Direct Synthesis of Ferrocenylmethylphosphines from Ferrocenylmethyl Alcohols and their Application as Ligands for Room Temperature Palladium(0)-Catalyzed Suzuki Coupling Reactions of Aryl Bromides

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General: NMR spectra were recorded on Varian 200 MHz or 600 MHz spectrometers. EI Mass measurement was carried out by CUNY-Hunter mass center. Elemental analysis was carried out by AtlanticMicro Analysis, Inc. Gel permeation chromatography was carried out by using Waters GPC with polystyrene standards in THF. Et₂O and THF were dried with sodium/benzophenone. Pd(OAc)₂, phenyl boronic acid, potassium fluoride diphenylphosphine (10% w. in hexanes), and phenylphosphine (10% w. in hexanes) were purchased from Strem and used directly. Other chemical reagents were purchased from Aldrich and used directly.

General procedure for the preparation of **4**

Procedure A: At 0°C, to a THF solution of ferrocene (5.60 g, 30.0 mmol) was added *t*-BuLi (14.75 mL, 1.7 M in hexanes, 25.0 mmol) under N₂. After stirring at 0°C for 30 min, aldehyde (19.3 mmol) was added. The mixture was allowed to stir for another 30 min. The reaction was quenched with H₂O and extracted with diethyl ether. The organic layer was washed with brine (3 times). Evaporation of solvents by using a rota-evaporator and flash chromatography on silica gel (hexane/Et₂O) gave ferrocenylmethyl alcohol **4**.

Procedure B: Under N₂, to a THF solution of benzoylferrocene (0.580 g, 2.0 mmol in 20 mL THF) was added PhLi (1.3 mL, 2.0 M in hexanes, 2.6 mmol) at -78°C. The mixture was allowed to stir for another 2 hr. The reaction was quenched with H₂O and extracted with diethyl ether. The organic layer was washed with brine. Evaporation of solvents by using a rota-evaporator and flash chromatography on silica gel (hexane/EtOAc) gave ferrocenylmethyl alcohol **4b** in 91.5% yield.

Procedure C: Under N₂ at 0°C, to a THF (5 mL) solution of (*S*)-Me CBS (0.5 mL, 1.1 M) and BH₃-SMe₂ solution (0.5 mL, 2.0 M in THF) were added benzoylferrocene (2.90 g, 10.0 mmol in 20 mL THF) and BH₃-SMe₂ (2.5 mL, 2.0 M in THF) simultaneously. After the addition, the mixture was allowed to stir at this temperature for another 5 min. The reaction was quenched with MeOH and extracted with diethyl ether. The organic layer was washed with brine. Evaporation of solvents by using a rota-evaporator gave a residue which was passed through a short silica gel (hexane/Et₂O). After recrystallization from Et₂O/hexanes, (R)-**4a** was obtained in 95% yield (2.75 g). [α]_D = -99.6 (c=1.008, THF). HPLC: 98% ee. (Chiralcel OD column, flow rate: 1.0 mL isopropanol/hexanes = 9:1): t_R = 16.34 min, t_S = 26.11 min.

4a (66% yield): ^1H NMR(CDCl_3 , 200 MHz) δ 7.406~7.241 (*m*, 5H), 5.473 (*d*, J = 3.4 Hz, 1H), 4.224~4.170 (*m*, 9H), 2.469 (*d*, J = 3.0 Hz, 1H). ^{13}C NMR(50 Hz, CDCl_3) δ 143.46, 128.45, 127.67, 126.44, 94.51, 72.23, 68.71, 68.40, 68.33, 67.66, 66.21. MS *m/e*: 292(M^+), 275 ($\text{M}^+ - \text{OH}$, 100). Anal. calcd for $\text{C}_{23}\text{H}_{20}\text{FeO}$: C, 69.90%; H, 5.52%. Found: C, 69.94%; H, 5.63%.

4b (78% yield): ^1H NMR (CDCl_3 , 200 MHz) δ 7.306~7.232 (*m*, 10H), 4.268 (*m*, 2H), 4.168 (*s*, 5H), 4.039 (*m*, 2H) 3.45 (*s*, 1H). ^{13}C NMR(50 Hz, CDCl_3) δ 147.17, 127.71, 127.24, 126.98, 99.62, 68.95, 68.80 68.63. MS *m/e*: 368(M^+), 351 (100). Anal. calcd for $\text{C}_{23}\text{H}_{20}\text{FeO}$: C, 75.02%; H, 5.47%. Found: C, 75.22%; H, 5.64%.

4c (33% yield): ^1H NMR(CDCl_3 , 200 MHz) δ 8.177~7.248 (*m*, 7H), 6.215 (*d*, J = 3.8 Hz, 1H), 4.326 (*d*, J = 1.2 Hz 1H), 4.264 (*br.s*, 5H), 4.210 (*t*, J = 1.2 Hz 1H), 4.166 (*d*, J = 1.2 Hz 1H), 4.129 (*t*, J = 2.4 Hz 1H), 2.729 (*d*, J = 3.8, 1H). ^{13}C NMR(50 Hz, CDCl_3) δ 139.19, 133.89, 131.13, 128.89, 128.35, 126.16, 125.73, 125.56, 124.15, 124.04, 94.50, 68.75, 68.45, 68.10, 67.91, 67.70. MS *m/e*: 342(M^+), 325 (100). Anal. calcd for $\text{C}_{21}\text{H}_{18}\text{FeO}$: C, 73.71%; H, 5.30. Found: C, 73.93%; H, 5.48 %.

4d (35% yield): ^1H NMR(CDCl_3 , 200 MHz) δ 7.372~7.191(*m*, 4 H), 5.802(*d*, J =5.2 Hz 1 H), 4.275~4.123(*m*, 9H), 3.841(*br.s*, 3H), 2.893(*d*, J =5.2 Hz 1H). ^{13}C NMR(50 Hz, CDCl_3) δ 156.68, 131.93, 128.68, 127.51, 120.86, 110.69, 93.26, 68.75, 68.00, 67.94, 67.73, 66.74, 55.55. MS *m/e*: 322(M^+), 305 (100). Anal. calcd for $\text{C}_{18}\text{H}_{18}\text{FeO}_2$: C, 67.11%; H, 5.63. Found: C, 67.16%; H, 5.76 %.

General procedure for the preparation of 5. Under N_2 to an acetic acid solution of **4** (1.0 mmol) at room temperature was added diphenylphosphine (4 mL, 10% weight in hexane). After stirring for 4-12 hours, the solvent was evaporated under vacuum. The residue was washed with methanol (3 times). **5** were obtained as yellow solids.

5a (83% yields): ^1H NMR(CDCl_3 , 200 MHz) δ 7.485~7.134(*m*, 15H), 4.282(*d*, J =6.2 Hz 1H), 4.117(*br.s*, 1H), 4.028(*br.s*, 1H), 3.821(*br.s*, 1H), 3.738(*br.s*, 5H), 3.424(*br.s*, 1H). ^{13}C NMR(CDCl_3 , 50 MHz) δ 142.49 (*d*, J = 11.0 Hz), 137.73(*d*, J = 16.4 Hz), 137.40(*d*, J = 16.7 Hz), 134.68(*d*, J = 20.1 Hz), 133.40(*d*, J = 18.2 Hz), 129.77(*d*, J = 9.44 Hz), 129.09, 128.52, 128.28, 128.15, 128.04(*d*, J = 2.6 Hz), 126.58, 90.47(*d*, J = 18.9 Hz), 69.92(*d*, J = 2.2 Hz), 68.87, 68.56, 68.14, 67.67(*d*, J = 5.3 Hz), 66.52, 47.23(*d*, J = 15.5 Hz). ^{31}P NMR(CDCl_3 , 81 MHz) δ 4.83. MS *m/e*: 461(M^+), 275(100). Anal. calcd for $\text{C}_{29}\text{H}_{25}\text{FeP}$: C, 75.67%; H, 5.47. Found: C, 75.84%; H, 5.57%.

5b (80% yield). ^1H NMR (CDCl_3 , 200 MHz) δ 7.462(*m*, 4H), 7.277-7.076(*m*, 12H), 6.896 (*m*, 4H), 4.174(*br.s*, 5H), 4.121 (*br.s*, 2H), 3.265 (*br.s*, 2H). ^{13}C NMR (CDCl_3 , 50 MHz) δ 145.73(*d*, J = 8.4 Hz), 136.82(*d*, J = 24.6 Hz), 135.72(*d*, J = 21.2 Hz), 131.46(*d*, J = 9.1 Hz), 129.01, 127.88(*d*, J = 7.2 Hz), 127.15, 126.54, 96.10(*d*, J = 6.5 Hz),, 71.27, 69.82, 69.79, 67.39. ^{31}P NMR(CDCl_3 , 81 MHz) δ 28.01. MS *m/e*: 536(M^+), 351(100). Anal. calcd for $\text{C}_{35}\text{H}_{29}\text{FeP}$: C, 78.37%; H, 5.45. Found: C, 77.51%; H, 5.49%.

5c (70% yield). ^1H NMR (CDCl_3 , 200 MHz) δ 8.438 (*d*, J =6.2Hz 2H), 8.051 (*d*, J =6.0Hz 2H), 7.859(*d*, J =7.8Hz, 2H), 7.734(*d*, J =8.0 Hz 2H), 7.620~6.960 (*m*, 9H), 5.189

(d, $J=7.2$ Hz 1H), 4.203 (s, 1H), 4.062(s, 1H), 3.820(s, 1H), 3.515(s, 1H), 3.417(br.s, 5H). ^{13}C NMR (CDCl_3 , 50 MHz) δ 139.21(d, $J = 10.6$ Hz), 138.54(d, $J = 17.0$ Hz), 137.66(d, $J = 17.4$ Hz), 134.71(d, $J = 19.7$ Hz), 134.18, 132.97(d, $J = 18.2$ Hz), 132.24, 129.32(d, $J = 18.6$ Hz), 128.61, 128.31, 128.04, 128.07, 127.99, 127.12, 126.74, 126.18, 125.63, 124.56, 123.46, 91.20(d, $J = 19.7$ Hz), 70.23, 69.15, 68.42, 68.16, 67.37(d, $J = 6.4$ Hz), 66.44, 39.46(d, $J = 13.3$ Hz). ^{31}P NMR(CDCl_3 , 81 MHz) δ 5.28. MS m/e : 510(M^+), 325(100). Anal. calcd for $\text{C}_{33}\text{H}_{27}\text{FeP}$: C, 77.66%; H, 5.33. Found: C, 77.71%; H, 5.43%.

5d (85% yield). ^1H NMR(CDCl_3 , 200 MHz) δ 7.730~6.777 (m, 14H), 5.048 (d, $J = 6.6$ Hz 1H), 4.144(br.s, 1H), 4.034(br.s, 1H), 3.858 (br.s, 4H), 3.761(br.s, 5H), 3.472(br.s, 1H). ^{13}C NMR (CDCl_3 , 50 MHz) δ 156.35, 138.34(d, $J = 16.7$ Hz), 137.60(d, $J = 16.7$ Hz), 134.72(d, $J = 19.8$ Hz), 133.36(d, $J = 18.6$ Hz), 130.94(d, $J = 10.6$ Hz), 130.37(d, $J = 15.9$ Hz), 129.02, 128.42, 128.11, 127.98, 127.86, 127.45, 120.63, 110.45, 89.98(d, $J = 20.8$ Hz), 70.38(d, $J = 2.6$ Hz), 68.60, 68.09, 67.72(d, $J = 4.6$ Hz), 66.66, 55.40, 36.50. ^{31}P NMR(CDCl_3 , 81 MHz) δ 4.61. MS m/e : 491($\text{M}^+ + 1$), 305(100). Anal. calcd for $\text{C}_{30}\text{H}_{27}\text{FeOP}$: C, 73.48%; H, 5.55. Found: C, 73.33%; H, 5.69%.

5e (75%). ^1H NMR(CDCl_3 , 200 MHz) δ 7.534(d, $J = 8.2$ Hz, 2H), 7.349 (t, $J=7.4$ Hz 2H), 7.218(t, $J = 7.2$ Hz, 1H), 4.260(m, 2H), 4.109(m, 1H), 4.038(m, 1H), 3.977(m, 1H), 3.615(m, 5H), 0.977(s, 9H), 0.931(s, 9H). ^{13}C NMR (CDCl_3 , 50 MHz) δ 147.34, 130.52, 128.08, 126.26, 94.98, 71.09, 69.69, 68.64, 68.16, 65.61, 43.23, 34.00, 31.56. ^{31}P NMR(CDCl_3 , 81 MHz) δ 60.88. MS m/e : 420(M^+), 275(100). Anal. calcd for $\text{C}_{25}\text{H}_{33}\text{FeP}$: C, 71.43%; H, 7.91. Found: C, 71.16%; H, 7.85%.

Preparation of 6. To an acetic acid solution of **4** (0.374 g, 1.1 mmol) at room temperature was added phenylphosphine (PhPH_2) (0.8 mL, 10% in hexanes) under N_2 . After 1~2 minute, yellow solid began to come out. The reaction mixture was allowed to stir for another 2 h. Evaporation of solvents gave a yellow residue. After washing with methanol (3 times) and drying under vacuum, **6** were obtained as yellow solids.

6 (83% yield). ^1H NMR (CDCl_3 , 200 MHz) δ 7.542~6.724 (m, 15H), 4.220(m, 0.5H), 4.020(m, 0.5H), 3.980(m, 0.5H), 3.857(m, 5H), 3.810(m, 1.5H), 3.771(s, 2.5H), 3.698(m, 1H), 3.679(s, 2.5H), 3.629 (s, 5H), 3.615(m, 1H). ^{13}C NMR (CDCl_3 , 50 MHz) δ 143.11(d, $J = 12.9$ Hz), 142.85 (d, $J = 12.5$ Hz), 142.44, 136.29(d, $J = 12.9$ Hz), 135.86(d, $J = 12.9$ Hz), 135.42(d, $J = 10.6$ Hz), 135.00(d, $J = 11.0$ Hz), 134.67, 134.21, 130.21(d, $J = 9.5$ Hz), 129.75, 129.58, 129.51, 129.42, 128.56, 128.21, 127.62, 127.50, 127.35, 127.20, 126.86(d, $J = 1.9$ Hz), 126.37(d, $J = 1.9$ Hz), 125.87, 91.51(d, $J = 21.2$ Hz), 90.65(d, $J = 16.0$ Hz), 90.38(d, $J = 11.4$ Hz), 69.84, 69.55, 69.33, 68.81, 68.53, 68.45, 67.95, 67.81, 67.73, 67.68, 66.72, 66.27, 66.21, 45.91(d, $J = 22.0$), 44.85(d, $J = 24.3$ Hz), 43.91(d, $J = 19.4$ Hz) (observed complexity due to C-P coupling). ^{31}P NMR(CDCl_3 , 81 MHz) δ 19.22, 17.40. m/e : 659($\text{M}^+ + 1$), 351(100). Anal. calcd for $\text{C}_{40}\text{H}_{35}\text{Fe}_2\text{P}$: C, 72.97%; H, 5.36. Found: C, 73.05%; H, 5.43%.

(*R,R*)-**6** (80% yield). $[\alpha]_{\text{D}} = -142.3$ ($c = 0.500$, THF). ^1H NMR (CDCl_3 , 200 MHz) δ 7.542~6.932 (m, 13H), 6.720~6.768(m, 2H), 4.203(m, 1H), 4.006(m, 1H), 3.968(m, 1H), 3.853(m, 4H), 3.813(m, 1H), 3.767(s, 5H), 3.674(m, 5H), 3.624 (m, 1H), 3.615(m, 1H). ^{13}C NMR (C_6D_6 , 50 MHz) δ 144.19, 143.38, 136.75, 136.32, 135.23, 130.84(d, $J = 9.4$

Hz), 130.04(d, $J = 4.2$ Hz), 129.83, 128.88, 128.38, 127.98, 127.90, 127.81, 127.66, 127.20, 126.35, 90.26, 70.45, 70.29, 70.22, 69.84, 69.38, 69.09, 68.45, 68.28, 67.2166.64, 45.60(d, $J = 25.0$), 44.72(d, $J = 20.1$ Hz) (observed complexity due to C-P coupling). ^{31}P NMR(CDCl_3 , 81 MHz) δ 17.41, 19.23 (53: 1).

General procedure for room temperature 5a or 5b/ $\text{Pd}(\text{OAc})_2$ -catalyzed Suzuki coupling reaction of aryl bromides:

In glove-box, to a vial containing $\text{Pd}(\text{OAc})_2$ (4.6 mg, 0.02 mmol) and ligand **5** (0.02 mmol), phenylboronic acid (1.5 mmol) and KF (3 mmol) was added 2 ml THF. After stirring for a few minutes, aryl bromide (1 mmol) was added. The mixture was stirred at room temperature in glove-box for 48 hours. After adding water to the reaction mixture, the mixture was extracted with Et_2O and washed with brine. Evaporation of solvent and flash chromatography on silica gel afforded the biaryl compounds.

2-Methybiiphenyl: ^1H NMR(CDCl_3 , 200 MHz) δ 7.466~7.279 (m, 9H), 2.327 (br.s, 3H). ^{13}C NMR(CDCl_3 , 50 MHz) δ 142.22, 135.61, 130.58, 130.07, 129.47, 129.03, 128.34, 127.52, 127.04, 126.04, 20.75.

4-Methoxybiphenyl: ^1H NMR(CDCl_3 , 200 MHz) δ 7.588~6.995 (m, 9H), 3.858 (s, 3H). ^{13}C NMR(CDCl_3 , 50 MHz) δ 141.058, 134.006, 128.955, 128.394, 126.929, 114.425, 55.569.

4-Acetylbiphenyl: ^1H NMR(CDCl_3 , 200 MHz) δ 8.066~7.395 (m, 9H), 2.639 (br.s, 3H). ^{13}C NMR(CDCl_3 , 50 MHz) δ 197.72, 146.00, 140.09, 136.08, 132.12, 130.077, 129.17, 128.47, 127.48, 26.90.

4-Formylbiphenyl: ^1H NMR(CDCl_3 , 200 MHz) δ 10.058 (br.s, 1H), 7.977~7.410 (m, 9H). ^{13}C NMR (CDCl_3 , 50 MHz) δ 192.186, 147.428, 139.944, 135.424, 132.679, 130.157, 129.528, 128.712, 127.931, 127.605.

4-Benzoylbiphenyl: ^1H NMR(CDCl_3 , 200 MHz) δ 7.918~7.446 (m, 14H). ^{13}C NMR(CDCl_3 , 50 MHz) δ 195.85, 137.403, 136.538, 132.913, 132.610, 131.844 (d, $J=2.3$ Hz), 130.964, 130.236, 130.176, 129.205, 128.545, 128.424, 127.749, 127.370.