Highly Stereocontrolled Synthesis of Trifluoromethylated Materials with Allylzincs and Allenylzincs Generated by Umpolung of Palladium Complexes

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The formation and chemical behaviors of trifluoromethylated allylzinc and allenylzinc reagents derived from the umpolung of allyl- or allenylpalladium complexes have been described. The reactions of these reagents with aldehydes proceeded smoothly to afford highly stereocontrolled γ-(trifluoromethyl)-δ-hydroxy α,β-unsaturated materials. Their configurations determined by the spectral data were *anti*, and *Z*-isomers were produced from the system of allylzinc reagents.

While we have reported the methodology and/or reagents suitable for the regio- or stereoselective introduction of a fluoroalkyl group onto the specific position of the molecules,[1] several problems remain to be solved in the field of fluorinated materials. In particular, the chemistry of β-fluorocarbanions which do not undergo elimination to form fluoroolefins has not been studied for the construction of regio- and stereocontrolled fluorinated materials.[2] The synthesis and chemical reactivity of such carbanions are of considerable interest. The generation and synthetic applications of these carbanions have been based on several methods: (1) use of nitrotrifluoroethane,[3] (2) the employment of dimethyl 2-(trifluoromethyl)malonate and/or dialkyl 2-bromo-2-(difluoromethyl)malonate,[4,5] (3) application of α-CF_3-silylenol ether and Reformatsky-type reactions of bromotrifluoro propionate,[6] (4) use of 2,3,3,3-tetrafluoropropionate and 2,3,3,3-tetrafluoropropionamide,[7] and (5) indium-mediated allylation using 1,1,1-trifluoro-4-bromo-2-butene.[8] Moreover, we have recently reported the palladium(0)-catalyzed allylation reactions under neutral condition in the system of a methylene group activated with fluoroalkyl and carbonyl groups.[9] However, except for indium-mediated allylation,[8] no other examples of highly stereocontrolled reactions using β-fluorocarbanions have been reported to our knowledge. While the chemistry of allylzinc[10] and allenylzinc[11] reagents generated from allylpalladium and allenylpalladium complexes and Et_2-Zn attracted our attention, their synthetic value in fluorine chemistry still appears to be grossly underestimated.

In our continuous study of stereocontrolled fluorinated materials,[1,12] we would like to describe the chemistry of allylzinc and allenylzinc reagents as a new route to the stereoselective construction on the continuous carbon atom with a trifluoromethyl group.

Results and Discussion

Allylzinc Species. To clarify the synthetic scope of the umpolung technique in the fluorine chemistry, we examined the allylation of aldehydes with derivatives **1** of 3-substituted 1-(trifluoromethyl)propen-3-ol.[12e] The reactions proceeded regioselectively under the conditions (**1** (1.0 equiv), aldehyde (1.2 equiv), diethylzinc (2.4 equiv), and $Pd(PPh_3)_4$ (0.05 equiv) in THF under an argon atmosphere), giving highly stereocontrolled homoallyl alcohols **3** with a trifluoromethyl group (Scheme 1). However, derivatives **2** of 1-substituted 3-(trifluorometh-

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Scheme 1. Umpolung of π-Allylpalladium

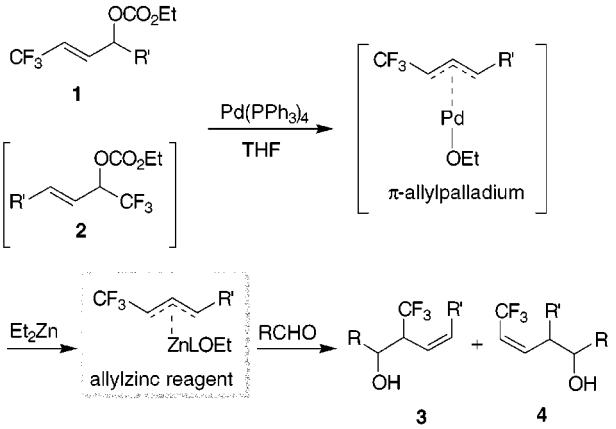
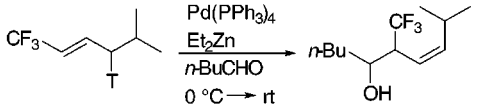


Table 1. Effect of Solvents and/or Leaving Groups



T	solvent	time (h)	yield (%)[b]	diastereomeric ratio[c]
OCOPh	THF	24	45	94:6
OCOPh	CH_2Cl_2	24	–	–
OCOPh	benzene	24	–	–
OCOPh	Et_2O	18	9	–
OCO_2Et	THF	20	66	97:3
OMs	THF	24	35	96:4

[a] Reaction condition: substrate (1 equiv), $Pd(PPh_3)_4$ (0.05 equiv), aldehyde (1.2 equiv), and Et_2Zn(2.4 equiv). [b] Yields were determined by ^{19}F NMR integral intensities. [c] The diastereomeric ratios were determined by ^{19}F NMR integral intensities.

yl)propen-3-ol did not react in this system, and the starting material **2** was recovered more than 95%. It is reported that the generation of π-palladium complex from the type of trifluoromethylated compound **2** is not easy,[13] and that an important factor is to find a matching between the palladium(0) catalyst and substrate to produce the palladium complex.[14] Therefore, we have examined several kinds of palladium(0) catalysts such as $Pd(PPh_3)_4$ and $Pd(dppe)_2$, however π-palladium complex did not produce.

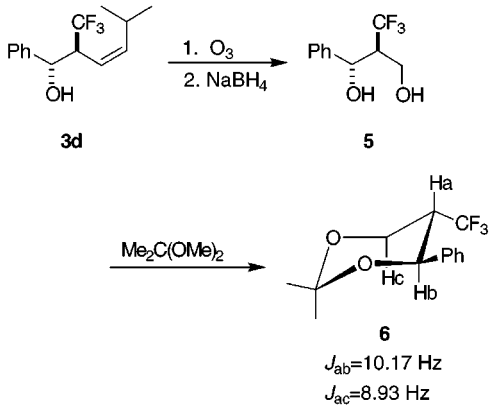
As the results show in Table 1, the solvent was an important factor in promoting present reaction. When dichloromethane and/or benzene was used as a solvent, the reaction did not proceed; however, in tetrahydrofuran the desired homoallylic alcohols with high diastereoselectivity were obtained. Further, the influence of the allylic substituent pattern of T group (from (ethoxycarbonyl)oxy or benzoyloxy to mesyloxy was directly apparent on the yield. The (ethoxycarbonyl)oxy group−THF system increased the chemical yield to 66%, and the diastereomeric ratio increased to 97:3. The generation of π-palladium complex is effective for both *E*- and *Z*-allylic carbonates. In the case of the *Z*-isomer ($CF_3CH{=}CHCH(OCO_2Et)CH(CH_3)_2$) instead of entry 1 (Table 2), the reaction proceeded to afford the product **3a** in 43% yield with diastereoselectivity (*anti*:*syn* = 98:2).

Table 2. Synthesis of Compound 3

entry	R′	RCHO R	yield[a] (%)	diastereomeric ratio (% de)[c]
1	*i*-Pr	*n*-Bu	66 (52) (**3a**)	97:3
2		*i*-Pr	46 (44) (**3b**)	95:5
2		*t*-Bu	–	–
4		Ph	83 (73) (**3c**)	>99:<1
5		(*E*)-PhCH=CH	60 (53)[b] (**3d**)	96:4
6	*n*-Bu	*n*-Bu	46 (36) (**3e**)	>99:<1
7	Ph	*n*-Bu	–	–
8	CH_2OBn	*n*-Bu	47 (25)[b] (**3f**)	96:4

[a] Yields were determined by ^{19}F NMR integral intensities. [b] Yields in the parentheses were isolated as an acetate derivative. [c] The diastereomeric ratios were determined by ^{19}F NMR integral intensities.

Scheme 2. Optimizing Structures of Acetonides



Our experimental results shown in Table 2, support the conclusion that allylzinc reagents generated from several kinds of (*E*)-3-(ethoxycarbonyl)oxy-3-substituted-1-(trifluoromethyl)propenes **1**, palladium(0) catalyst, and diethylzinc react smoothly with aldehydes to produce the corresponding γ-(trifluoromethyl)-δ-hydroxy α,β-unsaturated materials with high regioselectivity and diastereoselectivity.

The diastereomeric ratio was determined by ^{19}F NMR integral intensities. The stereochemistry of these products was established in the NMR studies. It is well-known that the coupling constant (^3J) of *Z*-isomer is 6−12 Hz, and that (^3J) of the *E*-isomer is 12−18 Hz.[15] Furthermore, the acetate derivative of compound **8a** was converted to the *Z*-isomer with Lindlar catalyst and H_2 system. On the basis of the comparison of its NMR spectrum of the acetate derivative of compound **3f** (see Experimental Section) and the above NMR studies, the stereochemistry of obtained materials is *Z*.

Moreover, NMR coupling constants of the acetonide derived from **3** have also led us to determine the relative configurations. Compound **3d** was transformed to 1,3-diol **5** by ozonolysis and hence to the acetonide **6** with ^1H NMR coupling constants (J_{Ha-Hb} = 10.17 Hz and J_{Ha-Hc} = 8.93 Hz). In comparison with the reported ^1H NMR coupling constants ($J_{Hax-Hax}$ = 8−10 Hz, $J_{Hax-Heq}$ = 2−3 Hz, and $J_{Heq-Heq}$ = 2−3 Hz),[15] all of their configurations were the axial. From this result, the stereochemistry of the major products of compounds **3** is *anti* (Scheme 2).

The excellent diastereoselectivity obtained in the allylation by trifluoromethylated allylzinc reagent can be

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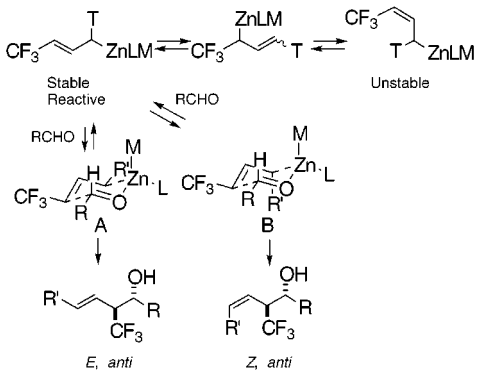

Figure 1. Six-membered transition state structures and the resulting products.

explained by the following mechanism. The folowing equilibrium might exist for the allylzinc species shown in Figure 1: a highly steric group (CF_3) and aldehyde substituent (R) will be in the equatorial position.[16] Moreover, structure **A** seem to be unfavorable because of the gauche interactions between the equatorial substituent (R′) and both the ligand L and the counterion M associated with the Zn^{2+} ion.[10] For example, on the basis of the above result, in the case of R′ being *i*-Pr (entries 1−5), the influence of the substitution pattern of the R group (from *n*-butyl and *i*-propyl to *tert*-butyl) directly affected the chemical yield. In sharp contrast to the present case, employment of the *tert*-butyl substituent (R = *tert*-Bu, entry 3) instead of *n*-butyl and/or *i*-propyl group (R) turned out to completely stop the desired reaction pathway.

Allenylzinc Species. Several examples of allenylmetal reagents were previously reported by Tamaru[10] and Marshall.[11] However, no examples for fluorine compounds showing high stereoselectivity have been reported. As this sequential procedure was also applicable to the formation of fluoromethylated allenylzinc reagent via the transmetalation of π-allenylpalladium, we carried out the propargylation of carbonyl compounds with Et_2Zn in the presence of catalytic $Pd(PPh_3)_4$. Propargylic mesylates with a trifluoromethyl group undergo highly diastereoselective propargylation of aldehydes with the $Et_2Zn-Pd(PPh_3)_4$ system in dichloromethane, affording the corresponding homopropargylic alcohols **8** with a trifluoromethyl group on the stereocenter. Furthermore, the influence of the organic solvents directly affected the reaction pathway (entries 11−14, Table 3). In sharp contrast to the present case, it is interesting to note that the reaction in tetrahydrofuran gave a poor yield (entry 11). The employment of a mesyloxy substituent (Z = OSO_2CH_3) and/or a (ethoxycarbonyl)oxy (entries 12−14) instead of a benzoyloxy (entry 10) group accelerated the desired reaction pathway to furnish the stereocontrolled homopropargyl alcohols.

The stereochemistry of products **8** had *anti* configuration which was confirmed by the ^1H NMR coupling constant (^3J = Hz) of the benzylidene acetal derived from **8b** and also led to determination of the relative configurations. Compound **8b** was reduced with Lindlar catalyst−H_2 to produce the corresponding *Z*-olefin. This *Z*-olefin was oxidized with O_3 and then reduced with $NaBH_4$ to give the 1,3-diol **11** and hence the benzylidene acetal **12** (Scheme 3**)** with ^1H NMR coupling constants J_{H1-H2} = 6.87 Hz and J_{H2-H3} = 5.22, 4.40 Hz. The configuration of benzylidene acetal **12** was determined from ^1H NMR coupling constants and molecular mechanics calculations. AM 1 calculations employing multiconformer analysis of the benzylidene acetal gave the global minimum conformations and the corresponding coupling constants as shown in Table 4. Comparison of the conformations gave the calculated coupling constants shown in Table 4. The ^1H NMR spectrum indicates an *anti* configuration for the major product, in accord with the calculated results. Further, in the comparison with the ^1H NMR coupling constant of acetonide **6**, the stereochemistry of acetonide derived from compound **8d** was the same configuration.

Furthermore, in the case of compound **13,** which was directly attached with a CF_3 group on a triple bond, the reaction proceeded on the carbon atom attached to the mesyloxy substituent, affording compound **14** with high diastereoselectivity (Table 5).

In the case of diethyl ketone as an acceptor shown in Scheme 4, the mixture of compounds **16** and **17** was obtained in the ratio of 1.6:1, and the isolation of both materials was difficult.

Furthermore, in the umpolung of palladium complex of 1,1-difluoro-4-[(ethyoxycarbonyl)oxy]-2-nonen **18**[12f,12 g] and/or 1-(benzyloxy)-4-(mesyloxy)-5,5-difluoro-2-pentyne **19**,[12f,12 g] instead of the corresponding trifluoromethylated derivatives, the starting materials were decomposed (Scheme 5). The difference of stability between the complex attached with CF_3 group and that of CHF_2 group is based on the fact that C−F bond length in CHF_2 group is longer than that of CF_3 group.[17]

In the allenylzinc system, it is important to note that two kinds of products, such as alkynes **8** with excellent diastereoselectivity and allenyl materials **9**, are obtained. Further, compound **13** as the starting material only produced the compound **14**. These observations might be explained by the steric hindrance between a highly steric group (CF_3) and aldehyde substituent (R), which led us to conclude that 1-substituted 3-(trifluoromethyl)-3-(mesyloxy)propyne derivatives were required as a starting material in the present stereoselective allenylzinc system. From the above results, the mechanism of the present reaction was explained as follows. The following equilibrium might exist for allenylzinc species shown in Figure 2. The stereoselective synthesis described above was thus attributed to the bulkiness of a CF_3 group, and thus ***TS*-1** is favored over ***TS*-2** of which the CF_3 and the R substituent are in a *syn* relationship.[18,19] Further, it seems that the unusually low regiocontrol featured by the reaction with diethyl ketone as acceptor (Scheme 4) might be due to the fact that ***TS*-1** and ***TS*-2** are equivalent: the CF_3 group experiences a destabilizing interaction with the ethyl groups of the ketone, thus making ***TS*-3** energetically comparable.

As depicted in the several types of combinations shown in Tables 2 and 3, we have found that these processes allowed convenient procedures for construction of the stereocenter on the carbon atom attached to a CF_3 group.

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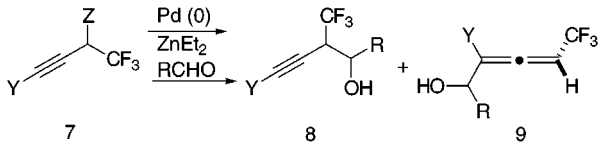
Table 3. Synthesis of Compounds 8 and 9

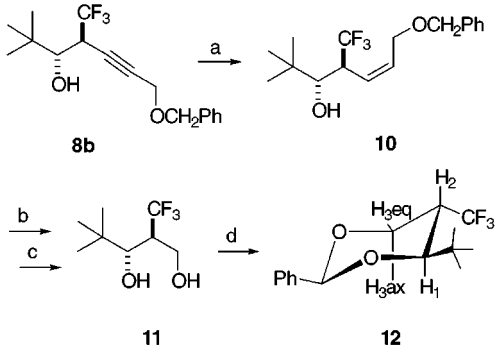


7 8 9

entry	Y	Z	RCHO R	solvent	yield (%)[a] 8	9	diastereomeric ratio (% de) of **8**
9	CH_2OBn	OCO_2Et	*n*-Bu	CH_2Cl_2	31 (**8a**)[b]		92:8
10	CH_2OBn	OCOPh	*n*-Bu	CH_2Cl_2	*c*		
11	CH_2OBn	OMs	*n*-Bu	THF	8 (**8a**)		
12	CH_2OBn	OMs	*n*-Bu	Et_2O	57 (**8a**)		91:9
13	CH_2OBn	OMs	*n*-Bu	benzene	53 (**8a**)		90:10
14	CH_2OBn	OMs	*n*-Bu	CH_2Cl_2	76 (52) (**8a**)		91:9
15	CH_2OBn	OMs	*t*-Bu	CH_2Cl_2	60 (43) (**8b**)		>99:1
16	CH_2OBn	OMs	(*E*)-PhCH=CH	CH_2Cl_2	69 (47) (**8c**)		81:19
17	CH_2OBn	OMs	Ph	CH_2Cl_2	55 (36) (**8d**)		87:13
18	CH_2OBn	OMs	$TBSOCH_2$	CH_2Cl_2	52 (33) (**8e**)		90:10
19	Ph	OMs	*n*-Bu	CH_2Cl_2	56 (42) (**8f**)	22 (18) (**9f**)	93:7
20	*n*-Pr	OMs	*n*-Bu	CH_2Cl_2	33 (20) (**8g**)	17 (12) (**9g**)	93:7
21	*t*-Bu	OMs	*n*-Bu	CH_2Cl_2	70 (66) (**8h**)		95:5

[a] Yields were determined by ^{19}F NMR integral intensities. Yields in parentheses were isolated. See Experimental Section with regard to isolated yields. [b] Compound **6** (Y = CH_2OBn, Z = OCO_2Et; 62%) was recovered. [c] Compound **6** (Y = CH_2OBn, Z = OCOPh; 95%) was recovered.

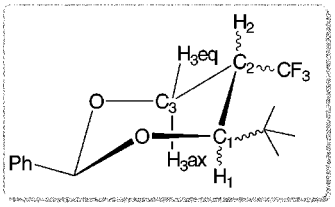
Scheme 3



[a] Key: (a) Lindlar, H_2 (b) O_3, MeOH (c) $NaBH_4$ (d) $PhCH(OMe)_2$, DMF, cat. TsOH

[a] Key: (a) Lindlar, H_2; (b) O_3, MeOH; (c) $NaBH_4$; (d) $PhCH(OMe)_2$, DMF, cat. TsOH.

Table 4. Coupling Constants by AM 1 Calculations



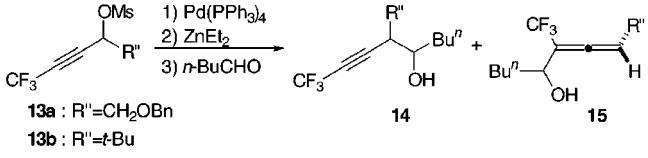
Ph	*t*-Bu	CF_3	H_1-H_2 (Hz)	H_2-H_{3ax} (Hz)	H_2-H_{3eq} (Hz)
e	e	e[a]	6.72	5.22	3.89
e	e	a	2.37	1.06	4.20
e	a	a	8.47	8.27	3.74
e	a	e	2.37	3.37	0.43

[a] eee means that each group is equatorial (Ph), equatorial (*t*-Bu), and equatorial (CH_3).

Experimental Section

General. All commercially available reagents were used without further purification. Chemical shifts of ^1H (300 MHz) and ^{13}C NMR (75 MHz) spectra were recorded in ppm (δ) downfield from the following internal standard (Me_4Si, δ 0.00) in $CDCl_3$. The ^{19}F (282 MHz) NMR spectra were recorded in ppm downfield from internal standard C_6F_6 in $CDCl_3$ using a VXR 300 instrument.

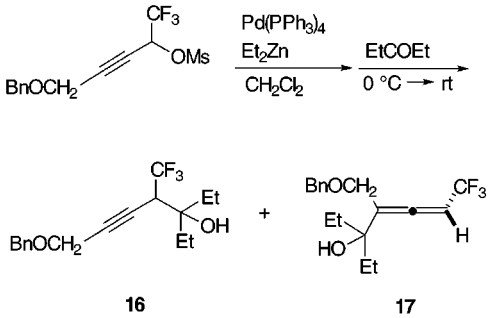
Table 5. Synthesis of Compounds 14



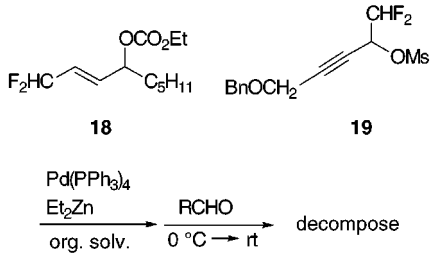
entry	R″	yield (%)[a]	diastereomeric ratio (% de) of **14**
22	CH_2OBn	61 (43)	89:11
23	*t*-Bu	72 (51)	>99:<1

[a] Yields were determined by ^{19}F NMR integral intensities. Yields in parentheses were isolated as an acetate derivative.

Scheme 4. Reaction of Allenylzinc Reagent with Diethyl Ketone



Scheme 5



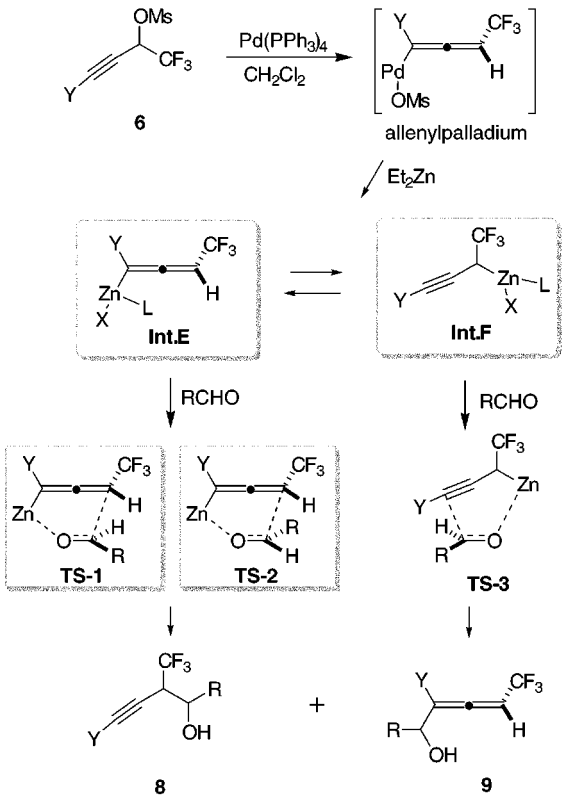


Figure 2. Reaction mechanism of the present allenylzinc reaction.

(*Z*)-2-Methyl-5-(trifluoromethyl)-6-hydroxy-3-decene 3a. (a) To a solution of $Pd(PPh_3)_4$ (0.05 equiv, 48 mg) and tetrahydrofuran (5 mL) were added 1,1,1-trifluoro-4-[(ethoxycarbonyl)oxy]-5-methyl-2-hexene (200 mg, 0.833 mmol) and pentanal (0.106 mL, 1.0 mmol) at 0 °C under an argon atmosphere, and then the mixture was stirred for a few minutes at that temperature. To the above solution was added Et_2Zn (2.0 mmol; 1 M solution in hexane), the whole was stirred for 20 h to warm from 0 °C to room temperature, and then the mixture was quenched with 1 N HCl. Oily materials were extracted with ethyl acetate, and the extract was washed with HCl, aq $NaHCO_3$, and brine and dried over $MgSO_4$. On removal of the solvent, the yield (66%) and diastereomeric ratio (97:3) were determined by the ^{19}F NMR integral intensities using benzotrifluoride ($PhCF_3$) as an internal standard. The resultant crude product was purified by chromatography on silica gel using a mixture solution of hexane and ethyl acetate in 53% yield (105 mg).

(b) In the above reaction, 1,1,1-trifluoro-4-(mesyloxy)-5-methyl-2-hexene (200 mg, 0.812 mmol), pentanal (0.104 mL, 1.0 mmol), $Pd(PPh_3)_4$ (0.05 equiv, 47 mg), and Et_2Zn (1.95 mmol; 1 M solution in hexane) in tetrahydrofuran (5 mL) were used and worked up similarly. The yield (35%) and diastereomeric ratio (96:4) were determined by the ^{19}F NMR integral intensities using benzotrifluoride as an internal standard.

Compound 3a. ^1H NMR ($CDCl_3$): δ 0.91 (3 H, t, J = 6.87 Hz), 0.98 (3 H, d, J = 6.59 Hz), 0.99 (3 H, d, J = 6.60 Hz), 1.30−1.55 (6 H, m), 2.52 (1 H, m), 3.08 (1 H, qind, J = 9.71, 2.30 Hz), 4.04 (1 H, m), 5.35 (1 H, t, J = 10.7 Hz), 5.68 ((1 H, t, J = 10.7 Hz);^{19}F NMR ($CDCl_3$): δ 94.17 (d, J = 9.48 Hz). ^{13}C NMR ($CDCl_3$): δ 14.51, 23.08, 23.17, 23.27, 27.98, 28.39, 35.22, 47.36 (q, J = 24.5 Hz), 69.56 (q, J = 2.3 Hz), 115.64 (q, J = 2.4 Hz), 127.24 (q, J = 280.9 Hz), 145.99. IR: 3636, 2960, 2870, 1724, 1660 cm^{-1}. Anal. Calcd for $C_{12}H_{21}F_3O$: C, 60.49; H, 8.88. Found. C, 60.26; H, 8.81.

(*Z*)-2,7-Dimethyl-5-(trifluoromethyl)-6-hydroxy-3-octene 3b. (a) In the above reaction, $Pd(PPh_3)_4$ (0.05 equiv, 48 mg), 1,1,1-trifluoro-4-[(ethoxycarbonyl)oxy]-5-methyl-2-hexene (200 mg, 0.833 mmol), and 2-methylpropanal (0.09 mL, 1.0 mmol) in tetrahydrofuran (5 mL) were used. To the solution was added Et_2Zn (1.8 mmol; 1 M solution in hexane) and then worked up similarly. On removal of the solvent, the yield (46%) and diastereomeric ratio (95:5) were determined by the ^{19}F NMR integral intensities. The resultant crude product was purified by chromatography on silica gel, using a mixture solution of hexane and ethyl acetate, in 44% yield (82 mg).

Compound 3b. ^1H NMR ($CDCl_3$): δ 0.89 (3 H, d, J = 6.60 Hz), 0.98 (3 H, d, J = 6.59 Hz), 0.99 (3 H, d, J = 6.59 Hz), 1.01 (3 H, d, J = 6.60 Hz), 1.6−1.7 (1 H, m), 2.4−2.6 (1 H, m), 3.26 (1 H, qind, J = 9.75, 2.41 Hz), 3.66 (1 H, dd, J = 8.24, 1.92 Hz), 5.37 (1 H, t, J = 10.72 Hz), 5.65 (1 H, t, J = 10.56 Hz). ^{19}F NMR ($CDCl_3$): δ 94.12 (d, J = 9.48 Hz). ^{13}C NMR ($CDCl_3$): δ 18.54, 19.07, 22.64, 22.77, 27.66, 31.37, 44.34 (q, J = 24.5 Hz), 74.17 (q, J = 2.2 Hz), 114.79 (q, J = 2.3 Hz), 126.66 (q, J = 280.2 Hz), 145.05. IR. 3636, 3455, 2865, 1725 cm^{-1}.

(*Z*)-2-Methyl-5-(trifluoromethyl)-6-hydroxy-6-phenyl-3-hexene 3c. In the above reaction, benzaldehyde (1.0 mmol) was used instead of pentanal. To the solution was added Et_2Zn (1.8 mmol; 1 M solution in hexane) and then worked up similarly. On removal of the solvent, the yield (83%) and diastereomeric ratio (>99:<1) were determined by the ^{19}F NMR integral intensities using benzotrifluoride as an internal standard. The resultant crude product was purified by chromatography on silica gel, using a mixture solution of hexane and ethyl acetate, in 73% yield (156 mg).

Compound 3c. ^1H NMR ($CDCl_3$): δ 0.41 (3 H, d, J = 6.59 Hz), 0.84 (3 H, d, J = 6.59 Hz), 1.98−2.10 (1 H, m), 2.14 (1 H, s), 3.30 (1 H, qind, J = 9.44, 2.86 Hz), 5.24 (1 H, s), 5.44 (1 H, t, J = 10.72 Hz), 5.54 (1 H, t, J = 10.44 Hz), 7.32 (Ar−H); ^{19}F NMR ($CDCl_3$): δ 93.9 (d, J = 9.46 Hz). ^{13}C NMR ($CDCl_3$): δ 21.67, 22.28, 26.94, 49.32 (q, J = 24.8 Hz), 71.02 (q, J = 2.5 Hz), 114.1 (q, J = 2.2 Hz), 125.8, 126.3 (q, J = 281 Hz), 127.5, 128.0, 141.5, 145.3. IR: 3457, 2962 cm^{-1}. Anal. Calcd for $C_{14}H_{17}F_3O$: C, 65.10; H, 6.63. Found. C, 64.68; H, 6.73.

(3*Z*,7*E*)-2-Methyl-5-(trifluoromethyl)-6-hydroxy-8-phenyl-3,7-octadiene 3d. In the above reaction, cinnamyl aldehyde (1.0 mmol) was used. To the solution was added Et_2Zn (1.8 mmol; 1 M solution in hexane) and then worked up similarly. On removal of the solvent, the yield (60%) and diastereomeric ratio (96:4) were determined by the ^{19}F NMR integral intensities using benzotrifluoride as an internal standard. As the product did not purify to take the spectral data, compound was converted to acetate derivative (53% yield, 143 mg, 0.438 mmol) by the reaction of crude product with acetyl chloride in CH_2Cl_2 at 0 °C.

Acetate Derivative of Compound 3d. ^1H NMR ($CDCl_3$): δ 0.95 (3 H, d, J = 6.59 Hz), 0.98 (3 H, d, J = 6.59 Hz), 2.09 (3 H, s), 2.54 (1 H, m), 3.40 (1 H, m), 5.37 (1 H, t, J = 10.99 Hz), 5.70 (1 H, t, J = 10.44 Hz), 5.81 (1 H, ddd, J = 7.90, 3.50, 0.89 Hz), 6.09 (1 H, dd, J = 15.93, 7.22 Hz), 6.68 (1 H, d, J = 15.93 Hz), 7.2−7.4 (Ar−H, m);^{19}F NMR ($CDCl_3$): δ 93.98 (d, J = 8.62 Hz). ^{13}C NMR ($CDCl_3$): δ 21.02, 22.54, 22.68, 27.23, 46.18 (q, J = 26.0 Hz), 71.46 (q, J = 2.4 Hz), 115.24 (q, J = 2.3 Hz), 120.0 (q, J = 280.9 Hz), 123.93,126.68, 128.31, 128.61, 134.46, 135.72, 145.52, 169.63. IR: 3030, 2963, 2872, 2362, 1747, 1658 cm^{-1}. Anal. Calcd for $C_{18}H_{21}F_3O_2$: C, 66.42; H, 6.49. Found. C, 66.62; H, 6.57.

(*Z*)-7-(Trifluoromethyl)-8-hydroxy-5-dodecene 3e. In the above reaction, $Pd(PPh_3)_4$ (0.05 equiv, 43 mg), 1,1,1-trifluoro-4-(ethoxycarbonyl)oxy-2-octene (200 mg, 0.746 mmol), and pentanal (0.094 mL, 0.895 mmol) in tetrahydrofuran (5 mL) were used.

To the solution was added Et_2Zn (1.8 mmol; 1 M solution in hexane) and then worked up similarly. On removal of the solvent, the yield (46%) and diastereomeric ratio (>99:<1) were determined by the ^{19}F NMR integral intensities using benzotrifluoride as an internal standard. The resultant crude product was purified by chromatography on silica gel using a mixture solution of hexane and ethyl acetate in 36% yield (68 mg).

Compound 3e. ^1H NMR ($CDCl_3$): δ 0.90 (6 H, t, J = 6.87 Hz), 1.25−1.45 (10 H, m), 2.03−2.12 (2 H, m), 3.08 (1 H, m), 4.04 (1 H, m), 5.47 (1 H, tt, J = 10.72, 1.65 Hz), 5.87 (1 H, dt, J = 10.08, 7.49 Hz); ^{19}F NMR ($CDCl_3$): δ 94.2 (d, J = 9.48

Hz). ^{13}C NMR ($CDCl_3$): δ 13.81, 13.89, 22.30, 22.46, 27.63, 27.81, 31.38, 34.58, 46.58 (q, J = 24.4 Hz), 69.12 (q, J = 2.3 Hz), 117.74 (q, J = 2.4 Hz), 138.3, 126.7 (q, J = 179.2 Hz). IR: 3420, 2933, 2866, 2364, 1724, 1462 cm^{-1}. Anal. Calcd for $C_{13}H_{23}F_3O$: C, 61.88; H, 9.19. Found. C, 61.65; H, 9.42.

1-(Benzyloxy)-5-(trifluoromethyl)-6-hydroxy-2-nonene 3f. In the above reaction, $Pd(PPh_3)_4$ (0.05 equiv, 36 mg), 1,1,1-trifluoro-4-(ethoxy-carbonyl)oxy-5-(benzyloxy)-2-pentene (200 mg, 0.629 mmol), and pentanal (0.755 mmol) in tetrahydrofuran (5 mL) were used. To the solution was added Et_2Zn (1.8 mmol; 1 M solution in hexane) and then worked up similarly. On removal of the solvent, the yield (47%) and diastereomeric ratio (96:4) were determined by the ^{19}F NMR integral intensities. As the product did not purify to take the spectral data, compound was converted to acetate derivative (29% yield, 56 mg, 0.156 mmol) by the reaction of crude product with acetyl chloride in CH_2Cl_2 at 0 °C.

Acetate Derivative of Compound 3f. ^{1}H NMR ($CDCl_3$): δ 0.86 (3 H, t, J = 7.00 Hz), 1.22−1.35 (4 H, m), 1.4−1.6 (2 H, m), 3.27 (1 H, m), 4.03 (1 H, ddd, J = 12,77, 5.90, 1.79 Hz), 4.14 (1 H, ddd, J = 12,78, 6.46, 1.79 Hz), 4.53 (2 H, s), 5.30 (1 H, ddd, J = 8.24, 5.49, 2.68 Hz), 5.65 (1 H, m), 6.07 (1 H, dt, J = 11.54, 5.86 Hz), 7.25−7.4 (Ar−H, m). ^{19}F NMR ($CDCl_3$): δ 93.8 (d, J = 8.62 Hz). ^{13}C NMR ($CDCl_3$): δ 13.95, 20.94, 23.34, 27.44, 32.03, 45.21 (q, J = 26.2 Hz), 65.88, 69.78 (q, J = 2.19 Hz), 72.57, 121.07 (q, J = 2.48 Hz), 125.62 (q, J = 270.3 Hz), 127.57, 127.66, 128.31, 134.44, 137.60, 169.82. IR: 2962, 1749 cm^{-1}. Anal. Calcd for $C_{19}H_{25}F_3O_3$: C, 63.67; H, 7.03. Found. C, 63.73; H, 7.02.

Acetonide 6. To a solution of compound **3c** (553 mg, 2.1 mmol) in methanol (10 mL) at −78 °C was bubbled excess O_3, and then the whole was stirred for several hours at −78 °C. To the above solution, $NaBH_4$ (320 mg, 8.4 mmol) was added, and the whole was stirred for 1 h at −78 °C. The mixture was quenched with aq NH_4Cl, oily materials were extracted with ethyl acetate, and the extract was washed with aq NH_4Cl and dried over $MgSO_4$. On removal of the solvent, the resultant crude product was used to produce the acetonide without purification. The crude product, benzene (10 mL), dimethylacetal (4.0 mmol), and a catalytic amount of TsOH (40 mg) were stirred for 5 h at 70 °C. On removal of the solvent, oily materials were extracted with ethyl acetate, and the extract was washed with aq $NaHCO_{34}$. The resultant crude product was purified by chromatography on silica gel using a mixture solution of hexane and ethyl acetate to give acetonide **6** (124 mg). ^{1}H NMR ($CDCl_3$): δ 1.48 (3 H, s), 1.57 (3 H, s), 2.76 (1 H, m), 4.07 (1 H, dd, J = 12.09, 8.79 Hz), 4.12 (1 H, dd, J = 12.09, 6.32 Hz), 4.93 (1 H, d, J = 10.17 Hz), 7.3−7.4 (Ar−H, m); ^{19}F NMR ($CDCl_3$): δ 94.74 (d, J = 7.76 Hz). ^{13}C NMR ($CDCl_3$): δ 19.56, 28.43, 45.75 (q, J = 23.6 Hz), 57.93 (q, J = 3.6 Hz), 70.97 (q, J = 2.1 Hz), 99.41, 125.18 (q, J = 279.4 Hz), 127.25, 128.39, 128.58, 138.96. IR: 2993, 1729, 1459 cm^{-1}. Anal. Calcd for $C_{13}H_{15}F_3O_2$: C, 60.00; H, 5.81. Found. C, 60.10; H, 6.09.

1-(Benzyloxy)-4-(trifluoromethyl)-5-hydroxy-2-nonyne 8a. (a) To a solution of $Pd(PPh_3)_4$ (0.05 equiv, 36 mg) and dichloromethane (5 mL) were added 1-(benzyloxy)-4-(mesyloxy)-5,5,5-trifluoro-2-pentyne (200 mg, 0.620 mmol) and pentanal (0.133 mL, 1.24 mmol) at 0 °C under an argon atmosphere, and then the mixture was stirred for a few minutes at that temperature. To the above solution was added Et_2Zn (1.48 mmol: 1 M solution in hexane), the whole was stirred for 8 h to warm from 0 °C to room temperature, and then the mixture was quenched with 1 N HCl. Oily materials were extracted with dichloromethane, and the extract was washed with aq $NaHCO_3$ and brine and dried over $MgSO_4$. On removal of the solvent, the yield (76%) and diastereomeric ratio (91:9) were determined by the ^{19}F NMR integral intensities using benzotrifluoride as an internal standard. The resultant crude product was purified by chromatography on silica gel using a mixture solution of hexane and ethyl acetate. As 1-(benzyloxy)-4-(trifluoromethyl)-5-hydroxy-2-nonyne was not sufficiently stable to undergo spectroscopy, the compound was converted to 1-(benzyloxy)-4-(trifluoromethyl)-5-(benzyloxy)-2-nonyne by the following method.

To a solution of the above isolated 1-(benzyloxy)-4-(trifluoromethyl)-5-hydroxy-2-nonyne, pyridine (1.5 mmol), and a catalytic amount of 4-(dimethylamino)pyridine in dichloromethane (7 mL) was added benzoyl chloride (1.5 mmol) at 0 °C under an argon atmosphere, and then the mixture was stirred at that temperature. The mixture was warmed to room tempetrature and then was quenched with aq NH_4Cl. Oily materials were extracted with dichloromethane, and the extract was dried over $MgSO_4$. On removal of the solvent, the crude product was purified by chromatography on silica gel using a mixture solution of hexane and ethyl acetate, giving the benzyloxy derivative in a 52% yield (136 mg).

Benzoate Derivative of Compound 8a.^{1}H NMR ($CDCl_3$): δ 0.9−1.0 (3 H, m), 1.3−1.4 (4 H, m), 1.8−1.9 (1 H, m), 1.9−2.0 (1 H, m), 3.4−3.6 (1 H, m), 4.28 (2 H, d, J = 1.92 Hz), 4.64 (2 H, s), 5.53 (1 H, ddd, J = 2.6, 5.2, 8.2 Hz), 7.3−8.1 (Ar−H); ^{19}F NMR ($CDCl_3$): δ 93.8 (d, J = 8.6 Hz). ^{13}C NMR ($CDCl_3$): δ 13.9, 22.3, 27.4, 32.2, 42.7 (q, J = 29.7 Hz), 57.0, 69.6, 71.4, 76.0 (q, J = 3.3 Hz), 82.4, 124.2 (q, J = 280 Hz), 127.8, 128.0, 128.2, 128.3, 129.5, 129.6, 133.0, 137.0, 165.2. IR: 3065, 3033, 2958, 2865, 1725, 1602, 1494, 1454 cm^{-1}. Anal. Calcd for $C_{24}H_{25}F_3O_3$: C, 68.89; H, 6.02. Found. C, 68.93; H, 6.35.

(b) In the above reaction, 1-(benzyloxy)-4-[(ethoxycarbonyl)-oxy]-5,5,5-trifluoro-2-pentyne (155 mg, 0.49 mmol), pentanal (0.104 mL, 0.98 mmol), Et_2Zn (1.18 mmol), and $Pd(PPh_3)_4$ (0.05 equiv, 28 mg) in dichloromethane (5 mL) were used in the same manner. After 1-(benzyloxy)-4-(trifluoromethyl)-5-hydroxy-2-nonyne (31%; diastereomeric ratio 92:8) and recovered starting material (63%, 97 mg, 0.31 mmol) were separated, the compound was converted to the corresponding benzyloxy derivative in a 13% yield (27 mg, 0.065 mmol).

1-(Benzyloxy)-4-(trifluoromethyl)-5-hydroxy-6,6-dimethyl-2-heptyne 8b. In the above reaction, 1-(benzyloxy)-4-(mesyloxy)-5,5,5-trifluoro-2-pentyne (200 mg, 0.620 mmol), 2,2-dimethylpropanal (0.124 mmol), Et_2Zn (1.48 mmol), and $Pd(PPh_3)_4$ (0.05 equiv, 36 mg) in dichloromethane (5 mL) were used in the same manner. Oily materials were extracted with dichloromethane, and the extract was washed with aq $NaHCO_3$ and brine and dried over $MgSO_4$. On removal of the solvent, the yield (60%) and diastereomeric ratio (>99:<1) were determined by the ^{19}F NMR integral intensities using benzotrifluoride as an internal standard. The resultant crude product was purified by chromatography on silica gel using a mixture solution of hexane and ethyl acetate, giving 1-(benzyloxy)-4-trifluoromethyl-5-hydroxy-6,6-dimethyl-2-heptyne in 43% yield (91 mg, 0.266 mmol).

Compound 8b. ^{1}H NMR ($CDCl_3$): δ 1.00 (9 H, s), 2.09 (1 H, d, J = 9.1 Hz), 3.4−3.5 (1 H, m), 3.62 (1 H, d, J = 8.8 Hz), 4.23 (2 H, d, J = 1.9 Hz), 4.60 (2 H, s), 7.3−7.4 (Ar−H). ^{19}F NMR ($CDCl_3$): δ 91.9 (d, J = 8.6 Hz). ^{13}C NMR ($CDCl_3$): δ 26.4, 36.4, 40.7 (q, J = 28.5 Hz), 57.6, 72.1, 74.8 (q, J = 1.6 Hz), 76.9 (q, J = 3.5 Hz), 125.7 (q, J = 281 Hz), 128.5, 128.7, 129.0, 137.6. IR: 3482, 1720 (CO) cm^{-1}. Anal. Calcd for $C_{17}H_{21}F_3O_2$: C, 64.96; H, 6.73. Found. C, 65.00; H, 6.79.

1-(Benzyloxy)-4-(trifluoromethyl)-5-hydroxy-7-phenyl-2-hept-6-en-2-yne 8c. In the above reaction, 1-(benzyloxy)-4-(mesyloxy)-5,5,5-trifluoro-2-pentyne (200 mg, 0.620 mmol), cinnamyl aldehyde (0.124 mmol), Et_2Zn (1.48 mmol), and $Pd(PPh_3)_4$ (0.05 equiv, 36 mg) in dichloromethane (5 mL) were used, and then worked up similarly. On removal of the solvent, the yield (68%) and diastereomeric ratio (81:19) were determined by the ^{19}F NMR integral intensities using benzotrifluoride as an internal standard. The resultant crude product was purified by chromatography on silica gel using a mixture solution of hexane and ethyl acetate. As 1-(benzyloxy)-4-(trifluoromethyl)-5-hydroxy-7-phenyl-2-hept-6-en-2-yne was not sufficiently stable to undergo spectroscopy, the compound was converted to 1-(benzyloxy)-4-(trifluoromethyl)-5-acetoxy-7-phenyl-2-hept-6-en-2-yne by the following method.

To a solution of the above isolated 1-(benzyloxy)-4-(trifluoromethyl)-5-hydroxy-7-phenyl-2-hept-6-en-2-yne, pyridine (1.5 mmol), and catalytic amount of 4-(dimethylamino)pyridine in dichloromethane (3 mL) was added acetyl chloride (1.0 mmol) at 0 °C under an argon atmosphere, and then the mixture was stirred at that temperature. The mixture was warmed to room

tempetrature and then was quenched with aq NH_4Cl. Oily materials were extracted with dichloromethane, and the extract was dried over $MgSO_4$. On removal of the solvent, the crude product was purified by chromatography on silica gel using a mixture solution of hexane and ethyl acetate, giving the acetoxy derivative in 47% yield (117 mg, 0.290 mmol).

Acetate Derivative of Compound 8c. ^{1}H NMR ($CDCl_3$): δ 2.12 (3 H, s), 3.49−3.60 (1 H, m), 4.61 (2 H, s), 4.25 (2 H, d, J = 1.93 Hz), 5.87 (1 H, ddd, J = 7.69, 3.57, 0.83 Hz), 6.25 (1 H, dd, J = 15.80, 7.56 Hz), 6.78 (1 H, d, J = 15.93 Hz), 7.2−7.4 (10 H, m). ^{19}F NMR ($CDCl_3$): δ 94.02 (d, J = 7.76 Hz) as major, 94.22 (d, J = 7.75 Hz) as minor. ^{13}C NMR ($CDCl_3$): δ 20.95, 42.54 (q, J = 29.5 Hz), 57.00, 70.13 (q, J = 1.91 Hz), 71.23, 75.90 (q, J = 3.34 Hz), 82.54, 122.76, 123.77 (q, J = 280.7 Hz), 126.67, 127.77, 127.96, 128.27, 128.38, 128.48, 135.03, 135.24, 136.92, 169.24. IR: 3031, 2919, 2859, 1956, 1880, 1748, 1655, 1582 cm^{-1}. Anal. Calcd for $C_{23}H_{21}F_3O_3$: C, 68.65; H, 5.26. Found. C, 68.39; H, 5.59.

1-(Benzyloxy)-4-(trifluoromethyl)-5-hydroxy-5-phenyl-2-pentyne 8d. In the above reaction, 1-(benzyloxy)-4-(mesyloxy)-5,5,5-trifluoro-2-pentyne (200 mg, 0.620 mmol), benzaldehyde (0.124 mmol), Et_2Zn (1.48 mmol), and $Pd(PPh_3)_4$ (0.05 equiv, 36 mg) in dichloromethane (5 mL) were used and then worked up similarly. On removal of the solvent, the yield (55%) and diastereomeric ratio (87:13) were determined by the ^{19}F NMR integral intensities. As 1-(benzyloxy)-4-(trifluoromethyl)-5-hydroxy-5-phenyl-2-pentyne **8d** was not sufficiently stable to undergo spectroscopy, the compound was converted to 1-(benzyloxy)-4-(trifluoromethyl)-5-acetoxy-5-phenyl-2-pentyne by the following method.

To a solution of 1-(benzyloxy)-4-(trifluoromethyl)-5-hydroxy-5-phenyl-2-pentyne **8d** were added pyridine (2.0 mmol) and acetyl chloride (1.5 mmol) at 0 °C under an argon atmosphere, and then the mixture was stirred at that temperature and then worked up similarly. On removal of the solvent, the crude product was purified by chromatography on silica gel using a mixture solution of hexane and ethyl acetate, giving acetoxy derivative in 36% yield (84 mg).

Acetate Derivative of Compound 8d. ^{1}H NMR ($CDCl_3$): δ 2.15 (3 H, s), 3.5−3.6 (1 H, m), 4.21 (2 H, d, J = 1.92 Hz), 4.57 (2 H, s), 6.16 (1 H, d, J = 3.02 Hz), 7.2−7.5 (10 H, m). ^{19}F NMR ($CDCl_3$): δ 93.28 (d, J = 7.75 Hz). ^{13}C NMR ($CDCl_3$): δ 20.90, 44.51 (q, J = 23.7 Hz), 57.01, 70.32 (q, J = 2.0 Hz), 71.19, 75.61 (q, J = 3.2 Hz), 83.01, 123.78 (q, J = 280.8 Hz), 127.81, 127.94, 128.31, 128.43, 128.68, 136.73, 136.99, 169.76. IR. 3034, 2859, 2365, 1958, 1752, 1604 cm^{-1}. Anal. Calcd for $C_{21}H_{19}F_3O_3$: C, 67.02; H, 5.09. Found. C, 66.84; H, 5.11.

1-(Benzyloxy)-4-(trifluoromethyl)-5-hydroxy-6-[(*tert*-butyldimethylsilyl)oxy]-2-hexyne 8e. (a) In the above reaction, $Pd(PPh_3)_4$ (0.05 equiv, 36 mg), 1-(benzyloxy)-4-(mesyloxy)-5,5,5-trifluoro-2-pentyne (200 mg, 0.620 mmol), and $TBSOCH_2CHO$ (2.0 equiv, 219 mg) in dichloromethane (2 mL) were used and then worked up similarly. To the above solution, Et_2Zn (2.4 equiv, 1.48 mL: 1 M solution in hexane) was added, the whole was stirred for 7 h to warm from 0 °C to room temperature, and then the mixture was quenched with 1 N HCl. Oily materials were extracted with dichloromethane, and the extract was washed with aq $NaHCO_3$ and brine and dried over $MgSO_4$. On removal of the solvent, the yield (52%) and diastereomeric ratio (90:10) were determined by the ^{19}F NMR integral intensities. As 1-(benzyloxy)-4-trifluoromethyl-5-hydroxy-5-phenyl-2-pentyne was not sufficiently stable to undergo spectroscopy, compound **8e** was converted to *p*-nitrobenzoate of compound **8e** by the following method.

(b) To a solution of 1-(benzyloxy)-4-(trifluoromethyl)-5-hydroxy-5-phenyl-2-pentyne (126 mg) and pyridine (0.12 mL) in dichloromethane (5 mL) was added *p*-nitrobenzyl chloride (185 mg, 1.0 mmol) at 0 °C under an argon atmosphere, and then the mixture was stirred overnight at room temperature and worked up similarly, giving *p*-nitrobenzoyloxy derivative in 33% total yield (113 mg).

***p*-Nitrobenzoate of Compound 8e**. ^{1}NMR ($CDCl_3$): δ 0.10 (3 H, s), 0.11 (3 H, s), 0.90 (9 H, s), 3,81−3.95 (3 H, m), 4.29 (2 H, d, J = 1.92 Hz), 4.63 (2 H, s), 5.53 (1 H, ddd, J = 7.97, 5.49, 2.56 Hz), 7.3−7.4 (5 H, m), 8.2−8.4 (Ar−H, m). ^{19}F NMR ($CDCl_3$): δ 93.2 (d, J = 8.61 Hz). ^{13}C NMR ($CDCl_3$): δ -5.40, −5.30, 18.23, 25.77, 38.63 (q, J = 30.5 Hz), 57.27, 60.86, 70.29 (q, J = 1.7 Hz), 71.58, 75.23 (q, J = 3.3 Hz), 82.71, 123.50, 124.30 (q, J = 279.9 Hz), 127.79, 127.99, 128.41. 130.77, 134.53, 136.89, 150.52, 163.15. IR. 2933, 2860, 2361, 1738, 1607, 1581 cm^{-1}. Anal. Calcd for $C_{27}H_{32}F_3NO_6Si$: C, 58.79; H, 5.58; N, 2.54. Found. C, 58.75; H, 5.95; N, 2.45.

1-Phenyl-3-(trifluoromethyl)-4-hydroxy-1-octyne 8f. In the above reaction, 1-phenyl-4,4,4-trifluoro-3-(mesyloxy)-1-butyne (200 mg, 0.718 mmol), pentanal (0.152 mL, 1.44 mmol), Et_2Zn (1.72 mmol), and $Pd(PPh_3)_4$ (0.05 equiv, 41 mg) in dichloromethane (5 mL) were used in the same manner. The yield (56%) and diastereomeric ratio (93:7) of compound **8f** and allenyl compound **9f** (22%) were determined by the ^{19}F NMR integral intensities using benzotrifluoride as an internal standard. The resultant crude product was purified by chromatography on silica gel using a mixture of hexane and ethyl acetate. As compounds **8f** and **9f** were not sufficiently stable to undergo spectroscopy, compounds were converted to acetoxy derivatives by the following method.

To a solution of the above isolated 1-phenyl-3-(trifluoromethyl)-4-hydroxy-1-octyne and pyridine (1.5 mmol) in dichloromethane (3 mL) was added acetyl chloride (1.0 mmol) at 0 °C under an argon atmosphere, and then the mixture was stirred at that temperature and then worked up similarly, giving acetoxy derivative in 42% yield (95 mg, 0.304 mmol). Moreover, the acetoxy derivative of allenyl compound was obtained in the same manner in 18% yield (41 mg, 0.131 mmol).

Acetate Derivative of Compound 8f. ^{1}H NMR ($CDCl_3$): δ 0.92 (3 H, t, J = 6.9 Hz), 1.3−1.4 (2 H, m), 1.7−1.9 (4 H, m), 3.55 (1 H, qt, J = 3.0, 8.1 Hz), 5.34 (1 H, ddd, J = 2.8, 5.6, 8.4 Hz), 7.3−7.5.^{19}F NMR ($CDCl_3$): δ 93.9 (d, J = 7.8 Hz). ^{13}C NMR ($CDCl_3$): δ 13.74, 20.71, 22.22, 27.41, 31.97, 41.95 (q, J = 29.6 Hz), 69.23 (q, J = 1.4 Hz), 78.39 (q, J = 3.5 Hz), 86.02, 122.00, 124.32 (q, J = 281 Hz), 128.25, 128.74, 131.86, 170.02. IR: 2960, 2868, 2363, 1747 cm^{-1}. Anal. Calcd for $C_{17}H_{19}F_3O_2$: C, 65.38; H, 6.13. Found. C, 65.70; H, 6.41.

Acetate Derivative of Compound 9f. ^{1}H NMR ($CDCl_3$): δ 0.86 (3 H, t, J = 7.0 Hz), 1.2−1.4 (4 H, m), 1.7−1.8 (2 H, m), 2.09 (3 H, s), 5.79 (1 H, ddd, J = 2.3, 5.6,7.4 Hz), 5.89 (1 H, qd, J = 2.3, 5.7 Hz), 7.3−7.4 (5 H, m). ^{19}F NMR ($CDCl_3$): δ 101.5 (d, J = 6.0 Hz). ^{13}C NMR ($CDCl_3$): δ 13.76, 20.87, 22.26, 27.20, 33.19, 71.41, 90.52 (q, J = 39 Hz), 115.64, 122.50 (q, J = 271 Hz), 127.05, 128.66, 128.89, 131.92, 170.24, 204.91 (q, J = 5.9 Hz). IR: 3027, 2958, 2868, 2363, 1969, 1744, 1599 cm^{-1}. Anal. Calcd for $C_{17}H_{19}F_3O_2$: C, 65.38; H, 6.13. Found. C, 65.40; H, 6.38.

1-Propyl-3-(trifluoromethyl)-4-hydroxy-1-octyne 8g. In the above reaction, 1-propyl-4,4,4-trifluoro-3-(mesyloxy)-1-butyne (200 mg, 0.819 mmol), pentanal (0.174 mL, 1.64 mmol), Et_2Zn (1.96 mmol), and $Pd(PPh_3)_4$ (0.05 equiv, 47 mg) in dichloromethane (5 mL) were used in the same manner. The yield (33%) and diastereomeric ratio (97:3) of octyne derivative and allenyl derivative (17%) were determined by the ^{19}F NMR integral intensities. Compound **8g** was converted to acetoxy derivatives (20% yield, 46 mg) by the above-mentioned method.

Acetate Derivaitve of Compound 8g. ^{1}H NMR ($CDCl_3$): δ 0.91 (3 H, t, J = 7.0 Hz), 1.0 (3 H, t, J = 7.4 Hz), 1.2−1.4 (4 H, m), 1.5−1.6 (2 H, m), 1.65−1.8 (2 H, m), 2.08 (3 H, s), 2.22 (2 H, td, J = 6.93, 2.29 Hz), 3.30 (1 H, qq, J = 2.51, 8.24 Hz), 5.23 (1 H, ddd, J = 2.75, 5.63, 8.38 Hz). ^{19}F NMR ($CDCl_3$): δ 93.3 (d, J = 8.6 Hz). ^{13}C NMR ($CDCl_3$): δ 13.12, 13.45, 20.52, 20.76, 21.81, 22.24, 27.42, 31.77, 41.26 (q, J = 29.4 Hz), 69.25 (q, J = 3.5 Hz), 69.34 (q, J = 1.8 Hz), 86.65, 124.49 (q, J = 280.8 Hz), 170.08. IR: 2963, 2872, 2247, 1748 cm^{-1}. Anal. Calcd for $C_{14}H_{21}F_3O_2$: C, 60.42; H, 7.61. Found. C, 60.37; H, 7.61.

Acetate of Allenyl Compound 9g. Yield. 12%, 28 mg.^{1}H NMR ($CDCl_3$): δ 0.87−0.97 (6 H, m), 1.26−1.37 (4 H, m), 1.47 (2 H, six, J = 7.44 Hz), 1.65−1.72 (2 H, m), 2.00−2.06 (2 H, m), 2.07 (3 H, s), 5.21 (1 H, td, J = 6.39, 1.92 Hz), 5.51−5.60 (1 H, m). ^{19}F NMR ($CDCl_3$): δ 101.2 (d, J = 6.03 Hz). ^{13}C NMR ($CDCl_3$): δ 13.62, 13.92, 20.36, 20.94, 22.41, 27.25, 30.78, 32.44, 72.60, 88.75 (q, J = 38.75 Hz), 113.14, 122.54 (q, J = 270.1

Hz), 170.06, 202.21 (q, J = 5.92 Hz). IR: 2961, 2872, 2363, 1980, 1744 cm^{-1}. Anal. Calcd for $C_{14}H_{21}F_3O_2$: C, 60.42; H, 7.61. Found. C, 60.06; H, 7.71.

1-*tert*-Butyl-3-(trifluoromethyl)-4-hydroxy-1-octyne 8h. In the above reaction, 1-*tert*-butyl-4,4,4-trifluoro-3-(mesyloxy)-1-butyne (200 mg, 0.774 mmol), pentanal (0.164 mL, 1.55 mmol), Et_2Zn (1.85 mmol), and $Pd(PPh_3)_4$ (0.05 equiv, 44 mg) in dichloromethane (5 mL) were used in the same manner. The yield (70%) and diastereomeric ratio (95:5) of compound **8h** was determined by the ^{19}F NMR integral intensities. Compound **8h** was converted to the acetoxy derivatives by the above-mentioned method in 66% yield (149 mg).

Acetate Derivative of Compound 8h. ^1H NMR ($CDCl_3$): δ 0.91 (3 H, t, J = 6.87 Hz), 1.23 (9 H, s), 1.29−1.40 (4 H, m), 1.68−1.76 (2 H, m), 2.08 (3 H, s), 3.28 (1 H, qd, J = 8.19, 3.23 Hz), 5.19 (1 H, ddd,J = 7.83, 5.91, 3.3 Hz). ^{19}F NMR ($CDCl_3$): δ 93.5 (d, J = 8.61 Hz). ^{13}C NMR ($CDCl_3$): δ 13.83, 20.80, 22.31, 27.49, 30.67, 31.64, 41.22 (q, J = 29.3 Hz), 67.74 (q, J = 3.58 Hz), 69.49, 94.84, 124.38 (q, J = 280 Hz), 169.85. IR. 2967, 2870, 2252, 1748 cm^{-1}.

Benzylidene Acetal 12. (a) A solution of Lindlar catalyst (120 mg), methanol (10 mL), and compound **8b** (804 mg, 2.35 mmol) under a hydrogen atmosphere was stirred for 6 days at room temperature. On removal of the solvent, the resultant crude product was purified by chromatography on silica gel using a mixture solution of hexane and ethyl acetate to give (*Z*)-1-(benzyloxy)-4-(trifluoromethyl)-5-hydroxy-6,6-dimethyl-2-heptene **10** (609 mg).

Compound 10. ^1H NMR ($CDCl_3$): δ 0.90 (9 H, s), 3.34 (1 H, qin, J = 9.96 Hz), 3.75 (1 H, s), 4.08 (1 H, ddd, J = 12.91, 5.22, 1.65 Hz), 4.17 (1 H, ddd, J = 12.91, 6.73, 1.38 Hz), 4.54 (2 H, d, J = 1.37 Hz), 5.85 (1 H, ddt, J = 11.41, 9.76, 1.69 Hz), 5.97 (1 H, ddd, J = 11.66, 6.73, 4.94 Hz), 7.2−7.4 (Ar−H, m). ^{19}F NMR ($CDCl_3$): δ 92.93 (d, J = 10.34 Hz). ^{13}C NMR ($CDCl_3$): δ 26.17, 35.60, 42.87 (q, J = 24.4 Hz), 66.52, 72.68, 75.19 (q, J = 2.2 Hz), 122.05 (q, J = 2.0 Hz),126.92 (q, J = 281.1 Hz), 127.70, 128.38, 132.95, 137.84. IR. 3480, 3034, 2961, 2870, 1717 cm^{-1}.

(b) To a solution of the above compound (500 mg, 1.58 mmol) in methanol (10 mL) at −78 °C was bubbled excess O_3, and then the whole was stirred for several hours at −78 °C. To the above solution was added $NaBH_4$, and the whole was stirred for 1 h at −78 °C and then was stirred for 1 h at −40 °C. Further, the mixture was stirred at room-temperature overnight. On removal of the solvent, product was purified by chromatography on silica gel using a mixture solution of hexane and ethyl acetate to give compound **11** (69 mg). Compound **11** (69 mg), DMF (5 mL), phenyldimethylacetal (0.67 mmol), and a catalytic amount of TsOH was stirred at 65 °C and worked up similarly. The resultant crude product was purified by chromatography on silica gel using a mixture solution of hexane and ethyl acetate, giving benzylidene acetal **12** (44 mg).

^1H NMR ($CDCl_3$): δ 1.05 (9 H, s), 2.65 (1 H, m), 3.71 (1 H, d, J = 6.87 Hz), 4.04 (1 H, dd, J = 11.68, 5.22 Hz), 4.22 (1 H, ddq, J = 11.61, 4.40, 1.28 Hz), 5.64 (1 H, s),7.3−7.5 (Ar−H, m); ^{19}F NMR ($CDCl_3$): δ 95.73 (d, J = 9.48 Hz). ^{13}C NMR ($CDCl_3$): δ 25.67, 35.30, 41.39 (q, J = 24.9 Hz), 60.51 (q, J = 4.3 Hz), 81.59 (q, J = 1.4 Hz), 98.79, 125.65, 126.20 (q, J = 279.3 Hz),128.11, 128.65, 138.84. IR. 2963, 2366 cm^{-1}. Anal. Calcd for $C_{15}H_{19}F_3O_2$: C, 62.49; H, 6.64. Found. C, 62.24; H, 6.51.

1-(Trifluoromethyl)-3-[(benzyloxy)methyl]-4-hydroxy-1-octyne 14a. (a) To a solution of $Pd(PPh_3)_4$ (0.05 equiv, 36 mg) and dichloromethane (5 mL) were added 5-(benzyloxy)-4-(mesyloxy)-1,1,1-trifluoro-2-pentyne **13a**[12e] (200 mg, 0.620 mmol) and pentanal (0.132 mL, 1.24 mmol) at 0 °C under an argon atmosphere, and then the mixture was stirred for a few minutes at that temperature. To the above solution was added Et_2Zn (1.49 mmol: 1 M solution in hexane), the whole was stirred for 7 h to warm from 0 °C to room temperature, and then the mixture was quenched with 1 N HCl and then worked up similarly. The yield (61%) and diastereomeric ratio (89:11) were determined by the ^{19}F NMR integral intensities using benzotrifluoride as an internal standard. As 1-(trifluoromethyl)-3-(benzyloxy)methyl-4-hydroxy-1-octyne **14a** was not purified for spectroscopy, the compound was converted to the acetate derivative by the following method.

To a solution of 1-(trifluoromethyl)-3-[(benzyloxy)methyl]-4-hydroxy-1-octyne **14a** and pyridine (1.5 mmol) in dichloromethane was added acetyl chloride (1.0 mmol) at 0 °C under an argon atmosphere, and then the mixture was stirred at that temperature. The mixture was warmed to room tempetrature and then worked up similarly. On removal of the solvent, the crude product was purified by chromatography on silica gel using a mixture solution of hexane and ethyl acetate, giving acetoxy derivative in a 43% yield (94 mg).

Acetate Derivative of Compound 14a. ^1H NMR ($CDCl_3$): δ 0.90 (3 H, t, J = 7.00 Hz), 1.2−1.4 (4 H, m), 1.6−1.8 (2 H, m), 2.04 (3 H, s), 3.00 (1 H, m), 3.51 (1 H, dd, J = 9.06, 7.14 Hz), 3.57 (1 H, dd, J = 9.21, 6.46 Hz), 4.52 (2 H, s), 5.14 (1 H, ddd, J = 8.10, 5.63, 3.57 Hz), 7.2−7.4 (Ar−H, m);^{19}F NMR ($CDCl_3$): δ 111.88 (d, J = 3.44 Hz). ^{13}C NMR ($CDCl_3$): δ 13.88, 20.79, 22.38, 27.47, 32.17, 36.79, 68.08, 70.53, 71.09 (q, J = 52.2 Hz), 73.27, 85.62 (q, J = 6.0 Hz), 113.78 (q, J = 256.3 Hz), 127.63, 127.71, 128.29, 137.27, 170.08. IR: 2959, 2271, 1743 cm^{-1}. Anal. Calcd for $C_{19}H_{23}F_3O_3$: C, 64.03; H, 6.51. Found. C, 64.04; H, 6.76.

1-(Trifluoromethyl)-3-*tert*-butyl-4-hydroxy-1-octyne 14b. (a) In the above reaction, $Pd(PPh_3)_4$ (0.05 equiv, 45 mg), 4-(mesyloxy)-5,5-dimethyl-1,1,1-trifluoro-2-pentyne **13b**[12e] (200 mg, 0.774 mmol), Et_2Zn (2.4 equiv, 1.85 mL; 1 M solution in hexane), and pentanal (2.0 equiv, 0.164 mL) in dichloromethane (5 mL) were used and worked up similarly. The yield (72%) and diastereomeric ratio (>99:<1) were determined by the ^{19}F NMR integral intensities. As 1-(trifluoromethyl)-3-*tert*-butyl-4-hydroxy-1-octyne **14b** was not purified for spectroscopy, the compound was converted to acetate derivative.

1-(Trifluoromethyl)-3-*tert*-butyl-4-hydroxy-1-octyne **14b**, pyridine (1.5 mmol), and acetyl chloride (1.0 mmol) in dichloromethane were used and worked up similarly. On removal of the solvent, the crude product was purified by chromatography on silica gel using a mixture solution of hexane and ethyl acetate, giving the acetoxy derivative in a 51% yield (116 mg).

Acetate Derivative of Compound 14b. ^1H NMR ($CDCl_3$): δ 0.90 (3 H, t, J = 7.14 Hz), 1.02 (9 H, s), 1.2−1.4 (4 H, m), 1.5−1.6 (1 H, m), 1.6−1.8 (1 H, m), 2.07 (3 H, s), 2.40 (1 H, qd, J = 3.71, 1.79 Hz), 5.15 (1 H, td, J = 6.87, 1.92 Hz);^{19}F NMR ($CDCl_3$): δ 112.40 (d, J = 4.31 Hz). ^{13}C NMR ($CDCl_3$): δ 13.76, 21.08, 22.36, 27.58, 27.96, 33.74, 34.40, 46.65, 70.34, 72.19 (q, J = 51.9 Hz), 87.11 (q, J = 6.4 Hz), 114.12 (q, J = 256.2 Hz), 170.30. IR: 2964, 2264, 1742 cm^{-1}. Anal. Calcd for $C_{15}H_{23}F_3O_2$: C, 61.63; H, 7.93. Found. C, 61.76; H, 7.82.

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