

A kinetic separation method for the stereoselective preparation of (*Z*)- and (*E*)-monofluoroenynes from *E/Z* mixtures of 1-bromo-1-fluoroolefins

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Abstract

Reaction of *E/Z* mixtures of 1-bromo-1-fluoroolefins with 1-alkynes and catalytic Pd(PPh₃)₂Cl₂ and CuI in triethylamine at room temperature gave (after 16–24 h) predominately the (*Z*)-monofluoroenyne (*Z/E* > 92/8) in good yields. Pure (*Z*)-monofluoroenyne could generally be obtained by chromatographic separation of the crude *Z/E* mixture. Pure (*Z*)-1-bromo-1-fluoroolefin could be recovered and reacted with 1-alkynes under similar conditions and longer reaction times (48 h) to give pure (*E*)-monofluoroenyne in excellent yields (78–89%). Thus, *E/Z* mixtures of 1-bromo-1-fluoroolefins could be kinetically separated into (*Z*)- and (*E*)-monofluoroenyne. This methodology provides a simple one-step unequivocal route to the isomerically pure (*Z*)- and (*E*)-monofluoroenyne from the readily available 1-bromo-1-fluoroolefins. © 2001 Elsevier Science B.V. All rights reserved.

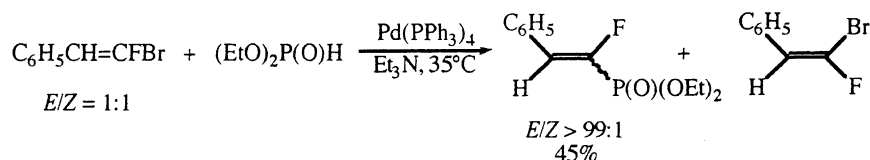
Keywords: Enynes; Monofluoroenyne; Kinetic separation; Palladium catalysis

1. Introduction

The chemistry and biology of conjugated enynes has recently received extensive attention [1,2]. Methods for the synthesis of fluorinated analogs have received increased attention, since many of these fluorinated analogs exhibit interesting biological activity [3–8]. The most popular approach to difluorinated enynes has been via palladium-catalyzed cross-coupling reactions of 1-alkynes with fluorinated vinyl bromides or iodides [9–14]. In contrast to the many examples of difluorinated or trifluorinated enynes, only a few reports of monofluoroenyne have been documented. Camps introduced fluorine to a pre-existing enyne via a multi-step sequence [15]. Rolando and co-workers employed a palladium-catalyzed cross-coupling reaction of 1-bromo-1-fluoro-2-arylethene with a terminal alkyne

[16,17]. This route was limited to aryl substituents on the olefinic carbon and required several steps to the 1-bromo-1-fluoro-arylethene. Similar palladium-catalyzed condensation of 1-halo-2-fluoroalkenes with 1-alkynes provided a route to 1-fluoro-1-en-3-yne derivatives [18]. α -Fluoropropargyl phosphonate ester condensation with aldehydes has also been successfully utilized for the preparation of conjugated fluoroenyne [19,20], and the addition–elimination sequence of acetylenic lithium reagents with 1,1-dichloro-2,2-difluoroethene also provided several monofluoroenyne [21].

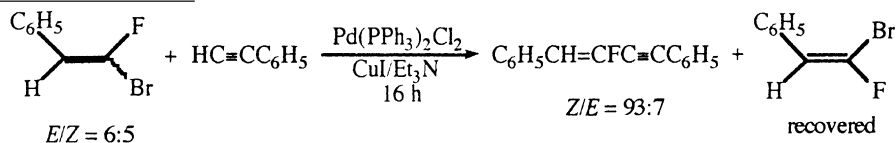
Recently, we reported a stereoselective preparation of pure (*E*)- and (*Z*)-1-fluorovinylphosphonates via a kinetic separation, utilizing a palladium-catalyzed phosphorylation reaction of *E/Z* mixtures of 1-bromo-1-fluoroolefins with dialkyl phosphites and triethylamine [22,23].



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The recovered (*Z*)-C₆H₅CH=CFBr could be stereospecifically converted to the (*Z*)-1-fluoro-vinylphosphonate by a

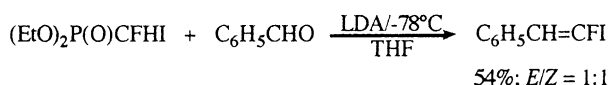
similar phosphorylation reaction at 70–80 °C [22]. Mechanistic experiments indicated that the kinetic separation occurred in the oxidative addition step of the vinyl bromide to Pd(0). Consequently, we reasoned that other Pd(0)-cata-



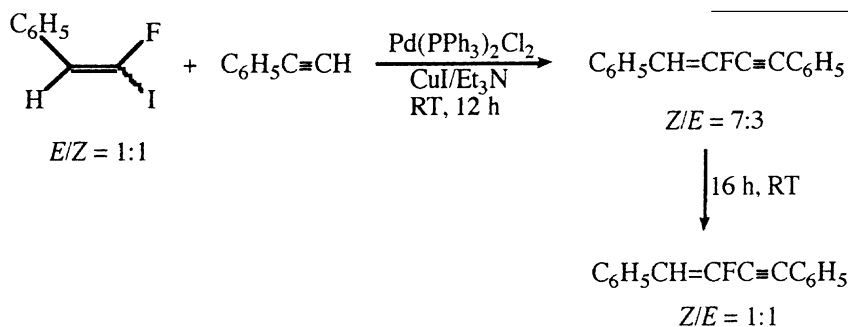
lyzed cross-coupling reactions of the *E/Z* mixture of the 1-bromo-1-fluoroolefins controlled by the rate of the oxidative addition step could also provide a novel utilization of both the (*E*)- and (*Z*)-olefins of the *E/Z* mixture for the stereoselective preparation of multi-functionalized derivatives. Herein, we report the extension of this kinetic separation methodology for the stereoselective synthesis of monofluoro-enynes [23].

2. Results and discussion

Our initial preparation of monofluorinated enynes utilized the palladium-catalyzed coupling reaction of 1-alkynes with an *E/Z* mixture of 1-fluoro-1-iodostyrene as a model reaction. The styrene was prepared via a Wittig–Horner reaction as outlined below [24]:



The 1-fluoro-1-iodostyrene reacted smoothly with phenylacetylene at room temperature in the presence of Pd(PPh₃)₂Cl₂, CuI and Et₃N.



Although the *Z/E* ratio (1:1) improved after a modest reaction time (*Z/E* = 7/3), it was obvious that both isomers of the vinyl iodide had reacted and eventually a 1:1 *Z/E* mixture was obtained after 16 h at room temperature. Similar results were obtained with 1-heptyne and (±) acetaldehyde ethyl propargyl acetal. Thus, although some kinetic separation was observed, the relative rate of the *E/Z*-olefin isomers with the 1-alkynes was not sufficiently different to be of practical value and paralleled similar observations in the attempted kinetic separation of 1-fluoro-1-iodoolefins via Pd(0)-catalyzed phosphorylation reactions [22].

However, when an *E/Z* mixture of 1-bromo-1-fluorostyrene was reacted with phenylacetylene under similar coupling conditions, a significantly better kinetic separation was observed, as outlined below:

At room temperature, the reaction was monitored (by ¹⁹F NMR) until all the (*E*)-olefin had been consumed (~16 h). The reaction was stopped at this stage, and the products separated by silica gel chromatography. Pure (*Z*)-C₆H₅CH=CFBr was recovered, and C₆H₅CH=CFC≡CC₆H₅ (*Z/E* = 93/7) was obtained, which on further purification (by recrystallization from pentane) gave 38% of pure (*Z*)-C₆H₅CH=CFC≡CC₆H₅, characterized by ¹H, ¹⁹F and ¹³C NMR and mass spectroscopy (both LRMS and HRMS). The (*Z*)- or (*E*)-configuration was assigned on the magnitude of *trans* ³J_{HF} > *cis* ³J_{HF}, cf. [16,17,22]. Thus, kinetic separation significantly enhances the formation of the (*Z*)-enyne. We chose to monitor the reaction until all the (*E*)-olefin had reacted—in order to maximize the amount and purity of the recovered (*Z*)-olefin (which, with longer reaction times) could be similarly coupled to give the (*E*)-enyne. If one wished only the (*Z*)-enyne, the reaction could be terminated earlier to increase the *Z/E* ratio of enyne product. When *E/Z* mixtures of 1-bromo-1-fluorostyrenes were treated similarly with a variety of 1-alkynes, the corresponding (*Z*)-enyne could be obtained in reasonable yields and high purity after chromatographic separation. These results are summarized in Table 1 (compounds 1–6). Similar kinetic separation was achieved with the *p*-chlorostyrene analog (compounds 7–8), as well as

with alkyl substituted 1-bromo-1-fluoroolefins (compounds 9–12). The recovered (*Z*)-1-bromo-1-fluoroolefins were subsequently coupled (with longer reaction times) to yield the corresponding (*E*)-monofluorinated enynes in excellent yields and high stereochemical purity (compounds 13–19).

The reactive Pd(0) is usually generated in situ, but one can also catalyze the reaction with Pd(PPh₃)₄ (cf. compound 6) in DMF/Et₃N. With the normal Pd(PPh₃)₂Cl₂/CuI/Et₃N system, the CuI is necessary for rapid reaction. In the absence of CuI, the conversion of (*E*)-olefins to (*Z*)-enyne takes ~1 week for total consumption of the (*E*)-olefin.

Table 1
The Pd(0)-catalyzed reaction of *E/Z*-1-bromo-1-fluoroolefins with 1-alkynes

$E/Z\text{-RCH=CFBr} + \text{HC}\equiv\text{CR}' \xrightarrow[\text{CuI/Et}_3\text{N/RT}]{\text{Pd(PPh}_3)_2\text{Cl}_2} \text{RCH=CFC}\equiv\text{CR}'$					
Compound no.	R	R'	<i>E/Z</i> ratio of olefin	Reaction conditions	Isolated yield (%) ^a <i>Z/E</i> ratio enyne
1	C ₆ H ₅	C ₆ H ₅	6/5	RT, 16 h	38 (100:0)
2	C ₆ H ₅	C ₅ H ₁₁	1/1	RT, 24 h	46 (98:2)
3	C ₆ H ₅	Acetal ^b	3/2	RT, 24 h	54 (95:5)
4	C ₆ H ₅	Si(CH ₃) ₃	6/5	RT, 16 h	23 (99:1)
5	C ₆ H ₅	CH(OH)CH ₃	1/1	RT, 24 h	49 (95:5)
6	C ₆ H ₅	Cyclohexanol	1/1	RT, 24 h	45 (99:1)
7	<i>p</i> -ClC ₆ H ₄	CH(OH)CH ₃	1/1	RT, 24 h	48 (99:1)
8	<i>p</i> -ClC ₆ H ₄	Acetal ^b	1/1	RT, 24 h	49 (99:1)
9	C ₇ H ₁₅	C ₆ H ₅	7/3	RT, 24 h	64 (90:10)
10	C ₇ H ₁₅	CH(OH)CH ₃	1/1	RT, 24 h	43 (98:2)
11	C ₇ H ₁₅	Acetal ^b	1/1	RT, 24 h	46 (93:7)
12	C ₆ H ₅ (CH ₃)CH	CH(OH)CH ₃	7/3	RT, 24 h	53 (92:8)
13	C ₆ H ₅	C ₆ H ₅	3/97	RT, 48 h	88 (3:97)
14	C ₆ H ₅	C ₅ H ₁₁	0/100	RT, 48 h	87 (0:100)
15	C ₆ H ₅	Acetal ^b	>2/98	RT, 48 h	89 (>2:98)
16	C ₆ H ₅	CH(OH)CH ₃	0/100	RT, 48 h	89 (>1:99)
17	<i>p</i> -ClC ₆ H ₄	CH(OH)CH ₃	0/100	RT, 48 h	77 (0:100)
18	<i>p</i> -ClC ₆ H ₄	Acetal ^b	0/100	RT, 48 h	89 (0:100)
19	C ₆ H ₅ (CH ₃)CH	CH(OH)CH ₃	0/100	RT, 48 h	78 (0:100)

^a *Z/E* ratio and yield of enyne after chromatography; yield is based on the amount of olefin consumed.

^b Acetal, R = CH₂OCH(OCH₂CH₃)CH₃.

3. Conclusions

This work demonstrates another useful practical application of kinetic separation in reactions of *E/Z*-1-bromo-1-fluoroolefins mediated by palladium catalysis [22]. By utilizing the difference in reactivity of the (*E*)- and (*Z*)-olefins, the conversion to (*Z*)-monofluorinated enynes can be achieved. In addition, the less reactive (*Z*)-olefin can be recovered and selectively converted to the corresponding (*E*)-monofluorinated enynes in high yields and high stereoselectivity. Consequently, the *E/Z*-1-bromo-1-fluoroolefins, which are readily prepared from aldehydes and the bromo-fluoromethylene ylide [25] can be employed to produce both the (*Z*)- and (*E*)-monofluorinated enynes, thus, providing a simple one-step route to both isomers of these useful compounds. Further applications of kinetic separation utilizing *E/Z* mixtures of 1-bromo-1-fluoroolefins are in progress and will be reported in due course.

4. Experimental

4.1. General

All reactions were monitored by ¹⁹F NMR analysis of the reaction mixture on a 90 or 300 MHz spectrometer. The ¹H, ¹⁹F and ¹³C NMR spectra of final products were obtained on a 300 MHz spectrometer (CDCl₃, CFCl₃ or TMS as internal references). FT-IR spectra were recorded on the pure sample on NaCl plates. Low resolution mass spectra analyses were

performed at 70 eV in the electron-impact mode on a single-quadrupole instrument interfaced to a gas chromatograph fitted with an OV-101 column. High resolution mass spectral analyses were performed by the High Resolution Mass Spectroscopy Facility, University of Iowa, at 70 eV in the electron-impact mode. GLPC analyses were performed on a 5% OV-101 column with a thermal conductivity detector.

4.2. Materials

The *E/Z* mixtures of 1-bromo-1-fluoroolefins were prepared from the corresponding aldehydes and [Ph₃P=CFBr] as described in the literature [25]. The *E/Z* mixtures of 1-fluoro-1-iodoolefins were prepared from the corresponding aldehydes and [(EtO)₂P(O)CFI] [24]. (EtO)₂P(O)CFHI was prepared by iodination of (EtO)₂P(O)CFHZnBr [26]. Tetrakis (triphenylphosphine) palladium was prepared by Coluson's procedure [27]. The aldehydes and 1-alkynes were commercial samples and were either distilled prior to use or used directly. Et₃N was dried over NaH and distilled from CaH₂. CuI was purified by the literature procedure [28]. Pd(PPh₃)₂Cl₂ was prepared by King and Negishi's procedure [29].

4.2.1. (*Z*)-1,4-diphenyl-3-fluoro-3-buten-1-yne (I)

To a mixture of 0.01 g (0.014 mmol) Pd(PPh₃)₂Cl₂, 0.01 g (0.05 mmol) CuI, 0.21 g (2.0 mmol) C₆H₅C≡CH and 2.0 ml of Et₃N was added 0.41 g (2.0 mmol) of an *E/Z* mixture (*E/Z* = 6/5) of C₆H₅CH=CFBr. The resulting mixture was stirred at room temperature until no (*E*)-olefin remained by

^{19}F NMR analysis of the reaction mixture (~ 16 h). The reaction mixture was directly purified by silica gel chromatography (hexane as eluant); 0.20 g of pure (*Z*)- $\text{C}_6\text{H}_5\text{CH}=\text{CFBr}$ was recovered (0.21 g olefin consumed) and 0.24 g of a white solid was obtained (*Z/E* = 93/7). Recrystallization from pentane gave 0.17 g (38%) of pure (**1**). ^1H NMR (CDCl_3): 7.21–7.55 (m, 10H), 6.13 (d, $J = 34.9$ Hz, 1H) ppm. ^{19}F NMR (CDCl_3): -104.7 (d, $J = 34.9$ Hz) ppm. ^{13}C NMR (CDCl_3): 141.2 (d, $J = 248.5$ Hz), 132.9 (d, $J = 6.1$ Hz), 131.7 (d, $J = 2.1$ Hz), 129.2 (d, $J = 4.3$ Hz), 129.1, 128.5, 128.4, 128.1 (d, $J = 2.6$ Hz), 121.4 (d, $J = 2.1$ Hz), 116.1 (d, $J = 12.8$ Hz), 92.4 (d, $J = 6.4$ Hz), 82.3 (d, $J = 41.8$ Hz) ppm. GC–MS: 222 (M^+ , 83), 220 (100), 202 (98), 194 (11), 110 (36), 98 (18). HRMS: Calcd for $\text{C}_{16}\text{H}_{11}\text{F}$: 222.0845; Found: 222.0859.

4.2.2. (*Z*)-2-fluoro-1-phenyl-1-nonen-3-yne (**2**)

To a mixture of 0.01 g (0.014 mmol) $\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$, 0.01 g (0.05 mmol) CuI , 0.19 g (2.0 mmol) $\text{CH}_3(\text{CH}_2)_4\text{C}\equiv\text{CH}$ and 2.0 ml of Et_3N was added 0.40 g (2.0 mmol) of an *E/Z* mixture of $\text{C}_6\text{H}_5\text{CH}=\text{CFBr}$ (*E/Z* = 1/1). The reaction mixture was stirred at room temperature until no (*E*)-olefin remained by ^{19}F NMR analysis of the reaction mixture (~ 24 h). The reaction mixture was directly purified by silica gel chromatography (hexanes). After solvent removal via rotary evaporation, excess olefin was removed under vacuum (0.02 mm Hg) and 0.20 g (46%) of (**2**) (*Z/E* = 98/2) was obtained. ^1H NMR (CDCl_3): 7.21–7.51 (m, 5H), 5.93 (d, $J = 35.2$ Hz, 1H), 2.39 (td, $J = 7.1$ Hz, $J = 5.0$ Hz, 2H), 1.29–1.64 (m, 6H), 0.92 (t, $J = 6.9$ Hz, 3H), ppm. ^{19}F NMR (CDCl_3): -102.3 (dt, $J = 35.0$ Hz, $J = 5.0$ Hz) ppm. ^{13}C NMR (CDCl_3): 141.4 (d, $J = 248.5$ Hz), 133.1 (d, $J = 6.1$ Hz), 128.9 (d, $J = 8.3$ Hz), 128.5, 127.7 (d, $J = 2.4$ Hz), 114.3 (d, $J = 13.4$ Hz), 94.4 (d, $J = 6.0$ Hz), 74.1 (d, $J = 41.5$ Hz), 31.0 (d, $J = 3.6$ Hz), 27.8 (d, $J = 1.6$ Hz), 22.1, 19.2 (d, $J = 2.2$ Hz), 13.9 ppm. GC–MS: 216 (M^+ , 53), 201 (2), 173 (12), 159 (100), 146 (50), 133 (63), 109 (12), 91 (21). FT-IR (neat, NaCl plate): 3091 (s), 3052 (s), 3025 (s), 2956 (w), 2221 (s), 1648 (m), 1467 (s). TLC: $R_f = 0.4$ (hexanes). HRMS: Calcd for $\text{C}_{15}\text{H}_{17}\text{F}$: 216.1314; Found: 216.1317.

4.2.3. (\pm) Acetaldehyde ethyl {(4*Z*)-4-fluoro-5-phenyl-4-penten-2-ynyl}acetal (**3**)

Similarly, 0.40 g (2.0 mmol) of an *E/Z* mixture of $\text{C}_6\text{H}_5\text{CH}=\text{CFBr}$ (*E/Z* = 3/2) was reacted with 0.26 g (2.0 mmol) of (\pm) acetaldehyde ethyl propargyl acetal in the presence of 0.01 g (0.014 mmol) of $\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$, 0.01 g (0.05 mmol) CuI and 2.0 ml Et_3N at room temperature until no (*E*)-olefin remained by ^{19}F NMR analysis of the reaction mixture (~ 24 h). The reaction mixture was directly purified by silica gel chromatography (hexanes, 100%; then 5:95 ethyl acetate:hexanes); 0.16 g of pure (*Z*)-olefin was recovered (0.24 g, 1.2 mmol of olefin consumed) and 0.27 g (54%) of (**3**) (*Z/E* = 95/5) was obtained. ^1H NMR (CDCl_3): 7.24–7.51 (m, 5H), 6.05 (d, $J = 34.9$ Hz, 1H), 4.88 (q, $J = 5.3$ Hz, 1H), 4.40 (d, $J = 4.9$ Hz, 2H), 3.47–3.73

(m, 2H), 1.36 (d, $J = 5.3$ Hz, 3H), 1.23 (t, $J = 7.0$ Hz, 3H) ppm. ^{19}F NMR (CDCl_3): -105.2 (dt, $J = 34.3$ Hz, $J = 4.5$ Hz) ppm. ^{13}C NMR (CDCl_3): 140.4 (d, $J = 248.7$ Hz), 132.6 (d, $J = 6.1$ Hz), 129.1 (d, $J = 8.0$ Hz), 128.6, 128.2 (d, $J = 2.8$ Hz), 116.3 (d, $J = 12.2$ Hz), 98.8, 89.2 (d, $J = 6.1$ Hz), 78.8 (d, $J = 42.1$ Hz), 60.8, 52.7 (d, $J = 1.9$ Hz), 19.6, 15.2 ppm. GC–MS: 248 (M^+ , 3), 233 (10), 185 (6), 176 (39), 159 (100), 146 (46), 133 (54), 72 (28). FT-IR (neat, NaCl plate): 3319 (s), 3027 (s), 2935 (vs), 2875 (s), 1664 (s), 1646 (vs). TLC: $R_f = 0.3$ (hexanes:ethyl acetate = 1:4).

4.2.4. (*3Z*)-3-fluoro-4-phenyl-1-trimethylsilyl-3-buten-1-yne (**4**)

Similarly, 0.40 g (2.0 mmol) of an *E/Z* mixture of $\text{C}_6\text{H}_5\text{CH}=\text{CFBr}$ (*E/Z* = 6/5) was reacted with 0.20 g (2.0 mmol) of $\text{Me}_3\text{SiC}\equiv\text{CH}$ in the presence of 0.01 g (0.014 mmol) $\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$, 0.01 g (0.05 mmol) CuI and 2.0 ml Et_3N at room temperature until no (*E*)-olefin remained by ^{19}F NMR analysis of the reaction mixture (~ 16 h). The reaction mixture was directly purified by silica gel chromatography (hexanes, 100%); 0.15 g of crude enyne (*Z/E* = 85/15) was obtained; after a second silica gel chromatography, 0.10 g of (**4**) (*Z/E* = 99/1) (23%) was obtained. ^1H NMR (CDCl_3): 7.25–7.50 (m, 5H), 6.06 (d, $J = 35.0$ Hz, 1H), 0.25 (s, 9H) ppm. ^{19}F NMR (CDCl_3): -105.8 (d, $J = 35.0$ Hz) ppm. ^{13}C NMR (CDCl_3): 140.8 (d, $J = 249.0$ Hz), 132.7 (d, $J = 6.1$ Hz), 129.1 (d, $J = 8.6$ Hz), 128.6, 128.2 (d, $J = 2.5$ Hz), 116.3 (d, $J = 12.2$ Hz), 99.0 (d, $J = 4.9$ Hz), 97.0 (d, $J = 40.3$ Hz), -0.48 ppm. GC–MS: 218 (M^+ , 49); 203 (20), 183 (11), 163 (5), 141 (36), 101 (100), 87 (5), 77 (36). FT-IR (neat, NaCl plate): 3056 (s), 3027 (s), 2962 (m), 2900 (s), 1643 (m).

4.2.5. (*5Z*)-5-fluoro-6-phenyl-5-hexen-3-yn-2-ol (**5**)

Similarly, 0.61 g (3.0 mmol) of an *E/Z* mixture of $\text{C}_6\text{H}_5\text{CH}=\text{CFBr}$ (*E/Z* = 1/1) was reacted with 0.21 g (3.0 mmol) of 1-butyne-3-ol in the presence of 0.01 g (0.014 mmol) of $\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$, 0.01 g (0.05 mmol) CuI and 2.0 ml Et_3N at room temperature until no (*E*)-olefin remained by ^{19}F NMR analysis of the reaction mixture (~ 24 h). The reaction mixture was directly purified by silica gel chromatography (hexanes, 100%; then 5:95 ethyl acetate:hexanes); 0.28 g of pure (*Z*)-olefin was recovered (0.33 g, 1.64 mmol of olefin consumed) and 0.28 g (49%) of (**5**) (*Z/E* > 95/5) was obtained. ^1H NMR (CDCl_3): 7.22–7.52 (m, 5H), 6.03 (d, $J = 35.0$ Hz, 1H), 4.73 (m, 1H), 2.51 (s, 1H), 1.52 (d, $J = 6.7$ Hz, 3H) ppm. ^{19}F NMR (CDCl_3): -105.2 (dd, $J = 34.9$ Hz, $J = 4.4$ Hz) ppm. ^{13}C NMR (CDCl_3): 140.4 (d, $J = 248.4$ Hz), 132.6 (d, $J = 6.1$ Hz), 129.1 (d, $J = 8.3$ Hz), 128.6, 128.2 (d, $J = 2.2$ Hz), 116.2 (d, $J = 12.5$ Hz), 94.1 (d, $J = 6.5$ Hz), 77.2 (d, $J = 42.1$ Hz), 58.4 (d, $J = 1.9$ Hz), 23.7 (d, $J = 1.5$ Hz) ppm. GC–MS: 190 (M^+ , 69), 175 (18), 155 (40), 146 (100), 133 (15), 127 (45). FT-IR (neat, NaCl plate): 3110 (s), 3091 (s), 3027 (m), 1683 (s), 1646 (w), 1496 (m). TLC: $R_f = 0.25$ (hexanes:ethyl acetate = 9:1).

4.2.6. (3'Z)-(3'-fluoro-4'-phenyl-3'-buten-1'-ynyl)-1-cyclohexanol (6)

To a mixture of 0.05 g (0.043 mmol) Pd(PPh₃)₄, 0.37 g (3.0 mmol) of 1-ethynyl-1-cyclohexanol, DMF (5 ml) and Et₃N (1 ml) was added 0.61 g (3.0 mmol) of an *E/Z* mixture of C₆H₅CH=CFBr (*E/Z* = 1/1). The resulting mixture was stirred at room temperature until no (*E*)-olefin remained by ¹⁹F NMR analysis of the reaction mixture (~24 h). The reaction mixture was then diluted with 100 ml of ether; the organic fraction was washed with saturated NH₄Cl solution (30 ml), water (3 × 20 ml) and brine solution (20 ml) and dried over anhydrous MgSO₄. Ether was removed via rotary evaporation and the residue was purified by silica gel chromatography (hexanes, 100%; then 50:50 ethyl acetate:hexanes); 0.20 g of pure (*Z*)-olefin was recovered (0.41 g, 2.0 mmol of olefin consumed) and 0.33 g (45%) of (6) was obtained (*Z/E* > 99/1). GLPC > 99%. ¹H NMR (CDCl₃): 7.15–7.46 (m, 5H), 5.96 (d, *J* = 34.9 Hz, 1H), 2.01 (s, 1H), 1.92 (m, 2H), 1.47–1.69 (m, 7H), 1.13–1.25 (m, 1H) ppm. ¹⁹F NMR (CDCl₃): –104.5 (d, *J* = 35.6 Hz) ppm. ¹³C NMR (CDCl₃): 140.7 (d, *J* = 249.2 Hz), 132.7 (d, *J* = 5.9 Hz), 129.1 (d, *J* = 8.0 Hz), 128.6, 128.1 (d, *J* = 2.9 Hz), 115.9 (d, *J* = 12.3 Hz), 96.1 (d, *J* = 6.5 Hz), 77.5 (d, *J* = 52.3 Hz), 69.0, 39.5, 25.0, 23.1 ppm. GC–MS: 244 (*M*⁺, 43), 226 (84), 196 (31), 183 (53), 159 (41), 146 (100), 133 (49), 125 (30). TLC: *R*_f = 0.2 (hexane:ethyl acetate = 9:1).

4.2.7. (5Z)-5-fluoro-6-(4'-chlorophenyl)-5-hexen-3-yn-2-ol (7)

Similarly, 0.71 g (3.0 mmol) of an *E/Z* mixture of *p*-ClC₆H₄CH=CFBr (*E/Z* = 1/1) was reacted with 0.21 g (3.0 mmol) of 1-butyn-3-ol in the presence of 0.01 g (0.014 mmol) Pd(PPh₃)₂Cl₂, 0.01 g (0.05 mmol) CuI and 2.0 ml Et₃N at room temperature until no (*E*)-olefin remained by ¹⁹F NMR analysis of the reaction mixture (~24 h). The reaction mixture was directly purified by silica gel chromatography (hexanes, 100%; then 10:90 ethyl acetate:hexanes); 0.31 g of pure (*Z*)-olefin was recovered (0.41 g, 1.7 mmol of olefin was consumed) and 0.32 g (48%) of (7) was obtained (*Z/E* > 99/1). ¹H NMR (CDCl₃): 7.20–7.33 (m, 4H), 5.89 (d, *J* = 33.5 Hz, 1H), 4.64 (m, 1H), 2.33 (s, 1H), 1.45 (d, *J* = 6.7 Hz, 3H) ppm. ¹⁹F NMR (CDCl₃): –104.3 (dd, *J* = 34.3 Hz, *J* = 4.5 Hz) ppm. ¹³C NMR (CDCl₃): 140.7 (d, *J* = 249.2 Hz), 133.9 (d, *J* = 4.1 Hz), 131.0 (d, *J* = 5.8 Hz), 130.3 (d, *J* = 8.3 Hz), 128.8, 115.1 (d, *J* = 12.3 Hz), 94.5 (d, *J* = 6.2 Hz), 77.0 (d, *J* = 41.8 Hz), 58.5 (d, *J* = 1.8 Hz), 23.7 (d, *J* = 1.8 Hz) ppm. GC–MS: 224 (*M*⁺, 44), 226 (11), 209 (22), 189 (22), 169 (14), 145 (100), 141 (8), 133 (5), 125 (17), 113 (4). TLC: *R*_f = 0.2 (hexanes:ethyl acetate = 9:1). HRMS: Calcd for C₁₂H₁₀F³⁷C₁₀: 226.0375; Found: 226.0379.

4.2.8. (±) Acetaldehyde ethyl{(4Z)-4-fluoro-5-(4'-chlorophenyl)-4-penten-2-ynyl}acetal (8)

Similarly, 0.47 g (2.0 mmol) of an *E/Z* mixture of *p*-ClC₆H₄CH=CFBr (*E/Z* = 1/1) was reacted with 0.26 g

(2.0 mmol) of (±) acetaldehyde ethyl propargyl acetal in the presence of 0.01 g (0.014 mmol) Pd(PPh₃)₂Cl₂, 0.01 g (0.05 mmol) CuI and 2.0 ml Et₃N at room temperature until no (*E*)-olefin remained by ¹⁹F NMR analysis of the reaction mixture (~24 h). The reaction mixture was directly purified by silica gel chromatography (hexanes; 100%, then 5:95 ethyl acetate:hexanes); 0.19 g of pure (*Z*)-olefin was recovered (0.28 g, 1.12 mmol of olefin was consumed) and 0.28 g (49%) of (8) was obtained (*Z/E* > 99/1). ¹H NMR (CDCl₃): 7.18–7.35 (m, 4H), 5.90 (d, *J* = 34.3 Hz, 1H), 4.78 (q, *J* = 5.4 Hz, 1H), 4.31 (d, *J* = 4.9 Hz, 2H), 3.40–3.64 (m, 2H), 1.27 (d, *J* = 5.4 Hz, 3H), 1.15 (t, *J* = 7.1 Hz, 3H) ppm. ¹⁹F NMR (CDCl₃): –104.1 (dt, *J* = 34.3 Hz, *J* = 5.1 Hz) ppm. ¹³C NMR (CDCl₃): 140.8 (d, *J* = 249.2 Hz), 133.9 (d, *J* = 4.4 Hz), 131.0 (d, *J* = 6.5 Hz), 130.3 (d, *J* = 8.0 Hz), 128.7, 115.2 (d, *J* = 12.3 Hz), 98.8, 88.7 (d, *J* = 5.8 Hz), 78.4 (d, *J* = 42.1 Hz), 60.7, 52.6 (d, *J* = 1.4 Hz), 19.6, 15.2 ppm. DIP–MS: 282 (*M*⁺, 6), 284 (2), 267 (10), 239 (5), 210 (74), 193 (53), 157 (79), 146 (100), 127 (51). FT-IR (neat, NaCl plate): 2980 (m), 2927 (m), 2868 (s), 1649 (m), 1223 (s), 1150 (m). *R*_f = 0.33 (hexanes:ethyl acetate = 9:1).

4.2.9. (3Z)-3-fluoro-1-phenyl-3-undecen-1-yne (9)

Similarly, 0.45 g (2.0 mmol) of an *E/Z* mixture of C₇H₁₅CH=CFBr (*E/Z* = 7/3) was reacted with 0.20 g (2.0 mmol) phenyl acetylene in the presence of 0.01 g (0.014 mmol) Pd(PPh₃)₂Cl₂, 0.01 g (0.05 mmol) CuI and 3.0 ml Et₃N at room temperature until no (*E*)-olefin remained by ¹⁹F NMR analysis of the reaction mixture (~24 h). The reaction mixture was directly purified by silica gel chromatography (hexane), and 0.31 g (64%) of (9) (*Z/E* = 90/10) was obtained. ¹H NMR (CDCl₃): 7.25–7.51 (m, 5H), 5.31 (dt, *J* = 33.5 Hz, *J* = 7.8 Hz, 1H), 2.22 (m, 2H), 1.29–1.44 (m, 10H), 0.88 (m, 3H) ppm. ¹⁹F NMR (CDCl₃): –111.6 (d, *J* = 33.7 Hz) ppm. ¹³C NMR (CDCl₃): 141.0 (d, *J* = 235.3 Hz), 131.6 (d, *J* = 1.8 Hz), 128.9, 128.4, 121.7 (d, *J* = 2.5 Hz), 118.1 (d, *J* = 20.1 Hz), 90.1 (d, *J* = 7.0 Hz), 81.5 (d, *J* = 43.7 Hz), 31.8, 29.1, 29.0, 28.9 (d, *J* = 1.8 Hz), 24.6 (d, *J* = 0.6 Hz), 22.6, 14.1 ppm. GC–MS: 244 (*M*⁺, 21), 215 (5), 173 (10), 159 (87), 146 (100), 133 (38). FT-IR (neat, NaCl plate): 3058 (s), 3035 (vs), 3021 (s), 2219 (s), 1708 (m), 1666 (m). HRMS: Calcd for C₁₇H₂₁F: 244.1627; Found: 244.1625.

4.2.10. (5Z)-5-fluoro-5-tridecen-3-yn-2-ol (10)

Similarly, 0.45 g (2.0 mmol) of an *E/Z* mixture of C₇H₁₅CH=CFBr (*E/Z* = 1/1) was reacted with 0.20 g (2.5 mmol) of 1-butyn-3-ol in the presence of 0.01 g (0.014 mmol) Pd(PPh₃)₂Cl₂, 0.01 g (0.05 mmol) CuI and 2.0 ml Et₃N at room temperature until no (*E*)-olefin remained by ¹⁹F NMR analysis of the reaction mixture (~24 h). The reaction mixture was directly purified by silica gel chromatography (hexanes, 100%; then 5:95 ethyl acetate:hexanes); 0.22 g of pure (*Z*)-olefin was recovered (0.23 g, 1.03 mmol of olefin consumed) and 0.18 g (43%) of (10) (*Z/E* > 98/2) was obtained. ¹H NMR (CDCl₃): 5.13

(dt, $J = 33.5$ Hz, $J = 7.8$ Hz, 1H), 4.58 (m, 1H), 2.04–2.12 (m, 3H), 1.41 (d, $J = 6.7$ Hz, 3H), 1.12–1.33 (m, 10H), 0.81 (t, $J = 6.4$ Hz, 3H) ppm. ^{19}F NMR (CDCl_3): -112.1 (d, $J = 33.1$ Hz) ppm. ^{13}C NMR (CDCl_3): 140.4 (d, $J = 235.5$ Hz), 118.3 (d, $J = 19.6$ Hz), 91.9 (d, $J = 7.3$ Hz), 77.5 (d, $J = 43.5$ Hz), 58.4 (d, $J = 1.4$ Hz), 31.8, 29.1, 28.9, 28.7 (d, $J = 1.5$ Hz), 24.4, 23.8 (d, $J = 1.4$ Hz), 22.6, 14.0 ppm. GC–MS: 212 (M^+ , 9), 165 (4), 141 (6), 121 (6), 109 (16), 99 (26), 79 (15), 55 (28), 43 (100). FT-IR (neat, NaCl plate): 3573 (s), 3373 (m), 3052 (m), 1667 (m), 1721 (s). TLC: $R_f = 0.25$ (hexanes:ethyl acetate = 9:1).

4.2.11. (\pm) Acetaldehyde ethyl{(4Z)-4-fluoro-4-dodecen-2-ynyl}acetal (**11**)

Similarly, 0.45 g (2.0 mmol) of an *E/Z* mixture of $\text{C}_7\text{H}_{15}\text{H}=\text{CFBr}$ ($E/Z = 1/1$) was reacted with 0.26 g (2.0 mmol) of (\pm) acetaldehyde ethyl propargyl acetal in the presence of 0.01 g (0.014 mmol) $\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$, 0.01 g (0.05 mmol) CuI and 2.0 ml Et_3N at room temperature until no (*E*)-olefin remained by ^{19}F NMR analysis of the reaction mixture (~24 h). The reaction mixture was directly purified by silica gel chromatography (hexanes, 100%; then 5:95 ethyl acetate:hexanes): 0.20 g of pure (*Z*)-olefin was recovered (0.25 g, 1.11 mmol of olefin was consumed) and 0.25 g (46%) of (**11**) ($Z/E = 93/7$) was obtained. ^1H NMR (CDCl_3): 5.15 (dt, $J = 33.5$ Hz, $J = 7.8$ Hz, 1H), 4.78 (q, $J = 5.3$ Hz, 1H), 4.27 (d, $J = 4.9$ Hz, 2H), 3.40–3.64 (m, 2H), 2.08 (qd, $J = 6.6$ Hz, $J = 1.8$ Hz, 2H), 1.12–1.32 (m, 16H), 0.81 (t, $J = 6.5$ Hz, 3H) ppm. ^{19}F NMR (CDCl_3): -112.1 (d, $J = 33.5$ Hz) ppm. ^{13}C NMR (CDCl_3): 140.4 (d, $J = 235.6$ Hz), 118.3 (d, $J = 19.8$ Hz), 98.7, 86.9 (d, $J = 7.0$ Hz), 78.0 (d, $J = 44.0$ Hz), 60.7, 52.6 (d, $J = 1.8$ Hz), 31.7, 28.9 (d, $J = 4.6$ Hz), 28.7 (d, $J = 1.8$ Hz), 24.4 (d, $J = 0.9$ Hz), 22.6, 19.6, 15.2, 14.0 ppm. GC–MS: no M^+ observed, 211 (2), 183 (10), 170 (8), 155 (5), 143 (8), 138 (100), 111 (26), 91 (36). FT-IR (neat, NaCl plate): 2955 (s), 2857 (s), 1666 (s), 1128 (s). TLC: $R_f = 0.33$ (hexane:ethyl acetate = 9:1).

4.2.12. (5Z)-5-fluoro-6-phenyl-5-octen-3-yn-2-ol (**12**)

Similarly, 0.69 g (3.0 mmol) of an *E/Z* mixture of $\text{Ph}(\text{CH}_3)\text{CHCH}=\text{CFBr}$ ($E/Z = 7/3$) was reacted with 0.21 g (3.0 mmol) of 1-butyne-3-ol in the presence of 0.01 g (0.014 mmol) $\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$, 0.01 g (0.05 mmol) CuI and 3.0 ml Et_3N at room temperature until no (*E*)-olefin remained by ^{19}F NMR analysis of the reaction mixture (~24 h). The reaction mixture was directly purified by silica gel chromatography (hexanes, 100%; then 50:50 ethyl acetate:hexanes); 0.23 g of pure (*Z*)-olefin was recovered (0.46 g, 2.0 mmol of olefin was consumed) and 0.23 g (53%) of (**12**) ($Z/E = 92/8$) was obtained. ^1H NMR (CDCl_3): 7.18–7.34 (m, 5H), 5.36 (dd, $J = 32.6$ Hz, $J = 9.8$ Hz, 1H), 4.59–4.67 (m, 1H), 3.96–4.04 (m, 1H), 2.08 (s, 1H), 1.46 (dd, $J = 6.6$ Hz, $J = 0.4$ Hz, 3H), 1.37 (d, $J = 7.1$ Hz, 3H) ppm. ^{19}F NMR (CDCl_3): -111.4 (dt, $J = 33.1$ Hz, $J = 3.1$ Hz) ppm. ^{13}C NMR (CDCl_3):

144.3 (d, $J = 1.8$ Hz), 139.3 (d, $J = 237.4$ Hz), 128.6, 126.8, 126.5, 122.5 (d, $J = 18.9$ Hz), 92.6 (d, $J = 6.8$ Hz), 76.3 (d, $J = 43.3$ Hz), 58.4 (d, $J = 1.2$ Hz), 35.2 (d, $J = 1.9$ Hz), 23.7 (d, $J = 1.8$ Hz), 21.1 (d, $J = 1.9$ Hz) ppm. GC–MS: 218 (M^+ , 4), 203 (13), 185 (23), 170 (12), 165 (23), 155 (23), 133 (15), 77 (20), 43 (100). FT-IR (neat, NaCl plate): 3380 (m), 3029 (s), 2977 (m), 1664 (m), 1236 (s). TLC: $R_f = 0.20$ (hexanes:ethyl acetate = 9:1).

4.2.13. (E)-1,4-diphenyl-3-fluoro-3-buten-1-yne (**13**)

To a mixture of 0.01 g (0.014 mmol) $\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$, 0.01 g (0.05 mmol) CuI and 0.21 g (2.0 mmol) $\text{C}_6\text{H}_5\text{C}\equiv\text{CH}$ and 2.0 ml Et_3N was added 0.41 g (2.0 mmol) of $\text{C}_6\text{H}_5\text{CH}=\text{CFBr}$ ($Z/E = 97/3$), and the reaction mixture was stirred at room temperature for 48 h. The reaction mixture was directly purified by silica gel chromatography (hexanes), followed by recrystallization from pentane to give 0.39 g (88%) of (**13**) ($E/Z > 97/3$). ^1H NMR (CDCl_3): 7.21–7.67 (m, 10H), 6.61 (d, $J = 16.1$ Hz, 1H) ppm. ^{19}F NMR (CDCl_3): -102.8 (d, $J = 16.6$ Hz) ppm. ^{13}C NMR (CDCl_3): 141.1 (d, $J = 232.2$ Hz), 132.2 (d, $J = 9.5$ Hz), 131.7 (d, $J = 2.6$ Hz), 129.6, 128.5 (d, $J = 5.1$ Hz), 128.2 (d, $J = 2.1$ Hz), 128.1 (d, $J = 3.3$ Hz), 121.3 (d, $J = 2.6$ Hz), 117.5 (d, $J = 33.1$ Hz), 97.3 (d, $J = 6.9$ Hz), 81.2 (d, $J = 41.1$ Hz) ppm. GC–MS: 222 (M^+ , 90), 220 (100), 202 (16), 194 (4), 150 (2), 110 (12), 98 (6), 85 (3), 74 (3).

4.2.14. (E)-2-fluoro-1-phenyl-1-nonen-3-yne (**14**)

Similarly, the reaction of 0.40 g (2.0 mmol) of (*Z*)- $\text{C}_6\text{H}_5\text{CH}=\text{CFBr}$ with 0.19 g (2.0 mmol) $\text{CH}_3(\text{CH}_2)_4\text{C}\equiv\text{CH}$ in the presence of 0.01 g (0.014 mmol) $\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$, 0.01 g (0.05 mmol) CuI and 2.0 ml Et_3N at room temperature for 48 h gave 0.37 g (87%) of (**14**), GLPC > 99%. ^1H NMR (CDCl_3): 7.20–7.58 (m, 5H), 6.48 (d, $J = 17.0$ Hz, 1H), 2.46 (td, $J = 7.0$ Hz, $J = 5.3$ Hz, 2H), 1.26–1.67 (m, 6H), 0.91 (t, $J = 7.0$ Hz, 3H) ppm. ^{19}F NMR (CDCl_3): -99.9 (dt, $J = 17.1$ Hz, $J = 5.0$ Hz) ppm. ^{13}C NMR (CDCl_3): 141.3 (d, $J = 232.2$ Hz), 132.4 (d, $J = 9.8$ Hz), 128.3, 127.8, 127.7, 115.7 (d, $J = 33.8$ Hz), 99.9 (d, $J = 6.5$ Hz), 73.0 (d, $J = 41.1$ Hz), 31.0, 27.6 (d, $J = 1.8$ Hz), 22.1, 19.5, 13.9 ppm. GC–MS: 216 (M^+ , 76), 201 (3), 187 (8), 173 (13), 159 (100), 146 (54), 133 (76), 109 (12). FT-IR (neat, NaCl plate): 3060 (s), 3027 (s), 2958 (w), 2933 (w), 2861 (m), 2225 (m), 1641 (w), 1448 (m). HRMS: Calcd for $\text{C}_{15}\text{H}_{17}\text{F}$: 216.1314; Found: 216.1319.

4.2.15. (\pm) Acetaldehyde ethyl{(4E)-4-fluoro-5-phenyl-4-penten-2-ynyl}acetal (**15**)

Similarly, the reaction of 0.40 g (2.0 mmol) of $\text{C}_6\text{H}_5\text{CH}=\text{CFBr}$ ($Z/E > 98/2$) with 0.26 g (2.0 mmol) of (\pm) acetaldehyde ethyl propargyl acetal in the presence of 0.01 g (0.014 mmol) $\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$, 0.01 g (0.05 mmol) CuI and 2.0 ml Et_3N at room temperature for 48 h gave 0.44 g (89%) of (**15**) ($E/Z > 98/2$). ^1H NMR (CDCl_3): 7.24–7.60 (m, 5H), 6.59 (d, $J = 17.0$ Hz, 1H), 4.88 (q, $J = 5.4$ Hz, 1H), 4.47 (dd, $J = 5.1$ Hz, $J = 1.6$ Hz,

2H), 3.47–3.71 (m, 2H), 1.36 (d, $J = 5.3$ Hz, 3H), 1.21 (t, $J = 7.0$ Hz, 3H) ppm. ^{19}F NMR (CDCl_3): -103.1 (dt, $J = 17.2$ Hz, $J = 5.1$ Hz) ppm. ^{13}C NMR (CDCl_3): 140.5 (d, $J = 232.5$ Hz), 131.7 (d, $J = 8.7$ Hz), 128.4, 128.2 (d, $J = 2.1$ Hz), 128.0, 117.8 (d, $J = 32.7$ Hz), 98.9, 94.3 (d, $J = 7.3$ Hz), 76.8 (d, $J = 41.5$ Hz), 61.0, 52.7 (d, $J = 2.2$ Hz), 19.6, 15.2 ppm. GC–MS: 248 (M^+ , 3), 233 (16), 219 (5), 205 (8), 185 (10), 176 (23), 159 (100), 146 (35), 133 (52), 128 (27). FT-IR (neat, NaCl plate): 3060 (s), 3027 (s), 2979 (m), 2931 (m), 1643 (m), 1448 (m), 1216 (m).

4.2.16. (5E)-5-fluoro-6-phenyl-5-hexen-3-yn-2-ol (**16**)

Similarly, the reaction of 0.40 g (2.0 mmol) of (Z)- $\text{C}_6\text{H}_5\text{CH}=\text{CFBr}$ with 0.21 g (3.0 mmol) of 1-butyne-3-ol in the presence of 0.01 g (0.014 mmol) $\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$, 0.01 (0.05 mmol) CuI and 2.0 ml Et_3N at room temperature for 48 h gave (after silica gel chromatography, 50:50 ethyl acetate:hexanes) 0.34 g (89%) of (**16**), GLPC > 99%. ^1H NMR (CDCl_3): 7.23–7.59 (m, 5H), 6.58 (d, $J = 17.0$ Hz, 1H), 4.75 (m, 1H), 2.39 (s, 1H), 1.54 (d, $J = 6.6$ Hz, 3H) ppm. ^{19}F NMR (CDCl_3): -103.2 (dd, $J = 16.5$ Hz, $J = 4.4$ Hz) ppm. ^{13}C NMR (CDCl_3): 140.4 (d, $J = 232.9$ Hz), 131.7 (d, $J = 9.4$ Hz), 128.4, 128.3 (d, $J = 1.8$ Hz), 127.9 (d, $J = 3.2$ Hz), 117.7 (d, $J = 32.3$ Hz), 99.1 (d, $J = 6.9$ Hz), 76.0 (d, $J = 41.4$ Hz), 58.6 (d, $J = 1.8$ Hz), 23.5 (d, $J = 2.2$ Hz) ppm. GC–MS: 190 (M^+ , 64), 175 (16), 155 (51), 146 (100), 133 (19), 127 (58), 122 (1), 107 (3), 94 (3), 75 (11). FT-IR (neat, NaCl plate): 3106 (s), 3085 (s), 2985 (m), 2935 (s), 2877 (s), 1675 (s), 1448 (m). TLC: $R_f = 0.25$ (hexanes:ethyl acetate = 9:1).

4.2.17. (5E)-5-fluoro-6-(4'-chlorophenyl)-5-hexen-3-yn-2-ol (**17**)

Similarly, the reaction of 0.24 g (1.0 mmol) of (Z)- $p\text{-ClC}_6\text{H}_4\text{CH}=\text{CFBr}$ with 0.1 g (1.3 mmol) of 1-butyne-3-ol in the presence of 0.01 g (0.014 mmol) $\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$, 0.01 g (0.05 mmol) CuI and 3.0 ml Et_3N at room temperature for 48 h gave (after silica gel chromatography, hexanes, 100%; then 50:50 ethyl acetate:hexanes) 0.17 g (77%) of (**17**). ^1H NMR (CDCl_3): 7.18–7.47 (m, 4H), 6.47 (d, $J = 16.5$ Hz, 1H), 4.64–4.75 (m, 1H), 2.08 (s, 1H), 1.49 (d, $J = 6.6$ Hz, 3H) ppm. ^{19}F NMR (CDCl_3): -102.2 (dd, $J = 17.6$ Hz, $J = 3.8$ Hz) ppm. ^{13}C NMR (CDCl_3): 140.7 (d, $J = 234.4$ Hz), 133.9 (d, $J = 2.2$ Hz), 130.3 (d, $J = 9.4$ Hz), 129.2 (d, $J = 2.9$ Hz), 128.7, 116.7 (d, $J = 33.4$ Hz), 99.6 (d, $J = 6.5$ Hz), 75.8 (d, $J = 41.7$ Hz), 58.6 (d, $J = 2.1$ Hz), 23.6 (d, $J = 1.8$ Hz) ppm. GC–MS: 224 (M^+ , 35), 226 (11), 209 (16), 189 (16), 169 (9), 145 (55), 141 (12), 133 (7), 125 (29), 113 (5), 43 (100). TLC: $R_f = 0.21$ (hexanes:ethyl acetate = 9:1). HRMS: Calcd for $\text{C}_{12}\text{H}_{10}\text{F}^{35}\text{ClO}$, 224.0404; Found: 224.0427.

4.2.18. (\pm) Acetaldehyde ethyl{(4E)-4-fluoro-5-(4'-chlorophenyl)-4-penten-2-ynyl}acetal (**18**)

Similarly, the reaction of 0.24 g (1.0 mmol) of (Z)- $p\text{-ClC}_6\text{H}_4\text{CH}=\text{CFBr}$ with 0.13 g (1.0 mmol) of (\pm) acetaldehyde

ethyl propargyl acetal in the presence of 0.01 g (0.014 mmol) $\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$, 0.01 g (0.05 mmol) CuI and 2.0 ml of Et_3N at room temperature for 48 h gave 0.25 g (89%) of (**18**). ^1H NMR (CDCl_3): 7.18–7.46 (m, 4H), 6.45 (d, $J = 16.4$ Hz, 1H), 4.79 (q, $J = 5.3$ Hz, 1H), 4.37 (d, $J = 5.1$ Hz, 2H), 3.38–3.62 (m, 2H), 1.27 (d, $J = 5.4$ Hz, 3H), 1.12 (t, $J = 7.1$ Hz, 3H) ppm. ^{19}F NMR (CDCl_3): -101.9 (dt, $J = 16.9$ Hz, $J = 5.1$ Hz) ppm. ^{13}C NMR (CDCl_3): 140.8 (d, $J = 234.4$ Hz), 133.8 (d, $J = 2.5$ Hz), 130.3 (d, $J = 9.2$ Hz), 129.1 (d, $J = 3.1$ Hz), 128.6, 116.7 (d, $J = 32.9$ Hz), 98.9, 95.0 (d, $J = 6.7$ Hz), 77.1 (d, $J = 43.4$ Hz), 60.9, 52.6 (d, $J = 1.8$ Hz), 19.6, 15.1 ppm. DIP–MS: 282 (M^+ , 4), 284 (1.3), 267 (10), 239 (8), 210 (55), 193 (70), 157 (100), 146 (96), 127 (49). FT-IR (neat, NaCl plate): 2980 (s), 2930 (s), 1642 (s), 1491 (s), 1150 (s). TLC: $R_f = 0.34$ (hexanes:ethyl acetate = 9:1). HRMS: Calcd for $\text{C}_{15}\text{H}_{16}^{35}\text{ClFO}_2$, 282.0823; Found: 282.0815.

4.2.19. (5E)-5-fluoro-6-phenyl-5-octen-3-yn-2-ol (**19**)

Similarly, the reaction of 0.23 g (1.0 mmol) of (Z)- $\text{C}_6\text{H}_5(\text{CH}_3)\text{CHCH}=\text{CFBr}$ with 0.10 g (1.3 mmol) of 1-butyne-3-ol in the presence of 0.01 g (0.014 mmol) $\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$, 0.01 g (0.05 mmol) CuI and 3.0 ml Et_3N at room temperature for 48 h gave 0.17 g (78%) of (**19**). ^1H NMR (CDCl_3): 7.18–7.34 (m, 5H), 5.73 (dd, $J = 14.3$ Hz, $J = 10.5$ Hz, 1H), 4.66–4.77 (m, 1H), 3.66–3.77 (m, 1H), 2.22 (s, 1H), 1.51 (d, $J = 6.3$ Hz, 3H), 1.39 (dd, $J = 6.8$ Hz, $J = 0.8$ Hz, 3H) ppm. ^{19}F NMR (CDCl_3): -109.7 (d, $J = 14.6$ Hz) ppm. ^{13}C NMR (CDCl_3): 144.5, 140.5 ($J = 233.7$ Hz) 128.5, 126.6 (d, $J = 23.3$ Hz), 122.3 (dd, $J = 22.6$ Hz, $J = 3.7$ Hz), 97.7 (d, $J = 6.7$ Hz), 74.4 (d, $J = 43.3$ Hz), 58.5, 37.2 (d, $J = 4.3$ Hz), 23.8, 21.4 (d, $J = 2.5$ Hz) ppm. GC–MS: 218 (M^+ , 1), 203 (3), 185 (9), 170 (5), 165 (7), 155 (8), 133 (45), 115 (9), 77 (23), 43 (100). FT-IR (neat, NaCl plate): 3334 (m), 3085 (s), 3029 (s), 2979 (m), 1654 (m), 1288 (w). TLC: $R_f = 0.20$ (hexanes:ethyl acetate = 9:1). HRMS: Calcd for $\text{C}_{14}\text{H}_{15}\text{FO}$, 218.1107; Found: 218.1094.

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