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Supporting Information

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The First General Catalysts for the Suzuki-Miyaura and Sonogashira Coupling of Aryl Chlorides and for the Coupling of Challenging Substrate Combinations in Water**

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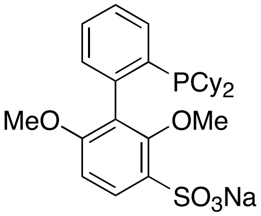
Experimental Details

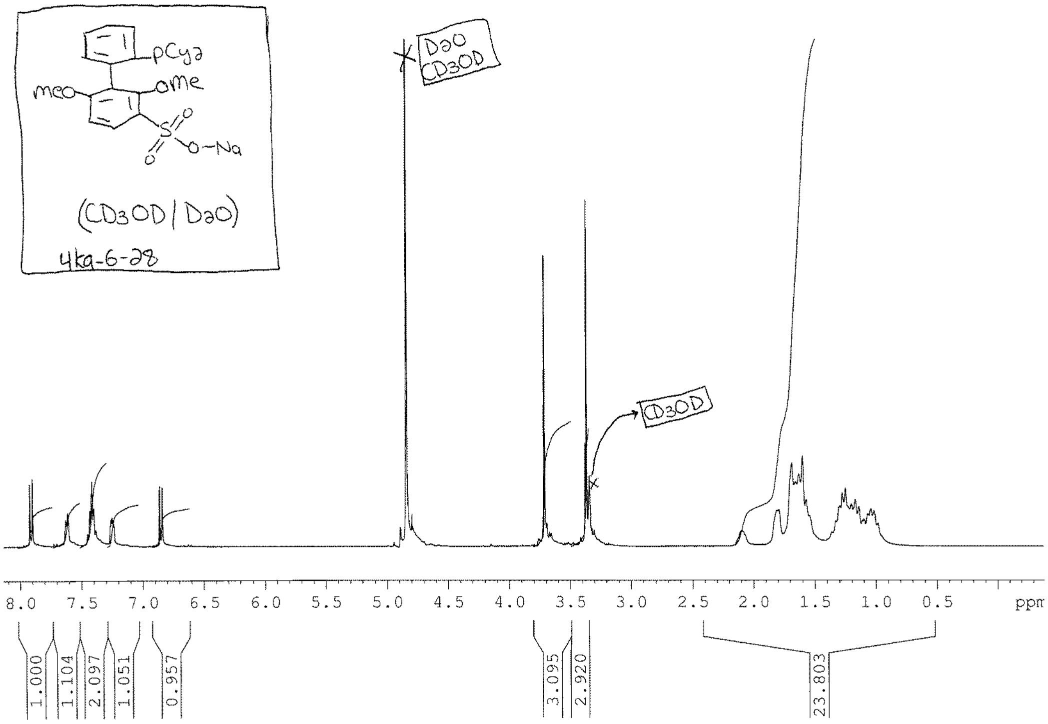
Reagents. $Pd(OAc)_2$ was obtained from Englehard and used without further purification. Dichloromethane was purchased from J. T. Baker in CYCLE-TAINER® solvent delivery kegs, which were vigorously purged with argon for 2 h, and further purified by passing the solvent through two packed columns of neutral alumina and copper (II) oxide under argon pressure. All other reagents were purchased from commercial sources and used without further purification. **Analytical methods.** All reactions were carried out under an argon atmosphere. IR spectra were obtained on a Perkin-Elmer Model 2000 FT-IR using NaCl plates (thin film). ^1H NMR and ^{13}C NMR spectra were recorded on a Bruker 400 Mhz NMR with chemical shifts reported in ppm relative to the residual deuterated solvent or the internal standard tetramethylsilane. Yield refers to isolated yields of compounds greater than 95% purity as determined by capillary gas chromatography (GC) and proton Nuclear Magnetic Resonance spectroscopy (^1H NMR) analysis. ^1H NMR and melting points (where applicable) of all known compounds were compared with those reported. All new compounds were further characterized by elemental analysis. Several of them are pending: copies of ^1H NMR spectra are included for those examples.

Preparation of Water-Soluble Ligand [Eq. (1)]:

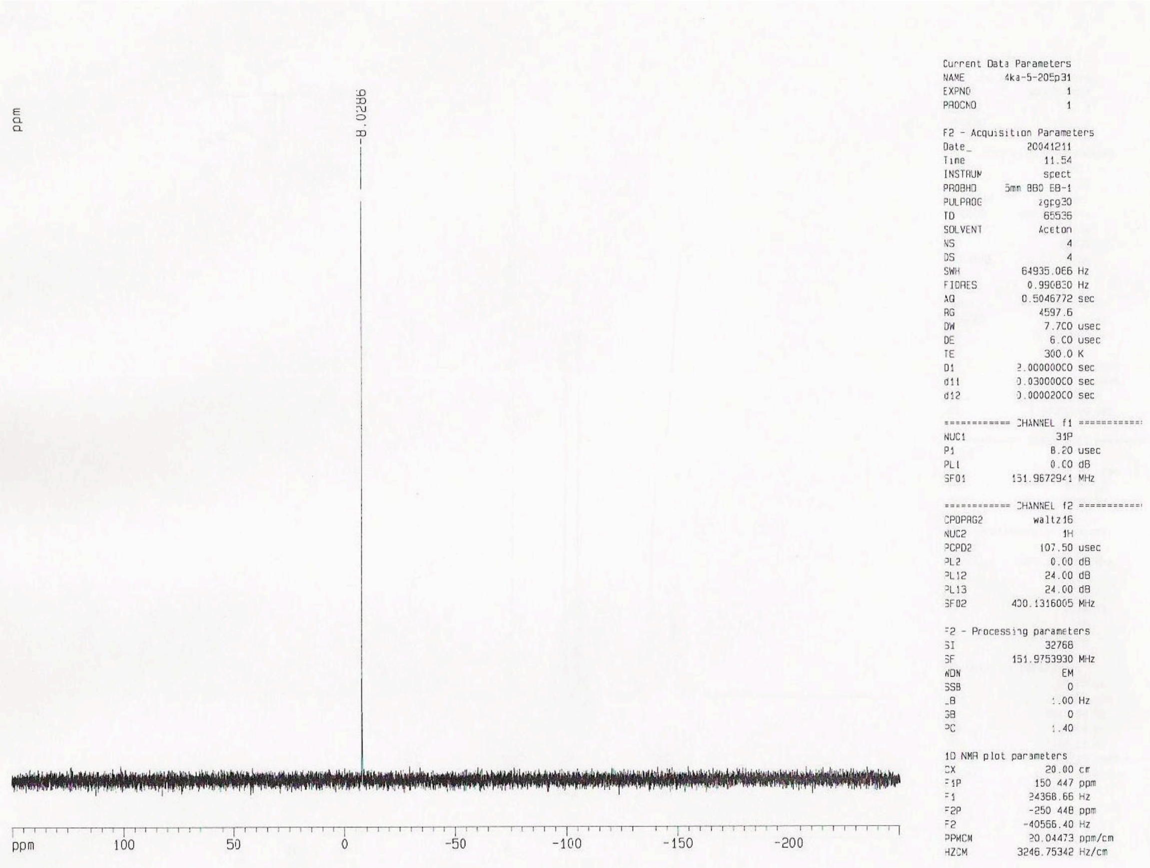


Sodium 2-Dicyclohexylphosphino-2',6'-dimethoxybiphenyl-3'-sulfonate [Eq. (1)], (2). To an oven-dried 25 mL round bottom flask equipped with a Teflon-coated magnetic stir bar and rubber septum was added 2-dicyclohexylphosphino-2'6'dimethoxybiphenyl (5.13 g, 12.5 mmol) and CH_2Cl_2 (5 mL). The solution was cooled to 0 °C using an ice/water bath and then concentrated H_2SO_4 (32.5 mL, 625 mmol) was added dropwise. The solution slowly turned yellow in color. The solution was heated to 40 °C in a preheated oil bath and was allowed stir for 24 h. At this time it was cooled to 0 °C using an ice/water bath and crushed ice (~50 g) was added. The solution turned cloudy and white in color. An aqueous solution of NaOH (6.0 M, ~200 mL) was then added dropwise to the cooled solution until it became neutral (pH ~7.0 as judged by pH paper). The aqueous solution was extracted with CH_2Cl_2 (3 x 300 mL) and concentrated under reduced pressure to give a light yellow solid. The crude material was then dissolved in a minimum amount of cold methanol (~20 mL), filtered and concentrated (this cycle was repeated) to give the desired product as a light yellow solid (6.35 g, 99%). Mp = 165 °C (turned red, dec.) ^{1}H NMR (400 MHz, CD_3OD) δ: 7.88 (d, 1H, J = 8.8 Hz), 7.60 (m, 1H), 7.36 (m, 2H), 7.22 (m, 1H), 6.76 (d, 1H, J = 8.8 Hz) 3.70 (s, 3H), 3.39 (s, 3H), 1.14-2.01 (m, 22H). ^{13}C NMR (125 MHz, CD_3OD) δ: 161.3, 157.1, 143.3, 142.9, 137.9, 137.8, 133.7, 133.6, 133.3, 133.2, 131.9, 130.0, 129.3, 128.0, 127.9, 127.8, 105.9, 61.6, 56.1, 50.0, 37.0, 36.9, 34.8, 34.6, 31.7, 31.6, 31.5, 31.2, 31.0, 30.8, 30.7, 28.9, 28.8, 28.7, 28.4, 28.34, 28.31, 28.2, 27.8, 27.7. ^{31}P NMR (162 MHz, CD_3OD) δ: -8.02. IR (neat, cm^{-1}): 3453, 2925, 2849, 1577, 1462, 1448, 1400, 1229, 1191, 1099, 1053, 736. Anal. Calcd for $C_{26}H_{34}NaO_5PS$: C, 60.92; H, 6.69. Found: C, 60.40; H, 6.85.

^{1}H NMR (d^4-MeOH/D$_2$O):



^{31}P NMR (d^4-MeOH):



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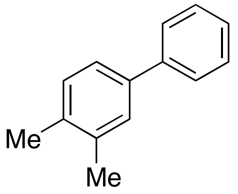
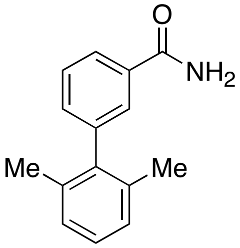
General Procedure for Suzuki-Miyaura coupling in Water. A disposable tube with a screw cap, Teflon septum and stir bar was charged with Pd(OAc)$_2$ (2.2 mg, 0.010 mmol, 1 mol %), sodium 2-dicyclohexylphosphino-2',6'-dimethoxybiphenyl-3'-sulfonate (10.0 mg, 0.0200 mmol, 2 mol %), aryl halide (1.00 mmol), boronic acid (1.20-1.50 mmol) and K_2CO_3 (276-690 mg, 2.00-5.00 mmol). The tube was evacuated and back-filled with argon (this was repeated two additional times). Degassed water (1.5-3.0 mL, sonicated under vacuum for 2 min) was added and the reaction mixture was allowed to stir at the noted temperature or submitted to microwave irradiation using a CEM Discover® LabMate microwave (300W, 150 °C, with cooling to optimize the power). After cooling to room temperature, the hydrophilic products were isolated by acidifying the reaction mixture with HCl (2.0 M) to pH~5 and extraction with ethyl acetate or diethyl ether. The organic layer was dried over anhydrous $MgSO_4$, filtered through celite and concentrated to give the crude product. The products were purified by crystallization from water to give pure compounds (as judged by ^{1}H NMR and elemental analysis). Hydrophobic products were extracted from the water layer with diethyl ether, dried over $MgSO_4$, filtered through celite and concentrated to dryness and purified by column chromatography on silica gel (eluting with hexanes).

Table 1: Suzuki-Miyaura coupling of aryl chorides using ligand **2**.

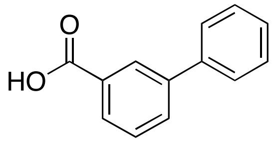


3,4-Dimethyl-biphenyl (Table 1, Entry 1)[1] The general procedure was used with 3,4-dimethyl-chlorobenzene (0.140 mL, 1.00 mmol), phenylboronic acid (157 mg, 1.20 mmol), Pd(OAc)$_2$ (4.5 mg, 0.020 mmol, 2 mol %), sodium 2-dicyclohexylphosphino-2',6'-dimethoxybiphenyl-3'-sulfonate (20.0 mg, 0.040 mmol, 4 mol %), K_2CO_3 (276 mg, 2.00 mmol), water (1.0 mL), 10 h, room temperature. The product was isolated as a colorless oil (151 mg, 99%). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.82 (d, 2H, J = 7.6 Hz), 6.81-7.55 (m, 6H), 2.24 (s, 6H).



2',6'-Dimethyl-biphenyl-3-carboxylic acid amide (Table 1, Entry 2). The general procedure was used with 3-chlorobenzamide (0.132 mL, 1.00 mmol), 2,6-dimethylphenylboronic acid (180 mg, 1.20 mmol), Pd(OAc)$_2$ (2.2 mg, 0.010 mmol, 1 mol %), sodium 2-dicyclohexylphosphino-2',6'-dimethoxybiphenyl-3'-sulfonate (10.0 mg, 0.020 mmol, 2 mol %), K_2CO_3 (414 mg, 3.00 mmol), water (2.0 mL),12 h, 100 °C. The product was isolated as a white solid (225 mg, 99%).

Using microwave irradiation: The general procedure was used with 3-chlorobenzamide (156 mg, 1.00 mmol), 2,6-dimethylphenylboronic acid (180 mg, 1.20 mmol), Pd(OAc)$_2$ (4.5 mg, 0.020 mmol, 2 mol %), sodium 2-dicyclohexylphosphino-2',6'-dimethoxybiphenyl-3'-sulfonate (20.0 mg, 0.0391 mmol, 4 mol %), K_2CO_3 (345 mg, 2.50 mmol), water (3.0 mL), 10 min, 150 °C (microwave irradiation with cooling). The product was isolated as a white solid (207 mg, 92%). Mp = 123-125 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.85 (d, 1H, J = 7.6 Hz), 7.67 (s, 1H), 7.50 (t, 1H, J = 7.6 Hz), 7.33 (d, 1H, J = 7.6 Hz), 7.20 (t, 1H, J = 7.4 Hz), 7.13 (d, 2H, J = 7.2 Hz), 6.87 (br-s, 1H), 6.69 (br-s, 1H), 2.03 (s, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 170.1, 141.6, 140.8, 135.9, 133.8, 132.8, 128.9, 128.1, 127.5, 126.0, 20.96. IR (neat, cm^{-1}): 3347 (br), 3197 (br), 1657, 1602, 1578, 1379, 1102, 770, 737, 703. Anal. Calcd for $C_{15}H_{15}NO$: C, 79.97; H, 6.71. Found: C, 79.98; H, 6.48.



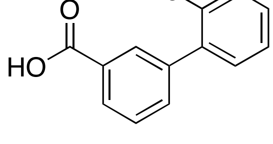
Biphenyl-3-carboxylic acid (Table 1, Entry 3)[2]

2 mol % Pd: The general procedure was used with 3-chlorobenzoic acid (157 mg, 1.00 mmol), phenylboronic acid (145 mg, 1.20 mmol), $Pd(OAc)_2$ (4.5 mg, 0.020 mmol, 2 mol %), sodium 2-dicyclohexylphosphino-2',6'-dimethoxybiphenyl-3'-sulfonate (20.0 mg, 0.040 mmol, 4 mol %), K_2CO_3 (345 mg, 2.50 mmol), water (1.5 mL), 2 h, room temperature. The product was isolated as a white solid (190 mg, 96%).

0.5 mol % Pd: The general procedure was used with 3-chlorobenzoic acid (157 mg, 1.00 mmol), phenylboronic acid (145 mg, 1.20 mmol), $Pd(OAc)_2$ (1.1 mg, 0.005 mmol, 0.5 mol %), sodium 2-dicyclohexylphosphino-2',6'-dimethoxybiphenyl-3'-sulfonate (5.0 mg, 0.010 mmol, 1 mol %), K_2CO_3 (345 mg, 2.50 mmol),water (1.5 mL), 8 h, room temperature. The product was isolated as a white solid (192 mg, 97%).

0.1 mol % Pd: The general procedure was used with 3-chlorobenzoic acid (157 mg, 1.00 mmol), phenylboronic acid (145 mg, 1.20 mmol), K_2CO_3 (345 mg, 2.50 mmol), water (1.5 mL), Pd/L solution (0.200 mL of a $Pd(OAc)_2$ (1.1 mg, 0.005 mmol, 0.5 mol %), sodium 2-dicyclohexylphosphino-2',6'-dimethoxybiphenyl-3'-sulfonate (5.0 mg, 0.010 mmol, 1 mol) in 1.0 mL water), 5 h, 100 °C. The product was isolated as a white solid (192 mg, 97%).

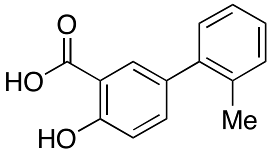
0.1 mol % Pd using microwave irradiation: The general procedure was used with 3-chlorobenzoic acid (157 mg, 1.00 mmol), phenylboronic acid (145 mg, 1.20 mmol), K_2CO_3 (345 mg, 2.50 mmol), water (1.5 mL), Pd/L solution (0.200 mL of a $Pd(OAc)_2$ (1.1 mg, 0.005 mmol, 0.5 mol %), sodium 2-dicyclohexylphosphino-2',6'-dimethoxybiphenyl-3'-sulfonate (5.0 mg, 0.010 mmol, 1 mol %) solution in 1.0 mL water), 10 min, 150 °C (microwave irradiation with cooling). The product was isolated as a white solid (192 mg, 97%). Mp = 164 °C (lit. = 165-166 °C)[3] ^1H NMR (400 MHz, $CDCl_3$) δ: 11.90 (br-s, 1H), 8.41 (s, 1H), 8.15 (d, 1H, J = 7.6 Hz), 7.88 (d, 1H, J = 7.6 Hz), 7.68 (d, 2H, J = 7.2 Hz), 7.60 (t, 1H, J = 6.4 Hz), 7.52 (t, 2H, J = 7.6 Hz), 7.43 (t, 1H, J = 7.2 Hz). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 172.6, 141.8, 140.1, 132.7, 130.0, 129.3, 129.2, 129.1, 129.0, 128.0, 127.4.



2'-Methyl-biphenyl-3-carboxylic acid (Table 1, Entry 4).

0.5 mol % Pd: The general procedure was used with 3-chlorobenzoic acid (157 mg, 1.00 mmol), *o*-tolylboronic acid (163 mg, 1.20 mmol), $Pd(OAc)_2$ (1.1 mg, 0.005 mmol, 0.5 mol %), sodium 2-dicyclohexylphosphino-2’,6’-dimethoxybiphenyl-3’-sulfonate (5.0 mg, 0.010 mmol, 1 mol %), K_2CO_3 (345 mg, 2.50 mmol), water (1.5 mL), 8 h, room temperature. The product was isolated as a white solid (201 mg, 95%).

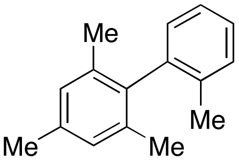
0.1 mol % Pd: The general procedure was used with 3-chlorobenzoic acid (157 mg, 1.00 mmol), *o*-tolylboronic acid (163 mg, 1.20 mmol), K_2CO_3 (345 mg, 2.50 mmol), water (1.5 mL), Pd/L solution (0.200 mL of a $Pd(OAc)_2$ (1.1 mg, 0.005 mmol, 0.5 mol %), sodium 2-dicyclohexylphosphino-2’,6’-dimethoxybiphenyl-3’-sulfonate (5.0 mg, 0.010 mmol, 1 mol %) solution in 1.0 mL water), 6 h,100 °C. The product was isolated as a white solid (203 mg, 96%). Mp = 127 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 12.9 (br-s, 1H), 8.01 (m, 2H), 7.46 (d, 1H, J = 7.6 Hz), 7.40 (t, 1H, J = 7.6 Hz), 7.20-7.14 (m, 4H), 2.17 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 172.8, 142.5, 140.8, 135.5, 134.8, 131.1, 130.7, 129.9, 129.4, 128.8, 128.5, 127.9, 125.2, 20.6. IR (neat, cm^{-1}): 2962, 1689, 1309, 1258, 747. Anal. Calcd for $C_{14}H_{12}O_2$: C, 79.22; H, 5.70. Found: C, 79.12; H, 5.62.



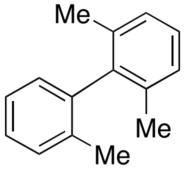
4-Hydroxy-2'-methyl-biphenyl-3-carboxylic acid (Table 1, Entry 5)[3]

2 mol % Pd: The general procedure was used with 5-chloro-2-hydroxy-benzoic acid (173 mg, 1.00 mmol), 2-methylphenylboronic acid (163 mg, 1.20 mmol), $Pd(OAc)_2$ (4.5 mg, 0.020 mmol, 2 mol %), sodium 2-dicyclohexylphosphino-2’,6’-dimethoxybiphenyl-3’-sulfonate (20.0 mg, 0.040 mmol, 4 mol %), K_2CO_3 (483 mg, 3.50 mmol), water (2.0 mL), 12 h, room temperature. The product was isolated as a white solid (227 mg, 99%).

0.1 mol % Pd: The general procedure was used with 5-chloro-2-hydroxy-benzoic acid (173 mg, 1.00 mmol), 2-methylphenylboronic acid (163 mg, 1.20 mmol), K_2CO_3 (345 mg, 2.50 mmol), water (2.0 mL), Pd/L solution (0.200 mL of a $Pd(OAc)_2$ (1.1 mg, 0.005 mmol, 0.5 mol %), sodium 2-dicyclohexylphosphino-2’,6’-dimethoxybiphenyl-3’-sulfonate (5.0 mg, 0.010 mmol, 1 mol %) solution in 1.0 mL water),12 h,100 °C. The product was isolated as a white solid (217 mg, 96%). Mp = 151 °C (lit. 150-152 °C)[4]. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 11.91 (br-s, 1H), 10.28 (br-s, 1H), 7.83 (d, 1H, J = 2.0 Hz), 7.42 (dd, 1H, J = 2.4 Hz, J = 8.6 Hz), 7.20-7.13 (m, 4H), 6.98 (d, 1H, J = 8.4 Hz), 2.20 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 175.4, 161.3, 140.4, 138.2, 135.6, 133.7, 131.4, 130.7, 129.9, 127.4, 126.2, 117.9, 111.2, 20.7 IR (neat, cm^{-1}): 3062, 1664, 1614, 1583, 1478, 1440, 1229, 1190, 728.

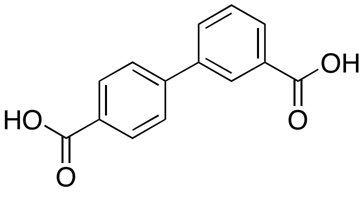


2,4,6,2'-Tetramethyl-biphenyl (Table 1, Entry 6)[4] The general procedure was used with 2-bromo-mesitylene (0.153 mL, 1.00 mmol), 2-methylphenylboronic acid (203 mg, 1.50 mmol), $Pd(OAc)_2$ (4.5 mg, 0.020 mmol, 2 mol %), sodium 2-dicyclohexylphosphino-2',6'-dimethoxybiphenyl-3'-sulfonate (20.0 mg, 0.040 mmol, 4 mol %), K_2CO_3 (276 mg, 2.00 mmol), water (1.5 mL), 22 h, room temperature. The product was isolated as a colorless oil (197 mg, 94%). ^1H NMR (400 MHz, $CDCl_3$) δ: 7.30-7.19 (m, 3H), 7.05-7.00 (m, 1H), 6.92 (s, 2H), 2.30 (2, 3H), 1.99 (s, 3H), 1.89 (s, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 140.9, 138.2, 136.4, 136.0, 135.9, 130.0, 129.2, 128.1, 127.1, 126.2, 21.4, 20.6, 19.9.



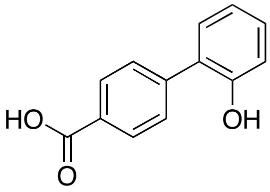
2,6,2'-Trimethyl-biphenyl (Table 1, Entry 7)[4]. The general procedure was used with 2-bromotoluene (0.120 mL, 1.00 mmol), 2,6-dimethylphenylboronic acid (225 mg, 1.50 mmol), $Pd(OAc)_2$ (4.5 mg, 0.020 mmol, 2 mol %), sodium 2-dicyclohexylphosphino-2',6'-dimethoxybiphenyl-3'-sulfonate (20.0 mg, 0.040 mmol, 4 mol %), K_2CO_3 (276 mg, 2.00 mmol), water (1.5 mL), 22 h, room temperature. The product was isolated as a colorless oil (190 mg, 97%). ^1H NMR (400 MHz, $CDCl_3$) δ: 7.30-7.10 (m, 6H), 7.02-7.00 (m, 1H), 1.99 (s, 3H), 1.96 (s, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 141.1, 140.7, 136.1, 135.9, 130.0, 129.1, 127.4, 127.1, 127.1, 126.1, 20.7, 19.7.

Table 2. Suzuki-Miyaura coupling of chlorobenzoic acids using ligand 2.

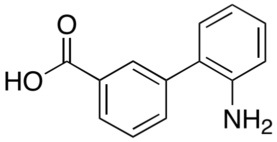


Biphenyl-3,4'-dicarboxylic acid (Table 2, Entry 1)[5] The general procedure was used with 4-chlorobenzoic acid (157 mg, 1.00 mmol), 3-carboxyphenylboronic acid (199 mg, 1.20 mmol), $Pd(OAc)_2$ (2.2 mg, 0.010 mmol, 1 mol %), sodium 2-dicyclohexylphosphino-2',6'-dimethoxybiphenyl-3'-sulfonate (10.0 mg, 0.020 mmol, 2 mol %), K_2CO_3 (414 mg, 3.00 mmol), water (3.0 mL), 8 h, 50 °C. The product was isolated as a white solid (241 mg, 99%).

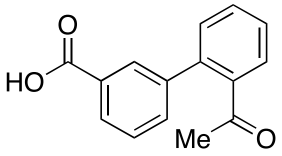
Using microwave irradiation: The general procedure was used with 4-chlorobenzoic acid (157 mg, 1.00 mmol), 3-carboxyphenylboronic acid (199 mg, 1.20 mmol), Pd(OAc)$_2$ (2.2 mg, 0.010 mmol, 1 mol %), sodium 2-dicyclohexylphosphino-2',6'-dimethoxybiphenyl-3'-sulfonate (10.0 mg, 0.020 mmol, 2 mol %), K$_2$CO$_3$ (414 mg, 3.00 mmol), water (3.0 mL), 10 min at 150 °C (using microwave irradiation with cooling). The product was isolated as a white solid (229 mg, 95%). Mp = >250 °C (lit. mp = 295 °C)[5]. ^{1}H NMR (400 MHz, d^6-DMSO/D$_2$O) δ: 8.22 (s, 1H), 8.42 (d, 2H, J = 7.6 Hz), 7.98 (d, 1H, J = 7.6 Hz), 7.91 (d, 1H, J = 7.6 Hz), 7.79 (d, 2H, J = 7.6 Hz), 7.59 (t, 1H, J = 7.2 Hz). ^{13}C NMR (125 MHz, d^6-DMSO/D$_2$O) δ: 167.5, 143.6, 139.7, 131.9, 131.7, 130.4, 130.3, 129.8, 129.4, 127.8, 127.2.



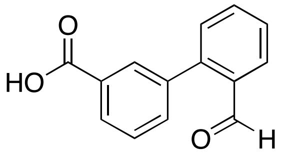
2'-Hydroxy-biphenyl-4-carboxylic acid (Table 2, Entry 2)[6] The general procedure was used with 4-chlorobenzoic acid (157 mg, 1.00 mmol), 2-hydroxyphenylboronic acid (166 mg, 1.20 mmol), Pd(OAc)$_2$ (2.2 mg, 0.010 mmol, 1 mol %), sodium 2-dicyclohexylphosphino-2',6'-dimethoxybiphenyl-3'-sulfonate (10.0 mg, 0.020 mmol, 2 mol %), K$_2$CO$_3$ (414 mg, 3.00 mmol), water (2.0 mL), 12 h, 100 °C. The product was isolated as a white solid (203 mg, 95%). Mp = 186 °C ^{1}H NMR (400 MHz, d^4-MeOH) δ: 8.04 (d, 2H, J = 8.4 Hz), 7.65 (d, 2H, J = 8.4 Hz), 7.25 (dd, 1H, J = 7.6 Hz, 1.6 Hz), 7.16 (td, 1H, J = 7.6 Hz, 1.6 Hz), 6.89 (m, 2H). ^{13}C NMR (125 MHz, d^4-MeOH) δ: 170.2, 155.6, 145.4, 131.7, 130.5 (2), 130.48, 130.4, 129.8, 128.7, 121.2, 117.2. IR (neat, cm^{-1}): 3391, 2529, 1683, 1274, 1008, 753.



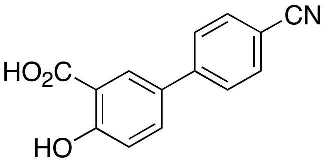
2'-Amino-biphenyl-3-carboxylic acid (Table 2, Entry 3)[7] The general procedure was used with 3-chlorobenzoic acid (157 mg, 1.00 mmol), 2-aminophenylboronic acid (205 mg, 1.50 mmol), Pd(OAc)$_2$ (2.2 mg, 0.010 mmol, 1 mol %), sodium 2-dicyclohexylphosphino-2',6'-dimethoxybiphenyl-3'-sulfonate (10.0 mg, 0.020 mmol, 2 mol %), K$_2$CO$_3$ (414 mg, 3.00 mmol), water (2.0 mL), 12 h, 100 °C. The product was isolated as a white solid (203 mg, 95%). Mp = 170 °C (lit. = 173-175 °C)[7] ^{1}H NMR (400 MHz, d^4-MeOH) δ: 8.07 (m, 1H), 7.99 (d, 1H, J = 7.6 Hz), 7.65 (d, 1H, J = 8.0 Hz), 7.53 (t, 1H, J = 7.6 Hz), 7.13 (td, 1H, J = 1.6 Hz, J = 7.6 Hz), 6.84 (d, 1H, J = 8.0 Hz), 6.77 (t, 1H, J = 7.6 Hz). ^{13}C NMR (125 MHz, d^4-MeOH) δ: 169.9, 145.1, 141.7, 134.8, 132.6, 131.4, 131.4, 130.1, 129.9, 129.5, 128.3, 120.0, 117.6.



2'-Acetyl-biphenyl-3-carboxylic acid (Table 2, Entry 3). The general procedure was used with 3-chlorobenzoic acid (157 mg, 1.00 mmol), 2-acetylphenylboronic acid (179 mg, 1.20 mmol), Pd(OAc)$_2$ (2.2 mg, 0.010 mmol, 1 mol %), sodium 2-dicyclohexylphosphino-2',6'-dimethoxybiphenyl-3'-sulfonate (10.0 mg, 0.020 mmol, 2 mol %), K$_2$CO$_3$ (414 mg, 3.00 mmol), water (2.0 mL), 10 h, 100 °C. The product was isolated as a light yellow solid (233 mg, 97%). Mp = 143 °C. ^{1}H NMR (400 MHz, CDCl$_3$) δ: 12.60 (br-s, 1H), 8.05 (m, 1H), 7.65 (d, 1H, J = 7.2 Hz), 7.58-7.55 (m, 3H), 7.49 (d, 1H, J = 7.2 Hz), 7.42 (d, 1H, J = 7.6 Hz), 2.16 (s, 3H). ^{13}C NMR (125 MHz, CDCl$_3$) δ: 204.3, 172.2, 141.7, 140.7, 139.9, 134.7, 131.5, 131.0, 130.7, 130.3, 129.9, 129.2, 128.7, 128.4, 30.8. IR (neat, cm^{-1}): 3419, 2517, 1686, 1018. Anal. Calcd for $C_{15}H_{12}O_3$: C, 74.99; H, 5.03. Found: C, 75.04; H, 5.06.

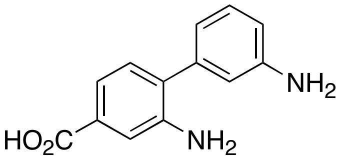


2'-Formyl-biphenyl-3-carboxylic acid monohydrate (Table 2, Entry 3)[8] The general procedure was used with 3-chlorobenzoic acid (157 mg, 1.00 mmol), 2-formylphenylboronic acid (225 mg, 1.50 mmol), Pd(OAc)$_2$ (2.2 mg, 0.010 mmol, 1 mol %), sodium 2-dicyclohexylphosphino-2',6'-dimethoxybiphenyl-3'-sulfonate (10.0 mg, 0.020 mmol, 2 mol %), K$_2$CO$_3$ (414 mg, 3.00 mmol), water (2.0 mL), 10 h, 80 °C. The product was isolated as a white solid (192 mg, 85%). Mp = 164-167 °C. ^{1}H NMR (400 MHz, d^4-MeOH, d^6-DMSO) δ: 8.07 (m, 2H), 7.68 (m, 1H), 7.63-7.52 (m, 2H), 7.46 (m, 2H), 7.30 (m, 1H), 5.10 (s, 1H), 4.98 (br-s, 2H). ^{13}C NMR (125 MHz, d^4-MeOH, d^6-DMSO) δ: 169.4, 142.1. 142.0, 137.0, 135.0, 131.9, 131.7, 131.2, 129.9, 129.8, 129.6, 128.9, 127.8, 103.6 [Ar-CH(OH)$_2$] IR (neat, cm^{-1}): 3066, 1694, 1260, 754.

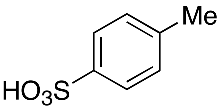


4'-Cyano-4-hydroxy-biphenyl-3-carboxylic acid (Table 2, Entry 4). The general procedure was used with 5-chloro-2-hydroxy-benzoic acid (173 mg, 1.00 mmol), 4-cyanophenylboronic acid (176 mg, 1.20 mmol), Pd(OAc)$_2$ (2.2 mg, 0.010 mmol, 1 mol %), sodium 2-dicyclohexylphosphino-2',6'-dimethoxybiphenyl-

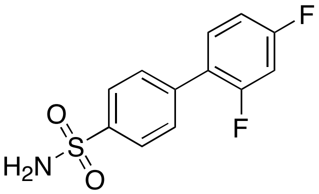
3'-sulfonate (10.0 mg, 0.020 mmol, 2 mol %), K_2CO_3 (552 mg, 4.00 mmol), water (2.0 mL), 12 h, 80 °C. The product was isolated as a white solid (220 mg, 92%). Mp = 227 °C. ^{1}H NMR (400 MHz, d^4-MeOH) δ: 8.11 (d, 1H, J = 2.4 Hz), 7.81-7.70 (m, 5H), 7.02 (d, 1H, J = 8.4 Hz). ^{13}C NMR (125 MHz, d^4-MeOH) δ: 173.2, 163.5, 145.5, 135.4, 134.0, 131.2, 130.1, 128.3, 120.1, 119.4, 114.6, 111.5. IR (neat, cm^{-1}): 3429, 2229, 1667, 750. Anal. Calcd for $C_{14}H_9NO_3$: C, 70.29; H, 3.79. Found: C, 69.96; H, 3.52.



2,3'-Diamino-biphenyl-4-carboxylic acid (Table 2, Entry 5). The general procedure was used with 3-Amino-4-chloro-benzoic acid (172 mg, 1.00 mmol), 3-aminophenylboronic acid (190 mg, 1.40 mmol), $Pd(OAc)_2$ (2.2 mg, 0.010 mmol, 1 mol %), sodium 2-dicyclohexylphosphino-2',6'-dimethoxybiphenyl-3'-sulfonate (10.0 mg, 0.020 mmol, 2 mol %), K_2CO_3 (552 mg, 4.00 mmol), water (3.0 mL), 12 h, 100 °C. The product was isolated as a light brown oil (254 mg, 99%). ^{1}H NMR (400 MHz, $CDCl_3$/d^4-MeOH) δ: 7.35 (m, 2H), 7.10 (t, 1H, J = 7.6 Hz), 7.02 (d, 1H, J = 8.0 Hz), 6.70-6.60 (m, 3H). ^{13}C NMR (125 MHz, $CDCl_3$/d^4-MeOH) δ: 169.4, 146.6, 143.4, 139.4, 132.4, 129.9, 129.7, 129.0, 119.8, 118.9, 115.8, 115.5, 114.8. IR (neat, cm^{-1}): 3419, 1645, 1016. EI-MS for $C_{13}H_{12}N_2O_2$: Theoretical [M + H] = 229.0977. Found: 229.0982. Anal. Calcd for $C_{13}H_{12}N_2O_2$: C, 68.41; H, 5.30. Found: C, 68.29; H, 5.29.

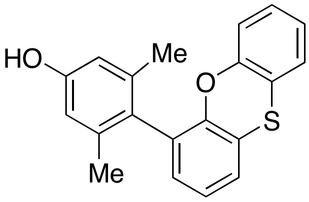


Toluene-4-sulfonic acid monohydrate (Table 2, Entry 6)[9] The general procedure was used with 4-chlorobenzenesulfonic acid (192 mg, 1.00 mmol), methylboronic acid (90 mg, 1.50 mmol), $Pd(OAc)_2$ (2.2 mg, 0.010 mmol, 1 mol %), sodium 2-dicyclohexylphosphino-2',6'-dimethoxybiphenyl-3'-sulfonate (10.0 mg, 0.020 mmol, 2 mol %), K_2CO_3 (414 mg, 3.00 mmol), water (2.0 mL), 12 h, 100 °C. The product was isolated as a white solid (207 mg, 99%). Mp = 104 °C (lit. = 106 °C)[9] ^{1}H NMR (400 MHz, d^4-MeOH) δ: 7.71 (d, 2H, J = 8.4 Hz), 7.24 (d, 2H, J = 8.4 Hz), 5.08 (s, H_2O), 2.37 (s, 3H).). ^{13}C NMR (125 MHz, d^4-MeOH) δ: 143.3, 142.0, 130.0, 127.1, 21.4.

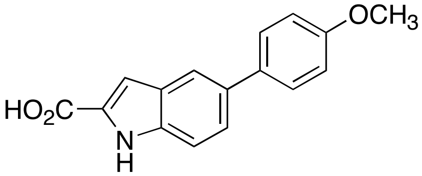


2',4'-Difluoro-biphenyl-4-sulfonic acid amide (Table 2, Entry 7). The general procedure was used with 4-chloro-benzenesulfonamide (192 mg, 1.00 mmol), 2,4-difluorophenylboronic acid (205 mg, 1.30 mmol), Pd(OAc)$_2$ (2.2 mg, 0.010 mmol, 1 mol %), sodium 2-dicyclohexylphosphino-2',6'-dimethoxybiphenyl-3'-sulfonate (10.0 mg, 0.020 mmol, 2 mol %), K$_2$CO$_3$ (414 mg, 3.00 mmol), water (2.0 mL), 12 h, 80 °C. The product was isolated as a white solid (258mg, 96%). Mp = 143 °C. ^{1}H NMR (400 MHz, d^4-MeOH) δ: 7.98 (d, 2H, J = 8.4 Hz), 7.87 (d, 1H, J = 8.4 Hz), 7.63 (d, 2H, J = 7.2 Hz), 7.49 (d, 2H, J = 8.4 Hz), 7.05-6.99 (m, 2H). ^{13}C NMR (125 MHz, d^4-MeOH) δ: 165.5 (d), 163.0 (d), 162.3 (d), 159.8 (d), 144.0, 143.6, 140.0, 139.3, 133.1 (d), 133.0 (d), 130.5 (d), 130.2, 128.9, 127.4, 125.1 (d), 124.9 (d), 113.2 (d), 113.0 (d), 105.4 (t). IR (neat, cm^{-1}): 3362, 3257, 1619, 1599, 1516, 1487, 1302, 1103, 965, 849, 809. Anal. Calcd for $C_{12}H_9F_2NO_2S$: C, 53.53; H, 3.37. Found: C, 53.34; H, 3.36.

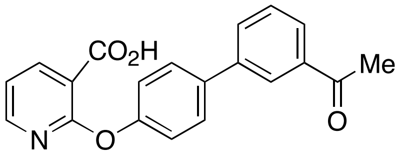
Table 3. Suzuki-Miyaura coupling of heterocyclic halides using ligand **2**.



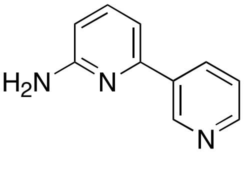
3,5-Dimethyl-4-phenoxathiin-4-yl-phenol (Table 3, Entry 1). The general procedure was used with 4-chloro-3,5-dimethyl-phenol (156 mg, 1.00 mmol), 4-phenoxathiineboronic acid (293 mg, 1.20 mmol), Pd(OAc)$_2$ (2.2 mg, 0.010 mmol, 1 mol %), sodium 2-dicyclohexylphosphino-2',6'-dimethoxybiphenyl-3'-sulfonate (10.0 mg, 0.020 mmol, 2 mol %), K$_2$CO$_3$ (414 mg, 3.00 mmol), water (3.0 mL), 12 h, 100 °C. The product was isolated as a colorless oil (277 mg, 85%), which became a white solid upon standing. Mp = 116 °C. ^{1}H NMR (400 MHz, CDCl$_3$) δ: 7.20 (m, 2H), 7.01-7.16 (m, 3H), 6.96 (d, 1H, J = 7.6 Hz), 6.73 (m, 3H), 5.64 (s, 1H), 2.04 (s, 6H). ^{13}C NMR (125 MHz, CDCl$_3$) δ: 154.6, 152.6, 149.9, 138.3, 130.2, 129.9, 129.5, 127.8, 126.8, 126.1, 124.7, 124.6, 121.2, 121.1, 118.2, 114.2, 20.9. IR (neat, cm^{-1}): 3367, 1593, 1471, 1419, 1311, 1265, 1223, 1154, 1026, 752. Anal. Calcd for $C_{20}H_{16}O_2S$: C, 74.97; H, 5.03. Found: C, 74.88; H, 4.99.



5-(4-Methoxy-phenyl)-1*H*-indole-2-carboxylic acid (Table 3, Entry 2). The general procedure was used with 5-chloro-1*H*-indole-2-carboxylic acid (194 mg, 1.00 mmol), 4-methoxyphenylboronic acid (207 mg, 1.50 mmol), $Pd(OAc)_2$ (2.2 mg, 0.010 mmol, 1 mol %), sodium 2-dicyclohexylphosphino-2',6'-dimethoxybiphenyl-3'-sulfonate (10.0 mg, 0.020 mmol, 2 mol %), K_2CO_3 (414 mg, 3.00 mmol), water (2.0 mL), 12 h, 80 °C. The product was isolated as a light yellow solid (246 mg, 93%). Mp = >230 °C. ^1H NMR (400 MHz, d^6-DMSO) δ: 11.81 (s, 1H), 7.84 (s, 1H), 7.58 (d, 2H, J = 8.8 Hz), 7.49 (m, 2H), 7.13 (d, 1H, J = 1.6 Hz), 6.99 (d, 2H, J = 8.4 Hz), 3.78 (s, 3H). ^{13}C NMR (125 MHz, d^6-DMSO) δ: 162.7, 158.3, 136.3, 133.7, 132.2, 129.0, 127.7, 127.5, 123.7, 119.1, 114.3, 112.8, 107.7, 55.1. IR (neat, cm^{-1}): 4320, 1700, 1183. Anal. Calcd for $C_{16}H_{13}NO_3$: C, 71.90; H, 4.90. Found: C, 71.94; H, 4.93.

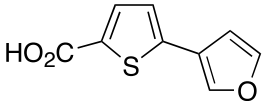


2-(3'-Acetyl-biphenyl-4-yloxy)-nicotinic acid (Table 3, Entry 3). The general procedure was used with 2-(4-chloro-phenoxy)-nicotinic acid (250 mg, 1.00 mmol), 3-acetylphenylboronic acid (246 mg, 1.50 mmol), $Pd(OAc)_2$ (2.2 mg, 0.010 mmol, 1 mol %), sodium 2-dicyclohexylphosphino-2',6'-dimethoxybiphenyl-3'-sulfonate (10.0 mg, 0.020 mmol, 2 mol %), K_2CO_3 (414 mg, 3.00 mmol), water (2.0 mL), 12 h, 80 °C. The product was isolated as a white solid (305 mg, 92%). Mp = 188 °C. ^1H NMR (400 MHz, d^6-DMSO) δ: 8.27 (m, 2H), 8.20 (s, 1H), 7.93 (d, 2H, J = 7.6 Hz), 7.77 (d, 2H, J = 8.8 Hz), 7.61 (t, 1H, J = 7.6 Hz), 7.23 (m, 3H), 2.66 (s, 3H). ^{13}C NMR (125 MHz, d^6-DMSO) δ: 198.0, 166.0, 160.7, 153.9, 150.3, 141.5, 140.0, 137.5, 135.6, 131.3, 129.4, 128.2, 126.9, 126.4, 121.9, 119.1, 117.2, 26.9. IR (neat, cm^{-1}): 3000-4000 (br), 1674, 1651, 1585, 1418, 1231, 896, 770. Anal. Calcd for $C_{20}H_{15}NO_4$: C, 72.06; H, 4.54. Found: C, 71.68; H, 4.41.



[2,3']Bipyridinyl-6-ylamine (Table 3, Entry 4). The general procedure was used with 6-chloro-pyridin-2-ylamine (129 mg, 1.00 mmol), 3-pyridylboronic acid (184 mg, 1.50 mmol), $Pd(OAc)_2$ (2.2 mg, 0.010 mmol, 1 mol %), sodium 2-

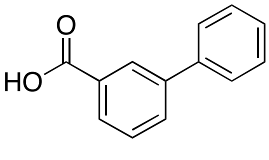
dicyclohexylphosphino-2’,6’-dimethoxybiphenyl-3’-sulfonate (10.0 mg, 0.020 mmol, 2 mol %), K_2CO_3 (414 mg, 3.00 mmol), water (2.0 mL), 12 h, 100 °C. The product was purified by column chromatography on silica gel (eluting with ethyl acetate/methanol, 9.5/0.5) to give the desired product as a white solid (145 mg, 85%). Mp = 108 °C. ^{1}H NMR (400 MHz, d^4-MeOH) δ: 8.69 (d, 1H, J = 4.8 Hz), 8.43 (dd, 1H, J = 4.8 Hz, 1.6 Hz), 8.19 (d, 1H, J = 4.8 Hz), 7.96 (dq, 1H, J = 8.0 Hz, 1.6 Hz, 0.4 Hz), 7.75 (dd, 1H, J = 8.8 Hz, 2.4 Hz), 7.44 (qd, 1H, J = 4.8 Hz, 8.8 Hz), 6.68 (d, 1H, J = 8.4 Hz). ^{13}C NMR (125 MHz, d^4-MeOH) δ: 161.0, 148.2, 147.4, 146.5, 137.9, 136.0, 135.4, 125.6, 123.4, 110.6. IR (neat, cm^{-1}): 3396 (br), 2522, 1633, 1018. EI-MS: Theoretical [M + H] = 172.0869. Found: 172.0868. Anal. Calcd for $C_{10}H_9N_3$: C, 70.16; H, 5.30. Found: C, 69.89; H, 5.25.



5-Furan-3-yl-thiophene-2-carboxylic acid (Table 3, Entry 5). The general procedure was used with 5-bromothiophene carboxylic acid (206 mg, 1.00 mmol), 3-furanboronic acid (168 mg, 1.50 mmol), $Pd(OAc)_2$ (2.2 mg, 0.010 mmol, 1 mol %), sodium 2-dicyclohexylphosphino-2’,6’-dimethoxybiphenyl-3’-sulfonate (10.0 mg, 0.020 mmol, 2 mol %), K_2CO_3 (414 mg, 3.00 mmol), water (5.0 mL), 12 h, 100 °C. The product was isolated as a white solid (181 mg, 94%).

Using microwave irradiation: The general procedure was used with 5-bromothiophene carboxylic acid (206 mg, 1.00 mmol), 3-furanboronic acid (168 mg, 1.50 mmol), $Pd(OAc)_2$ (2.2 mg, 0.010 mmol, 1 mol %), sodium 2-dicyclohexylphosphino-2’,6’-dimethoxybiphenyl-3’-sulfonate (10.0 mg, 0.020 mmol, 2 mol %), K_2CO_3 (414 mg, 3.00 mmol), water (5.0 mL), 10 min, 150 °C (using microwave irradiation with cooling). The product was isolated as a white solid (183 mg, 95%). Mp = 147 °C. ^{1}H NMR (400 MHz, d^4-MeOH) δ: 7.89 (m, 1H), 7.65 (d, 1H, J = 4.0 Hz), 7.54 (t, 1H, J = 1.6 Hz), 7.15 (d, 1H, J = 4.0 Hz), 6.69 (m, 1H). ^{13}C NMR (125 MHz, d^4-MeOH) δ: 165.4, 145.6, 143.7, 140.9, 135.5, 132.9, 125.2, 121.5, 109.9. IR (neat, cm^{-1}): 3200 (br), 1672, 1287. Anal. Calcd for $C_9H_6O_3S$: C, 55.66; H, 3.11. Found: C, 55.50; H, 3.32.

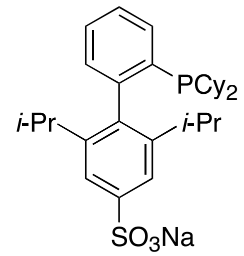
Table 4. Screening of conditions of Suzuki-Miyaura coupling of **1** and **2**.



Biphenyl-3-carboxylic acid[2] The general procedure was used with 3-chlorobenzoic acid (157 mg, 1.00 mmol), phenylboronic acid (145 mg, 1.20 mmol), $Pd(OAc)_2$ (4.5 mg, 0.020 mmol, 2 mol %), sodium 2-

dicyclohexylphosphino-2',6'-dimethoxybiphenyl-3'-sulfonate (20.0 mg, 0.040 mmol, 4 mol %), K_2CO_3 (345 mg, 2.50 mmol), solvent (see Table 4) (2.0 mL), 14 h, temperature. The conversion and yield were determined using ^{1}H NMR.

Preparation of Water-Soluble Ligand [Eq. (3)]:



Sodium 2'-(Dicyclohexyl-phosphanyl)-2,6-diisopropyl-biphenyl-4-sulfonate [Eq. (3)], (4). To an oven-dried 25 mL round bottom flask equipped with a Teflon-coated magnetic stir bar and rubber septum was added dicyclohexyl-(2',4',6'-triisopropyl-biphenyl-2-yl)-phosphane (476 mg, 1.00 mmol) and CH_2Cl_2 (1.0 mL). The solution was cooled to 0 °C using an ice/water bath and then concentrated H_2SO_4 (1.00 mL) and fuming sulfuric acid (3.0 mL, 20% SO_3) were added dropwise. The solution was allowed to warm to room temperature and stir for 24 h. At this time it was cooled to 0 °C using an ice/water bath and crushed ice (~10 g) was added. The solution turned cloudy and white in color. An aqueous solution of NaOH (6.0 M, ~20.0 mL) was then added dropwise to the cooled solution until it became neutral (pH ~7.0 as judged by pH paper). The aqueous solution was extracted with CH_2Cl_2 (3 x 50 mL) and concentrated under reduced pressure to give a beige solid. The crude material was then dissolved in a minimum amount of cold methanol (~20 mL), filtered and concentrated (this cycle was repeated) to give the desired product as a beige solid (503 mg, 94%). Mp = >250 °C ^{1}H NMR (400 MHz, CD_3OD) δ: 7.52 (s, 2H), 7.46 (m, 1H), 7.22 (m, 2H), 6.90 (m, 1H), 2.24 (m, 1H), 0.71-1.83 (34H). ^{13}C NMR (125 MHz, CD_3OD) δ: 148.4, 147.9, 147.8, 147.5, 145.6, 142.8, 137.4, 137.2, 133.92, 133.91, 132.43, 132.42, 129.3, 128.1, 121.3, 121.0, 40.1, 39.9, 39.7, 39.5, 39.3, 38.8, 35.8, 35.7, 32.5, 32.3, 31.9, 30.8, 30.6, 28.7, 28.6, 28.4, 28.3, 27.7, 26.0, 25.9, 23.3, 23.1. ^{31}P NMR (162 MHz, CD_3OD) δ: -10.7. IR (neat, cm^{-1}): 3459, 2927, 2851, 1634, 1463, 1447, 1184, 1078, 1040. Anal. Calcd for $C_{30}H_{42}NaO_3PS$: C, 67.14; H, 7.89. Found: C, 66.93; H, 7.77.

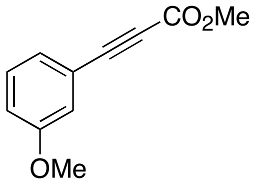
General Procedure for Sonogashira coupling in Water/Acetonitrile. A disposable tube with a screw cap, Teflon septum and stir bar was charged with $PdCl_2(CH_3CN)_2$ (3.2 mg, 0.0125 mmol, 1.25 mol %), sodium 2'-(dicyclohexyl-phosphanyl)-2,6-diisopropyl-biphenyl-4-sulfonate (20.0 mg, 0.0375 mmol, 3.75 mol %), aryl halide (0.500 mmol) and Cs_2CO_3 (406-813 mg, 1.25-2.50 mmol). The tube was evacuated and back-filled with argon (this was repeated two additional times). Acetonitrile (3.0 mL) was added and the reaction mixture was allowed to stir at room temperature for 20 minutes. The alkyne (0.650 mmol) and degassed water (1.0-1.5 mL, sonicated under vacuum for 2 min) were added and the reaction mixture was allowed to stir at the noted temperature. After cooling to room temperature the following work-up procedure was followed:

Table 5, entries 1,2,4,8: The reaction mixture was acidified with HCl (2.0 M) to pH~5 (as judged by pH paper) and extracted out with ethyl acetate. The organic layer was dried over anhydrous $MgSO_4$, filtered through celite and concentrated to give the crude product. To the crude material was added diethyl ether (10.0 mL), methanol (5.0 mL) and then trimethylsilyldiazomethane (2.0 mL, 2.0 M solution in dietyl ether, 4.0 mmol). The solution was allowed to stir for 5 minutes after which it was filtered and concentrated. The product was purified by column chromatography on silica gel (eluting with ether/hexane mixtures).

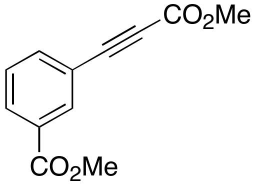
Table 5, entries 6,7: The products were extracted out of the water layer with ethyl acetate, dried over $MgSO_4$, filtered through celite and concentrated to dryness. The product was purified by column chromatography on silica gel (eluting with hexanes).

Table 5, entries 3,5: The reaction was acidified with HCl (2.0 M) to pH~5 (as judged by pH paper) and extracted out with ethyl acetate. The organic layer was dried over anhydrous $MgSO_4$, filtered through celite and concentrated to give the crude product. The product was purified by crystallization from water.

Table 5. Sonogashira coupling of aryl halides using ligand **4**.

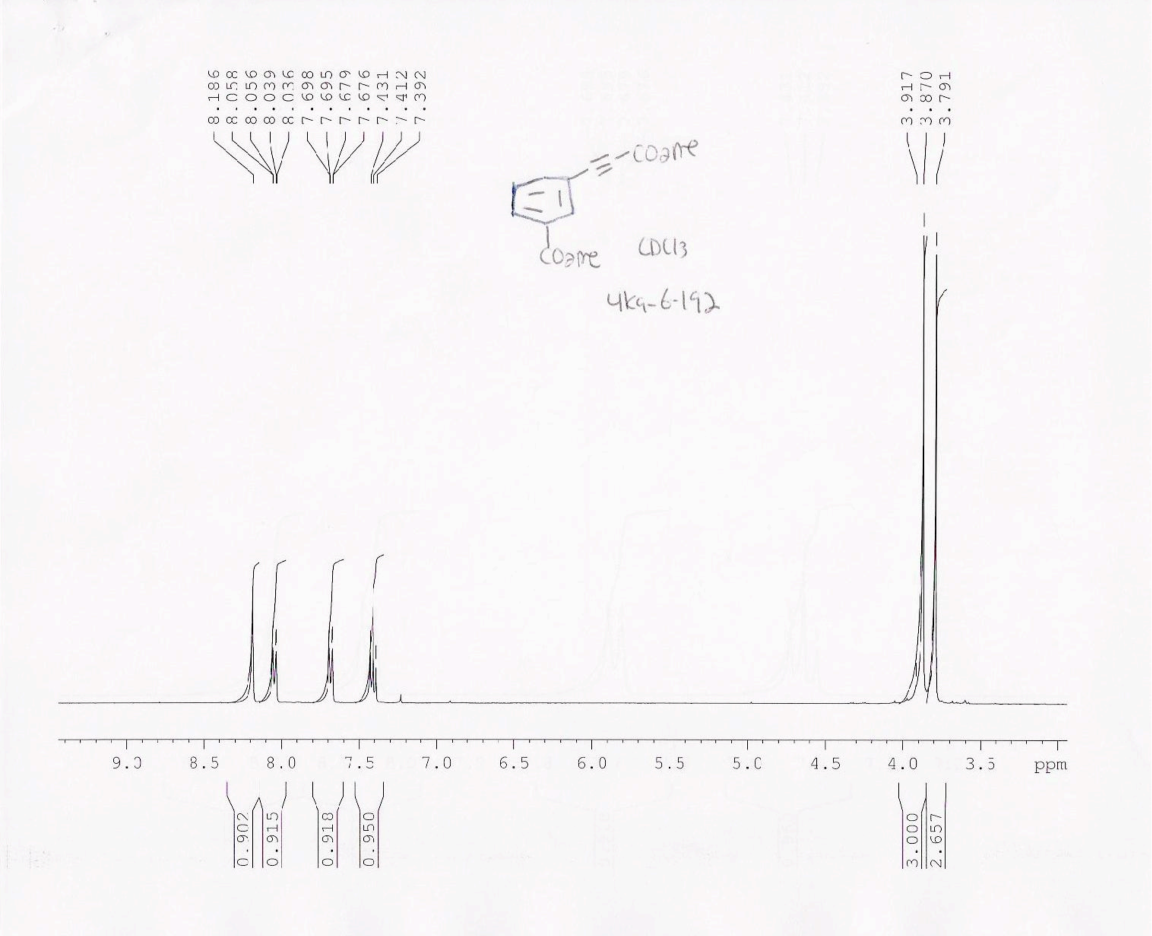


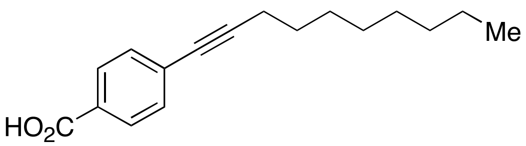
(3-Methoxy-phenyl)-propynoic acid methyl ester (Table 5, entry 1).[10] The general procedure was used with 3-bromoanisole (0.063 mL, 0.50 mmol), propiolic acid (added at 0 °C) (0.050 mL, 0.65 mmol), $PdCl_2(CH_3CN)_2$ (3.2 mg, 0.0125 mmol, 1.25 mol %), sodium 2'-(dicyclohexyl-phosphanyl)-2,6-diisopropyl-biphenyl-4-sulfonate (20.0 mg, 0.0375 mmol, 3.75 mol %), Cs_2CO_3 (650 mg, 2.00 mmol), water (1.0 mL), acetonitrile (1.0 mL), 12 h, 60 °C. The product was isolated as a colorless oil (66 mg, 69%). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.28 (t, 1H, J = 7.6 Hz, 8.4 Hz), 7.17 (dt, 1H, J = 1.2 Hz, 7.6 Hz), 7.09 (m, 1H), 7.00 (qd, 1H, J = 1.2 Hz, 2.4 Hz, 8.4 Hz), 3.84 (s, 3H), 3.80 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 159.4, 154.6, 129.9, 125.6, 120.5, 117.7, 117.6, 86.6, 80.2, 55.5, 52.9.



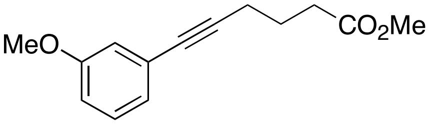
3-Methoxycarbonylethynyl-benzoic acid methyl ester (Table 5, entry 2). The general procedure was used with 3-bromobenzoic acid (101 mg, 0.50 mmol), propiolic acid (added at 0 °C) (0.050 mL, 0.65 mmol), $PdCl_2(CH_3CN)_2$ (3.2 mg, 0.0125 mmol, 1.25 mol %), sodium 2'-(dicyclohexyl-phosphanyl)-2,6-diisopropyl-biphenyl-4-sulfonate (20.0 mg, 0.0375 mmol, 3.75 mol %), Cs_2CO_3 (813 mg, 2.50 mmol), water (1.0 mL), acetonitrile (1.0 mL), 12 h, 60 °C. The product was isolated as a white solid (77 mg, 70%). Mp = 96-97 °C ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.19 (m, 1H), 8.04 (d, 1H, J = 8.0 Hz), 7.68 (d, 1H, J = 7.6 Hz), 7.41 (t, 1H, J = 7.6 Hz), 3.87 (s, 3H), 3.79 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 165.9, 154.3, 136.9, 134.2, 131.7, 130.9, 128.9, 120.1, 85.1, 81.0, 53.0, 52.6. IR (neat, cm^{-1}): 3022, 2963, 2231, 1738, 1718, 1437, 1290, 1259, 1197, 1173, 1101, 749. Anal. Calcd for $C_{12}H_{10}O_4$: C, 66.05; H, 4.62. Found: C, 65.95; H, 4.60

^{1}H NMR ($CDCl_3$):



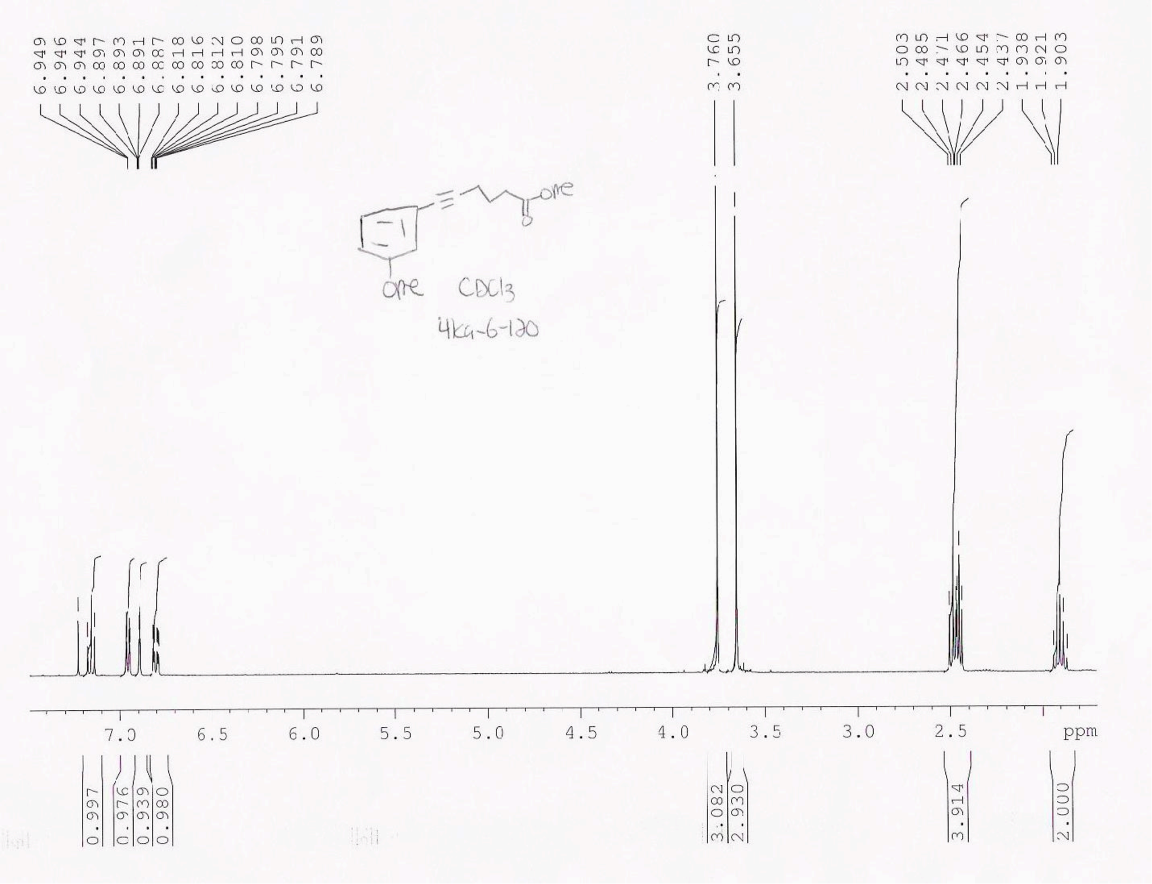


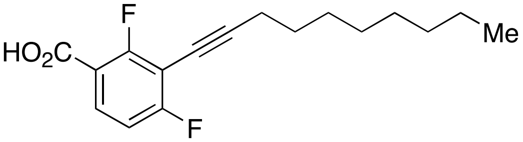
4-Dec-1-ynyl-benzoic acid (Table 5, entry 3). The general procedure was used with 4-chlorobenzoic acid (79 mg, 0.50 mmol), 1-decyne (0.136 mL, 0.75 mmol), $PdCl_2(CH_3CN)_2$ (3.2 mg, 0.0125 mmol, 1.25 mol %), sodium 2'-(dicyclohexyl-phosphanyl)-2,6-diisopropyl-biphenyl-4-sulfonate (20.0 mg, 0.0375 mmol, 3.75 mol %), Cs_2CO_3 (650 mg, 2.00 mmol), water (1.0 mL), acetonitrile (1.0 mL), 12 h, 100 °C. The product was isolated as a white solid (111 mg, 86%). Mp = 103 °C. ^1H NMR (400 MHz, $CDCl_3$) δ: 11.0 (br-s, 1H), 8.04 (d, 2H, J = 8.4 Hz), 7.49 (d, 2H, J = 8.4 Hz), 2.46 (t, 2H, J = 6.8 Hz), 1.64 (p, 2H, J = 6.8 Hz), 0.89-1.49 (m, 13H). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 169.3, 132.6, 130.9, 130.8, 130.4, 94.6, 81.2, 33.2, 30.5, 30.4, 30.2, 29.9, 23.9, 20.2, 14.6 IR (neat, cm^{-1}): 3402 (br), 2920, 2849, 2214, 1686, 1607, 1428, 1319, 1283, 1178, 1112, 929, 862, 769. Anal. Calcd for $C_{17}H_{22}O_2$: C, 79.03; H, 8.58. Found: C, 78.84; H, 8.48.



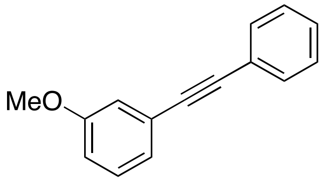
6-(3-Methoxy-phenyl)-hex-5-ynoic acid methyl ester (Table 5, entry 4). The general procedure was used with 3-chloroanisole (0.061 mL, 0.50 mmol), 5-hexynoic acid (0.072 mL, 0.65 mmol), $PdCl_2(CH_3CN)_2$ (3.2 mg, 0.0125 mmol, 1.25 mol %), sodium 2'-(dicyclohexyl-phosphanyl)-2,6-diisopropyl-biphenyl-4-sulfonate (20.0 mg, 0.0375 mmol, 3.75 mol %), Cs_2CO_3 (650 mg, 2.00 mmol), water (1.0 mL), acetonitrile (1.0 mL), 10 h, 100 °C. The product was isolated as a colorless oil (60 mg, 85%). ^1H NMR (400 MHz, $CDCl_3$) δ: 7.16 (t, 1H, J = 8.0 Hz), 6.96 (dt, 1H, J = 1.2 Hz, 7.6 Hz), 6.89 (m, 1H), 6.80 (qd, 1H, J = 1.2 Hz, 2.4 Hz, 8.4 Hz), 3.76 (s, 3H), 3.66 (s, 3H), 2.48 (t, 2H, J = 7.2 Hz), 2.45 (t, 2H, J = 6.8 Hz), 1.90 (q, 2H, J = 6.8 Hz). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 173.8, 159.4, 129.5, 124.9, 124.3, 116.6, 114.5, 88.9, 81.6, 55.4, 51.8, 33.1, 24.1, 19.1. IR (neat, cm^{-1}): 2952, 2232, 1737, 1598, 1574, 1481, 1434, 1316, 1287, 1206, 1164, 1045, 854, 786, 688. Anal. Calcd for $C_{14}H_{16}O_3$: C, 72.39; H, 6.94. Found: C, 72.22; H, 6.85

^{1}H NMR ($CDCl_3$):

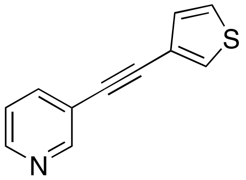




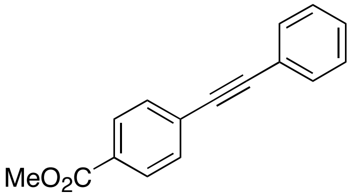
3-Dec-1-ynyl-2,4-difluoro-benzoic acid (Table 5, entry 5). The general procedure was used with 3-chloro-2,4-difluoro-benzoic acid (97 mg, 0.50 mmol), 1-decyne (0.136 mL, 0.75 mmol), $PdCl_2(CH_3CN)_2$ (3.2 mg, 0.0125 mmol, 1.25 mol %), sodium 2'-(dicyclohexyl-phosphanyl)-2,6-diisopropyl-biphenyl-4-sulfonate (20.0 mg, 0.0375 mmol, 3.75 mol %), Cs_2CO_3 (650 mg, 2.00 mmol), water (1.0 mL), acetonitrile (1.0 mL), 12 h, 100 °C. The product was isolated as a white solid (102 mg, 70%). Mp = 117 °C. ^{1}H NMR (400 MHz, d^6-DMSO) δ: 10.1 (br-s, 1H), 7.88 (q, 1H, J = 8.8 Hz), 7.26 (t, 1H, J = 8.4 Hz), 2.51 (t, 2H, J = 6.8 Hz), 1.57 (p, 2H, J = 6.8 Hz), 0.80-1.43 (m, 13H). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 168.7, 167.9, 165.3, 162.6, 132.3, 132.2, 114.1, 111.7, 111.5, 104.8, 103.1, 66.7, 32.0, 29.4, 29.3, 28.9, 28.5, 22.9, 20.0, 14.3. IR (neat, cm^{-1}): 3428 (br), 2922, 2848, 2235, 1689, 1611, 1406, 1268, 1242, 1051, 1036. Anal. Calcd for $C_{17}H_{20}F_2O_2$: C, 69.37; H, 6.85. Found: C, 69.13; H, 6.80.



1-Methoxy-3-(phenlethynyl)-benzene (Table 5, entry 6).[11] The general procedure was used with 3-chloroanisole (0.063 mL, 0.50 mmol), phenylacetylene (0.072 mL, 0.65 mmol), $PdCl_2(CH_3CN)_2$ (3.2 mg, 0.0125 mmol, 1.25 mol %), sodium 2'-(dicyclohexyl-phosphanyl)-2,6-diisopropyl-biphenyl-4-sulfonate (20.0 mg, 0.0375 mmol, 3.75 mol %), Cs_2CO_3 (650 mg, 2.00 mmol), water (1.0 mL), acetonitrile (1.5 mL), 12 h, 100 °C. The product was isolated as a white solid (99 mg, 95%). Mp = 70 °C (lit. 72-74 °C)[11]. ^1H NMR (400 MHz, $CDCl_3$) δ: 7.62 (m, 2H), 7.41 (m, 3H), 7.32 (t, 1H, J = 7.6 Hz), 7.23 (dt, 1H, J = 1.2 Hz, 7.6 Hz), 7.15 (m, 1H), 6.96 (qd, 1H, J = 1.2 Hz, 2.4 Hz, 7.6 Hz). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 159.5, 131.8, 129.6, 128.5, 128.48, 124.4, 124.3, 123.3, 116.5, 115.1, 89.5, 89.4, 55.4.



3-(3-Thienylethynyl)-pyridine (Table 5, entry 7).[12] The general procedure was used with 3-chloropyridine (0.050 mL, 0.50 mmol), 3-ethynylthiophene (0.074 mL, 0.75 mmol), $PdCl_2(CH_3CN)_2$ (3.2 mg, 0.0125 mmol, 1.25 mol %), sodium 2'-(dicyclohexyl-phosphanyl)-2,6-diisopropyl-biphenyl-4-sulfonate (20.0 mg, 0.0375 mmol, 3.75 mol %), Cs_2CO_3 (650 mg, 2.00 mmol), water (1.0 mL), acetonitrile (1.5 mL), 10 h, 100 °C. The product was isolated as a white solid (86 mg, 93%). Mp = 62 °C (lit. 65.5-64.0 °C)[12]. ^1H NMR (400 MHz, $CDCl_3$) δ: 8.75 (d, 1H, J = 1.6 Hz), 8.54 (dd, 1H, J = 2.0 Hz, 5.2 Hz), 7.79 (dt, 1H, J = 8.0 Hz, 2.0 Hz), 7.57 (dd, 1H, J = 2.8 Hz, 1.2 Hz), 7.32 (dd, 1H, J = 5.2 Hz, 2.8 Hz), 7.27 (qd, 1H, J = 0.8 Hz, 4.8 Hz, 3.2 Hz), 7.21 (dd, 1H, J = 1.2 Hz, 5.2 Hz). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 152.4, 148.7, 138.5, 129.9, 129.6, 125.9, 123.2, 121.8, 120.6, 87.9, 85.7.



Methyl-4-(phenylethynyl) benzoate (Table 5, entry 8).[13] The general procedure was used with 4-chlorobenzoic acid (79 mg, 0.50 mmol), phenylacetylene (0.072 mL, 0.65 mmol), $PdCl_2(CH_3CN)_2$ (3.2 mg, 0.0125 mmol, 1.25 mol %), sodium 2'-(dicyclohexyl-phosphanyl)-2,6-diisopropyl-biphenyl-4-sulfonate (20.0 mg, 0.0375 mmol, 3.75 mol %), Cs_2CO_3 (650 mg, 2.00 mmol), water (1.0 mL), acetonitrile (1.5 mL), 12 h, 100 °C. The product was isolated as a white solid (101 mg, 86%). Mp = 114 °C (lit. 113-115 °C)[13]. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.04 (d, 2H, J = 8.4 Hz), 7.61 (d, 2H, J = 8.4 Hz), 7.57 (m, 2H), 7.39 (m, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 166.6, 131.9, 131.6, 129.64, 129.56, 128.9, 128.6, 128.1, 122.8, 92.5, 88.8, 52.3.

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