Supporting Information

Suzuki-Miyaura Coupling Reaction Using Pentafluorophenylboronic Acid

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Experimental Section

General Experimental Methods. All reactions were carried out under an argon atmosphere with dry solvents under anhydrous conditions, unless otherwise noted. Dehydrated 1,2-dimethoxyethane (DME), toluene, and *N,N*-dimethylformamide (DMF) were purchased from Kanto Chemical Co. and then were stored in Schlenk tubes under an argon atmosphere. Reagents were purchased at the highest commercial quality and used without further purification, unless otherwise stated. As a usual workup procedure, the reaction mixture was extracted with ethyl acetate (EtOAc). The organic layer was dried over MgSO_4 , filtrated with suction, and then concentrated under reduced pressure. Preparative column chromatography was carried out by using silica gel (Fuji Silysia BW-127 ZH, 100-270 mesh). ^1H NMR and ^{13}C NMR spectra were measured at 300 MHz and 75 MHz, respectively, and chemical shifts are given relative to tetramethylsilane (TMS). ^{19}F NMR spectra were measured at 282 MHz, and chemical shifts are given relative to CCl_3F using C_6F_6 as secondary reference (-162.9 ppm).

Typical procedure of the coupling reaction with condition A.

2,3,4,5,6-Pentafluoro-1,1'-biphenyl (**3a**).^{1,2}

A 20 mL of dry Schlenk tube was charged with iodobenzene (34 μL , 0.30 mmol) and DME (1 mL) under an argon atmosphere. Argon was bubbled through the solution for 10 min. To the solution were added pentafluorophenylboronic acid (**1**) (70 mg, 0.33 mmol), tetrakis(triphenylphosphine)palladium (10 mg, 9.0 μmol), cesium fluoride (91 mg, 0.60 mmol), and silver(I) oxide (83 mg, 0.36 mmol) with a gentle flow of argon. The reaction mixture was stirred at 70 $^{\circ}\text{C}$ for 12 h. The resulting mixture was filtered through a pad of Celite[®]. The filtrate was extracted with EtOAc (three times), and treated in a usual manner to give a crude product. The resulting solid was purified by silica gel column chromatography (hexane) to give 2,3,4,5,6-pentafluoro-1,1'-biphenyl (**3a**) as a white solid (66 mg, 90% yield): mp 110 – 111 $^{\circ}\text{C}$ (lit. mp 111 – 112 $^{\circ}\text{C}$); R_f = 0.38 (SiO_2 , hexane); ^1H NMR (300 MHz, CDCl_3) δ 7.39 – 7.43 (m, 2H), 7.45 – 7.49 (m, 3H); ^{13}C NMR (75 MHz, CDCl_3 (except for C_6F_5)) δ 126.3, 128.7, 129.2, 130.1; ^{19}F NMR (282 MHz, CDCl_3) δ -163.4 (m, 2F), -156.8 (t, J = 20.9 Hz, 1F), -144.6 (dd, J = 7.1, 23.4 Hz, 2F); IR (KBr) 1526, 1497, 1063, 983, 853, 797, 750, 721, and 694 cm^{-1} .

Typical procedure of the coupling reaction with condition B.

4'-Methyl-2,3,4,5,6-pentafluoro-1,1'-biphenyl (**3b**).^{1,3}

A 20 mL of dry Schlenk tube was charged with 4-bromotoluene (37 μ L, 0.30 mmol) and DMF (3 mL) under an argon atmosphere. Argon was bubbled through the solution for 10 min. To the solution were added pentafluorophenylboronic acid (**1**) (70 mg, 0.33 mmol), tris(dibenzylideneacetone)dipalladium (14 mg, 15 μ mol), cesium fluoride (91 mg, 0.60 mmol), silver(I) oxide (83 mg, 0.36 mmol), and tri-*tert*-butylphosphine (11 μ L, 45 μ mol) with a gentle flow of argon. The reaction mixture was stirred at 100 $^{\circ}$ C for 12 h. The resulting mixture was filtered through a pad of Celite[®]. The filtrate was extracted with EtOAc (three times), and treated in a usual manner to give a crude product. The resulting solid was purified by silica gel column chromatography (hexane) to give 4'-methyl-2,3,4,5,6-pentafluoro-1,1'-biphenyl (**3b**) as a white solid (72 mg, 93% yield) : mp 118 – 119 $^{\circ}$ C (lit. mp 117 – 119 $^{\circ}$ C); R_f = 0.43 (SiO₂, hexane); ¹H NMR (300 MHz, CDCl₃) δ 2.42 (s, 3H), 7.31 (s, 4H); ¹³C NMR (75 MHz, CDCl₃ (except for C₆F₅)) δ 21.3, 123.3, 129.4, 129.9, 139.4; ¹⁹F NMR (282 MHz, CDCl₃) δ -163.4 (m, 2F), -156.5 (t, J = 21.2 Hz, 1F), -141.7 (dd, J = 7.1, 23.2 Hz, 2F); IR (KBr) 2926, 1526, 1493, 1065, 982, 860, 826, and 777 cm⁻¹.

3'-Methyl-2,3,4,5,6-pentafluoro-1,1'-biphenyl (**3c**).⁴

3c: mp 43 – 45 $^{\circ}$ C (lit. mp 44 $^{\circ}$ C); R_f = 0.42 (SiO₂, hexane); ¹H NMR (300 MHz, CDCl₃) δ 2.42 (s, 3H), 7.21 – 7.28 (m, 3H), 7.35 – 7.40 (m, 1H); ¹³C NMR (75 MHz, CDCl₃ (except for C₆F₅)) δ 21.4, 126.2, 127.2, 128.6, 130.1, 130.7, 138.5; ¹⁹F NMR (282 MHz, CDCl₃) δ -163.5 (m, 2F), -157.1 (t, J = 21.0 Hz, 1F), -144.4 (dd, J = 7.1, 23.4 Hz, 2F); IR (KBr) 2962, 1518, 1487, 1070, 988, 920, 883, 802, 783, 764, 694, and 654 cm⁻¹.

2'-Methyl-2,3,4,5,6-pentafluoro-1,1'-biphenyl (3d).¹

3d: mp 38 – 39 °C (lit. mp 39 – 40 °C); R_f = 0.37 (SiO₂, hexane); ¹H NMR (300 MHz, CDCl₃) δ 2.19 (s, 3H), 7.18 – 7.41 (m, 4H); ¹³C NMR (75 MHz, CDCl₃ (except for C₆F₅)) δ 19.6, 125.8, 126.0, 129.6, 130.5, 130.6, 137.3; ¹⁹F NMR (282 MHz, CDCl₃) δ –163.6 (m, 2F), –157.3 (t, J = 20.9 Hz, 1F), –144.5 (dd, J = 7.1, 23.4 Hz, 2F); IR (KBr) 2928, 1522, 1494, 1063, 988, and 864 cm⁻¹.

4'-Methoxy-2,3,4,5,6-pentafluoro-1,1'-biphenyl (3e).¹

3e: mp 121 – 123 °C (lit. mp 123 – 124 °C); R_f = 0.35 (SiO₂, hexane); ¹H NMR (300 MHz, CDCl₃) δ 3.86 (s, 3H), 6.99 – 7.03 (m, 2H), 7.33 – 7.37 (m, 2H); ¹³C NMR (75 MHz, CDCl₃ (except for C₆F₅)) δ 55.3, 114.2, 118.3, 131.4, 160.2; ¹⁹F NMR (282 MHz, CDCl₃) δ –163.7 (m, 2F), –157.7 (t, J = 21.0 Hz, 1F), –144.9 (dd, J = 7.1, 23.1 Hz, 2F); IR (KBr) 2964, 1612, 1514, 1491, 1256, 1067, 982, 862, and 827 cm⁻¹.

3'-Methoxy-2,3,4,5,6-pentafluoro-1,1'-biphenyl (3f).⁵

3f: R_f = 0.33 (SiO₂, hexane); ¹H NMR (300 MHz, CDCl₃) δ 3.84 (s, 3H), 6.93 (m, 1H), 6.96 – 7.01 (m, 2H), 7.40 (m, 1H); ¹³C NMR (75 MHz, CDCl₃ (except for C₆F₅)) δ 55.3, 114.8, 115.8, 122.5, 123.7, 129.7, 159.6; ¹⁹F NMR (282 MHz, CDCl₃) δ –163.4 (m, 2F), –156.8 (t, J = 20.9 Hz, 1F), –144.1 (dd, J = 7.1, 23.1 Hz, 2F); IR (KBr) 2939, 1581, 1521, 1491, 1246, 1067, 989, 916, and 781 cm⁻¹.

2-Pentafluorophenylnaphthalene (**3g**).⁶

3g: mp 157 – 158 °C; R_f = 0.35 (SiO₂, hexane); ¹H NMR (300 MHz, CDCl₃) δ 7.47 – 7.59 (m, 3H), 7.87 – 7.96 (m, 4H); ¹³C NMR (75 MHz, CDCl₃ (except for C₆F₅)) δ 123.7, 126.7, 127.0, 127.2, 127.8, 128.3, 128.4, 130.1, 133.0, 133.2; ¹⁹F NMR (282 MHz, CDCl₃) δ –163.3 (m, 2F), –156.6 (t, J = 21.0 Hz, 1F), –144.1 (dd, J = 9.3, 23.1 Hz, 2F); IR (KBr) 1526, 1510, 1487, 1062, 986, 829, 781, and 746 cm^{–1}.

2,3,4,4',5,6-Hexafluoro-1,1'-biphenyl (**3h**).^{7,8}

3h: mp 116 – 118 °C (lit. mp 118 – 119 °C); R_f = 0.37 (SiO₂, hexane); ¹H NMR (300 MHz, CDCl₃) δ 7.16 – 7.22 (m, 2H), 7.37 – 7.41 (m, 2H); ¹³C NMR (75 MHz, CDCl₃ (except for C₆F₅)) δ 116.0 (d, J = 21.9 Hz), 122.2, 132.0 (d, J = 8.4 Hz), 163.1 (d, J = 248 Hz); ¹⁹F NMR (282 MHz, CDCl₃) δ –163.1 (m, 2F), –156.4 (t, J = 20.9 Hz, 1F), –144.6 (dd, J = 9.3, 23.4 Hz, 2F), –112.8 (s, 1F); IR (KBr) 1602, 1529, 1495, 1227, 1163, 1067, 986, 866, 847, and 779 cm^{–1}.

Ethyl 2,3,4,5,6-pentafluoro-1,1'-biphenyl-4-carboxylate (**3i**).⁸

3i: mp 149 – 150 °C; R_f = 0.28 (SiO₂, hexane); ¹H NMR (300 MHz, CDCl₃) δ 1.42 (t, J = 7.2 Hz, 3H), 4.42 (q, J = 7.2 Hz, 2H), 7.50 – 7.53 (m, 2H), 8.15 – 8.18 (m, 2H); ¹³C NMR (75 MHz, CDCl₃ (except for C₆F₅)) δ 14.3, 61.3, 129.8, 130.2, 130.7, 131.2, 165.8; ¹⁹F NMR (282 MHz, CDCl₃) δ –162.8 (m, 2F), –155.3 (t, J = 20.9 Hz, 1F), –144.0 (dd, J = 7.1, 23.2 Hz, 2F); IR (KBr) 2359, 1722, 1558, 1489, 1279, 1130, 1065, 984, and 756 cm^{–1}.

2,3,4,5,6-Pentafluoro-4'-trifluoromethyl-1,1'-biphenyl (3j).⁹

3j: R_f = 0.43 (SiO₂, hexane); ¹H NMR (300 MHz, CDCl₃) δ 7.54 – 7.57 (m, 2H), 7.74 – 7.77 (m, 2H); ¹³C NMR (75 MHz, CDCl₃ (except for C₆F₅)) δ 123.5 (q, J = 265 Hz), 125.6, 125.7, 130.9; ¹⁹F NMR (282 MHz, CDCl₃) δ –162.5 (m, 2F), –155.0 (t, J = 20.9 Hz, 1F), –144.3 (dd, J = 9.3, 23.4 Hz, 2F), –64.9 (s, 3F); IR (KBr) 1533, 1485, 1325, 1148, 1063, 986, 860, 847, and 770 cm^{–1}.

4'-Nitro-2,3,4,5,6-Pentafluoro-1,1'-biphenyl (3k).^{7,8}

3k: mp 85 – 87 °C (lit. mp 87 – 89 °C); R_f = 0.35 (SiO₂, hexane); ¹H NMR (300 MHz, CDCl₃) δ 7.61 – 7.66 (m, 2H), 8.35 – 8.39 (m, 2H); ¹³C NMR (75 MHz, CDCl₃ (except for C₆F₅)) δ 123.9, 131.3, 132.9, 148.2; ¹⁹F NMR (282 MHz, CDCl₃) δ –161.9 (m, 2F), –153.6 (t, J = 20.9 Hz, 1F), –143.7 (dd, J = 8.9, 21.2 Hz, 2F); IR (KBr) 1522, 1497, 1348, 1063, 988, 864, 839, and 729 cm^{–1}.

References

- (1) Chen, Q.-Y.; Li, Z.-T. *J. Org. Chem.* **1993**, 58, 2599.
- (2) Pushkina, L. N.; Stepanov, A. P.; Zhukov, V. S. *Org. Magnet. Reson.* **1972**, 4, 607.
- (3) Xiao, J.-C.; Ye, C.; Shreeve, J. M. *Org. Lett.* **2005**, 7, 1963.
- (4) Claret, P. A.; Coulson, J.; Williams, G. H. *Chem. Ind.* **1965**, 5, 228.
- (5) Kamigata, N.; Yoshikawa, M.; Shimizu, T. *J. Fluorine Chem.* **1998**, 87, 91.
- (6) Birchall, J.; *J Chem Soc, Perkin Trans I* **1974**, 1740.
- (7) Sheppard, W. A. *J. Am. Chem. Soc.* **1970**, 92, 5419.
- (8) Frohn, H.-J.; Adonin, N. Y.; Bardin, V. V.; Starichenko, V. F. *J. Fluorine Chem.* **2002**, 117, 115.
- (9) Frohn, H. J.; Klose, A.; Bardin, V. V. *J. Fluorine Chem.* **1993**, 64, 201.

Pulse Sequence: s2pul
Solvent: CDCl3
Ambient temperature
Mercury-300BB "gcmr2"

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 3.200 sec
Width 5402.5 Hz
14 Repetitions
OBSERVE H1, 300.0673700 MHz
DATA PROCESSING
F1 size 65536
Total time 2 min, 33 sec

3a

PULSE SEQUENCE
 Relax delay 1.000 sec
 Pulse 75.4 degrees
 Acq. time 3.200 sec
 Width 5402.5 Hz
 128 repetitions

OBSERVE H1, 300.0673668

DATA PROCESSING
 FT size 65536
 Total time 8 minutes

Pulse Sequence: s2pul
 Solvent: CDCl₃
 Ambient temperature
 File: P-methyl-
 Mercury-300 "mp300"

Pulse Sequence: 42pul
 Solvent: CDCl3
 Ambient temperature
 Mercury-300BB "scomr2"
 Relax. delay 1.000 sec
 Pulse 45.0 degrees
 Acq. time 3.200 sec
 Width 5402.5 Hz
 11 repetitions
 OBSERVE H1, 200.067366 MHz
 DATA PROCESSING
 FT size 65536
 Total time 2 min, 33 sec

Pulse Sequence: s2pul
 Solvent: CDCl3
 Ambient temperature
 Mercury-300B "cmar2"
 Relax. delay 1.000 sec
 Pulse 45.0 degrees
 Acq. time 3.200 sec
 Width 5402.5 Hz
 11 repetitions
 OBSERVE H1, 200.0673700 MHz
 DATA PROCESSING
 FT date 65516
 Total time 2 min, 33 sec

3g

Pulse Sequence: s2pul
 Solvent: CDCl3
 Ambient temperature
 Mercury-300BB *scmr2*
 Relax. delay 1.000 sec
 Pulse 45.0 degrees
 Acq. time 3.200 sec
 Width 5402.5 Hz
 14 Repetitions
 OBSERVE H1, 300.0673700 MHz
 DATA PROCESSING
 FT size 65536
 Total time 1 min, 16 sec

Pulse Sequence: a2pul
 Solvent: CDCl3
 Ambient temperature
 Mercury-300BB "ecmar2"
 Relax. delay 1.000 sec
 Pulse 45.0 degrees
 Acq. time 3.200 sec
 Width 5402.5 Hz
 13 repetitions
 OBSERVE H1, 300.0673696 MHz
 DATA PROCESSING
 FT size 65526
 Total time 2 min, 33 sec

Pulse Sequence: s2pul
Solvent: CDCl₃
Ambient temperature
File: p-Co2Et-h
Mercury-300 "mp300"

DATA PROCESSING
FT size 65536
Total time 8 minutes

OBSERVE H1, 300.0673668

PULSE SEQUENCE
Relax delay 1.000 sec
Pulse 76.4 degrees
Acq. time 3.200 sec
Width 5402.5 Hz
128 repetitions

Pulse Sequence: w2pul
 Solvent: CDCl3
 Ambient temperature
 Mercury-300BB "schem2"
 Relax. delay 1.000 sec
 Pulse 45.0 degrees
 Acq. time 3.200 sec
 Width 5402.5 Hz
 17 repetitions
 OBSERVE H1, 300.0673696 MHz
 DATA PROCESSING
 FT size 65536
 Total time 2 min, 33 sec

Pulse Sequence: s2pul
 Solvent: CDCl3
 Ambient temperature
 File: p-nitro-h
 Mercury-300 "mp100"

DATA PROCESSING
 FT size 65536
 Total time 8 minutes

OBSERVE H1, 300.0673669

PULSE SEQUENCE
 Relax delay 1.000 sec
 Pulse 76.4 degrees
 Acq. time 3.200 sec
 Width 5402.5 Hz
 128 repetitions

Cartesian coordinates of pentafluorophenylboronic acid (**1**)

Optimization at B3LYP/6-31+G* level

1	C	0.000000	1.186557	-0.144049
2	C	-0.004500	1.205697	1.248298
3	C	0.000000	0.000000	1.945487
4	C	0.004500	-1.205697	1.248298
5	C	0.000000	-1.186557	-0.144049
6	C	0.000000	0.000000	-0.881424
7	B	0.000000	0.000000	-2.458933
8	O	0.873626	0.842778	-3.085524
9	O	-0.873626	-0.842778	-3.085524
10	F	-0.024565	2.372240	-0.774128
11	F	-0.018059	2.364618	1.918628
12	F	0.000000	0.000000	3.281142
13	F	0.018059	-2.364618	1.918628
14	F	0.024565	-2.372240	-0.774128
15	H	0.812026	0.847990	-4.051801
16	H	-0.812026	-0.847990	-4.051801

Cartesian coordinates of trihydroxy pentafluorophenylborate.

Optimization at B3LYP/6-31+G* level

1	C	0.119363	1.201282	-0.000441
2	C	1.516223	1.183727	-0.008483
3	C	2.190748	-0.030546	-0.011872
4	C	1.451928	-1.207811	-0.004266
5	C	0.061083	-1.134643	0.000778
6	C	-0.671853	0.051508	-0.005775
7	B	-2.385239	0.030454	0.009050
8	O	-2.707034	-0.324370	1.398868
9	O	-2.963208	1.319955	-0.360487
10	O	-2.860499	-0.947295	-0.994879
11	H	-3.590434	0.034284	1.571134
12	H	-3.366262	1.204946	-1.232495
13	H	-2.671975	-1.841744	-0.681395
14	F	-0.432529	2.438688	0.026868
15	F	2.232267	2.337316	-0.007953
16	F	3.545631	-0.067918	-0.019925
17	F	2.099619	-2.401025	-0.000455
18	F	-0.578782	-2.342304	0.015893

Cartesian coordinates of phenylboronic acid.

Optimization at B3LYP/6-31+G* level

1	C	-0.000493	1.205242	0.551496
2	C	-0.000532	1.209046	1.946040
3	C	0.000000	0.000000	2.645696
4	C	0.000532	-1.209046	1.946040
5	C	0.000493	-1.205242	0.551496
6	C	0.000000	0.000000	-0.173143
7	B	0.000000	0.000000	-1.734873
8	O	0.000000	1.212702	-2.385002
9	O	0.000000	-1.212702	-2.385002
10	H	-0.000283	1.154026	-3.350561
11	H	0.000283	-1.154026	-3.350561
12	H	0.000874	-2.147396	0.009999
13	H	0.000922	-2.151386	2.488344
14	H	0.000000	0.000000	3.733084
15	H	-0.000922	2.151386	2.488344
16	H	-0.000874	2.147396	0.009999

Cartesian coordinates of trihydroxy phenylborate.

Optimization at B3LYP/6-31+G* level

1	C	-0.850299	1.204317	0.001301
2	C	-2.251353	1.191357	0.021315
3	C	-2.944037	-0.024768	0.020385
4	C	-2.212865	-1.219217	-0.004840
5	C	-0.813664	-1.185504	-0.026482
6	C	-0.086262	0.021491	-0.019258
7	B	1.564491	0.028388	0.007943
8	O	2.120003	-1.104844	-0.809609
9	O	2.013226	1.344011	-0.507651
10	O	2.083251	-0.191838	1.383967
11	H	-0.320019	2.154518	-0.005536
12	H	-2.805834	2.130873	0.036144
13	H	-4.033752	-0.042635	0.035507
14	H	-2.737074	-2.176036	-0.010210
15	H	-0.257417	-2.121595	-0.057870
16	H	2.086137	-0.837592	-1.738489
17	H	2.901889	1.478109	-0.146508
18	H	2.562660	-1.032284	1.359066

³¹P NMR (in DME with capillary containing C₆D₆)