Supporting Information for

**The Use of Polymer Supported Pd Reagents for Rapid and Efficient
Suzuki Reactions Using Microwave Heating**

Ying Wang and Daryl R. Sauer

*High-Throughput Organic Synthesis Group, Global Pharmaceutical Research and Development,
Abbott Laboratories, 100 Abbott Park Road, Abbott Park, Illinois 60064-6113.*

Experimental Section.

General Methods.

All reagents were obtained from commercial suppliers and were used without further purification. All microwave reactions were performed in septa capped SmithTM process vials (2-5 mL) using an EmrysTM Optimizer with stirring. Reaction times under microwave conditions reflect total irradiation times rather than actual reaction times at a given temperature. Power required to maintain target temperature was controlled by EmrysTM Optimizer Software. When required, compounds were purified by MPLC on an Analogix IntelliFlash 280 using Analogix RS-4 silica cartridges with a gradient mobile phase (hexane:ethyl acetate, 0-10% ethyl acetate). Reactions were monitored by TLC and LC/MS. Unless otherwise noted, all ¹H and ¹³C spectra were recorded in DMSO-d₆. ¹H-NMR was recorded on a Varian Unity-500 (500 MHz), Varian Unity-400 (400 MHz) or Varian Unity-300 (300 MHz). Chemical shifts are reported in parts per million (ppm) downfield from TMS which was added as an internal standard. Data are reported as follows: Chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), integration and coupling constant. ¹³C-NMR was recorded on a Varian Unity-500 (125 MHz), Varian Unity-400 (100 MHz) or Varian Unity-300 (75 MHz) spectrometer, using broadband proton decoupling. Chemical shifts are reported in parts per million (ppm) downfield from TMS which was added as an internal standard. Analytical LC/MS was performed on a Waters Alliance HPLC ZMD mass spectrometer system running MassLynx 3.4 and Openlynx 3.4 software. The ZMD mass spectrometer was operated under positive APCI ionization conditions. The HPLC system was composed of a Waters 2795 autosampler, a Waters 996 diode-array detector, and a Sedere Sedex-75 evaporative light-scattering detector (ELSD). The column used was a Phenomenex Luna Combi-HTS C8(2), 5 μm, 2.1 x 30 mm. A gradient of 10-100% acetonitrile (A)/0.1% trifluoroacetic acid in water (B) was used at a flow rate of 1.5 mL/min (0-0.1 min 10% A, 0.1-3.1 min 10-100% A, 3.1-3.9 min 100-10% A, 3.9-4.0 min 100-10% A). Reaction conversion percents and purity for all compounds was established by monitoring four methods of detection (UV 220 and 254 nm, ELSD, and ion chromatograph).

Typical experimental procedure for the Suzuki coupling protocol.

A Smith Process vial (2-5 ml) was charged with a stir bar, 0.2 mmol of the aryl halide or aryl triflate, 0.24 mmol of the boronic acid and 2-3 ml EtOH¹ (in the case of aryl chloride, 0.3 mmol boronic acid was used). Base, (0.24 ml of 1M aq. K₂CO₃) was added to above solution followed by 3 mol % of the polymer supported reagent. The reaction vessel was sealed and heated to the desired temperature for the indicated amount of time. After cooling, the reaction mixture was transferred to a pre-packed column of Si-Carbonate (2g, 0.79 mmol/g), which had been conditioned with MeOH/CH₂Cl₂ (1:1). The elutant was collect via gravity filtration. The column was then washed with MeOH/CH₂Cl₂ (1:1) (3 X 3 ml). The combined elutants were concentrated and purified by flash chromatography. In some cases (Table 4, entries 2-5, and 8) no further purification was required after the Si-carbonate filtration process. All products were greater than 98% pure as determined by LC/MS analysis.

4'-Methyl-biphenyl-4-carbonitrile (Table 1, entry 1).² ¹H NMR (400 MHz) δ 2.36 (s, 3H), 7.32 (d, 2H, 7.9 Hz), 7.64 (d, 2H, 7.9 Hz), 7.85 (d, 2H, 8.7 Hz), 7.89 (d, 2H, 8.7 Hz); ¹³C NMR (100 MHz) δ 20.7, 109.6, 118.8, 126.8, 127.2, 129.7, 132.7, 135.3, 138.3, 144.5; MS (DCI/NH₃) m/z 211.1 (M + NH₃).

1-(5-p-Tolyl-2,3-dihydro-indol-1-yl)-ethanone (Scheme 1). ¹H NMR (400 MHz) δ 2.17 (s, 3H), 2.33 (s, 3H), 3.19 (t, 2H, J = 8.5 Hz), 4.12 (t, 2H, J = 8.5 Hz), 7.23 (d, 2H, J = 7.6

¹ DME may be used to increase solubility of substrates if needed.

² Hassan, J.; Hathroubi, C.; Gozzi, C.; Lemaire, M. *Tetrahedron*. **2001**, 57, 7845-7856

Hz), 7.42 (d, 1H, J = 8.1 Hz), 7.51 (d, 2H, J = 7.6 Hz), 7.51 (s, 1H), 8.07 (d, 1H, J = 8.1 Hz); ^{13}C NMR (100 MHz) δ 20.6, 23.9, 27.4, 48.3, 115.9, 122.7, 125.1, 126.0, 129.4, 131.5, 132.5, 135.0, 136.0, 137.1, 142.1; MS (DCI/ NH_3) m/z 252.1 (M + H).

1-[5-(4-Fluoro-phenyl)-2,3-dihydro-indol-1-yl]-ethanone (Table 4, entry 1). ^1H NMR (400 MHz) δ 2.16 (s, 3H), 3.17 (t, 2H, J = 8.5 Hz), 4.11 (t, 2H, J = 8.5 Hz), 7.23 (t, 2H, J = 8.7 Hz), 7.41 (d, 1H, J = 8.4 Hz), 7.49 (s, 1H), 7.63 (dd, 2H, J = 8.7, 5.3 Hz), 8.07 (d, 1H, J = 8.4 Hz); ^{13}C NMR (100 MHz) δ 23.9, 27.3, 48.3, 115.5 (d, J = 21.2 Hz), 115.9, 122.9, 125.4, 128.1, 132.8 (d, J = 34.9 Hz), 136.5, 142.4, 160.3, 162.7, 168.5; MS (DCI/ NH_3) m/z 256.1 (M + NH_3).

3'-Methoxy-biphenyl-4-carbonitrile (Table 4, entry 2).³ ^1H NMR (400 MHz) δ 3.32(s, 3H), 7.00 (dd, 1H, J = 8.4, 1.8 Hz), 7.25 (t, 1H, J = 2.0 Hz), 7.28 (d, 1H, J = 7.8 Hz), 7.41 (t, 1H, J = 8.1 Hz), 7.86-7.90 (m, 3H); ^{13}C NMR (100 MHz) δ 55.2, 110.0, 112.4, 114.4, 119.3, 127.7, 130.2, 132.7, 139.7, 144.5, 159.8; MS (DCI/ NH_3) m/z 227.1 (M + NH_3).

4'-Fluoro-biphenyl-4-carbonitrile (Table 4, entry 3).⁴ ^1H NMR (400 MHz) δ 7.33 (t, 2H, J = 8.7 Hz), 7.80 (dd, 2H, J = 5.3 Hz, 8.7 Hz), 7.86 (d, 2H, J = 8.4 Hz), 7.90 (d, 2H, J = 8.4 Hz); ^{13}C NMR (100 MHz) δ 110.0, 115.9 (d, J = 21.9 Hz), 118.7, 127.5, 129.2 (d, J = 9.1 Hz), 132.8, 134.7, 143.5, 163.8; MS (DCI/ NH_3) m/z 215.0 (M + NH_3).

³ Molander, G. A.; Biolatto, B. *J. Org. Chem.* **2003**, 68, 4302-4314

⁴ Dewar, M. J. S.; Marchand, A. P. *J. Amer. Chem. Soc.* **1966**, 88, 3318-3327

2-p-Tolyl-quinoline (Table 4, entry 4).⁵ ¹H NMR (400 MHz) δ 2.48 (s, 3H), 7.37 (d, 2H, J = 8.1 Hz), 7.58 (m, 1H), 7.77 (m, 1H), 7.99 (dd, 1H, J = 8.1, 1.8 Hz), 8.05 (m, 1H), 8.13 (d, 1H, J = 8.5 Hz), 8.19 (m, 2H), 8.44 (d, 1H, J = 9.5 Hz); ¹³C NMR (100 MHz) δ 20.8, 118.5, 126.2, 127.0, 127.7, 129.4, 129.8, 135.8, 137.0, 139.2, 147.5, 156.0; MS (DCI/NH₃) m/z 220.0 (M + H).

3-Quinolin-2-yl-benzonitrile (Table 4, entry 5). ¹H NMR (400 MHz) δ 7.65 (m, 1H), 7.81 (m, 2H), 7.98 (dt, 1H, J = 7.5, 1.4 Hz), 8.05 (dd, 1H, J = 8.1, 1.0 Hz), 8.13 (d, 1H, J = 9.2 Hz), 8.28 (d, 1H, J = 7.6 Hz), 8.54 (d, 1H, J = 7.5 Hz), 8.64 (dt, 1H, J = 7.5, 1.4 Hz), 8.72 (t, 1H, J = 1.7 Hz); ¹³C NMR (100 MHz) δ 112.0, 118.6, 162.9, 127.2, 127.8, 192.1, 130.1, 130.1, 130.6, 131.7, 132.9, 137.6, 137.6, 139.6, 147.4, 153.8; MS (DCI/NH₃) m/z 231.0 (M + H).

3-Methoxy-4'-methyl-biphenyl (Table 4, entry 6).⁶ ¹H NMR (400 MHz) δ 2.34 (s, 3H), 3.81 (s, 3H), 6.90 (dd, 1H, J = 7.9, 1.9 Hz), 7.15 (d, 1H, J = 1.9 Hz), 7.20 (d, 1H, J = 7.6 Hz), 7.25 (d, 2H, J = 8.0 Hz), 7.35 (dd, 1H, J = 7.9, 7.6 Hz), 7.55 (d, 2H, J = 8.0 Hz); ¹³C NMR (100 MHz) δ 20.6, 55.0, 111.9, 112.6, 118.7, 126.5, 129.4, 129.8, 136.8, 137.1, 141.6, 159.7; MS (DCI/NH₃) m/z 199.0 (M + H).

4'-Fluoro-4-methyl-biphenyl (Table 4, entry 7).⁷ ¹H NMR (400 MHz) δ 2.34 (s, 3H), 7.26 (m, 4H), 7.53 (d, 2H, J = 8 Hz), 7.66 (dd, 2H, J = 6.8, 3.4 Hz); ¹³C NMR (100 MHz)

⁵ Inada, K.; Miyaura, N.; *Tetrahedron*. **2000**, 56, 8657-8660

⁶ Parrish, C. A.; Buchwald, S. L. *J. Org. Chem.* **2001**, 66, 3820-3827

⁷ Roy, A. H.; Hartwig, J. F. *J. Amer. Chem. Soc.* **2003**, 125, 8704-8705

δ 20.6, 115.5 (d, $J = 21.2$ Hz), 126.4, 128.2, 129.5, 136.2, 136.6, 160.4, 162.8; MS (DCI/ NH_3) m/z 186.0 (M^+).

3-p-Tolyl-pyridine (Table 4, entry 8).⁸ ^1H NMR (400 MHz) δ 2.35 (s, 3H), 7.31 (d, 2H, $J = 8.0$ Hz), 7.47 (m, 1H), 7.62 (d, 2H, $J = 8.0$ Hz), 8.04 (m, 1H), 8.55 (m, 1H), 8.87 (d, 1H, $J = 1.9$ Hz); ^{13}C NMR (100 MHz) δ 20.6, 123.7, 126.6, 129.6, 133.7, 134.1, 135.4, 137.5, 147.4, 148.1; MS (DCI/ NH_3) m/z 170.0 ($\text{M} + \text{H}$).

4-Methyl-4'-nitro-biphenyl (Table 4, entry 9).⁹ ^1H NMR (400 MHz) δ 2.37 (s, 3H), 7.35 (d, 2H, $J = 8.0$ Hz), 7.69 (d, 2H, $J = 8.0$ Hz), 7.94 (d, 2H, $J = 8.9$ Hz), 8.28 (d, 2H, $J = 8.9$ Hz); ^{13}C NMR (100 MHz) δ 20.7, 124.0, 127.0, 127.4, 129.8, 134.8, 138.7, 146.4, 146.5; MS (DCI/ NH_3) m/z 212.0 ($\text{M} - \text{H}$).

1-(3'-Methoxy-biphenyl-4-yl)-ethanone (Table 4, entry 10).¹⁰ ^1H NMR (400 MHz) δ 2.66 (s, 3H), 3.85 (s, 3H), 7.00 (dd, 1H, $J = 8.8, 2.5$ Hz), 7.26 (d, 1H, $J = 2.5$ Hz), 7.29 (d, 1H, $J = 8.8$ Hz), 7.42 (t, 1H, $J = 7.8$ Hz), 7.61 (t, 1H, $J = 7.8$ Hz), 7.94 (m, 2H), 8.18 (s, 1H); ^{13}C NMR (100 MHz) δ 26.8, 55.1, 112.4, 113.4, 119.2, 126.4, 127.1, 129.2, 130.0, 131.4, 137.4, 140.8, 159.8, 197.9; MS (DCI/ NH_3) m/z 244.1 ($\text{M} + \text{NH}_3$).

⁸ Inada, K.; Miyaura, N.; *Tetrahedron*. **2000**, 56, 8657-8660

⁹ Shudo, K.; Ohta, T.; Okamoto, T. *J. Amer. Chem. Soc.* **1981**, 103, 645-653

¹⁰ Hatanaka, Y.; Goda, K.; Okahara, Y.; Hiyama, T. *Tetrahedron*. **1994**, 50, 8301-8316

3'-Ethoxy-3-methoxy-biphenyl (Table 4, entry 11). ^1H NMR (400 MHz) δ 1.35 (t, 3H, $J = 6.9$ Hz), 3.82 (s, 3H), 4.10 (q, 2H, $J = 6.9$ Hz), 6.93 (m, 2H), 7.16 (m, 2H), 7.21 (m, 2H), 7.35 (m, 2H); ^{13}C NMR (100 MHz) δ 14.6, 55.1, 63.0, 112.2, 112.7, 112.8, 113.1, 113.5, 119.0, 119.0, 129.8, 141.6, 141.6, 158.9, 159.6; MS (DCI/ NH_3) m/z 228.9 ($\text{M} + \text{H}$).

Spectral Data For All Compounds Follows