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New methods for the synthesis of fluoroolefins via the palladium catalyzed cross-coupling reaction of 1-fluorovinyl halides with organoboranes and organostannanes

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Abstract

The palladium catalyzed cross-coupling reaction of 1-fluorovinyl halides with organoboranes and organostannanes provide two new facile methods to 1-substituted 1-fluoroolefins. The reactions proceed with retention of configuration in good to excellent yields.

Keywords: Palladium catalyst; Cross-coupling; Fluoroolefin

1. Introduction

New methods to fluoroorganic compounds are of considerable interest [1,21–23], in part because of the change in biological activity often observed by the introduction of fluorine into compounds synthesized by medicinal chemists [2,24]. For this reason fluoroolefins [3,25] have been of special interest as enzyme inhibitors (see [4,26] and references therein.). Recently, we reported the stereospecific Pd(0)/Cu(I) catalyzed cross-coupling of 1-fluorovinylstannanes with aryl iodides under Stille conditions to afford substituted fluoroolefins [5,27]. The method requires somewhat forcing conditions since CuI is necessary as a co-catalyst to obtain good yields of product and to avoid the formation of large amounts of side products. Herein we report two new palladium-catalyzed cross-coupling reactions (for the palladium(0) catalyzed coupling reaction of 1-fluorovinyl bromides with terminal alkynes, see [6]) of 1-fluorovinyl halides with organoboranes or organostannanes that provide more facile stereospecific methods to 1-substituted 1-fluoroolefins. A rationale for the increased facility of the two new methods to substituted fluoroolefins compared with the Pd(0)/Cu(I)/1-fluorovinylstannanes method will be discussed based on the electronic effects of fluorine. A portion of this work was published as a communication The coupling reaction of 1-fluorovinylstannane with iodobenzene proceeded very slowly under standard Stille conditions (without CuI) to give a very poor yield of the desired product, see [7,28].

2. Results and discussion

The required 1-fluorovinyl bromides or chlorides **1–4** are readily available, as a separable mixture of *E*, *Z* isomers, by the condensation of aldehydes with fluorotribromomethane or fluorotrichloromethane in the presence of triphenylphosphine and zinc [8,29–31]. Alternatively, bromination of *E*-2-fluoro-3-phenylacrylic acid [6] followed by debromocarboxylation yields pure isomer *Z*-**1**. The corresponding *E*-isomer [9] *E*-**1** was obtained in 92% isomeric purity by isomerization of *Z*-**1** with a catalytic amount of bromine in chloroform.

The coupling of (*E*)-**1**-fluoro-2-phenylvinyl bromide *E*-1 with phenylboronic acid (**5a**) proceeded in the presence of 5 mol% of $Pd(PPh_3)_4$ under Suzuki conditions (1 M aq. Na_2CO_3, benzene–ethanol, reflux; cross-coupling of carbon substituted vinyl halides with arylboronic acids catalyzed by palladium(0) has been reported [10,32]) to afford β-fluorostilbene *Z*-**6a**[2] exclusively in 86% isolated yield (Table 1). In addition, under these conditions *E*-**1** coupled with aryl-

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[2]The *E* or *Z* configuration of the product olefins was assigned from the $^3J_{H-F}$ coupling constant: 14–18 Hz for a *cis* H–F coupling. 33–36 Hz for a *trans* coupling.

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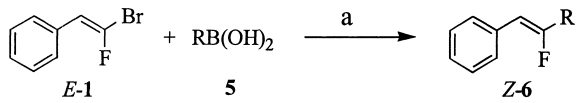
Table 1
Cross-coupling of (*E*)-β-bromo-β-fluorostyrene with organoboranes



E-**1** **5** *Z*-**6**

(a: $Pd(PPh_3)_4$, Na_2CO_3, benzene–EtOH–H_2O, reflux)

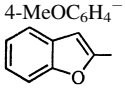
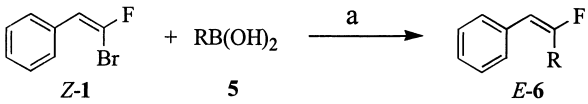
Entry	R		Time (h)	Product	Yield (%)
1	$C_6H_5^-$	(**5a**)	1	*Z*-**6a**	86
2	4-$ClC_6H_4^-$	(**5b**)	1	*Z*-**6b**	89
3	4-$MeOC_6H_4^-$	(**5c**)	3	*Z*-**6c**	91
4		(**5d**)	3	*Z*-**6d**	83
5	*E*-*n*-C_4H_9CH=CH-	(**5e**)	3	*Z*-**6e**	81

Table 2
Cross-coupling of (*Z*)-β-bromo-β-fluorostyrene with organoboranes

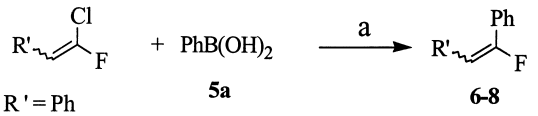


Z-**1** **5** *E*-**6**

(a: $Pd(PPh_3)_4$, Na_2CO_3, benzene–EtOH–H_2O, reflux)

Entry	R		Time (h)	Product	Yield (%)
1	Ph	(**5a**)	4	*E*-**6a**	92
2	4-$ClC_6H_4^-$	(**5b**)	4	*E*-**6b**	90
3	4-$MeOC_6H_4^-$	(**5c**)	6	*E*-**6c**	85
4	*E*-*n*-C_4H_9CH=CH-	(**5e**)	4	*E*-**6e**	82
5	1-Naphthyl	(**5f**)	5	*E*-**6f**	78

Table 3
Cross-coupling of (*E*, *Z*)-1-chloro-1-fluoroolefins **2–4** with phenylboronic acid (**5a**)



5a **6-8**

2, R' = Ph
3, R' = 4-$MeOC_6H_4$
4, R' = $PhCH_2CH_2$

(a: $Pd(PPh_3)_4/Na_2CO_3$/benzene–EtOH–H_2O/reflux)

Entry	R'		Ratio (*E*/*Z*)	Time (h)	Product	Yield (%)	Ratio (*Z*/*E*)
1	Ph	(**2**)	44/56	4	**6a**	92	50/50
2	4-$MeOC_6H_4^-$	(**3**)	44/56	8	**7**	80	47/53
3	$PhCH_2CH_2^-$	(**4**)	47/53	24[a]	**8**	83	45/55

[a] $Pd(PPh_3)_2Cl_2$/dioxane/aq.Na_2CO_3/reflux.

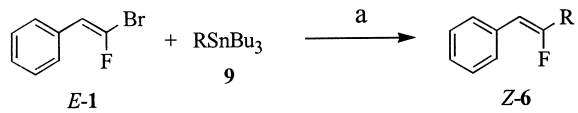
boronic acids **5b–d** and vinylboronic acid **5e** to give fluoroolefins *Z*-**6b–e** in 81–91% yields.

The coupling reaction of the *Z*-isomer *Z*-**1** with organoboronic acids **5a–c**, **5f** and vinylboronic acid **5e** also proceeded smoothly to give the corresponding *E* isomers *E*-**6a–c** and *E*-**6e–f** exclusively in 78–92% yields (see Table 2).

It is noteworthy that the coupling reaction also proceeded with 1-fluorovinyl chlorides **2–4** (Table 3). Reaction of 1-fluoro-2-phenylvinyl chloride **2** (mixture of *E*/*Z* isomers with a ratio of *E*/*Z* = 44/56) with phenylboronic acid (**5a**) under Suzuki conditions gave the fluorinated olefin **6a** as a mixture of *E* and *Z* isomers with a 1 : 1 ratio based on GC-MS and ^{19}F NMR analysis of the crude reaction mixture. These two isomers were separated by chromatography (*Z*-**6a**, 43% and *E*-**6a**, 49%) (Table 3). The coupling reaction of 1-fluoro-2-(4-methoxyphenyl)vinyl chloride **3** (*E*/*Z* = 44 : 56) with phenylboronic acid (**5a**) provided the products *Z*-**7** and *E*-**7** in 80% isolated yield (*Z*/*E* = 47 : 53). This reaction required approximately 8 h for complete conversion to **7** vs 4 h for the unsubstituted phenyl fluoroolefin **6a**, which can be attributed to the electron-donating 4-methoxy group. Reaction of 1-fluoro-2-phenethylvinyl chloride **4** with phenylboronic acid (3 equiv.) was not complete after 48 h when catalyzed by tetrakis(triphenylphosphine)palladium(0). However, the reaction proceed to completion in 24 h when catalyzed by $Pd(PPh_3)_2Cl_2$ in refluxing dioxane to afford the desired product in 83% yield as an inseparable mixture of *Z*-**8** and *E*-**8** in a ratio of 45 : 55.

An alternative method to 1-substituted 1-fluoroolefins, that compliments the Sonogashira reaction conditions reported by Mestdagh and co-workers for the synthesis of fluorinated enynes and dienes [6,11], is the palladium catalyzed coupling of 1-fluorovinyl bromides *E*-**1** and *Z*-**1** with organostannanes (**9**). Condensation of phenyltributylstannane (**9a**) with *E*-**1** using 5 mol% $Pd(PPh_3)_4$ as the catalyst in refluxing dioxane provided high yields of the corresponding *Z*-**6a** with retention of double bond geometry. Several examples of the reaction with *E*-**1** are summarized in Table 4 showing good to excellent isolated yields. The reaction of *E*-**1** with (tributylstannyl) phenylacetylene (**9g**) to provide *Z*-**6g** (75% isolated yield) was carried out for direct comparison with the Sonogashira conditions reported with acetylenes and haloolefins. The yield of *Z*-**6g** was identical by our new route and by the coupling reaction of β-bromo-β-fluorostyrene with phenylacetylene under Sonogashira conditions [11]. It should also be noted that

Table 4
Cross-coupling of (*E*)-β-bromo-β-fluorostyrene with organostannanes

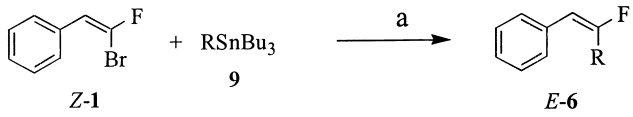


E-**1** **9** *Z*-**6**

(a: $Pd(PPh_3)_4$, dioxane, reflux)

Entry	R		Time (h)	Product	Yield (%)
1	Ph	(**9a**)	16	*Z*-**6a**	86
2		(**9f**)	16	*Z*-**6f**	80
3	PhC≡C-	(**9g**)	2	*Z*-**6g**	75
4		(**9h**)	16	*Z*-**6h**	78

Table 5
Cross-coupling of (*Z*)-β-bromo-β-fluorostyrene with organostannanes



Z-**1** **9** *E*-**6**

(a: $Pd(PPh_3)_4$, dioxane, reflux)

Entry	R		Time (h)	Product	Yield (%)
1	Ph	(**9a**)	16	*E*-**6a**	94
2		(**9f**)	16	*E*-**6f**	81
3	PhC≡C-	(**9g**)	16	*E*-**6g**	74

the reaction proceeds just as efficiently with *Z*-**1** to yield *E*-**6g** in 74% (Table 5). This new method provides the preparation of 1-aryl-1-fluoroolefins as well as dienes and enynes and thus compliments the above use of boronic acids for the cross-coupling reaction.

The cross-coupling reaction proceeds in very good yield with the more hindered *Z*-**1** as can be seen in Table 5 by comparing the three entries with entries 1–3 in Table 4. In addition, it should be noted that the cross-coupling of *E*-**1** with tributylstannyl-1-ethoxyethene (**10**) is a high yielding reaction by ^{19}F NMR to form the very labile vinyl ether **11** (Scheme 1). Aqueous work-up of the reaction mixture resulted in the hydrolysis of the vinyl ether to the α-fluoro-α,β-unsaturated ketone **12**, that proved difficult to isolate. Percy and Wilkes [12] reported the synthesis of a series of more stable β-fluorvinyl ethers by a palladium(0)-catalyzed coupling of vinyltributylstannane with 1-iodo-1-fluoro-2-substituted vinyl MEM ethers.

The facility of these two new methods for the preparation of 1-substituted 1-fluoroolefins can be rationalized by the −I electron withdrawing effect of fluorine, which would increase the ease of the palladium insertion between the carbon–bromine and carbon–chlorine bond in the reaction illustrated in Fig. 1, and is in contrast to the observations usually made with aryl and vinyl chlorides. (The low reactivity of aryl chlorides in cross-coupling reactions is apparently due to their reluctance to oxidatively add to

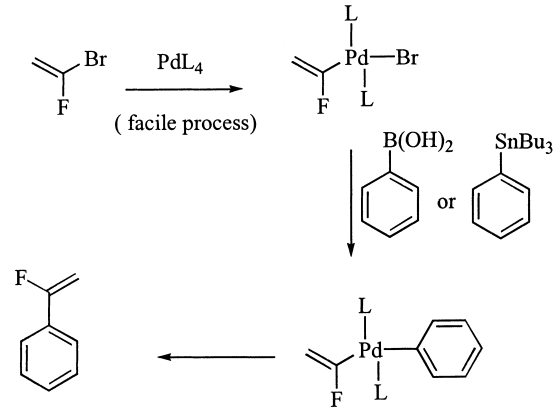
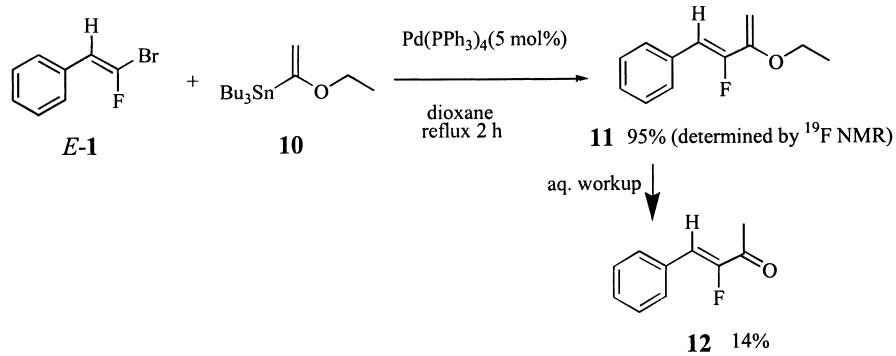


Fig. 1. Proposed mechanism for the palladium(0) insertion into an 1-bromo-1-fluoroolefin followed by nucleophilic attack by an arylboronic acid or an arylstannane.

Pd(0). For a discussion see [13]. For two recent exceptions to this problem see [33,34].) Consistent with the observation is the facility of Pd(0) insertions into electron deficient heteroaryl chlorides. See, for example, the coupling reaction of 2,5-dichloropyridine with phenylboronic acid proceeds under Suzuki conditions to give 5-chloro2-phenylpyridine in 83% yield [14].

Likewise, the −I effect of fluorine is consistent with the "copper effect" observed for the cross-coupling of fluorovinylstannanes with aryl iodides that we recently reported [7,28]. The fluorovinylstannane would presumably be a poorer nucleophile than the nonfluorinated stannane, thus requiring CuI to increase the electrophilicity of the palladium(II) ligand–solvent intermediate (see Fig. 2) For key references on the "copper-effect" for Stille coupling, see: [15,35]. For an example of the reaction of nonfluorinated vinylstannanes with aryl iodides which does not require CuI to proceed in good yield, see [16,36].

In summary, the palladium-catalyzed cross-coupling reactions of 1-fluorovinyl halides with organoboranes or organostannanes take advantage of the −I effect of fluorine to provide facile and convenient methods for the stereospecific synthesis of 1-substituted 1-fluoroolefins in high yields.



E-**1** **10** **11** 95% (determined by ^{19}F NMR)

12 14%

Scheme 1. Formation of α-fluoro-α,β-unsaturated kenone **12**.

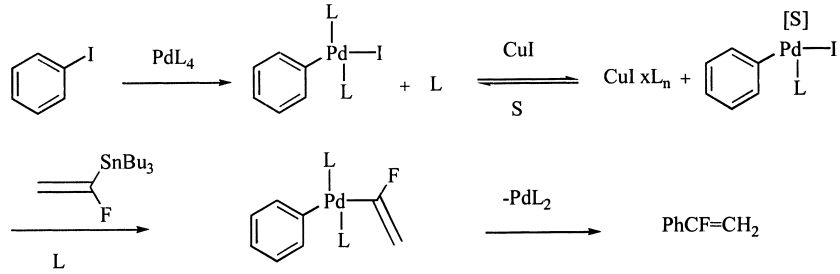


Fig. 2. Proposed mechanism for the palladium(0) insertion into an aryl iodide followed by nucleophilic attack by a fluorovinylstannane.

3. Experimental

3.1. General

High-field NMR spectra were recorded on a Varian XL-300 (^{1}H at 300 MHz, ^{13}C at 75.5 MHz) in $CDCl_3$. ^{19}F chemical shifts are reported in δ (ppm) relative to fluorotrichloromethane ($CFCl_3$, 0 ppm). GC-MS spectra were recorded on Hewlett-Packard 5890 Series II with a 5972 mass selective detector. Thin-layer chromatography was performed on silica gel 60 F_{254} plates from Whatman. (*Z*)-1-Bromo-1-fluoro-2-phenylethene (*Z*-**1**) and (*E*)-1-bromo-1-fluoro-2-phenylethene (*E*-**1**) [11], (*Z*,*E*)-1-chloro-1-fluoro-2-phenylethene (**2**) [17,37], (*Z*,*E*)-1-chloro-1-fluoro-2-(4-methoxyphenyl) (**3**) [18,21] and (*Z*,*E*)-1-chloro-1-fluoro-2-phenethylethene (**4**) were synthesized according to literature methods.

3.1.1. (Z,E)-1-Chloro-1-fluoro-2-phenethylethene (4)

Mixture of *E* and *Z* isomers (47 : 53 ratio); colorless oil; ^{1}H NMR ($CDCl_3$) δ: *Z*-isomer: 2.43 (m, 2H); 2.70 (m, 2H); 5.29 (d*t*, $J = 10.5$, 7.8 Hz, 1H), 7.27 (m, 5H); *E*-isomer: 2.36 (m, 2H), 2.70 (m, 2H), 4.87 (d*t*, $J = 29.1$, 7.6 Hz, 1H), 7.27 (m, 5H); ^{19}F NMR ($CDCl_3$) δ : −78.9 (*Z*-isomer, d, $J = 9.0$ Hz); −81.6 (*E*-isomer, d, $J = 30.0$ Hz); GCMS (EI): *m/e* 182 (M^+).

3.2. Palladium catalyzed cross-coupling reaction of β-bromo-β-fluorostyrene with organoboronic acid

3.2.1. General procedure

A mixture of (*Z*)- or (*E*)-1-bromo-1-fluoro-2-phenylethene (201 mg, 1.0 mmol), organoboronic acid (1.2 mmol), potassium carbonate (420 mg, 3.0 mmol) in benzene (15 ml), ethanol (3 ml) and water (3 ml) was treated with tetrakis(triphenylphosphine)palladium(0) (60 mg, 0.05 mmol) under nitrogen and then heated at reflux for 1–6 h. This mixture was diluted with ethyl acetate (100 ml), dried over $MgSO_4$, filtrated and concentrated in vacuo. The residue was chromatographed on silica gel with hexanes to give the desired product.

For compounds *Z*-**6a**, **6b**, **6c**, and **6e** see reference [5,27]

*(Z)-1-(Benzofuran-2-yl)-1-fluoro-2-phenylethene (Z-**6d**)* White solid, m.p. 101–3°C, yield: 83%; ^{1}H NMR ($CDCl_3$) δ: 6.52 (d, $J = 39.3$ Hz, 1H), 6.96 (d, $J = 2.1$ Hz, 1H), 7.25–7.42 (m, 5H), 7.49 (d, $J = 8.7$ Hz, 1H), 7.58 (d, $J = 8.1$ Hz, 1H), 7.66 (dm, $J = 7.2$ Hz, 2H); ^{19}F NMR ($CDCl_3$) δ: −125.7 (d, $J = 39.5$ Hz); ^{13}C NMR ($CDCl_3$) δ: 104.2 (d, $J = 1.1$ Hz), 107.1 (d, $J = 5.4$ Hz), 111.1 (d, $J = 1.1$ Hz, 121.4 (s), 123.2 (s), 125.3 (s), 127.7 (d, $J = 2.3$ Hz), 128.6 (S), 129.1 (d, $J = 7.8$ Hz), 132.7 (d, $J = 3.5$ Hz), 148.8 (d, $J = 49.0$ Hz), 149.1 (d, $J = 247.5$ Hz), 154.9 (s); GCMS (EI): *m/e* 238 (M^+); Anal for $C_{16}H_{11}FO$ (238.26), calcd. C, 80.66; H, 4.65; found C, 80.41; H, 4.78.

*(E)-1,2-Diphenyl-1-fluoroethene (E-**6a**)* Colorless oil [5,27,19], 92% yield; ^{1}H NMR ($CDCl_3$) δ: 6.45 (d, $J = 21.3$ Hz, 1H), 7.20 (m, 4H), 7.32 (m, 3H), 7.41 (m, 2H), 7.60 (m, 1H); ^{19}F NMR ($CDCl_3$) δ: −96.5 (d, $J = 21.5$ Hz); ^{13}C NMR ($CDCl_3$) δ: 109.2 (d, $J = 30.9$ Hz), 127.0 (d, $J = 13.7$ Hz), 128.1 (s), 128.2 (s), 128.3 (s), 128.7 (d, $J = 2.9$ Hz), 129.4 (d, $J = 1.5$ Hz), 131.7 (d, $J = 29.2$ Hz), 133.6 (d, $J = 12.6$ Hz), 157.6 (d, $J = 246.0$ Hz); GCMS (EI): *m/e* 198 (M^+).

*(E)-1-(4-Chlorophenyl)-1-fluoro-2-phenylethene (E-**6b**)* White solid, m.p. 133–7°C, yield: 90%; ^{1}H NMR ($CDCl_3$) δ: 6.46 (d, $J = 21.6$ Hz), 7.13–7.50 (m, 9H); ^{19}F NMR ($CDCl_3$) δ: −98.0 (d, $J = 21.2$ Hz); ^{13}C NMR ($CDCl_3$) δ: 106.3 (d, $J = 30.6$ Hz, 123.6 (d, $J = 26.9$ Hz), 124.6 (s), 125 (s), 125.2 (d, $J = 2.9$ Hz), 126.0 (d, $J = 5.2$ Hz), 126.7 (d, $J = 29.5$ Hz), 129.8 (d, $J = 12.1$ Hz), 134.8 (s), 153.0 (d, $J = 245.6$ Hz); GCMS (EI): *m/e* 232 (M^+); Anal for $C_{14}H_{11}F$ (198.24), calcd. C, 84.82; H, 5.59; found C, 84.49; H, 5.67.

*(E)-1-Fluoro-1-(4-methoxyphenyl)-2-phenylethene (E-**6c**)* Colorless oil, yield: 85%; ^{1}H NMR ($CDCl_3$) δ: 3.81 (s, 3H), 6.36 (d, $J = 21.6$ Hz, 1H), 6.82 (d,$J = 8.7$ Hz, 2H), 7.18 (m, 5H), 7.36 (d, $J = 8.7$ Hz, 2H); ^{19}F NMR ($CDCl_3$) δ: −95.7 (d, $J = 21.4$ Hz); GCMS (EI): *m/e* 228 (M^+); HRMS for $C_{15}H_{13}FO$ (M^+): calcd. 228.0950; found 228.0961.

*2-Fluoro-1-phenyl-Octa-1E,3E-diene (E-**6e**)* Colorless oil, yield: 82%; ^{1}H NMR ($CDCl_3$) δ: 0.92 (t, $J = 7.2$ Hz, 3H), 1.36 (m, 4H), 2.16 (m, 2H), 5.53 (d, $J = 38.4$ Hz, 1H), 5.90 (ddt, $J = 1.2$, 15.9, 25.8 Hz, 1H), 6.12 (dt, $J = 7.2$, 15.9 Hz, 1H), 7.15–7.56 (m, 5H); ^{19}F NMR ($CDCl_3$) δ: −107.4 (dd, $J = 27.4$, 39.5 Hz); GCMS (EI): *m/e* 204 (M^+); HRMS for $C_{14}H_{17}F$ (M^+), calcd. 204.1314; found 204.1323.

*(E)-1-Fluoro-1-(1-naphthyl)-2-phenylethene (E-**6f**)* Colorless oil, yield: 78%; ^{1}H NMR ($CDCl_3$) δ: 6.73 (d,

$J = 20.1$ Hz, 1H), 6.90 (m, 2H), 7.06 (m, 3H), 7.44 (t, $J = 7.2$ Hz, 1H), 7.53 (m, 3H), 7.93 (t, $J = 9.0$ Hz, 2H), 8.08 (m, 1H); ^{19}F NMR ($CDCl_3$) δ: −84.8 (d, $J = 18.3$ Hz); GCMS (EI): *m/e* 248 (M^+); HRMS for $C_{18}H_{13}F$ (M^+), calcd. 248.1003; found 248.1012.

3.3. Palladium catalyzed cross-coupling reaction of 1-fluorovinyl chloride (E, Z mixture) with arylboronic acids.

*(E)- and (Z)-1-fluoro-1-(4-methoxyphenyl)-2-phenylethene (**7**)* A mixture of (*E*, *Z*)-1-chloro-1-fluoro-2-(4-methoxyphenyl)ethene (*E*/*Z* = 44 : 56, 93 mg, 0.5 mmol), phenylboronic acid (74 mg, 0.6 mmol), potassium carbonate (210 mg, 1.5 mmol) in benzene (8 ml), ethanol (1.5 ml) and water (1.5 ml) was treated with tetrakis(triphenylphosphine)palladium(0) (30 mg, 0.025 mmol) under nitrogen and heated at reflux for 8 h. This mixture was diluted with ethyl acetate (100 ml), dried over $MgSO_4$, filtrated and concentrated in vacuo. GC-MS analysis of the crude products showed a mixture of (*E*)- and (*Z*)-**7** with a ratio of 47 : 53 (*Z*/*E*). Attempts to separate these two isomers on silica gel failed, and the product was obtained, after chromatography, as a colorless oil (80% yield). ^{1}H NMR ($CDCl_3$) δ: (*Z*-**7**) 3.82 (s, 3H), 6.26 (d, $J = 40.2$ Hz, 1H), 6.91 (d, $J = 9.0$ Hz, 2H), 6.30–6.46 (m, 3H), 7.60 (m, 4H); (E-**7**) 3.77 (s, 3H), 6.40 (d, $J = 21.9$ Hz, 1H), 6.76 (d, $J = 8.7$ Hz, 2H), 7.08 (d, $J = 8.7$ Hz, 2H), 6.30–6.46 (m, 5H); ^{19}F NMR ($CDCl_3$) δ: −117.7 (*Z*-isomer, d, $J = 39.8$ Hz); −98.6 (*E*-isomer, d, $J = 21.5$ Hz); MS (EI): *m/e* 228 (M^+); HRMS for $C_{15}H_{13}FO$ (M^+), calcd. 228.0950; found 228.0970.

*(E)-1-Fluoro-1,4-diphenylbutene and (Z)-1-Fluoro-1,4-diphenylbutene (**8**)* GC-MS analysis of the crude products shown a mixture of *Z*/*E* = 45 : 55. The two isomers were not separated by silica gel. Colorless oil, 83% yield; ^{1}H NMR ($CDCl_3$) δ: (*Z*-isomer) 2.60 (m, 2H), 2.78 (m, 2H), 5.48 (dt, $J = 37.2$, 7.5 Hz, 1H), 7.15–7.50 (m,10H); ^{19}F NMR ($CDCl_3$) δ: −120.5 (*Z*-isomer, d, $J = 36.7$ Hz); −101.74 (d, $J = 23.0$ Hz); MS (EI): *m/e* 226 (M^+); HRMS for $C_{16}H_{15}F$ (M^+): calcd. 226.1258; found 226.1263.

3.4. Palladium catalyzed cross-coupling reaction of (E)-β-bromo-β-fluorostyrene with organostannanes.

*(Z) 1-Fluoro-1-(2-furanyl)-2-phenylethene (Z-**6f**)* A mixture of (*E*)-1-fluoro-1-bromo2-phenylethene (100 mg, 0.50 mmol), 2-(tributylstannyl)furan (195 mg, 0.55 mmol), tetrakis(triphenylphosphine)palladium(0) (32 mg, 0.025, 5 mol%) in dioxane (5 ml) was refluxed under nitrogen overnight. The ^{19}F NMR was performed on a sample of the reaction mixture to determine yield (97%, D_2O insert for signal lock-on; C_6F_6 as external standard). The reaction mixture was concentrated in vacuo and purified by flash chromatography on silica gel (eluted with hexane, R_f0.5) to provide (*Z*)-**6f** as a colorless oil (75 mg, 80%). ^{1}H NMR ($CDCl_3$) δ: 6.25 (d, $J = 40.2$ Hz, 1H), 6.48 (m, 1H), 6.60–6.62 (m, 1H), 7.22–7.28 (m, 1H), 7.33–7.39 (m, 2H), 7.44–7.46 (m, 1H), 7.57–7.61 (m, 2H); ^{19}F NMR ($CDCl_3$) δ: −120.82 (d, $J = 39.9$ Hz); GCMS (EI): *m/e* 188 (M^+) at $t_r = 4.91$ min; HRMS: *m/e* for $C_{12}H_9FO$ [$M + H^+$] calcd. 189.0716; found 189.0723.

*(Z)-1,4-Diphenyl-2-fluoro-1-buten-3-yne (Z-**6g**)* Colorless oil, 75% yield; ^{1}H NMR: 6.15 (d, $J = 35.1$ Hz, 1H), 6.48 (m, 1H), 7.25–7.39 (m, 6H), 7.50–7.57 (m, 4H); ^{19}F NMR ($CDCl_3$) δ: −100.63 (d, $J = 35.0$ Hz); GCMS: *m/e* 222 (M^+) at $t_r = 6.31$ min; HRMS: *m/e* for $C_{16}H_{11}F$ [$M + H^+$] calcd. 223.0923; found 223.0931.

*(Z)-1-Fluoro-1-(2-thienyl)-2-phenylethene (Z-**6h**)* Colorless oil, 78% yield; ^{1}H NMR: 6.15 (d, $J = 39.3$ Hz, 1H), 7.03–7.07 (m, 1H), 7.22–7.39 (m, 5H), 7.57–7.61 (m, 2H); ^{19}F NMR:−104.19 (d, $J = 38.8$ Hz); GCMS: *m/e* 204 (M^+) at $t_r = 5.65$ min; HRMS: *m/e* for $C_{12}H_9FS$ [$M + H^+$] calcd. 205.0487; found 205.0494.

*(Z)-2-Fluoro-3-ethoxy-1-phenyl-1,3-butadiene (**11**)* Colorless oil, 9% yield: ^{1}H NMR: ($CDCl_3$) δ: 1.41 (t, $J = 7.0$ Hz, 3H), 3.89 (q, $J = 7.0$ Hz, 2H), 4.32 (m, 1H), 4.74 (dd, $J = 39.5$ Hz, 1H), 6.23 (m, 1H), 7.25–7.42 (m, 3H), 7.53–7.59 (m, 2H); ^{19}F NMR ($CDCl_3$) δ: -120.04 (d, $J = 39.2$ Hz); GCMS: *m/e* 192 (M^+).

3.5. Palladium catalyzed cross-coupling reaction of (Z)-β-bromo-β-fluorostyrene with organostannanes.

*(E)-1-Fluoro-1,2-diphenylethene (E-**6a**)* A solution of (*Z*)-1-bromo-1-fluoro-2-phenylethene (100 mg, 0.5 mmol), tributylphenyltin (240 mg, 0.65 mmol) in dioxane was treated with tetrakis(triphenylphosphine)palladium(0) (30 mg, 0.025 mmol) under nitrogen and heated at reflux for 16 h. Chromatography of the reaction mixture on silica gel with hexanes gave *E*-**6a** in 94% isolated yield.

*(E)-1-Fluoro-1-(2-furfuryl)-2-phenylethene (E-**6f**)* Colorless oil, 81% yield; ^{1}H NMR ($CDCl_3$) δ: 6.40 (m, 1H), 6.41 (d, $J = 24.0$ Hz, 1H), 7.23 (m, 1H), 7.51 (m, 5H); GCMS (EI): *m/e*188 (M^+).

*(Z)-3-Fluoro-4-phenyl-3-buten-2-one (**12**)* A mixture of (*E*)-β-bromo-β-fluorostyrene (100 mg, 0.50 mmol), 1-(tributylstannyl)vinyl ethyl ether (**10**) (200 mg, 0.55 mmol), tetrakis(triphenylphosphine)palladium(0) (32 mg, 0.025, 5 mol%) in dioxane (5 ml) was refluxed under nitrogen overnight. The ^{19}F NMR was performed on a sample of the reaction mixture to determine yield (95%, D_2O insert for signal lock-on; C_6F_6 as external standard). The reaction mixture was concentrated in vacuo, dissolved in ether, washed with KF solution and brine. The ether was concentrated, purified by preparative TLC plates to provide *Z*-**12** [20] in 14% yield. ^{1}H NMR: 2.42 (d, $J = 1.8$ Hz, 3H), 6.63 (d, $J = 36.6$ Hz, 1H), 7.38–7.44 (m, 3H), 7.64–7.72 (m, 2H); GCMS: *m/e* 164 (M^+) at $t_r = 4.31$ min; HRMS: *m/e* for $C_{16}H_{11}F$ [$M + H^+$] calcd. 165.0716; found 165.0722.

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