5** did not react with $CrCl_2$ in THF at room temperature (entry 1), while a combination of $CrCl_2$ and Mn powder in THF at the same

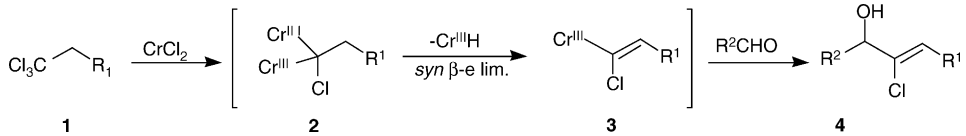


Scheme 3.

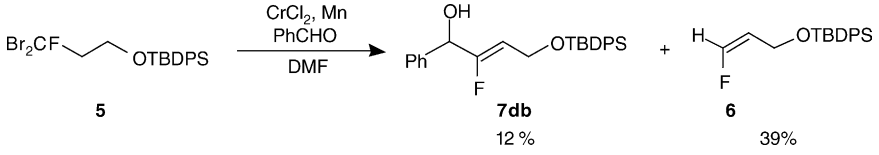
temperature promoted the reaction giving rise to (*Z*)-fluoroalkene **6** in 16% yield after 20 h (entry 2). In DMF reaction proceeded smoothly consuming **5** within 6 h to give fluoroalkene **6** in 75% yield with complete *Z*-selectivity after aqueous work-up (entry 3). Furthermore, it was found that treatment of the reaction mixture obtained under the same conditions with D_2O or benzaldehyde instead of aqueous work-up resulted in the formation of fluoroalkene **6** as a sole product, and any deuterium incorporation or fluoroalkenylation of aldehyde was not observed (entries 4–6).

Under the Barbier's conditions, namely when a mixture of **5**, benzaldehyde, $CrCl_2$ and Mn powder in DMF was stirred at room temperature, we obtained the fluoroallyl alcohol **7db** in only 12% yield along with the isolation of **6** in 39% yield, still as a major product (Scheme 4).

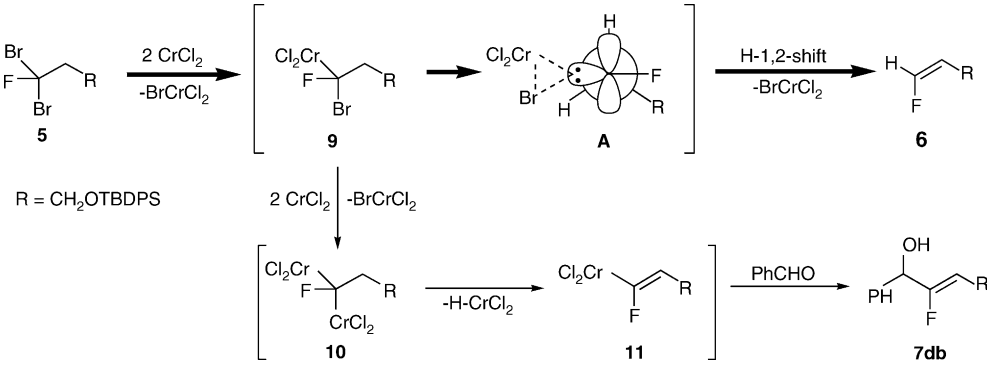
Possible reaction pathway is illustrated in Scheme 5. From these results and the efficient fluoroalkenylation of aldehyde with 1-bromo-1-fluoroalkene mediated by $CrCl_2$/$NiCl_2$ in DMF (vide infra), it would be likely that the formation of fluoroalkenyl chromium species **11** is not the major reaction pathway in the reaction of dibromofluoroalkane **5** with $CrCl_2$ and Mn powder in DMF. On the other hand, the 1,2-shift of β-hydrogen to divalent carbon resulting in the formation of an alkene is well known reaction via carbene and carbenoid intermediate [20]. Likewise, the reaction pathway to the major product fluoroalkene **6** from dibromofluoride **5** possibly involves the generation of chromium carbenoid intermediate **9** as the first step, and then α-elimination of bromine accompanying the concomitant 1,2-shift of β-hydrogen prior to the second reaction of the carbenoid intermediate **9** with $CrCl_2$ to generate bischromium intermediate **10** (Scheme 5). Mechanistic detail is the future subject.



Scheme 2.



Scheme 4.

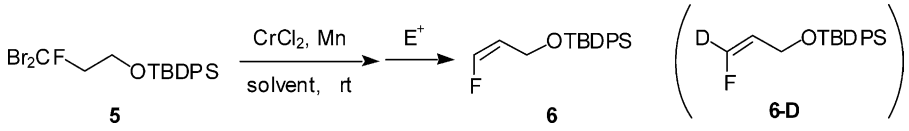


Scheme 5.

Since it was difficult to achieve chromium-mediated fluoroalkenylation of aldehyde using 1,1-dibromo-1-fluoroalkane, we next examined the N–H–K reaction using a *E/Z* mixture of 1-bromo-1-fluoroalkene. According to the reported procedure [21], 1-bromo-1-fluoroalkenes **8a–8d** were prepared as an almost 1:1 *E/Z* mixture, which was used chromium-mediated reaction with aldehyde. Results are summarized in Table 2. When a mixture of the 1-bromo-1-fluorostyrene **8a** (*E/Z* = 45:55, 4 equiv), 3-phenylpropanal (1 equiv), $CrCl_2$ (8 equiv) and a catalytic amount of $NiCl_2$ (8 mol %) in DMF was stirred at room temperature for 4 h, the fluoroallyl alcohol **7aa** was isolated in 74% yield as a single (*Z*)-isomer (entry 1). Similarly, with benzaldehyde the adduct **7ab** consisting of only (*Z*)-isomer was obtained in 62% yield (entry 2). The alkyl group substituted substrate **8b** showed lower reactivity than styrene derivative **8a**, requiring much more $NiCl_2$ for the reaction to proceed smoothly. Thus, on using 80 mol% $NiCl_2$, the reaction of **8b** (*E/Z* = 47:53) with 3-phenylpropanal gave the adduct **7ba** in 75% yield, and with benzaldehyde the product **7bb** was obtained in 70% yield (entries 3, 4). In these cases, a high *Z* selectivity of the isolated fluoroallyl alcohol derivative was observed, **7ba**; *Z/E* = 94:6 and **7bb**; *Z/E* = 92:8, respectively. Under the similar conditions, the homoallyl ether derivative **8c** reacted with 3-phenylpropanal and benzaldehyde to give the corresponding adduct **7ca** in 70% yield (*Z/E* = 93:7) and **7cb** in 73% yield (*Z/E* = 95:5), respectively (entries 5, 6). In the case of the allyl ether derivative **8d**, while a longer reaction time was required, highly *Z* selective formation of the adducts **7da** and **7db** was also observed (*Z/E* > 95:5) (entries 7,8).

To see the difference in reactivity due to the olefin geometry, we carried out the reaction of (*Z*)-isomer of bromofluoroalkene (*Z*)-**8d** with 2 equiv of benzaldehyde (Scheme 6). Reaction proceeded rather sluggishly to give the (*E*)-isomer of alkenylated product (*E*)-**7db** in 10% yield

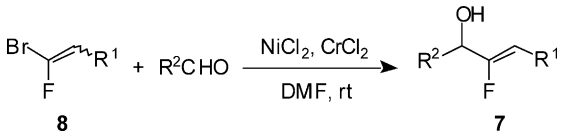
Table 1
Reaction of dibromofluoroalkane **5** with CrCl

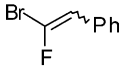
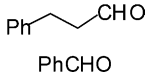
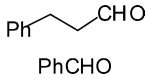
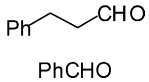
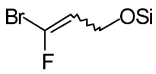
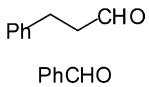


Entry	$CrCl_2$ (equiv)	Mn (equiv)	Solvent	Time (h)	E^+	**6** yield (%)[a]
1	4.8	0	THF	12	H_2O	No reaction
2	2	4	THF	20	H_2O	16
3	2	4	DMF	6	H_2O	75
4	2	4	DMF	6	D_2O	73[b]
5	2	4	DMF–d_7	6	H_2O	66[b]
6	2	4	DMF	6	PhCHO	60[c]

[a] Isolated yield.
[b] **6-D** was not detected.
[c] 2-Fluoroallylic alcohol **7db** was not detected.

Table 2
Synthesis of 2-fluoroallyl alcohol derivatives **7**



Entry	**8** (*E*/*Z*)	R^2CHO	Method[a]	Time (h)	**7**	Yield[b] (%)	*Z*/*E*[c]
1			A	4	**7aa**	74	100:0
2	**8a** (45:55)	PhCHO	A	4	**7ab**	62	100:0
3			B	4	**7ba**	75	94:6
4	**8b** (47:53)	PhCHO	B	4	**7bb**	70	92:8
5			B	4	**7ca**	70	93:7
6	**8c** (45:55)	PhCHO	B	4	**7cb**	73	95:5
7			B	12	**7da**	64	>95:5
8	**8d** (42:58)	PhCHO	B	12	**7db**	60	>95:5

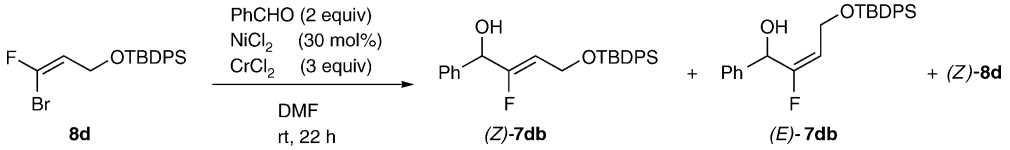
[a] *Method A:* 8 mol% of $NiCl_2$, 8 equiv of $CrCl_2$ and 4 equiv of **8** were employed in DMF (0.03 M); *method B:* 8 mol% of $NiCl_2$, 8 equiv of $CrCl_2$ and 4 equiv of **8** were employed in DMF (0.06 M).
[b] Isolated yield based on the aldehyde.
[c] *Z*/*E* ratio was determined by 300 MHz ^1H NMR.

along with the recovery of (*Z*)-**8d** in 4% yield, but (*Z*)-isomer of alkenylated product (*Z*)-**7db** was not detected. Besides, these compounds, formation of homocoupling products of **8d** seemed to make this reaction rather complicated [17c,d]. Similar reaction using *E*/*Z* mixture (ratio 44:56) gave (*Z*)-**7db** in 89% yield based on the starting (*E*)-isomer of the bromide (*E*)-**8d**, and (*E*)-**7db** in 11% yield based on (*Z*)-**8d** along with the recovery of (*Z*)-**8d** in 11%. From these results, (*E*)-isomer of the bromide **8** shows highly efficient reactivity with $CrCl_2$/$NiCl_2$ to form (*E*)-fluroalkenyl chromium species, which reacts with aldehyde to give the (*Z*)-fluoroallylic alchohol. On the other hand, compared with the (*E*)-isomer, (*Z*)-isomer reacts with $CrCl_2$/$NiCl_2$ much more slowly to form the (*Z*)-alkenylchromium species stereospecifically leading to (*E*)-fluoroallylic alchohol although yield is quite low. Therefore, when the reaction is conducted using excess amount of bromofluoroalkene **8** relative to aldehyde, highly *Z*-selective fluoroalkenylation reaction can be achieved.

In summary, $CrCl_2$–$NiCl_2$-mediated reaction of an *E*/*Z* mixture of 1-bromo-1-fluoroalkene with aldehyde provided a highly *Z*-selective alkenylation product. Furthermore, the reaction of 1,1-dibromo-1-fluoroalkane with $CrCl_2$ was found to give (*Z*)-fluoroalkene derivative via α-elimination reaction of the chromium carbenoid intermediate accompanying the concomitant 1,2-shift of β-hydrogen.

3. Experimental details

General: $CrCl_2$, $NiCl_2$ and Mn are available commercially. All reactions were carried out under argon atmosphere. ^1H and ^{13}C NMR spectra were taken on a Bruker dpx400 spectrometer, and chemical shifts were reported in



8d	(*Z*) **-7db**	(*E*)- **7db**	(*Z*) **8d**
Z only	0%	10%	4%
E/*Z* = 44:56	89%	11%	11%

Scheme 6.

parts per million (ppm) using $CHCl_3$ (7.26 ppm) in $CDCl_3$ for ^1H NMR, and $CDCl_3$ (77.01 ppm) for ^{13}C NMR as an internal standard, respectively. ^{19}F NMR spectra were taken on a Bruker dpx400 spectrometer, and chemical shifts were reported in parts per million using benzotrifluoride as a standard. Infrared (IR) spectra were recorded on a JASCO FT/IR-620 infrared spectrophotometer. Mass spectra (MS) were obtained on a VG Auto Spec. Medium pressure liquid chromatography (MPLC) was performed using prepacked column (silica-gel, 50 μm) with RI detector.

3.1. Preparation of (1,1-dimethylethyl)(diphenyl)silyl 3,3-dibromo-3-fluoropropyl ether (**5**)

Under an argon atmosphere, to a solution of $LiBH_4$ (230 mg, 10.6 mmol) in Et_2O (6 mL), ethyl 3,3-dibromo-3-fluoropropionate [22] (2.7 g, 9.7 mmol) in Et_2O (4 mL) and trimethyl borate (200 μL, 1.8 mmol) were added at 0 °C. After being stirred at the same temperature for 2 h and then at room temperature for 5 h, addition of NH_4Cl aq. followed by extractive work-up gave 3,3-dibromo-3-fluoropropanol, which was used without purification. A mixture of this alcohol, *tert*-butyldiphenylchlorosilane (1.5 mL, 5.8 mmol) and imidazole (550 mg, 8.1 mmol) in THF (6 mL) was stirred at room temperature for 5 h. Addition of H_2O followed by extractive work-up and purification by column chromatograpy (hexane/AcOEt = 100:1) gave the product **5** (2.5 g, 5.2 mmol, 54% yield).

*(1,1-Dimethylethyl)(diphenyl)silyl 3,3-dibromo-3-fluoropropyl ether (**5**)*: Colorless oil. IR (neat) ν cm^{-1}; 3071, 2931, 2858, 1472, 1428, 1113, 823, 739, 702. ^1H NMR (400 MHz, $CDCl_3$) δ; 1.09 (9H, s), 3.04 (2H, dt, J = 15.8, 6.7 Hz), 4.00 (2H, t, J = 6.7 Hz), 7.40–7.48 (6H, m), 7.69–7.72 (4H, m). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ; 19.1, 26.8, 54.8 (d, J = 18.0 Hz), 61.0 (d, J = 2.9 Hz), 93.0 (d, J = 319.7 Hz), 127.8, 129.9, 133.1, 135.6. ^{19}F NMR (376.5 MHz, $CDCl_3$) δ; 19.1 (1F, t, J = 15.8 Hz). EI–MS m/z: 291 (M^+–$C_6H_{11}BrF$). HRMS calcd for $C_{13}H_{12}BrOSi$: 290.9841 (M^+–$C_6H_{11}BrF$), Found: 290.9814. Anal. Calcd for $C_{19}H_{23}Br_2FOSi$: C, 48.12; H, 4.89. Found: C, 48.39; H, 4.91.

3.2. Reaction of 1,1-dibromo-1-fluoroalkane with $CrCl_2$

Under an argon atmosphere, to a mixture of $CrCl_2$ (94.0 mg, 0.77 mmol) and Mn (55.0 mg, 1.0 mmol) in DMF (3 mL) sonicated for 10 min, was added a solution of **5** (120 mg, 0.25 mmol) and benzaldehyde (50 μL, 0.49 mmol) in DMF (2 mL). After being stirred at room temperature for 14 h, addition of H_2O followed by extractive work-up and separation by column chromatography gave a fraction containing **6** (hexane/AcOEt = 50:1) and allylic alcohol **7db** (12.4 mg, 0.03 mmol, 12%, hexane/AcOEt = 6:1). The former was further separated by MPLC (hexane/AcOEt = 50:1, flow rate 7.0 mL/min) to give **6** (31.2 mg, 0.1 mmol, 39% yield).

*(1,1-Dimethylethyl)(diphenyl)silyl (Z)-3-fluoro-2-propenyl ether (**6**)*: Colorless oil. IR (neat) ν cm^{-1}; 3071, 2931, 2858, 1472, 1428, 1112, 740, 702. ^1H NMR (400 MHz, $CDCl_3$) δ; 1.06 (9H, s), 4.37 (2H, ddd, J = 6.6, 2.2, 1.5 Hz), 5.03 (1H, dtd, J = 42.2, 6.6, 4.8 Hz), 5.40 (1H, ddt, J = 84.0, 4.8, 1.5 Hz), 7.33–7.47 (6H, m), 7.61–7.73 (4H, m). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ; 19.2, 26.8, 56.3 (d, J = 7.6 Hz), 111.1 (d, J = 3.0 Hz), 127.7, 129.7, 133.6, 135.6, 147.7 (d, J = 260.4 Hz). ^{19}F NMR (376.5 MHz, $CDCl_3$) δ; −64.3 (1F, ddt, J = 84.0, 42.2, 2.2 Hz). EI–MS m/z: 257 (M^+–C_4H_9). HRMS calcd for $C_{15}H_{14}FOSi$: 257.0798 (M^+–C_4H_9). Found: 257.0805.

*(Z)-4-{ [(1,1-Dimethylethyl)(diphenyl)silyl]oxy}-2-fluoro -1-phenyl-2-buten-1-ol (**7db**)*: Colorless oil. IR (neat) ν cm^{-1}; 3398, 3070, 2931, 2858, 1472, 1428, 1111, 1060, 741, 702. ^1H NMR (400 MHz, $CDCl_3$) δ; 1.07 (9H, s), 2.16 (1H, br. s), 4.39 (2H, d, J = 6.6 Hz), 5.14 (1H, dd, J = 11.1, 4.4 Hz), 5.21 (1H, dt, J = 36.6, 6.6 Hz), 7.34–7.46 (11H, m), 7.67–7.70 (4H, m). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ; 19.1, 26.8, 57.1 (d, J = 6.8 Hz), 72.4 (d, J = 32.0 Hz), 107.2 (d, J = 11.0 Hz), 126.7, 127.7, 128.4, 128.6, 129.6, 133.6, 135.6, 139.1, 158.7 (d, J = 260.4 Hz). ^{19}F NMR (376.5 MHz, $CDCl_3$) fδ; −55.9 (1F, dd, J = 36.6, 11.1 Hz). EI–MS m/z: 285 (M^+–$C_{10}H_{15}$). HRMS calcd for $C_{16}H_{16}FO_2Si$: 285.0747 (M^+–$C_{10}H_{15}$). Found: 285.0756. Anal. Calcd for $C_{26}H_{29}FO_2Si$: C, 74.25; H, 6.95. Found: C, 73.90; H, 7.03.

3.3. General procedure for preparation of 1-bromo-1-fluoroalkene: preparation of 1-[(E)- and (Z)-2-bromo-2-fluoroethenyl]benzene (**8a**)

Under an argon atmosphere, to a suspension of Zn (1.2 g, 18.4 mmol) and triphenylphosphine (3.1 g, 11.8 mmol) in THF (30 mL), a solution of benzaldehyde (0.6 mL, 5.9 mmol) and tribromofluoromethane (4.8 g, 17.7 mmol) in THF (10 mL) was added at room temperature. After being refluxed for 2 h, usual work-up and purification by column chromatography (hexane/Et_2O = 100:1) gave the product **8a** (1.1 g, 5.3 mmol, 89% yield, E/Z = 45:55).

*1-[(E)- and (Z)-2-bromo-2-fluoroethenyl]benzene (**8a**)*: ^1H and ^{19}F NMR spectra of this compound was identical with those reported by Burton and co-workers [21].

*1-[(E)- and (Z)-4-bromo-4-fluoro-3-butenyl]benzene (**8b**)*: ^1H and ^{19}F NMR spectra of this compound was identical with those reported by Hiyama and co-workers [23].

*(E)- and (Z)-4-bromo-4-fluoro-3-butenyl (1,1-dimethylethyl)(diphenyl)silyl ether (**8c**)*: Colorless oil. IR (neat) ν cm^{-1}; 3071, 2931, 2858, 1472, 1428, 1112, 1024, 822, 740, 702. ^1H NMR (400 MHz, $CDCl_3$) δ; 1.09 (9H, s), 2.30 (*Z*–2H, dt, J = 7.4, 6.6 Hz), 2.38 (*E*–2H, dt, J = 7.7, 6.4 Hz), 3.69–3.76 (2H, m), 5.14 (*E*–1H, dt, J = 31.3, 7.7 Hz), 5.60 (*Z*–1H, dt, J = 13.4, 7.4 Hz), 7.40–7.49 (6H, m), 7.68–7.77 (4H, m). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ; 19.2, 26.8, 29.2, 31.1, 62.3, 62.4, 107.1 (d, J = 16.5 Hz), 109.6 (d, J = 12.4 Hz), 127.7, 129.7, 132.4 (d, J = 316.1 Hz), 133.6, 135.6, 136.0 (d, J = 317.9 Hz). ^{19}F NMR (376.5 MHz,

$CDCl_3$) δ; −7.5 (*Z*–1F, d, J = 13.4 Hz), −12.0 (*E*–1F, d, J = 31.3 Hz). EI–MS *m/z*: 349 (M^+–C_4H_9). HRMS calcd for $C_{16}H_{15}BrFOSi$: 349.0060 (M^+–C_4H_9). Found: 349.0054.

*(E)- and (Z)-3-bromo-3-fluoro-2-propenyl (1,1-dimethylethyl)(diphenyl)silyl ether (**8d**)*: Colorless oil. IR (neat) ν cm^{-1}; 3071, 2958, 2857, 1472, 1428, 1113, 1070, 822, 740, 702. ^1H NMR (400 MHz, $CDCl_3$) δ; 1.09 (9H, s), 4.24 (*Z*–2H, dd, J = 6.8, 2.2 Hz), 4.28 (*E*–2H, dd, J = 6.9, 2.7 Hz), 5.30 (*E*–1H, dd, J = 30.6, 6.9 Hz), 5.74 (*Z*–1H, dd, J = 12.3, 6.8 Hz), 7.35–7.53 (6H, m), 7.62–7.78 (4H, m). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ; 19.1, 26.8, 57.9 (*E*, d, J = 3.3 Hz), 61.0 (*Z*, d, J = 7.3 Hz), 109.8 (*Z*, d, J = 14.7 Hz), 112.4 (*E*, d, J = 10.7 Hz), 127.8, 129.8, 133.2 (*E*), 133.2 (*Z*), 133.4 (*E*, d, J = 322.5 Hz), 135.5 (*E*), 135.6 (*Z*), 136.2 (*Z*, d, J = 318.6 Hz). ^{19}F NMR (376.5 MHz, $CDCl_3$) δ; −6.6 (*Z*–1F, dd, J = 12.3, 2.2 Hz), −8.8 (*E*–1F, dd, J = 30.6, 2.7 Hz). EI–MS *m/z*: 335 (M^+–C_4H_9). HRMS calcd for $C_{15}H_{13}BrFOSi$: 334.9903 (M^+–C_4H_9). Found: 334.9908. Anal. Calcd for $C_{19}H_{22}BrFOSi$: C, 58.01; H, 5.64. Found: C, 58.18; H, 5.73.

3.4. General procedure for $CrCl_2$/$NiCl_2$-mediated reaction of 1-bromo-1-fluoroalkene with aldehyde

Under an argon atmosphere, to a mixture of $CrCl_2$ (185 mg, 1.5 mmol) and $NiCl_2$ (2.0 mg, 15 μmol) in DMF (4 mL) sonicated for 10 min, was added a solution of **8a** (120 mg, 0.25 mmol) and 3-phenylpropanal (50 μL, 0.49 mmol) in DMF (2 mL). After being stirred at room temperature for 4 h, addition of H_2O followed by extractive work-up and purification by column chromatography (hexane/AcOEt = 5:1) gave the product **7aa** (35.4 mg, 0.14 mmol, 74% yield).

*(Z)-2-Fluoro-1,5-diphenyl-1-penten-3-ol (**7aa**)*: Colorless oil. IR (neat) ν cm^{-1}; 3365, 3027, 2926, 1495, 1451, 1032, 752, 695. ^1H NMR (400 MHz, $CDCl_3$) δ; 2.02–2.18 (2H, m), 2.72–2.86 (2H, m), 4.24 (1H, ddd, J = 15.2, 7.2, 6.2 Hz), 5.78 (1H, d, J = 39.6 Hz), 7.20–7.37 (8H, m), 7.49–7.53 (2H, m). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ; 31.5, 35.5, 70.6 (d, J = 30.1 Hz), 106.5 (d, J = 6.7 Hz), 126.0, 127.4, 128.5, 128.7, 128.7, 132.7, 141.2, 160.1 (d, J = 269.7 Hz). ^{19}F NMR (376.5 MHz, $CDCl_3$) δ; −55.2 (1F, dd, J = 39.6, 15.2 Hz). EI–MS *m/z*: 256 (M^+). HRMS calcd for $C_{17}H_{17}FO$: 256.1263 (M^+). Found: 256.1252. Anal. Calcd for $C_{17}H_{17}FO$: C, 79.66; H, 6.69. Found: C, 79.27; H, 6.94.

*(Z)-2-Fluoro-1,3-diphenyl-2-propen-1-ol (**7ab**)*: ^1H and ^{19}F NMR spectra of this compound was identical with those reported by Hiyama et al [24].

*(Z)-4-Fluoro-1,7-diphenyl-4-hepten-3-ol (**7ba**)*: Colorless oil. IR (neat) ν cm^{-1}; 3377, 3027, 2925, 2858, 1496, 1454, 1030, 748, 699. ^1H NMR (400 MHz, $CDCl_3$) δ; 1.86 (1H, br. s), 1.91–2.05 (2H, m), 2.47 (2H, dt, J = 7.5, 7.5 Hz), 2.59–2.78 (4H, m), 4.06 (1H, ddd, J = 16.6, 7.3, 6.5 Hz), 4.85 (1H, dt, J = 37.5, 7.5 Hz), 7.15–7.26 (6H, m), 7.29–7.33 (4H, m). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ; 24.9 (d, J = 4.3 Hz), 31.4, 35.3, 35.4, 70.1 (d, J = 30.3 Hz), 105.9 (d, J = 13.9 Hz), 126.0, 126.0, 128.3, 128.4, 141.3, 159.5 (d, J = 257.4 Hz). ^{19}F NMR (376.5 MHz, $CDCl_3$) δ; −61.5 (1F, dd, J = 37.5, 16.6 Hz). EI–MS *m/z*: 284 (M^+). HRMS calcd for $C_{19}H_{21}FO$: 284.1576 (M^+). Found: 284.1565. Anal. Calcd for $C_{19}H_{21}FO$: C, 80.25; H, 7.44. Found: C, 79.98; H, 7.49.

*(Z)-2-Fluoro-1,5-diphenyl-2-penten-1-ol (**7bb**)*: Colorless oil. IR (neat) ν cm^{-1}; 3389, 3028, 2926, 2859, 1496, 1453, 1024, 748, 700. ^1H NMR (400 MHz, $CDCl_3$) δ; 2.26 (1H, br. s), 2.48 (2H, dt, J = 7.5, 7.5 Hz), 2.73 (2H, t, J = 7.5 Hz), 4.95 (1H, dt, J = 36.9, 7.5 Hz), 5.17 (1H, d, J = 12.7 Hz), 7.19–7.25 (3H, m), 7.28–7.39 (7H, m). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ; 25.1 (d, J = 4.0 Hz), 35.3, 72.7 (d, J = 32.0 Hz), 106.7 (d, J = 13.3 Hz), 126.0, 126.6, 128.2, 128.3, 128.4, 128.5, 139.5, 141.3, 158.8 (d, J = 256.5 Hz). ^{19}F NMR (376.5 MHz, $CDCl_3$) δ; −59.4 (1F, dd, J = 36.9, 12.7 Hz). EI–MS *m/z*: 256 (M^+). HRMS calcd for $C_{17}H_{17}FO$: 256.1263 (M^+). Found: 256.1256.

*(Z)-7-{[(1,1-Dimethylethyl)(diphenyl)silyl]oxy}-4-fluoro -1-phenyl-4-hepten-3-ol (**7ca**)*: Colorless oil. IR (neat) ν cm^{-1}; 3388, 3070, 2930, 2858, 1472, 1428, 1111, 740, 701. ^1H NMR (400 MHz, $CDCl_3$) δ; 1.09 (9H, s), 1.91–2.09 (2H, m), 2.40 (2H, dt, J = 7.4, 6.4 Hz), 2.66–2.85 (2H, m), 3.73 (2H, t, J = 6.4 Hz), 4.07 (1H, ddd, J = 15.8, 9.4, 6.2 Hz), 4.92 (1H, dt, J = 37.8, 7.4 Hz), 7.18–7.26 (3H, m), 7.28–7.33 (2H, m), 7.37–7.47 (6H, m), 7.69–7.71 (4H, m). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ; 19.6, 27.3, 27.4 (d, J = 3.9 Hz), 32.0, 35.8, 63.5, 70.5 (d, J = 30.2 Hz), 103.8 (d, J = 13.7 Hz), 126.4, 128.1, 128.9, 128.9, 130.0, 134.3, 136.0, 141.8, 160.6 (d, J = 257.5 Hz). ^{19}F NMR (376.5 MHz, $CDCl_3$) δ; −61.9 (1F, dd, J = 37.8, 15.8 Hz). EI–MS *m/z*: 230 (M^+–$C_{16}H_{21}F$). HRMS calcd for $C_{13}H_{14}O_2Si$: 230.0763 (M^+–$C_{16}H_{21}F$). Found: 230.0780. Anal. Calcd for $C_{29}H_{35}FO_2Si$: C, 75.28; H, 7.62. Found: C, 75.38; H, 7.66.

*(Z)-5-{ [(1,1-Dimethylethyl)(diphenyl)silyl]oxy}-2-fluoro -1-phenyl-2-penten-1-ol (**7cb**)*: Colorless oil. IR (neat) ν cm^{-1}; 3397, 3070, 2930, 2858, 1472, 1428, 1111, 739, 702. ^1H NMR (400 MHz, $CDCl_3$) δ; 1.06 (9H, s), 2.20 (1H, br. s), 2.40 (2H, dt, J = 7.4, 6.4 Hz), 3.71 (2H, t, J = 6.4 Hz), 5.00 (1H, dt, J = 37.3, 7.4 Hz), 5.21 (1H, dd, J = 12.3, 3.5 Hz), 7.33–7.47 (11H, m), 7.66–7.71 (4H, m). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ; 19.2, 26.8, 27.0 (d, J = 3.7 Hz), 63.0, 72.8 (d, J = 31.7 Hz), 104.5 (d, J = 13.3 Hz), 126.7, 127.6, 128.3, 128.5, 129.6, 133.8, 135.6, 139.5, 159.5 (d, J = 257.0 Hz). ^{19}F NMR (376.5 MHz, $CDCl_3$) δ; −58.7 (1F, dd, J = 37.3, 12.3 Hz). EI–MS *m/z*: 299 (M^+–$C_{10}H_{15}$). HRMS calcd for $C_{17}H_{18}FO_2Si$: 299.0904 (M^+–$C_{10}H_{15}$). Found: 299.0893. Anal. Calcd for $C_{27}H_{31}FO_2Si$: C, 74.61; H, 7.19. Found: C, 74.37; H, 7.33.

*(Z)-6-{ [(1,1-Dimethylethyl)(diphenyl)silyl]oxy}-4-fluoro -1-phenyl-4-hexen-3-ol (**7da**):* Colorless oil. IR (neat) ν cm^{-1}; 3388, 3070, 2931, 2858, 1471, 1428, 1111, 1065, 740, 701. ^1H NMR (400 MHz, $CDCl_3$) δ; 1.08 (9H, s), 1.72 (1H, br. s), 1.87–2.01 (2H, m), 2.64–2.81 (2H, m), 4.04 (1H,

ddd, J = 14.3, 7.1, 7.1 Hz), 4.38 (2H, d, J = 6.6 Hz), 5.09 (1H, dt, J = 37.1, 6.6 Hz), 7.19–7.24 (3H, m), 7.29–7.33 (2H, m), 7.38–7.45 (6H, m), 7.69–7.72 (4H, m). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ; 19.1, 26.8, 31.4, 35.2, 57.0 (d, J = 7.0 Hz), 69.6 (d, J = 30.0 Hz), 106.5 (d, J = 11.4 Hz), 126.0, 127.7, 128.5, 129.7, 133.6, 135.6, 141.2, 159.5 (d, J = 261.2 Hz). ^{19}F NMR (376.5 MHz, $CDCl_3$) δ; −58.8 (1F, dd, J = 37.1, 14.3 Hz). EI–MS m/z: 313 (M^+–$C_{10}H_{15}$). HRMS calcd for $C_{18}H_{18}FO_2Si$: 313.1060 (M^+–$C_{10}H_{15}$). Found: 313.1037. Anal. Calcd for $C_{28}H_{33}FO_2Si$: C, 74.96; H, 7.41. Found: C, 74.84; H, 7.46.

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