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Highly Stereoselective Synthesis of Fluoroalkene Dipeptides via the Novel Chromium(II)-Mediated Carbon–Fluorine Bond Cleavage/New Carbon–Carbon Bond Formation

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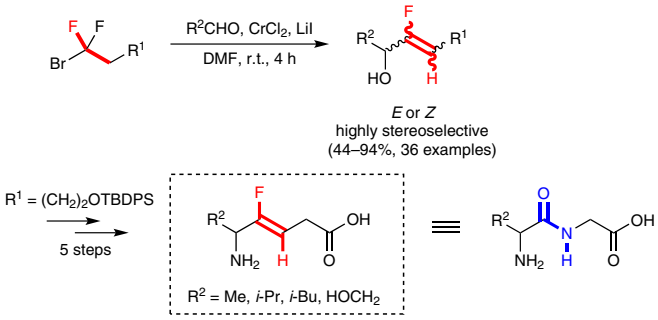

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Abstract An efficient chromium(II)-mediated reductive coupling reaction of various $CBrF_2$-containing molecules and aldehydes has been developed. This reaction proceeds presumably via the monofluorinated dichromium(III) intermediate generated by the carbon–fluorine bond activation, and provides a general and straightforward access to synthesize a variety of (*E*)- or (*Z*)-β-fluoroallylic alcohols in a highly stereoselective manner. Based on the novel reductive coupling, four types of fluoroalkene dipeptide analogues could be stereoselectively prepared.

Key words β-fluoroallylic alcohol derivatives, carbon–fluorine bond activation, chromium(II) chloride, stereoselective, fluoroalkene bioisosteres

Fluoroalkenes have been well recognized as among the most important and valuable peptide bond bioisosteres because the fluoroalkene and the peptide bond frameworks are closely similar in the structural and electronic properties. More specifically, an amide bond in bioactive peptides is sometimes easily hydrolyzed by an enzyme in vivo, resulting in the inactivation of the peptide, but due to hydrolytic stability of the fluoroalkene framework, peptidomimetics, in which the amide bond is replaced with the fluoroalkene unit, maintain the original bioactivity and often simultaneously provoke very interesting additional biological activities.[1] For this reason, a large number of synthetic methods, such as electrophilic fluorination of various vinylmetal species,[2] Horner–Wadsworth–Emmons reaction of monofluorinated phosphonate with aldehydes,[3] S_N2' reaction of α,α-difluoroallylic compounds with organocopper reagents,[4] and others,[5] have been developed for the incorporation of a fluoroalkene skeleton into a wide range of bioactive peptides. Although such synthetic procedures absolutely play an important role in synthesizing a variety of stereochemically defined fluoroalkenes, they also have various drawbacks, like difficulties on the preparation of the substrates, narrow range of applicable substrates, etc. As a consequence, it has still been a very important subject to explore a new methodology for constructing fluoroalkene frameworks stereoselectively.

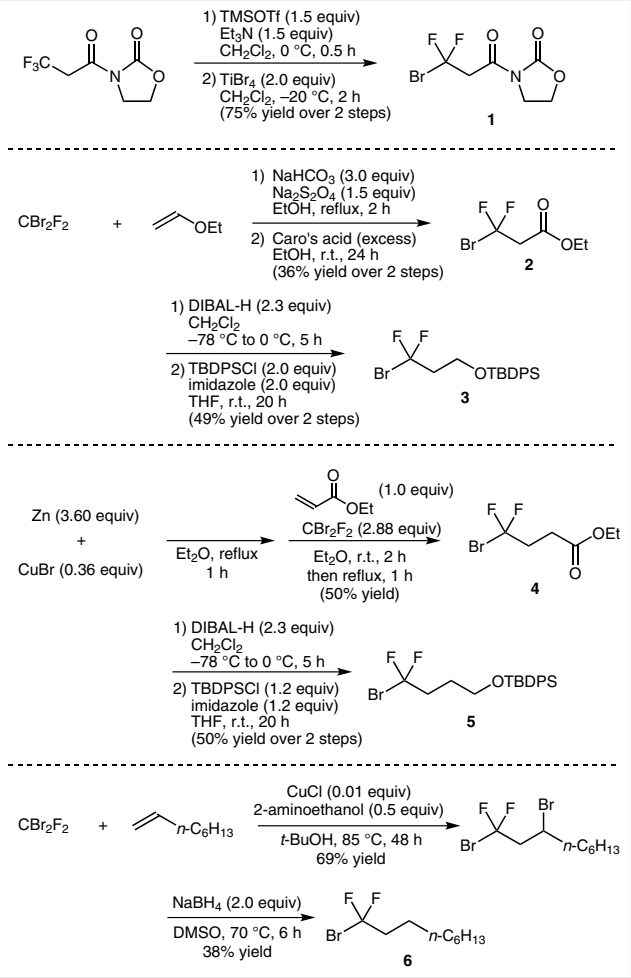
Carbon–fluorine (C–F) bond has a very large bond energy and has been known as the most chemically stable bond. Accordingly, reactions that efficiently cleave this C–F bond and subsequently create a new carbon–carbon (C–C) bond are significantly attractive from the viewpoint of a new synthetic methodology. In recent years, such carbon elongations have come under the spotlight.[6]

In this article, we describe a highly stereoselective synthesis of various (*E*)- or (*Z*)-β-fluoroallylic alcohols based on C–F bond cleavage of $CBrF_2$-containing molecules in the presence of the early transition metal, chromium(II)[7] followed by the addition reaction of the resultant α-fluorovinyl chromium species with various aldehydes in detail.[8] Additionally, we also report the stereoselective synthesis of various fluoroalkene dipeptides through the above Cr(II)-mediated reductive coupling reaction.

Scope and Limitations

For this investigation, we first selected several $CBrF_2$-containing substrates, such as the imide **1**,[9] the esters **2**[10] and **4**,[11] the silyl ethers **3** and **5**,[10] and also the alkane **6**.[12] These substrates were easily prepared as shown in Scheme 1. Treatment of 3,3,3-trifluoropropanoyloxazolidinone with

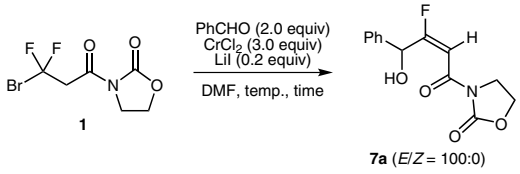
1.5 equivalents each of TMSOTf and Et_3N in CH_2Cl_2 at 0 °C for 0.5 hour afforded the corresponding silyl enol ether, which was subsequently subjected to 2.0 equivalents of $TiBr_4$ in CH_2Cl_2 at –20 °C for 2 hours, leading to 3-(3-bromo-3,3-difluoropropanoyl)-2-oxazolidinone (**1**) in 75% isolated yield over two steps. The radical addition of CBr_2F_2 toward ethyl vinyl ether in the presence of $NaHCO_3$ and $Na_2S_2O_4$ in EtOH at the reflux temperature for 2 hours, followed by treating the resultant reaction mixture with an excess amount of Caro's acid for 24 hours, gave ethyl 3-bromo-3,3-difluoropropionate (**2**) in 36% combined yield. This ester **2** was reduced with 2.3 equivalents of DIBAL-H to provide the corresponding alcohol, which was subjected to 2.0 equivalents each of TBDPSCl and imidazole in THF for 20 hours to afford the desired 1-bromo-3-(*tert*-butyldiphenylsilyloxy)-1,1-difluoropropane (**3**) in 49% yield over two steps. The radical addition of CBr_2F_2 toward ethyl acrylate in the presence of Zn and CuBr in Et_2O also proceeded to give the corresponding ethyl 4-bromo-4,4-difluorobutyrate (**4**) in an acceptable yield, which could be converted to 1-bromo-4-(*tert*-butyldiphenylsilyloxy)-1,1-difluorobutane (**5**) by the similar procedure used to prepare compound **3**. Finally, the radical adduct, which could be readily prepared through the reaction of CBr_2F_2 with oct-1-ene in the presence of CuCl (0.01 equiv) and 2-aminoethanol (0.5 equiv) in *tert*-BuOH at 85 °C for 48 hours, was treated with 2.0 equivalents of $NaBH_4$ in DMSO at 70 °C for 6 hours to afford 1-bromo-1,1-difluorononane (**6**) in 38% yield.



Scheme 1 Preparation of various $CBrF_2$-containing substrates

With various substrates **1**–**6** in hand, the reaction of **1** with benzaldehyde in the presence of $CrCl_2$ was first examined as shown in Table 1. On treating **1** with 2.0 equivalents of benzaldehyde in the presence of 3.0 equivalents of $CrCl_2$ and a catalytic amount of LiI (0.2 equiv) in DMF at –20 °C for 4 hours, the corresponding β-fluoroallylic alcohol **7a** was obtained in only 15% yield (Table 1, entry 1). Longer reaction time was not effective to increase the yield (entry 2). In each case, the starting material **1** was completely consumed. The yield of **7a** was greatly improved from 18% to 84–86% when the reaction was carried out at 0 °C to room temperature (entries 3 and 4), though higher temperature such as 60 °C rather decreased the yield (entry 5). Using only 2.0 equivalents of $CrCl_2$ brought about a significant drop in the yield (entry 6). The yield somewhat decreased even when only 1.2 equiv of benzaldehyde was used or LiI was not used[13] (entries 7 and 8). Finally, the use of 4.0 equiv of $CrCl_2$ led to the best reaction yield (entry 9). In all cases, only the *E*-isomer was obtained.[14]

Table 1 Reaction of **1** with Benzaldehyde in the Presence of $CrCl_2$

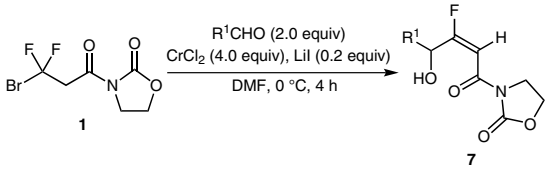


Entry	Temp (°C)	Time (h)	Yield (%)[a,b] of **7a**	Recovery (%)[a] of **1**
1	–20	4	15	trace
2	–20	20	18	trace
3	0	4	86	trace
4	r.t.	4	84	0
5	60	4	27	0
6[c]	0	4	13	21
7[d]	0	4	76	4
8[e]	0	4	64	9
9[f]	0	4	89 (84)	0

[a] Determined by ^{19}F NMR spectroscopy. Value in parentheses is of isolated yield.
[b] In all cases, (*E*)-**7a** was obtained as the sole isomer.
[c] Only 2.0 equiv of $CrCl_2$ was used.
[d] Only 1.2 equiv of PhCHO was used.
[e] Without LiI.
[f] Four equiv of $CrCl_2$ was used.

Upon optimization of the reaction conditions (Table 1, entry 9), a series of aldehydes were tested by using **1** to explore the generality of this Cr(II)-mediated reductive coupling reactions. The results are summarized in Table 2.

Table 2 Reaction of **1** with Various Aldehydes



Entry[a]	R^1	Product	Yield (%)[b,c]	Ratio (*E*/*Z*)[b]
1	Ph	**7a**	89 (84)	100:0
2	4-MeC_6H_4	**7b**	77 (64)	100:0
3	4-$MeOC_6H_4$	**7c**	73 (69)	100:0
4	4-FC_6H_4	**7d**	94 (90)	100:0
5	4-$F_3CC_6H_4$	**7e**	26	100:0
6	*n*-Pr	**7f**	70 (68)	100:0
7	*i*-Pr	**7g**	80 (77)	100:0
8	*t*-Bu	**7h**	88 (77)	100:0
9	(*E*)-MeCH=CH	**7i**	23	100:0

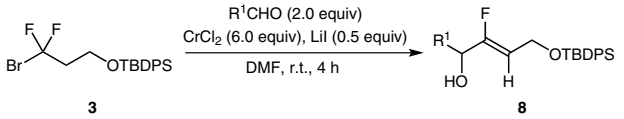
[a] Reaction conditions: **1** (0.5 mmol), R^1CHO (1.0 mmol), $CrCl_2$ (2.0 mmol), LiI (0.1 mmol), DMF (1.5 mL) at 0 °C for 4 h under argon.
[b] Determined by ^{19}F NMR spectroscopy.
[c] Values in parentheses are of isolated yield.

The reaction with aromatic aldehydes bearing an electron-donating group (Me, MeO; Table 2, entries 2 and 3) or an electron-withdrawing group (F substituent, entry 4) at the *para* position of the benzene ring proceeded efficiently to give the corresponding β-fluoroallylic alcohols **7b**–**d** in good to high yields. Various aliphatic aldehydes, such as butyraldehyde (entry 6) and isobutyraldehyde (entry 7), also showed satisfactory results. Notably, even much bulkier pivalaldehyde provided the corresponding adduct **7h** in a high yield (entry 8). Disappointingly, a strongly electron-withdrawing group, like a CF_3 group, on the benzene ring hampered the desired reaction proceeding (entry 5). In addition, α,β-unsaturated aldehyde, like crotonaldehyde, resulted in a significant decrease of the yield (entry 9). In all cases, only (*E*)-β-fluoroallylic alcohols were observed and no *Z*-isomer was detected.

Next, our attention was directed toward the Cr(II)-mediated reaction of 1-bromo-3-(*tert*-butyldiphenylsilyloxy)-1,1-difluoropropane (**3**) with various aldehydes under the same reaction conditions as employed in Table 2. The results are collected in Table 3.

First of all, the desired β-fluoroallylic alcohol **8a** was obtained in only 44% yield under the reaction conditions employed for the reaction of **1** (Table 3, entry 1). In this case, 40% of the starting material **3** still remained unreacted. Therefore, the amounts of $CrCl_2$ and LiI were increased from

Table 3 Reaction of **3** with Various Aldehydes



Entry[a]	R^1	Product	Yield[b,c] (%)	Ratio (*E*/*Z*)[b]
1[d]	Ph	**8a**	44[e]	0:100
2	Ph	**8a**	68 (56)	0:100
3	4-MeC_6H_4	**8b**	64 (48)	0:100
4	4-$MeOC_6H_4$	**8c**	78 (52)	0:100
5	4-FC_6H_4	**8d**	64 (56)	0:100
6	4-$F_3CC_6H_4$	**8e**	10	0:100
7	*n*-Pr	**8f**	79 (57)	1:99
8	*i*-Pr	**8g**	77 (59)	1:99
9	*t*-Bu	**8h**	78 (63)	0:100
10	(*E*)-MeCH=CH	**8i**	17	0:100

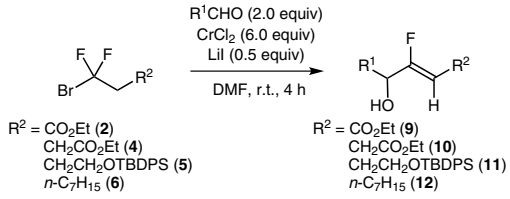
[a] Reaction conditions: **3** (0.3 mmol), aldehyde (0.6 mmol), $CrCl_2$ (1.8 mmol), LiI (0.15 mmol), DMF (1.2 mL) at r.t. for 4 h under argon.
[b] Determined by ^{19}F NMR spectroscopy.
[c] Values in parentheses are of isolated yield.
[d] Reaction conditions: **3** (0.3 mmol), aldehyde (0.6 mmol), $CrCl_2$ (1.2 mmol), LiI (0.06 mmol), DMF (1.2 mL) at 0 °C for 4 h under argon.
[e] The starting material **3** was recovered in 40% yield.

4.0 to 6.0 equivalents and from 0.2 to 0.5 equivalent, respectively. As a result, the starting material **3** was completely consumed and the corresponding β-fluoroallylic alcohol **8a** was obtained in 68% yield (entry 2). Surprisingly, only the *Z*-isomer was obtained[14] and no trace of *E*-isomer was detected. The reactions with various aromatic aldehydes, such as *p*-tolualdehyde, *p*-anisaldehyde, and 4-fluorobenzaldehyde, also took place smoothly to give the corresponding adducts in an exclusive *Z*-selective manner (entries 3, 4, and 5). Similarly, various aliphatic aldehydes, such as butyraldehyde, isobutyraldehyde, and pivalaldehyde, also gave the corresponding β-fluoroallylic alcohol derivatives with high *Z*-selectivity in high yields (entries 7–9). As observed in the Cr(II)-mediated reductive coupling of **1**, both 4-trifluoromethylbenzaldehyde and crotonaldehyde gave poor yields (entries 6 and 10).

In an analogous way, ethyl 3-bromo-3,3-difluoropropionate (**2**), ethyl 4-bromo-4,4-difluorobutyrate (**4**), 1-bromo-4-(*tert*-butyldiphenylsilyloxy)-1,1-difluorobutane (**5**), and 1-bromo-1,1-difluorononane (**6**) were also subjected to the same reaction conditions as used in Table 3. The results are listed in Table 4.

The reaction of **2** with benzaldehyde did not give any desired coupling product **9a**, and ethyl β,β-difluoroacrylate (**13**) was obtained in only 18% yield (Figure 1).[15] On the other hand, the ester **4**, in which the carbon framework has one carbon extension from **2**, underwent a smooth reductive coupling with benzaldehyde to give the corresponding

Table 4 Reaction of **2**, **4**–**6** with Various Aldehydes



R^2 = CO_2Et (**2**)
CH_2CO_2Et (**4**)
$CH_2CH_2OTBDPS$ (**5**)
n-C_7H_{15} (**6**)

R^2 = CO_2Et (**9**)
CH_2CO_2Et (**10**)
$CH_2CH_2OTBDPS$ (**11**)
n-C_7H_{15} (**12**)

Entry[a]	Substrate	R^1	Product	Yield (%)[b,c]	Ratio (*E*/*Z*)[b]
1	**2**	Ph	**9a**	0[d]	–
2	**4**	Ph	**10a**	76 (55)	2:98
3	**4**	4-MeC_6H_4	**10b**	47 (40)	1:99
4	**4**	4-$MeOC_6H_4$	**10c**	52 (51)	1:99
5	**4**	4-FC_6H_4	**10d**	59 (49)	0:100
6	**4**	4-$F_3CC_6H_4$	**10e**	4[e]	–[f]
7	**4**	*n*-Pr	**10f**	53 (42)	0:100
8	**4**	*i*-Pr	**10g**	58 (54)	1:99
9	**4**	*t*-Bu	**10h**	44 (31)	0:100
10	**4**	(*E*)-MeCH=CH	**10i**	26	1:99
11	**5**	Ph	**11a**	78 (67)	0:100
12	**5**	4-$MeOC_6H_4$	**11c**	80 (54)	0:100
13	**5**	Me	**11j**	83 (69)	0:100
14	**5**	*i*-Pr	**11g**	81 (67)	0:100
15	**5**	*i*-Bu	**11h**	71 (61)	0:100
16[g]	**5**	*s*-Bu	**11k**	64 (49)	0:100
17	**5**	CH_2OPMB	**11l**	57 (38)	0:100
18[g]	**5**	CHMe(OBn)	**11m**	75	0:100
19	**6**	Ph	**12a**	94 (76)	2:98
20	**6**	4-MeC_6H_4	**12b**	75	2:98
21	**6**	4-$MeOC_6H_4$	**12c**	90 (80)	0:100
22	**6**	4-FC_6H_4	**12d**	93 (78)	0:100
23	**6**	4-$F_3CC_6H_4$	**12e**	6[h]	–[f]
24	**6**	*n*-Pr	**12f**	94 (81)	2:98
25	**6**	*i*-Pr	**12g**	91 (70)	1:99
26	**6**	*t*-Bu	**12h**	82	1:99
27	**6**	(*E*)-MeCH=CH	**12i**	18[i]	–[f]

[a] Reaction conditions: **2** and **4**–**6** (0.3 mmol), aldehyde (0.6 mmol), $CrCl_2$ (1.8 mmol), LiI (0.15 mmol), DMF (1.2 mL) at r.t. for 4 h under Ar atmosphere.
[b] Determined by ^{19}F NMR spectroscopy.
[c] Values in parentheses are of isolated yield.
[d] Ethyl β,β-difluoroacrylate (**13**) was obtained in 18% yield.
[e] The starting material **4** was recovered in 47% yield.
[f] Not determined.
[g] The diastereomeric ratio was at 45:55 (entry 16) and at 62:38 (entry 18).
[h] The starting material **6** was recovered in 44% yield.
[i] The starting material was recovered in 7% yield.

adduct **10a** in 76% yield. Furthermore, various aromatic as well as aliphatic aldehydes could participate well in the reductive coupling reaction to afford the corresponding adducts **10b**–**d**,**f**–**h** in acceptable yields. As observed in the reaction of **1** and **3**, however, neither 4-trifluoromethylbenzaldehyde nor crotonaldehyde afforded the desired products **10e** and **10i** in good yields.

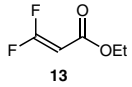


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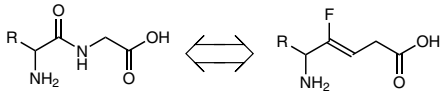
Figure 1 Ethyl β,β-difluoroacrylate

In the same way, the other starting materials **5** and **6** could be also successfully applied for the reductive coupling reaction with various aldehydes, except for 4-trifluoromethylbenzaldehyde and crotonaldehyde, with various β-fluoroallylic alcohols **11a**,**c**,**g**,**h**,**j**–**m**, and **12a**–**d**,**f**–**h** being obtained in high to excellent yields. In all cases, a high *Z*-stereoselection was observed.

With the highly selective preparation of fluoroalkenes in hand, the investigation was next shifted to their synthetic application. As mentioned previously, fluoroalkene is one of the important bioisosteres found occasionally in medicinal chemistry (Figure 2).



glycine dipeptide

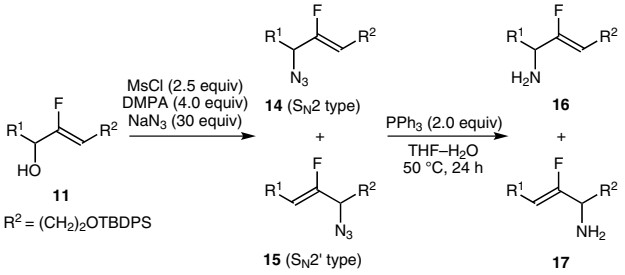
fluoroalkene bioisostere of glycine dipeptide

Figure 2 Glycine dipeptide and its fluoroalkene bioisostere

To prove our concept, (*Z*)-fluoroalkene **11** was chosen as the ideal starting material.[16] First, alcohol moiety was reacted with sodium azide to afford β-fluoroallylic azides as a regioisomeric mixture of **14** and **15**, which were generated through an S_N2 and S_N2' reaction pathway, respectively[5j,17] (Table 2). Regioselectivity was highly dependent on the substrates. If R^1 is aromatic, compound **15** is the major product, if R^1 is aliphatic, the major product is the desired product **14**, and interestingly, when R^1 is CH_2OPMB, only the S_N2 type of product **14** was observed. The products **14** and **15** were unable to separate by the standard condition of silica gel chromatography, therefore the following reduction step was conducted with a mixture of starting materials. However, fortunately, their amine products after reduction were easily separated and used for further chemical transformation (Table 5). Next, after protection of amine moiety by Boc, the desilylation was conducted smoothly,

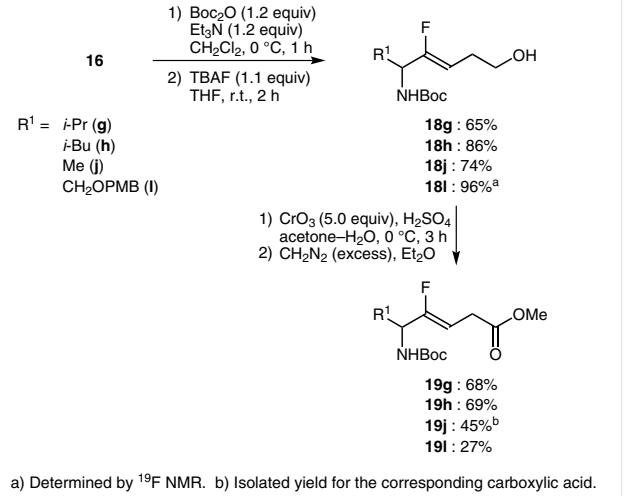
and Jones oxidation, followed by esterification with diazomethane, gave the desired fluoroalkene bioisosteres of Boc-protected glycine dipeptide analogues (Scheme 2).

Table 5 Synthesis of β-Fluoroamine Analogues



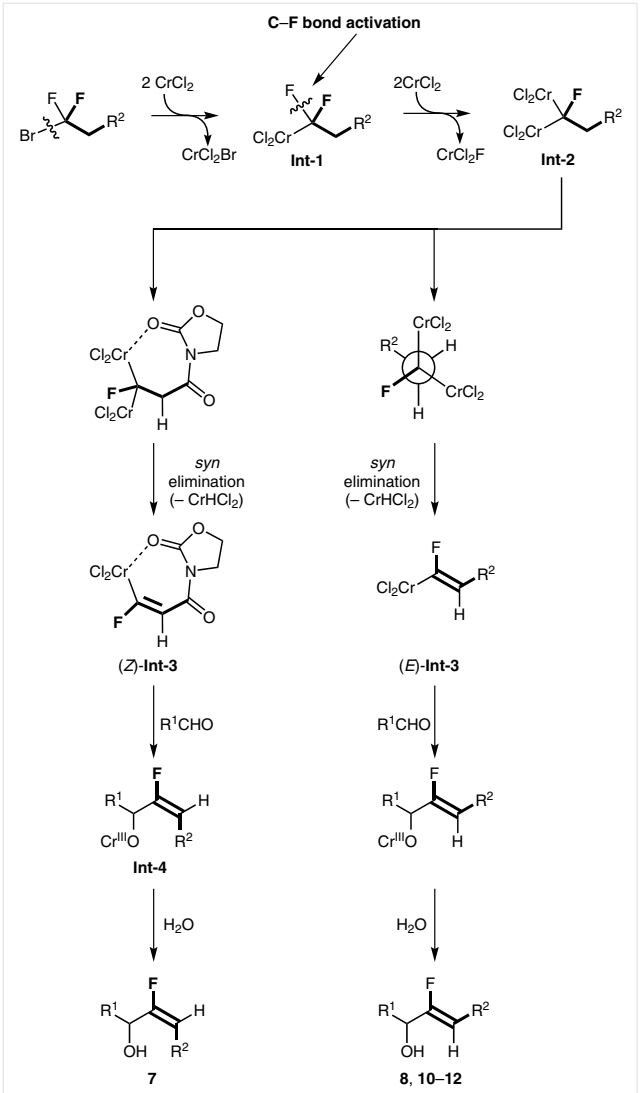
Entry	R^1		Yield[a] of **14** and **15** (ratio **14**/**15**)[b]	Combined yield (%)[a] (yield (%) of **16** and **17**)
1	Ph	**a**	60 (0:100)	85 (0, 85)
2	*p*-$MeOC_6H_4$	**c**	45 (0:100)	84 (0, 84)
3	*i*-Pr	**g**	69 (52:48)	52 (35, 17)
4	*i*-Bu	**h**	74 (49:51)	82 (28, 54)
5	Me	**j**	85 (78:22)	82 (49, 33)
6	*s*-Bu	**k**	40 (68:32)[c]	83 (52, 31)[d]
7	CH_2OPMB	**l**	85 (100:0)	85 (85, 0)
8	CHMe(OBn)	**m**	28 (52:48)[e]	88[f] (40, 48)[g]

[a] Isolated yield.
[b] Values in parentheses are the ratio of regioisomer determined by ^{19}F NMR spectroscopy.
[c] The diastereomeric ratio was 50:50.
[d] The diastereomeric ratios of **16** and **17** were 48:52 and 49:51, respectively.
[e] The diastereomeric ratios of **14** and **15** were 30:70 and 31:69, respectively.
[f] Isolation of the product was not possible. The yield was determined by ^{19}F NMR spectroscopy.
[g] The diastereomeric ratios of **16** and **17** were 27:73 and 27:73, respectively.



Scheme 2 Synthesis for bioisosteres of glycine dipeptide

Based on our experimental results, the reaction mechanism can be proposed as follows (Scheme 3). Thus, the starting $CBrF_2$-containing substrates can be converted into the corresponding difluorinated chromium species **Int-1** via the single electron-transfer mechanism. In **Int-1**, the C–F bond may be a little bit longer than that in the starting $CBrF_2$-containing substrates due to the nature of a carbenoid. Therefore, the C–F bond activation by $CrCl_2$ presumably takes place to provide the corresponding dichromium species **Int-2**.



Scheme 3 Proposed reaction mechanism

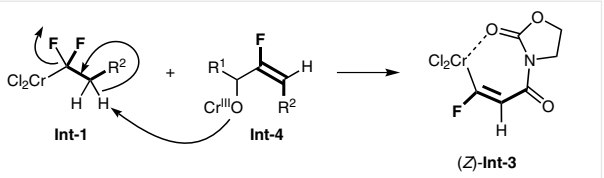
When **1** was employed as the substrate, the Lewis acidic chromium metal can coordinate with the carbonyl oxygen of the oxazolidinone moiety in **Int-2** to form a stable seven-membered intermediate. Additionally, this intermediate is more stabilized because the dipole moment vectors on each carbonyl group facing the opposite direction cancel each

other. Then, *syn*-elimination of $CrHCl_2$ takes place to afford the corresponding (*Z*)-fluorovinyl chromium reagent (*Z*)-**Int-3**,[18] which can react with aldehydes to produce the corresponding (*E*)-β-fluoroallylic alcohols **7**.

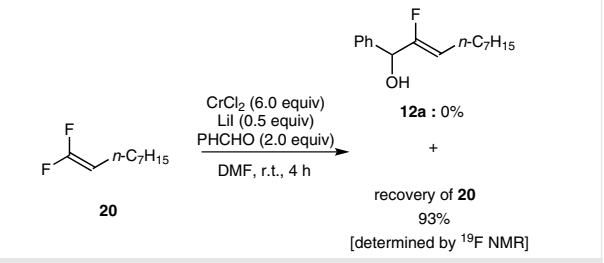
In the case of **3**–**6**, which do not have any functionality capable of coordinating with the chromium metal, β-elimination of $CrHCl_2$ from the most stable conformer, in which R^2 and $CrCl_2$ substituents are located in the antiperiplaner position, avoiding a large steric repulsion, occurs in a *syn*-fashion, resulting in the formation of a thermodynamically stable (*E*)-fluorovinyl chromium reagents (*E*)-**Int-3**, which can react with various aldehydes to yield the corresponding (*Z*)-β-fluoroallylic alcohols **8** and **10**–**12**.

In the reaction of **1**, β-elimination of HF from **Int-1** by the chromium alkoxide **Int-4** may also be possible due to a highly acidic α-proton of the carbonyl (Scheme 4). In this case, **Int-1** can be directly converted into (*Z*)-**Int-3**, bypassing the formation of the dichromium species **Int-2**.

Given that the reaction of **1** with benzaldehyde in the presence of only 3.0 equivalents of $CrCl_2$ proceeded efficiently, this β-elimination may play an important role in the Cr(II)-mediated reductive coupling. In fact, some of the steps of this new reaction mechanism depicted in Scheme 3 conflicts with the one described in our previous paper,[8] thus the difluoroalkene could be possibly formed after β-elimination from **Int-1**, which was initially thought as the key intermediate transformed to fluorovinylchromium species (*Z*)- or (*E*)-**Int-3** via single electron transfer. In fact, according to the control reaction described in Scheme 5, treating difluoroalkene **20**[19] with benzaldehyde under the standard reaction condition did not give the corresponding desired product **12a** with almost quantitative recovery of starting material **20**. This fact strongly indicates that the reaction does not proceed via a 1,1-difluoroalkene intermediate.



Scheme 4 β-Elimination



Scheme 5 Control reaction

In summary, we have investigated the highly stereoselective synthesis of (*E*)- or (*Z*)-β-fluoroallylic alcohol derivatives based on $CrCl_2$-mediated C–F bond activation reaction. As a result, the substrate **1** having a Lewis basic group, like an oxazolidinone substituent, afforded *E*-isomers in a highly stereoselective manner, while substrates **3**–**6** without a Lewis basic substituent gave the *Z*-isomers stereoselectively. It was proposed that this stereoselection was derived from the interaction of chromium metal and a carbonyl oxygen in the dichromium intermediates. In addition, the novel Cr(II)-mediated reductive coupling reaction could be successfully applied to the stereoselective synthesis of fluoroalkene dipeptide analogues.

IR spectra were recorded as a liquid film between NaCl plates or KBr disk method for solids with a JASCO FT/IR-4100 type A spectrometer. ^1H and ^{13}C NMR spectra were recorded on a JEOL JNM-AL 400 NMR spectrometer in $CDCl_3$ solution with TMS as an internal reference. A JEOL JNM-AL 400 NMR spectrometer was used for determining the yield of the products with C_6F_6. ^{19}F NMR (376.05 MHz) spectra were recorded on a JEOL JNM-AL 400 NMR spectrometer in $CDCl_3$ solution with $CFCl_3$ as an internal standard. High-resolution mass spectra (HRMS) were recorded on a JEOL JMS-700MS spectrometer by electron impact (EI), chemical ionization (CI), and fast atom bombardment (FAB) methods.

All reactions were routinely monitored by ^{19}F NMR spectroscopy or TLC, and carried out under an atmosphere of argon. EtOH was fleshly distilled from Mg. DMF were freshly distilled from CaH_2. All chemicals were of reagent grade and, if necessary, were purified in the usual manner prior to use. TLC was done with Merck silica gel 60 F254 plates, and column chromatography was carried out with Wako gel C-200.

1-Bromo-3-(*tert*-butyldiphenylsilyloxy)-1,1-difluoropropane (3); Typical Procedure

Under an argon atmosphere, a solution of ethyl 3-bromo-3,3-difluoropropanoate (**2**; 0.65 g, 3.0 mmol) in CH_2Cl_2 was added dropwise to DIBAL-H (6.9 mmol) at –78 °C. The reaction mixture was stirred at that temperature for 2 h and then stirred at 0 °C for 3 h. The reaction was quenched with aq 10% HCl and the mixture was extracted with CH_2Cl_2 (3 ×). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated under reduce pressure. The resulting residue was used in the next step without further purification. A mixture of the above crude alcohol, *t*-$BuPh_2SiCl$ (1.65 g, 6.0 mmol), and imidazole (0.41 g, 6.0 mmol) in THF (6 mL) was stirred at r.t. for 20 h. Addition of H_2O followed by extractive workup and purification by silica gel column chromatography (hexane–EtOAc, 80:1) afforded the desired product; yield: 0.60 g (49%, 1.46 mmol) over two steps; colorless oil.

IR (neat): 3072, 3000, 2932, 2858, 1960, 1590, 1472, 1428, 1362, 1283, 1188, 1114, 998, 880, 823, 702, 613 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.07 (9 H, s), 2.63–2.69 (2 H, tt, *J* = 6.59, 13.35 Hz), 3.93 (2 H, t, *J* = 6.59 Hz), 7.39–7.46 (6 H, m), 7.67–7.69 (4 H, m).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 19.1, 26.7, 46.7 (t, *J* = 20.7 Hz), 58.8 (t, *J* = 4.1 Hz), 121.2 (t, *J* = 305.4 Hz), 127.8, 129.8, 133.1, 135.5.

^{19}F NMR (376 MHz, $CDCl_3$): δ = –42.39 (2 F, t, *J* = 13.35 Hz).

HRMS (FAB+): *m*/*z* [M + H]$^+$ calcd for $C_{19}H_{24}BrF_2OSi$: 413.0748; found: 413.0751.

1-Bromo-4-(*tert*-butyldiphenylsilyloxy)-1,1-difluorobutane (5)

Yield: 3.72 g (69%, 8.70 mmol) over two steps; colorless oil.

IR (neat): 3071, 2932, 2858, 1472, 1428, 1216, 1186, 1112, 1023, 997, 932, 823, 740, 702 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.06 (9 H, s), 1.81–1.88 (2 H, m), 2.45–2.55 (2 H, m), 3.72 (2 H, t, *J* = 5.99 Hz), 7.38–7.46 (6 H, m), 7.64–7.66 (4 H, m).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 19.1, 26.8, 27.1 (d, *J* = 2.5 Hz), 41.2 (t, *J* = 21.5 Hz), 62.0, 123.2 (d, *J* = 304.5 Hz), 127.7, 129.7, 133.5, 135.5.

^{19}F NMR (376 MHz, $CDCl_3$): δ = –43.76 (2 F, t, *J* = 14.67 Hz).

HRMS (FAB+): *m*/*z* [M + H]$^+$ calcd for $C_{20}H_{26}BrF_2OSi$: 427.0904; found: 427.0896.

1-Bromo-1,1-difluorononane (6)

Under an argon atmosphere, a three-necked, round-bottomed flask equipped with an efficient magnetic stirring bar was charged with CuCl (0.040 g, 0.4 mmol), 2-aminoethanol (1.22 g, 20.0 mmol), *t*-BuOH (6.6 mL), oct-1-ene (4.49 g, 40 mmol), and CBr_2F_2 (16.8 g, 80 mmol), and the mixture was stirred at 85 °C for 48 h. Then, all organic materials were filtered through silica gel, which was rinsed with hexanes. The resulting colorless filtrate was concentrated by evaporation and subjected to fractional distillation under reduced pressure, affording 1,3-dibromo-1,1-difluorononane (8.86 g, 27.7 mmol, 69%) as a colorless liquid. Under an argon atmosphere, a three-necked round-bottomed flask equipped with an ice-H_2O condenser was charged with 1,3-dibromo-1,1-difluorononane (8.86 g, 27.7 mmol) dissolved in anhydrous DMSO (28 mL). $NaBH_4$ (1.51 g, 40 mmol) was then added in small portions with vigorous stirring over the course of 15 min. After the addition was complete, the bath temperature was raised to 70 °C and the mixture was stirred at this temperature for 6 h. The flask was cooled to r.t., the contents were transferred to an Erlenmeyer flask, and the reaction was quenched with chips of ice. The resulting mixture was carefully acidified with concd HCl, and the aqueous DMSO layer was extracted with Et_2O (3 ×). The combined Et_2O layers were washed with H_2O, dried (Na_2SO_4), and subjected to fractional distillation under the ambient pressure affording the known compound, 1-bromo-1,1-difluorononane (contaminated with a small amount of 1,1-difluorononane); yield: 1.87 g (38%, 7.7 mmol) as a colorless liquid. The analytical and spectral data were in conformity with the literature.[12]

***E*-Selective Chromium(II)-Mediated Reductive Coupling Reaction of 3-(3-Bromo-3,3-difluoropropanoyl)-2-oxazolidinone (1) with Aldehydes; 3-[(*E*)-3-Fluoro-4-hydroxy-4-phenylbut-2-enoyl]-2-oxazolidinone (7a); Typical Procedure**

To a suspension of anhydrous $CrCl_2$ (0.25 g, 2.0 mmol) and LiI (0.013 g, 0.1 mmol) in DMF (1.5 mL) were added benzaldehyde (0.11 g, 1.0 mmol) and imide (0.13 g, 0.5 mmol) at 0 °C. After stirring at that temperature for 4 h, the reaction was quenched with ice-cold H_2O. The mixture was extracted with Et_2O (3 ×). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated in vacuo. The resulting residue was purified by silica gel column chromatography (benzene–EtOAc, 3:1) to afford the pure product **7a**; yield: 0.11 g (84%, 0.42 mmol); yellow oil.

^{1}H NMR (400 MHz, acetone-d_6): δ = 4.12 (2 H, t, *J* = 8.03 Hz), 4.48–4.52 (2 H, m), 5.31 (1 H, d, *J* = 6.00 Hz), 6.47 (1 H, dd, *J* = 6.00, 27.23 Hz), 7.04 (1 H, d, *J* = 21.33 Hz), 7.31–7.59 (5 H, m).

^{13}C NMR (100 MHz, acetone-d_6): δ = 43.6, 63,2, 69.0 (d, *J* = 22.0 Hz), 101.8 (d, *J* = 30.2 Hz), 127.2, 128.7, 129.1, 140.5 (d, *J* = 1.3 Hz), 154.4, 164.5 (d, *J* = 24.7 Hz), 175.4 (d, *J* = 280.6 Hz).

^{19}F NMR (376 MHz, acetone-d_6): δ = –97.43 (1 F, dd, *J* = 21.33, 27.23 Hz).

HRMS (FAB+): *m*/*z* [M]$^+$ calcd for $C_{13}H_{12}FNO_4$: 265.0750; found: 265.0750.

3-[(*E*)-3-Fluoro-4-hydroxy-4-(4-methylphenyl)but-2-enoyl]-2-oxazolidinone (7b)

Yield: 0.089 g (64%, 0.32 mmol); yellow oil.

^{1}H NMR (400 MHz, acetone-d_6): δ = 2.36 (3 H, s), 4.13 (2 H, t, *J* = 8.06 Hz), 4.48–4.52 (2 H, m), 5.26 (1 H, d, *J* = 6.11 Hz), 6.47 (1 H, dd, *J* = 6.11, 27.13 Hz), 7.11 (1 H, d, *J* = 21.36 Hz), 7.22 (2 H, d, *J* = 7.97 Hz), 7.51 (2 H, d, *J* = 7.97 Hz).

^{13}C NMR (100 MHz, acetone-d_6): δ = 21.1, 43.6, 63.1, 69.0 (d, *J* = 22.1 Hz), 101.6 (d, *J* = 30.2 Hz), 127.2, 129.7, 137.5, 138.3, 154.4, 164.5 (d, *J* = 24.7 Hz), 175.6 (d, *J* = 280.6 Hz).

^{19}F NMR (376 MHz, acetone-d_6): δ = –98.73 (1 F, dd, *J* = 21.36, 27.13 Hz).

HRMS (FAB+): *m*/*z* [M]$^+$ calcd for $C_{14}H_{14}FNO_4$: 279.0907; found: 279.0916.

3-[(*E*)-3-Fluoro-4-hydroxy-4-(4-methoxylphenyl)but-2-enoyl]-2-oxazolidinone (7c)

Yield: 0.10 g (69%, 0.35 mmol); yellow oil.

^{1}H NMR (400 MHz, acetone-d_6): δ = 3.79 (3 H, s), 4.11 (2 H, t, *J* = 8.05 Hz), 4.46–4.51 (2 H, m), 5.18 (1 H, d, *J* = 6.00 Hz), 6.39 (1 H, dd, *J* = 6.00, 27.01 Hz), 6.92 (2 H, d, *J* = 8.58 Hz), 7.04 (1 H, d, *J* = 21.31 Hz), 7.49 (2 H, d, *J* = 8.58 Hz).

^{13}C NMR (100 MHz, acetone-d_6): δ = 43.6, 55.5, 63.1, 68.7 (d, *J* = 22.0 Hz), 101.4 (d, *J* = 30.2 Hz), 114.5, 128.5, 132.5, 154.4, 160.5, 164.1 (d, *J* = 24.7 Hz), 175.6 (d, *J* = 280.6 Hz).

^{19}F NMR (376 MHz, acetone-d_6): δ = –98.67 (1 F, dd, *J* = 21.31, 27.01 Hz).

HRMS (FAB+): *m*/*z* [M]$^+$ calcd for $C_{14}H_{14}FNO_5$: 295.0856; found: 295.0863.

3-[(*E*)-3-Fluoro-4-(4-fluorophenyl)-4-hydroxybut-2-enoyl]-2-oxazolidinone (7d)

Yield: 0.13 g (90%, 0.45 mmol); yellow oil.

^{1}H NMR (400 MHz, acetone-d_6): δ = 4.13 (2 H, t, *J* = 8.17 Hz), 4.47–4.53 (2 H, m), 5.37 (1 H, d, *J* = 5.84 Hz), 6.46 (1 H, dd, *J* = 5.84, 27.09 Hz), 7.06 (1 H, d, *J* = 21.29 Hz), 7.14 (2 H, m), 7.58–7.63 (2 H, m).

^{13}C NMR (100 MHz, acetone-d_6): δ = 43.6, 63.2, 68.3 (d, *J* = 21.9 Hz), 101.9 (d, *J* = 29.8 Hz), 115.8 (d, *J* = 21.6 Hz), 129.2 (d, *J* = 8.2 Hz), 136.6, 154.4, 163.3 (d, *J* = 244.4 Hz), 164.5 (d, *J* = 24.4 Hz), 175.6 (d, *J* = 280.4 Hz).

^{19}F NMR (376 MHz, acetone-d_6): δ = –115.06 to –114.87 (1 F, m), –98.29 (1 F, dd, *J* = 21.29, 27.09 Hz).

HRMS (FAB+): *m*/*z* [M + H]$^+$ calcd for $C_{13}H_{12}F_2NO_4$: 284.0734; found: 284.0726.

3-[(*E*)-3-Fluoro-4-hydroxyhept-2-enoyl]-2-oxazolidinone (7f)

Yield: 0.079 g (68%, 0.34 mmol); yellow oil.

^{1}H NMR (400 MHz, acetone-d_6): δ = 0.94 (3 H, t, J = 7.38 Hz), 1.35–1.78 (4 H, m), 4.07 (2 H, t, J = 8.05 Hz), 4.43–4.49 (3 H, m), 5.10–5.25 (1 H, m), 6.99 (1 H, d, J = 22.83 Hz).

^{13}C NMR (100 MHz, acetone-d_6): δ = 14.1, 19.3, 36.6, 43.5, 63.1, 67.6 (d, J = 22.9 Hz), 101.3 (d, J = 30.9 Hz), 154.4, 164.2 (d, J = 25.02 Hz), 177.5 (d, J = 280.4 Hz).

^{19}F NMR (376 MHz, acetone-d_6): δ = –97.38 (1 F, dd, J = 22.83, 26.89 Hz).

HRMS (FAB+): m/z [M + H]$^+$ calcd for $C_{10}H_{15}FNO_4$: 232.0985; found: 232.0993.

3-[(*E*)-3-Fluoro-4-hydroxy-5-methylhex-2-enoyl]-2-oxazolidinone (7g)

Yield: 0.088 g (77%, 0.38 mmol); yellow oil.

^{1}H NMR (400 MHz, acetone-d_6): δ = 0.92 (3 H, d, J = 6.82 Hz), 1.05 (3 H, d, J = 6.66 Hz), 1.91–1.99 (1 H, m), 4.06 (2 H, t, J = 8.03 Hz), 4.48 (2 H, t, J = 8.03 Hz), 4.57 (1 H, d, J = 7.08 Hz), 4.80–4.90 (1 H, m), 7.05 (1 H, d, J = 21.83 Hz).

^{13}C NMR (100 MHz, acetone-d_6): δ = 18.85, 18.86, 32.4, 43.5, 63.0, 73.1 (d, J = 22.5 Hz), 102.2 (d, J = 30.7 Hz), 154.3, 164.4 (d, J = 25.5 Hz), 177.0 (d, J = 280.6 Hz).

^{19}F NMR (376 MHz, acetone-d_6): δ = –95.00 (1 F, dd, J = 21.83, 29.33 Hz).

HRMS (FAB+): m/z [M + H]$^+$ calcd for $C_{10}H_{15}FNO_4$: 232.0985; found: 232.0984.

3-[(*E*)-3-Fluoro-4-hydroxy-5,5-dimethylhex-2-enoyl]-2-oxazolidinone (7h)

Yield: 0.095 g (77%, 0.39 mmol); yellow oil.

^{1}H NMR (400 MHz, acetone-d_6): δ = 1.00 (9 H, s), 4.07 (2 H, dt, J = 2.11, 8.00 Hz), 4.48 (2 H, t, J = 8.00 Hz), 4.63 (1 H, d, J = 6.93 Hz), 5.04 (1 H, dd, J = 6.93, 30.24 Hz), 7.09 (1 H, d, J = 23.08 Hz).

^{13}C NMR (100 MHz, acetone-d_6): δ = 26.5, 36.3, 43.6, 63.0, 74.4 (d, J = 20.5 Hz), 103.0 (d, J = 31.3 Hz), 154.4, 164.5 (d, J = 25.9 Hz), 176.6 (d, J = 282.8 Hz).

^{19}F NMR (376 MHz, acetone-d_6): δ = –87.58 (1 F, dd, J = 23.08, 30.24 Hz).

HRMS (FAB+): m/z [M + H]$^+$ calcd for $C_{11}H_{17}FNO_4$: 246.1142; found: 246.1141.

Z-Selective Chromium(II)-Mediated Reductive Coupling Reaction of 1-Bromo-3-(*tert*-butyldiphenylsilyloxy)-1,1-difluoropropane (3) with Aldehydes; (*Z*)-4-(*tert*-Butyldiphenylsilyloxy)-2-fluoro-1-phenylbut-2-en-1-ol (8a); Typical Procedure

To a suspension of anhydrous $CrCl_2$ (0.22 g, 1.8 mmol) and LiI (0.020 g, 0.15 mmol) in DMF (1.2 mL) were added benzaldehyde (0.064 g, 0.6 mmol) and the silyl ether **3** (0.12 g, 0.30 mmol) at 0 °C. After stirring at r.t. for 4 h, the reaction was quenched with H_2O. The mixture was extracted with Et_2O (3 ×). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated in vacuo. The resulting residue was purified by silica gel column chromatography (hexane–EtOAc, 5:1) to afford the pure product; yield: 0.071 g (56%, 0.17 mmol); yellow oil.

IR (neat): 3392, 3070, 2931, 2858, 1709, 1589, 1494, 1472, 1428, 1262, 1164, 1111, 1060, 885, 740, 701, 612 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.95 (9 H, s), 2.01 (1 H, br s), 4.26 (2 H, dd, J = 2.00, 6.79 Hz), 5.03 (1 H, d, J = 11.91 Hz), 5.09 (1 H, dt, J = 36.72, 6.79 Hz), 7.20–7.34 (11 H, m), 7.56–7.57 (4 H, m).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 19.1, 26.8, 57.1 (d, J = 6.6 Hz), 72.3 (d, J = 32.2 Hz), 107.0, (d, J = 10.7 Hz), 126.7, 127.6, 128.4, 128.5, 129.6, 133.5, 135.5, 139.1, 158.8 (d, J = 260.3 Hz).

^{19}F NMR (376 MHz, $CDCl_3$): δ = –119.05 (1 F, dd, J = 11.91, 36.72 Hz).

HRMS (FAB+): m/z [M + Na]$^+$ calcd for $C_{26}H_{29}FO_2SiNa$: 443.1819; found: 443.1815.

(*Z*)-4-(*tert*-Butyldiphenylsilyloxy)-2-fluoro-1-(4-methylphenyl)but-2-en-1-ol (8b)

Yield: 0.063 g (48%, 0.14 mmol); yellow oil.

IR (neat): 3395, 3071, 2930, 2858, 1079, 1513, 1472, 1428, 1362, 1163, 1111, 1062, 800, 740, 702 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.05 (9 H, s), 2.31 (1 H, br s), 2.35 (3 H, s), 4.36 (2 H, dd, J = 1.60, 6.49 Hz), 5.09 (1 H, d, J = 11.86 Hz), 5.19 (1 H, dt, J = 36.52, 6.49 Hz), 7.15–7.44 (10 H, m), 7.64–7.70 (4 H, m).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 19.1, 21.2, 26.7, 57.1 (d, J = 6.6 Hz), 72.2 (d, J = 32.2 Hz), 106.9 (d, J = 9.9 Hz), 126.6, 127.6, 129.2, 129.6, 133.6, 135.6, 136.2, 138.2, 158.8 (d, J = 259.5 Hz).

^{19}F NMR (376 MHz, $CDCl_3$) δ = –119.12 (1 F, dd, J = 11.86, 36.52 Hz).

HRMS (FAB+): m/z [M + Na]$^+$ calcd for $C_{27}H_{31}FO_2SiNa$: 457.1975; found: 457.1972.

(*Z*)-4-(*tert*-Butyldiphenylsilyloxy)-2-fluoro-1-(4-methoxyphenyl)but-2-en-1-ol (8c)

Yield: 0.070 g (52%, 0.16 mmol); yellow oil.

IR (neat): 3419, 3071, 2931, 2857, 1709, 1611, 1512, 1464, 1428, 1250, 1111, 1036, 739, 703 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.04 (9 H, s), 2.00 (1 H, br s), 3.82 (3 H, s), 4.36 (2 H, dd, J = 2.20, 6.59 Hz), 5.09 (1 H, dd, J = 3.20, 10.09 Hz), 5.19 (1 H, dt, J = 36.63, 6.59 Hz), 6.88–6.90 (2 H, m), 7.23–7.44 (8 H, m), 7.63–7.68 (4 H, m).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 19.1, 26.8, 55.3, 57.8 (d, J = 6.6 Hz), 72.0 (d, J = 32.2 Hz), 106.8 (d, J = 11.6 Hz), 113.9, 127.6, 128.1, 129.6, 131.3, 133.6, 135.6, 158.9 (d, J = 259.5 Hz), 159.7.

^{19}F NMR (376 MHz, $CDCl_3$): δ = –118.95 (1 F, dd, J = 10.09, 36.63 Hz).

HRMS (FAB+): m/z [M – H]$^+$ calcd for $C_{27}H_{30}FO_3Si$: 449.1948; found: 449.1938.

(*Z*)-4-(*tert*-Butyldiphenylsilyloxy)-2-fluoro-1-(4-fluorophenyl)but-2-en-1-ol (8d)

Yield: 0.073 g (56%, 0.17 mmol); yellow oil.

IR (neat): 3402, 3071, 2931, 2858, 1709, 1605, 1509, 1472, 1428, 1227, 1111, 1064, 908, 739, 703 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.06 (9 H, s), 2.17 (1 H, br s), 4.37 (2 H, d, J = 6.39 Hz), 5.12 (1 H, d, J = 12.11 Hz), 5.18 (1 H, dt, J = 36.72, 6.39 Hz), 7.03–7.07 (2 H, m), 7.32–7.46 (8 H, m), 7.64–7.72 (4 H, m).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 19.1, 26.8, 57.0 (d, J = 6.6 Hz), 71.7 (d, J = 32.2 Hz), 107.3 (d, J = 11.7 Hz), 115.4 (d, J = 27.8 Hz), 127.6, 128.5 (d, J = 8.2 Hz), 129.7, 133.5, 134.8 (d, J = 2.4 Hz), 135.5, 158.5 (d, J = 258.5 Hz), 162.6 (d, J = 246.2 Hz).

^{19}F NMR (376 MHz, $CDCl_3$): δ = –119.38 (1 F, dd, J = 12.11, 36.72 Hz).

HRMS (FAB+): m/z [M]$^+$ calcd for $C_{26}H_{28}F_2O_2Si$: 438.1827; found: 438.1833.

(*Z*)-1-(*tert*-Butyldiphenylsilyloxy)-3-fluorohept-2-en-4-ol (8f)

Yield: 0.066 g (57%, 0.17 mmol); yellow oil.

IR (neat): 3389, 3071, 3050, 2999, 2959, 2932, 2859, 1709, 1589, 1471, 1428, 1305, 1264, 1185, 1112, 939, 852, 822, 740, 702 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 0.95 (3 H, t, *J* = 7.39 Hz), 1.07 (9 H, s), 1.26–1.70 (4 H, m), 1.79 (1 H, br s), 4.00–4.07 (1 H, m), 4.37 (2 H, dd, *J* = 2.20, 6.59 Hz), 5.07 (1 H, dt, *J* = 37.41, 6.59 Hz), 7.36–7.47 (6 H, m), 7.68–7.73 (4 H, m).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.8, 18.5, 19.1, 26.8, 35.8, 57.0 (d, *J* = 7.43 Hz), 70.2 (d, *J* = 29.8 Hz), 106.1 (d, *J* = 11.7 Hz), 127.6, 129.6, 133.6, 135.5, 159.8 (d, *J* = 261.2 Hz).

^{19}F NMR (376 MHz, $CDCl_3$): δ = –122.19 (1 F, dd, *J* = 15.61, 37.41 Hz).

HRMS (FAB+): *m*/*z* $[M + Na]^+$ calcd for $C_{23}H_{31}FO_2SiNa$: 409.1975; found: 409.1976.

(*Z*)-6-(*tert*-Butyldiphenylsilyloxy)-4-fluoro-2-methylhex-4-en-3-ol (8g)

Yield: 0.069 g (59%, 0.18 mmol); yellow oil.

IR (neat): 3404, 3071, 3050, 2960, 2931, 2858, 1708, 1471, 1428, 1264, 1112, 1059, 1026, 939, 876, 822, 782, 740, 702 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 0.92 (3 H, d, *J* = 6.79 Hz), 0.97 (3 H, d, *J* = 6.79 Hz), 1.07 (9 H, s), 1.69 (1 H, br s), 1.87–1.91 (1 H, m), 3.73 (1 H, dd, *J* = 6.59, 17.05 Hz), 4.37 (2 H, d, *J* = 6.49 Hz), 5.07 (1 H, dt, *J* = 37.12, 6.49 Hz), 7.37–7.46 (6 H, m), 7.69–7.71 (4 H, m).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 17.5, 18.8, 19.1, 26.5, 26.8, 57.0 (d, *J* = 7.4 Hz), 75.8 (d, *J* = 28.9 Hz), 107.1 (d, *J* = 11.6 Hz), 127.7, 129.7, 133.7, 135.6, 159.1 (d, *J* = 261.1 Hz).

^{19}F NMR (376 MHz, $CDCl_3$): δ = –121.25 (1 F, dd, *J* = 17.05, 37.12 Hz).

HRMS (FAB): *m*/*z* $[M + Na]^+$ calcd for $C_{23}H_{31}FO_2SiNa$: 409.1975; found: 409.1976.

(*Z*)-6-(*tert*-Butyldiphenylsilyloxy)-4-fluoro-2,2-dimethylhex-4-en-3-ol (8h)

Yield: 0.076 g (63%, 0.19 mmol); yellow oil.

IR (neat): 3442, 3071, 2957, 2958, 1702, 1671, 1472, 1428, 1264, 1186, 1070, 1014, 937, 822, 788, 740, 612 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 0.94 (9 H, s), 1.05 (9 H, s), 1.71 (1 H, br s), 3.68 (1 H, d, *J* = 18.81 Hz), 4.35–4.36 (2 H, m), 5.03 (1 H, dt, *J* = 37.38, 6.79 Hz), 7.37–7.44 (6 H, m), 7.67–7.71 (4 H, m).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 19.1, 25.8, 26.8, 34.8, 60.0 (d, *J* = 7.43 Hz), 78.2 (d, *J* = 27.31 Hz), 107.5 (d, *J* = 11.7 Hz), 127.7, 129.6, 133.7, 135.5, 159.1 (d, *J* = 262.0 Hz).

^{19}F NMR (376 MHz, $CDCl_3$): δ = –114.51 (1 F, dd, *J* = 18.81, 37.38 Hz).

HRMS (FAB+): *m*/*z* $[M – H]^+$ calcd for $C_{24}H_{32}FO_2Si$: 399.2156; found: 399.2152.

Z-Selective Chromium(II)-Mediated Reductive Coupling Reaction of Ethyl 4-Bromo-4,4-difluorobutyrate (4) with Aldehydes; Ethyl (*Z*)-4-Fluoro-5-hydroxy-5-phenylpent-3-enoate (10a); Typical Procedure

To a suspension of anhydrous $CrCl_2$ (0.22 g, 1.8 mmol) and LiI (0.020 g, 0.15 mmol) in DMF (1.2 mL) were added benzaldehyde (0.064 g, 0.6 mmol) and the ester **4** (0.065 g, 0.3 mmol) at 0 °C. After stirring at r.t. for 4 h, the reaction was quenched with H_2O and the mixture was extracted with Et_2O (3 ×). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated in vacuo. The resulting residue was purified by silica gel column chromatography (hexane–EtOAc, 3:1) to afford the pure product; yield: 0.040 g (55%, 0.17 mmol); yellow oil.

IR (neat): 3448, 3032, 2983, 1736, 1495, 1454, 1372, 1266, 1189, 1094, 1060, 1027, 955, 887, 804, 701 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.26 (3 H, t, *J* = 7.09 Hz), 2.50 (1 H, br s), 3.17 (2 H, d, *J* = 7.19 Hz), 4.15 (2 H, q, *J* = 7.09 Hz), 5.22 (1 H, dt, *J* = 35.26, 7.19 Hz), 5.24 (1 H, d, *J* = 11.25 Hz), 7.29–7.45 (5 H, m).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.1, 29.2 (d, *J* = 4.9 Hz), 60.9, 72.4 (d, *J* = 31.4 Hz), 99.5 (d, *J* = 9.8 Hz), 126.7, 128.4, 128.5, 139.1, 160.4 (d, *J* = 260.3 Hz), 171.2 (d, *J* = 2.5 Hz).

^{19}F NMR (376 MHz, $CDCl_3$): δ = –119.34 (1 F, dd, *J* = 11.25, 35.26 Hz).

HRMS (FAB+): *m*/*z* $[M]^+$ calcd for $C_{13}H_{15}FO_3$: 238.1005; found: 238.1009.

Ethyl (*Z*)-4-Fluoro-5-hydroxy-5-(4-methylphenyl)pent-3-enoate (10b)

Yield: 0.031 g (40%, 0.12 mmol); yellow oil.

IR (neat): 3438, 2982, 2925, 1737, 1514, 1372, 1264, 1186, 1024, 955, 805, 770, 734 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.26 (3 H, t, *J* = 7.19 Hz), 1.61 (1 H, br s), 2.35 (3 H, s), 3.17 (2 H, d, *J* = 6.99 Hz), 4.15 (2 H, q, *J* = 7.19 Hz), 5.19–5.22 (1 H, m), 5.22 (1 H, dt, *J* = 35.66, 6.99 Hz), 7.17–7.33 (4 H, m).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.1, 21.2, 29.2 (d, *J* = 4.9 Hz), 60.9, 72.3 (d, *J* = 32.2 Hz), 99.3 (d, *J* = 12.4 Hz), 126.7, 129.3, 136.2, 138.3, 160.5 (d, *J* = 259.5 Hz), 171.2 (d, *J* = 1.7 Hz).

^{19}F NMR (376 MHz, $CDCl_3$): δ = –119.31 (1 F, dd, *J* = 11.09, 35.66 Hz).

HRMS (FAB+): *m*/*z* $[M]^+$ calcd for $C_{14}H_{17}FO_3$: 252.1162; found: 252.1163.

Ethyl (*Z*)-4-Fluoro-5-hydroxy-5-(4-methoxyphenyl)pent-3-enoate (10c)

Yield: 0.041 g (51%, 0.15 mmol); yellow oil.

IR (neat): 3449, 2982, 2839, 1736, 1611, 1586, 1513, 1465, 1372, 1304, 1251, 1180, 1113, 1032, 955, 834, 775, 736 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.26 (3 H, t, *J* = 7.49 Hz), 2.63 (1 H, br s), 3.16 (2 H, d, *J* = 7.19 Hz), 3.80 (3 H, s), 4.14 (2 H, q, *J* = 7.49 Hz), 5.20 (1 H, dt, *J* = 36.03, 7.19 Hz), 5.24 (1 H, m), 6.89 (2 H, d, *J* = 8.59 Hz), 7.35 (2 H, d, *J* = 8.59 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.1, 29.2 (d, *J* = 4.9 Hz), 55.3, 60.9, 72.0 (d, *J* = 31.1 Hz), 99.2 (d, *J* = 11.7 Hz), 113.9, 128.1, 131.3, 159.7, 160.6 (d, *J* = 259.5 Hz), 171.2 (d, *J* = 2.4 Hz).

^{19}F NMR (376 MHz, $CDCl_3$): δ = –119.13 (1 F, dd, *J* = 9.78, 36.03 Hz).

HRMS (FAB+): *m*/*z* $[M]^+$ calcd for $C_{14}H_{17}FO_4$: 268.1111; found: 268.1118.

Ethyl (*Z*)-4-Fluoro-5-(4-fluorophenyl)-5-hydroxypent-3-enoate (10d)

Yield: 0.038 g (49%, 0.15 mmol); yellow oil.

IR (neat): 3431, 2985, 1735, 1604, 1509, 1414, 1373, 1225, 1190, 1158, 1098, 1027, 956, 839, 784, 736 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.32 (3 H, t, *J* = 7.19 Hz), 2.84 (1 H, br s), 3.23 (2 H, d, *J* = 7.29 Hz), 4.21 (2 H, q, *J* = 7.19 Hz), 5.27 (1 H, dt, *J* = 35.26, 7.29 Hz), 5.28 (1 H, d, *J* = 11.25 Hz), 7.10–7.14 (2 H, m), 7.46–7.49 (2 H, m).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.1, 29.1 (d, *J* = 5.8 Hz), 61.0, 71.7 (d, *J* = 31.3 Hz), 99.6 (d, *J* = 11.6 Hz), 115.4, 128.5 (d, *J* = 8.2 Hz), 134.9 (d, *J* = 3.3 Hz), 160.3 (d, *J* = 260.3 Hz), 162.7 (d, *J* = 246.3 Hz), 171.2 (d, *J* = 2.5 Hz).

^{19}F NMR (376 MHz, $CDCl_3$): δ = –114.14 to –114.22 (1 F, m), –119.43 (1 F, dd, *J* = 11.25, 35.26 Hz).

HRMS (FAB+): *m*/*z* [M]$^+$ calcd for $C_{13}H_{14}F_2O_3$: 256.0911; found: 256.0914.

Ethyl (*Z*)-4-Fluoro-5-hydroxyoct-3-enoate (10f)

Yield: 0.026 g (42%, 0.13 mmol); yellow oil.

IR (neat): 3437, 2961, 2874, 1739, 1466, 1372, 1188, 1118, 1028, 953 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.94 (3 H, t, *J* = 7.39 Hz), 1.26 (3 H, t, *J* = 6.79 Hz), 1.37–1.46 (2 H, m), 1.60–1.66 (2 H, m), 2.08 (1 H, br s), 3.14 (2 H, d, *J* = 7.19 Hz), 4.08–4.17 (3 H, m), 5.07 (1 H, dt, *J* = 36.77, 7.19 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.8, 14.1, 18.5, 29.1 (d, *J* = 5.8 Hz), 35.8, 60.9, 70.2 (d, *J* = 28.9 Hz), 98.5 (d, *J* = 12.3 Hz), 161.4 (d, *J* = 261.2 Hz), 171.3 (d, *J* = 2.5 Hz).

^{19}F NMR (376 MHz, $CDCl_3$): δ = –122.41 (1 F, dd, *J* = 15.79, 36.77 Hz).

HRMS (FAB+): *m*/*z* [M + Na]$^+$ calcd for $C_{10}H_{17}FO_3Na$: 227.1059; found: 227.1062.

Ethyl (*Z*)-4-Fluoro-5-hydroxy-6-methylhept-3-enoate (10g)

Yield: 0.033 g (54%, 0.16 mmol); yellow oil.

IR (neat) 3445, 2965, 2875, 1738, 1469, 1371, 1259, 1189, 1123, 1123, 1024, 956, 879, 831 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.95 (3 H, d, *J* = 6.59 Hz), 0.99 (3 H, d, *J* = 6.59 Hz), 1.26 (3 H, t, *J* = 7.09 Hz), 1.78 (1 H, br s), 1.89–1.96 (1 H, m), 3.16 (2 H, dm, *J* = 7.24 Hz), 3.82 (1 H, dd, *J* = 6.99, 17.25 Hz), 4.15 (2 H, q, *J* = 7.09 Hz), 5.07 (1 H, dt, *J* = 36.58, 7.24 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.1, 17.6, 18.8, 29.1 (d, *J* = 5.7 Hz), 31.2, 60.9, 75.9 (d, *J* = 28.1 Hz), 99.4 (d, *J* = 12.5 Hz), 160.7 (d, *J* = 261.2 Hz), 171.3 (d, *J* = 1.6 Hz).

^{19}F NMR (376 MHz, $CDCl_3$): δ = –119.59 (1 F, dd, *J* = 17.25, 36.58 Hz).

HRMS (FAB+): *m*/*z* [M – H]$^+$ calcd for $C_{10}H_{16}FO_3$: 203.1083; found: 203.1088.

Ethyl (*Z*)-4-Fluoro-5-hydroxy-6,6-dimethylhept-3-enoate (10h)

Yield: 0.020 g (31%, 0.09 mmol); yellow oil.

IR (neat): 3461, 2958, 2908, 2873, 1793, 1479, 1467, 1370, 1330, 1261, 1188, 1076, 1018, 957, 911, 849, 770 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.97 (9 H, s), 1.26 (3 H, t, *J* = 7.19 Hz), 1.99 (1 H, br s), 3.15 (2 H, m), 3.78 (1 H, d, *J* = 19.13 Hz), 4.15 (2 H, q, *J* = 7.19 Hz), 5.03 (1 H, dt, *J* = 36.52, 7.29 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.1, 25.8, 29.2 (d, *J* = 5.7 Hz), 34.9, 60.9, 78.2 (d, *J* = 28.1 Hz), 100.3 (d, *J* = 12.5 Hz), 160.7 (d, *J* = 262.0 Hz), 171.2 (d, *J* = 1.7 Hz).

^{19}F NMR (376 MHz, $CDCl_3$): δ = –114.92 (1 F, dd, *J* = 19.13, 36.52 Hz).

HRMS (FAB+): *m*/*z* [M + H]$^+$ calcd for $C_{11}H_{20}FO_3$: 219.1396; found: 219.1389.

Z-Selective Chromium(II)-Mediated Reductive Coupling Reaction of 1-Bromo-4-(*tert*-butyldiphenylsilyloxy)-1,1-difluorobutane (5) with Benzaldehyde; (*Z*)-8-(*tert*-Butyldiphenylsilyloxy)-5-fluoro-2-methyloct-5-en-4-ol (11h); Typical Procedure

To a suspension of anhydrous $CrCl_2$ (1.11 g, 9.0 mmol) and LiI (0.10 g, 0.75 mmol) in DMF (6 mL) were added isovaleraldehyde (0.26 g, 3.0 mmol) and 1-bromo-4-(*tert*-butyldiphenylsilyloxy)-1,1-difluorobutane (**5**; 0.64 g, 1.5 mmol) at 0 °C. After stirring at r.t. for 4 h, the reaction was quenched with ice-cold H_2O and the mixture was extracted with Et_2O (3 ×). The combined organic layers were dried (Na_2SO_4); filtered, and concentrated in vacuo. The resulting residue was purified by silica gel column chromatography (hexane–EtOAc, 5:1) to afford the pure product **11h**; yield: 0.38 g (61%, 0.92 mmol); yellow oil.

IR (neat): 3388, 3071, 2957, 2931, 2859, 1709, 1471, 1428, 1388, 1362, 1111, 937, 823, 738, 702 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.926 (3 H, d, *J* = 6.39 Hz), 0.932 (3 H, d, *J* = 6.39 Hz), 1.05 (9 H, s), 1.45–1.60 (3 H, m), 1.75 (1 H, m), 2.36 (2 H, q, *J* = 6.66 Hz), 3.69 (2 H, t, *J* = 6.66 Hz), 4.12 (1 H, dt, *J* = 15.79, 7.99 Hz), 4.88 (1 H, dt, *J* = 38.40, 6.66 Hz), 7.36–7.45 (6 H, m), 7.65–7.68 (4 H, m).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 19.2, 22.1, 23.0, 24.3, 26.8, 42.9, 63.1, 69.3 (d, *J* = 28.9 Hz), 103.1 (d, *J* = 14.1 Hz), 127.6, 129.6, 133.8, 135.6, 160.6 (d, *J* = 257.1 Hz).

^{19}F NMR (376 MHz, $CDCl_3$): δ = –125.73 (1 F, dd, *J* = 15.79, 38.40 Hz).

HRMS (FAB+): *m*/*z* [M + Na]$^+$ calcd for $C_{25}H_{35}FO_2SiNa$: 437.2288; found: 437.2294.

(*Z*)-5-(*tert*-Butyldiphenylsilyloxy)-2-fluoro-1-phenylpent-2-en-1-ol (11a)

Yield: 0.30 g (67%, 0.68 mmol); yellow oil.

Physical and spectral data were in accordance with the literature values.[20]

(*Z*)-5-(*tert*-Butyldiphenylsilyloxy)-2-fluoro-1-(4-methoxyphenyl)pent-2-en-1-ol (11c)

Yield: 0.13 g (54%, 0.28 mmol); yellow oil.

IR (neat): 3405, 3070, 2930, 2857, 1611, 1512, 1471, 1427, 1249, 1174, 1111, 1035, 823, 740, 703 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.03 (9 H, s), 2.06 (1 H, d, *J* = 4.80 Hz), 2.37 (2 H, q, *J* = 6.59 Hz), 3.68 (2 H, t, *J* = 6.59 Hz), 3.80 (3 H, s), 4.96 (1 H, dt, *J* = 37.95, 6.59 Hz), 5.15 (1 H, dd, *J* = 4.80, 11.34 Hz), 6.87–6.89 (2 H, m), 7.32–7.44 (8 H, m), 7.63–7.67 (4 H, m).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 19.2, 26.8, 27.0 (d, *J* = 4.1 Hz), 55.2, 63.0 (d, *J* = 1.6 Hz), 72.3 (d, *J* = 32.1 Hz), 104.1 (d, *J* = 13.3 Hz), 113.9, 127.6, 128.0, 129.6, 131.7, 133.8, 135.5, 159.5, 159.7 (d, *J* = 256.2 Hz).

^{19}F NMR (376 MHz, $CDCl_3$): δ = –121.83 (1 F, dd, *J* = 11.34, 37.95 Hz).

HRMS (FAB+): *m*/*z* [M + Na]$^+$ calcd for $C_{28}H_{33}FO_3SiNa$: 487.2081; found: 487.2075.

(*Z*)-6-(*tert*-Butyldiphenylsilyloxy)-3-fluorohex-3-en-2-ol (11j)

Yield: 0.39 g (69%, 1.04 mmol); colorless oil.

IR (neat): 3362, 3071, 3050, 2957, 2931, 2858, 1709, 1472, 1428, 1389, 1362, 1111, 1005, 937, 823, 738, 702 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.05 (9 H, s), 1.34 (3 H, d, *J* = 6.31 Hz), 1.55–1.65 (1 H, m), 2.35 (2 H, m), 3.69 (2 H, t, *J* = 6.79 Hz), 4.26 (1 H, dq, *J* = 13.74, 6.31 Hz), 4.88 (1 H, dt, *J* = 38.93, 6.79 Hz), 7.36–7.45 (6 H, m), 7.65–7.67 (4 H, m).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 19.1, 20.1 (d, *J* = 1.7 Hz), 26.8, 26.9 (d, *J* = 1.6 Hz), 63.0 (d, *J* = 1.6 Hz) 66.5 (d, *J* = 30.5 Hz), 102.0 (d, *J* = 14.0 Hz), 127.6, 129.6, 133.8, 135.6, 161.3 (d, *J* = 256.2 Hz).

^{19}F NMR (376 MHz, $CDCl_3$): δ = –124.45 (1 F, dd, *J* = 13.74, 38.93 Hz).

HRMS (FAB+): *m*/*z* [M + Na]$^+$ calcd for $C_{22}H_{29}FO_2SiNa$: 395.1819; found: 395.1826.

(*Z*)-7-(*tert*-Butyldiphenylsilyloxy)-4-fluoro-2-methylhept-4-en-3-ol (11g)

Yield: 0.40 g (67%, 1.00 mmol); yellow oil.

Physical and spectral data were in accordance with the literature values.[20]

(*Z*)-8-(*tert*-Butyldiphenylsilyloxy)-5-fluoro-3-methyloct-5-en-4-ol (11k)

Yield: 0.41 g (49%, 0.99 mmol); diastereomeric ratio: 45:55; yellow oil.

IR (neat): 3404, 3071, 2961, 2931, 2858, 1707, 1463, 1428, 1384, 1362, 1262, 1111, 937, 822, 739, 702 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.87–0.95 (6 H, m), 1.05 (9 H, s), 1.40–1.84 (4 H, m), 2.39 (2 H, q, *J* = 6.39 Hz), 3.72 (2 H, t, *J* = 6.39 Hz), 3.79 and 3.89 (1 H, dd and dd, *J* = 7.19, 19.48 Hz and *J* = 5.99, 15.69 Hz), 4.87 and 4.88 (1 H, dt and dt, *J* = 7.19, 38.64 Hz and *J* = 7.19, 38.50 Hz), 7.36–7.45 (6 H, m), 7.66–7.68 (4 H, m).

^{19}F NMR (376 MHz, $CDCl_3$): δ = –123.86 and –124.94 (1 F, dd and dd, *J* = 19.48, 38.64 Hz and 15.69, 38.50 Hz).

HRMS (FAB+): *m*/*z* [M + Na]$^+$ calcd for $C_{25}H_{35}FO_2SiNa$: 437.2288; found: 437.2285.

(*Z*)-6-(*tert*-Butyldiphenylsilyloxy)-3-fluoro-1-(4-methoxybenzyloxy)hex-3-en-2-ol (11l)

Yield: 0.20 g (38%, 0.39 mmol); colorless oil.

IR (neat): 3434, 3070, 2931, 2858, 1616, 1514, 1471, 1428, 1249, 1111, 1035, 822, 740, 703 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.04 (9 H, s), 1.40–2.00 (1 H, m), 2.37 (2 H, q, *J* = 6.66 Hz), 3.50 (1 H, dd, *J* = 7.59, 9.59 Hz), 3.61 (1 H, dd, *J* = 4.00, 9.59 Hz), 3.67 (2 H, t, *J* = 6.66 Hz), 3.80 (3 H, s), 4.28 (1 H, ddd, *J* = 4.00, 7.59, 11.39 Hz), 4.48 (1 H, d, *J* = 11.99 Hz), 4.52 (1 H, d, *J* = 11.99 Hz), 4.99 (1 H, dt, *J* = 36.71, 6.66 Hz), 6.86–6.89 (2 H, m), 7.23–7.25 (2 H, m), 7.34–7.64 (6 H, m,), 7.65–7.66 (4 H, m).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 19.2, 26.8, 26.9 (d, *J* = 1.7 Hz), 55.3, 63.0 (d, *J* = 1.7 Hz), 69.4 (d, *J* = 32.2 Hz), 71.0, 73.1, 104.1 (d, *J* = 12.4 Hz), 113.9, 127.6, 129.48, 129.58, 129.62, 133.8, 135.5, 157.7 (d, *J* = 255.4 Hz), 159.4.

^{19}F NMR (376 MHz, $CDCl_3$): δ = –123.36 (1 F, dd, *J* = 11.39, 36.71 Hz).

HRMS (FAB+): *m*/*z* [M + Na]$^+$ calcd for $C_{30}H_{37}FO_4SiNa$: 531.2353; found: 531.2353.

(*Z*)-2-Benzyloxy-7-(*tert*-butyldiphenylsilyloxy)-4-fluorohept-4-en-3-ol (11m)

This compound was inseparable from by-products; yield: 75% (^{19}F NMR yield); diastereomeric ratio: 62:38.

Major Isomer (more polar)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.05 (9 H, s), 1.19 (3 H, d, *J* = 6.39 Hz), 1.50–1.80 (1 H, m), 2.38 (2 H, q, *J* = 7.06 Hz), 3.68 (2 H, t, *J* = 7.06 Hz), 3.85–3.95 (1 H, m) 4.20–4.30 (1 H, m), 4.42–4.70 (2 H, m), 5.00 (1 H, dt, *J* = 38.43, 7.06 Hz), 7.26–7.44 (11 H, m), 7.65–7.67 (4 H, m).

^{19}F NMR (376 MHz, $CDCl_3$): δ = –123.04 (1 F, dd, *J* = 10.91, 38.43 Hz).

HRMS (FAB+): *m*/*z* [M + Na]$^+$ calcd for $C_{30}H_{37}FO_3SiNa$: 515.2389; found: 515.2394.

Minor Isomer (less polar)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.02 (1 H, dt, *J* = 37.37, 7.86 Hz).

^{19}F NMR (376 MHz, $CDCl_3$): δ = –123.94 (1 F, dd, *J* = 15.80, 37.37 Hz).

Z-Selective Chromium(II)-Mediated Reductive Coupling Reaction of 1-Bromo-1,1-difluorononane (6) with Benzaldehyde; (*Z*)-2-Fluoro-1-phenyldec-2-en-1-ol (12a); Typical Procedure

To a suspension of anhydrous $CrCl_2$ (0.22 g, 1.8 mmol) and LiI (0.020 g, 0.15 mmol) in DMF (1.2 mL) were added benzaldehyde (0.064 g, 0.6 mmol) and the substrate **6** (0.073 g, 0.3 mmol) at 0 °C. After stirring at r.t. for 4 h, the reaction was quenched with H_2O and the mixture was extracted with Et_2O (3 ×). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated in vacuo. The resulting residue was purified by silica gel column chromatography (hexane–EtOAc, 3:1) to afford the pure product **12a**; yield: 0.056 g (76%, 0.22 mmol); yellow oil.

IR (neat): 3364, 3032, 2926, 2856, 1708, 1495, 1455, 1379, 1273, 1192, 1111, 1024, 700 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.88 (3 H, t, *J* = 6.79 Hz), 1.27–1.39 (10 H, m), 2.08–2.18 (3 H, m), 4.90 (1 H, dt, *J* = 37.87, 7.19 Hz), 5.21 (1 H, d, *J* = 13.17 Hz), 7.31–7.45 (5 H, m).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.1, 22.6, 23.3, 29.0, 29.1, 29.2, 31.8, 72.8 (d, *J* = 32.2 Hz), 107.8 (d, *J* = 13.3 Hz), 126.6, 128.2, 128.5, 139.7, 158.3 (d, *J* = 255.4 Hz).

^{19}F NMR (376 MHz, $CDCl_3$): δ = –124.22 (1 F, dd, *J* = 13.17, 37.87 Hz).

HRMS (FAB+): *m*/*z* [M]$^+$ calcd for $C_{16}H_{23}FO$: 250.1733; found: 250.1729.

(*Z*)-2-Fluoro-1-(4-methylphenyl)dec-2-en-1-ol (12b)

Yield: 76% (^{19}F NMR yield). This compound could not be separated from the small amount of impurities.

IR (neat): 3368, 2925, 2856, 1708, 1514, 1459, 1273, 1111, 1044, 819, 768 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.90 (3 H, t, *J* = 5.60 Hz), 1.20–1.40 (10 H, m), 2.12 (2 H, q, *J* = 7.19 Hz), 2.26 (1 H, br s), 2.37 (3 H, s), 4.90 (1 H, dt, *J* = 37.03, 7.19 Hz), 5.16 (1 H, d, *J* = 12.41 Hz), 7.13–7.33 (4 H, m).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.1, 21.1, 22.6, 23.3, 29.0, 29.1, 29.2, 31.8, 72.6 (d, *J* = 32.1 Hz), 107.6 (d, *J* = 14.1 Hz), 126.6, 129.2, 136.8, 138.0, 158.5 (d, *J* = 254.6 Hz).

^{19}F NMR (376 MHz, $CDCl_3$): δ = –124.11 (1 F, dd, *J* = 12.41, 37.03 Hz).

HRMS (FAB+): *m*/*z* [M]$^+$ calcd for $C_{17}H_{25}FO$: 264.1889; found: 264.1884.

(*Z*)-2-Fluoro-1-(4-methoxyphenyl)dec-2-en-1-ol (12c)

Yield: 0.065 g (80%, 0.23 mmol); yellow oil.

IR (neat): 3399, 2926, 2855, 1707, 1612, 1585, 1512, 1464, 1304, 1249, 1174, 1109, 1036, 832, 774 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.88 (3 H, t, *J* = 6.79 Hz), 1.20–1.35 (11 H, m), 2.11 (2 H, q, *J* = 7.13 Hz), 3.81 (3 H, s), 4.89 (1 H, dt, *J* = 38.34, 7.13 Hz), 5.15 (1 H, dd, *J* = 3.60, 12.21 Hz), 6.90 (2 H, d, *J* = 8.59 Hz), 7.35 (2 H, d, *J* = 8.59 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.1, 22.6, 23.3, 28.99, 29.04, 29.2, 31.8, 55.2, 72.3 (d, *J* = 32.2 Hz), 107.4 (d, *J* = 13.3 Hz), 113.8, 127.9, 132.0, 158.6 (d, *J* = 254.6 Hz), 159.4.

^{19}F NMR (376 MHz, $CDCl_3$): δ = –123.86 (1 F, dd, *J* = 12.21, 38.34 Hz).

HRMS (FAB+): *m*/*z* [M]$^+$ calcd for $C_{17}H_{25}FO$: 264.1889; found: 264.1894.

(*Z*)-2-Fluoro-1-(4-fluorophenyl)dec-2-en-1-ol (12d)

Yield: 0.061 g (78%, 0.23 mmol); yellow oil.

IR (neat): 3358, 2926, 2856, 1707, 1605, 1509, 1465, 1227, 1157, 1097, 1015, 837, 783 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.88 (3 H, t, *J* = 6.79 Hz), 1.20–1.40 (10 H, m), 2.10 (2 H, q, *J* = 7.19 Hz), 2.44 (1 H, br s), 4.89 (1 H, dt, *J* = 37.68, 7.19 Hz), 5.18 (1 H, d, *J* = 12.79 Hz), 7.03–7.09 (2 H, m), 7.38–7.41 (2 H, m).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.1, 22.6, 23.3, 28.99, 29.09, 29.14, 31.8, 72.1 (d, *J* = 32.2 Hz) 107.9 (d, *J* = 14.1 Hz), 115.3 (d, *J* = 21.5 Hz), 128.4 (d, *J* = 8.3 Hz), 135.5 (d, *J* = 2.5 Hz) 158.2 (d, *J* = 254.6 Hz), 162.6 (d, *J* = 246.4 Hz).

^{19}F NMR (376 MHz, $CDCl_3$): δ = –124.41 (1 F, dd, *J* = 12.79, 37.68 Hz).

HRMS (FAB+): *m*/*z* [M]$^+$ calcd for $C_{16}H_{22}F_2O$: 268.1639; found: 268.1632.

(*Z*)-5-Fluoro-5-tridecen-4-ol (12f)

Yield: 0.051 g (81%, 0.24 mmol); yellow oil.

IR (neat): 3349, 2959, 2927, 2857, 1708, 1466, 1379, 1253, 1127, 1029, 845 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.88 (3 H, t, *J* = 6.79 Hz), 0.94 (3 H, t, *J* = 7.19 Hz), 1.20–1.45 (12 H, m), 1.61–1.70 (3 H, m), 2.04–2.09 (2 H, m), 4.06 (1 H, dt, *J* = 17.25, 13.19 Hz), 4.79 (1 H, dt, *J* = 37.97, 7.19 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.8, 14.1, 18.7, 22.6, 23.2, 29.0, 29.1, 29.3, 31.8, 36.0, 70.8 (d, *J* = 29.8 Hz), 106.7 (d, *J* = 14.1 Hz), 159.2 (d, *J* = 255.4 Hz).

^{19}F NMR (376 MHz, $CDCl_3$): δ = –127.84 (1 F, dd, *J* = 17.25, 37.97 Hz).

HRMS (EI+): *m*/*z* [M]$^+$ calcd for $C_{13}H_{25}FO$: 216.1889; found: 216.1891.

(*Z*)-4-Fluoro-2-methyldodec-4-en-3-ol (12g)

Yield: 0.044 g (70%, 0.20 mmol); yellow oil.

IR (neat): 3387, 2958, 2926, 2857, 1707, 1467, 1381, 1281, 1168, 1103, 1021, 934, 831 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.88 (3 H, t, *J* = 6.79 Hz), 0.91 (3 H, d, *J* = 6.79 Hz), 0.98 (3 H, d, *J* = 6.79 Hz), 1.20–1.40 (10 H, m), 1.70–1.75 (1 H, m), 1.85–1.95 (1 H, m), 2.09 (2 H, q, *J* = 7.59 Hz), 3.72 (1 H, dt, *J* = 19.37, 6.79 Hz), 4.77 (1 H, dt, *J* = 37.41, 7.59 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.1, 17.9, 18.9, 22.6, 23.2, 29.0, 29.1, 29.3, 31.3, 31.8, 76.5 (d, *J* = 32.2 Hz), 107.6 (d, *J* = 14.1 Hz), 158.5 (d, *J* = 256.2 Hz).

^{19}F NMR (376 MHz, $CDCl_3$): δ = –126.97 (1 F, dd, *J* = 19.37, 37.41 Hz).

HRMS (EI+): *m*/*z* [M]$^+$ calcd for $C_{13}H_{25}FO$: 216.1889; found: 216.1897.

(*Z*)-4-Fluoro-2,2-dimethyldodec-4-en-3-ol (12h)

Yield: 82% (^{19}F NMR yield). This compound could not be separated from the small amount of impurities.

IR (neat): 3421, 2956, 2926, 2857, 1703, 1466, 1365, 1288, 1114, 1065, 1013, 910, 848, 768 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.88 (3 H, t, *J* = 6.39 Hz), 0.96 (9 H, s), 1.20–1.35 (11 H, m), 2.09 (2 H, q, *J* = 7.19 Hz), 3.71 (1 H, d, *J* = 20.64 Hz), 4.75 (1 H, dt, *J* = 37.88, 7.19 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.1, 22.6, 23.2, 26.0, 29.1, 29.31, 29.32, 31.8, 34.8, 78.8 (d, *J* = 27.3 Hz), 108.5 (d, *J* = 14.1 Hz), 158.4 (d, *J* = 257.9 Hz).

^{19}F NMR (376 MHz, $CDCl_3$): δ = –120.38 (1 F, dd, *J* = 20.64, 37.88 Hz).

HRMS (FAB+): *m*/*z* [M]$^+$ calcd for $C_{14}H_{27}FO$: 230.2046; found: 230.2043.

Azide Compounds; (*Z*)-2-Azido-6-(*tert*-butyldiphenylsilyloxy)-3-fluoro-1-(4-methoxybenzyloxy)hex-3-ene (14l), Typical Procedure

To a mixture of β-fluoroallylic alcohol derivative **11l** (0.26 g 0.51 mmol), NaN_3 (0.96 g, 15 mmol), and DMAP (0.25 g, 2.02 mmol) in CH_2Cl_2 (5.1 mL) were added MsCl (0.14 g, 1.26 mmol) at 0 °C. The mixture was stirred at r.t. for 30 min. Then, DMSO (3.37 mL) was added to the reaction mixture and the whole was stirred for additional 3 h. The reaction was quenched with H_2O and the mixture was extracted with Et_2O (3 ×). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated in vacuo. The resulting residue was purified by silica gel column chromatography (hexane–EtOAc, 3:1) to afford the pure product **14l**; yield: 0.23 g (85%, 0.43 mmol); pale yellow oil.

In the case of **11a** and **11c**, the reaction proceeded in a highly regioselective manner to afford the corresponding azide compounds, **15a** and **15c** in a pure form. For other substrates, the reaction took place in a low regioselective manner to give the corresponding adducts as an inseparable regioisomeric mixture. Therefore, the mixture was employed for the next reaction without further purification.

IR (neat): 2931, 2857, 2103, 1613, 1514, 1471, 1428, 1362, 1303, 1250, 1173, 1111, 1037, 822, 739, 703 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.04 (9 H, s), 2.38 (2 H, q, *J* = 6.29 Hz), 3.55 (1 H, dd, *J* = 7.98, 9.59 Hz), 3.64–3.70 (1 H, m), 3.68 (2 H, t, *J* = 6.29 Hz), 3.80 (3 H, s), 4.08 (1 H, ddd, *J* = 4.79, 7.98, 17.15 Hz), 4.48 (1 H, d, *J* = 11.49 Hz), 4.52 (1 H, d, *J* = 11.49 Hz) 5.00 (1 H, dt, *J* = 36.92, 6.29 Hz), 6.87–6.88 (2 H, m), 7.24–7.45 (8 H, m), 7.65–7.66 (4 H, m).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 19.2, 26.8, 27.1 (d, *J* = 4.1 Hz), 55.2, 61.6 (d, *J* = 29.0 Hz), 62.8 (d, *J* = 1.6 Hz), 69.2, 73.2, 106.9 (d, *J* = 12.5 Hz), 113.9, 127.6, 129.4, 129.5, 129.6, 133.7, 135.5, 154.4 (d, *J* = 256.2 Hz), 159.4.

^{19}F NMR (376 MHz, $CDCl_3$): δ = –120.86 (1 F, dd, *J* = 17.15, 36.92 Hz).

HRMS (FAB+): *m*/*z* [M + Na]$^+$ calcd for $C_{30}H_{36}FN_3O_3SiNa$: 556.2408; found: 556.2401.

(*Z*)-3-Azido-5-(*tert*-butyldiphenylsilyloxy)-2-fluoro-1-phenylpent-1-ene (15a)

Yield: 0.19 g (60%, 0.41 mmol); yellow oil.

IR (neat): 3070, 2958, 2931, 2857, 2101, 1471, 1428, 1251, 1112, 822, 739, 700 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.07 (9 H, s), 1.90–2.08 (1 H, m), 2.00–2.03 (1 H, m), 3.80 (2 H, m), 4.34 (1 H, dt, *J* = 22.39, 7.29 Hz), 5.77 (1 H, d, *J* = 38.65 Hz), 7.29–7.44 (9 H, m), 7.50–7.52 (2 H, m), 7.63–7.68 (4 H, m).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 19.2, 26.8, 33.9, 59.7, 60.2 (d, *J* = 7.2 Hz), 109.2 (d, *J* = 6.5 Hz), 127.7 (d, *J* = 4.1 Hz), 127.9 (d, *J* = 2.5 Hz), 128.6, 128.9 (d, *J* = 7.4 Hz), 129.8 (d, *J* = 4.1 Hz), 132.2 (d, *J* = 2.5 Hz), 133.3 (d, *J* = 4.9 Hz), 135.5 (d, *J* = 2.4 Hz), 156.2 (d, *J* = 268.7 Hz).

^{19}F NMR (376 MHz, $CDCl_3$): δ = –116.84 (1 F, dd, *J* = 22.39, 38.65 Hz).

HRMS (FAB+): *m*/*z* [M]$^+$ calcd for $C_{27}H_{30}FN_3OSi$: 459.2142; found: 459.2148.

(*Z*)-3-Azido-5-(*tert*-butyldiphenylsilyloxy)-2-fluoro-1-(4-methoxyphenyl)pent-1-ene (15c)

Yield: 0.12 g (45%, 0.24 mmol); yellow oil.

IR (neat): 3071, 2957, 2931, 2857, 2101, 1608, 1513, 1463, 1428, 1299, 1254, 1180, 1112, 1034, 860, 823, 739, 702 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.06 (9 H, s), 1.90–1.98 (1 H, m), 1.99–2.07 (1 H, m), 3.72–3.89 (2 H, m), 3.83 (3 H, s), 4.32 (1 H, dt, *J* = 21.99, 7.39 Hz), 5.70 (1 H, d, *J* = 38.65 Hz), 6.88–6.90 (2 H, m), 7.31–7.47 (8 H, m), 7.62–7.70 (4 H, m).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 19.2, 26.8, 33.9, 55.3, 59.8, 60.4 (d, *J* = 27.3 Hz), 108.8 (d, *J* = 7.4 Hz), 114.0, 124.8 (d, *J* = 3.3 Hz), 127.7 (d, *J* = 4.2 Hz), 129.8 (d, *J* = 4.2 Hz), 130.3 (d, *J* = 7.4 Hz), 133.3 (d, *J* = 5.7 Hz), 135.5 (d, *J* = 2.5 Hz), 154.8 (d, *J* = 226.8 Hz), 159.1 (d, *J* = 2.5 Hz).

^{19}F NMR (376 MHz, $CDCl_3$): δ = –119.91 (1 F, dd, *J* = 21.99, 38.65 Hz).

HRMS (FAB+): *m*/*z* [M]$^+$ calcd for $C_{28}H_{32}FN_3O_2Si$: 489.2248; found: 489.2245.

β-Fluoroallylic Amines 16 and 17; (*Z*)-5-(*tert*-Butyldiphenylsilyloxy)-2-fluoro-1-phenylpent-1-en-3-amine (17a); Typical Procedure

To a solution of the azide compound **15a** (0.19 g 0.41 mmol) in THF (1.37 mL)–H_2O (0.075 mL) was added PPh_3 (0.22 g, 0.82 mmol) at r.t. The mixture was stirred at 50 °C for 24 h. The reaction mixture was purified by silica gel column chromatography (hexane–EtOAc, 2:1) to afford the pure product **17a**; yield: 0.15 g (85%, 0.35 mmol); yellow oil.

IR (neat): 3070, 2930, 2857, 1687, 1589, 1492, 1471, 1448, 1427, 1389, 1111, 1049, 998, 937, 915, 823, 739, 702, 613 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.06 (H, s), 1.70 (2 H, br s), 1.82–1.89 (1 H, m), 1.93–1.98 (1 H, m), 3.74–3.86 (3 H, m), 5.70 (1 H, d, *J* = 40.20 Hz), 7.22–7.49 (11 H, m), 7.64–7.68 (4 H, m).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 19.2, 26.8, 36.9, 51.3 (d, *J* = 28.1 Hz), 61.1, 105.4 (d, *J* = 7.4 Hz), 127.0 (d, *J* = 7.4 Hz), 127.7 (d, *J* = 2.4 Hz), 128.4, 128.6 (d, *J* = 6.6 Hz), 129.6 (d, *J* = 2.4 Hz), 133.3 (d, *J* = 4.1 Hz), 133.5 (d, *J* = 4.1 Hz), 135.5, 162.2 (d, *J* = 267.8 Hz).

^{19}F NMR (376 MHz, $CDCl_3$): δ = –117.59 (1 F, dd, *J* = 18.24, 40.20 Hz).

HRMS (FAB+): *m*/*z* [M + H]$^+$ calcd for $C_{27}H_{33}FNOSi$: 434.2315; found: 434.2324.

(*Z*)-7-(*tert*-Butyldiphenylsilyloxy)-4-fluoro-2-methylhept-4-en-3-amine (16g)

Yield: 0.095 g (35%); 0.24 mmol; colorless oil.

IR (neat): 3071, 2958, 2930, 2857, 1703, 1589, 1471, 1428, 1386, 1362, 1260, 1111, 936, 822, 738, 702 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.92 (3 H, d, *J* = 6.79 Hz), 0.95 (3 H, d, *J* = 6.79 Hz), 1.05 (9 H, s), 1.41 (2 H, br s), 1.80 (1 H, m), 2.36 (2 H, q, *J* = 6.93 Hz), 2.99 (1 H, dd, *J* = 6.79, 20.23 Hz), 3.68 (2 H, t, *J* = 6.93 Hz), 4.74 (1 H, dt, *J* = 38.01, 6.93 Hz), 7.36–7.45 (6 H, m), 7.66–7.68 (4 H, m).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 18.4, 19.1, 19.6, 26.8, 27.0 (d, *J* = 16.6 Hz), 31.1, 59.1 (d, *J* = 27.3 Hz), 63.3 (d, *J* = 1.7 Hz), 102.2 (d, *J* = 14.9 Hz), 127.6, 129.5, 133.8, 135.5, 161.8 (d, *J* = 257.0 Hz).

^{19}F NMR (376 MHz, $CDCl_3$): δ = –122.52 (1 F, dd, *J* = 20.23, 38.01 Hz).

HRMS (FAB+): *m*/*z* [M + H]$^+$ calcd for $C_{24}H_{35}FNOSi$: 400.2472; found: 400.2481.

(*Z*)-8-(*tert*-Butyldiphenylsilyloxy)-5-fluoro-2-methyloct-5-en-4-amine (16h)

Yield: 0.077 g (28%, 0.19 mmol); yellow oil.

IR (neat): 3071, 2956, 2930, 2857, 1703, 1471, 1428, 1386, 1362, 1111, 1022, 937, 822, 738, 702 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.90 (6 H, d, *J* = 6.39 Hz), 1.05 (9 H, s), 1.26–1.36 (1 H, m), 1.42–1.56 (3 H, m), 1.62–1.72 (1 H, m), 2.34 (2 H, q, *J* = 6.69 Hz), 3.32 (1 H, dt, *J* = 20.63, 7.39 Hz), 3.67 (2 H, t, *J* = 6.69 Hz), 4.74 (1 H, dt, *J* = 38.04, 6.69 Hz), 7.36–7.45 (6 H, m), 7.66–7.68 (4 H, m).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 19.2, 22.4, 22.6, 24.9, 26.8, 27.0 (d, *J* = 4.1 Hz), 43.1, 51.2 (d, *J* = 28.0 Hz), 63.2 (d, *J* = 1.6 Hz), 101.3 (d, *J* = 14.9 Hz), 127.6 (d, *J* = 5.8 Hz), 129.5, 133.8 (d, *J* = 1.6 Hz), 135.5, 162.6 (d, *J* = 257.1 Hz).

^{19}F NMR (376 MHz, $CDCl_3$): δ = –125.31 (1 F, dd, *J* = 20.63, 38.04 Hz).

HRMS (FAB+): *m*/*z* [M + H]$^+$ calcd for $C_{25}H_{37}FNOSi$: 414.2628; found: 414.2630.

(*Z*)-6-(*tert*-Butyldiphenylsilyloxy)-3-fluorohex-3-en-2-amine (16j)

Yield: 0.16 g (49%, 0.43 mmol); colorless oil.

IR (neat): 3072, 3049, 2959, 2931, 2858, 1704, 1472, 1428, 1389, 1112, 1027, 937, 823, 791, 737, 703, 613 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.06 (9 H, s), 1.23 (3 H, d, *J* = 6.79 Hz), 1.41 (2 H, br s), 2.31–2.38 (2 H, m), 3.46 (1 H, dq, *J* = 14.67, 6.79 Hz), 3.68 (2 H, t, *J* = 6.59 Hz), 4.75 (1 H, dt, *J* = 37.35, 7.49 Hz), 7.36–7.45 (6 H, m), 7.67–7.69 (4 H, m).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 19.2, 20.4 (d, *J* = 1.7 Hz), 26.8, 26.9 (d, *J* = 4.9 Hz), 48.0 (d, *J* = 29.8 Hz), 63.2 (d, *J* = 1.6 Hz), 99.9 (d, *J* = 15.8 Hz), 127.6, 129.5, 133.8, 135.5, 163.7 (d, *J* = 256.2 Hz).

^{19}F NMR (376 MHz, $CDCl_3$): δ = –121.96 (1 F, dd, *J* = 14.67, 37.35 Hz).

HRMS (FAB+): *m*/*z* [M + H]$^+$ calcd for $C_{22}H_{31}FNOSi$: 372.2159; found: 372.2158.

(*Z*)-8-(*tert*-Butyldiphenylsilyloxy)-5-fluoro-3-methyloct-5-en-4-amine (16k)

Yield: 0.082 g (52%, 0.20 mmol); yellow oil; diastereomeric ratio: 48:52.

IR (neat): 3071, 2960, 2931, 2858, 1472, 1428, 1111, 1021, 823, 738, 701, 613 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.898 (3 H, t, *J* = 7.19 Hz), 0.900 (3 H, d, *J* = 6.79 Hz), 1.05 (9 H, s), 1.16 (1 H, m), 1.44 (2 H, br s), 1.46–1.63 (2 H, m), 2.35 (2 H, q, *J* = 7.29 Hz), 3.08 and 3.15 (1 H, dd and dd, *J* = 6.79, 20.73 Hz and 5.60, 18.19 Hz), 3.68 (2 H, t, *J* = 7.29 Hz), 4.73 and 4.75 (1 H, dt and dt, *J* = 38.17, 7.29 Hz), 7.30–7.50 (6 H, m), 7.60–7.70 (4 H, m).

^{19}F NMR (376 MHz, $CDCl_3$): δ = –121.26 (1 F, dd, *J* = 18.19, 38.17 Hz), –122.36 (1 F, dd, *J* = 20.73, 38.17 Hz).

HRMS (FAB+): *m*/*z* [M + H]$^+$ calcd for $C_{25}H_{37}FNOSi$: 414.2628; found: 414.2627.

(*Z*)-6-(*tert*-Butyldiphenylsilyloxy)-3-fluoro-1-(4-methoxybenzyloxy)hex-3-en-2-amine (16l)

Yield: 0.17 g (85%, 0.34 mmol); colorless oil.

IR (neat): 3070, 2931, 2857, 1612, 1587, 1514, 1471, 1428, 1362, 1302, 1249, 1173, 1111, 1037, 822, 739, 703 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.05 (9 H, s), 1.55–1.65 (2 H, br s), 2.35 (2 H, q, *J* = 6.79 Hz), 3.36–3.42 (1 H, m), 3.55–3.64 (1 H , m), 3.66 (2 H, t, *J* = 6.79 Hz), 3.80 (3 H, s), 4.47 (2 H, s), 4.86 (1 H, dt, *J* = 38.11, 6.79 Hz), 6.37 (2 H, d, *J* = 8.59 Hz), 7.23 (2 H, d, *J* = 8.59 Hz), 7.27–7.44 (6 H, m), 7.65–7.67 (4 H, m).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 19.1, 26.8, 26.9 (d, *J* = 4.2 Hz), 52.6 (d, *J* = 28.9 Hz), 55.1, 63.1 (d, *J* = 1.7 Hz), 71.9, 72.9, 102.5 (d, *J* = 14.1 Hz), 113.7, 127.6, 129.3, 129.5, 129.9, 133.5, 133.8, 159.2, 160.0 (d, *J* = 255.4 Hz).

^{19}F NMR (376 MHz, $CDCl_3$): δ = –120.58 (1 F, dd, *J* = 13.53, 38.11 Hz).

HRMS (FAB+): *m*/*z* [M + Na]$^+$ calcd for $C_{30}H_{38}FNO_3SiNa$: 530.2503; found: 530.2493.

(*Z*)-2-Benzyloxy-7-(*tert*-butyldiphenylsilyloxy)-4-fluorohept-4-en-3-amine (16m)

Yield: 0.028 g (40%, 0.057 mmol); colorless oil; diastereomeric ratio: 27:73.

^{19}F NMR (376 MHz, $CDCl_3$): δ = –119.75 and –121.13 (dd and dd, *J* = 14.67, 39.11 Hz).

(*Z*)-5-(*tert*-Butyldiphenylsilyloxy)-2-fluoro-1-(4-methoxyphenyl)pent-1-en-3-amine (17c)

Yield: 0.69 g (84%, 0.20 mmol); colorless oil.

IR (neat): 3070, 2999, 2931, 2857, 1608, 1512, 1464, 1428, 1389, 1297, 1251, 1179, 1111, 1036, 937, 855, 823, 739, 703, 613 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.06 (9 H, s), 1.69 (2 H, br s), 1.84 (1 H, m), 1.95 (1 H, m), 3.80 (3 H, m), 3.82 (3 H, s), 5.63 (1 H, d, *J* = 40.87 Hz), 6.87 (2 H, m), 7.31–7.44 (8 H, m), 7.65–7.69 (4 H, m).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 19.2, 26.8, 36.9, 51.2 (d, *J* = 28.1 Hz), 55.2, 61.1, 104.9 (d, *J* = 7.4 Hz), 113.8, 125.9 (d, *J* = 2.5 Hz), 127.7 (d, *J* = 2.4 Hz), 129.6 (d, *J* = 2.5 Hz), 129.8 (d, *J* = 6.6 Hz), 133.5 (d, *J* = 2.4 Hz), 135.5, 158.5 (d, *J* = 2.5 Hz), 160.8 (d, *J* = 264.5 Hz).

^{19}F NMR (376 MHz, $CDCl_3$): δ = –120.64 (1 F, dd, *J* = 19.55, 40.87 Hz).

HRMS (FAB+): *m*/*z* [M + H]$^+$ calcd for $C_{28}H_{35}FNO_2Si$: 464.2421; found: 464.2420.

(*Z*)-1-(*tert*-Butyldiphenylsilyloxy)-4-fluoro-6-methylhept-4-en-3-amine (17g)

Yield: 0.045 g (17%, 0.11 mmol); colorless oil.

IR (neat): 3385, 3071, 2958, 2931, 2858, 1702, 1589, 1471, 1428, 1389, 1278, 1112, 1047, 936, 823, 738, 702 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 0.95 (3 H, d, *J* = 6.92 Hz), 0.98 (3 H, d, *J* = 6.92 Hz), 1.04 (9 H, s), 1.46 (2 H, br s), 1.68–1.76 (1 H, m), 1.80–1.88 (1 H, m), 2.72 (1 H, dsept, *J* = 9.65, 6.92 Hz), 3.56 (1 H, dt, *J* = 18.51, 6.79 Hz), 3.74 (2 H, m), 4.55 (1 H, dd, *J* = 9.65, 38.18 Hz), 7.36–7.44 (6 H, m), 7.65–7.68 (4 H, m).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 19.2, 23.0, 23.1 (d, *J* = 1.7 Hz), 23.6 (d, *J* = 4.5 Hz), 26.8, 36.9, 50.3 (d, *J* = 28.9 Hz), 61.1, 112.5 (d, *J* = 14.9 Hz), 127.7 (d, *J* = 1.7 Hz), 129.6, 133.7 (d, *J* = 4.5 Hz), 135.5, 159.5 (d, *J* = 254.5 Hz).

^{19}F NMR (376 MHz, $CDCl_3$): δ = –126.64 (1 F, dd, *J* = 18.51, 38.18 Hz).

HRMS (FAB+): *m*/*z* [M + H]$^+$ calcd for $C_{24}H_{35}FNOSi$: 400.2472; found: 400.2481.

(*Z*)-1-(*tert*-Butyldiphenylsilyloxy)-4-fluoro-7-methyloct-4-en-3-amine (17h)

Yield: 0.150 g (54%, 0.36 mmol); yellow oil.

IR (neat): 3385, 3071, 2956, 2930, 2858, 1702, 1471, 1428, 1388, 1111, 1048, 823, 737, 702, 613 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 0.88 (3 H, d, *J* = 6.79 Hz), 0.89 (3 H, d, *J* = 6.39 Hz), 1.05 (9 H, s), 1.56 (2 H, br s), 1.57–1.60 (1 H, m), 1.70–1.78 (1 H, m), 1.81–1.91 (1 H, m), 1.92–1.97 (2 H, m), 3.61 (1 H, dt, *J* = 19.17, 6.79 Hz), 3.70–3.81 (2 H, m), 4.69 (1 H, dt, *J* = 38.54, 7.79 Hz), 7.36–7.48 (6 H, m), 7.65–7.68 (4 H, m).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 19.1, 22.17, 22.19, 26.8, 28.3 (d, *J* = 1.6 Hz), 32.3 (d, *J* = 4.1 Hz), 36.9, 50.4 (d, *J* = 29.0 Hz), 61.1, 103.7 (d, *J* = 14.9 Hz), 127.6 (d, *J* = 2.4 Hz), 129.6, 133.6 (d, *J* = 5.0 Hz), 135.5, 161.5 (d, *J* = 255.4 Hz).

^{19}F NMR (376 MHz, $CDCl_3$): δ = –125.85 (1 F, dd, *J* = 19.17, 38.54 Hz).

HRMS (FAB+): *m*/*z* [M + H]$^+$ calcd for $C_{25}H_{37}FNOSi$: 414.2628; found: 414.2625.

(*Z*)-1-(*tert*-Butyldiphenylsilyloxy)-4-fluorohex-4-en-3-amine (17j)

Yield: 0.11 g (33%, 0.29 mmol); colorless oil.

IR (neat): 3384, 3071, 3050, 2930, 2858, 1709, 1589, 1482, 1428, 1390, 1112, 1048, 984, 823, 739, 702, 688 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.05 (9 H, s), 1.55–1.59 (5 H, m), 1.71–1.76 (1 H, m), 1.80–1.88 (1 H, m), 3.62 (1 H, dt, *J* = 19.37, 6.79 Hz), 3.75 (2 H, m), 4.71 (1 H, dq, *J* = 37.42, 6.79 Hz), 7.36–7.45 (6 H, m), 7.65–7.68 (4 H, m).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 8.5 (d, *J* = 6.6 Hz), 19.1, 26.8, 36.8, 50.3 (d, *J* = 28.1 Hz), 61.0, 99.3 (d, *J* = 15.8 Hz), 127.6, 129.6, 133.6, 135.5, 161.7 (d, *J* = 255.4 Hz).

^{19}F NMR (376 MHz, $CDCl_3$): δ = –126.69 (1 F, dd, *J* = 19.37, 37.42 Hz).

HRMS (FAB+): *m*/*z* [M + H]$^+$ calcd for $C_{22}H_{31}FNOSi$: 372.2159; found: 372.2149.

(*Z*)-1-(*tert*-Butyldiphenylsilyloxy)-4-fluoro-6-methyloct-4-en-3-amine (17k)

Yield: 0.050 g (31%, 0.12 mmol); colorless oil; diastereomeric ratio: 49:51.

IR (neat): 3071, 2959, 2930, 2857, 1472, 1461, 1428, 1112, 1048, 823, 738, 702, 613 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 0.81 and 0.85 (3 H, t and t, *J* = 7.19 Hz), 0.94 and 1.00 (3 H, d and d, *J* = 6.79 Hz), 1.05 (9 H, s), 1.16–1.23 (1 H, m), 1.24–1.40 (1 H, m), 1.50–1.70 (2 H, br s), 1.68–1.80 (1 H, m), 1.80–1.90 (1 H, m), 2.47 (1 H, m), 3.59 (1 H, m), 3.75 (2 H, m), 4.41 and 4.49 (1 H, dd and dd, *J* = 8.34, 38.36 Hz and 7.79, 38.86 Hz), 7.35–7.44 (6 H, m), 7.65–7.68 (4 H, m).

^{19}F NMR (376 MHz, $CDCl_3$): δ = –126.21 (1 F, dd, *J* = 17.11, 38.36 Hz), –126.95 (1 F, dd, *J* = 19.55, 39.86 Hz).

HRMS (FAB+): *m*/*z* [M + H]$^+$ calcd for $C_{25}H_{37}FNOSi$: 414.2628; found: 414.2627.

(*Z*)-6-Benzyloxy-1-(*tert*-butyldiphenylsilyloxy)-4-fluorohept-4-en-3-amine (17m)

Yield: 0.034 g (48%, 0069 mmol); yellow oil; diastereomeric ratio: 27:73.

^{19}F NMR (376 MHz, $CDCl_3$): δ = –120.55 and –121.15 (dd and dd, *J* = 17.93, 36.66 Hz).

tert-Butyl (*Z*)-3-Fluoro-6-hydroxyhex-3-en-2-ylcarbamate (18j); Typical Procedure

To a solution of (*Z*)-6-(*tert*-butyldiphenylsilyloxy)-3-fluorohex-3-en-2-amine (**16j**; 0.19 g, 0.5 mmol) and Et_3N (0.05 mL, 0.6 mmol) in CH_2Cl_2 (1.7 mL) was added $(Boc)_2O$ (0.13 g, 0.6 mmol) at 0 °C. The mixture was stirred at r.t. for 1 h. Then, the reaction was quenched with H_2O and the mixture was extracted with CH_2Cl_2 (3 ×). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated in vacuo. The resulting residue was used in the next step without further purification. To a THF solution of the above alcohol was added TBAF (0.55 mL, 0.55 mmol) at r.t. After stirring the mixture at that temperature for 2 h, addition of H_2O followed by extractive workup and purification by column chromatography (hexane–EtOAc, 2:1) afforded the desired alcohol **18j**; yield: 0.086 g (74%, 0.37 mmol); colorless oil.

IR (neat): 3328, 2979, 2933, 1692, 1527, 1454, 1428, 1391, 1367, 1251, 1171, 1112, 1056, 862, 735, 703 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.26 (3 H, d, *J* = 6.96 Hz), 1.40 (9 H, s), 1.65 (1 H, br s), 2.23–2.36 (2 H, m), 3.61 (2 H, t, *J* = 6.32 Hz), 4.22–4.26 (1 H, m), 4.63 (1 H, br s), 4.78 (1 H, dt, *J* = 37.20, 7.52 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 18.5, 27.0 (d, *J* = 3.9 Hz), 28.3, 47.4 (d, *J* = 27.7 Hz), 61.7, 79.7, 101.6 (d, *J* = 14.4 Hz), 154.9, 160.3 (d, *J* = 257.6 Hz).

^{19}F NMR (376 MHz, $CDCl_3$): δ = –123.24 (1 F, dd, *J* = 16.18, 37.20 Hz).

HRMS (FAB+): *m*/*z* [M + Na]$^+$ calcd for $C_{11}H_{20}FNO_3Na$: 256.1325; found: 256.1319.

tert-Butyl (*Z*)-4-Fluoro-7-hydroxy-2-methylhept-4-en-3-ylcarbamate (18g)

Yield: 0.39 g (65%, 1.48 mmol); yellow oil.

IR (neat): 3334, 2966, 2933, 2875, 1696, 1504, 1469, 1391, 1367, 1251, 1171, 1044, 1011, 876, 737, 479, 418 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.926 (3 H, d, *J* = 6.76 Hz), 0.933 (3 H, d, *J* = 6.76 Hz), 1.43 (9 H, s), 1.86 (1 H, octet, *J* = 6.90 Hz), 1.99 (1 H, br s), 2.31–2.40 (2 H, m), 3.62 (2 H, t, *J* = 6.36 Hz), 3.86 (1 H, dt, *J* = 21.91, 8.48 Hz), 4.77 (1 H, dt, *J* = 37.60, 7.58 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 18.6, 19.5, 27.2 (d, *J* = 4.1 Hz), 28.4, 30.1, 58.0 (d, *J* = 27.6 Hz), 61.9, 79.8, 103.6 (d, *J* = 14.2 Hz), 155.5, 158.6 (d, *J* = 258.0 Hz).

^{19}F NMR (376 MHz, $CDCl_3$): δ = –122.98 (1 F, dd, *J* = 21.91, 37.60 Hz).

HRMS (FAB+): *m*/*z* [M + H]$^+$ calcd for $C_{13}H_{25}FNO_3$: 262.1818; found: 262.1820.

tert-Butyl (*Z*)-5-Fluoro-8-hydroxy-2-methyloct-5-en-4-ylcarbamate (18h)

Yield: 0.22 g (86%, 0.80 mmol); yellow oil.

IR (neat): 3330, 2959, 2871, 1692, 1527, 1470, 1391, 1367, 1283, 1252, 1171, 1117, 1046, 872 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.916 (3 H, d, *J* = 6.60 Hz), 0.919 (3 H, d, *J* = 6.52 Hz), 1.43 (9 H, s), 1.35–1.55 (2 H, m), 1.56–1.70 (1 H, m), 1.80–1.95 (1 H, br s), 2.25–2.44 (2 H, m), 3.63 (2 H, t, *J* = 6.34 Hz), 4.08–4.24 (1 H, m), 4.63–4.67 (1 H, m), 4.80 (1 H, dt, *J* = 37.41, 7.56 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 22.6, 22.7, 25.0, 27.5 (d, *J* = 3.7 Hz), 28.6, 41.5, 50.8 (d, *J* = 28.2 Hz), 62.0, 80.0, 103.1 (d, *J* = 14.1 Hz), 155.5, 159.6 (d, *J* = 258.2 Hz).

^{19}F NMR (376 MHz, $CDCl_3$): δ = –125.09 (1 F, dd, *J* = 21.76, 37.41 Hz).

HRMS (FAB+): *m*/*z* [M + Na]$^+$ calcd for $C_{14}H_{26}FNO_3Na$: 298.1794; found: 298.1804.

tert-Butyl (*Z*)-3-Fluoro-6-hydroxy-1-(4-methoxybenzyloxy)hex-3-en-2-ylcarbamate (18l)

Due to unidentified inseparable by-products, this compound could not be isolated in pure form; yield: 96% (^{19}F NMR yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.44 (9 H, s), 1.85–2.05 (1 H, m), 2.29–2.43 (2 H, m), 3.53 (1 H, dd, *J* = 4.98, 9.66 Hz), 3.62 (2 H, t, *J* = 6.32 Hz), 3.60–3.65 (1 H, m), 3.81 (3 H, s), 4.37 (1 H, br s), 4.47 (2 H, s), 4.86 (1 H, dt, *J* = 37.32, 7.60 Hz), 4.96–5.11 (1 H, m), 6.88 (2 H, d, *J* = 8.64 Hz), 7.23 (2 H, d, *J* = 8.64 Hz).

^{19}F NMR (376 MHz, $CDCl_3$): δ = –120.70 (1 F, dd, *J* = 11.14, 37.32 Hz).

HRMS (FAB+): *m*/*z* [M + Na]$^+$ calcd for $C_{19}H_{28}FNO_5Na$: 392.1849; found: 392.1850.

The corresponding carboxylic acid was converted into the methyl ester through treatment of the acid with an excess amount of diazomethane.

Methyl (*Z*)-5-(*tert*-Butoxycarbonylamino)-4-fluoro-7-methyloct-3-enoate (19h); Typical Procedure

To a solution of *tert*-butyl (*Z*)-5-fluoro-8-hydroxy-2-methyloct-5-en-4-yl carbamate (**18h**; 0.21 g, 0.76 mmol) in acetone (9.45 mL) was added Jones reagent [readily prepared by mixing of CrO_3 (0.39 g, 3.91 mmol), H_2O (1.15 mL), and H_2SO_4 (0.38 mL) at 0 °C] at 0 °C. The mixture was stirred at that temperature for 3.5 h. The reaction was quenched with *i*-PrOH–H_2O (1:1 v/v) and the mixture was extracted with EtOAc (3 ×), and washed with brine. The combined organic layers were dried (Na_2SO_4), filtered, and concentrated in vacuo to give the corresponding carboxylic acid. Thus obtained carboxylic acid was dissolved in Et_2O (10 mL), and the mixture was cooled to 0 °C. To this reaction mixture was added dropwise an excess amount of an ethereal solution of diazomethane [readily prepared via heating the mixture of KOH (0.56 g, 9.89 mmol), *N*-methyl-*N*-nitroso-*p*-toluenesufonamide (1.81 g, 8.45 mmol) in Et_2O (ca. 20 mL)/H_2O (ca. 1 mL)] at 0 °C. After about 1 h, the reaction was quenched with AcOH, and the mixture was concentrated in vacuo. The residue was neutralized with sat. aq $NaHCO_3$ and extracted with EtOAc (3 ×). The combined organic layers were dried (Na_2SO_4), filtered, and concentrated in vacuo. The crude material was purified by silica gel column chromatography (hexane–EtOAc, 3:1) to give **19h**; yield: 0.16 g (69%, 0.52 mmol) over 2 steps; yellow oil.

IR (neat): 3360, 2958, 2871, 1712, 1518, 1439, 1367, 1252, 1170, 1044, 1023, 951, 907, 780 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.92 (6 H, d, *J* = 6.60 Hz), 1.43 (9 H, s), 1.35–1.55 (2 H, m), 1.58–1.70 (1 H, m), 3.10–3.15 (2 H, m), 3.68 (3 H, s), 4.15–4.35 (1 H, m), 4.62 (1 H, d, *J* = 8.44 Hz), 5.01 (1 H, dt, *J* = 36.29, 7.00 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 22.5, 22.8, 25.0, 28.6, 29.3 (d, *J* = 5.7 Hz), 41.6, 50.3 (d, *J* = 28.1 Hz), 52.2, 79.9, 98.6 (d, *J* = 13.1 Hz), 155.2, 160.2 (d, *J* = 260.7 Hz), 171.7 (d, *J* = 1.7 Hz).

^{19}F NMR (376 MHz, $CDCl_3$): δ = –121.50 (1 F, dd, *J* = 19.54, 36.29 Hz).

HRMS (FAB+): *m*/*z* [M + Na]$^+$ calcd for $C_{12}H_{26}FNO_4Na$: 326.1744; found: 326.1751.

Methyl (*Z*)-5-(*tert*-Butoxycarbonylamino)-4-fluoro-6-methylhept-3-enoate (19g)

Yield: 0.29 g (68%, 0.99 mmol); yellow oil.

IR (neat): 3362, 2970, 1744, 1709, 1513, 1469, 1438, 1391, 1367, 1255, 1171, 1041, 1011, 949, 879, 808, 487 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 0.93 (3 H, d, *J* = 6.74 Hz), 0.94 (3 H, d, *J* = 6.74 Hz), 1.43 (9 H, s), 1.89 (1 H, octet, *J* = 6.74 Hz), 3.14 (2 H, m), 3.68 (3 H, s), 3.97 (1 H, dt, *J* = 19.98, 8.57 Hz), 4.72 (1 H, d, *J* = 9.16 Hz), 4.97 (1 H, dt, *J* = 36.49, 7.16 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 18.2, 19.3, 28.3, 29.0 (d, *J* = 5.9 Hz), 30.1, 51.8, 57.2 (d, *J* = 27.2 Hz), 79.5, 99.1 (d, *J* = 13.0 Hz), 155.2, 159.2 (d, *J* = 261.0 Hz), 171.4 (d, *J* = 1.8 Hz).

^{19}F NMR (376 MHz, $CDCl_3$): δ = –119.72 (1 F, dd, *J* = 19.98, 36.49 Hz).

HRMS (FAB+): *m*/*z* $[M + H]^+$ calcd for $C_{14}H_{25}FNO_4$: 290.1768; found: 290.1769.

(*Z*)-5-(*tert*-Butoxycarbonylamino)-4-fluorohex-3-enoic Acid (19j)

The methyl esterification with diazomethane was not carried out because the corresponding carboxylic acid could be isolated in a pure form; yield: 47 mg (45%, 0.19 mmol); colorless oil.

IR (neat): 3327, 2980, 2934, 1715, 1524, 1455, 1394, 1368, 1252, 1169, 1105, 1059, 951, 914, 864, 735 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.31 (3 H, d, *J* = 6.96 Hz), 1.44 (9 H, s), 3.18 (2 H, d, *J* = 7.04 Hz), 4.33–4.35 (1 H, m), 4.68 (1 H, m), 5.02 (1 H, dt, *J* = 35.96, 7.04 Hz), 9.20–9.40 (1 H, m).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 18.5, 28.3, 28.9 (d, *J* = 3.9 Hz), 47.0 (d, *J* = 23.6 Hz), 80.0, 97.1 (d, *J* = 16.5 Hz), 154.8, 160.8 (d, *J* = 261.2 Hz), 176.1.

^{19}F NMR (376 MHz, $CDCl_3$): δ = –119.48 (1 F, dd, *J* = 14.34, 35.96 Hz).

HRMS (FAB+): *m*/*z* $[M + Na]^+$ calcd for $C_{11}H_{18}FNO_4Na$: 270.1118; found: 270.1116.

Methyl (*Z*)-5-(*tert*-Butoxycarbonylamino)-4-fluoro-6-(4-methoxybenzyloxy)hex-3-enoate (19l)

Yield: 0.25 g (27%, 0.62 mmol); yellow oil.

IR (neat): 3359, 2977, 1741, 1713, 1613, 1586, 1514, 1458, 1391, 1366, 1249, 1172, 1101, 1034, 949, 821, 491 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.44 (9 H, s), 3.16–3.18 (2 H, m), 3.54 (1 H, dd, *J* = 4.62, 9.70 Hz), 3.61–3.64 (1 H, m), 3.68 (3 H, s), 3.80 (3 H, s), 4.42 (1 H, br s), 4.46 (2 H, s), 5.00–5.11 (1 H, m), 5.10 (1 H, dt, *J* = 36.23, 6.99 Hz), 6.85–6.89 (2 H, m), 7.21–7.24 (2 H, m).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 28.4, 29.3 (d, *J* = 5.8 Hz), 51.2 (d, *J* = 31.7 Hz), 52.1, 55.4, 68.8, 73.0, 80.1, 99.2 (d, *J* = 12.4 Hz), 113.9, 129.4, 129.8, 155.1, 158.2 (d, *J* = 257.9 Hz), 159.4, 171.5 (d, *J* = 1.2 Hz).

^{19}F NMR (376 MHz, $CDCl_3$): δ = –117.61 (1 F, dd, *J* = 8.98, 36.23 Hz).

HRMS (FAB+): *m*/*z* $[M + Na]^+$ calcd for $C_{20}H_{28}FNO_6Na$: 420.1798; found: 420.1795.

Supporting Information

Supporting information for this article is available online at http://dx.doi.org/10.1055/s-0035-1560390.

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(15) When the reaction was carried out at –40 °C for 16 h in the presence of 2.0 equiv of $Ti(O\textit{i}\text{-}Pr)_4$, instead of a catalytic amount of LiI, **13** was obtained in 40% yield.
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