Nucleophilic Substitution and Claisen Rearrangement Reactions of Model Fluoroalkenes of General Structure R−CF=CF−CF_3

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Fluoroalkenes of general structure R−CF=CF−CF_3 (**2a**, R = cyclopentyl and **2b**, R = cyclohexyl), prepared in high yield in two steps from hexafluoropropene and the appropriate cycloalkane, react with oxygen, carbon, and hydrogen nucleophiles to give R−CX=CF−CF_3 derivatives (X = H, OR, R, Ar). Reaction of fluoroalkenes **2a** and **2b** with allylic alkoxides gave products arising from Claisen rearrangement, providing access to keto-alkenes bearing >$CFCF_3$ units in mid-aliphatic chain positions.

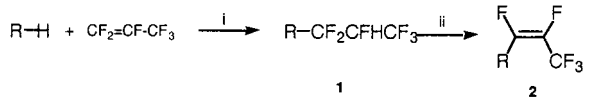
Introduction

There is continuing interest, in both academia and industry, in the development of efficient and general methodology for the selective introduction of fluorine and perfluoroalkyl groups into organic systems. This is exemplified by the fact that many commercially significant pharmaceuticals and plant protection agents owe their biological activity to the presence of, for example, a trifluoromethyl group within their structures,[1] e.g., the well-known antidepressant drug Prozac.

Syntheses of systems bearing perfluoroalkyl substituents remains a significant research challenge, and two approaches to the problem of introducing a perfluoroalkyl group into an organic molecule have been adopted. Although several effective perfluoroalkylating reagents have been developed,[2−4] a complementary "building block" approach[5] to the synthesis of molecules bearing perfluoroalkyl groups potentially offers greater synthetic applicability and versatility, provided, of course, a range of suitable "building-blocks" bearing perfluoroalkyl substituents are readily available.

The use of the carbon−hydrogen bond as a functional group in reactions between carbon-centered radicals, generated by carbon−hydrogen bond homolysis, with various fluoroalkenes has been developed considerably in these laboratories[6] In particular, reactions of various alkane,[7] alcohol,[6] and ether[8−10] substrates, initiated by either gamma rays or peroxides, with industrially available hexafluoropropene, are very efficient processes, and a range of polyfluorinated products have been synthesized on a preparatively useful scale (Scheme 1). It is perhaps worth reemphasizing here that no highly toxic tin derivatives (e.g., Bu_3SnH) are used as initiators, and so all these processes are appropriate for scale-up.

Scheme 1



Subsequent dehydrofluorination of the polyfluoroalkylated adducts **1** were accomplished[7] stereospecifically using sodium or potassium *tert*-butoxide, giving ready access to a range of potentially synthetically versatile fluoroalkenes **2** of general formula R−CF=CF−CF_3. (Scheme 1)

Of course, perfluoroalkenes are very susceptible to nucleophilic attack and, indeed, an extensive chemistry involving such processes has emerged.[11] However, related studies concerning nucleophilic substitution reactions involving alkenes bearing both perfluoroalkyl and alkyl groups, such as **2**, are relatively scarce. Consequently, we have explored reactions between model fluoroalkenes **2a** and **2b** and a range of nucleophiles, thus developing the use of such fluoroalkenes as "building-blocks" for the synthesis of organic derivatives bearing perfluoroalkyl units.

Results and Discussion

Fluoroalkenes **2a** and **2b** were prepared stereoselectively in two steps from hexafluoropropene and cyclopentane and -hexane, respectively, as described previously.[7] Reaction of **2b** with sodium methoxide, ethoxide, and cyclohexanoxide salts gave, upon heating in THF, **3**, **4**, and **5**, respectively (Table 1).

Nucleophilic substitution of the vinyllic fluorine atom at the R−CF= site, rather than the =$CFCF_3$ position,

(1) Banks, R. E.; Smart, B. E.; Tatlow, J. C., Eds. *Organofluorine Chemistry. Principles and Commercial Applications*; Plenum: New York, 1994.
(2) Dolbier, W. R. *Top. Curr. Chem.* **1997**, *192*, 97.
(3) Prakash, G. K. S.; Yudin, A. K. *Chem. Rev.* **1997**, *97*, 757.
(4) Umemoto, T. *Chem. Rev.* **1996**, *96*, 1757.
(5) Percy, J. M. *Top. Curr. Chem.* **1997**, *193*, 131.
(6) Chambers, R. D.; Diter, P.; Dunn, S. N.; Farren, C.; Sandford, G.; Batsanov, A. S.; Howard, J. A. K. *J. Chem. Soc., Perkin Trans 1* **2000**, 1639.
(7) Chambers, R. D.; Fuss, R. W.; Greenhall, M. P.; Spink, R. C. H.; Batsanov, A. S.; Howard, J. A. K. *J. Chem. Soc., Perkin Trans 1* **2000**, 1623.
(8) Chambers, R. D.; Grievson, B. *J. Chem. Soc., Perkin Trans. 1* **1985**, 2215.
(9) Chambers, R. D.; Grievson, B. *J. Fluorine Chem.* **1985**, *29*, 323.
(10) Chambers, R. D.; Grievson, B.; Kelly, N. M. *J. Chem. Soc., Perkin Trans. 1* **1985**, 2209.
(11) Chambers, R. D. *Fluorine in Organic Chemistry*; John Wiley and Sons: New York, 1973.

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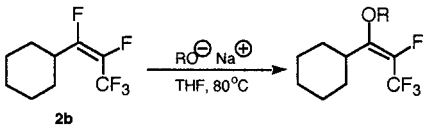
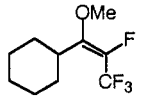
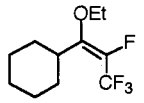
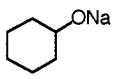
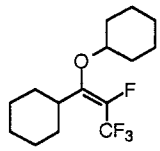
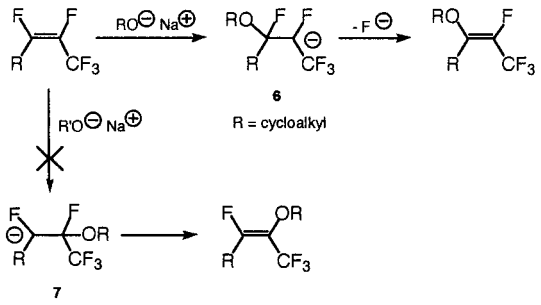
Table 1



2b

$RO^{\ominus}Na^{\oplus}$	Product Yield (%)
MeONa	 **3**, 72%, Z:E 31:1
EtONa	 **4**, 58%
	 **5**, 67%

Scheme 2



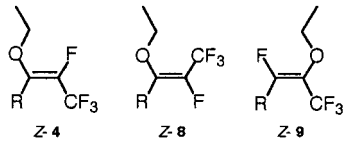
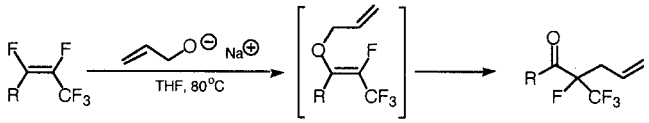
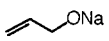
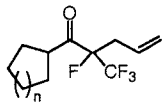
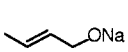
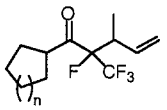
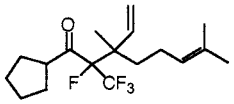
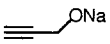
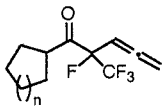


Figure 1.

Table 2



Substrate	Nucleophile	Product Yield (%)
2a **2b**		 **10a**, n = 1, 59% **10b**, n = 2, 52%
2a **2b**		 **11a**, n = 1, 69% **11b**, n = 2, 37%
2a	geraniol	 **12**, 73%
2a **2b**		 **13a**, n = 1, 54% **13b**, n = 2, 49%

occurs exclusively, to the limits of detection by ^{19}F NMR, because substitution proceeds via the most stable carbanion transition state **6**, in which the negative charge is located on a carbon atom attached to a highly stabilizing trifluoromethyl group, rather than less stable carbanion **7** (Scheme 2).

In the case of methoxide substitution, a small amount of the thermodynamically more stable *E*-alkene *E*-**3** was formed in addition to the major *Z*-alkene (*Z*:*E* 31:1 by ^{19}F NMR), whereas in similar reactions involving ethoxide and cyclohexanoxide the *Z*-fluoroalkene derivatives **4** and **5** were obtained exclusively, indicating that these nucleophilic substitution reactions give products resulting from kinetic control.

The regio- and stereochemistry of the products were established by NMR analysis, and a discussion of the spectral data obtained for the ethoxide derivative **4** is given below as an example.

The regiochemistry of the nucleophilic substitution, giving **4** rather than **9** (Figure 1), was determined by a comparison of ^{19}F NMR shift literature data.[12]

The stereochemistry of the fluoroalkene *Z*-**4** was established by heteronuclear ($^1H-^{19}F$) nOe experiments. Irradiation of the ^{19}F NMR resonance attributed to the vinyllic fluorine atom in **4** ($\delta_F = -160.9$ ppm) gave an enhanced signal on the ^1H NMR spectrum for the resonance corresponding to the CH_2O group ($\delta_H = 4.13$ ppm), indicating that the CH_2O and F substituents must be close to each other in space and, therefore, in the *Z*, rather than the *E*, configuration.

Reaction of alkenes **2a** and **2b** with various allyl alcohol salts in THF (80 °C) gave, keto-alkenes **10**−**13** in one-pot processes (Table 2). Claisen rearrangement of the enol ether intermediates **14**, formed initially by nucleophilic substitution, accounts for the reaction mechanism.

^{19}F NMR analysis of the crude reaction mixtures indicate that Claisen rearrangement products are formed exclusively. However, isolation and purification of the products was difficult because product degradation occurs on silica gel, precluding the use of column chromatography, and some degree of polymerization occurs upon distillation.

By a similar rearrangement process, reaction between **2a** and **2b** with propargyl alcohol gave allenes **13a** and **13b**, respectively.

Reaction of **2a** with benzyl alcohol gave the ether derivative **15** (Scheme 3). In contrast to the Claisen processes described above, rearrangement of **15** did not occur under the reaction conditions or after heating at high temperature.

(12) Berger, S.; Braun, S.; Kalinowski, H. O. *NMR Spectroscopy of the Non-Metallic Elements*; Wiley-Interscience: New York, 1997.

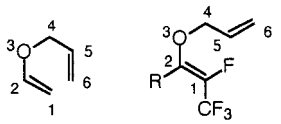
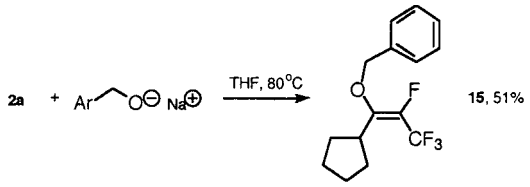


Figure 2.

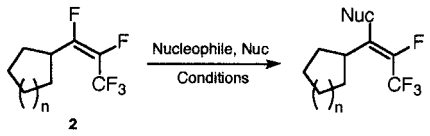
Scheme 3

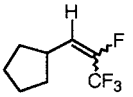
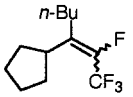
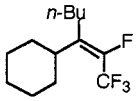
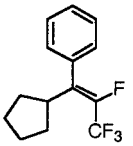


Of course, [3,3] sigmatropic rearrangement reactions offer very versatile carbon−carbon bond forming methodology, and processes involving fluorinated systems have been reviewed.[13] In general, Claisen rearrangements of nonfluorinated substrates require high temperatures (>150 °C) for useful reaction[14] but, in the cases described here, full conversion of the enol ether to product ketoalkene occurs readily (80 °C in THF). The effect of fluorine and fluorinated substituents on the rate of Claisen rearrangement processes has been debated,[13,15] and, in general, it is found that trifluoromethyl groups located at C-1 (Figure 2) has little effect on rate. Fluorine at C-1 is dependent on the nature of the adjacent alkene substituents, and an electron-donating group at C-2 is rate accelerating.

A qualitative Frontier Orbital approach can be used to rationalize these findings.[16] It is well established that[16] [3,3] sigmatropic rearrangements can be considered as [4 + 2] cycloaddition processes involving overlap between a 2-electron LUMO (C-5−C-6 π-bond; Figure 2) and a four-electron HOMO component (σ bond, C-4−O and π bond C-2−C-1, Figure 2). The rate of rearrangement is increased if the energy difference between the HOMO and LUMO components is decreased and, also, if the size of the orbital coefficient on C-1 is increased. Photoelectron spectroscopy studies[17−19] have shown that fluorine, attached directly to a carbon−carbon double bond, has little effect on orbital energies with respect to hydrogen whereas a trifluoromethyl group both lowers HOMO energy and increases the HOMO coefficient at C-2. In contrast, electron-releasing substituents, such as cycloalkyl groups, significantly raise the energy of the HOMO and increase the orbital coefficient at C-1. However, the energy and coefficients of a carbon−carbon double bond HOMO are affected more significantly by an electron-releasing substituent (typically raise HOMO energy by 1.4 eV) than by an electron-withdrawing substituent (lower HOMO energy by −0.4 eV). Consequently, for transformation of **2** to **10**−**13**, the rise in HOMO energy attributed to the electron-releasing alkyl group more than compensates for the lowering in HOMO energy by the trifluoromethyl group, and the overall effect on the system is a rise in HOMO energy and an increase in the coefficient at C-1. Consequently, the HOMO/LUMO energy difference in **2** is lowered and the coefficient at C-1 is increased in size by the presence of F, CF_3, and alkyl substituents, and this enables the rearrangement process to occur relatively readily. Thus, the ease of rearrangement for the transformation of **2** to **10**−**13** is due to the rate-enhancing effect of the electron-releasing cycloalkyl substituent located at C-2 rather than the presence of the fluorine and trifluoromethyl substituents.

Table 3



Substrate	Nucleophile	Conditions	Product Yield (%)
2a	$LiAlH_4$	A	 **16**, 85%, Z:E 6:5
2a	*n*-BuLi	B	 **17**, 53%, Z:E 33:1
2b	*n*-BuLi	C	 **18**, 58%
2a	PhLi	B	 **19**, 34%, Z:E 33:1

A, tetraglyme, r.t.
B, THF, 80°C
C, THF, -78°C

In related nucleophilic substitution processes, reaction of carbon (*n*-BuLi and PhLi) and hydrogen ($LiAlH_4$) nucleophiles with fluoroalkene **2a** and **2b** led to substituted products indicated in Table 3. The regio- and stereochemistry of each of these reactions were also established by NMR studies, as described above.

In conclusion, fluoroalkenes **2**, efficiently prepared in two steps from industrially available chemicals, react effectively with various oxygen and carbon nucleophiles. In particular, Claisen rearrangement processes lead to the synthesis of keto-alkenes bearing a $CFCF_3$ group in mid-aliphatic chain positions. Thus, the chemistry of "building-blocks" derived from free radical chemistry as an approach to the synthesis of organic molecules bearing fluorine atoms, has been further extended.[20]

(13) Purrington, S. T.; Weeks, S. C. *J. Fluorine Chem.* **1992**, *56*, 165.
(14) March, J. *Advanced Organic Chemistry*, 3rd ed.; Wiley-Interscience: New York, 1985.
(15) Gajewski, J. J.; Kee, K. R.; Jurayj, J. *J. Org. Chem.* **1990**, *55*, 1813.
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(17) White, D. H.; Condit, P. B.; Bergman, R. G. *J. Am. Chem. Soc.* **1972**, *94*, 1348.
(18) Dommelsmith, L. N.; Houk, K. N.; Piedrahita, C.; Dolbier, W. R. *J. Am. Chem. Soc.* **1978**, *100*, 6908.
(19) Bryce, M. R.; Chambers, R. D.; Taylor, G. *J. Chem. Soc., Perkin Trans. 1* **1984**, 509.

Experimental Section

All solvents were dried before use by literature procedures. NMR spectra were recorded on either a Varian Gemini 200, a Varian VXR 400S or a Bruker AC250 NMR spectrometer with tetramethylsilane and trichlorofluoromethane as internal standards and deuteriochloroform as solvent, unless otherwise stated. In ^{19}F NMR spectra, upfield shifts are quoted as negative. Coupling constants are given in Hz. Mass spectra were recorded on a Fisons VG Trio 1000 spectrometer coupled with a Hewlett-Packard 5890 series II gas chromatograph. Accurate mass measurements were performed by the EPSRC Mass Spectrometry Service, Swansea. IR spectra were recorded on a Perkin-Elmer 1600 FT IR spectrometer using KBr plates while elemental analyses were obtained on either a Perkin-Elmer 240 or a Carlo Erba Elemental Analyzer. Melting and boiling points were recorded at atmospheric pressure and are uncorrected. Superscript numbers given as part of boiling point data indicate the pressure (in mmHg) during measurement. Distillations were carried out using a Fischer Spahltrohr MS200 microdistillation apparatus. Column chromatography was performed on silica gel (Merck no. 1-09385), and TLC analysis was performed on silica gel TLC plates (Merck).

Fluoroalkenes **2a** and **2b** were prepared using procedures described previously.[7] **CAUTION**: All fluoroalkenes described in this paper must be assumed to be toxic and handled accordingly.

For clarity, when mixtures of diastereoisomers were obtained, the NMR and mass spectral data of the major diastereoisomer obtained is recorded only. Minor diastereoisomers give very similar chemical shift data in all cases.

Reactions with Oxygen Nucleophiles. General Procedure. Sodium or sodium hydride (60% dispersion in oil, removed by repeated washing with hexane) was added to the alcohol in THF (or methanol for methoxide reactions) under nitrogen and the mixture stirred at 50 °C. The fluoroalkene was added dropwise and the reaction mixture heated at reflux at 80 °C until complete reaction had occurred. The crude reaction mixture was extracted into dichloromethane and dried ($MgSO_4$), and solvent was removed by rotary evaporation. Purification was achieved either by distillation or by column chromatography using 5% diethyl ether/cyclohexane as eluent.

1-Cyclohexylmethoxy-2,3,3,3-tetrafluoroprop-1-ene 3. Sodium (0.86 g, 37 mmol), methanol (2.4 g, 75 mmol), and **2b** (4.0 g, 19 mmol) gave 1-cyclohexylmethoxy-2,3,3,3-tetrafluoroprop-1-ene **3** (3.1 g, 72%) as a colorless oil and as a mixture of isomers (*Z*:*E* 31:1 by ^{19}F NMR); bp 168 °C (Found: C, 53.1; H, 6.2. $C_{10}H_{14}F_4O$ requires C, 53.1; H, 6.2%); ν_{max}/cm^{-1} 1680 (C=C), 2857 and 2933 (C−H); δ_H 1.1−1.2 (5 H, m, CH_2 axial), 1.4−1.7 (5 H, m, C*H*$_2$ equatorial), 2.2 (1 H, m, C*H*), 3.8 (3 H, d, $^5J_{H-F}$ 5.2, C*H*$_3$); δ_C 25.6 (s, C-4), 25.8 (s, C-3), 29.3 (s, C-2), 38.4 (s, C-1), 60.8 (d, $^4J_{C-F}$ 12, *C*H_3), 121.2 (qd, $^1J_{C-F}$ 270, $^2J_{C-F}$ 37, *C*F_3), 133.7 (dq, $^1J_{C-F}$ 243, $^2J_{C-F}$ 39, *C*F), 151.5 (m, =*C*O); δ_F −63.3 (3 F, d, $^3J_{F-F}$ 9.0, C*F*$_3$), −161.5 (1 F, m, C*F*); *m*/*z* (EI$^+$) 226 (M$^+$, 15%), 184 (17), 171 (23), 159 (11), 125 (21), 101 (11), 97 (15), 93 (17), 82 (44), 8 (29), 79 (23), 77 (21), 71 (23), 69 (22), 67 (100). The *E* isomer was observed by NMR; δ_F −67.2 (3F, d, $^3J_{F-F}$ 9.0), −162.3 (1F, d, $^5J_{F-H}$ 7.1).

(1*Z*)-1-Cyclohexyl-1-ethoxy-2,3,3,3-tetrafluoroprop-1-ene 4. Sodium (0.55 g, 24 mmol), ethanol (1.10 g, 24 mmol), and **2b** (3.42 g, 16 mmol) gave (1*Z*)-1-cyclohexyl-1-ethoxy-2,3,3,3-tetrafluoroprop-1-ene **4** (2.50 g, 58%) as a clear yellow oil; bp 178 °C (Found: C, 55.2; H, 6.9. $C_{11}H_{16}F_4O$ requires C, 55.0; H, 6.7%); R_f 0.3; ν_{max}/cm^{-1} 1678 (C−O), 1732 (C=C), 2859, 2934 and 2982 (C−H); δ_H 1.1−1.75 (10 H, m, C*H*$_2$), 1.29 (3 H, t, $^3J_{H-H}$ 7.2, C*H*$_3$), 2.3 (1 H, m, C*H*), 4.13 (2 H, qd, $^3J_{H-H}$ 7.2, $^5J_{H-F}$ 3.6, C*H*$_2$CH$_3$); δ_C 15.5 (s, CH_3), 25.6 (s, C-4), 25.9 (s, C-3), 29.5 (s, C-2), 38.2 (s, C-1), 68.9 (d, $^4J_{C-F}$ 12, *C*H_2CH$_3$), 121.3 (qd, $^1J_{C-F}$ 268, $^2J_{C-F}$ 37, *C*F_3), 133.4 (dq, $^1J_{C-F}$ 240, $^2J_{C-F}$ 39, CF), 150.5 (s, =C−O); δ_F −63.1 (3 F, d, $^3J_{F-F}$ 8.6, C*F*$_3$), −160.9 (1 F, q, $^3J_{F-F}$ 8.6, C*F*); *m*/*z* (EI$^+$) 240 (M$^+$, 41%), 221 (11), 111 (13), 83 (22), 82 (21), 81 (14), 79 (10), 69 (20).

(1*Z*)-1-Cyclohexyl-1-cyclohexyloxy-2,3,3,3-tetrafluoroprop-1-ene 5. Sodium hydride (0.43 g, 18 mmol), cyclohexanol (1.80 g, 18 mmol), and **2b** (3.22 g, 18 mmol) gave (1*Z*)-1-cyclohexyl-1-cyclohexyloxy-2,3,3,3-tetrafluoroprop-1-ene **5** (3.60 g, 67%) as a clear yellow oil; bp 205 °C (Found: C, 61.2; H, 7.5. $C_{15}H_{22}F_4O$ requires C, 61.2; H, 7.5%); R_F 0.25; ν_{max}/cm^{-1} 1674 (C=C), 2859 and 2934 (C−H); δ_H 1.1−1.9 (20 H, m, CH_2), 2.29 (1 H, m, =C−CH), 4.33 (1 H, m C*H*−O); δ_C 23.7 (s, *C*H_2-CH_2CH_2CHC=), 25.5 (s, *C*$H_2CH_2CH_2CHO$), 25.7 (s, *C*H_2CH_2-CHO), 25.9 (s, CH_2CH_2CHC=), 29.9 (s, *C*H_2CHC=), 32.5 (s, *C*H_2CHO), 38.3 (s, *C*HC=), 79.2 (d, $^4J_{C-F}$ 11, *C*HO), 121.4 (qd, $^1J_{C-F}$ 270, $^2J_{C-F}$ 37, *C*F_3), 132.1 (dq, $^1J_{C-F}$ 241, $^2J_{C-F}$ 39, *C*F) 151.0 (s, *C*O); δ_F −62.0 (3 F, d, $^3J_{FF}$ 8.6, C*F*$_3$), −160.7 (1 F, m, C*F*); *m*/*z* (EI$^+$) 294 (M$^+$, 3%), 212 (49), 170 (13), 111 (17), 83 (100), 82 (84).

Claisen Rearrangement Reactions

1-Cyclopentyl-2-fluoro-2-(trifluoromethyl)pent-4-en-1-one 10a. Allyl alcohol (2.6 g, 45 mmol), sodium (0.9 g, 37.5 mmol), THF (15 mL), and **2a** (3.0 g, 15.0 mmol) gave, after distillation at reduced pressure, 1-cyclopentyl-2-fluoro-2-(trifluoromethyl)pent-4-en-1-one **10a** (2.4 g, 59%) as a colorless oil; bp 50 °C (6 mmHg); (Found: M$^+$, 238.096216. $C_{14}H_{14}F_4O$ requires M$^+$, 238.098078); γ_{max}/cm^{-1} 2853−2954 (C−H), 1731 (C=O), 1645 (C=C); δ_H 1.6−1.8 (8H, m, CH_2), 5.2 (2H, m, =CH_2), 5.6 (1H, m, =CH); δ_F -77.7 (3F, d, $^3J_{FF}$ 7.5, CF_3), −180.0 (1F, dm, $^3J_{HF}$ 35.4, CF); δ_C 22.9 (s, C-3′), 26.1 (d, $^4J_{CF}$ 5.0, C-2′), 36.0 (d, $^2J_{CF}$ 20.2, **C**H$_2$−CF), 47.3 (s, **C**H−C=O), 97.8 (dq, $^1J_{CF}$ 201.6, $^2J_{CF}$ 29.0, CF), 121.9 (dq, $^1J_{CF}$ 285.7, $^2J_{CF}$ 28.7, CF_3), 122.2 (s, =CH_2), 127.7 (d, $^3J_{CF}$ 2.7, −CH=), 206.9 (d, $^2J_{CF}$ 27.5, C=O); *m*/*z* (EI$^+$) 239 (MH$^+$, 8%), 97 (52), 70 (11), 69 (100).

1-Cyclohexyl-2-fluoro-2-(trifluoromethyl)pent-4-en-1-one 10b. Sodium (1.07 g, 47 mmol), allyl alcohol (3.25 g, 56 mmol), and **2b** (4.0 g, 19 mmol) gave 1-cyclohexyl-2-fluoro-2-(trifluoromethyl)pent-4-ene-1-one **10b** (2.62 g, 52% yield) as a colorless oil; bp 216 °C; (Found: C, 56.9; H, 6.2. $C_{12}H_{16}F_4O$ requires C, 57,15; H, 6.35%); ν_{max}/cm^{-1} 1645 (C=C), 1729 (C=O) 2859 and 2935 (C−H); δ_H 1.2−1.3 (5H, m, C*H*$_2$ axial), 1.6−1.8 (5H, m, C*H*$_2$ equatorial), 2.69 (1H, m, CHCO), 2.84 (2H, m, C*H*CH=CH_2), 5.20 (1H, dm, $^3J_{H-Htrans}$ 9.6, =CH_2), 5.23 (1H, m, =CH_2), 5.64 (1H, ddt, $^3J_{H-Htrans}$ 9.6, $^3J_{H-Hcis}$ 7.6, $^3J_{H-H}$ 7.2, −CH=); δ_C 25.6 (s, C-4), 25.8 (s, C-3), 27.8 (d, $^4J_{C-F}$ 7.8, C-2), 35.8 (d, $^2J_{C-F}$ 20.2, **C**H$_2$CF), 46.4 (s, **C**H−C=O), 98.1 (dq, $^1J_{C-F}$ 202, $^2J_{C-F}$ 29, CF), 121.8 (qd, $^1J_{C-F}$ 286, $^2J_{C-F}$ 29, CF_3), 122.2 (s, =CH_2), 127.7 (s, −CH=), 207.0 (d, $^2J_{C-F}$ 27, *C*=O); δ_F −77.6 (3F, d, $^3J_{F-F}$ 7.5, CF_3) −181.5 (1F, dm, $^3J_{F-H}$ 35, CF); *m*/*z* (CI$^+$) 253 (M$^+$ + 1, 59%), 235 (14), 233 (11), 215 (11), 212 (28), 211 (19), 75 (10), 58 (100).

1-Cyclohexyl-2-fluoro-3-methyl-2-(trifluoromethyl)-pent-4-en-1-one 11. Sodium (2.69 g, 120 mmol), crotyl alcohol (10.1 g, 140 mmol), and **2b** (10.0 g, 47 mmol) gave 1-cyclohexyl-2-fluoro-3-methyl-2-(trifluoromethyl)pent-4-en-1-one **11** (4.65 g, 37%) as a colorless oil and as a mixture of diastereoisomers (4.5:1); bp 222 °C (Found: C, 58.8; H, 6.8. $C_{13}H_{18}F_4O$ requires C, 58.65; H, 6.8%); ν_{max}/cm^{-1} 1642 (C=C), 1727 (C=O), 2857 and 2933 (C−H); δ_H 1.10 (3H, d, $^3J_{HH}$ 6.8, CH_3),1.0−1.4 (5H, m, C*H*$_2$ axial), 1.6−1.9 (5H, m, C*H*$_2$ equatorial), 2.75 (1H, m, CH−C=O), 3.0 (1 H, m, C*H*-CH_3), 5.07 (1 H, d, $^3J_{HHtrans}$ 17.2, =CH_2), 5.10 (1 H, d, $^3J_{HHcis}$ 9.6, =CH_2), 5.66 (1 H, ddd, $^3J_{HHtrans}$ 17.2, $^3J_{HHcis}$ 9.6, $^3J_{HH}$ 9.6, −CH=); δ_C 13.9 (s, CH_3), 25.7 (s, C-4), 27.2 (s, C-3), 28.3 (s, C-2), 41.8 (d, $^3J_{C-F}$ 20, **C**HCH$_3$), 46.7 (s, **C**H−C=O), 99.95 (dq, $^1J_{C-F}$ 206, $^2J_{C-F}$ 28, *C*F), 119.0 (s, CH=*C*H$_2$), 121.9 (qd, $^1J_{C-F}$ 287, $^2J_{C-F}$ 30, *C*F_3), 135.1 (s, −CH=), 208.0 (d, $^2J_{C-F}$ 27, *C*=O); δ δ_C both); δ_F −68.5 (3F, s, C*F*$_3$), −186.5 (1F, s, C*F*); *m*/*z* (EI$^+$) 266 (M$^+$, 14%), 111 (34), 83 (100), 67 (21), 65 (10).

(6*E*)-1-Cyclopentyl-2-fluoro-3,7-dimethyl-2-(trifluoromethyl)-3-vinyloct-6-en-1-one 12. Geraniol (6.9 g, 45 mmol), sodium (0.9 g, 37.5 mmol) in THF (15 mL), and **2a** (3.0 g, 15 mmol) gave after distillation at reduced pressure (6*E*)-1-cyclopentyl-2-fluoro-3,7-dimethyl-2-(trifluoromethyl)-3-vinyl-

(20) Since this manuscript was submitted, a communication describing related Claisen rearrangement reactions of allyl fluorovinyl ethers derived from 1,1,3,3,3-pentafluoropropene has been published. See, Tellier, F.; Audoin, M.; Sauvetre, R.; *Tetrahedron Lett.*, **2001**, *42*, 2665.

oct-6-en-1-one **12** (3.6 g, 73%) as a colorless oil and a mixture of diastereoisomers (6.8:1); bp 110−120 °C (7 mmHg); (Found: C, 64.3; H, 7.9. $C_{18}H_{26}F_4O$ requires C, 64.7; H, 7.8%); γ_{max}/cm^{-1} 2873−2963 (C−H), 1727 (C=O), 1639 (C=C); δ_H 1.2 (3H, s, CH_3), 1.5−2.0 (8H, m, CH_2), 1.5 (3H, s, CH_3), 1.7 (3H, s, CH_3), 3.3 (1H, m, CH), 4.95 (1 H, m, =CH-), 5.04 (1H, dm, $^3J_{HHtrans}$ 17.6, $=CH_2$), 5.17 (1H, d, $^3J_{HHtrans}$ 10.8, $=CH_2$), 5.8 (1H, dd, $^3J_{HHtrans}$ 17.6, $^3J_{HHcis}$ 10.8, =CH); δ_F −68.7 (3F, d, $^3J_{FF}$ 5.6, CF_3), −177.9 (1F, m, CF); δ_C 16.0 (m, CH_3), 17.8 (s, CH_3), 22.3 (s, C-3′), 25.8 (s, CH_3), 26.4 (s, C-2′), 28.2 (s, C-5), 31.2 (s, C-4), 46.3 (d, $^2J_{CF}$ 19.1, C-3), 48.5 (s, CH−C=O), 100.0 (dq, $^1J_{CF}$ 204.3, $^2J_{CF}$ 26.8, CF), 117.5 (s, $=CH_2$), 122.3 (qd, $^1J_{CF}$ 288.4, $^2J_{CF}$ 30.0, CF_3), 124.0 (s, C-6), 132.2 (s, C-7), 138.6 (d, $^3J_{CF}$ 3.1, CH), 207.9 (d, $^2J_{CF}$ 29.0, C=O); *m/z* (EI^+) 334 (M^+, 1%), 231 (26), 136 (29), 135 (13), 121 (12), 97 (35), 93 (19), 82 (44), 69 (100), 55 (68).

1-Cyclopentyl-2-fluoro-2-(trifluoromethyl)penta-3,4-dien-1-one 13a. Propargyl alcohol (2.6 g, 45 mmol), sodium (0.9 g, 37.5 mmol) in THF (15 mL), and **2a** (3.0 g, 15 mmol) gave, after distillation at reduced pressure, 1-cyclopentyl-2-fluoro-2-(trifluoromethyl)penta-3,4-dien-1-one **13a** (1.9 g, 54%) as a colorless oil; bp 110−135 °C (20 mmHg); (Found: C, 56.3; H, 5.2. $C_{11}H_{12}F_4O$ requires C, 55.9; H, 5.1%); γ_{max}/cm^{-1} 2875−2961 (C−H), 1955−1983 (C=C=C), 1732 (C=O); δ_H 1.6−1.8 (8H, m, CH_2), 3.3 (1H, ttd, $^3J_{HH}$ 8.0, $^3J_{HH}$ 4.0, $^4J_{HF}$ 4.0, CH), 5.15 (1H, d, $^2J_{HH}$ 3.6, $=CH_2$), 5.16 (1H, d, $^2J_{HH}$ 3.6, $=CH_2$), 5.4 (1H, dt, $^3J_{HF}$ 16.5, $^4J_{HH}$ 6.5, =CH); δ_F −77.8 (3F, d, $^3J_{FF}$ 8.7, CF_3), −171.3 (1F, m, CF); δ_C 26.2 (s, C-3′), 26.3 (s, C-4′), 29.2 (d, $^4J_{CF}$1.5, C-2′), 29.4 (d, $^4J_{CF}$1.4, C-5′), 46.9 (s, CH−C=O), 81.3 (s, $=CH_2$), 85.4 (dm, $^2J_{CF}$ 23.9, =CH), 93.7 (dq, $^1J_{CF}$ 202.0, $^2J_{CF}$ 30.5, CF), 121.5 (qd, $^1J_{CF}$ 285.8, $^3J_{CF}$ 30.0, CF_3), 204.1 (d, $^2J_{CF}$ 26.4, C=O), 209.3 (d, $^3J_{CF}$ 8.4, =C=); *m/z* (EI^+) 237 (MH^+, 6%), 236 (3), 119 (16), 97 (100), 70 (11), 69 (100), 55 (30).

1-Cyclohexyl-2-fluoro-2-(trifluoromethyl)penta-3,4-dien-1-one 13b. Sodium (2.7 g, 120 mmol), propargyl alcohol (7.9 g, 140 mmol), and **2b** (10.0 g, 47 mmol) gave 1-cyclohexyl-2-fluoro-2-(trifluoromethyl)penta-3,4-dien-1-one **13b** (5.4 g, 49%) as a colorless oil; bp 208 °C; (Found: C, 57.7; H, 5.6. $C_{12}H_{14}F_4O$ requires C, 57.6; H, 5.6%); ν_{max}/cm^{-1} 1733 (C=O), 1955 and 1982 (C=C=C), 2859 and 2936 (C−H); δ_H 1.1−1.4 (5H, C*H*$_2$ axial), 1.5−1.8 (5H, C*H*$_2$ equatorial), 2.92 (1H, m, C*H*CO), 5.15 (2H, m, $=CH_2$), 5.41 (1H, dt, $^3J_{H-F}$ 16.4, $^4J_{H-H}$ 6.8, =CH−); δ_C 25.4 (s, C-4), 27.6 (s, C-3), 28.8 (s, C-2), 46.1 (s, **C**H−C=O), 81.0 (s, $=CH_2$), 85.1 (dm, $^2J_{C-F}$ 22, −CH=), 93.7 (dq, $^1J_{C-F}$ 203, $^2J_{C-F}$ 30, CF), 121.2 (qd, $^1J_{C-F}$ 286, $^2J_{C-F}$ 30, CF_3), 204.1 (d, $^2J_{C-F}$ 26, C=O), 209.0 (d, $^3J_{C-F}$ 8.5, =C=); δ_F −77.8 (3F, d, $^3J_{F-F}$ 8.6, CF_3), −172.5 (1F, m, CF); *m/z* (EI^+) 250 (M^+, 2%), 119 (10), 111 (65), 84 (11), 83 (100), 69 (10).

1-Cyclopentyl-2, 3, 3, 3-tetrafluoro-1-(phenylmethoxy)-prop-1-ene 15. Benzyl alcohol (4.9 g, 45 mmol), sodium (0.9 g, 37.5 mmol) in THF (30 mL), and **2a** (3.0 g, 15 mmol) gave, after distillation at reduced pressure, 1-cyclopentyl-2,3,3,3-tetrafluoro-1-(phenylmethoxy)prop-1-ene **15** (2.2 g, 51%) as a colorless oil and a mixture of isomers (ratio *Z*:*E*, 320:1); bp 56 °C (5 mmHg); (Found: C, 62.6; H, 5.5. $C_{15}H_{16}F_4O$ requires C, 62.5; H, 5.6%); γ_{max}/cm^{-1} 1679 (C=C); δ_H 1.6−1.8 (8H, m, CH_2), 2.9 (1H, quint, $^3J_{HH}$ 7.0, CH), 5.2 (2H, d, $^2J_{HH}$ 3.0, O−CH_2), 7.4 (5H, m, 5CH); δ_F -63.0 (3F, d, $^3J_{FF}$ 8.7, CF_3), −156.9 (1F, qd, $^3J_{FF}$ 8.7, $^4J_{HF}$ 3.0, CF); δ_C 26.4 (s, C-3′), 30.3 (d, $^4J_{CF}$ 1.9, C-2′), 38.8 (m, C-1′), 74.9 (d, $^4J_{CF}$ 12.9, OCH_2), 121.4 (qd, $^1J_{CF}$ 270.4, $^2J_{CF}$ 36.9, CF_3), 128.0 (s, Ar_{para}), 128.5 (s, Ar_{meta}), 128.8 (s, Ar_{ortho}), 134.0 (dq, $^1J_{CF}$ 242.4, $^2J_{CF}$ 39.0, CF), 137.0 (d, $^5J_{CF}$ 2.0, Ar_{ipso}), 149.3 (dq, $^2J_{CF}$ 3.0, $^3J_{CF}$ 3.0, =C−O); *m/z* (EI^+) 92 (23%), 91 (100), 69 (12).

1-Cyclohexyl-2,3,3,3-tetrafluoroprop-1-ene 16. 2b (3.6 g, 17 mmol) and lithium aluminum hydride (1.48 g, 30 mmol) in tetraglyme (10 mL) at room temperature gave 1-cyclohexyl-2,3,3,3-tetrafluoroprop-1-ene **16** (2.84 g, 85%) as a colorless volatile liquid and as a mixture of isomers (*Z*:*E* 6:5); bp 146 °C (Found: C, 55.1; H, 6.2. $C_9H_{12}F_4$ requires C, 55.1; H, 6.1%); ν_{max}/cm^{-1} 1702 (C=C), 2855 and 2933 (C−H); δ_H 1.2 (5H, m, C*H*$_2$ axial), 1.7 (5H, m, C*H*$_2$ equatorial), 2.4 (1H, m, C*H*CH), 5.40 (1H, dd, $^3J_{H-F}$ 34, $^3J_{H-H}$ 9.6, =CH− *E* isomer), 5.52 (1H, dd, $^3J_{H-F}$ 22, $^3J_{H-H}$ 11, =CH− *Z* isomer); δ_C 25.4 and 25.5 (both s, C-4), 25.6 and 25.7 (both s, C-3), 32.2 and 33.2 (both s, C-2), 33.1 and 33.5 (both m, C-1), 118.2 (dq, $^2J_{C-F}$ 8.8, $^3J_{C-F}$ 3.0, *C*HCF), 118.9 (qd, $^1J_{C-F}$ 269, $^2J_{C-F}$ 63, CF_3), 119.1 (qd, $^1J_{C-F}$ 269, $^2J_{C-F}$ 59, CF_3), 121.1 (dq, $^2J_{C-F}$ 13, $^3J_{C-F}$ 2.6, *C*HCF), 144.3 (dq, $^1J_{C-F}$ 248, $^2J_{C-F}$ 39, *C*FCF$_3$), 144.8 (dq, $^1J_{C-F}$ 253, $^2J_{C-F}$ 38, *C*FCF$_3$); δ_F −68.1 (3F, d, $^3J_{F-F}$ 9, CF_3 *Z* isomer), −73.3 (3F, d, $^3J_{F-F}$ 5.6, CF_3 *E* isomer), −131.2 (1 F, q, $^3J_{F-F}$ 9.8, C*F* *Z* isomer), −138.3 (1 F, q, $^3J_{F-F}$ 11, C*F*, *E* isomer); *m/z* (EI^+) 196 (M^+, 0.46%), 140 (20), 90 (13), 85 (10), 82 (100), 81 (21), 77 (23), 69 (28), 67 (92).

Reactions with Organolithium Reagents

General Procedure. A three-necked flask, equipped with a septum, was charged with the organolithium derivative in hexane, THF, and 1-(pentafluoroprop-2-enyl) cyclopentane, under nitrogen at −78 °C. The mixture was stirred and warmed at 80 °C. After cooling to room temperature, the reaction mixture was poured into ice/water, neutralized with aqueous HCl (10%), and extracted into dichloromethane. The solvents were removed by rotary evaporation and further distillation, under reduced pressure, gave the desired product.

3-Cyclopentyl-1,1,1,2-tetrafluorohept-2-ene 17a. *n*-Butyllithium (15.6 mL, 25 mmol) in hexane, THF (15 mL), and **2a** (2.0 g, 10 mmol) gave 3-cyclopentyl-1,1,1,2-tetrafluorohept-2-ene **17a** (1.3 g, 53%) as a colorless liquid and as a mixture of isomers (*Z*:*E*, 33.4:1.0); bp 32 °C (7 mmHg); (Found: C, 60.5; H, 7.7. $C_{12}H_{18}F_4$ requires C, 60.5; H, 7.6%); γ_{max}/cm^{-1} 2875−2960 (C−H), 1688 (C=C), 1468 (CH_3), 1457 (CH_2); δ_H 0.9 (3H, t, $^3J_{HH}$ 6.8, CH_3), 1.4−1.8 (12H, m, CH_2) (4H, m, $-CH_2-CH_2-CH_3$), 2.1 (2H, m, =C−CH_2), 2.9 (1H, m, CH); δ_F -64.2 (3F, d, $^3J_{FF}$ 7.2, CF_3), −131.3 (1F, m, CF); δ_C 13.8 (s, CH_3), 23.3 (s, **C**H_2CH_3), 25.6 (d, $^5J_{CF}$ 0.7, C-3′), 25.8 (d, $^3J_{CF}$ 5.4, **C**H_2−C=), 31.0 (s, C-2′), 31.02 (s, C-5′), 31.6 (m, **C**H_2CH_2C=), 38.5 (m, CH), 120.1 (qd, $^1J_{CF}$ 272.8, $^2J_{CF}$ 43.1, CF_3), 131.3 (dq, $^2J_{CF}$ 8.7, $^3J_{CF}$ 2.6, CH−**C**=), 142.2 (dq, $^1J_{CF}$ 246.8, $^2J_{CF}$ 37.4, CF); *m/z* (EI^+) 238 (M^+, 4%), 181 (47), 97 (11), 81 (14), 77 (18), 68 (100).

(2*E*)-3-Cyclohexyl-1,1,1,2-tetrafluorohept-2-ene 17b. *n*-Butyllithium (1.6 M in hexanes, 20 mL, 30 mmol) and **2b** (2.0 g, 10 mmol) in THF (20 mL) at −78 °C gave (2*E*)-3-cyclohexyl-1,1,1,2-tetrafluorohept-2-ene **17b** (1.81 g, 58%) as a colorless oil and as a mixture of isomers (*Z*:*E* 1:4.5); bp 228 °C (Found: C, 61.7; H, 8.1. $C_{13}H_{20}F_4$ requires C, 61.9; H, 7.9%); ν_{max}/cm^{-1} 1687 (C=C), 2853 and 2932 (C−H); δ_H 0.85 (3H, t, $^3J_{H-H}$ 7.6, CH_3), 1.2−1.4 and 1.7−2.2 (16H, m, CH_2), 2.45 (1H, m, CH); δ_C 13.8 (s, CH_3), 23.1 (s, *C*H_2CH_3), 25.5 (s, *C*$H_2CH_2CH_3$), 25.7 (s, C-4), 25.8 (s, C-3), 26.0 (s, C-2), 30.8 (s, *C*H_2C=CF), 37.9 (s, C-1), 120.1 (qd, $^1J_{C-F}$ 273, $^2J_{C-F}$ 44, CF_3), 133.4 (m, *C*=CF), 142.1 (dq, $^1J_{C-F}$ 248, $^2J_{C-F}$ 39, *C*F); δ_F −62.2 (3F, m, CF_3), −131.0 (1F, m, C*F*); *m/z* (EI^+) 252 (M^+, 2%), 195 (3), 127 (6), 95 (14), 83 (42). The *Z* isomer was observed (4.5:1 by ^{19}F NMR); δ_F −56.0 (3 F, s, CF_3), −104.0 (1 F, s, C*F*); unidentifiable higher adducts in trace amounts were detected by GLC/MS with M = 290 and M = 270.

(1-Cyclohexyl-2,3,3,3-tetrafluoroprop-1-enyl)benzene 18. Phenyllithium (16.7 mL, 30 mmol) in hexane, THF (15 mL), and **2a** (3.0 g, 15 mmol) gave (1-cyclohexyl-2,3,3,3-tetrafluoroprop-1-enyl)benzene **18** (1.3 g, 34%) as a colorless liquid and as a mixture of isomers (*Z*:*E*, 33:1); bp 66−70 °C (1 mmHg); (Found: M^+, 258.103130 $C_{14}H_{14}F_4$ requires M, 258.103164); γ_{max}/cm^{-1} 2958 (ArCH), 2873 (CH_2), 1681 (C=C); δ_H 1.4−1.8 (8H, m, CH_2), 3.2 (1H, m, CH), 7.2 (2H, dm, $^3J_{HH}$ 7.8, ArH_{ortho}), 7.4 (3H, m, ArH); δ_F -64.5 (3F, d, $^3J_{FF}$ 7.5, CF_3), −125.0 (1F, q, $^3J_{FF}$ 7.2, CF); δ_C 24.9 (s, C-3′), 31.1 (d, $^4J_{CF}$ 3.1, C-2′), 38.9 (d, $^3J_{CF}$ 1.5, C-1′), 120.2 (qd, $^1J_{CF}$ 273.2, $^2J_{CF}$ 43.3, CF_3), 128.2 (s, Ar_{para}), 128.4 (s, Ar_{meta}), 129.1 (s, Ar_{ortho}), 131.9 (dq, $^2J_{CF}$ 9.9, $^3J_{CF}$ 2.7, Ar−C=), 132.8 (d, $^3J_{CF}$ 3.4, Ar_{ipso}), 142.0 (dq, $^1J_{CF}$ 249.6, $^2J_{CF}$ 37.8, CF); *m/z* (EI^+) 258 (M^+, 65%), 229 (10), 216 (15), 195 (14), 190 (79), 41 (100).

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