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Synthesis of Trifluoro- or Difluoromethylated Olefins by Regio- and Stereocontrolled S_N2' Reactions of *gem*-Difluorinated Vinyloxiranes

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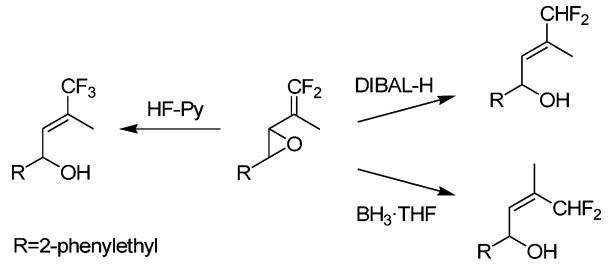

This paper presents a highly stereoselective synthesis of trifluoro- or difluoromethylated olefins via an S_N2' type fluorination or reductions of *gem*-difluorinated vinyloxiranes. Their fluorination with HF-Py furnished trifluoromethylated allylic alcohols with exclusive *E* selectivity. On the other hand, their reduction with DIBAL-H afforded difluoromethylated *E*-allylic alcohols predominantly, whereas the corresponding *Z* isomers were formed exclusively by treatment with BH_3·THF.

Introduction

Introduction of fluorine atoms into organic molecules often significantly alters the physical, chemical, and biological properties of the compounds.[1] Among fluorinated compounds, fluoromethylated ($-CH_{3-n}F_n$; $n = 1, 2, 3$) compounds are the most fundamental and widely used, since the degree of fluorination in such groups is sometimes significantly important, especially in the medicinal and agrochemical field.[1,2] For instance, monofluoroacetic acid possesses a high toxicity, inhibiting the aconitase activity in the TCA cycle, whereas di- and trifluoroacetic acids do not exhibit such inhibition[3] because of the altered steric and electronic properties by the substitution of a hydrogen with a fluorine atom.[2b,4] On the other hand, β-fluoroalanines are well-known as suicide substrates, and are reported to show different metabolic pathways depending on the degree of fluorination.[5] Moreover, fluoromethylated sulfonanilides possess a herbicidal activity; among them, the trifluoromethlated one is the most effective due to increasing lipophilicity and electronegativity.[6] Furthermore, fluoromethyl ketones, which are known to inhibit acetylcholineesterase and carboxylesterases, show an increase in activity as the degree of fluorination increases,[7] since fluorine substitution enhances the stability of intermediate geminal diols or hydrates.[8]

However, in general, different synthetic strategies and different starting materials were necessary to prepare the useful fluoromethylated compounds depending on the degree of fluorination desired. Moreover, highly stereocontrolled synthetic methods for the preparation of such compounds are sometimes quite difficult.[9] To overcome such drawbacks, we reported the highly stereoselective introduction of fluorine-containing methyl groups from a single starting compound by the application of

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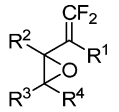
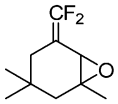


1

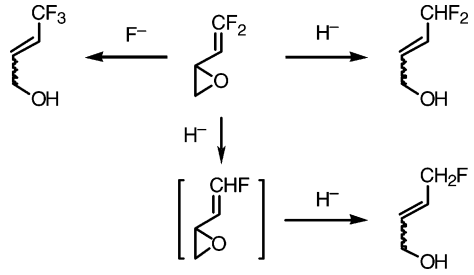
R^1=Me, R^2=R^4=H, R^3=2-Phenylethyl (**a**)
R^1=Et, R^2=Me, R^3=2-Phenylethyl, R^4=H (**b**)
R^1=Me, R^2=R^4=H, R^3=Ph (**c**)
R^1=Me, R^2=R^4=H, R^3=4-NO_2-C_6H_4 (**e**)
R^1=Me, R^2=R^4=H, R^3=4-Me-C_6H_4 (**f**)
R^1=Me, R^2=Bn, R^3=R^4=H (**g**)
R^1=Me, R^2=H, R^3=R^4=2-Phenylethyl (**h**)
R^1=2-Phenylethyl, R^2=R^3=R^4=H (**i**)
R^1=Me, R^2=R^3=H, R^4=Ph (**j**)
R^1=R^3=Ph, R^2=R^4=H (**j**)



1d

FIGURE 1. Various difluorinated vinyloxiranes **1a**−**k**.

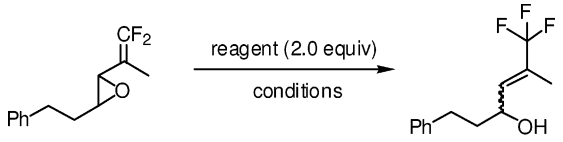
SCHEME 1



the readily available D-glucose with *gem*-difluoroolefine as a key intermediate.[10]

Recently, we have established the preparation of *gem*-difluorinated vinyloxiranes **1a**−**k** (Figure 1) which have significant potential as versatile building blocks for fluorinated compounds, utilizing their intrinsic reactivity.[11] Although they possess three reaction sites for nucleophiles, we have demonstrated their ability to undergo highly regio- and stereoselective reactions depending on the employed organometallic reagents[11,12] or halogenating reagents.[13] Very recently, we reported selective synthesis of difluoromethylated olefins utilizing S_N2' reductions of *gem*-difluorinated vinyloxiranes, generally proceeding with a high level of regio- and stereocontrol.[14] These successful results prompt us to investigate their regio- and stereoselective reductions and fluorinations for the synthesis of fluoromethylated olefins (Scheme 1), since their selective syntheses are not particularly easy.[15,16] Therefore, in this article, the full details of the preparation of di- and trifluoromethylated olefins from a key synthetic intermediate, *gem*-difluorinated vinyloxiranes, are described.

TABLE 1. Fluorination of 1a with Fluorinating Reagents[a]



1a **2a**

entry	reagent	conditions	yield of **2a** (%)	*E*/*Z*
1	TBAF	THF, rt, 24 h	*b*	−/−
2		THF, reflux, 24 h	>55	80/20
3		CH_3CN, reflux, 7 h	>58	88/12
4		DMF, 100 °C, 1.5 h	>38	>99/<1
5	HF-Py	CH_2Cl_2, 0 °C, 1 h	>99	>99/<1

[a] Yields and ratios were determined by ^{19}F NMR. [b] No reaction.

Results and Discussion

Selective S_N2' Fluorination of *gem*-Difluorinated Vinyloxiranes. As we reported previously,[13a] an S_N2' type fluorination of **1a** by MgF_2 as well as LiF/AcOH resulted in the complete recovery of the starting material, while selective S_N2' brominations and chlorinations were realized under similar conditions. Such drawbacks prompted us to investigate their reactivity utilizing several fluorinating reagents (Table 1). The application of KF and CsF failed to provide the corresponding products even at high temperature and prolonged reaction times. KHF_2, which is often used for oxirane-opening reactions,[17] also demonstrated poor reactivity, even in the presence of 12-crown-4 or Ph_3P.[18] Although no product was observed with the application of TBAF (tetrabutylammonium fluoride) at ambient temperature, complete consumption of **1a** and formation of an *E*,*Z* mixture of the S_N2' product **2a** was observed at higher temperature (entries 1 and 2). Unfortunately the products were not easy to isolate from unidentified byproducts. Also the application of other solvents yielded similar results (entries 3 and 4). On the other hand, further fluorination to the OH moiety of **2a** occurred to afford tetrafluorinated compound **3**, when DAST (diethylaminosulfur trifluoride) and Ishikawa reagent (hexafluoropropene diethylamine)[19] were employed as a fluorinating reagent (Scheme 2).[20] As we reported previously,[13a] strong Brønsted acids, with pK_a, which is lower than 4.0, can react with **1a** smoothly in an S_N2' manner to afford *E*-allylic alcohols exclusively. Inspired by these experimental facts, we decided to conduct the reaction with HF-Py,[21] which is frequently used for an oxirane-opening fluorination,[22,23] and the desired trifluorinated allylic alcohol was obtained in quantitative yield with exclusive *E* selectivity (entry 5).

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(16) In the preparation of them by a transition metal catalyzed cross-coupling reaction, the olefinic stereochemistries were excellent, but in some cases the regioselectivity is not perfect, moreover, quite a few examples of difluoromethylated olefins are described. See: (a) Konno, T.; Chae, J.; Tanaka, T.; Ishihara, T.; Yamanaka, H. *Chem. Commun.* **2004**, 690. (b) Konno, T.; Nagata, K.; Ishihara, T.; Yamanaka, H. *J. Org. Chem.* **2002**, *67*, 1768.

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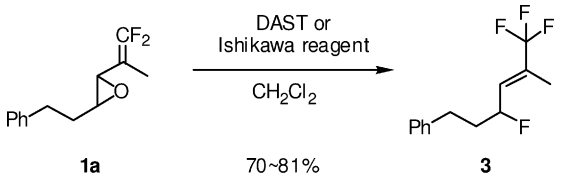
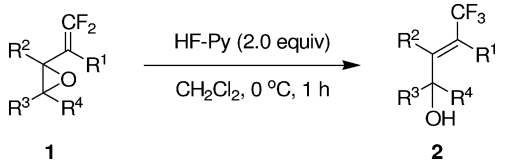
SCHEME 2



Yields were determined by ^{19}F NMR.

TABLE 2. Stereoselective S_N2' Fluorination of 1[a]



entry	1	isolated yield (%)	product
1	**1a**	95	**2a**
2	**1b**	90[b]	**2b**
3	**1c**	67	**2c**
4	**1d**	64[c]	**2d**
5	**1e**	91	**2e**
6	**1f**	*d*	
7	**1g**	90[e]	**2g**
8	**1h**	>99	**2h**
9	**1i**	88	**2i**
10	**1j**	64	**2c**
11	**1k**	53	**2k**

[a] *E*/*Z* ratios were determined by ^{19}F NMR. [b] *E*/*Z* = 72/28. [c] Low yield was attained because of a high volatility of the product. [d] Complex mixture. [e] *E*/*Z* = 71/29.

Next, to explore the scope and limitation of this selective S_N2' type fluorination, other *gem*-difluorinated vinyloxiranes were applied to the standard conditions. All examples listed in Table 2, except for **1f**, demonstrated the selective S_N2' fluorination with high stereoselectivity; the olefinic stereochemistry was determined by the NOESY spectroscopy of **2c**. However, this methodology has some limitations as listed below. In the R^2 substituted cases (entries 2 and 7), poor olefinic stereoselectivities were observed, and some byproducts were formed when both epoxide carbons were activated by the adjacent sp^2 system presumably due to accompanying regiorandom reactions and/or rearrangements (entries 3, 10, and 11).

The proposed reaction mechanism is depicted in Figure 2. At the first stage, a proton could activate the substrate strongly, weakening the allylic epoxide C−O bond and producing intermediates **Int-A** or **-B**.[22a] Then, the hard fluoride nucleophile

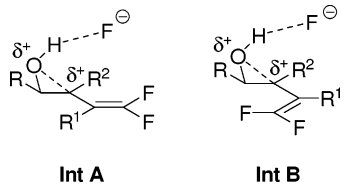
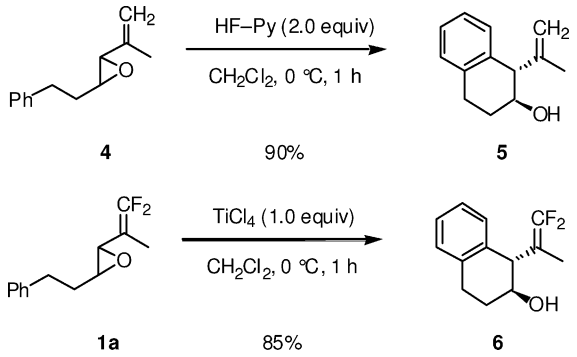


FIGURE 2.

SCHEME 3



would react at the most electrophilic reaction site terminal-fluorine-attached carbon selectively. With respect to the olefinic stereochemistry, **Int-A** would afford the *E*-allylic alcohols whereas the corresponding *Z* isomers could be formed from **Int-B**; therefore, taking into account the results from the application of **1b** and **1g** (Table 2, entries 2 and 7), the steric repulsions present in **Int-A** and **-B** would determine olefinic stereochemistry of the products.

To understand the role of fluorine atoms in this selective fluorination, the corresponding nonfluorinated prototype of **1a** was applied to the standard conditions (Scheme 3). Interestingly, the treatment of **4** with HF-Py did not result in fluorination, but the formation of **5** was observed as a sole product by way of an intramolecular Friedel−Crafts reaction, implying HF was only playing a role as an acid to activate the substrate in this case. This unexpected reaction outcome could be rationalized by the presence or absence of the extraordinarily high electrophilicity at the terminal sp^2 carbon in **Int-A** and **-B** introduced by the fluorine atoms (Figure 2). The 6-*exo-tet* cyclization would occur because of delocalization of the positive charge in the case of **4**. It should be mentioned that the corresponding difluorinated intramolecular Friedel−Crafts product **6** was obtained selectively by a completely different method,[13a] clearly indicating that fluorine substitutions significantly altered the compounds' chemical properties.

Selective S_N2' Reductions of *gem*-Difluorinated Vinyloxirane. Here the reductions of nonfluorinated vinyloxiranes are systematically investigated by using several reducing reagents: $LiAlH_4$,[24] DIBAL-H (diisobutylaluminum hydride),[24e,25] boron reagents,[26] Pd/RCOOH,[27] and others.[28] From the preliminary

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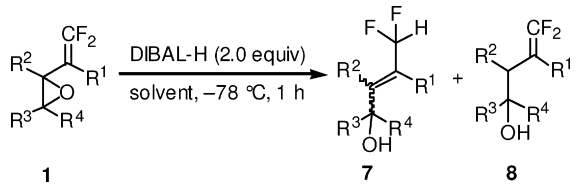
TABLE 3. Reduction of 1 with DIBAL-H[a]



1 **7** **8**

entry	1	solvent	yield (%) 7	yield (%) 8	*E*/*Z* of 7	recovery (%)
1	**1a**	*n*-hexane	(64): **7a**	(<1)	>99/<1	*b*
2		CH_2Cl_2	77	(<1)	>99/<1	*b*
3	**1b**	*n*-hexane	(47): **7b**	(<1)	65/35	0
4		CH_2Cl_2	(31)	(<1)	86/15	0
5	**1c**	*n*-hexane	(39): **7c**	(14): **8c**	>99/<1	0
6		CH_2Cl_2	62	(6)	>99/<1	0
7	**1d**	*n*-hexane		59[c] (96): **8d**		0
8		CH_2Cl_2		41[c] (86)		0
9	**1e**	CH_2Cl_2	75: **7e**			7
10	**1f**	CH_2Cl_2	(33): **7f**		>99/<1	0
11	**1g**	*n*-hexane	(16): **7g**		45/55	0
12		CH_2Cl_2	(21)		69/31	0
13	**1h**	CH_2Cl_2	complex mixture			28
14	**1i**	*n*-hexane	(<1)	81: **8i**		0
15	**1j**	*n*-hexane	(2): **7c**	87: **8c**	>99/<1	7
16		CH_2Cl_2	(4)	(79)	>99/<1	0
17	**1k**	*n*-hexane	66: **7k**		92/8	0
18		CH_2Cl_2	66		92/8	0

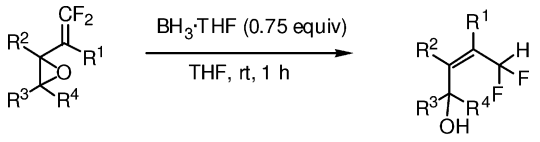
[a] Yields in parentheses, ratios, and recoveries were determined by ^{19}F NMR. [b] The remaining **1a** decomposed during workup. [c] Low isolated yield was attained because of a high volatility of the product.

results of screening (see the Supporting Information), the selective S_N2' reduction of **1a** was realized by using DIBAL-H to prepare difluorinated *E*-allylic alcohols, while BH_3·THF furnished *Z*-allylic alcohols exclusively.[14]

Thus, various kinds of *gem*-difluorinated vinyloxiranes **1a**−**k** were treated with DIBAL-H under the standard conditions (Table 3). The site selectivity of the reduction, by DIBAL-H, highly depended on the structure and substituents of the substrate. Besides **1a**, selective S_N2' reactions with excellent *E* selectivity were realized in the case of **1c**, **1e**, and **1k** (entries 5, 6, 9, 17, and 18). When applied to the R^2 substituted substrates **1b** and **1g** (entries 3, 4, 11, and 12), the yield and olefinic stereoselectivity decreased presumably due to steric effects. Stereoisomeric **1c** and **1j** were found to exhibit a remarkable regioselective difference: the former *E*-oxirane demonstrating the S_N2' selectivity whereas the S_N2 product **8** was formed selectively in the latter *Z*-oxirane case (entries 5, 6, 15, and 16). This unexpected S_N2 selectivity was also observed when **1d** and **1i** were used as a substrate (entries 7, 8, and 14).

Next, to investigate the generality of the reaction with BH_3·THF, *gem*-difluorinated vinyloxiranes were applied to the standard conditions (Table 4). The *Z* selective S_N2' reaction was realized in almost all examples except for the substrate possessing the substituents at the R^4 moiety (entries 4, 8, and 10).

TABLE 4. Stereoselective S_N2' Reduction of 1 with BH_3·THF[a]

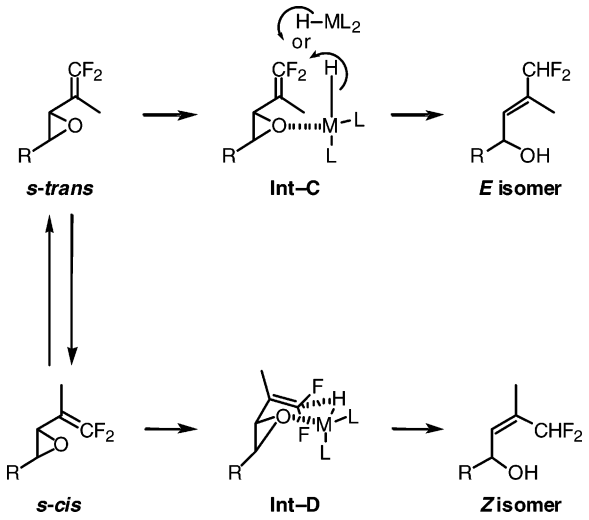


1 ***Z*-7**

entry	1	yield (%)	recovery (%)
1	**1a**	95: **7a**	0
2	**1b**	85: **7b**	0
3	**1c**	71: **7c**	13
4	**1d**	23:[b] **7d**	45
5	**1e**	77:[c] **7e**	17
6	**1f**	85: **7f**	7
7	**1g**	89: **7g**	0
8	**1h**	trace	88
9	**1i**	75: **7i**	0
10	**1j**	13:[d,e] **7c**	87
11	**1k**	91: **7k**	0

[a] *E*/*Z* ratios and recoveries were determined by ^{19}F NMR. [b] *E* isomer. [c] *E*/*Z*=13/87. [d] *E*/*Z*=23/77. [e] Determined by ^{19}F NMR.

SCHEME 4



The olefinic stereochemistry was determined by the analysis of NOESY spectrums of **7a**, **7c**, and **7k** cases, indicating that DIBAL-H attained the *E* isomer of **7** selectively while the corresponding *Z* isomer was formed from the reaction with BH_3·THF.

To account for the current olefinic stereochemical outcome of **7a**−**k** from the reduction of **1a**−**k** with DIBAL-H and BH_3·THF, a plausible reaction mechanism of them is described in Scheme 4. DIBAL-H and BH_3 could activate the oxirane moiety strongly leading to an intramolecular hydride shift to the fluorine-attached-terminal carbon. The *E* isomer would be furnished from the *s-trans* conformer by way of **Int-C**, while **Int-D** could be generated from the *s-cis* conformer to afford the *Z* isomer. The chair-like six-membered-ring conformation of **Int-D** would be favorable in the case of reducing reagents with relatively small ligands (L) such as BH_3·THF producing the *Z* product easily. On the other hand, in the case of DIBAL-H whose L are relatively large, steric repulsion between the L and

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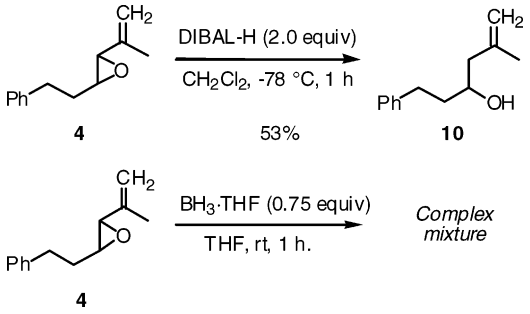
SCHEME 5



the epoxide moiety in **Int-D** could inhibit the reaction pathway to the *Z* product therefore leading to the formation of the *E* isomer.

The corresponding nonfluorinated prototype of **1a** was reduced under the standard selective S_N2' reductions as a comparison (Scheme 5). To our surprise, no S_N2' product was obtained by DIBAL-H, instead a homoallylic alcohol **10** was formed selectively, while high S_N2' selectivity was observed in the fluorinated case (see, Table 3, entry 2). This difference in regioselectivity based on the degree of fluorine could be attributed to the positive charge on the reaction sites: the terminal sp^2 carbon of *gem*-difluorinated vinyloxiranes possesses the most electropositive charge due to the strong electronic repulsion between lone pairs of fluorine atoms and π-electrons,[11b] whereas the allylic epoxide carbon would be expected to be the most electropositive in the case of the nonfluorinated prototype. In other words, the site selectivity of the reduction with DIBAL-H would be determined by the positive charges on the carbons if a substrate has small steric encumbrance. On the other hand, the reduction of **4** with BH_3·THF resulted in a complex mixture while *Z*-**7** was obtained exclusively in the fluorinated case (see, Table 4, entry 1). These different experimental results could be explained by the computational results.[11b] These results indicate that the HOMO of *gem*-difluorinated vinyloxiranes lies on the epoxide oxygen atom whereas it is on the olefin moiety in the nonfluorinated case. In the former case BH_3 can activate the epoxide moiety to produce **Int-D** smoothly, while such side reactions as hydroboration would occur easily to retard the S_N2' selectivity in the latter case.

As described above, we have established the regio- and stereoselective synthetic methods for tri- and difluoromethylated olefins from *gem*-difluorinated vinyloxiranes. Then, our attention was turned to the preparation of monofluorinated olefins from the same key intermediate *gem*-difluorinated vinyloxirane. Following the strategy depicted in Scheme 1, we decided to investigate a selective reduction from *gem*-difluoro olefins to the corresponding monofluorinated ones. However, the attempt by $LiAlH_4$[29] or Red-Al (bis(2-methoxyethoxy)aluminum dihydride)[30] was not successful. After an extensive study, we found an alternative method to prepare monofluorinated vinyloxirane **11** (see the Supporting Information). Although the isolated **11** is not a useful synthetic intermediate because of the low yield and the inherent low stability, independent reductions of the monofluorinated vinyloxirane **11** by DIBAL-H and BH_3·THF were performed under the standard conditions. However, to our disappointment, both reactions resulted in a complex mixture, and we could not obtain the desired monofluoromethylated allylic alcohol (see the Supporting Information). From the obtained results, it was proved that two fluorine atom substitutions on an olefin moiety are crucial for the selective S_N2' reductions.

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Conclusion

In summary, *gem*-difluorinated vinyloxiranes **1** were demonstrated as useful synthetic intermediates for the preparation of tri- and difluoromethylated olefins utilizing their selective S_N2' fluorination and reductions. HF-Py worked effectively for fluorine introduction to *gem*-difluorinated vinyloxiranes at the terminal-fluorine-attached carbon to afford trifluoromethylated allylic alcohols in the *E* form exclusively. Their reductions with DIBAL-H led to the selective formation of *E*-difluoromethylated olefins whereas the corresponding *Z* isomers were obtained exclusively by BH_3·THF. Compared with the results from mono- and nonfluorinated vinyloxiranes, the highly regio- and stereocontrol could be attributed to the alternating properties by the two fluorine atoms on the olefin moiety. These highly selective S_N2' reactions allowed an access to various geometrically controlled alkenes with a tri- or difluoromethyl group.

Experimental Sections

General Procedure for the Fluorination of 1 with HF-Py. The reaction of **1a** is described as a representative example. HF-Py (0.022 mL, 0.89 mmol) was added to a flask containing **1a** (0.10 g, 0.45 mmol) in 5 mL of CH_2Cl_2 at 0 °C under Ar atmosphere and the reaction mixture was stirred for 1 h. Then, the reaction was quenched with H_2O and the organic layer was extracted with Et_2O three times and dried over anhydrous $MgSO_4$. Removal of the solvents and purification with slica gel column chromatography (*n*-hexane:AcOEt = 4:1) furnished the pure desired **2a** in 91%.

(*E*)-1-Phenyl-5-trifluoromethylhex-4-en-3-ol (2a): ^{1}H NMR δ 1.75 (3 H, d, J = 1.10 Hz), 1.82 (1 H, dddd, J = 14.5, 9.07, 6.87, 5.22 Hz), 1.98 (1 H, dddd, J = 14.0, 8.79, 7.68, 6.32 Hz), 2.68 (1 H, ddd, J = 14.0, 8.79, 6.87 Hz), 2.75 (1 H, ddd, J = 14.0, 9.07, 6.32 Hz), 4.42 (1 H, m), 6.07 (1 H, dddd, J = 8.52, 3.02, 3.02, 1.37 Hz), 7.16−7.34 (5 H, m). ^{19}F NMR δ 91.7 (s). ^{13}C NMR δ 11.0 (dd, J = 2.57, 1.43 Hz), 31.3, 38.1 (dd, J = 4.01, 2.86 Hz), 67.0, 123.7 (q, J = 272.9 Hz), 126.0, 126.4 (q, J = 24.5 Hz), 128.2, 128.3, 134.7 (dd, J = 11.0, 5.44 Hz), 140.9. IR (neat) ν 670, 747, 892, 1030, 1118, 1177, 1335, 1455, 1496, 2863, 2933, 3029, 3064, 3375. Anal. Calcd for $C_{13}H_{15}F_3O$: C, 63.93; H, 6.19. Found: C, 63.97; H, 6.05.

Typical Procedure for the Reduction of 1 with DIBAL-H. The reaction of (*E*)-3,4-epoxy-1,1-difluoro-2-methyl-6-phenylhex-1-ene **1a** in CH_2Cl_2 is described as a representative example. To a solution of **1a** (0.10 g, 0.45 mmol) in 5 mL of dry CH_2Cl_2 was added 2.0 equiv of DIBAL-H (0.89 mmol) at −78 °C under argon. After 1.0 h of stirring, the reaction was quenched with 3 N HCl aq, and the organic layer was extracted with CH_2Cl_2 three times and dried over anhydrous $MgSO_4$. Removal of the solvents and purification with silica gel column chromatography (*n*-hexane: AcOEt = 4:1) afforded the pure *E*-**7a** in 66% yield.

Typical Procedure for the Reduction of 1 with BH_3·THF. The reaction of (*E*)-3,4-epoxy-1,1-difluoro-2-methyl-6-phenylhex-1-ene **1a** is described as a representative example. To a solution of **1a** (0.10 g, 0.45 mmol) in 5 mL of dry THF was added 0.75 equiv of BH_3·THF THF solution (0.33 mmol) under argon. After 1.0 h of stirring at room temperature, the reaction was quenched with 3

N NaOH aq, and the organic layer was extracted with Et_2O three times, washed with brine, and dried over anhydrous $MgSO_4$. Removal of the solvents and purification with silica gel column chromatography (*n*-hexane:AcOEt = 4:1) afforded the pure ***Z*-7a** in 95% yield.

6,6-Difluoro-5-methyl-1-phenylhex-4-en-3-ol (7a): IR (neat) ν 509, 698, 748, 822, 841, 883, 918, 1018, 1092, 1153, 1207, 1339, 1362, 1396, 1454, 1497, 1524, 1585, 1605, 1655, 1674, 1686, 1717, 1751, 1802, 1871, 1948, 2862, 2928, 3028, 3063, 3086, 3368, 3530, 3568, 3588 cm^{-1}. Anal. Calcd for $C_{13}H_{16}F_2O$: C, 69.01; H, 7.13. Found: C, 69.28; H, 6.92. ***E* isomer:** ^1H NMR δ 1.71 (3 H, dd, J = 1.48, 0.38 Hz), 1.80 (1 H, dddd, J = 13.7, 9.61, 6.87, 5.77 Hz), 1.95 (1 H, dddd, J = 13.7, 8.79, 7.42, 6.32 Hz), 2.67 (1 H, ddd, J = 13.7, 8.79, 6.60 Hz), 2.74 (1 H, ddd, J = 14.0, 9.34, 6.32 Hz), 4.44 (1 H, m), 5.74 (1 H, m), 5.92 (1 H, t, J = 56.2 Hz), 7.10−7.35 (5 H, m). ^{19}F NMR δ 45.8 (1 F, dd, J = 299.0, 56.0 Hz), 46.9 (1 F, dd, J = 299.0, 56.0 Hz). ^{13}C NMR δ 9.66 (dd, J = 2.29, 2.01 Hz), 31.4, 38.3 (t, J = 1.72 Hz), 67.0, 117.1 (t, J = 236.8 Hz), 125.9, 128.2, 128.3, 131.1 (dd, J = 21.8, 21.5 Hz), 135.2 (dd, J = 10.0, 9.73 Hz), 141.1. ***Z* isomer:** ^1H NMR δ 1.81 (1 H, dddd, J = 12.7, 9.15, 6.96, 5.83 Hz), 1.83 (3 H, m), 1.95 (1 H, dddd, J = 13.7, 8.91, 7.32, 6.38 Hz), 2.67 (1 H, ddd, J = 13.9, 8.91, 6.96 Hz), 2.70 (1 H, ddd, J = 14.0, 9.16, 6.47 Hz), 4.44 (1 H, m), 5.63 (1 H, m), 6.42 (1 H, t, J = 55.7 Hz), 7.16−7.32 (5 H, m). ^{19}F NMR δ 44.8 (d, J = 55.6 Hz). ^{13}C NMR δ 15.7 (t, J = 3.01 Hz), 31.4, 38.9 (t, J = 1.14 Hz), 66.5 (t, J = 0.86 Hz), 112.0 (t, J = 233.9 Hz), 125.9, 128.2, 128.3, 131.2 (t, J = 22.5 Hz), 136.3 (t, J = 8.88 Hz), 141.0.

Supporting Information Available: Experimental procedures, characterization data for all new compounds, reduction of **1a** with various reducing reagents (Table 5), reaction of **1a** with DIBAL-H (Table 6), reaction of **1a** with BH_3·THF (Table 7), ^1H NMR spectra of *E*-**2a**, *E*-**7a**, and *Z*-**7a**. This material is available free of charge via the Internet at http://pubs.acs.org.

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