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The polar effect on the regiochemistry of nucleophilic substitution of trifluoromethylated π-allylpalladium complex

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Abstract

Allylic nucleophilic substitution of trifluoromethyl-group substituted cinnamyl carbonate with diethyl malonate anion in the presence of palladium complex catalyst gave regio- and stereoselectively the S_N2' product. The regiochemistry caused by the polar effect of trifluoromethyl group was opposite to the methylated cinnamyl substrate in a similar steric environment. The sterically more hindered mesityl and *tert*-butyl substrates than phenyl derivative also gave the products reacted at the more hindered sites. Although *o*-substituted substrates expecting intramolecular coordination to affect regiochemistry were examined, no alternative regioisomers were detected.

Keywords: π-Allylpalladium complexes; Regiochemistry; Trifluoromethyl group; σ-Acceptor

1. Introduction

Nucleophilic substitution reactions of π-allylpalladium complexes with soft carbon nucleophiles have attracted much attention as useful transformations for the introduction of new carbon–carbon bonds into allylic oxygenated compounds [1]. Since the reaction proceeds through π-allylpalladium complexes as the intermediates, a problem of regiochemistry arising from unsymmetrically substituted substrates is which terminal carbon is attacked by the soft carbon nucleophiles such as enolate anions [2]. Generally, the least-substituted carbons are attacked by the nucleophiles [3]. A conjugated carbonyl group (π-acceptor) on a terminal carbon also controls the regiochemistry to form a new C–C bond at the other terminal carbon [4]. Alternatively, π-donor/σ-acceptor alkoxy substituent directs the substitution to the oxygenated terminal [5]. For a pure σ-acceptor trifluoromethyl group, Kobayashi and co-workers reported several trifluoromethylated allyl acetates and carbonates regioselectively gave the products [6]. Nevertheless, it still remains unclear if the polar effect prevails over the steric effect. In the course of our investigation of stereoselective synthesis of aliphatic linear molecules with a trifluoromethyl group for the building block of fluorine-containing functional materials [7], we found that the regiochemistry is predominantly determined by the polar effect. In this paper, we report the regioselective nucleophilic substitution of trifluoromethylated allyl carbonates (Scheme 1).

2. Results and discussion

Trifluoromethylated carbonates **1a**–**f** were prepared starting from trifluoromethylenones **2a**–**f** as described in Section 3 (vide infra).

Nucleophilic substitution of carbonate **1a** with diethyl malonate–NaOEt was firstly examined using $Pd(PPh_3)_4$ as a Pd(0) catalyst. While a mixture of *E*/*Z* isomers of S_N2' products were given, the yield was low. After several Pd catalysts were examined, allylpalladium complex $[(\eta^3\text{-}CH_2CHCH_2)PdCl]_2$ (**4**) was found to be useful as an effective allylation catalyst. Carbonate **1a**

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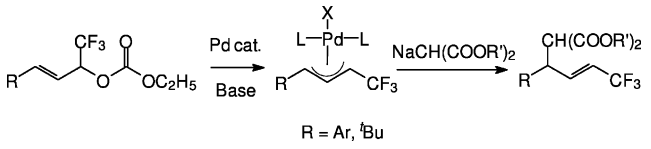
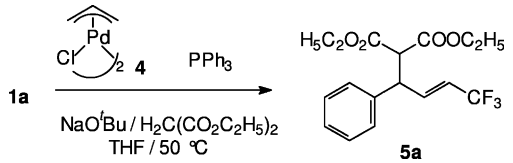
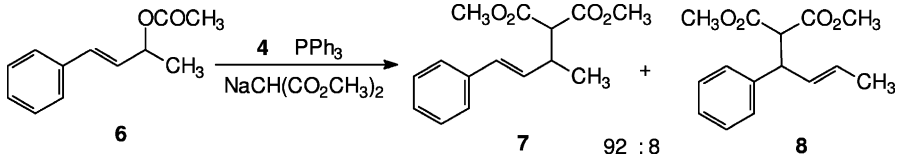


Scheme 1.

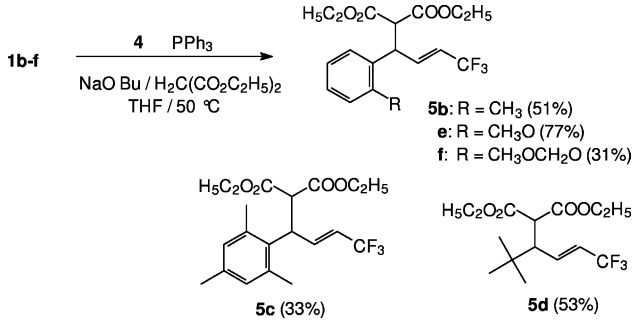
was reacted with diethyl malonate–NaOEt in the presence of 10% of allylpalladium **4** and 20% of PPh_3 to give **5a** stereoselectively in 58% yield with a small amount of alcohol **3a**, which was presumably yielded by the transesterification of **1a** with NaOEt. The regio- and stereochemistry were confirmed by the ^{1}H-NMR spectrum, in which a vinylic proton signal (δ 5.65; J_{H-H} = 15.9 and J_{H-F} = 6.3 Hz) revealed that the oxygenated terminal carbon bearing the trifluoromethyl group was converted to an unsaturated carbon. In the Pd(0)-assisted nucleophilic substitution reaction of allyl carbonates with malonates, mechanistically, addition of base is not necessary because of the formation of alkoxide anion during the palladium complexation to allyl carbonates [8]. However, the reaction under the above-mentioned conditions without addition of NaOEt resulted in no change in carbonate **1a**. Just after the addition of an excess amount of NaOEt, the reaction mixture turned brown and the product **5a** was detected by TLC analysis. This suggests the strongly basic conditions are necessary for the formation of trifluoromethylated palladium π-allyl complex from **1a**. When NaH was used as base to generate enolate, the yield of **5a** was lower (38%) than alkoxide base. Kitazume et al. have already reported the difficulty of generation of π-palladium complexes from this type of trifluoromethylated aryl starting materials, but seemingly they used no strong base [9]. Finally, to avoid transesterification of **1a** with NaOEt, sterically hindered NaO^{t}Bu was used and **5a** was obtained regio- and stereoselectively in 71% yield.



In general, the steric effect mainly determines the regiochemistry of palladium-assisted nucleophilic substitution of allyl esters [3]. There are several reports describing nucleophilic substitution of structurally related methyl derivative **6** with sodium dimethyl malonate in the presence of π-palladium complex catalyst **4**, and the major product was alternative regioisomer **7** [10]. In this case, the regiochemistry was controlled by the difference in the steric bulk of substituents on the terminal carbons of the π-allylpalladium complex, and the less hindered methylated carbon terminal was attacked by the malonate nucleophile. The size of a trifluoromethyl group (A value = 2.4–2.5 kcal mol^{-1}: $-\Delta G^\circ$ for axial–equatorial cyclohexane interconversion [11]) is considerably larger than that of a methyl group (A value = 1.7 kcal mol^{-1}), but it is still somewhat smaller than that of a phenyl group (A value = 2.8 kcal mol^{-1}). The absence of production of the regioisomer of **5a** suggests that for the trifluoromethylated π-allylpalladium complex formed from **1a** the regiochemistry is determined by the polar effect of the strongly electron-withdrawing σ-acceptor, CF_3-group, and the nucleophile attacks at the terminal carbon with the more hindered phenyl group.



To confirm importance of the polar effect, carbonates **1b–d** with more sterically hindered reaction sites were examined. As shown in Scheme 2, methyl groups at ortho position of the phenyl ring (**1b**,**c**) have no effect to determine the regiochemistry. Furthermore, even *tert*-butyl derivative **1d** gave the more sterically crowded product **5d**. In order to control the regiochemistry of the nucleophilic substitution, intramolecular coordination



Scheme 2.

to palladium has been employed [12]. Although *o*-alkoxy derivatives **1e**,**f** were employed in anticipation of intramolecular coordination of oxygen atom, only the normal products **5e**,**f** were also given.

The polar effect of a trifluoromethyl group for the regiochemical selection of nucleophilic substitution of cinnamyl carbonates prevails over the steric effect, which has been recognized as the major factor for the regiochemical control in palladium-assisted nucleophilic substitution. For the regiospecific substitution of the allylic system with a π-acceptor (an alkoxycarbonyl group), an unsymmetrical π-palladium complex or σ-complex intermediate was invoked [4a]. In the non-conjugated trifluoromethyl system, these unsymmetrical complex structures are also conceivable. In the palladium catalyzed allyl nucleophilic substitution, both σ- and π-acceptors act as the regio-controlling substituents to afford the allylic products with a new C–C bond at the terminal carbon opposite to the electron-withdrawing group.

3. Experimental

3.1. General

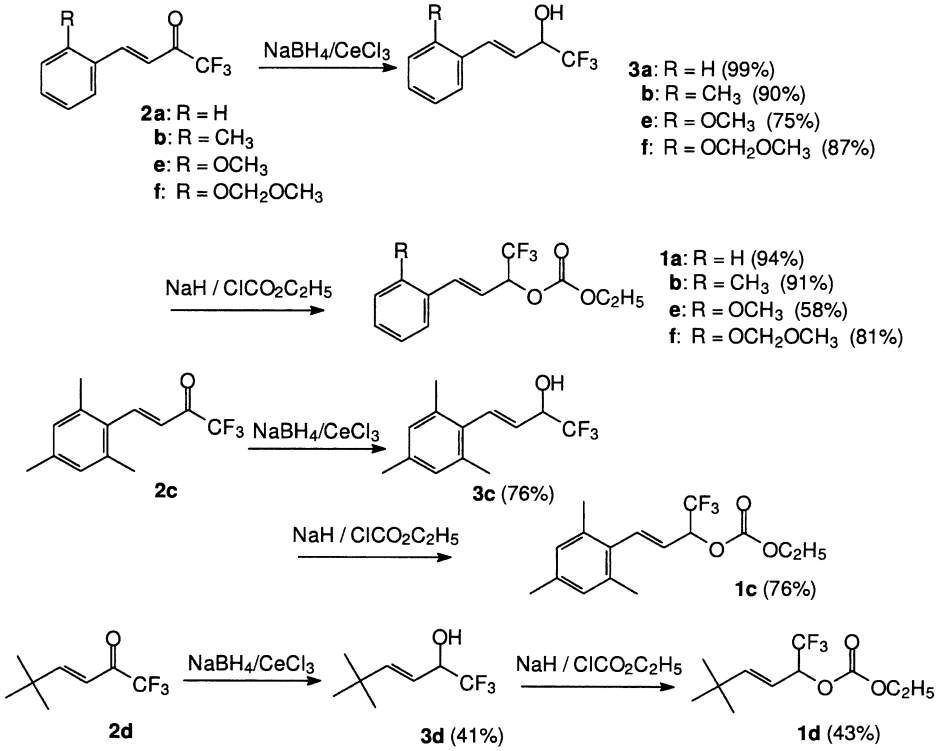
^{1}H- and ^{13}C-NMR spectra were collected in $CDCl_3$ in the presence of Me_4Si as an internal standard at 300 and 75.4 MHz, respectively. ^{19}F-NMR spectra (282 MHz) were recorded in $CDCl_3$, and referenced based on internal $CF_3COOC_2H_5$ whose chemical shift was set at −75.75 ppm downfield (δ) from internal $CFCl_3$ in $CDCl_3$.

3.2. Preparation of carbonate substrates (*1a–f*)

Trifluoromethylated carbonates **1a–f** were prepared starting from the $NaBH_4$–$CeCl_3$ reduction of the corresponding (*E*)-trifluoromethylenones **2a–f** followed by deprotonation of the resulting alcohols **3a–f** with NaH and the reaction with ethyl chlorocarbonate (Scheme 3). The isolate yields of *tert*-butyl derivatives **2d** and **1d** were relatively lower than corresponding aryl derivatives due to their volatility.

3.2.1. (*E*)-1,1,1-Trifluoro-4-(*o*-tolyl)-3-buten-2-ol (*3b*)

To a stirred mixture of ketone **2b** (3.63 g, 15.7 mmol) and cerium chloride heptahydrate (5.96 g, 16 mmol) in methanol (40 ml), $NaBH_4$ (605 mg, 16.0 mmol) was added in portions at 0 °C. The mixture was stirred at room temperature for 10 min, and then aqueous NH_4Cl solution was added into the mixture. The mixture was extracted with hexane and Et_2O. The combined extracts were dried over $MgSO_4$ and the solvents were removed under reduced pressure. The residue was chromatographed on a silica gel column (5:2 hexane–CH_2Cl_2) to obtain pure **3b** as colorless solid: 3.30 g (90%); mp: 51.0–51.6 °C; ^{1}H-NMR ($CDCl_3$): δ 2.371 (s, 3H), 2.48 (m, 1H), 4.658 (tq, $J = 6.3$, 6.1 Hz, 1H), 6.092 (dd, $J =$ 15.9, 6.3 Hz, 1H), 7.096 (d, $J = 15.9$ Hz, 1H), 7.15–7.25



Scheme 3.

(m, 3H), 7.456 (dd, $J = 6.0$, 2.4 Hz, 1H); ^{13}C-NMR ($CDCl_3$): δ 19.65, 71.75 (q, $J = 32$ Hz), 121.95 (q, $J = 2$ Hz), 124.25 (q, $J = 281$ Hz), 125.92, 126.23, 128.56, 130.44, 134.29, 134.51, 135.97; ^{19}F-NMR ($CDCl_3$): δ −79.57 (d, $J = 6.1$ Hz); EI-MS *m/z* (%) 217 (12), 216 (M^+, 86), 147 (100), 129 (52), 115 (37), 105 (27), 91 (28). Anal. Calc. for $C_{11}H_{11}F_3O$: C, 61.11; H, 5.13. Found: C, 61.08; H, 5.24%.

3.2.2. (*E*)-4-Mesityl-1,1,1-trifluoro-3-buten-2-ol (**3c**)

Alcohol **3c** was obtained as above: colorless oil, yield 76%; m.p.: ^{1}H-NMR ($CDCl_3$): δ 2.253 (s, 6H), 2.268 (s, 3H), 4.639 (sex, $J = 5.9$ Hz, 1H), 5.710 (dd, $J = 16.2$, 6.5, 1 Hz), 6.838 (d, $J = 16.2$ Hz, 1H), 6.869 (s, 3H); ^{13}C-NMR ($CDCl_3$): δ 20.75, 21.04, 71.87 (q, $J = 32$ Hz), 124.21 (q, $J = 281$ Hz), 125.93 (q, $J = 2$ Hz), 126.28, 132.13, 134.27, 135.75, 136.97; ^{19}F-NMR ($CDCl_3$): δ −80.28 (d, $J = 6.1$ Hz); EI-MS *m/z* (%) 245 (14, $M^+ + 1$), 244 (100, M^+), 210 (11), 176 (10), 175 (75), 157 (39), 145 (25), 142 (13), 133 (36), 130 (15), 129 (22), 128 (23), 115 (17), 105 (11), 91 (19), 87 (149, 80 (11), 77 (19), 65 (11), 55 (93), 51 (12). Anal. Calc. for $C_{13}H_{15}F_3O$: C, 63.93; H, 6.19. Found: C, 63.87; H, 6.24%.

3.2.3. (*E*)-1,1,1-Trifluoro-5,5-dimethyl-3-buten-2-ol (**3d**)

Alcohol **3d** was obtained as above as volatile colorless oil: yield 41%; bp 65 °C (17 mmHg); ^{1}H-NMR ($CDCl_3$): δ 1.047 (s, 9H), 2.2 (br s, 1H), 4.379 (quintet of d, $J =$ 6.7, 1.2 Hz, 1H), 5.416 (dd, $J = 15.9$, 6.7 Hz, 1H), 5.981 (dd, $J = 15.9$, 1.2 Hz, 1H); ^{19}F-NMR ($CDCl_3$): δ −75.23 (d, $J = 6.2$ Hz); EI-MS *m/z* (%) 164 (10, $M^+ - H_2O$), 149 (17), 113 (16), 91 (20), 83 (34), 77 (21), 69 (45), 67 (12), 65 (17), 63 (16), 59 (11), 57 (11), 55 (80), 51 (21), 43 (100).

3.2.4. (*E*)-4-(*o*-Anisyl)-1,1,1-trifluoro-3-buten-2-ol (**3e**)

Alcohol **3e** was obtained as above: colorless solid, yield 75%; m.p.: 64.5–65.5 °C; ^{1}H-NMR ($CDCl_3$): δ 2.260 (d, $J = 6$ Hz, 3H), 3.868 (s, 3H), 4.637 (dqd, $J =$ 7.1, 6.1, 6 Hz, 1H), 6.258 (dd, $J = 16.2$, 7.1 Hz, 1H), 6.898 (dd, $J = 7.5$, 0.9 Hz, 1H), 6.951 (ddd, $J = 7.7$, 6.6, 0.9 Hz, 1H), 7.171 (d, $J = 16.2$ Hz, 1H), 7.292 (ddd, $J =$ 7.5, 6.6, 1.8 Hz, 1H), 7.452 (dd, $J = 7.7$, 1.8 Hz, 1H); ^{13}C-NMR ($CDCl_3$): δ 55.43, 72.13 (q, $J = 32$ Hz), 110.96, 120.68, 121.20 (q, $J = 2$ Hz), 124.25, 124.34 (q, $J = 281$ Hz), 127.46, 129.87, 131.59, 157.08; ^{19}F-NMR ($CDCl_3$): δ −79.52 (d, $J = 6.1$ Hz); EI-MS *m/z* (%) 233 (12), 232 (M^+, 100), 163 (85), 121 (140), 107 (28), 91 (40), 77 (27), 55 (61). Anal. Calc. for $C_{11}H_{11}F_3O_2$: C, 56.90; H, 4.77. Found: C, 57.08; H, 4.91%.

3.2.5. (*E*)-1,1,1-Trifluoro-4-[*o*-(methoxymethoxy)phenyl]-3-buten-2-ol (**3f**)

Alcohol **3f** was obtained as above: colorless solid, yield 87%; m.p.: 75.1–76.5 °C; ^{1}H-NMR ($CDCl_3$): δ 2.345 (d, $J = 5.7$ Hz, 1H), 3.493 (s, 3H), 4.648 (tqd, $J =$ 6.8, 6.1, 1.8 Hz, 1H), 5.231 (s, 2H), 6.245 (dd, $J = 16.2$, 6.9 Hz, 1H), 7.003 (td, $J = 7.5$, 1.2 Hz, 1H), 7.118 (dd, $J = 7.5$, 1.2 Hz, 1H), 7.199 (dd, $J = 16.2$, 1.8 Hz, 1H), 7.260 (td, $J = 7.7$, 1.5 Hz, 1H), 7.471 (dd, $J = 7.5$, 1.5 Hz); ^{13}C-NMR ($CDCl_3$): δ 56.22, 72.04 (q, $J = 32$ Hz), 94.63, 114.75, 121.35 (q, $J = 2$ Hz), 121.97, 124.32 (q, $J = 281$ Hz), 125.05, 127.25, 129.88, 131.34, 154.76; ^{19}F-NMR ($CDCl_3$): δ −79.56 (d, $J = 6.1$ Hz); EI-MS *m/z* (%) 263 (6), 262 (M^+, 48), 230 (44), 131 (100), 91 (31), 51 (23). Anal. Calc. for. $C_{12}H_{13}F_3O_3$: C, 54.96; H, 5.00. Found: C, 54.97; H, 5.16%.

3.2.6. Ethyl (*E*)-3-phenyl-1-(trifluoromethyl)allyl carbonate (**1a**)

To a stirred suspension of NaH (60% oil dispersion; 396 mg, 10.0 mmol) in anhydrous THF (30 ml) at 0 °C under Ar atmosphere, a solution of alcohol **3a** (2.02 g, 10.0 mmol) in THF (5 ml) was added dropwise in 1 h, and then ethyl chloroformate (6.51 g, 60.0 mmol) was added in one portion. After stirring the mixture for 24 h, water was added and the mixture was extracted with $CHCl_3$. The combined extracts were washed successively with 1 M HCl, water, and sat. aq. $NaHCO_3$ solution. The $CHCl_3$ solution was dried over $MgSO_4$. The solvents were removed under reduced pressure. The residue was chromatographed on a silica gel column (1:1 hexane–CH_2Cl_2) to obtain pure **1a** as colorless oil: 2.57 g (94%); ^{1}H-NMR ($CDCl_3$): δ 1.348 (t, $J = 7.2$ Hz, 3H), 4.274 (q, $J = 7.2$ Hz, 2H), 5.629 (dq, $J = 7.8$, 6.1 Hz, 1H), 6.142 (dd, $J = 16.0$ Hz, 7.8 Hz, 1H), 6.913 (d, $J =$ 16.0 Hz, 1H), 7.29–7.40 (m, 3H), 7.41–7.46 (m, 2H); ^{13}C-NMR ($CDCl_3$): δ 14.10, 65.20, 74.72 (q, $J = 34$ Hz), 116.69 (q, $J = 2$ Hz), 122.88 (q, $J = 280$ Hz), 127.08, 128.74, 129.15, 134.83, 139.20, 153.56; ^{19}F-NMR ($CDCl_3$): δ −77.21 (d, $J = 6.1$ Hz); EI-MS *m/z* (%) 275 (2), 274 (M^+, 12), 254 (59), 201 (28), 185 (35), 165 (35), 134 (51), 133 (100), 115 (91). Anal. Calc. for $C_{13}H_{13}F_3O_3$: C, 56.94; H, 4.78. Found: C, 56.94; H, 4.95%.

3.2.7. Ethyl (*E*)-3-(*o*-tolyl)-1-(trifluoromethyl)allyl carbonate (**1b**)

Carbonate **1b** was obtained as above: yield 91%; ^{1}H-NMR ($CDCl_3$): δ 1.351 (t, $J = 7.2$ Hz, 3H), 2.371 (s, 3H), 4.278 (q, $J = 7.2$ Hz, 2H), 5.636 (dq, $J = 8.0$, 6.1 Hz, 1H), 6.142 (dd, $J = 16.0$, 8.0 Hz, 1H), 7.10–7.24 (m, 4H), 7.455 (dd, $J = 7.0$, 2.1 Hz, 1H); ^{13}C-NMR ($CDCl_3$): δ 14.15, 19.70, 65.20, 74.91 (q, $J = 34$ Hz), 118.11 (q, $J = 1$ Hz), 122.90 (q, $J = 280$ Hz), 126.03, 126.28, 128.97, 130.52, 134.09, 136.25, 137.28, 153.59; ^{19}F-NMR ($CDCl_3$): δ −77.23 (d, $J = 6.1$ Hz); EI-MS *m/z*

(%) 289 (2), 288 (M^+, 13), 199 (24), 198 (21), 147 (20), 129 (100), 125 (32). Anal. Calc. for $C_{14}H_{15}F_3O_3$: C, 58.33; H, 5.24. Found: C, 58.45; H, 5.45%.

3.2.8. Ethyl (*E*)-3-mesityl-1-(trifluoromethyl)allyl carbonate (*1c*)

Carbonate **1c** was obtained as above: yield 76%; ^{1}H-NMR ($CDCl_3$): δ 1.266 (t, $J = 7.3$ Hz, 3H), 2.165 (s, 6H), 2.191 (s, 3H), 4.206 (q, $J = 7.3$ Hz, 2H), 5.47–5.64 (m, 2H), 6.789 (s, 2H), 6.847 (d, $J = 15.1$ Hz, 1H); ^{13}C-NMR ($CDCl_3$): δ 14.22, 20.65, 21.04, 65.16, 74.98 (q, $J = 34$ Hz), 122.15 (q, $J = 2$ Hz), 122.83 (q, $J = 280$ Hz), 128.59, 131.71, 135.76, 137.24, 137.50, 153.40; ^{19}F-NMR ($CDCl_3$): δ −77.87 (d, $J = 6.1$ Hz); EI-MS *m/z* (%) 317 (5, $M^+ + 1$), 316 (26, M^+), 227 (26), 226 (25), 210 (33), 158 (14), 157 (100), 143 (13), 142 (18), 129 (13), 128 (149, 120 (15), 91 (12). Anal. Calc. for $C_{16}H_{19}F_3O_3$: C, 60.75; H, 6.05. Found: C, 60.65; H, 6.12%.

3.2.9. (*E*)-4,4-Dimethyl-1-(trifluoromethyl)-2-pentenyl ethyl carbonate (*1d*)

Carbonate **1d** was obtained as above: yield 43%; ^{1}H-NMR ($CDCl_3$): δ 1.043 (s, 9H), 1.340 (t, $J = 7.2$ Hz, 3H), 4.258 (q, $J = 7.2$ Hz, 2H), 5.33–5.47 (m, 2H), 6.076 (d, $J = 15.0$ Hz, 1H); ^{19}F-NMR ($CDCl_3$): δ −78.27 (d, $J = 6.1$ Hz); EI-MS *m/z* (%) 165 (3, $M^+ - OCOOC_2H_5$), 163 (12), 162 (16), 161 (20), 160 (14), 159 (15), 127 (14), 126 (23), 125 (33), 124 (27), 123 (24), 91 (29), 90 (13), 87 (15), 78 (13), 64 (14), 63 (54), 61 (649, 60 (100), 59 (97), 54 (12), 53 (13). Anal. Calc. for $C_{11}H_{17}F_3O_3$: C, 51.97; H, 6.74. Found: C, 52.00; H, 6.71%.

3.2.10. (*E*)-3-(*o*-Anisyl)-1-(trifluoromethyl)allyl ethyl carbonate (*1e*)

Carbonate **1e** was obtained as above: yield 75%; ^{1}H-NMR ($CDCl_3$): δ 1.343 (t, $J = 7.2$ Hz, 3H), 3.860 (s, 3H), 4.266 (q, $J = 7.2$ Hz, 2H), 5.630 (dq, $J = 8.1$, 6.1 Hz, 1H), 6.215 (dd, $J = 16.1$, 8.1 Hz, 1H), 6.888 (dd, $J = 8.4$, 1.0 Hz, 1H), 6.942 (td, $J = 7.5$, 1.0 Hz, 1H), 7.216 (dd, $J = 16.1$ Hz, 1H), 7.296 (ddd, $J = 8.4$, 7.5, 1.5 Hz, 1H), 7.440 (dd, $J = 7.5$, 1.5 Hz, 1H); ^{13}C-NMR ($CDCl_3$): δ 14.10, 55.40, 75.43 (q, $J = 33$ Hz), 110.97, 117.10 (q, $J = 2$ Hz), 120.61, 122.99 (q, $J = 280$ Hz), 123.74, 127.79, 130.27, 130.27, 134.65, 153.59, 157.36; ^{19}F-NMR ($CDCl_3$): δ −77.22 (d, $J = 6.1$ Hz); EI-MS *m/z* (%) 305 (16), 304 (M^+, 96), 284 (33), 231 (49), 215 (100), 163 (38), 145 (33), 131 (48), 121 (75), 108 (74), 107 (66). Anal. Calc. for $C_{14}H_{15}F_3O_4$: C, 55.26; H, 4.97. Found: C, 55.19; H, 4.92%.

3.2.11. Ethyl (*E*)-3-[*o*-(methoxymethyl)phenyl]-1-(trifluoromethyl)allyl carbonate (*1f*)

Carbonate **1f** was obtained as above: yield 81%; ^{1}H-NMR ($CDCl_3$): δ 1.346 (t, $J = 7.2$ Hz, 3H), 3.492 (s, 3H), 4.272 (q, $J = 7.2$ Hz, 2H), 5.233 (s, 2H), 5.644 (dq, $J = 8.4$, 6.1 Hz, 1H), 6.198 (dd, $J = 16.5$, 8.4 Hz, 1H), 7.001 (t, $J = 7.5$ Hz, 1H), 7.121 (d, $J = 8.0$ Hz, 1H), 7.22–7.31 (m, 2H), 7.469 (dd, $J = 7.5$ Hz, 1H); ^{13}C-NMR ($CDCl_3$): δ 14.12, 56.23, 75.30 (q, $J = 33$ Hz), 114.79, 117.33 (q, $J = 2$ Hz), 119.22 (q, $J = 280$ Hz), 121.92, 124.58, 127.51, 130.29, 134.41, 153.60, 155.01; ^{19}F-NMR ($CDCl_3$): δ −77.23 (d, $J = 6.1$ Hz); EI-MS *m/z* (%) 335 (2), 334 (M^+, 8), 245 (5), 213 (10), 200 (21), 199 (9), 132 (10), 131 (100). Anal. Calc. for $C_{15}H_{17}F_3O_5$: C, 53.89; H, 5.13. Found: C, 53.79; H, 5.05%.

3.2.12. Ethyl (*E*)-2-ethoxycarbonyl-6,6,6-trifluoro-3-phenyl-4-hexenoate (*5a*)

To a mixture of carbonate **1a** (54 mg, 0.20 mmol), allylpalladium complex **4** (7.3 mg, 20 μmol), triphenylphosphine (10.4 mg, 40 μmol) in anhydrous THF (1 ml), a mixture of diethyl malonate (96 mg, 0.30 mmol) and NaO^tBu (58 mg, 0.60 mmol) in THF (0.6 ml) was added under Ar atmosphere. The resulting mixture was stirred at room temperature for 1 h, and then quenched with water. The reaction mixture was extracted with $CHCl_3$. The combined extracts were dried over $MgSO_4$, and the solvents were removed under reduced pressure. The residue was chromatographed on a silica gel column to give pure ester **5a** as pale yellow oil: 51 mg (74%); ^{1}H-NMR ($CDCl_3$): δ 1.002 (t, $J = 7.2$ Hz, 3H), 1.276 (t, $J = 7.2$ Hz, 3H), 3.839 (d, $J = 10.8$ Hz, 1H), 3.969 (q, $J = 7.2$ Hz, 2H), 4.16–4.26 (m, 3H), 5.656 (dqd, $J = 15.9$, 6.1, 1.8 Hz, 1H), 6.566 (ddq, $J = 15.9$, 8.1, 1.0 Hz, 1H), 7.19–7.37 (m, 5H); ^{13}C-NMR ($CDCl_3$): δ 13.71, 13.98, 47.35, 56.77, 61.65, 61.94, 120.26 (q, $J = 33$ Hz), 122.64 (q, $J = 269$ Hz), 127.79, 128.12, 128.91, 137.80, 139.45 (q, $J = 6$ Hz), 166.79, 167.32; ^{19}F-NMR ($CDCl_3$): δ −64.85 (d, $J = 6.1$ Hz); EI-MS *m/z* (%) 344 (M^+, 0.6), 271 (100), 243 (26), 201 (44), 185 (43), 173 (28), 165 (40), 129 (24), 128 (22), 115 (26). Anal. Calc. for $C_{17}H_{19}F_3O_4$: C, 59.30; H, 5.56. Found: C, 59.22; H, 5.44%.

3.2.13. Ethyl (*E*)-2-ethoxycarbonyl-6,6,6-trifluoro-3-(*o*-tolyl)-4-hexenoate (*5b*)

Ester **5b** was obtained as above: yield 51%; ^{1}H-NMR ($CDCl_3$) 0.969 (t, $J = 7.2$ Hz, 3H), 1.291 (t, $J = 7.2$ Hz, 3H), 2.397 (s, 3H), 3.919 (d, $J = 11.3$ Hz, 1H), 3.949 (q, $J = 7.2$ Hz, 2H), 4.241 (q, $J = 7.2$ Hz, 2H), 4.488 (dddq, $J = 11.3$, 7.8, 1.5, 1.2 Hz, 1H), 5.573 (dqd, $J = 15.9$, 6.1, 1.5 Hz, 1H), 6.458 (ddq, $J = 15.9$, 7.8, 2.4 Hz, 1H), 7.26–7.14 (m, 4H); ^{13}C-NMR ($CDCl_3$): δ 13.81, 14.16, 19.80, 42.76, 51.44, 61.15, 61.78, 120.20 (q, $J = 34$ Hz), 122.86 (q, $J = 270$ Hz), 126.66, 126.79, 127.65, 131.18, 136.15, 136.87, 139.56 (q, $J = 6$ Hz), 166.97, 167.75; ^{19}F-NMR ($CDCl_3$): δ −64.75 (d, $J = 6.1$ Hz); EI-MS *m/z* (%) 358 (M^+, 2), 199 (31), 179 (28), 164 (34), 129 (100), 128 (28), 115 (45), 91 (38). Anal. Calc. for $C_{18}H_{21}F_3O_4$: C, 60.33; H, 5.91. Found: C, 60.16; H, 5.91%.

*3.2.14. Ethyl (E)-2-ethoxycarbonyl-6,6,6-trifluoro-3-mesityl-4-hexenoate (**5c**)*

Ester **5c** was obtained as above: yield 33%; ^{1}H-NMR ($CDCl_3$) 1.268 (t, $J = 7.2$ Hz, 3H), 1.308 (t, $J = 7.2$ Hz, 3H), 2.228 (s, 3H), 2.32 (br s, 6H), 4.122 (d, $J = 11.7$ Hz, 1H), 4.203 (q, $J = 7.2$ Hz, 2H), 4.278 (q, $J = 7.2$ Hz, 2H), 4.72–4.83 (m, 1H), 5.408 (dqd, $J = 14.7$, 6.3, 2.1 Hz, 1H), 6.588 (ddq, $J = 15.9$, 4.2, 2.4 Hz, 1H), 6.817 (s, 2H); ^{19}F-NMR ($CDCl_3$): δ −65.03 (br s); EI-MS *m/z* (%) 386 (4, M^+), 368 (19), 267 (25), 239 (12), 238 (11), 228 (15), 227 (100), 226 (44), 212 (12), 211 (16), 158 (10), 157 (58), 143 (17), 142 (13), 141 (11), 119 (41), 91 (13). Anal. Calc. for $C_{20}H_{25}F_3O_4$: C, 62.17; H, 6.52. Found: C, 62.21; H, 6.73%.

*3.2.15. Ethyl (E)-3-tert-butyl-2-ethoxycarbonyl-6,6,6-trifluoro-4-hexenoate (**5d**)*

Ester **5d** was obtained as above: yield 53%; ^{1}H-NMR ($CDCl_3$) 0.925 (s, 9H), 1.255 (t, $J = 7.1$ Hz, 3H), 1.250 (t, $J = 7.2$ Hz, 3H), 2.846 (dd, $J = 11.1$, 6.3 Hz, 1H), 3.612 (d, $J = 6.3$ Hz, 1H), 4.137 (q, $J = 7.2$ Hz, 2H), 4.195 (q, $J = 7.1$ Hz, 2H), 5.701 (dq, $J = 15.3$, 6.3 Hz, 1H), 6.481 (ddq, $J = 15.3$, 8.7, 1.8 Hz, 1H); ^{19}F-NMR ($CDCl_3$): δ −65.32 (d, $J = 6.0$ Hz); EI-MS *m/z* (%) 309 (2, $M^+ - CH_3$), 268 (59), 232 (11), 222 (15), 217 (12), 195 (22), 194 (15), 176 (12), 125 (10), 115 (11), 97 (14), 87 (10), 57 (100). Anal. Calc. for $C_{15}H_{23}F_3O_4$: C, 55.55; H, 7.15. Found: C, 55.53; H, 7.17%.

*3.2.16. Ethyl (E)-3-(o-anisyl)-2-ethoxycarbonyl-6,6,6-trifluoro-4-hexenoate (**5e**)*

Ester **5e** was obtained as above: yield 77%; ^{1}H-NMR ($CDCl_3$): δ 0.987 (t, $J = 7.2$ Hz, 3H), 1.264 (t, $J = 7.2$ Hz, 3H), 3.858 (s, 3H), 3.943 (q, $J = 7.2$ Hz, 2H), 4.164 (d, $J = 10.5$ Hz, 1H), 4.205 (q, $J = 7.2$ Hz, 2H), 4.4389 (dddq, $J = 10.4$, 8.6, 1.5, 1.2 Hz, 1H), 5.667 (dqd, $J = 15.6$, 6.1, 1.2 Hz, 1H), 6.458 (ddq, $J = 15.6$, 8.7, 2.1 Hz, 1H), 6.875 (dd, $J = 8.4$, 1.5 Hz, 1H), 6.898 (dt, $J = 7.5$, 1.5 Hz, 1H), 7.141 (dd, $J = 7.5$, 1.5 Hz, 1H), 7.246 (ddd, $J = 8.4$, 7.5, 1.5 Hz, 1H); ^{19}F-NMR ($CDCl_3$): δ −64.71 (d, $J = 6.1$ Hz); EI-MS *m/z* (%) 374 (M^+, 10), 302 (15), 301 (88), 282 (13), 273 (20), 255 (18), 231 (38), 215 (100), 203 (13), 180 (13), 159 (12), 131 (13). Anal. Calc. for $C_{18}H_{21}F_3O_5$: C, 57.75; H, 5.65. Found: C, 57.77; H, 5.55%.

*3.2.17. Ethyl (E)-2-ethoxycarbonyl-6,6,6-trifluoro-3-[o-(methoxymethyl)phenyl]-4-hexenoate (**5f**)*

Ester **5f** was obtained as above: yield 31%; ^{1}H-NMR ($CDCl_3$): δ 0.979 (t, $J = 7.2$ Hz, 3H), 1.272 (t, $J = 7.2$ Hz, 3H), 3.495 (s, 3H), 3.940 (q, $J = 7.2$ Hz, 2H), 4.145 (d, $J = 10.8$ Hz, 1H), 4.219 (q, $J = 7.2$ Hz, 2H), 4.438 (dd, $J = 10.8$, 8.7 Hz, 1H), 5.236 (s, 2H), 5.657 (dq, $J = 16.2$, 6.1 Hz, 1H), 6.668 (ddq, $J = 15.6$, 7.8, 1.5 Hz, 1H), 6.945 (t, $J = 7.8$ Hz, 1H), 7.110 (d, $J = 8.4$ Hz, 1H), 7.152 (dd, $J = 7.8$, 1.8 Hz, 1H), 7.221 (ddd, $J = 8.4$, 7.8, 1.8 Hz, 1H); ^{13}C-NMR ($CDCl_3$): δ 13.65, 13.96, 43.91, 54.67, 56.10, 61.39, 61.74, 94.18, 114.23, 120.01 (q, $J = 33$ Hz), 121.81, 122.83 (q, $J = 270$ Hz), 126.22, 128.78 (q, $J = 7$ Hz), 129.05, 129.80, 154.95, 167.08, 167.71; ^{19}F-NMR ($CDCl_3$): δ −64.72 (d, $J = 6.1$ Hz); EI-MS *m/z* (%) 405 (5), 404 (M^+, 20), 314 (12), 313 (56), 285 (22), 267 (31), 244 (22), 241 (100), 219 (22), 213 (30), 160 (28), 131 (39). Anal. Calc. for $C_{19}H_{23}F_3O_6$: C, 56.43; H, 5.73. Found: C, 56.22; H, 6.00%.

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