

Advanced
**Synthesis &
Catalysis**

Supporting Information

© Copyright Wiley-VCH Verlag GmbH & Co. KGaA, 69451 Weinheim, 2008

Supporting information

**Efficient and Practical Cross-Coupling of Arenediazonium
Tetrafluoroborate Salts with Boronic Acids Catalyzed by
Palladium(0)/Barium Carbonate**

François-Xavier Felpin* and Eric Fouquet

*Université Bordeaux 1, UMR CNRS 5255, Institut des Sciences Moléculaires, 351 Cours de la
Libération, 33405 Talence Cedex, France*

** Corresponding author, Email address: fx.felpin@ism.u-bordeaux1.fr*

General Remarks

Chemical shifts from proton and carbon NMR spectra are reported in ppm relative to the CDCl₃ peak at 7.26 ppm (¹H) or 77.0 ppm (¹³C), DMSO at 2.50 ppm (¹H) or 39.5 ppm (¹³C). Infrared (IR) spectra were recorded as neat samples on NaCl plates or with KBr pellets. Yields refer to isolated material determined to be pure by NMR spectroscopy and thin layer chromatography (TLC), unless specified otherwise in the text. Diazonium salts used in this study were all known and prepared as described. 10% Pd(0)/C, 20% Pd(OH)₂/C and 5% Pd(0)/BaSO₄ was purchased from Aldrich®. 5% Pd(0)/Al₂O₃, 5% Pd(0)/CaCO₃ and 5% Pd(0)/BaCO₃ was purchased from Alfa Aesar®.

General procedure for the preparation of biphenyl

To a solution of diazonium salt (1.2 mmol) in MeOH (4.8 mL) were added ArB(OH)₂ (1 mmol) and 5% Pd(0)/BaCO₃ (0.1-2 mol%, see Table 2). The resulting mixture was stirred for 12 hours at 25 °C and then concentrated under reduced pressure. The crude was purified by flash chromatography to give the corresponding cross-coupled product.

4-Methoxy-2'-nitrobiphenyl (3). Purification by flash chromatography (5% EtOAc-petroleum ether) gave a yellow solid. mp 62 °C [Lit.^[1] 62-64 °C]. IR (KBr) $\tilde{\nu}$ 1611, 2844, 2920, 3010 cm⁻¹. ¹H NMR (CDCl₃, 250 MHz) δ 3.85 (s, 3H), 6.96 (dt, 2H, J = 3.1, 8.8 Hz), 7.26 (dt, 2H, J = 2.8, 8.9 Hz), 7.41-7.48 (m, 2H), 7.56-7.62 (m, 1H), 7.80 (dd, 1H, J = 1.8, 8.6 Hz). ¹³C NMR (CDCl₃, 75 MHz) δ 55.3, 114.2, 124.0, 127.7, 129.1, 129.4, 131.9, 132.1, 135.8, 149.4, 159.7. MS (EI) m/z 229 (M).

4-Methoxy-4'-nitrobiphenyl (4). Purification by flash chromatography (5% EtOAc-petroleum ether) gave a yellow solid. mp 106 °C [Lit.^[2] 107-108 °C]. IR (KBr) $\tilde{\nu}$ 2930, 2968, 3052 cm⁻¹. ¹H NMR (CDCl₃, 250 MHz) δ 3.88 (s, 3H), 7.02 (dt, 2H, J = 3.1, 8.9 Hz), 7.58 (dt, 2H, J = 3.1, 8.9 Hz), 7.69 (dt, 2H, J = 2.4, 9.2 Hz), 8.27 (dt, 2H, J = 2.4, 9.2 Hz). ¹³C NMR (CDCl₃, 75 MHz) δ 55.4, 114.6, 124.1, 127.0, 128.5, 131.0, 146.5, 147.2, 160.4. MS (EI) m/z 229 (M).

4-Chloro-2'-methoxy-3'-nitrobiphenyl (5). Purification by flash chromatography (10% EtOAc-petroleum ether) gave a white solid. mp 127 °C [Lit.^[3] 120-122 °C]. IR (KBr) $\tilde{\nu}$ 1584, 1615, 2844, 2922, 2980, 3090 cm⁻¹. ¹H NMR (CDCl₃, 300 MHz) δ 3.94 (s, 3H), 7.04 (d, 1H, J = 7.5 Hz), 7.40-7.48 (m, 4H), 8.19 (d, 1H, J = 2.2 Hz), 8.25 (dd, 1H, J = 2.2, 7.5 Hz). ¹³C NMR (CDCl₃, 75 MHz) δ 56.3, 110.8, 125.1, 126.1, 128.5, 130.1, 130.7, 134.1, 134.5, 141.5, 161.3. MS (EI) m/z 265 (M, ³⁵Cl), 265 (M, ³⁷Cl), 264 (M+H⁺, ³⁵Cl), 266 (M+H⁺, ³⁷Cl).

2-Methoxy-4-Nitrobiphenyl (6). Purification by flash chromatography (10% EtOAc-petroleum ether) followed by recrystallization (Et₂O-petroleum ether) gave a pale yellow solid. mp 90 °C [Lit.^[4] 90-91 °C]. IR (KBr) $\tilde{\nu}$ 1625, 2949, 3014, 3064, cm⁻¹. ¹H NMR (CDCl₃, 250 MHz) δ 4.00 (s, 3H), 7.17 (d, 1H, J = 8.9 Hz), 7.35-7.49 (m, 3H), 7.53-7.57 (m, 2H), 7.77 (dd, 1H, J = 2.5, 8.9 Hz), 8.09 (d, 1H, J = 2.4 Hz). ¹³C NMR (CDCl₃, 50 MHz) δ 56.6, 113.9, 124.0, 126.7, 127.8, 129.0, 132.5, 133.8, 138.3, 152.2. MS (EI) m/z 229 (M).

^[1] S. E. Denmark, M. H. Ober, *Org. Lett.* **2003**, 5, 1357-1360.

^[2] S. M. Rubenstein, V. Baichwal, H. Beckmann, D. L. Clark, W. Frankmoelle, D. Roche, E. Santha, S. Schwender, M. Thoolen, Q. Ye, J. C. Jaen, *J. Med. Chem.* **2001**, 44, 3599-3605.

^[3] J. Hung, L. M. Werbel, *Eur. J. Med. Chem.* **1983**, 18, 61-66.

^[4] Y. Ahmad, M. I. Qureshi, M. I. Baig, *Can. J. Chem.* **1967**, 45, 1539-1542.

3,4-Dimethoxy-3'-trifluoromethylbiphenyl (7). Purification by flash chromatography (10% EtOAc- petroleum ether) gave a pale yellow oil. IR (KBr) $\tilde{\nu}$ 2838, 2939, 3002 cm^{-1} . ^1H NMR (CDCl_3 , 250 MHz) δ 3.94 (s, 3H), 3.97 (s, 3H), 6.97 (d, 1H, J = 6.9 Hz), 7.09 (d, 1H, J = 1.9 Hz), 7.16 (dd, 1H, J = 1.6, 6.9 Hz), 7.50-7.58 (m, 2H), 7.73 (d, 1H, J = 6.0 Hz), 7.79 (s, 1H). MS (EI) m/z 282 (M). HRMS (electrospray) calcd for $\text{C}_{15}\text{H}_{13}\text{O}_2\text{F}_3\text{Na}$ ($\text{M}+\text{Na}^+$) 305.0765, found 305.0768.

2,3-Dimethoxybiphenyl (8). Purification by flash chromatography (10% EtOAc- petroleum ether) gave a colorless oil. IR (KBr) $\tilde{\nu}$ 2835, 2933, 2998, 3061 cm^{-1} . ^1H NMR (CDCl_3 , 300 MHz) δ 3.60 (s, 3H), 3.92 (s, 3H), 6.95 (dt, 2H, J = 1.5, 9.2 Hz), 7.12 (t, 1H, J = 7.9 Hz), 7.32-7.38 (m, 1H), 7.43 (tm, 2H, J = 7.2 Hz), 7.55-7.59 (m, 2H). ^{13}C NMR (CDCl_3 , 75 MHz) δ 55.9, 60.5, 111.5, 122.7, 124.0, 127.0, 128.0, 129.2, 136.0, 138.2, 146.6, 153.1. MS (EI) m/z 214 (M), 199 (M- CH_3).

2,3-Dimethoxy-2'-nitrobiphenyl (9). Purification by flash chromatography (20% EtOAc- petroleum ether) gave a yellow solid. mp 103 $^\circ\text{C}$. IR (KBr) $\tilde{\nu}$ 1539, 2840, 2933, 2966, 3065 cm^{-1} . ^1H NMR (CDCl_3 , 250 MHz) δ 3.58 (s, 3H), 3.88 (s, 3H), 6.87 (dd, 1H, J = 1.5, 7.6 Hz), 6.98 (dd, 1H, J = 1.2, 7.9 Hz), 7.14 (t, 1H, J = 8.2 Hz), 7.41-7.52 (m, 2H), 7.61 (dt, 2H, J = 1.2, 7.6 Hz), 7.96 (dd, 1H, J = 1.0, 8.0 Hz). ^{13}C NMR (CDCl_3 , 75 MHz) δ 55.8, 60.3, 112.8, 121.2, 123.9, 124.2, 128.1, 132.0, 132.4, 132.9, 145.7, 149.3, 152.4. HRMS (electrospray) calcd for $\text{C}_{14}\text{H}_{13}\text{NO}_4\text{Na}$ ($\text{M}+\text{Na}^+$) 282.0742, found 282.0741.

3,4-methylenedioxy-4'-methoxybiphenyl (10). Purification by flash chromatography (5% EtOAc- petroleum ether) gave a white solid. mp 93 $^\circ\text{C}$ [Lit.^[5] 95-96 $^\circ\text{C}$]. IR (KBr) $\tilde{\nu}$ 1608, 2838, 2908, 2955 cm^{-1} . ^1H NMR (CDCl_3 , 300 MHz) δ 3.85 (s, 3H), 5.99 (s, 2H), 6.85-6.88 (m, 1H), 6.87-7.04 (m, 4H), 7.42-7.48 (m, 2H). ^{13}C NMR (CDCl_3 , 75 MHz) δ 55.3, 101.0, 107.3, 108.5, 114.1, 120.0, 127.8, 133.5, 135.3, 146.5, 148.0, 158.8. MS (EI) m/z 228 (M), 213 (M- CH_3).

^[5] S. Schneider, W. Bannwarth, *Helv. Chim. Acta.* **2001**, *84*, 735-742.

2-Bromo-2'-methylbiphenyl (11). Purification by flash chromatography (100% petroleum ether) gave a colorless oil. IR (KBr) $\tilde{\nu}$ 1465, 2922, 3018, 3057 cm^{-1} . ^1H NMR (CDCl_3 , 250 MHz) δ 2.12 (s, 3H), 7.11-7.15 (m, 1H), 7.19-7.40 (m, 6H), 7.64-7.69 (m, 1H). ^{13}C NMR (CDCl_3 , 62.5 MHz) δ 19.8, 123.7, 125.5, 127.2, 127.9, 128.7, 129.2, 129.8, 130.8, 132.5, 135.9, 141.1, 142.6. MS (EI) m/z 248 (M, ^{81}Br), 246 (M, ^{79}Br).

4-Bromobiphenyl (12). Purification by flash chromatography (100% petroleum ether) gave a white solid. mp 89 °C [Lit.^[6] 89 °C]. IR (KBr) $\tilde{\nu}$ 3055 cm^{-1} . ^1H NMR (CDCl_3 , 250 MHz) δ 7.34-7.49 (m, 5H), 7.54-7.59 (m, 4H). ^{13}C NMR (CDCl_3 , 62.5 MHz) δ 121.5, 126.9, 127.6, 128.7, 128.9, 131.8, 140.0, 140.1. MS (EI) m/z 234 (M+H, ^{81}Br), 232 (M+H, ^{79}Br).

4-Bromo-3'-nitrobiphenyl (13). Purification by flash chromatography (5% EtOAc-petroleum ether) gave a white solid. mp 93 °C [Lit.^[7] 94 °C]. IR (KBr) $\tilde{\nu}$ 3091 cm^{-1} . ^1H NMR (CDCl_3 , 250 MHz) δ 7.49 (dm, 2H, $J = 8.6$ Hz), 7.59-7.65 (m, 3H), 7.88 (d, 1H, $J = 7.6$ Hz), 8.22 (dm, 1H, $J = 8.3$ Hz), 8.41 (t, 1H, $J = 1.8$ Hz). ^{13}C NMR (CDCl_3 , 62.5 MHz) δ 122.1, 122.8, 123.4, 129.1, 130.3, 132.7, 133.2, 137.9, 142.0. MS (EI) m/z 279 (M, ^{81}Br), 277 (M, ^{79}Br).

4-Iodobiphenyl (14). Purification by flash chromatography (100% petroleum ether) gave a white solid. mp 112 °C [Lit.^[7] 109 °C]. IR (KBr) $\tilde{\nu}$ 1474, 3050 cm^{-1} . ^1H NMR (CDCl_3 , 300 MHz) δ 7.32-7.40 (m, 3H), 7.45 (tm, 2H, $J = 7.1$ Hz), 7.56 (dm, 2H, $J = 7.9$ Hz), 7.77 (tm, 2H, $J = 8.3$ Hz). ^{13}C NMR (CDCl_3 , 50 MHz) δ 93.0, 126.9, 127.7, 128.9, 129.0, 137.8, 140.0, 140.7. MS (EI) m/z 280 (M), 152 (M-HI).

3,4-Dimethoxy-*p*-terphenyl (18). To a solution of 4-iodobenzenediazonium tetrafluoroborate salt **16** (1.2 mmol) in MeOH (4.8 mL) were added PhB(OH)₂ **15** (122 mg, 1 mmol) and Pd/BaCO₃ (106 mg, 5 mol%). The reaction was stirred for 8 h at 25 °C. Then 2M aqueous Na₂CO₃ solution (1.5 mL) and 3,4-dimethoxyboronic acid (1.5 mmol) was added dropwise. The resulting mixture was stirred for 12 h at 70 °C. The catalyst was filtered, washed with

^[6] M. J. S. Dewar, L. S. Hart, *Tetrahedron* **1970**, *26*, 1001-1008.

^[7] S. Darses, T. Jeffery, J.-L. Brayer, J.-P. Demoute, J.-P. Genêt, *Bull. Soc. Chim. Fr.* **1996**, *133*, 1095-1102.

CH₂Cl₂ (2 x 5 mL) and water (5 mL). The aqueous layer was extracted with CH₂Cl₂ (3x), the collected organic extracts were dried (MgSO₄) and concentrated under reduced pressure. Purification by flash chromatography (50% CH₂Cl₂- petroleum ether) gave **18** (239 mg, 92%) a white solid. mp 158 °C [Lit.^[8] 157 °C]. IR (KBr) ν 2934, 3002, 3081 cm⁻¹. ¹H NMR (CDCl₃, 250 MHz) δ 3.94 (s, 3H), 3.98 (s, 3H), 6.97 (d, 1H, J = 8.2 Hz), 7.17 (d, 1H, J = 2.1 Hz), 7.21 (dd, 1H, J = 2.1, 8.2 Hz), 7.35-7.40 (m, 1H), 7.47 (tm, 2H, J = 7.0 Hz), 7.62-7.70 (m, 6H). ¹³C NMR (CDCl₃, 75 MHz) δ 56.0, 56.0, 110.4, 111.6, 119.4, 127.0, 127.2, 127.3, 127.4, 128.8, 133.7, 139.7, 140.0, 140.7, 148.8, 149.3. MS (EI) m/z 291 (M+H), 290 (M), 275 (M-CH₃). HRMS (electrospray) calcd for C₂₀H₁₉O₂ (M+H) 291.1204, found 291.1206.

4-Methoxy-3-nitroaniline. This compound was prepared according a reported procedure.^[9] To a solution of 3-nitro-4-fluoroaniline (1.67 g, 10.7 mmol) in distilled MeOH (11 mL) at room temperature was added MeONa (2.31 g, 42.8 mmol) and the resulting mixture was stirred for 20 hours at 70 °C. After cooling to 0 °C, the reaction was quenched successively with concentrated HCl (1.34 mL) and water (25 mL). The aqueous phase was extracted with Et₂O (3x). The collected organic extracts were (MgSO₄) and concentrated under reduced pressure to give the title compound (1.65 g, 92%) as a dark orange solid which was used without further purification. ¹H NMR (DMSO, 300 MHz) δ 3.77 (s, 3H), 5.26 (br s, 2H), 6.86 (dd, 1H, J = 2.6, 8.7 Hz), 7.03 (d, 1H, J = 2.6 Hz), 7.07 (d, 1H, J = 8.7 Hz).

3-Nitro-4-methoxybenzenediazonium tetrafluoroborate (20). To a solution of aniline (1.59 g, 10.39 mmol) in H₂O (2.8 mL) and HBF₄ (50% solution in Et₂O, 2.8 mL) at 0 °C was added dropwise a solution of sodium nitrite (717 mg, 10.39 mmol) in H₂O (2.8 mL). The resulting heterogeneous mixture was stirred for 30 minutes at 0 °C, filtered, washed with cold EtOH (5 mL) and Et₂O (3 x 10 mL). The solid was dissolved in acetone and precipitated in Et₂O. The white solid was collected and stored at -20 °C. ¹H NMR (DMSO, 300 MHz) δ 4.22 (s, 3H), 7.91 (d, 1H, J = 9.8 Hz), 8.87 (dd, 1H, J = 2.6, 9.4 Hz), 9.40 (d, 1H, J = 2.6 Hz). ¹³C NMR (DMSO, 75 MHz) δ 59.3, 104.8, 117.8, 131.7, 138.3, 139.0, 161.4.

^[8] G. R. Ames, W. Davey, *J. Chem. Soc.* **1958**, 1794-1799.

^[9] S. M. Rubenstein, V. Baichwal, H. Beckmann, D. L. Clark, W. Frankmoelle, D. Roche, E. Santha, S. Schwender, M. Thoolen, Q. Ye, J. C. Jaen, *J. Med. Chem.* **2001**, *44*, 3599-3605.

2-Methoxy-5-phenylaniline (21). A solution of **6** (300 mg, 1.31 mmol) in MeOH (8 mL) was added 5% Pd/BaCO₃ (55.5 mg, 2 mol%). The resulting mixture was stirred at room temperature for 12 hours under H₂ atmosphere. After filtration over a pad of celite, the title compound **21** was obtained as a white powder (240 mg, 92%). For analytical purposes, it could be purified by flash chromatography (15% EtOAc-petroleum ether).

One-Pot process: To a solution of diazonium tetrafluoroborate salt **20** (320 mg, 1.2 mmol) in MeOH (4.8 mL) were added PhB(OH)₂ **15** (122 mg, 1 mmol) and 5% Pd/BaCO₃ (21.2 mg, 2 mol%). The resulting mixture was stirred for 8 hours at 25 °C under air and then 12 hours under hydrogen atmosphere. The crude was concentrated under reduced pressure and purified by flash chromatography (15% EtOAc-petroleum ether) to give the title product **21** (169 mg, 85%). mp 81 °C [Lit.^[10] 80-81 °C]. IR (KBr) $\tilde{\nu}$ 1525, 1609, 2840, 2942, 3000, 3033, 3361, 3454 cm⁻¹. ¹H NMR (CDCl₃, 200 MHz) δ 3.87 (s, 2H), 3.92 (s, 3H), 6.87-6.91 (m, 1H), 7.00-7.05 (m, 2H), 7.30-7.49 (m, 3H), 7.56-7.62 (m, 2H). ¹³C NMR (CDCl₃, 50 MHz) δ 55.5, 110.5, 113.7, 117.1, 126.5, 126.7, 128.5, 134.2, 136.2, 141.2, 146.9. MS (EI) m/z 199 (M).

Bifenazate (22). The transformation of **21** into **22** was realized according reported procedures.^[11] mp 122 °C. IR (KBr) $\tilde{\nu}$ 1699, 2936, 2977, 3033, 3079, 3314, 3350 cm⁻¹. ¹H NMR (CDCl₃, 250 MHz) δ 1.26 (m, 6H), 3.90 (s, 3H), 4.97 (hept, 1H, J = 6.4 Hz), 6.31 (br s, 1H), 6.44 (br s, 1H), 6.88 (d, 1H, J = 8.2 Hz), 7.06-7.10 (m, 2H), 7.27-7.37 (m, 1H), 7.40 (dd, 2H, J = 7.0, 8.2 Hz), 7.53 (d, 2H, J = 8.3 Hz). ¹³C NMR (CDCl₃, 50 MHz) δ 22.0, 55.7, 69.6, 110.4, 111.0, 119.1, 126.6, 126.9, 128.6, 134.3, 137.6, 141.3, 146.5, 156.6. MS (EI) m/z 300 (M), 258 (M-iPr), 214 (M-COOiPr).

^[10] D. S. Tarbell, H. P. Hirschler, T. J. Hall, *J. Am. Chem. Soc.* **1953**, *75*, 1985-1987.

^[11] (a) M. A. Dekeyser, P. T. McDonald, Insecticidal phenylhydrazine derivatives. US Patent 5,367,093, November 22, 1994. (b) S. B. Park, G.-L. Chee, M. A. Dekeyser, 4-Methoxybiphenyl hydrazone derivatives. US Patent 6,706,895, March 16, 2004.