

Palladium catalyzed cross-coupling reaction of organoboronic acids with β -(perfluoroalkyl)ethyl iodides

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Abstract

Palladium catalyzed Suzuki cross-coupling reaction of β -(perfluoroalkyl)ethyl iodides with organoboronic acids proceeds smoothly to provide the corresponding cross-coupling products in the presence of the weak base NaHCO_3 in aqueous ethylene glycol dimethyl ether (DME) in moderate to good yields. © 1999 Elsevier Science S.A. All rights reserved.

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1. Introduction

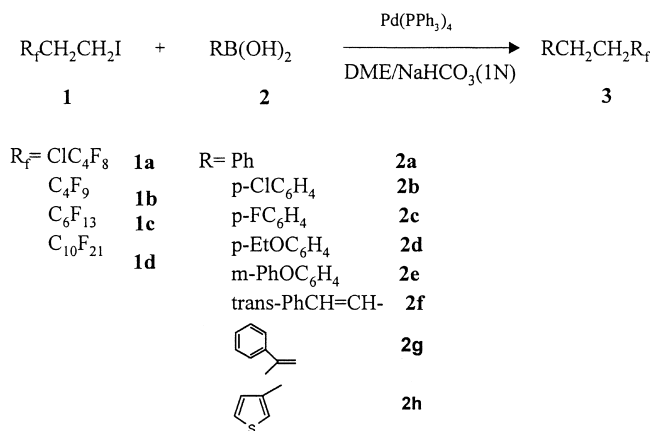
Cross-coupling reactions catalyzed by transition-metals have become powerful and widely used tools for carbon–carbon bond formation in organic syntheses [1,2]. Useful methods based on Pd-catalysis cross-coupling reactions forming carbon–carbon bonds have been well developed over the last decades [3]. Suzuki cross-coupling reaction of organoboranes with aryl halides or triflates containing functional groups has proved very versatile in organic syntheses [4–6]. On the other hand, it is well known that organofluorine compounds usually show unique reactivities in transition-metal catalyzed reactions. For example, Fuchikami and co-workers reported that β -(perfluoroalkyl) substituted alkyl halides took part in a carbonylation cross-coupling reaction in a Still cross-coupling reaction [7–10] and a Grignard cross-coupling reaction catalyzed by copper salts [7–10] and showed different reactivities from non-fluorinated alkyl halides; in the latter case the β -hydrogen was usually eliminated [11]. Here, we would like to report a Suzuki cross-coupling reaction of β -(perfluoroalkyl)ethyl iodides (**1**) with organoboronic acids (**2**) using a palladium-phosphine catalyst.

2. Results and discussions

β -(Perfluoroalkyl)ethyl benzene and its derivatives of substituted benzene could not be prepared by free radical addition of perfluoroalkyl iodide to styrene and its derivatives due to polymerization of the styrene. Suzuki cross-coupling reaction provides a practical method of forming a carbon–carbon bond in the presence of a catalytic amount of palladium complex and a base. Thus, we first examined the reaction of phenyl boronic acid (**2a**) with perfluoroalkyl iodide (**1a**) in the presence of 5 mol% of $\text{Pd}(\text{PPh}_3)_4$ and a weak base NaHCO_3 (1 N). Refluxing DME under an Ar atmosphere for 5 h gave the desired cross-coupling product **3a** in 68% yield (Eq. (1)). Only a small amount of byproduct biphenyl formed. The product was easily purified by column chromatography on silica gel eluted with petroleum ether.

The results of the present Suzuki cross-coupling reactions are summarized in Scheme 1 and Table 1. The reaction without palladium catalyst (Entry 1) did not occur in the above reaction conditions and both starting materials were recovered. The reaction of iodide **1a** with phenyl boronic acid **2a** in the presence of 5 mol% $\text{Pd}(\text{PPh}_3)_4$, K_3PO_4 in dioxane at 85°C for 5 h resulted in a lower yield (37%) (Entry 2). Little change was observed in reaction yield when the perfluoroalkyl iodides with different chain length were coupled in the same conditions (Entry 3–6). The reaction of aryl boronic acids substituted with different functional groups, such as fluorine, ethoxy, chlorine and phenoxy carried out smoothly to give a 66–79% yield (Entry 3, 7–

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Scheme 1.

10). 3-Thienyl boronic acid (**2h**) was treated with **1a** and **1d** to afford **3ah** and **3dh** in 68% and 58% yield respectively. In addition, vinyl boronic acid with α or β -phenyl groups could also react with iodide **1a** under the same condition; but **2g** bearing an α -phenyl group gave a rather lower yield than **2f** with a β -phenyl group probably due to steric hindrance. It is interesting that the reaction of phenyl boronic acid **2a** with $\text{CF}_3\text{CH}_2\text{I}$ or $\text{CF}_3(\text{CH}_2)_4\text{I}$ did not give the desired coupling product, but the starting materials were recovered. In conclusion, we have presented a practical method for introduction of the β -(perfluoroalkyl)ethyl group into organic molecules.

3. Experimental

All reactions were monitored by TLC (silica gel, developing solvent: petroleum ether). IR spectra were recorded with a Shimadzu IR-440 spectrometer in liquid films and KBr pellets for solids. The ^1H NMR, ^{19}F NMR spectra of final products were obtained on a 300 MHz spectrometer (TMS as ^1H internal reference or TFA as ^{19}F external

reference). Mass spectra were taken on a Finnigan GC-MS-4021 spectrometer. Elemental analysis data were measured by the elemental analysis group of SIOC.

3.1. General procedure

To a mixture of β -(perfluoroalkyl)ethyl iodide (**1**, 2.2 mmol), organoboronic acid (**2**, 2 mmol), 10 ml DME and 5 ml NaHCO_3 (aq., 1 N) was added $\text{Pd(PPh}_3)_4$ (0.0578 g, 0.05 mmol) under Ar. The mixture was stirred at reflux for 5 h. After the reaction was completed, it was cooled to room temperature; the ether phase was separated. The aqueous phase was extracted with three 5 ml portions of diethyl ether and the combined organic phase was washed with water and saturated brine, then dried over Na_2SO_4 . The organic solvents were evaporated in vacuo. The residue was purified by flash chromatography using petroleum ether as eluent.

Compound **3aa**: colourless oil, ν_{max} (cm^{-1}) 3000, 2900, 1600, 1485, 1200, 1120. ^1H NMR (CDCl_3), δ_{H} (ppm) 2.40 (m, 2H), 2.95 (m, 2H), 7.3 (m, 5H). ^{19}F NMR (CDCl_3), δ_{F} (ppm) 46 (m, 2F), 43 (m, 2F), 38 (m, 2F), -9 (t, $^3J_{\text{FF}}=13.0$ Hz, 2F). MS (m/z): 342 (M^++2 , 0.47), 341 (M^++1 , 3.52), 340 (M^+ , 1.65), 339 (M^+-1 , 10.78), 91 (C_7H_7^+ , 100). Elemental analysis (for $\text{C}_{12}\text{H}_9\text{ClF}_8$): found: C: 41.98, H: 2.61; calcd.: C: 42.30, H: 2.64%.

Compound **3ab**: colourless oil, ν_{max} (cm^{-1}) 3000, 2900, 1500, 1460, 1200, 1130. ^1H NMR (CDCl_3), δ_{H} (ppm) 2.38 (m, 2H), 2.90 (m, 2H), 7.15 (d, $^3J_{\text{HH}}=10.8$ Hz, 2H), 7.30 (d, $^3J_{\text{HH}}=10.80$ Hz, 2H). ^{19}F NMR (CDCl_3), δ_{F} (ppm) 46 (m, 2F), 43 (m, 2F), 38 (m, 2F), -9 (t, $^3J_{\text{FF}}=13.0$ Hz, 2F). MS (m/z): 376 (M^++2 , 3.11), 375 (M^++1 , 22.07), 374 (M^+ , 1.65), 125 ($\text{C}_7\text{H}_7\text{Cl}^+$, 100). Elemental analysis (for $\text{C}_{12}\text{H}_8\text{Cl}_2\text{F}_8$): found: C: 38.45, H: 2.07; calcd.: C: 38.41, H: 2.13%.

Compound **3ac**: colourless oil, ν_{max} (cm^{-1}) 3000, 2900, 1600, 1500, 1460, 1200, 1130. ^1H NMR (CDCl_3), δ_{H} (ppm) 2.35 (m, 2H), 2.90 (m, 2H), 7.00 (m, 2H), 7.18 (m, 2H).

Table 1

Suzuki cross-coupling reaction of β -(perfluoroalkyl)ethyl iodides (**1**) with organoboronic acids (**2**) using $\text{Pd(PPh}_3)_4$ as a catalyst

Entry	$\text{R}_f\text{CH}_2\text{CH}_2\text{I}$	RB(OH)_2	Catalyst/base	Product, isolated yield (%)
1	1a	2a	None/ NaHCO_3	—
2	1a	2a	$\text{Pd(PPh}_3)_4/\text{K}_3\text{PO}_4$	3aa , 37%
3	1a	2a	$\text{Pd(PPh}_3)_4/\text{NaHCO}_3$	3aa , 68%
4	1b	2a	$\text{Pd(PPh}_3)_4/\text{NaHCO}_3$	3ba , 64%
5	1c	2a	$\text{Pd(PPh}_3)_4/\text{NaHCO}_3$	3ca , 70%
6	1d	2a	$\text{Pd(PPh}_3)_4/\text{NaHCO}_3$	3da , 68%
7	1a	2b	$\text{Pd(PPh}_3)_4/\text{NaHCO}_3$	3ab , 77%
8	1a	2c	$\text{Pd(PPh}_3)_4/\text{NaHCO}_3$	3ac , 72%
9	1a	2d	$\text{Pd(PPh}_3)_4/\text{NaHCO}_3$	3cd , 66%
10	1a	2e	$\text{Pd(PPh}_3)_4/\text{NaHCO}_3$	3ah , 79%
11	1c	2b	$\text{Pd(PPh}_3)_4/\text{NaHCO}_3$	3cb , 80%
12	1a	2h	$\text{Pd(PPh}_3)_4/\text{NaHCO}_3$	3ah , 68%
13	1a	2f	$\text{Pd(PPh}_3)_4/\text{NaHCO}_3$	3af , 80%
14	1a	2g	$\text{Pd(PPh}_3)_4/\text{NaHCO}_3$	3ag , 30%
15	1d	2h	$\text{Pd(PPh}_3)_4/\text{NaHCO}_3$	3dh , 58%

^{19}F NMR (CDCl_3), δ_{F} (ppm) 45.8 (m, 2F), 43.0 (m, 2F), 39.2 (m, 1F), 37.9 (m, 2F), -9.0 (t, $^3J_{\text{FF}}=13.1$ Hz, 2F). MS (m/z): 360 (M^++2 , 0.67), 359 (M^++1 , 5.06), 358 (M^+ , 2.36), 357 (M^+-1 , 15.74), 109 ($\text{C}_7\text{H}_7\text{F}^+$, 100). Elemental analysis (for $\text{C}_{12}\text{H}_8\text{ClF}_9$): found: C: 40.18, H: 2.18; calcd.: C: 40.17, H: 2.23%.

Compound **3ad**: colourless oil, ν_{max} (cm^{-1}) 3000, 2900, 1605, 1500, 1470, 1200, 1120. ^1H NMR (CDCl_3), δ_{H} (ppm) 1.43 (t, $^3J_{\text{HH}}=7.0$ Hz, 3H), 2.38 (m, 2H), 2.87 (m, 2H), 4.2 (q, $^3J_{\text{HH}}=7.0$ Hz, 2H), 6.85 (d, $^3J_{\text{HH}}=9.46$ Hz, 2H), 7.15 (d, $^3J_{\text{HH}}=9.46$ Hz, 2H). ^{19}F NMR (CDCl_3), δ_{F} (ppm): 46.0 (m, 2F), 43.0 (m, 2F), 38.0 (m, 2F), -9.0 (t, $^3J_{\text{FF}}=13.0$ Hz, 2F). MS (m/z): 386 (M^++2 , 1.64), 385 (M^++1 , 10.31), 384 (M^+ , 5.63), 135 ($\text{C}_9\text{H}_{11}\text{O}^+$, 41.43), 107 (100). Elemental analysis (for $\text{C}_{14}\text{H}_{13}\text{ClF}_8\text{O}$): found: C: 43.63, H: 3.33; calcd.: C: 43.70, H: 3.38%.

Compound **3ae**: colourless oil, ν_{max} (cm^{-1}) 3000, 2900, 1600, 1500, 1470, 1200, 1130. ^1H NMR (CDCl_3), δ_{H} (ppm) 2.40 (m, 2H), 2.93 (m, 2H), 6.9–7.4 (m, 9H). ^{19}F NMR (CDCl_3), δ_{F} (ppm) 46.0 (m, 2F), 43.0 (m, 2F), 38.0 (m, 2F), -9.0 (t, $^3J_{\text{FF}}=13.0$ Hz, 2F). MS (m/z): 434 (M^++2 , 34.57), 433 (M^++1 , 22.18), 432 (M^+ , 100), 183 ($\text{C}_{13}\text{H}_{11}\text{O}^+$, 45.01). HRMS for $\text{C}_{18}\text{H}_{13}\text{ClF}_8\text{O}$: found: 432.0532; calcd.: 432.0527.

Compound **3af**: colourless oil, ν_{max} (cm^{-1}) 3000, 2900, 1500, 1470, 1200, 1120. ^1H NMR (CDCl_3), δ_{H} (ppm) 2.30 (m, 2H), 2.57 (m, 2H), 6.20 (d, $^3J_{\text{HH}}=15.8$ Hz, 1H), 6.50 (d, $^3J_{\text{HH}}=15.8$ Hz, 1H). ^{19}F NMR (CDCl_3), δ_{F} (ppm) 46.0 (m, 2F), 43.0 (m, 2F), 37.6 (m, 2F), -9.0 (t, $^3J_{\text{FF}}=12.9$ Hz, 2F). MS (m/z): 368 (M^++2 , 12.80), 367 (M^++1 , 7.55), 366 (M^+ , 37.23), 117 (C_9H_9^+ , 100). Elemental analysis (for $\text{C}_{14}\text{H}_{11}\text{ClF}_8$): found: C: 45.41, H: 2.82; calcd.: C: 45.84, H: 3.00%.

Compound **3ag**: colourless oil, ν_{max} (cm^{-1}) 3000, 2900, 1640, 1500, 1460, 1200, 1130. ^1H NMR (CDCl_3), δ_{H} (ppm) 2.20 (m, 2H), 2.80 (m, 2H), 5.15 (s, 1H), 5.38 (s, 1H), 7.32 (m, 5H). ^{19}F NMR (CDCl_3), δ_{F} (ppm) 45.8 (m, 2F), 43.0 (m, 2F), 37.7 (m, 2F), -9.0 (t, $^3J_{\text{FF}}=12.6$ Hz, 2F). MS (m/z): 368 (M^++2 , 5.63), 367 (M^++1 , 35.27), 366 (M^+ , 15.29), 131 ($\text{C}_{10}\text{H}_{11}^+$, 100). Elemental analysis (for $\text{C}_{14}\text{H}_{11}\text{ClF}_8$): found: C: 45.70, H: 2.88; calcd.: C: 45.84, H: 3.00%.

Compound **3ah**: colourless oil, ν_{max} (cm^{-1}) 3000, 2880, 1500, 1460, 1200, 1130. ^1H NMR (CDCl_3), δ_{H} (ppm) 2.40 (m, 2H), 2.95 (m, 2H), 7.00 (m, 2H), 7.30 (m, 1H). ^{19}F NMR (CDCl_3), δ_{F} (ppm) 46.0 (m, 2F), 43.0 (m, 2F), 38.0 (m, 2F), -9.0 (t, $^3J_{\text{FF}}=13.0$ Hz, 2F). MS (m/z): 348 (M^++2 , 1.42), 347 (M^++1 , 11.51), 346 (M^+ , 4.39), 345 (M^+-1 , 29.99), 97 ($\text{C}_5\text{H}_5\text{S}^+$, 100). HRMS (for $\text{C}_{10}\text{H}_7\text{ClF}_8\text{S}$): found: 345.9821; calcd.: 345.9829.

Compound **3ca**: colourless oil, ν_{max} (cm^{-1}) 3000, 2900, 1600, 1500, 1460, 1200, 1130. ^1H NMR (CDCl_3), δ_{H} (ppm) 2.40 (m, 2H), 2.90 (m, 2H), 7.26 (m, 5H). ^{19}F NMR (CDCl_3), δ_{F} (ppm) 49.2 (m, 2F), 46.5 (m, 2F), 45.9 (m, 2F), 45.0 (m, 2F), 38 (m, 2F), -3.8 (t, $^3J_{\text{FF}}=10.0$ Hz, 3F). MS (m/z) 424 (M^+ , 22.88), 91 (C_7H_7^+ , 100). Elemental analysis (for $\text{C}_{14}\text{H}_9\text{F}_{13}$): found: C: 39.43, H: 2.20; calcd.: C: 39.62, H: 2.12.

Compound **3cb**: colourless oil, ν_{max} (cm^{-1}) 3000, 2900, 1600, 1500, 1450, 1200, 1120. ^1H NMR (CDCl_3), δ_{H} (ppm) 2.35 (m, 2H), 2.90 (m, 2H), 7.18 (d, $^3J_{\text{HH}}=8.4$ Hz, 2H), 7.28 (d, $^3J_{\text{HH}}=8.40$ Hz, 2H). ^{19}F NMR (CDCl_3), δ_{F} (ppm) 49.0 (m, 2F), 46.6 (m, 2F), 46.0 (m, 2F), 45.0 (m, 2F), 37.7 (m, 2F), -3.9 (t, $^3J_{\text{FF}}=9.62$ Hz, 3F). MS (m/z): 460 (M^++2 , 8.70), 459 (M^++1 , 4.67), 458 (M^+ , 25.99), 125 ($\text{C}_7\text{H}_6\text{Cl}^+$, 100). Elemental analysis (for $\text{C}_{14}\text{H}_8\text{ClF}_{13}$): found: C: 36.76, H: 1.88; calcd.: C: 36.64, H: 1.74.

Compound **3da**: white solid m.p.: 46.5–47.5°C, ν_{max} (cm^{-1}) 3000, 2900, 1600, 1500, 1460, 1200, 1130. ^1H NMR (CDCl_3), δ_{H} (ppm) 2.40 (m, 2H), 2.90 (m, 2H), 7.28 (m, 5H). ^{19}F NMR (CDCl_3), δ_{F} (ppm) 49.0 (m, 2F), 46.4 (m, 2F), 45.7 (m, 2F), 44.8 (m, 10F), 38 (m, 2F), -3.7 (t, $^3J_{\text{FF}}=10.0$ Hz, 3F). MS (m/z) 625 (M^+ , 8.83), 91 (C_7H_7^+ , 100). HRMS (for $\text{C}_{18}\text{H}_9\text{F}_{21}$): found: 624.0351; calcd.: 624.0368.

Compound **3dh**: wax solid, ν_{max} (cm^{-1}) 3000, 2800, 1500, 1200, 1130. ^1H NMR (CDCl_3), δ_{H} (ppm) 2.40 (m, 2H), 2.90 (m, 2H), 7.00 (m, 1H), 7.10 (m, 1H), 7.35 (m, 1H). ^{19}F NMR (CDCl_3), δ_{F} (ppm) 49.0 (m, 2F), 46.5 (m, 2F), 45.2 (m, 2F), 49.5 (m, 10F), 35 (m, 2F), -3.5 (t, $^3J_{\text{FF}}=10.0$ Hz, 3F). MS (m/z): 631 (M^++1 , 14.04), 97 (100).

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