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Synthetic Organic Chemistry with 2-Ethoxy-2-(phenylselenenyl)perfluoroalk-2-enenitrile: Application to α-Cyanoperfluoroacylation of Aldehydes

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(*Z*)- and (*E*)-2-Ethoxyperfluoro-2-(phenylselenenyl)alk-2-enenitriles **2**−**4** prepared by our original method underwent transmetalation on treatment with *n*-BuLi or EtMgBr, and the successive reaction with aldehyde and ketones afforded the corresponding allylic alcohols **10a**−**f**, **9a**, and **11a**,**b** in good to high yields. Hydrolysis of the alcohols gave α-cyano-α,*β*-unsaturated perfluoroalkyl ketones **13a**−**c**, **13e**, **12a**, and **15a**. α-Cyanoperfluoroalkyl ketones were easily converted to α,*β*-unsaturated 3-aryl-2-cyanoallylic alcohols **18**−**22** having interesting biological activities and chemical reactivities.

While Knoevenagel reactions are well-known as a useful synthetic procedure for the preparation of α,*β*-unsaturated ketones and esters,[1] application of this method to the preparation of the α,*β*-unsaturated perfluoroalkyl ketones is difficult.[2] These compounds have been widely utilized as novel starting materials to obtain fluorine-containing biologically active compounds[3] via other multistep routes.[4] Therefore, intensive efforts have been made by organic and fluorine chemists to find new methodology for praparation of α,*β*-unsaturated perfluoroalkyl ketones. Recently, we have reported both perfluoroacylation[5] and α-cyano formylation[6] of aldehydes and ketones based on a Wittig-type olefination using *β*-alkoxy alkenyllithium. A simple two-step process is shown in Figure 1: electrophilic addition of the *β*-alkoxy alkenyllithium with aldehydes or ketones, followed by hydrolysis of the allylic alcohols obtained from the first step. α-Cyano-α,*β*-unsaturated perfluoroalkyl ketones are also an almost unknown chemical species for the same above reasons. If a novel α-cyano perfluoroacylation of aldehydes and ketones is achieved, it will provide a novel and convenient method for α,*β*-unsaturated α-cyano perfluoroalkyl ketones as shown in Figure 1. We selected

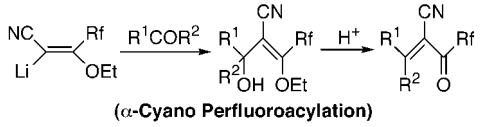
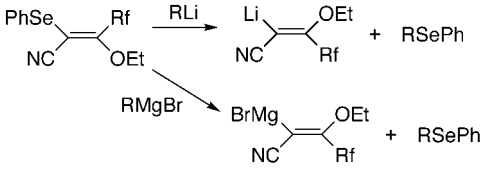
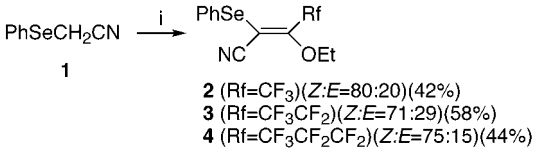


FIGURE 1.

SCHEME 1. Transmetalation of *β*-Ethoxy-*β*-perfluoroalkyl-α-(phenylselenenyl)acrylonitrile



SCHEME 2[a]



[a] Reagents: (i) lithium 2,2,6,6-tetramethylpiperidide (LTMP)/−78 °C/RfCO$_2$Et/MsCl.

new vinylic selenides as a precursor for the *β*-alkoxy alkenyllithiums. α-Cyano vinylic selenides would provide two kinds of alkenylmetals via transmetalation of the *β*-ethoxy-*β*-perfluoroalkyl-α-(phenylselenenyl)acrylonitriles as shown in Scheme 1. Here we report a novel preparation of α-cyano-α,*β*-unsaturated perfluoroalkyl ketones via a Wittig-type olefination and its convenient conversion to 2-cyanoallylic alcohols.

We first examined the preparation of vinylic selenides **2**−**4** by our original method using (phenylselenenyl)-acetonitrile **1** as shown in Scheme 2. Acetonitrile **1** was treated with lithium 2,2,6,6-tetramethylpiperidide (LTMP)

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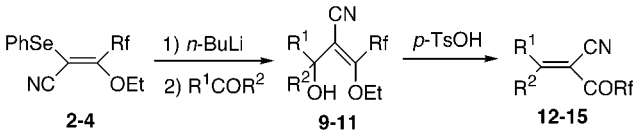
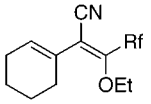
TABLE 1. α-Cyanoperfluoroacylation of Aldehydes and Ketones with *β*-Ethoxy Alkenyllithium



2-4 9-11 12-15

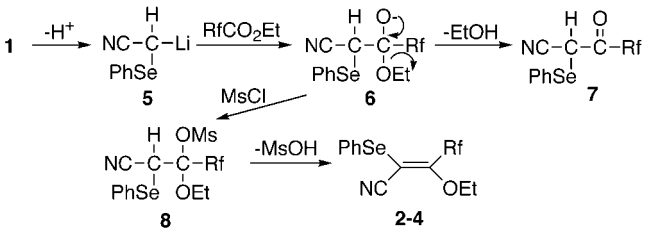
entry	vinyl selenide (Rf)	conditions[a]	R^1	R^2	alcohol (% yield)	product (% yield)
1	**3** (CF_2CF_3)	A	mesityl	H	**10a** (67)	**13a** (54)
2		B	mesityl	H	**10a** (47)	
3		A	*p*-methoxyphenyl	H	**10b** (54)	**13b** (46)
4		A	*p*-bromophenyl	H	**10c** (54)	**13c** (10)
5		A	$(CH_2)_5$		**10d** (31)	**14** (43)[b]
6		B	$(CH_2)_5$		**10d** (57)	
7		A	styryl	H	**10e** (46)	**13e** (55)
8		A	phenylethynyl	H	**10f** (60)	
9	**2** (CF_3)	A	mesityl	H	**9a** (17)	**12a** (78)
10		B	mesityl	H	**9a** (51)	
11	**4** ($CF_2CF_2CF_3$)	A	mesityl	H	**11a** (50)	**15a** (59)
12		B	mesityl	H	**11a** (78)	
13		A	$(CH_2)_5$		**11b** (49)	**16** (40)[b]

[a] Condition A: *n*-BuLi/THF/−78 °C. Condition B: $EtMgBr/Et_2O$/−78 °C. [b] Structure for **14** and **16**:



14 ($Rf=CF_2CF_3$)
16 ($Rf=CF_2CF_2CF_3$)

SCHEME 3



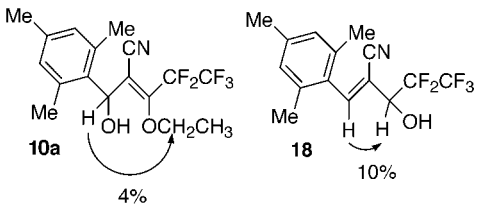
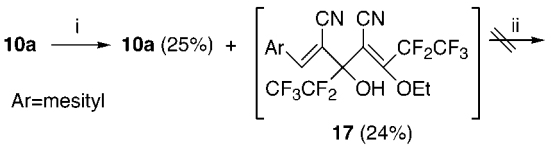


FIGURE 2.

at −78 °C, and the successive addition of $RfCO_2Et$ and then MsCl gave the corresponding vinylic selenides **2**−**4**, respectively. The mechanism of the new preparative method for the vinylic selenides is shown in Scheme 3. Deprotonation of **1** with LTMP gives α-seleno carbanion **5**, which is treated with ethyl perfluoroalkanoate to give the intermediate **6**. Since perfluoroalkyl ketone **7** could not be detected in the reaction products, the rate of the de-ethoxylation of **6** would be very slow. Methanesulfonylation of **6** affords **8**, which undergoes demethanesulfonylation to give the desired selenides **2**−**4**.

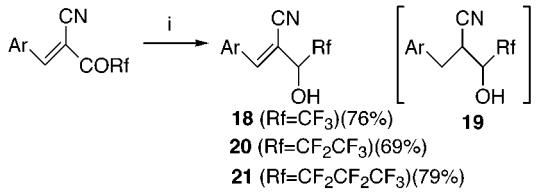
The transmetalation of **3** with *n*-BuLi (condition A) easily proceeded, and successive treatment with mesityl aldehyde afforded the allylic alcohol (*E*)-**10a** in good yield. The structure of **10a** was determined by the IR spectral data, showing the absorption in both hydroxy and cyano groups at ν 3750−3150 and 2220 cm^{-1} by ^1H NMR spectral data and the hydroxy and its α-proton at δ 2.97 (br s, OH) and 5.93 (br s, CHOH). Mass and elemental analyses show the molecular formula as $C_{17}H_{18}F_5NO_2$. The stereochemistry of **10a** was determined as *E* by NOE enhancement as shown in Figure 2. Irradiation of the ethoxy methylene protons of **10a** increased the intensity of the α-proton of the hydroxy group. The reaction of **3** with EtMgBr (condition B)/mesityl aldehyde gave **10a** in almost the same yield. However, trifluoromethyl vinylic selenide **2** resulted in a low yield of alcohol **9a** by condition A. We observed the changes in the reaction mixture after the addition of *n*-BuLi to a THF solution of **2**. The color of the reaction mixture quickly changed to red and then to a dark-brown suspension. Nevertheless, the addition of aldehyde to the mixture gave rise to low yields of the products. On the other hand, condition B succeeded in providing allylic alcohol **9a** in moderate yield (entry 10). The reactions with various aldehydes and ketones were examined and the results are shown in Table 1. Next, we performed the hydrolysis of **10a** using protic or Lewis acids and found that *p*-toluenesulfonic acid was effective for the α-cyano perfluoroacylation. The hydrolysis of **10a**−**c**, **9a**, and **11a** afforded the corresponding α,*β*-unsaturated perfluoroalkyl ketones **13a**−**c**, **13e**, and **12a**, respectively. The representative structure of α,*β*-unsaturated perfluoroalkyl ketone **13a** is shown as follows. The IR spectrum shows two characteristic absorptions of both cyano and carbonyl groups at ν 2220 (CN) and 1720 (CO) cm^{-1}. Furthermore, ^1H NMR exhibits an olefinic proton at δ 6.98 ppm as a singlet. ^{19}F NMR also exhibits a single isomer of the pentafluoroethyl absorptions at δ −46.87 and −3.67 ppm. Mass and elemental analyses show the corresponding molecular formula as $C_{15}H_{12}F_5NO$. The stereochemistry of **13a** was determined after leading to allylic alcohol **18** by the reduction of **13a** as shown below. NOE enhancement between the olefinic and the methine protons of **18** was observed as 10%. The elimination of allylic alcohols **10d** and **11b** gave the dienes **14** and **16**, not the α,*β*-unsaturated ketones. Next, we attempted a tandem

SCHEME 4[a]



[a] Reagents: (i) *n*-BuLi/PhSe(NC)C=C(OEt)CF_2CF_3/−78 °C; (ii) *p*-TosOH/$ClCH_2CH_2Cl$/83 °C.

SCHEME 5[a]



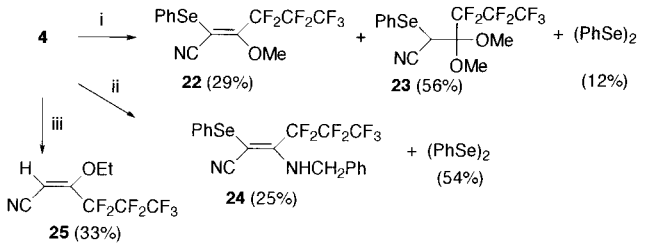
[a] Reagent: (i) $NaBH_4$/EtOH/0 °C.

α-cyano perfluoroacylation; however, the hydroysis of the penta-1,4-dien-3-ol **17** afforded a complex mixture (Scheme 4).

On the other hand, 3-substituted 2-cyanoallylic alcohols have been an important raw material in food chemistry,[7] in the synthesis of nuciferol precursors[8] and naturally occurring derivatives which have been used for fragnance enhancement. A few multistep routes are known in the literature. One strategy is based on the use of epoxide functionalization of 2-cyanoacrylic acid esters involving epoxidation−reduction−de-epoxidation.[9] Another pathway to the 2-cyanoallylic alcohols is based on rearrangement of the Baylis−Hillman products involving a bromination−formylation−hydrolysis process.[10] It is not possible to reduce the 2-cyanoacrylic acid ester or its derivatives even under mild conditions by using $NaBH_4$/EtOH to provide the saturated alcohols, exclusively. A simple and general synthetic method for the preparation of 2-cyanoallylic alcohols has not been reported. The products we obtained here are novel precursors for the fluorine-containing 2-cyanoallylic alcohol by a convenient method. The trifluoromethyl ketone **12a** was reduced under the conditions ($NaBH_4$/EtOH/0 °C) to give 2-cyanoallylic alcohol **18** in 76% yield (Scheme 5). The further reduced product **19** was not observed. Pentafluoroethyl and heptafluoropropyl ketone **13a** and **15a** provided the corresponding alcohols **20** and **21**, respectively.

Furthermore, we examined the transformation of the new α-cyanovinylic selenides as shown in Scheme 6. The nucleophilc reaction with sodium methoxide to **4** occurred at the *β*-position of the cyano group and afforded *β*-methoxy vinylic selenide **22** and acetal **23**. The reaction with benzylamine gave the *β*-amino vinylic selenide **24**, accompanied by diphenyl diselenide. Surprisingly, the reaction with sodium benzenethiolate underwent reduction of the selenenyl function of the vinylic selenide **4** to give the acrylonitrile in 33% yield.

SCHEME 6[a]



[a] Reagents: (i) MeONa/0 °C; (ii) $BnNH_2$/$ClCH_2CH_2Cl$/83 °C; (iii) PhSNa/THF/0 °C.

Experimental Section[5]

The elemental analysis were measured by the Yanako CHN corder (MT-6) by the autosampling system at the Center of Instrumentation of Gifu University. The stereochemistries of the vinylic selenides **2**−**4** were determined by the NOE enhancements between the ethoxy methylene protons and the ortho-aromatic protons. High-resolution mass was obtained by using a JEOL Gcmate spectrometer with a direct-insertion probe at an ionization voltage of 70 eV.

Preparation of (*Z*)- and (*E*)-3-Ethoxy-4,4,5,5,5-pentafluoro-2-(phenylseleno)-2-pentenenitrile (3), Typical Procedure. Under an Ar atmosphere, a THF (5.00 mL) solution of phenylselenoacetonitrile (2.89 g, 14.7 mmol) was added dropwise to a THF (20.0 mL) solution of 2,2,6,6-tetramethylpiperidide (prepared from 2,2,6,6-tetramethylpiperidine (4.16 g, 29.5 mmol) and *n*-BuLi (14.7 mL, 22.1 mmol)) at −78 °C. After the mixture was stirred for 10 min, ethyl pentafluoropropionate (3.36 mL, 22.1 mmol) and then a THF (5.00 mL) solution of methanesulfonyl chloride (2.53 g, 22.1 mmol) were added dropwise. The whole solution was stirred for 10 min and poured into water (150 mL). The organic solvent was removed and the aqueous layer was extracted with ether. The combined organic layer was dried over $MgSO_4$. The solvent was removed under reduced pressure. The residue was purified by column chromatography on silica gel eluting with EtOAc−*n*-hexane (1:20) to give (*Z*)- and (*E*)-3-ethoxy-4,4,5,5,5-pentafluoro-2-(phenylseleno)-2-pentenenitrile (**3**) as a yellow oil. The stereochemistries of (*E*)- and (*Z*)-**3**, **2**, and **4** were determined by the NOE enhacements of (*Z*)-isomers. Irradiation of the ethoxy methylene protons increased the intensities of the ortho-aromatic protons as follows ((*Z*)-**3** (1%), (*Z*)-**2** (1%), (*Z*)-**4** (7%)).

(*Z*)- and (*E*)-3-Ethoxy-4,4,5,5,5-pentafluoro-2-(phenylseleno)-2-pentenenitrile (3): *Z*:*E* = 71:29; IR (film, cm^{-1}) 2210 (CN); ^1H NMR *δ* 1.39 (t, *J* = 7 Hz, *Z*-Me), 1.45 (t, *J* = 7 Hz, *E*-Me), 4.25 (q, *J* = 7 Hz, *E*-CH_2), 4.45 (q, *J* = 7 Hz, *Z*-CH_2), 7.38−7.50 (m, *E*- and *Z*-ArH), 7.65−7.69 (m, *E*- and *Z*-ArH); ^{19}F NMR *δ* −36.20 (d, *J* = 3 Hz, *E*-CF_2), −34.25 (d, *J* = 2 Hz, *Z*-CF_2), −34.24 (d, *J* = 2 Hz, *Z*-CF_2), −5.13 (t, *J* = 2 Hz, *E*-CF_3), −4.39 (t, *J* = 2 Hz, *Z*-CF_3); MS *m*/*z* 371 (M^+). Anal. Calcd for $C_{13}H_{10}F_5NOSe$: C, 42.18; H, 2.72; N, 3.78. Found: C, 42.55; H, 2.84; N, 3.75.

(*Z*)- and (*E*)-3-Ethoxy-4,4,4-trifluoro-2-(phenylseleno)-2-butenenitrile (2): a yellow oil; *Z*:*E* = 80:20; IR (film, cm^{-1}) 2200 (CN); ^1H NMR (400 MHz, $CDCl_3$) *δ* 1.40 (t, *J* = 7 Hz, *Z*-Me), 1.45 (t, *J* = 7 Hz, E-Me), 7.36−7.49 (m, ArH), 7.60−7.72 (m, ArH); MS *m*/*z* 241 (M^+). Anal. Calcd for $C_{12}H_{10}F_3NOSe$: C, 45.02; H, 3.15; N, 4.37. Found: C, 44.72; H, 3.21; N, 3.54.

(*Z*)- and (*E*)-3-Ethoxy-4,4,5,5,6,6,6-heptafluoro-2-(phenylseleno)-2-hexenenitrile (4): a yellow oil; *Z*:*E* = 75:15; IR

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(film, cm^{-1}) 2210 (CN); ^1H NMR (400 MHz, $CDCl_3$) δ 1.38 (t, J = 7 Hz, *Z*-Me), 1.46 (t, J = 7 Hz, *E*-Me), 4.25 (q, J = 7 Hz, *E*-OCH_2), 4.42 (q, J = 7 Hz, *Z*-OCH_2), 7.25−7.48 (m, ArH), 7.64−7.68 (m, ArH); ^{19}F NMR δ −48.42 (s, *E*-CF_2), −47.93 (t, J = 12 Hz, *Z*-CF_2), −33.97 (d, J = 9 Hz, *E*-CF_2), −32.67 (br d, J = 9, *Z*-CF_2), −2.77 (t, J = 9 Hz, *E*-CF_3), −2.73 (t, J = 9 Hz, *Z*-CF_3); MS *m*/*z* 421 (M^+). Anal. Calcd for $C_{14}H_{10}F_7NOSe$: C, 40.01; H, 2.39; N, 3.33. Found: C, 39.65; H, 2.56; N, 3.32.

Reactions of 2-Lithio-3-ethoxy-3-perfluoroalkyl-2-alkenenitrile with Aldehydes and Ketones, Typical Procedure. Under an Ar atmosphere, *n*-BuLi (0.50 mL, 0.75 mmol) was added dropwise to a THF (3.00 mL) solution of **3** (0.18 g, 0.50 mmol) at −78 °C and the mixture was stirred for 10 min. Then a THF (1.00 mL) solution of mesityl aldehyde (0.11 g, 0.73 mmol) was added to the mixture. The whole solution was stirred for 10 min and poured into water (100 mL). The organic layer was separated and the aqueous layer was extracted with ether. The combined organic layer was dried over $MgSO_4$. The solvent was removed under reduced pressure. The residue was purified by preparative TLC on silica gel eluting with AcOEt−hexane (1:3). (*E*)-2-Cyano-3-ethoxy-4,4,5,5,5-pentafluoro-1-mesitylpent-2-en-1-ol (**10a**) (0.12 g, 67%) was obtained as colorless prisms (mp 60−63 °C).

10a: IR (film, cm^{-1}) 3750−3160 (OH), 2220 (CN); ^1H NMR (400 MHz, $CDCl_3$) δ 0.96 (3H, t, J = 7 Hz, Me), 2.25 (3H, s, Me), 2.40 (6H, s, Mex2), 2.97 (1H, br s, OH), 3.14−3.19 (1H, m, OCH_2), 3.84−3.92 (1H, m, OCH_2), 5.93 (1H, br s, CHO), 6.84 (2H, br s, ArH); ^{19}F NMR δ −36.62 (1F, d, J = 282 Hz, CF_2), −34.87 (1F, d, J = 282 Hz, CF_2), −5.02 (3F, t, J = 2 Hz, CF_3); MS *m*/*z* 363 (M^+). Anal. Calcd for $C_{17}H_{18}F_5NO_2$: C, 56.20; H, 4.99; N, 3.85. Found: C, 56.09; H, 5.01; N, 3.79.

Reaction of 3-Ethoxy-3-perfluoroalkyl-2-alkenenitril-2-yl Magnesium Bromide with Aldehydes and Ketones, Typical Procedure. An Et_2O solution of EtMgBr (1.00 mL, 1.00 mmol) was added dropwise to a THF (2.00 mL) solution of **3** (0.10 g, 0.27 mmol) under an Ar atmosphere. The reaction mixture was stirred for 10 min. Then the electrophile was added to the mixture at the same temperature. The workup procedure afforded the results as shown in Table 1.

(*E*)-2-Cyano-3-ethoxy-4,4,5,5,5-pentafluoro-1-(4-methoxyphenyl)pent-2-en-1-ol (10b): IR (film, cm^{-1}) 3800−3160 (OH), 2300 (CN); ^1H NMR (400 MHz, $CDCl_3$) δ 1.24 (3H, t, J = 7 Hz, Me), 3.48 (1H, br s, OH), 3.79 (3H, s, OMe), 4.02−4.15 (2H, m, OCH_2), 5.79 (1H, s, CHO), 6.94 (2H, d, J = 9 Hz, ArH), 7.28 (2H, d, J = 9 Hz, ArH); ^{19}F NMR δ −37.20 (2F, d, J = 3 Hz, CF_2), −5.22 (3F, t, J = 2 Hz, CF_3); MS *m*/*z* 351 (M^+). Anal. Calcd for $C_{15}H_{14}F_5NO_3$: C, 51.29; H, 4.02; N, 3.99. Found: C, 51.69; H, 4.31; N, 3.70.

(*E*)-2-Cyano-3-ethoxy-4,4,5,5,5-pentafluoro-1-(4-bromophenyl)pent-2-en-1-ol (10c): IR (film, cm^{-1}) 3600−3300 (OH), 2250 (CN); ^1H NMR (400 MHz, $CDCl_3$) δ 1.38 (3H, t, J = 7 Hz, Me), 3.69 (1H, br s, OH), 4.13 (2H, q, J = 7 Hz, OCH_2), 5.80 (1H, s, CHO), 7.26 (2H, br d, J = 8 Hz, ArH), 7.49 (2H, br d, J = 8 Hz, ArH); ^{19}F NMR δ −37.12 (2F, d, J = 10 Hz, CF_2), −5.23 (3F, t, J = 2 Hz, CF_3); MS *m*/*z* 399 (M^+). Anal. Calcd for $C_{14}H_{11}BrF_5NO_2$: C, 42.02; H, 2.77; N, 3.50. Found: C, 42.34; H, 3.03; N, 3.23.

(*E*)-1-[2-(3-Ethoxy-4,4,5,5,5-pentafluoro-2-pentenenitrilyl)]cyclohexanol (10d): IR (film, cm^{-1}) 3600−3300 (OH), 2200 (CN); ^1H NMR (400 MHz, $CDCl_3$) δ 1.22−1.32 (1H, m, CH_2), 1.41 (3H, t, J = 7 Hz, Me), 1.57−1.92 (10H, m, CH_2), 3.01 (1H, br s, OH), 4.18 (2H, q, J = 7 Hz, OCH_2); ^{19}F NMR δ −35.29 (2F, s, CF_2), −5.15 (3F, t, J = 1 Hz, CF_3); MS *m*/*z* 320 (M^+).

(1*E*,4*E*)-4-Cyano-5-ethoxy-6,6,7,7,7-pentafluoro-1-phenylhepta-1,4-dien-3-ol (10e): a yellow oil; IR (film, cm^{-1}) 3600−3300 (OH), 2220 (CN); ^1H NMR (400 MHz, $CDCl_3$) δ 1.39 (3H, t, J = 7 Hz, Me), 3.41 (1H, br s, OH), 4.07−4.18 (2H, m, OCH_2), 5.40 (1H, d, J = 6 Hz, CHO), 6.28 (1H, dd, J = 16 and 7 Hz, olefinic H), 6.74 (1H, d, J = 16 Hz, olefinic H), 7.24−7.34 (3H, m, ArH), 7.36−7.40 (2H, m, ArH); ^{19}F NMR δ −37.29 (2F, s, CF_2), −5.13 (3F, d, J = 2 Hz, CF_3); MS *m*/*z* 347 (M^+). Anal. Calcd for $C_{16}H_{14}F_5NO_2$: C, 55.33; H, 4.06; N, 4.03. Found: C, 55.61; H, 4.23; N, 3.63.

(*E*)-4-Cyano-5-ethoxy-6,6,7,7,7-pentafluoro-1-phenylhept-4-en-1-yn-3-ol (10f): a yellow oil; IR (film, cm^{-1}) 3600−3300 (OH), 2230 (CN); ^1H NMR (400 MHz, $CDCl_3$) δ 1.40 (3H, t, J = 7 Hz, Me), 3.50 (1H, br s, OH), 4.20 (2H, q, J = 7 Hz, OCH_2), 5.65 (1H, br s, CHO), 7.24−7.38 (3H, m, ArH), 7.43−7.81 (2H, m, ArH); ^{19}F NMR δ −37.61 (2F, t, J = 3 Hz, CF_2), −5.05 (3F, br s, CF_3); MS *m*/*z* 345 (M^+). Anal. Calcd for $C_{16}H_{12}F_5NO_2$: C, 56.66; H, 3.58; N, 4.05. Found: C, 56.32; H, 3.76; N, 3.88.

(*E*)-2-Cyano-3-ethoxy-4,4,4-trifluoro-1-mesitylbut-2-en-1-ol (9a): a yellow oil; IR (film, cm^{-1}) 3650−3000 (OH), 2250 (CN); ^1H NMR (400 MHz, $CDCl_3$) δ 0.97 (3H, t, J = 7 Hz, Me), 2.25 (3H, s, Me), 2.41 (6H, s, Mex2), 2.62 (1H, br s, OH), 3.21−3.30 (1H, m, OCH_2), 3.85−3.94 (1H, m, OCH_2), 5.91 (1H, br d, J = 2 Hz, CHO), 6.85 (2H, br s, ArH); ^{19}F NMR δ −14.25 (3F, s, CF_3); MS *m*/*z* 313 (M^+). Anal. Calcd for $C_{16}H_{18}F_3NO_2$: C, 61.34; H, 5.79; N, 4.47. Found: C, 60.94; H, 5.69; N, 4.38.

(*E*)-2-Cyano-3-ethoxy-4,4,5,5,6,6,6-heptafluoro-1-mesitylhex-2-en-1-ol (11a): white powders, mp 56−58 °C; IR (film, cm^{-1}) 3600−3300 (OH), 2230 (CN); ^1H NMR (400 MHz, $CDCl_3$) δ 1.05 (3H, t, J = 7 Hz, Me), 2.26 (3H, s, Me), 2.40 (1H, br s, OH), 2.43 (6H, s, Mex2), 3.20−3.26 (1H, m, OCH_2), 3.89−3.95 (1H, m, OCH_2), 6.02 (1H, br d, J = 2 Hz, CHO), 6.87 (2H, br s, ArH); ^{19}F NMR δ −48.56 (1F, d, J = 290 Hz, CF_2), −47.43 (1F, d, J = 290 Hz, CF_2), −33.97 (1F, dd, J = 293 and 7 Hz, CF_2), −32.76 (1F, dd, J = 293 and 7 Hz, CF_2), −2.75 (3F, t, J = 9 Hz, CF_3); MS *m*/*z* 413 (M^+). Anal. Calcd for $C_{18}H_{18}F_7NO_2$: C, 52.30; H, 4.39; N, 3.38. Found: C, 52.09; H, 4.42; N, 3.41.

(*E*)-1-[2-(3-Ethoxy-4,4,5,5,6,6,6-heptafluoro-2-hexenenitrilyl)cyclohexanol (11b): a yellow oil; IR (film, cm^{-1}) 3600−3200 (OH), 2210 (CN); ^1H NMR (400 MHz, $CDCl_3$) δ 1.24−1.30 (1H, m, CH_2), 1.41 (3H, t, J = 7 Hz, Me), 1.58−1.93 (9H, m, CH_2), 2.35 (1H, br s, OH), 4.19 (2H, q, J = 7 Hz, OCH_2); ^{19}F NMR δ −48.42 (2F, s, CF_2), −33.29 (2F, q, J = 9 Hz, CF_2), −2.97 (3F, t, J = 9 Hz, CF_3); MS *m*/*z* 149.

(1*Z*,4*E*)-2,4-Dicyano-5-ethoxy-6,6,7,7,7-pentafluoro-1-mesityl-3-pentafluoroethylhept-1,4-dien-3-ol (17): colorless prisms, mp 126−128 °C; IR 3500−3200 (OH), 2250 (CN); ^1H NMR (400 MHz, $CDCl_3$) δ 1.46 (3H, t, J = 7 Hz, Me), 2.21 (6H, s, Mex2), 2.28 (3H, s, Me), 4.31−4.43 (2H, m, OCH_2), 5.69 (1H, br s, OH), 6.91 (2H, s, ArH), 7.77 (1H, s, olefinic H); ^{19}F NMR δ −41.16 (2F, s, CF_2), −35.38 (2F, s, CF_2), −6.12 (3F, s, CF_3), −5.39 (3F, s, CF_3); MS *m*/*z* 532 (M^+). Anal. Calcd for $C_{22}H_{18}F_{10}N_2O_2$: C, 49.63; H, 3.41; N, 5.26. Found: C, 49.61; H, 3.56; N, 5.19.

Hydration of Allylic Alcohols 9−11, Typical Procedure. A $ClCH_2CH_2Cl$ (2.00 mL) solution of (*E*)-2-cyano-3-ethoxy-4,4,5,5,5-pentafluoro-1-mesitylpent-2-en-1-ol (**10a**) (0.17 g, 0.47 mmol) and *p*-toluenesulfonic acid (89 mg, 0.47 mmol) was refluxed for 10 min. A cooled mixture was poured into saturated $NaHCO_3$ (50 mL) and the organic layer was separated. The aqueous layer was extracted with $CHCl_3$. The combined organic layer was dried over $MgSO_4$. The solvent was removed under reduced pressure. The residue was purified by preparative TLC on silica gel eluting with AcOEt−hexane (1:3). (*E*)-2-Cyano-1-mesityl-4,4,5,5,5-pentafluoro-1-penten-3-one (**13a**) was obtained as a brown oil. **13a**: IR (film, cm^{-1}) 2200 (CN), 1720 (CO); ^1H NMR (400 MHz, $CDCl_3$) δ 2.32 (6H, s, Mex2), 2.33 (3H, s, Me), 6.98 (2H, s, ArH), 8.71 (1H, s, olefinic H); ^{19}F NMR δ −46.87 (2F, s, CF_2), −3.67 (3F, s, CF_3); MS *m*/*z* 317 (M^+). Anal. Calcd for $C_{15}H_{12}F_5NO$: C, 56.79; H, 3.81; N, 4.42. Found: C, 56.47; H, 4.18; N, 3.99.

(*E*)-2-Cyano-1-(4-methoxyphenyl)-4,4,5,5,5-pentafluoro-1-penten-3-one (13b): yellow plates, mp 66−73 °C; IR (film, cm^{-1}) 2200 (CN), 1700 (CO); ^1H NMR (400 MHz, $CDCl_3$) δ 3.95 (3H, s, OMe), 7.05 (2H, d, J = 7 Hz, ArH), 8.16 (2H, d, J = 7 Hz, ArH), 8.32 (1H, s, olefinic H); ^{19}F NMR δ −39.78 (2F, d, J = 1 Hz, CF_2), −3.74 (3F, d, J = 1 Hz, CF_3); MS *m*/*z* 305 (M^+).

Anal. Calcd for $C_{13}H_8F_5NO_2$: C, 51.16; H, 2.64; N, 4.59. Found: C, 51.18; H, 2.78; N, 4.61.

(*E*)-2-Cyano-1-(4-bromophenyl)-4,4,5,5,5-pentafluoro-1-penten-3-one (13c): yellow needles, mp 33 °C; IR (film, cm^{-1}) 2210 (CN), 1710 (CO); ^1H NMR (400 MHz, $CDCl_3$) δ 7.72 (2H, d, J = 7 Hz, ArH), 7.98 (2H, d, J = 7 Hz, ArH), 8.33 (1H, s, olefinic H); ^{19}F NMR δ −39.84 (2F, d, J = 1 Hz, CF_2), −3.72 (3F, s, CF_3); MS m/z 353 (M^+). Anal. Calcd for $C_{12}H_5BrF_5NO$: C, 40.71; H, 1.42; N, 3.96. Found: C, 40.53; H, 1.85; N, 3.25.

(*E*)-2-(1-Cyclohexenyl)-3-ethoxy-4,4,5,5,5-pentafluoropent-2-enenitrile (14): a yellow oil; IR (film, cm^{-1}) 2260 (CN); ^1H NMR (400 MHz, $CDCl_3$) δ 1.31 (3H, t, J = 7 Hz, Me), 1.61−1.74 (4H, m, CH_2), 2.21−2,23 (4H, m, CH_2), 4.00 (2H, q, J = 7 Hz, OCH_2), 6.12 (1H, br s, olefinic H); ^{19}F NMR δ −37.84 (2F, s, CF_2), −4.85 (3F, s, CF_3); MS m/z 295 (M^+).

(1*E*,4*E*)-4-Cyano-6,6,7,7,7-pentafluoro-1-phenylhepta-1,3-dienenitrile (13e): orange needles, mp 67−69 °C; IR 2210 (CN); ^1H NMR (400 MHz, $CDCl_3$) δ 7.41−7.68 (5H, m, ArH), 7.75−7.82 (2H, m, olefinic H), 8.32 (1H, d, J = 8 Hz, olefinic H); ^{19}F NMR δ −39.80 (2F, s, CF_2), −3.97 (3F, d, J = 1 Hz, CF_3); MS m/z 301 (M^+). Anal. Calcd for $C_{14}H_8F_5NO$: C, 55.83; H, 2.68; N, 4.65. Found: C, 55.46; H, 2.80; N, 4.57.

(*E*)-2-Cyano-4,4,4-trifluoro-1-mesityl-1-buten-3-one (12a): a yellow oil; IR 2250 (CN), 1620 (CO); ^1H NMR (400 MHz, $CDCl_3$) δ 2.20 (6H, s, Mex2), 2.27 (3H, s, Me), 6.92 (2H, s, ArH), 7.84 (1H, s, olefinic H); ^{19}F NMR δ − 5.12 (3F, s, CF_3); MS m/z 267 (M^+).

(*E*)-2-Cyano-4,4,5,5,6,6,6-heptafluoro-1-mesitylhex-1-en-3-one (15a): IR 2230 (CN), 1720 (CO); ^1H NMR (400 MHz, $CDCl_3$) δ 2.31 (6H, s, Mex2), 2.32 (3H, s, Me), 6.98 (2H, s, ArH), 8.70 (1H, s, olefinic H); ^{19}F NMR δ −48.05 (2F, t, J = 7 Hz, CF_2), −38.00 (2F, q, J = 10 Hz, CF_2), −2.78 (3F, t, J = 10 Hz, CF_3); MS m/z 367 (M^+). Anal. Calcd for $C_{16}H_{12}F_7NO$: C, 53.80; H, 3.28; N, 3.92. Found: C, 53.52; H, 3.27; N, 3.78.

(*E*)-2-(1-Cyclohexenyl)-3-ethoxy-4,4,5,5,6,6,6-heptafluoro-2-hexenenitrile (16): a yellow oil; IR 2220 (CN); ^1H NMR (400 MHz, $CDCl_3$) δ 1.31 (3H, t, J = 7 Hz, Me), 1.62−1.68 (2H, m, CH_2), 1.70−1.76 (2H, m, CH_2), 2.20−2.25 (4H, m, CH_2), 4.00 (2H, q, J = 7 Hz, OCH_2), 6.12 (1H, d, J = 2 Hz, olefinic H); ^{19}F NMR δ −48.35 (2F, t, J = 12 Hz, CF_2), −35.84 (2F, q, J = 9 Hz, CF_2), −2.89 (3H, t, J = 9 Hz, CF_3); MS m/z 318 (M^+ − Et).

Reduction of (*E*)-2-Cyano-4,4,4-trifluoro-1-mesityl-1-buten-3-one (13a), Typical Procedure. $NaBH_4$ (28.0 mg, 0.74 mmol) was added to a EtOH (2.00 mL) solution of the titled compound **13a** (0.10 g, 0.37 mmol) at 0 °C. The reaction mixture was stirred for 30 min. The workup procedure afforded (*E*)-2-cyano-4,4,4-trifluoro-1-mesityl-1-buten-3-ol (**18**) (76.0 mg, 76%) as colorless prisms.

18: mp 110−112 °C; IR 3441 (OH), 2260 (CN); ^1H NMR (400 MHz, $CDCl_3$) δ 2.19 (6H, s, Mex2), 2.27 (3H, s, Me), 4.12 (1H, q, J = 6 Hz, OH), 4.68 (1H, q, J = 6 Hz, CHO), 6.89 (2H, s, ArH), 7.57 (1H, s, olefinic H); ^{19}F NMR δ −0.30 (3F, d, J = 6 Hz, CF_3); MS m/z 269 (M^+). Anal. Calcd $C_{14}H_{14}F_3NO$: C, 62.45; H, 5.24; N, 5.20. Found: C, 62.29; H, 5.24; N, 5.05.

(*E*)-2-Cyano-4,4,5,5,5-pentafluoro-1-mesityl-1-penten-3-ol (20): mp 102−103 °C; IR 3392 (OH), 2245 (CN); ^1H NMR (400 MHz, $CDCl_3$) δ 2.18 (6H, s, Mex2), 2.27 (3H, s, Me), 4.02 (1H, br s, OH), 4.80 (1H, dd, J = 5 and 17 Hz, CHO), 6.89 (2H, s, ArH), 7.53 (1H, s, olefinic H); ^{19}F NMR δ −52.19 (2F, dd, J = 17 and 278 Hz, CF_2), −42.02 (2F, dd, J = 5 and 278 Hz, CF_2), −3.74 (3F, s, CF_3); MS m/z 302 (M^+ − OH). Anal. Calcd for $C_{14}H_{14}F_5NO$: C, 56.43; H, 4.42; N, 4.39. Found: C, 56.15; H, 4.45; N, 4.30.

(*E*)-2-Cyano-4,4,5,5,6,6,6-heptafluoro-1-mesityl-1-hexen-3-ol (21): mp 94−96 °C; IR 3395 (OH), 2246 (CN); ^1H NMR (400 MHz, $CDCl_3$) δ 2.19 (6H, s, Mex2), 2.27 (3H, s, Me), 4.13 (1H, br s, OH), 4.88 (1H, br d, J = 17 Hz, CHO), 6.89 (2H, s, ArH), 7.55 (1H, s, olefinic H); ^{19}F NMR δ −47.31 (2F, ddd, J = 5 and 11 and 293 Hz, CF_2), −39.53 (2F, br d, J = 287 Hz, CF_2), −3.40 (3F, dd, J = 8 and 11 Hz, CF_3); MS m/z 369 (M^+). Anal. Calcd for $C_{16}H_{14}F_7NO$: C, 52.04; H, 3.82; N, 3.79. Found: C, 51.79; H, 3.95; N, 3.61.

Reaction of (*Z*)- and (*E*)-3-Ethoxy-4,4,5,5,6,6,6-heptafluoro-2-(phenylselenenyl)-2-hexenenitrile (4) with NaOMe. NaOMe (1.00 mL, 1.00 mmol) in MeOH was added to a dry MeOH (1.00 mL) solution of **4** (0.20 g, 0.48 mmol) at 0 °C. The reaction mixture was stirred for 10 min and poured into water (100 mL). The organic layer was separated and the aqueous layer was extracted with ether. The combined organic layer was dried over $MgSO_4$. The solvent was removed under reduced pressure. The residue was purified by TLC on silica gel eluting with AcOEt−*n*-hexane (1:40) to give *(E)*-4,4,5,5,6,6,6-heptafluoro-2-(phenylselenenyl)-2-hexenenitrile (**22**) (0.06 g, 29%) and 4,4,5,5,6,6,6-heptafluoro-3,3-dimethoxy-2-(phenylselenenyl)hexanenitrile (**23**) (0.12 g, 56%) as a yellow oil, accompanied by diphenyl diselenide (0.01 g, 12%).

22: *E*:*Z* = 18:82; IR (cm^{-1}) 2250 (CN); ^1H NMR (400 MHz, $CDCl_3$) δ 4.00 (3H, s, OMe), 7.39−7.52 (3H, m, ArH), 7.66−7.70 (2H, m, ArH); (*E*)-**22** could not be detected by the ^1H NMR spectrum. ^{19}F NMR δ −48.99 (s, *E*-CF_2), −48.42 (s, *Z*-CF_2), −34.11 (q, J = 9 Hz, *E*-CF_2), −33.98 (2F, q, J = 9 Hz, *Z*-CF_2), −3.08 to −2.76 (m, *E*- and *Z*-CF_3); MS m/z 407 (M^+). Anal. Calcd for $C_{13}H_8NOSe$: C, 38.44; H, 1.98; N, 3.45. Found: C, 38.51; H, 2.31; N, 2.99.

23: IR (cm^{-1}) 2250 (CN); ^1H NMR (400 MHz, $CDCl_3$) δ 3.61 (3H, s, OMe), 3.66 (3H, s, OMe), 4.31 (1H, br s, CH), 7.35−7.47 (3H, m, ArH), 7.72−7.78 (2H, m, ArH); ^{19}F NMR δ −46.67 to −46.41 (2F, m, CF_2), −36.62 to −36.44 (2F, m, CF_2), −2.91 to −2.84 (3F, m, CF_3); MS m/z 392, 352, 312, 157 (PhSe). Anal. Calcd for $C_{14}H_{12}F_7O_2Se$: C, 38.37; H, 2.76; N, 3.20. Found: C, 38.63; H, 2.29; N, 3.02.

Reaction of 4 with Benzylamine. A benzene (2.00 mL) solution of **4** (0.20 g, 0.48 mmol) and benzylamine (0.10 g, 0.95 mmol) was refluxed for 10 h. The solvent was evaporated and the residue was purified by TLC on silica gel eluting with AcOEt−*n*-hexane (1:10) to give *(Z)*-3-benzylamino-4,4,5,5,6,6,6-heptafluoro-2-(phenylselenenyl)-2-hexenenitrile (**24**) (0.04 g, 54%) as a brown oil.

24: IR (cm^{-1}) 2220 (CN); ^1H NMR (400 MHz, $CDCl_3$) δ 4.52 (2H, d, CH_2), 7.00 (1H, s, NH), 7.30−7.42 (8H, m, ArH), 7.67−7.69 (2H, m, ArH); ^{19}F NMR δ −49.20 (2F, s, CF_2), −42.95 (2F, q, J = 8 Hz, CF_2), −2.86 (3F, t, J = 8 Hz, CF_3); MS m/z 180, 165, 152, 89, 76. Anal. Calcd for $C_{19}H_{13}F_7N_2Se$: C, 47.42; H, 2.72; N, 5.82. Found: C, 45.56; H, 3.13; N, 5.95.

Reaction of 4 with PhSNa. A THF (1.50 mL) solution of **4** (0.20 g, 0.48 mmol) was added to a THF (2.00 mL) solution of PhSNa (prepared from thiophenol (0.06 g, 0.57 mmol) and NaH (0.03 g, 0.71 mmol)) at 0 °C. The reaction mixture was stirred for 1 h and poured into water (50.0 mL). The organic layer was separated and the aqueous layer was extracted with ether. The combined organic layer was dried over $MgSO_4$. The solvent was removed under reduced pressure. The residue was purified by preparative TLC on silica gel eluting with AcOEt−*n*-hexane (1:10) to give *(E)*-3-ethoxy-4,4,5,5,6,6,6-heptafluoro-2-hexenenitrile (**25**) (0.03 g, 33%) as a pale yellow oil, accompanied by diphenyl diselenide (0.10 g, 55%).

25: IR (cm^{-1}) 2230 (CN); ^1H NMR (400 MHz, $CDCl_3$) δ 1.48 (3H, t, J = 7 Hz, Me), 3.98 (2H, q, J = 7 Hz, CH_2), 4.99 (1H, s, olefinic H); ^{19}F NMR δ −49.48 (2F, s, CF_2), −38.65 (2F, q, J = 9 Hz, CF_2), −3.36 (3F, t, J = 9 Hz, CF_3); MS m/z 259 (small M^+).

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