Supplementary Material (ESI) for Chemical Communications

Simple mixed Fe-Zn catalysts for the Suzuki couplings of tetraarylborates with benzyl halides and 2-halopyridines

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Electronic Supporting Information

General information. All reagents were purchased from commercial suppliers and used without further purification. All experiments were carried out under nitrogen. Solvents were dried and purified using Anhydrous Engineering double alumina and alumina-copper catalyst dry columns then degassed prior to use. Flash chromatography was carried out with fluorochem silica gel LC60A-40-63 micron. ^{1}H-NMR and ^{13}C-NMR (300 or 400 MHz and 100 MHz, respectively) spectra were recorded on a Varian 400MHz or 500MHz spectrometers using $CDCl_3$ as solventMass spectra were recorded on a VG Autospec Triple Sector Mass Spectrometer or a Waters Micromass ZQ LC-MS system.

Synthesis of di-*p*-tolylzinc, 0.25M in THF. Anhydrous $ZnCl_2$ beads (1.362 g, 10 mmol) were added to a Schlenk tube under nitrogen and dissolved in THF (20 ml). *p*-Tolylmagnesium chloride (2.0M in THF, 10 ml) was added dropwise while stirring. The resultant mixture was filtered *via* cannula into a Young's flask and made up to a total volume of 40 ml with THF.

Synthesis of Li[BPhBu$_3$]. A solution of tributyl borane (1M in Et_2O) was cooled down to -78 °C and 1 eq. of a cold (5 °C) phenyllithium solution (1.8M in *n*-Bu_2O) was added slowly. The resulting solution was stirred for another 30 min at -78 °C before allowing it to warm to room temperature and stirring for f further 30 min. The resulting solution was then ready for use.

General Procedure for the iron-catalysed Negishi Coupling of pyridine derivatives with di-*p*-tolyl zinc, GP 1 (Table 1). Complex **1** (0.05 g, 0.05 mmol) and the appropriate pyridine compound (1.0 mmol) were added to a Radleys® Carousel tube under nitrogen. Toluene (6 ml) was added and the mixture was stirred and heated to 100 ^{o}C. Pre-prepared di-*p*-tolylzinc (0.25 M, 4.8 ml) was added and the reaction stirred at 100^{o}C for 4 hour. Upon cooling, the reaction was quenched with H_2O (5 ml), extracted into CH_2Cl_2 (3x10 ml), dried over $MgSO_4$ and filtered. 1,3,5-Trimethoxybenzene (1 mmol) was added as an internal standard. An aliquot (2 ml) was removed from which the solvent was removed at room temperature under reduced pressure. The residue was dissolved in $CDCl_3$ (approx. 0.7 ml) and the conversion to coupled product was determined by ^{1}H NMR spectroscopy. Alternatively the crude product obtained after the filtration step was purified by flash chromatography.

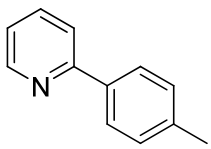
Optimisation of iron-catalysed Suzuki coupling of benzyl halides co-catalysed by zinc reagents (Table 2). To a THF solution of anhydrous $ZnCl_2$ (0.7M, 0.14 ml) in a Radleys® Carousel tube under nitrogen was added the appropriate arylmagnesium bromide (THF solution, 1.0M, 0.20 mmol). Toluene (2 ml) was added and the mixture stirred for 1 hour at room temperature. Alternatively, where specified in Table 2, the diarylzinc solution was replaced with either a hexane solution of $ZnEt_2$ (1M, 0.10 ml) and toluene (2 ml) or a THF solution of anhydrous $ZnCl_2$ (0.7M, 0.14 ml) and toluene (2 ml). Complex **1** (0.050 g, 0.05 mmol), the appropriate boron source (1.25 mmol), the appropriate benzyl halide (1.00 mmol) and toluene (6 ml) were added. The reaction was warmed to 85 °C (external

temperature) and stirred for 4 hours. The reaction was quenched with H_2O (5 ml) and the organic component extracted with CH_2Cl_2 (2 x 10 ml), dried over $MgSO_4$ and then filtered. 1,3,5-Trimethoxybenzene (1.00 ml, 1.00 M in CH_2Cl_2) was added as an internal standard. An aliquot (2 ml) was removed from which the solvent was removed at room temperature under reduced pressure. The residue was dissolved in $CDCl_3$ (approx. 0.7 ml) and the conversion to coupled product was determined by ^1H NMR spectroscopy. Alternatively the crude product obtained after the filtration step was purified by flash chromatography.

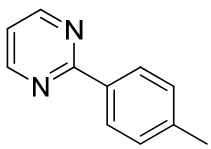
General procedure for the iron-catalysed Suzuki coupling of benzyl halides co-catalysed by diarylzinc reagents, GP 2 (Table 3, entries 1 – 13). To a THF solution of anhydrous $ZnCl_2$ (0.7M, 0.14 ml) in a Radleys® Carousel tube under nitrogen was added 4-anisylmagnesium bromide (THF solution, 1.0M, 0.20 mmol). Toluene (2 ml) was added and the mixture stirred for 1 hour at room temperature to produce the diarylzinc reagent. Complex **1** (0.050 g, 0.05 mmol), the appropriate tetraarylborate salt (1.25 mmol), the appropriate benzyl halide (1.00 mmol) and toluene (6 ml) were added. The reaction was warmed to 85 °C (external temperature) and stirred for 4 hours. Analysis and work-up as described above.

General procedure for the iron-catalysed Suzuki coupling of 2-bromopyridine derivatives co-catalysed by diarylzinc reagents, GP 3 (Table 3, entries 14 – 18). To a THF solution of anhydrous $ZnCl_2$ (0.7M, 1.4 ml) in a Radleys® Carousel tube under nitrogen was added 4-anisylmagnesium bromide (THF solution, 1.0M, 2.00 mmol) and the mixture stirred for 1 hour at room temperature to produce the diarylzinc reagent. Complex **1** (0.050 g, 0.05 mmol), sodium tetraphenylborate (0.427 g, 1.25 mmol), the appropriate 2-halopyridine (1.00 mmol) and toluene (6 ml) were added. The reaction was heated to 115 °C (external temperature) and stirred for 16 hours. Analysis and work-up as described above.

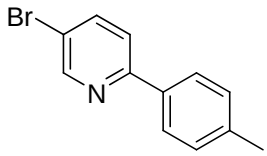
2-(*p*-tolyl)pyridine (Table 1, entry 1). Prepared according to the **GP 1** using 2-bromopyridine (95 µl, 1.0 mmol) and di-*p*-tolylzinc (1.2 mmol). Purification by flash chromatography (silica, hexane/DCM, 2:1 → DCM) yielded the coupling product as a colourless oil (0.083g, 49%). NMR: δ_H (400 MHz, $CDCl_3$) 8.68 (dt, J = 4.95, 1.28 Hz, 1H), 7.89 (dt, J = 8.43, 2.02 Hz, 2H), 7.67-7.74 (m, 2H), 7.28 (d, J = 8.43 Hz, 2H), 7.17-7.21 (m, 1H), 2.40 (s, 3H); δ_C (100 MHz, $CDCl_3$) 157.5, 149.6, 138.9, 136.6, 129.4, 126.7, 121.8, 120.2, 21.2. MS-EI: (m/z): 169 ($[M]^+$, 100), 168 (85), 167 (32), 86 (17), 84 (27).



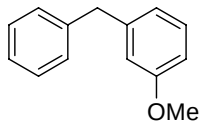
2-(*p*-tolyl)pyrimidine (Table 1, entry 6). Prepared according to **GP 1** using 2-bromopyrimidine (159 mg, 1.00 mmol) and di-*p*-tolylzinc (1.2 mmol). Purification by flash chromatography (silica, hexane/DCM, 2:1 → DCM) yielded the coupling product as a white solid (0.100g, 58%), NMR: δ_H (400 MHz, $CDCl_3$) 8.76 (d, J = 4.77 Hz, 2H), 8.33 (dt, J = 8.25, 1.83 Hz, 2H), 7.30 (d, J = 8.25 Hz, 2H), 7.13 (t, J = 4.86 Hz, 1H), 2.41 (s, 3H); δ_C (100 MHz, $CDCl_3$) 165.0, 157.1, 141.2, 135.0, 129.3, 128.0, 118.7, 21.4. MS-EI: (m/z): 170 ($[M]^+$, 100), 169 (97), 117 (40), 116 (18), 84 (18).



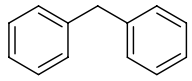
2-(*p*-tolyl)-5-bromopyridine (Table 1, entry 10). Prepared according to **GP 1** using 2,5-dibromopyridine (159 mg, 1.00 mmol) and di-*p*-tolylzinc (1.2 mmol). Purification by flash chromatography (silica, hexane/DCM, 2:1 → DCM) yielded the coupling product as a white solid (0.123g, 50%), NMR: δ_H (400 MHz, $CDCl_3$) 8.70 (dd, J = 2.38, 0.73 Hz, 1H), 7.81-7.88 (m, 3H), 7.59 (dd, J = 8.43, 0.73 Hz, 1H), 7.27 (d, J = 7.88 Hz, 2H), 2.41 (s, 3H); δ_C (100 MHz, $CDCl_3$) 155.9, 150.6, 139.4, 139.2, 135.4, 129.6, 126.6, 121.3, 118.9, 21.3. MS-EI: (m/z): 247 ($[M]^+$, 100), 246 (58), 167 (36), 86 (40), 84 (64).



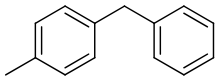
1-Benzyl-3-methoxybenzene (3-Benzylanisole) (Table 3, entry 1). Prepared according to **GP 2** using 3-methoxybenzyl bromide (0.201 g, 1.00 mmol) and sodium tetraphenylborate (0.427 g, 1.25 mmol). Purification by flash chromatography (silica, hexane/ethyl acetate 99:1) yielded the coupling product as a yellow oil (0.174 g, 88%). NMR: (400 MHz, $CDCl_3$) δ_H 7.29-7.33 (m, 2H), 7.20-7.25(m, 4H), 6.82 (d, J = 7.6 Hz, 1H),6.76-6.79 (m, 2H), 3.98 (s,2H), 3.79 (s, 3H); δ_C (100 MHz, $CDCl_3$) 42.0, 55.1, 111.3, 114.8, 121.4, 126.1, 128.4, 128.9, 129.4, 140.9, 142.7, 159.7. MS-EI: (m/z): 198 ($[M]^+$, 100), 183 (20), 167 (49), 153 (24), 91 (31).



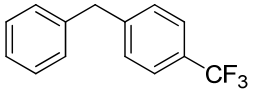
Diphenylmethane (Table 3, entry 3). Prepared according to **GP 2** using benzyl bromide (0.171 g, 1.00 mmol) and sodium tetraphenylborate (0.427 g, 1.25 mmol). Purification by flash chromatography (silica, hexane/DCM 99.5:0.5) yielded the coupling product as a colourless oil (0.106 g, 63%). NMR: δ_H (400 MHz, $CDCl_3$) 7.31-7.34 (m, 4H) 7.22-7.25 (m, 6H), 4.02 (s, 2H); δ_C (100 MHz, $CDCl_3$) 41.9, 126.0, 128.4, 128.9, 141.1. MS-EI: (m/z): 168 ($[M]^+$, 100), 152 (21), 91 (28).



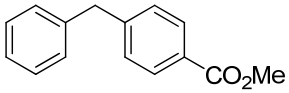
1-Benzyl-4-methylbenzene (Table 3, entries 5 and 12). Prepared according to **GP 2** using 4-methylbenzyl bromide (0.185 g, 1.00 mmol) and sodium tetraphenylborate (0.427 g, 1.25 mmol) *or* using benzyl bromide (0.086 g, 0.50 mmol) and potassium tetratolylborate (0.310 g, 0.625 mmol). Purification (entry 5) by flash chromatography (silica, hexane/DCM 99.5:0.5) yielded the coupling product as a colourless oil (0.110 g, 61%). NMR: δ_H (400 MHz, $CDCl_3$) 7.29-7.33 (m, 2H), 7.19-7.24 (m, 2H), 7.12 (s, 4H), 3.98 (s, 2H), 2.35 (s, 3H); δ_C (100 MHz, $CDCl_3$) 21.0, 41.5, 125.9, 128.4, 128.8, 128.9, 129.1, 135.5, 138.0, 141.4. MS-EI: (m/z): 182 ($[M]^+$, 75), 167 (75), 152(12), 91 (17), 84 (50).



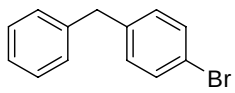
1-Benzyl-4-(trifluoromethyl)benzene (Table 3, entry 6). Prepared according to **GP 2** using 1-bromo-4-(trifluoromethyl)benzene (0.239 g, 1.00 mmol) and sodium tetraphenylborate (0.427 g, 1.25 mmol). Purification by flash chromatography (silica, hexane/ethyl acetate/NEt_3 98.5:0.5:1) yielded the coupling product as a colourless oil (0.212 g, 90%). NMR: δ_H 7.55 (d, *J*= 7.83 Hz, 2H), 7.30-7.34 (m, 4H), 7.22-7.26 (m, 1H), 7.19 (dd, *J*= 7.83 Hz, *J*= 0.98 Hz, 2H), 4.05 (s, 2H), δ_C (125 MHz, $CDCl_3$) 41.7, 124.3 (q, *J*= 272 Hz), 125.4 (q, *J*= 4 Hz), 126.5, 128.5 (q, *J*= 33 Hz), 128.6, 128.9, 129.2, 140.0, 145.2.



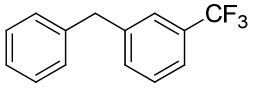
Methyl 4-benzylbenzoate (Table 3, entry 7). Prepared according to **GP 2** using methyl 4-(bromomethyl)benzoate (0.229 g, 1.00 mmol) and sodium tetraphenylborate (0.427 g, 1.25 mmol). Purification by flash chromatography (silica, hexane/ethyl acetate 95:5) yielded the coupling product as a yellow oil (0.180 g, 80%). NMR: δ_H 7.97 (d, *J*= 8.31 Hz, 2H), 7.28-7.33 (m, 3H), 7.22-7.26 (m, 2H), 7.17-7.20, 4.05 (s, 2H), 3.91 (3 H); δ_C (100 MHz, $CDCl_3$) 41.9, 52.0, 126.4, 128.1, 128.6, 128.9, 129.8, 140.1, 146.5, 167.0. MS-EI: (m/z): 226 ($[M]^+$, 47), 195 (42), 167 (100), 152 (27), 91 (40).



1-Benzyl-4-bromobenzene (Table 3, entry 8). Prepared according to **GP 2** using 4-bromobenzyl bromide (0.250 g, 1.00 mmol) and sodium tetraphenylborate (0.427 g, 1.25 mmol). Purification by flash chromatography (silica, hexane/ethyl acetate 99:1) yielded the coupling product as a colourless oil (0.194 g, 79%). NMR: δ_H (400 MHz, $CDCl_3$) 7.41-7.44 (m, 2H) 7.30-7.34 (m, 2H), 7.22-7.26 (m, 1H), 7.17-7.20 (m, 2H), 7.07-7.10 (m, 2H), 3.96 (s,2H); δ_C (100 MHz, $CDCl_3$) 41.3, 119.9, 126.3, 128.5, 128.8, 130.6, 131.5, 140.1, 140.4. MS-EI: (m/z): 246 ($[M]^+$, 45), 167 (100), 152 (28).

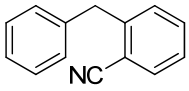


1-Benzyl-3-(trifluoromethyl)benzene (Table 3, entry 10). Prepared according to **GP 2** using 1-bromo-3-(trifluoromethyl)benzene (0.239 g, 1.00 mmol) and sodium tetraphenylborate (0.427 g, 1.25 mmol). Purification by flash chromatography (silica, hexane/ethyl acetate/NEt_3 98.5:0.5:1) yielded the coupling product as a colourless oil (0.174 g, 74%). NMR: δ_H 7.45-7.51 (m, 2H), 7.31-7.43 (m, 4H), 7.23-7.26 (m, 1H), 7.18-7.21 (m, 2H), 4.05 (s, 2H).

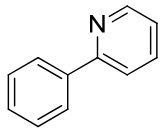


2-Benzylbenzonitrile (Table 3, entry 11). Prepared according to **GP 2** using 2-(bromomethyl)benzonitrile (0.196 g, 1.00 mmol) and sodium tetraphenylborate (0.427 g, 1.25 mmol). Purification by flash chromatography (silica, hexane/ethyl acetate 98:2) yielded the coupling product as a colourless oil (0.135 g, 73%). NMR: δ_H (400 MHz, $CDCl_3$) 7.64 (dd, *J*= 7.70 Hz, *J*= 0.86 Hz, 1H), 7.50 (td, *J*= 7.70 Hz, *J*= 1.22 Hz, 1H), 7.29-7.34 (m, 3H), 7.22-7.34 (m, 3H), 4.22 (s, 2H; δ_C (100 MHz, $CDCl_3$) 40.2, 112.6, 118.2, 126.7, 126.8, 128.7,

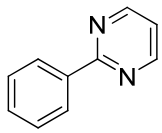
129.0, 130.0, 132.8, 132.9, 138.8, 144.9. MS-EI: (m/z): 193 ([M]$^+$, 100), 192 (57), 165 (40). 91 (28).



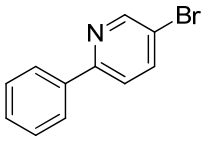
2-Phenylpyridine (Table 3, entry 14). Prepared according to **GP 3** using 2-bromopyridine (0.158 g, 1.00 mmol) and sodium tetraphenylborate (0.427 g, 1.25 mmol). Purification by flash chromatography (silica, hexane/DCM/ethyl acetate 8:1:1) yielded the coupling product as a yellow oil (0.098 g, 64%). NMR: δ_H (400 MHz, $CDCl_3$) 8.71 (dt, *J*=5.01, 1.16 Hz, 1 H) 7.98 - 8.03 (m, 1 H) 7.72 - 7.80 (m, 1 H) 7.46 - 7.53 (m, 1 H) 7.40 - 7.46 (m, 1 H) 7.19 - 7.27 (m, 1 H); δ_C (100 MHz, $CDCl_3$) 120.6, 122.1, 126.9, 128.7, 128.9, 136.7, 139.4, 149.6, 157.5. MS-CI: (m/z): 156 ([M+H]$^+$, 100), 155 ([M]$^+$,27), 154(7), 87 (4), 85 (5).



2-Phenylpyrimidine (Table 3, entry 15). Prepared according to **GP 3** using 2-bromopyrimidine (0.159 g, 1.00 mmol) and sodium tetraphenylborate (0.427 g, 1.25 mmol). Purification by flash chromatography (silica, hexane/DCM/ethyl acetate 12:1:1) yielded the coupling product as a white wax (0.080 g, 51%). NMR: δ_H (400 MHz, $CDCl_3$) 8.83 (d, *J*= 4.89 Hz, 2 H) 8.45 (dd, *J*= 6.85 Hz, 3.18 Hz, 2 H) 7.47-7.54 (m, 3 H) 7.21 (t, *J*= 4.77 Hz, 1 H); δ_C (100 MHz, $CDCl_3$) 119.1, 128.1, 128.6, 130.8, 137.6, 157.2, 164.8. MS-CI: (m/z): 157 ([M+H]$^+$, 100), 156 ([M]$^+$,20), 103 (4), 87 (13), 85 (21), 63 (3).

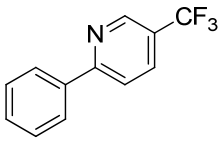


5-Bromo-2-phenylpyridine (Table 3, entry 16). Prepared according to **GP 3** using 2,5-dibromopyridine (0.237 g, 1.00 mmol) and sodium tetraphenylborate (0.427 g, 1.25 mmol). Purification by flash chromatography (silica, hexane/THF 20:1) yielded the coupling product as a white solid (0.090 g, 38%). NMR: δ_H (400 MHz, $CDCl_3$) 8.75 (dd, *J*= 2.45 Hz, *J*= 0.49 Hz, 1 H), 7.94-8.00 (m, 2 H), 7.88 (dd, *J*= 8.56 Hz, *J*= 2.45 Hz, 1 H), 7.64 (d, *J*= 8.31 Hz, 1 H), 7.43-7.53 (m, 4 H); δ_C (100 MHz, $CDCl_3$) 119.3, 121.6, 126.7, 128.9, 129.3, 138.2, 139.3, 150.7, 155.9. MS-CI: (m/z): 234 ([M+H]$^+$, 100), 233 ([M]$^+$, 64), 183 (11), 155 (10), 154 (21).



2-Phenyl-5-(trifluoromethyl)pyridine (Table 3, entry 17). Prepared according to **GP 3** using 2-bromo-5-(trifluoromethyl)pyridine (0.226 g, 1.00 mmol) and sodium tetraphenylborate (0.427 g, 1.25 mmol). Purification by flash chromatography (silica, hexane/DCM/NEt_3 84:16:1) yielded the coupling product as a white solid(0.119 g, 53%). NMR: δ_H (400 MHz, $CDCl_3$) 8.96 (s, 1 H) 8.05 (dd, *J*=8.07, 1.47 Hz, 2 H) 8.00 (dd, *J*=8.31,

2.45 Hz, 1 H) 7.86 (d, *J*=8.31 Hz, 1 H) 7.46-7.56 (m, 3 H). MS-CI: (m/z): 224 ($[M+H]^+$, 100), 223 ($[M]^+$, 32), 204 (68), 100 (6), 87 (28), 85 (42).



Methyl 2-phenylisonicotinate (Table 3, entry 18). Prepared according to **GP 3** using methyl 2-bromoisonicotinate (0.216 g, 1.00 mmol) and sodium tetraphenylborate (0.427 g, 1.25 mmol). Purification by flash chromatography (silica, hexane/DCM/ethyl acetate 85:10:5) yielded the coupling product as a yellow oil (0.110 g, 52%). NMR: δ_H (400 MHz, $CDCl_3$) 8.85 (d, *J*= 5.14 Hz, 1 H), 8.32 (s, 1 H), 8.05-8.10 (m, 2 H), 7.79 (dd, *J*= 4.89 Hz, 1.47 Hz, 1 H), 7.43-7.55 (m, 3 H), 4.01 (s, 3 H); δ_C (100 MHz, $CDCl_3$) 52.8, 119.7, 121.1, 127.0, 128.9, 129.5, 138.2, 138.5, 150.5, 158.5, 165.8. MS-CI: (m/z): 214 ($[M+H]^+$, 100), 213 ($[M]^+$, 33), 182 (4), 155 (11), 154 (4), 127 (3).