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# Stereoselective Preparation of (*E*)- and (*Z*)-α-Fluorostilbenes via Palladium-Catalyzed Cross-Coupling Reaction of High *E*/*Z* Ratio and (*Z*)-1-Bromo-1-fluoroalkenes

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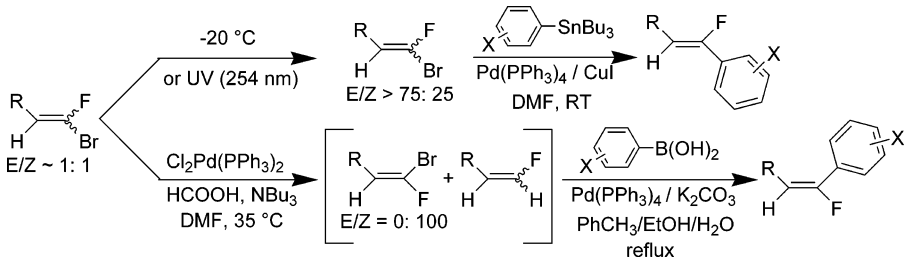
*Received January 11, 2006*




A highly stereoselective method to prepare both (*E*)- and (*Z*)-α-fluorostilbenes is described. 1-Bromo-1-fluoroalkenes (*E*/*Z* ≈ 1:1), a readily available starting material, isomerizes to high *E*/*Z* ratios by storage at −20 °C or by photolysis at 254 nm. Stille coupling between these high *E*/*Z* 1-bromo-1-fluoroalkenes and aryl stannanes gave (*Z*)-α-fluorostilbenes in high stereoselectivity. (*Z*)-1-Bromo-1-fluoroalkenes, which were kinetically separated from 1-bromo-1-fluoroalkenes (*E*/*Z* ≈ 1:1), can participate in Suzuki coupling reactions to give (*E*)-α-fluorostilbenes stereoselectively.

## Introduction

Monofluorinated analogues of natural products have received increased attention in medicinal chemistry and agrochemistry.[1] As fluorine is small (similar in size to oxygen) and has very strong electronegativity, it is believed that fluorine can modify the biological activity by altering the physicochemical properties of these fluorinated compounds.[2] α-Fluorostilbenes, for example, as an important class of fluoroolefins,[3] have been recently explored as potential enzyme inhibitors,[4] anti-carcinogenic agents, and anti-oestrogenic agents.[5]

The preparation, especially the stereospecific preparation of (*E*)- and (*Z*)-α-fluorostilbenes, has not been fully investigated, however. Several research groups have reported a base-induced elimination reaction to prepare (*E*) and (*Z*) mixtures of α-fluorostilbenes, such as dehydrofluorination[6] and dehydrochlorination.[7] Most of these reactions showed little stereoselectivity. Under certain reaction conditions, in some base-promoted eliminations it has been reported that (*E*)-α-fluorostilbene dominated the (*E*,*Z*) mixture of products.[6(c)] Unfortunately, this reaction was not fully investigated, and the mechanism is not clear. Wadsworth−Horner−Emmons olefination has also been explored to prepare α-fluorostilbenes.[8] For example, diethyl α-fluorobenzylphosphonate reacted with aldehydes and base at low temperature to afford α-fluorostilbenes in good yields. Again, this reaction showed little stereoselectivity.[8] McCarthy and coworkers have described the stereospecific preparation of 1-fluoro-2-substituted-vinyl stannanes[9,10] and their Stille coupling reaction with organic halides to prepare (*Z*)-α-fluorostilbenes.[10] The

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10.1021/jo060068i CCC: $33.50 
Published on Web 04/20/2006

drawbacks of this methodology are: the preparation of the starting (*E*)-1-fluorovinyl stannanes takes several steps; and the separation of the intermediate (*E*) and (*Z*) isomers of 1-fluoro-2-phenylvinyl sulfones is time-consuming. McCarthy and co-workers also studied the separation of 1-bromo-1-fluorostyrene (*E*,*Z* mixtures) using gas chromatography and separated the (*Z*) isomer from the (*E*) isomer (actual *E*/*Z* = 92:8).[11] A Suzuki coupling reaction between aryl boronic acids and (*E*)- or (*Z*)-1-bromo-1-fluorostyrene was successfully utilized to prepare (*Z*)- or (*E*)-α-fluorostilbenes.[11] This method is straightforward compared to the previous Stille coupling reaction between 1-fluoro-2-phenylvinyl stannanes and aryl halides.[10] However, the availability of the starting (*E*)- and (*Z*)-1-bromo-1-fluoroalkenes is a problem. In most of these reactions, mmol amounts of 1-bromo-1-fluorostyrenes, obtained from gas chromatography separation, were used as the starting materials, which is unlikely to be efficient for large-scale preparative purposes. Another synthetic method to prepare (*Z*)-1-bromo-1-fluoroalkenes from (*E*)-2-fluoro-3-phenylacrylic acid takes several steps, and the isomerization catalyzed by $Pd(OAc)_2$ from (*Z*) to high *E*/*Z* ratio 1-bromo-1-fluoroalkenes was not fully studied.[12] McCarthy and co-workers mentioned another isomerization method from (*Z*)-1-bromo-1-fluorostyrene to *E*/*Z* = 92:8 isomer mixtures catalyzed by bromine in chloroform.[11a] This isomerization was shown to be low-yielding (<20%) in our hands due to the domination of saturated products, which were formed by the addition of bromine to the alkenes. Recently, one example was reported for the stereoselective preparation of (*Z*)-α-fluorostilbene via α-fluorinated vinyl sulfone and α-fluorinated vinyl germanium intermediates;[13] however, this method was not studied in detail.

As most literature methods for the preparation of (*E*)- and (*Z*)-α-fluorostilbenes either lack stereoselectivity or suffer from difficulty in the preparation of the starting materials, an efficient and stereospecific method to prepare this class of compounds is needed in medicinal chemistry and agrochemistry. Herein, we wish to report our preparation of high *E*/*Z* and (*Z*)-1-bromo-1-fluoroalkenes and their coupling reactions to synthesize (*Z*)- and (*E*)-α-fluorostilbenes. A portion of this research was reported as a preliminary communication.[14]

## Results and Discussion

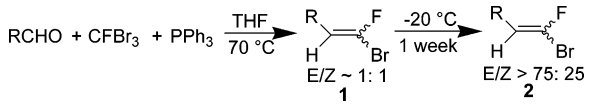
**Preparation and Isomerization of 1-Bromo-1-fluoroalkenes.** 1-Bromo-1-fluoroalkenes (*E*/*Z* ≈ 1:1) **1**, which were readily prepared from RCHO, $CFBr_3$, and $PPh_3$,[15] could potentially serve as valuable starting materials for the preparation of (*Z*)- and (*E*)-α-fluorostilbenes. Recently, we found that they cleanly isomerize to high *E*/*Z* (*E*/*Z* > 75:25) ratio **2** when they are stored at −20 °C for 1 week (Scheme 1),[14] or alternatively by photolysis at 254 nm for 1 h. As illustrated in Table 1, for **1** (R = aryl groups), clean isomerization occurs, and **2** (*E*/*Z* > 75:25) were successfully obtained; for **1** (R = 1-naphthyl or alkyl groups), no obvious isomerization was observed, however (Table 1). This isomerization could be catalyzed by a trace amount of bromine in the mixture of **1**.

**TABLE 1. Preparation and Isomerization of 1-Bromo-1-fluoroalkenes 1**

| entry | R | time (hr) | yield (%) | *E*/*Z* of **1** | *E*/*Z* of **2**[a] |
|---|---|---|---|---|---|
| 1 | Ph− | 6 | 77 | 44:56 | 85:15[b] |
| 2 | *o*-$ClC_6H_4$− | 6 | 67 | 48:52 | 82:18[c] |
| 3 | *p*-$MeOC_6H_4$− | 6 | 62 | 66:34 | 81:19[d] |
| 4 | *p*-$FC_6H_4$− | 6 | 45 | 72:28 | 87:13 |
| 5 | *m*-$NO_2C_6H_4$− | 8 | 53 | 63:37 | 76:24[e] |
| 6 | 1-naphthyl− | 7 | 46 | 49:51 | 49:51[f] |
| 7 | PhCH(Me)− | 8 | 52 | 42:58 | 42:58[f] |
| 8 | *n*-$C_7H_{15}$ | 5 | 72 | 46:54 | 46:54[f] |

[a] *E*/*Z* ratios after leaving **1** in the freezer for 1 week. [b] *E*/*Z* ratio was 88:12 in 3 months. [c] Photolysis of this substrate at 254 nm for 1 h gave an *E*/*Z* ratio of 78:22 from a starting *E*/*Z* ratio of 63:37. [d] *E*/*Z* ratio was 83:17 in 3 months. [e] *E*/*Z* ratio was 81:19 in 3 months. [f] No obvious isomerization was observed.

**SCHEME 1**




**Preparation of (*Z*)-α-Fluorostilbenes from High *E*/*Z* 1-Bromo-1-fluoroalkenes.** Recently we reported that the (*E*)-isomer of 1-bromo-1-fluoroalkenes reacts faster than the corresponding (*Z*)-isomer at room temperature in palladium-catalyzed coupling reactions at room temperature.[16−18] It provides a novel and important strategy to prepare monofluorinated olefins stereoselectively. Therefore, we examined the coupling reactions of **2** to synthesize (*Z*)-α-fluorostilbenes.

Both Stille and Suzuki coupling reactions could be utilized to synthesize (*Z*)-α-fluorostilbenes. Therefore, we tested the coupling reaction of **2** by both methods. Under Stille coupling reaction conditions, PhCH═CFBr (*E*/*Z* = 88:12) reacted smoothly with $PhSnBu_3$, $Pd(PPh_3)_4$/CuI in DMF at room temperature for 20 h. $^{19}F$ NMR analysis of the reaction mixture showed that all the (*E*) isomer was consumed and the *Z*/*E* ratio of the crude product was 98:2. Under Suzuki coupling reaction conditions, 1-bromo-1-fluoro-2-phenylethene (*E*/*Z* = 88:12) reacted with phenylboronic acid in the presence of $Pd(PPh_3)_4$ in $PhCH_3$/EtOH/$H_2O$. When this reaction was carried out at room temperature, it was very slow. When the above Suzuki reaction was carried out at reflux temperature, the *Z*/*E* ratio of α-fluorostilbene in the mixture was 94:6, which is not as good as the *Z*/*E* ratio (98:2) under Stille coupling conditions. Therefore, we selected Stille coupling reaction conditions for the preparation of (*Z*)-α-fluorostilbenes.

The coupling reaction of **2** with phenyltributyltin or substituted phenyltributyltin proceeded smoothly in DMF at room temperature, with $Pd(PPh_3)_4$ (4%) and CuI (50%) as catalyst (Scheme 2). CuI has been shown to be a very effective cocatalyst

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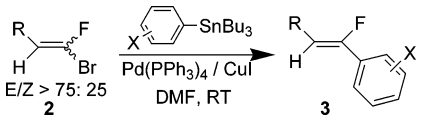
**TABLE 2. Preparation of (*Z*)-α-Fluorostilbenes 3 by Stille Coupling Reaction from 2**

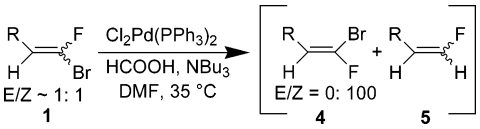
| entry | R | X | *E*/*Z* of **2** | time (hr) | mixture *Z*/*E*[c] | product[a] (*Z*/*E*)[b] | yield[d] (conversion) |
|---|---|---|---|---|---|---|---|
| 1 | Ph− | H | 88:12 | 20 | 98:2 | **3a** (100:0) | 73 (83) |
| 2 | Ph− | *p*-F | 88:12 | 16 | 98:2 | **3b** (100:0) | 67 (76) |
| 3 | *o*-$ClC_6H_4$− | H | 82:18 | 15 | 94:6 | **3c** (100:0) | 71 (87) |
| 4 | *o*-$ClC_6H_4$− | *p*-F | 82:18 | 16 | 94:6 | **3d** (100:0) | 52 (63) |
| 5 | *p*-$MeOC_6H_4$− | H | 83:17 | 22 | 93:7 | **3e** (100:0) | 61 (74) |
| 6 | *p*-$FC_6H_4$− | H | 87:13 | 16 | 96:4 | **3f** (100:0) | 69 (80) |
| 7 | *m*-$NO_2C_6H_4$− | H | 76:24 | 16 | 87:13 | **3g** (100:0) | 53 (70) |
| 8 | *p*-$ClC_6H_4$− | *p*-F | 88:12 | 12 | 98:2 | **3h** (100:0) | 72 (82) |
| 9 | PhC(Me)H− | H | 79:21 | 26[e] | 95:5 | **3i** (100:0) | 36 (45) |

[a] All products gave satisfactory $^{19}F$, $^{1}H$, and $^{13}C$ NMR and HRMS data. [b] *Z*/*E* ratio of isolated product. [c] *Z*/*E* ratios of α-fluorostilbenes were determined by $^{19}F$ NMR analysis of the reaction mixture when the reaction was completed. [d] Isolated yield. Conversion was calculated based on the amount of (*E*)-1-bromo-1-fluoroalkenes in the starting (*E*,*Z*) mixtures. [e] The reaction was carried out at 95 °C instead of at rt.

**SCHEME 2**




**SCHEME 3**

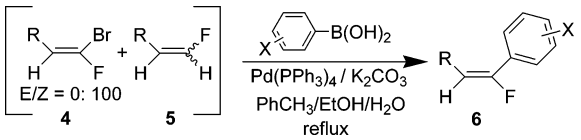



in Stille coupling reactions.[10b,19] The reaction was shown to be stereoselective, and high *Z*/*E* ratios were observed for the crude products in the reaction mixture by $^{19}F$ NMR analysis. Pure (*Z*)-α-fluorostilbenes were isolated in good yields (Table 2) by either column chromatography or column chromatography followed by recrystallization. The reaction conditions for the preparation of (*Z*)-α-fluorostilbenes are very mild. Various combinations of functional groups on both phenyl rings are available and permutation is also possible, as demonstrated in Table 2 (entries 2 and 6). Alkyl group substituted 1-bromo-1-fluoroalkene can also selectively couple with aryl stannane at higher temperature (95 °C) to afford the corresponding (*Z*)-monofluoroalkene (Table 2, entry 9).

Recently, Rolando and co-workers synthesized two (*Z*)-α-fluorostilbenes, fluorinated resveratrol and pterostilbene, by Suzuki coupling of 1-bromo-1-fluoroalkenes ((*E*,*Z*) mixtures).[5] High yields (71−86%) of products were achieved in this Suzuki coupling step, starting from 1-bromo-1-fluoroalkenes (*E*/*Z* ≈ 1:1 when they were prepared). Probably the selectivity is partially due to the high *E*/*Z* ratio of the starting materials before the coupling reaction.

**Preparation of (*E*)-α-Fluorostilbenes from (*Z*)-1-Bromo-1-fluoroalkenes.** (*Z*)-1-Bromo-1-fluoroalkenes have been shown to participate in Suzuki coupling reactions to give (*E*)-α-fluorostilbenes.[11] Recently we reported the preparation of (*Z*)-1-bromo-1-fluoroalkenes **4** by the kinetic reduction method from **1** using $HCOOH/NBu_3$/DMF.[18] Most (*Z*) isomers **4** were not separated from the corresponding reduced products **5** at this stage (Scheme 3). As **4** has been shown to be a good starting material in a series of palladium-catalyzed coupling reactions to prepare (*Z*)-1-fluorovinyl phosphonates,[16] (*E*)-monofluoroenynes,[12,20] and (*E*)-α-fluoro-α,β-unsaturated esters,[18] we

**SCHEME 4**




tested the preparation of (*E*)-α-fluorostilbenes starting from the mixture of **4** and **5**.

Similar to the preparation of (*Z*)-α-fluorostilbenes **3**, we can choose either the Stille or the Suzuki coupling reaction to prepare (*E*)-α-fluorostilbenes. However, here we prefer Suzuki coupling reaction conditions. The reasons include the following: the coupling reactions of (*Z*)-1-bromo-1-fluoroalkenes **4** normally occur at 70 °C or higher temperature, which is close to the refluxing temperature of $PhCH_3/EtOH/H_2O$ in a typical Suzuki coupling reaction; a variety of substituted aryl boronic acids are commercially available; and no side product of tributyltin halide, which is usually difficult to separate.

Following typical Suzuki coupling reaction conditions (with minor changes, such as $C_6H_6$ is replaced by toluene and $Na_2CO_3$ is replaced by $K_2CO_3$),[11a,21] a mixture of **4** and **5** reacted with $Pd(PPh_3)_4$, $XC_6H_4B(OH)_2$ (X= substituted groups), and $K_2CO_3$ in $PhCH_3/EtOH/H_2O$ at reflux temperature (Scheme 4). $^{19}F$ NMR analysis of the reaction mixture showed that all the (*Z*)-1-bromo-1-fluoroalkene **4** was consumed; the crude product had a *Z*/*E* ratio of 0:100; and the reduced products did not participate in the reaction. Workup followed by column chromatography gave the desired (*E*)-α-fluorostilbenes **6** in high yields (Table 3). Some products, however, were found to have an obvious tendency to isomerize in the course of separation (Table 3, entries 3 and 5). This Suzuki coupling reaction also works very well for those **4** whose R = alkyl groups, where the corresponding (*E*)-monofluoroalkene products were successfully separated in high yields (Table 3, entries 5−7).

## Conclusion

A straightforward method to prepare both (*Z*)- and (*E*)-α-fluorostilbenes has been developed. 1-Bromo-1-fluoroalkenes (*E*/*Z* ≈ 1:1) were found to isomerize to high *E*/*Z* ratios after storage at −20 °C or by photolysis at 254 nm. These high *E*/*Z* ratio 1-bromo-1-fluoroalkenes can undergo a Stille coupling reaction with aryl stannanes to afford (*Z*)-α-fluorostilbenes

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**TABLE 3. Preparation of 6 by Suzuki Coupling Reaction from 4**

| entry | R | *E*/*Z* of **4** | X | time (hr) | *Z*/*E* of **6**[a] | yield[b] (%) |
|---|---|---|---|---|---|---|
| 1 | Ph− | 0:100 | *m*-Ac | 4 | 0:100 **6a** | 83 |
| 2 | *o*-$ClC_6H_4$− | 0:100 | H | 8 | 0:100[c] **6b** | 82 |
| 3 | *o*-$ClC_6H_4$− | 0:100 | *m*-$NO_2$ | 8 | 11:89[d] **6c** | 90 |
| 4 | *o*-$ClC_6H_4$− | 0:100 | *o*-Cl | 6 | 5:95[c] **6d** | 90 |
| 5 | 1-naphthyl− | 0:100 | H | 10 | 4:96[d] **6e** | 85 |
| 6 | $PhC(CH_3)H$− | 0:100 | *o*-Cl | 6 | 0:100 **6f** | 92 |
| 7 | $PhC(CH_3)H$− | 0:100 | *m*-Ac | 8 | 0:100 **6g** | 93 |

[a] All products gave satisfactory $^{19}F$, $^1H$, and $^{13}C$ NMR, GC-MS, and HRMS data. [b] The yield of **6** is based on the amount of **4** in a starting material mixture of **4** and **5**. [c] The product contains 2−3% of (1*E*,3*E*)-*o*-Cl−$C_6H_4$−CH═CF−CH═CF−$C_6H_4$−Cl-*o* that could not be separated. [d] The product had an obvious tendency to isomerize at room temperature in the course of separation.

stereoselectively. (*Z*)-1-Bromo-1-fluoroalkenes could be obtained after kinetic reduction of the *E*/*Z* ≈ 1:1 mixture by HCOOH/$NBu_3$/DMF. The Suzuki coupling reaction between aryl boronic acids and a mixture of (*Z*)-1-bromo-1-fluoroalkene and the reduced products lead to (*E*)-α-fluorostilbenes stereoselectively. This route to both (*Z*)- and (*E*)-α-fluorostilbenes is highly stereoselective, highly efficient, and should be suitable for scale-up preparation compared to existing methods.

## Experimental Section

The preparation and characterization of **3a**, **3b**, **3c**, **3d**, **3e**, **3f**, **3g**, and **3h** were described in the preliminary communication;[14] their $^1H$ and $^{13}C$ NMR spectra are included in the Supporting Information of this article.

**General Procedure for the Preparation of (*Z*)-α-Fluorostilbenes 3.** To a round-bottom flask containing $Pd(PPh_3)_4$ (4 mol %) and dry DMF, 1-bromo-1-fluorostyrene (high *E*/*Z* ratio, includes (*E*) isomer 1.0 equiv) was added, and the resulting solution was stirred at room temperature for 15 min. Following the addition of CuI (0.5 equivalent) and phenyltributyltin (1.2 equivalent), the resulting mixture was stirred at room temperature. When the reaction was completed, $Co(OAc)_2 \cdot 4H_2O$ (1.6 equivalent) was added to the mixture to remove tributyltin halide side products.[22] The mixture was added directly to a silica gel column. Subsequent recrystallization from hexanes gives white crystals if the product is a solid.

**(*Z*)-1-Fluoro-1,3-diphenyl-1-butene (3i).** Similarly, a mixture of 1-bromo-1-fluoro-3-phenyl-1-butene (0.229 g, 1.0 mmol, *E*/*Z* = 79:21), $Pd(PPh_3)_4$ (0.037 g, 0.032 mmol), $PhSnBu_3$ (0.51 g, 1.40 mmol, 1.8 equiv), and CuI (0.08 g, 0.40 mmol) in DMF (4 mL) was reacted at 95 °C for 26 h. $^{19}F$ NMR analysis of the reaction mixture showed that the *Z*/*E* ratio of the crude product was 95:5. Silica gel column chromatography (ethyl acetate/hexanes = 10:90, $R_f$ = 0.67) gave a colorless liquid (0.08 g), yield 36% (the conversion is 45% based on the amount of the consumed (*E*)-1-bromo-1-fluoroalkenes). (*Z*) 100%. $^{19}F$ NMR ($CDCl_3$) δ −121.3 (d, $^3J_{FH(trans)}$ = 37.6 Hz) ppm; $^1H$ NMR ($CDCl_3$) δ 7.17−7.62 (m, 10H), 5.54 (dd, $^3J_{HF(trans)}$ = 36.6 Hz, *J* = 9.5 Hz, 1H), 4.14 (dq, *J* = 9.4 Hz, *J* = 7.0 Hz, 1H); 1.46 (d, *J* = 9.0 Hz, 3H) ppm; $^{13}C$ NMR ($CDCl_3$) δ 155.6 (d, $^1J_{CF}$ = 245.9 Hz), 145.6, 132.5 (d, *J* = 29.5 Hz), 128.5 (d, *J* = 2.4 Hz), 128.4 (d, *J* = 2.5 Hz), 127.2 (d, *J* = 6.1 Hz), 126.8, 126.2, 124.0 (d, *J* = 7.8 Hz), 111.2 (d, *J* = 17.6 Hz), 34.7 (d, *J* = 5.4 Hz), 21.8 ppm; GC-MS *m*/*z* (relative intensity) 226 ($M^+$, 37), 211 (86), 191 (21), 133 (100), 109 (20), 77 (19); HRMS calculated 226.1158 for $C_{16}H_{15}F$; observed, 226.1149.

(22) Blumenthal, E. J. Ph.D. Thesis, University of Iowa, Iowa City, Iowa, 2000; p 128.

**General Procedure for the Preparation of (*E*)-α-Fluorostilbenes 6.** To a round-bottom flask containing $Pd(PPh_3)_4$ (0.046 g, 0.04 mmol, 4 mol %), $K_2CO_3$ (0.415 g, 3.0 mmol), and toluene/EtOH/$H_2O$ (15 mL, 3 mL, 3 mL respectively), a mixture of **4** and **5** (contains **4** 1.0 mmol) was added, and the resulting suspension was stirred at room temperature for 15 min. Following the addition of aryl boronic acid (1.2 mmol), the resulting mixture was refluxed for 8 h. After the reaction was completed, the reaction mixture was transferred to a separatory funnel with 200 mL of ethyl ether. The organic phase was washed with water (3 × 20 mL) and brine (3 × 20 mL) and dried over anhydrous $MgSO_4$. The solvent was removed by rotary evaporation, and the resulting mixture was separated by silica gel column chromatography.

**(*E*)-1-(3-Acetylphenyl)-1-fluoro-2-phenylethene (6a).** Similarly, a mixture of (*Z*)-1-bromo-1-fluoro-2-phenyl-ethene (contains (*Z*)-1-bromo-1-fluoroalkene, 0.10 g, 0.5 mmol, *E*/*Z* = 0:100) and the reduced products, $Pd(PPh_3)_4$ (0.023 g, 0.02 mmol), $K_2CO_3$ (0.207 g, 1.5 mmol), and *m*-$AcC_6H_4B(OH)_2$ (0.098 g, 0.6 mmol), was reacted in toluene/EtOH/$H_2O$ (15 mL/3 mL/3 mL) for 4 h. After workup and silica gel column chromatography (ethyl acetate/hexanes = 10:90, $R_f$ = 0.31), 0.10 g of liquid was obtained, yield 83%. $^{19}F$ NMR ($CDCl_3$) δ −99.1 (d, $^3J_{FH(cis)}$ = 20.2 Hz, 1F) ppm; $^1H$ NMR ($CDCl_3$) δ7.97 (m, 1H), 7.92 (dm, *J* = 7.9 Hz, 1H), 7.60 (d, *J* = 7.6 Hz, 1H), 7.39 (t, *J* = 7.7 Hz, 1H), 7.22−7.26 (m, 3H), 7.16−7.19 (m, 2H), 6.56 (d, $^3J_{HF(cis)}$ = 21.3 Hz, 1H), 2.44 (s, 3H) ppm; $^{13}C$ NMR ($CDCl_3$) δ 197.2, 156.6 (d, $^1J_{CF}$ = 246.8 Hz), 137.0, 133.3 (d, *J* = 12.2 Hz), 132.3 (d, *J* = 5.2 Hz), 131.9, 128.8, 110.1 (d, *J* = 30.9 Hz) ppm; GC-MS *m*/*z* (relative intensity) 241 ($M^+$ + 1, 16), 240 ($M^+$, 96), 226 (11), 225 (76), 207 (19), 197 (81), 196 (100), 177 (21), 176 (25), 170 (26), 98 (28); HRMS calculated 240.0950 for $C_{16}H_{13}OF$; observed, 240.0948.

**(*E*)-2-(2-Chlorophenyl)-1-fluoro-1-phenylethene (6b).** Similarly, a mixture of (*Z*)-1-bromo-1-fluoro-2-(2-chlorophenyl)-ethene (contains (*Z*)-1-bromo-1-fluoroalkene, 0.236 g, 1.0 mmol, *E*/*Z* = 0:100) and the reduced products, $Pd(PPh_3)_4$ (0.046 g, 0.04 mmol), $K_2CO_3$ (0.415 g, 3.0 mmol), and $PhB(OH)_2$ (0.146 g, 1.2 mmol), was reacted in toluene/EtOH/$H_2O$ (15 mL/3 mL/3 mL) for 8 h. After workup and silica gel column chromatography (hexanes 100%, $R_f$ = 0.44), 0.19 g of a colorless liquid was obtained (contains 2% (*E*,*E*)-*o*-$ClC_6H_4CH$═$CFCF$═$CHC_6H_4Cl$-*o*, which could not be separated), yield 82%. $^{19}F$ NMR ($CDCl_3$) δ −96.6 (d, $^3J_{FH(cis)}$ = 20.5 Hz, 1F) ppm; $^1H$ NMR ($CDCl_3$) δ 7.23−7.41 (m, 6H), 7.16 (td, *J* = 7.7 Hz, *J* = 1.6 Hz, 1H), 7.09 (dd, *J* = 7.8 Hz, *J* = 1.5 Hz, 1H), 7.02 (tm, *J* = 7.4 Hz, 1H), 6.53 (d, $^3J_{HF(cis)}$ = 20.5 Hz, 1H) ppm; $^{13}C$ NMR ($CDCl_3$) δ 158.7 (d, $^1J_{CF}$ = 246.7 Hz), 133.9 (d, *J* = 3.9 Hz), 132.7 (d, *J* = 13.2 Hz), 131.3 (d, *J* = 30.4 Hz), 130.8, 129.5 (d, *J* = 6.3 Hz), 128.6, 128.2, 127.9 (d, *J* = 5.8 Hz), 127.1, 126.5, 106.6 (d, *J* = 32.8 Hz) ppm; GC-MS *m*/*z* (relative intensity) 235 (4), 234 ($M^+$ + 2, 30), 233 ($M^+$ + 1, 13), 232 ($M^+$, 58), 198 (17), 197 (31), 196 (100), 194 (20), 177 (33), 176 (21), 170 (20), 98 (38), 97 (13), 88 (19), 85 (39), 75 (16); HRMS calculated 232.0455 for $C_{14}H_{10}F^{35}Cl$; observed, 232.0462.

**(*E*)-2-(2-Chlorophenyl)-1-fluoro-1-(3-nitrophenyl)ethene (6c).** Similarly, a mixture of (*Z*)-1-bromo-1-fluoro-2-(2-chlorophenyl)-ethene (contains (*Z*)-1-bromo-1-fluoroalkene, 0.236 g, 1.0 mmol, *E*/*Z* = 0:100) and the reduced products, $Pd(PPh_3)_4$ (0.046 g, 0.04 mmol), $K_2CO_3$ (0.415 g, 3.0 mmol), and *m*-$NO_2C_6H_4B(OH)_2$ (0.200 g, 1.2 mmol), was reacted in toluene/EtOH/$H_2O$ (15 mL/3 mL/3 mL) for 8 h. After workup and silica gel column chromatography (ethyl acetate/hexanes = 7:93, $R_f$ = 0.32), 0.25 g of a colorless liquid was obtained, yield 90%. *Z*/*E* = 11:89 (The product partially isomerized in the course of separation). $^{19}F$ NMR ($CDCl_3$) δ −100.3 (d, $^3J_{FH(cis)}$ = 20.7 Hz, 1F) ppm; $^1H$ NMR ($CDCl_3$) δ 8.22 (m, 1H), 8.16 (dm, *J* = 8.4 Hz, 1H), 7.60 (dm, *J* = 7.7 Hz, 1H), 7.45 (dd, *J* = 7.8 Hz, *J* = 3.7 Hz, 2H), 7.22−7.28 (m, 1H), 7.07−7.13 (m, 2H), 6.69 (d, $^3J_{HF(cis)}$ = 20.0 Hz, 1H) ppm; $^{13}C$ NMR ($CDCl_3$) δ 155.9 (d, $^1J_{CF}$ = 249.6 Hz), 148.1, 134.0 (d, *J* = 2.9 Hz), 133.4 (d, *J* = 5.0 Hz), 132.9 (d, *J* = 28.7 Hz), 131.5 (d, *J* = 12.6 Hz), 130.5, 129.9, 129.4, 129.3, 127.0, 124.1, 122.6, 129.0 (d, *J* = 32.1 Hz)

ppm; GC-MS *m*/*z* (relative intensity) 280 (2), 279 ($M^+ + 2$, 10), 278 (4), 277 ($M^+$, 30), 232 (6), 230 (12), 225 (10), 224 (11), 212 (7), 197 (15), 196 (100), 195 (28), 194 (45), 183 (24), 175 (27), 170 (30), 169 (189), 168 (17), 99 (18), 98 (18), 87 (18), 75 (34), 74 (27); HRMS calculated 277.0306 for $C_{14}H_9NO_2F^{35}Cl$; observed, 277.0297.

**(*E*)-1,2-Di(2-chlorophenyl)-1-fluoroethene (6d).** Similarly, a mixture of (*Z*)-1-bromo-1-fluoro-2-(2-chlorophenyl)-ethene (contains (*Z*)-1-bromo-1-fluoroalkene, 0.118 g, 0.5 mmol, *E*/*Z* = 0:100) and the reduced products, $Pd(PPh_3)_4$ (0.023 g, 0.02 mmol), $K_2CO_3$ (0.207 g, 1.5 mmol), and *o*-$ClC_6H_4B(OH)_2$ (0.094 g, 0.6 mmol), was reacted in toluene/EtOH/$H_2O$ (15 mL/3 mL/3 mL) for 6 h. After workup and silica gel column chromatography (ethyl acetate/hexanes = 5:95, $R_f$ = 0.36), 0.12 g of a colorless liquid was obtained (contains 3% (*E*,*E*) *o*-$ClC_6H_4CH{=}CFCF{=}CHC_6H_4Cl$-*o*, which could not be separated), yield 90%. $^{19}F$ NMR ($CDCl_3$) $\delta$ −88.9 (d, $^3J_{FH(cis)}$ = 18.3 Hz, 1F) ppm; $^1H$ NMR ($CDCl_3$) $\delta$ 7.43 (d, *J* = 8.1 Hz, 1H), 7.35 (d, *J* = 8.1 Hz, 2H), 7.28 (d, *J* = 7.8 Hz, 1H), 7.21 (d, *J* = 8.1 Hz, 1H), 7.09 (t, *J* = 7.9 Hz, 1H), 6.92 (t, *J* = 7.5 Hz, 1H), 6.78 (d, $^3J_{HF(cis)}$ = 17.9 Hz, 1H), 6.77 (d, *J* = 8.1 Hz, 1H) ppm; $^{13}C$ NMR ($CDCl_3$) $\delta$ 157.0 (d, $^1J_{CF}$ = 252.2 Hz), 134.1, 133.8 (d, *J* = 4.5 Hz), 131.9, 131.7 (d, *J* = 13.1 Hz), 131.2 (d, *J* = 2.6 Hz), 130.8, 130.1, 129.8, 129.3, 128.5, 126.9, 126.4, 109.6 (d, *J* = 31.3 Hz) ppm; GC-MS m/z (relative intensity) 270 ($M^+ + 4$, 2), 268 ($M^+ + 2$, 11), 266 ($M^+$, 17), 231 (7), 230 (7), 196 (100), 194 (16), 176 (6), 175 (9), 170 (6), 115 (8), 97 (20); HRMS calculated 266.0065 for $C_{14}H_9{}^{35}Cl_2F$; observed, 266.0056.

**(*E*)-1-Fluoro-1-phenyl-2-(1-naphthyl)ethene (6e).** Similarly, a mixture of (*Z*)-1-bromo-1-fluoro-2-(naphthalene-2-yl)-ethene (contains (*Z*)-1-bromo-1-fluoroalkene, 0.251 g, 1.0 mmol, *E*/*Z* = 0:100) and the reduced products, $Pd(PPh_3)_4$ (0.046 g, 0.04 mmol), $K_2CO_3$ (0.415 g, 3.0 mmol), and $PhB(OH)_2$ (0.146 g, 1.2 mmol), was reacted in toluene/EtOH/$H_2O$ (15 mL/3 mL/3 mL) for 10 h. After workup and silica gel column chromatography (ethyl acetate/hexanes = 3:97, $R_f$ = 0.28), 0.21 g of a colorless liquid was obtained, yield 85%. *Z*/*E* = 4:96 (The product partially isomerized in the course of separation). $^{19}F$ NMR ($CDCl_3$) $\delta$ −99.9 (d, $^3J_{FH(cis)}$ = 21.7 Hz, 1F) ppm; $^1H$ NMR ($CDCl_3$) $\delta$ 8.09 (dd, *J* = 6.3 Hz, *J* = 3.7 Hz, 1H), 7.86 (dd, *J* = 6.3 Hz, *J* = 3.5 Hz, 1H), 7.74−7.79 (m, 1H), 7.51 (dd, *J* = 6.4 Hz, *J* = 3.3 Hz, 2H), 7.25−7.33 (m, 4H), 7.11−7.22 (m, 3H), 6.87 (d, $^3J_{HF(cis)}$ = 21.2 Hz, 1H) ppm; $^{13}C$ NMR ($CDCl_3$) $\delta$ 158.3 (d, $^1J_{CF}$ = 247.1 Hz), 133.6, 131.9 (d, *J* = 2.8 Hz), 131.7, 131.3 (d, *J* = 3. 6 Hz), 131.1, 129.1, 128.5, 128.0, 127.9, 127.6 (d, *J* = 6.1 Hz), 127.4, 126.2 (d, *J* = 13.8 Hz), 125.6, 124.7, 107.0 (d, *J* = 30.8 Hz) ppm; GC-MS *m*/*z* (relative intensity) 249 ($M^+ + 1$, 21), 248 ($M^+$, 100), 246 (44), 244 (21), 233 (28), 228 (50), 226 (38), 220 (15), 170 (29), 123 (20), 113 (22), 110 (20); HRMS calculated 248.1001 for $C_{18}H_{13}F$; observed, 248.1004.

**(*E*)-1-(2-Chlorophenyl)-1-fluoro-3-phenyl-1-butene (6f).** Similarly, a mixture of (*Z*)-1-bromo-1-fluoro-3-phenylethene (contains (*Z*)-1-bromo-1-fluoroalkene, 0.229 g, 1.0 mmol, *E*/*Z* = 0:100) and the reduced products, $Pd(PPh_3)_4$ (0.046 g, 0.04 mmol), $K_2CO_3$ (0.415 g, 3.0 mmol), and *o*-$ClC_6H_4B(OH)_2$ (0.188 g, 1.2 mmol), was reacted in toluene/EtOH/$H_2O$ (15 mL/3 mL/3 mL) for 6 h. After workup and silica gel column chromatography (ethyl acetate/hexanes = 1:99, $R_f$ = 0.25), 0.24 g of a colorless liquid was obtained, yield 92%. $^{19}F$ NMR ($CDCl_3$) $\delta$ −96.8 (d, $^3J_{FH(cis)}$ = 18.0 Hz, 1F) ppm; $^1H$ NMR ($CDCl_3$) $\delta$ 7.47 (dm, *J* = 8.0 Hz, 1H), 7.36−7.40 (m, 1H), 7.25−7.35 (m, 4H), 7.18−7.22 (m, 2H), 7.16 (m, 1H), 5.69 (dd, $^3J_{HF(cis)}$ = 18.2 Hz, *J* = 11.0 Hz, 1H), 3.25 (dqd, *J* = 10.8 Hz, *J* = 7.0 Hz, *J* = 3.4 Hz, 1H), 1.37 (dd, *J* = 7.0 Hz, *J* = 0.9 Hz, 3H) ppm; $^{13}C$ NMR ($CDCl_3$) $\delta$ 154.2 (d, $^1J_{CF}$ = 247.4 Hz), 145.1, 134.2, 131.7, 131.0 (d, *J* = 28.7 Hz), 130.9, 129.9, 128.5, 126.6, 126.57, 126.3, 115.4 (d, *J* = 21.5 Hz), 36.6 (d, *J* = 5.8), 22.3 ppm; GC-MS, *m*/*z* (relative intensity) 263 ($M^+ + 3$, 6), 262 ($M^+ + 2$, 39), 261 ($M^+ + 1$, 15), 260 ($M^+$, 85), 247 (60), 245 (100), 225 (71), 210(64), 209 (42), 207 (22), 189 (27), 183 (22), 169 (37), 167 (74), 147 (27), 143 (24), 133 (61), 109 (37), 104 (23), 101 (23). HRMS calculated 260.0768 for $C_{16}H_{14}F^{35}Cl$; observed, 260.0760.

**(*E*)-1-(3-Acetylphenyl)-1-fluoro-3-phenyl-1-butene (6g).** Similarly, a mixture of (*Z*)-1-bromo-1-fluoro-3-phenyl-1-butene (contains (*Z*)-1-bromo-1-fluoroalkene, 0.229 g, 1.0 mmol, *E*/*Z* = 0:100) and the reduced products, $Pd(PPh_3)_4$ (0.046 g, 0.04 mmol), $K_2CO_3$ (0.415 g, 3.0 mmol), and *m*-$AcC_6H_4B(OH)_2$ (0.197 g, 1.2 mmol), was reacted in toluene/EtOH/$H_2O$ (15 mL/3 mL/3 mL) for 8 h. After workup and silica gel column chromatography (ethyl acetate/hexanes = 10:90, $R_f$ = 0.33), 0.25 g of a colorless liquid was obtained, yield 93%. $^{19}F$ NMR ($CDCl_3$) $\delta$ −102.2 (d, $^3J_{FH(cis)}$ = 21.7 Hz, 1F) ppm; $^1H$ NMR ($CDCl_3$) $\delta$ 7.97 (d, *J* = 8.4 Hz, 2H), 7.63 (d, *J* = 7.6 Hz, 1H), 7.50 (tm, *J* = 7.6 Hz, 1H), 7.21−7.38 (m, 5H), 5.72 (dd, $^3J_{HF(cis)}$ = 21.8 Hz, *J* = 10.9 Hz, 1H), 3.68 (dqd, *J* = 10.6 Hz, *J* = 6.8 Hz, *J* = 2.6 Hz, 1H), 2.53 (s, 3H), 1.43 (dm, *J* = 6.9 Hz, 3H) ppm; $^{13}C$ NMR ($CDCl_3$) $\delta$ 196.0, 154.2 (d, $^1J_{CF}$ = 244.3 Hz), 144.4 (d, *J* = 2.4 Hz), 136.0, 131.1 (d, *J* = 29.9 Hz), 130.8, 130.75, 127.7, 127.6, 126.6 (d, *J* = 5.0 Hz), 125.6, 125.4, 112.9 (d, *J* = 23.3 Hz), 35.6 (d, *J* = 9.5 Hz), 25.3, 22.8 ppm; GC-MS m/z (relative intensity) 269 ($M^+ + 1$, 7), 268 ($M^+$, 46), 254 (15), 253 (88), 225 (16), 209 (17). 205 (16), 191 (20), 189 (15), 175 (31), 147 (17), 133 (32), 119 (22), 109 (19), 95 (17), 77 (17); HRMS calculated 268.1263 for $C_{18}H_{17}FO$; observed, 268.1251.

**Acknowledgment.** We thank the National Science Foundation for their financial support of this work.

**Supporting Information Available:** Experimental procedures for the synthesis of **3a**, **3b**, **3c**, **3d**, **3e**, **3f**, **3g**, and **3h** and their characterization by $^{19}F$, $^1H$, and $^{13}C$ NMR, GC-MS, and HRMS; copies of $^1H$ and $^{13}C$ NMR spectra of compounds **3a**−**3i**, and **6a**−**6g**; and photolytic isomerization example of **1** to **2**. This material is available free of charge via the Internet at http://pubs.acs.org.

JO060068I