Suzuki coupling of aryl chlorides with phenylboronic acid in water using microwave heating with simultaneous cooling

Riina K. Arvela and Nicholas. E. Leadbeater

Department of Chemistry, University of Connecticut, Unit 3060, 55 North Eagleville Road, Storrs, CT 06269-3060, USA

nicholas.leadbeater@uconn.edu

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General experimental

Unless noted otherwise, all materials were obtained from commercial suppliers and used without further purification. 10% Palladium on carbon was purchased from Aldrich. All reactions were carried out in air. Reactions were conducted using a focused microwave unit. The machine consists of a continuous focused microwave power delivery system with operator selectable power output from 0-300 W. Reactions were performed in glass vessels (capacity 10 mL) sealed with a pressure lock. The pressure is controlled by a load cell connected directly to the vessel. The temperature of the contents of the vessel was monitored using a calibrated fiber-optic device inserted in to the reaction vessel to a level 1.5 cm from the bottom of the tube. ^1H - and ^{13}C -NMR spectra were recorded at 293 K on a 500 MHz spectrometer.

Typical experimental procedure

In a 10 mL glass tube was placed aryl chloride (1.0 mmol), phenylboronic acid (0.159 g, 1.3 mmol), Na_2CO_3 (392 mg, 3.7 mmol), tetrabutylammonium bromide (322 mg, 1.0 mmol), 10% Pd/C (10.6 mg, 0.01 mol Pd) water (2 mL) and magnetic stir bar. The vessel was placed into the microwave cavity and sealed with a pressure lock. A fiber optic temperature measurement device was inserted to reaction vessel through the pressure lock. Before the reaction were run, the mixture was stirred for 20 seconds to ensure sufficient mixing of the reagents. The microwave source was then turned on and microwave irradiation of 300 W was used to ramp the temperature from r.t. to 120 °C where it was held by modulating the microwave power until a total reaction time of 10 minutes had elapsed. After allowing the reaction mixture to cool down to r.t., the vessel was opened and the contents poured into a separatory funnel. Water (30 mL) and ethyl acetate (30 mL) were added and the organic material extracted and removed. After further extraction of the aqueous layer with ethyl acetate, combining the organic washings and drying them over MgSO_4 , the solvent was removed in vacuo leaving the crude product. Products were purified and isolated by chromatography using hexane / ethyl acetate as eluent.

Spectroscopic data

4-Methylbiphenyl (compound 1): ^1H NMR (500 MHz, CDCl_3) δ 7.64 (d, J = 7.1 Hz, 2H), 7.55 (d, J = 8.1 Hz, 2H), 7.48 (t, J = 7.5 Hz, 2H), 7.37 (t, J = 7.3 Hz, 1H), 7.30 (d, J = 7.9 Hz, 2H), 2.45 (s, 3H); ^{13}C NMR (500 MHz, CDCl_3) δ 141.2, 138.4, 137.0, 129.5, 128.7, 127.2, 127.0, 21.1.

4-Acetylbiphenyl (compound 2): ^1H NMR (500 MHz, CDCl_3) δ 8.06 (d, J = 8.2 Hz, 2H), 7.72 (d, J = 8.2 Hz, 2H), 7.66 (d, J = 7.7 Hz, 2H), 7.50 (t, J = 7.5 Hz, 2H), 7.43 (t, J = 7.3 Hz, 1H), 2.67 (s, 3H); ^{13}C NMR (500 MHz, CDCl_3) δ 197.8, 145.8, 139.9, 135.9, 129.0, 128.9, 128.3, 127.3, 127.2, 26.7.

4-Nitrobiphenyl (compound 3): ^1H NMR (500 MHz, CDCl_3) δ 8.32 (d, J = 8.4 Hz, 2H), 7.76 (d, J = 8.4 Hz, 2H), 7.66 (d, J = 7.5 Hz, 2H), 7.53 (t, J = 7.4 Hz, 2H), 7.46-7.49 (m, 1H); ^{13}C NMR (500 MHz, CDCl_3) δ 147.6, 147.1, 138.8, 129.2, 129.0, 127.8, 127.4, 124.1.

4-Cyanobiphenyl (compound 4): ^1H NMR (500 MHz, CDCl_3) δ 7.75 (d, J = 8.5 Hz, 2H), 7.71 (d, J = 8.5 Hz, 2H), 7.62 (d, J = 7.7 Hz, 2H), 7.52 (t, J = 7.5 Hz, 2H), 7.46 (t, J = 7.4 Hz, 1H); ^{13}C NMR (500 MHz, CDCl_3) δ 145.7, 139.2, 132.6, 129.1, 128.7, 127.8, 127.3, 119.0, 110.9.

2-Methylbiphenyl (compound 5): ^1H NMR (500 MHz, CDCl_3) δ 7.45 (t, J = 7.3 Hz, 2H), 7.35-7.39 (m, 3H), 7.27-7.30 (m, 4H), 2.31 (s, 3H); ^{13}C NMR (500 MHz, CDCl_3) δ 142.0, 135.4, 130.3, 129.8, 129.2, 128.0, 127.3, 126.8, 125.8, 20.5.

Biphenyl (compound 6): ^1H NMR (500 MHz, CDCl_3) δ 7.64 (dd, $J = 8.5$ Hz, $J = 1.2$ Hz, 4H), 7.48 (t, $J = 7.7$ Hz, 4H), 7.39 (tt, $J = 7.4$ Hz, $J = 1.4$ Hz, 2H); ^{13}C NMR (500 MHz, CDCl_3) δ 141.3, 128.8, 127.3, 127.2.

4-Methoxybiphenyl (compound 7): ^1H NMR (500 MHz, CDCl_3) δ 7.53-7.58 (m, 4H), 7.43 (t, $J = 7.7$ Hz, 2H), 7.32 (t, $J = 7.4$ Hz, 1H), 6.99 (d, $J = 8.8$ Hz, 2H), 3.86 (s, 3H); ^{13}C NMR (500 MHz, CDCl_3) δ 159.2, 140.9, 133.8, 128.7, 128.2, 126.8, 126.7, 114.2, 55.4.

2-Methoxybiphenyl (compound 8): ^1H NMR (500 MHz, CDCl_3) δ 7.60 (d, $J = 7.7$ Hz, 2H), 7.47 (t, $J = 7.6$ Hz, 2H), 7.37-7.40 (m, 3H), 7.10 (d, $J = 7.5$ Hz, 1H), 7.04 (d, $J = 8.6$ Hz, 1H), 3.87 (s, 3H); ^{13}C NMR (500 MHz, CDCl_3) δ 156.5, 138.6, 130.9, 130.8, 129.6, 128.7, 128.0, 127.0, 120.9, 111.3, 55.6.

4-Phenylaniline (compound 9): ^1H NMR (500 MHz, CDCl_3) δ 7.56 (d, $J = 7.4$ Hz, 2H), 7.40-7.45 (m, 4H), 7.28-7.31 (m, 1H), 6.79 (dd, $J = 8.2$ Hz, $J = 1.6$ Hz, 2H), 3.7 (bs, 2H); ^{13}C NMR (500 MHz, CDCl_3) δ 145.8, 141.2, 131.6, 128.7, 128.0, 126.4, 126.3, 115.4.

4-Methylbiphenyl

4-Methylbiphenyl

4-Acetylbiphenyl

4-Acetylbiphenyl

4-Nitrobiphenyl

4-Nitrobiphenyl

4-Cyanobiphenyl

4-Cyanobiphenyl

2-Methylbiphenyl

2-Methylbiphenyl

Biphenyl

Biphenyl

4-Methoxybiphenyl

4-Methoxybiphenyl

2-Methoxybiphenyl

2-Methoxybiphenyl

4-Phenylaniline

4-Phenylaniline

Temperature, pressure and microwave power profiles for the reaction mixture corresponding to Table 1, entry 1 (no simultaneous cooling)

Stage	1	2
Power	0	300
Ramp	0:00	0:00
Hold	0:20	10:00
Temp	24	120
Press	300	300
Stirring	On	On
Cooling	Off	Off
Solvent: Water		
Boiling Point: 100		

Temperature, pressure and microwave power profiles for the reaction mixture corresponding to Table 1, entry 5 (with simultaneous cooling)

Stage	1	2
Power	0	300
Ramp	0:00	0:00
Hold	0:20	10:00
Temp	24	120
Press	300	300
Stirring	On	On
Cooling	On	On
Solvent: Water		
Boiling Point: 100		