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Supporting Information

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Medium Ring and Iodinated Biaryl Synthesis via Organocuprate Oxidation

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General Information: ^{1}H NMR Spectra were recorded on Bruker DPX 400 or 500 spectrometers in deuterochloroform operating at 400 and 500 MHz respectively. ^{13}C NMR Spectra were recorded on a Bruker 400 or 500 operating at 100 and 125 MHz respectively. Chemical shifts are quoted relative to residual solvent (7.26 ppm for $CHCl_3$ and 77.0 ppm for ^{13}C of $CDCl_3$, 2.54 ppm for DMSO and 40.45 ppm for ^{13}C of d_6-DMSO) and coupling constants (J) are given in Hz. The following abbreviations are used to indicate the multiplicity of signals: s singlet, d doublet, t triplet, q quartet, dd doublet of doublets, dt doublet of triplets, m multiplet and b broad. NMR spectra were acquired at 300 K unless otherwise indicated.

High resolution mass spectrometric (HRMS) analyses were measured on a Micromass Q-TOF or a Micromass LCT Premier spectrometer at the Department of Chemistry, University of Cambridge or on a Finnigan MAT 900 XLT or a Finnigan MAT 95XP spectrometer at the EPSRC National Mass Spectrometry Service Centre, Swansea.

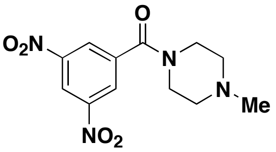
Infrared spectra were recorded on a Perkin Elmer 1 FT-IR Spectrometer fitted with an Attenuated Total Reflectance (ATR) sampling accessory as thin films or flattened solids. Absorption maxima (ν_{max}) are reported in wavenumbers (cm^{-1}).

Optical rotations were recorded on a Perkin Elmer 343 polarimeter. $[\alpha]_D^{25}$ values are reported in 10^{-1} deg cm^2 g^{-1} at 589 nm, concentration (c) is given in g(100mL)$^{-1}$.

Melting points were determined on a Reichert hot stage apparatus and are uncorrected.

Full spectral data for all novel compounds are given below, all previously characterised compounds gave spectra consistent with the literature.

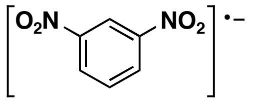
Except as otherwise indicated, reactions were carried out in oven-dried glassware under an atmosphere of nitrogen with dry, freshly distilled solvents. Tetrahydrofuran was distilled from $LiAlH_4$ with triphenylmethane as indicator. All chemicals were purchased from The Aldrich Chemical Company or Avocado. Copper(I) bromide-dimethyl sulfide complex was purified before use according to the procedure of House.[1] *i*PrMgCl solution was titrated with 1,10-phenanthroline and menthol before use. All flash chromatography was carried out using slurry-packed Merck 9385 Kieselgel 60 silca gel.



Synthesis of 3: 3,5-Dinitrobenzoic acid (21.2 g, 0.1 mol) was dissolved in thionyl chloride (100 mL), the solution heated at reflux for 10 h and then allowed to cool to 20 °C. Excess thionyl chloride was removed under reduced pressure and by azeotropic distillation with toluene. The residue was dissolved in chloroform (200 mL) and added dropwise to a stirred slurry of 1-methylpiperazine (12.0 g, 0.12 mol) and potassium carbonate (14 g, 0.1 mol) in chloroform (200 mL) at 0 °C. The reaction mixture was allowed to warm to 20 °C over 1 h and then washed with water (4 × 400 mL), dried (K_2CO_3) and the solvent removed under reduced pressure. The residue was recrystallized (hexanes) as yellow needles (20.4 g, 70%); mp 138-141 °C; ν_{max}(film)/cm^{-1} 1633, 1531, 1435, 1339, 1295, 1277, 1133, 995, 917, 908, 720, 681; δ_H (500 MHz; d_6-DMSO; 393 K) 8.87 (1 H, t, J 2.0), 8.56 (2 H, d, J 2.0), 3.54 (4 H, br), 2.42 (4 H, t, J 5.0), 2.27 (3 H, s); δ_C (125 MHz; d_6-DMSO; 393 K) 165.5, 149.1, 139.8, 127.6, 119.4, 54.7, 45.7; HRMS found ESI $[M+H]^+$ 295.1042, $[C_{12}H_{15}N_4O_5]^+$ requires 295.1043.

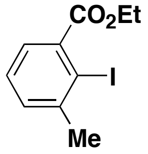
General procedure for the studies on oxidant to substrate ratio:
Phenyl magnesium bromide (1 mL of a 1 M solution in THF, 1 mmol) was added to a stirred suspension of copper(I) bromide-dimethyl sulfide complex (0.103 g, 0.5 mmol) in THF (3 mL) at –78 °C. The resulting yellow slurry was stirred at –78 °C for 10 min and then a solution of oxidant in THF was added. The solution was allowed to warm to 20 °C and the reaction mixture filtered through a pad of silica eluting with hexane-EtOAc (1:1). The filtrate was concentrated under reduced pressure and the residue purified by flash column chromatography on silica gel to yield biphenyl.

Preparation of potassium dinitrobenzenide:[2] Potassium (0.42 g, 10.7 mmol) was heated with a heat gun in a Schlenk flask under reduced pressure (0.5 mmHg) until sublimation occurred. The flask was back-filled with argon and degassed THF (30 mL) was added. A solution of *meta*-dinitrobenzene (1.49 g, 8.9 mmol) in THF (10 mL) was added, the solution sonicated for 1 h and then used immediately.

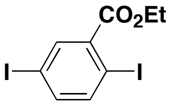


General procedure for synthesis of 1b, 1g, 1h: The benzoic acid was dissolved in thionyl chloride and heated at reflux for 1 h. The solution was allowed to cool to 20 °C and excess thionyl chloride removed under reduced pressure and by azeotropic distillation with toluene. The residue was cooled to 0 °C and excess ethanol added dropwise. The resulting solution was stirred at room temperature overnight and excess ethanol removed under reduced pressure. The residue was purified by flash column chromatography on silica gel.

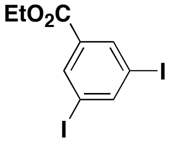
1b: ν_{max}(film)/cm^{-1} 1722, 1279, 1179, 1139, 1097, 1012, 751; δ_H (500 MHz; CDCl$_3$) 7.35 (2 H, m), 7.27 (1 H, t, *J* 7.5), 4.41 (2 H, q, *J* 7.0), 2.51 (3 H, s), 1.42 (3 H, t, *J* 7.0); δ_C (125 MHz; CDCl$_3$) 168.4, 143.3, 138.9, 131.6, 127.8, 126.9, 99.8, 61.7, 29.6, 14.2; ; HRMS found EI [M]$^+$ 289.9800, [C$_{10}$H$_{11}$IO$_2$]$^+$ requires 289.9798.



1g: mp 59-60 °C (lit.,[3] 65 °C); ν_{max}(film)/cm^{-1} 1726, 1276, 1233, 1148, 1098, 1081, 1008, 815, 774; δ_H (500 MHz; CDCl$_3$) 8.09 (1 H, d, *J* 2.0), 7.69 (1 H, d, *J* 8.5), 7.46 (1 H, dd, *J* 8.5, 2.0), 4.42 (2 H, q, *J* 7.0), 1.43 (3 H, t, *J* 7.0); δ_C (125 MHz; CDCl$_3$) 165.1, 142.7, 141.3, 139.5, 137.2, 93.3, 93.0, 62.1, 14.2; HRMS found EI [M]$^+$ 401.8626, [C$_9$H$_8$I$_2$O$_2$]$^+$ requires 401.8614.

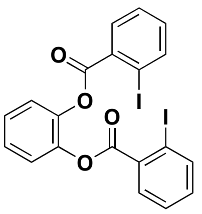


1h: mp 86-88 °C; ν_{max}(film)/cm^{-1} 1716, 1542, 1256, 1129, 1104, 1020, 874, 761, 706, 660; δ_H (500 MHz; CDCl$_3$) 8.34 (2 H, d, *J* 2.0), 8.24 (1 H, d, *J* 2.0), 4.39 (2 H, q, *J* 7.0), 1.41 (3 H, t, *J* 7.0); δ_C (125 MHz; CDCl$_3$) 163.7, 149.1, 137.7, 133.6, 94.3, 61.8, 14.2; HRMS found ESI [M+Na]$^+$ 424.8501, [C$_9$H$_8$I$_2$NaO$_2$]$^+$ requires 424.8506.

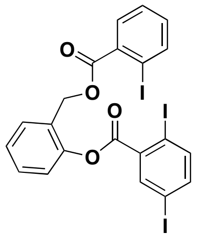


General procedure for synthesis of 1i, 1j, 1k, 1l:[4] A solution of 2-iodobenzoic acid (5.46 g, 22 mmol) in CH_2Cl_2 (30 mL) was added to a solution of diol (10 mmol), NEt_3 (3.3 mL, 2.4 g, 24 mmol) and 4-(dimethylamino)pyridine (0.012 g, 0.1 mmol) in CH_2Cl_2 at 0 °C and stirred at 20 °C for 12 h. The reaction mixture was washed with water, the organic layer separated, dried ($MgSO_4$) and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel.

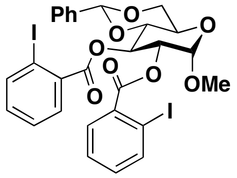
1j: mp 99-102 °C; ν_{max}(film)/cm^{-1} 1744, 1579, 1491, 1232, 1070, 1010, 763, 740, 729, 682; δ_H (400 MHz; $CDCl_3$) 8.00 (4 H, m), 7.45-7.33 (6 H, m), 7.15 (2 H, dt, *J* 7.0, 2.0); δ_C (125 MHz; $CDCl_3$) 163.6, 142.3, 141.9, 133.5, 132.8, 132.1, 128.3, 127.1, 123.6, 95.1; HRMS found ESI $[M+NH_4]^+$ 587.9164, $[C_{20}H_{16}I_2NO_4]^+$ requires 587.9163.



1l: ν_{max}(film)/cm^{-1} 1724, 1274, 1215, 1174, 1131, 1088, 1066, 1006, 738; δ_H (500 MHz; $CDCl_3$) 8.36 (1 H, d, *J* 2.0), 7.99 (1 H, dd, *J* 8.0, 1.0), 7.79 (1 H, dd, *J* 8.0, 1.5), 7.77 (1 H, d, *J* 8.0), 7.63 (1 H, dd, *J* 7.5, 1.5), 7.53 (1 H, dd, *J* 8.0, 2.0), 7.48 (1 H, td, *J* 8.0, 1.5), 7.39-7.33 (3 H, m), 7.15 (1 H, td, *J* 8.0, 2), 5.42 (2 H, s); δ_C (125 MHz; $CDCl_3$) 165.9, 163.1, 149.2, 143.2, 142.3, 141.4, 140.2, 135.2, 134.4, 132.8, 131.3, 131.0, 130.1, 128.0, 127.7, 126.7, 122.6, 94.4, 94.2, 93.3, 62.8; HRMS found ESI $[M+Na]^+$ 732.7844, $[C_{28}H_{24}NaI_2O_8]^+$ requires 732.7948.

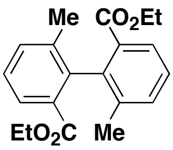


Synthesis of 1m: 2-Iodobenzoic acid (18 g, 72.6 mmol), (+)-(4,6-*O*-benzylidene)methyl-α-D-glucopyranoside (10 g, 35.4 mmol), 1,3-dicyclohexylcarbodiimide (15.3 g, 74.3 mmol) and 4-(dimethylamino)pyridine (1.3 g, 10.6 mmol) were dissolved in CH_2Cl_2 (700 mL) and the solution stirred at 20 °C for 18 h. The resulting slurry was filtered through Celite® and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel to yield **1m** as a white solid; mp 92-96 °C; $[\alpha]_D^{25}$ +13.6 (*c* = 1.0, $CHCl_3$); ν_{max}(film)/cm^{-1} 1730, 1287, 1242, 1092, 1047, 1014, 992, 737, 697; δ_H (500 MHz; $CDCl_3$) 7.97 (2 H, t, *J* 7.0), 7.90 (1 H, d, *J* 8.0), 7.73 (1 H, dd, *J* 8.0,1.5), 7.53 (2 H, dd, *J* 8.0, 2.0), 7.35 (5 H, m), 7.13 (1 H, td, *J* 7.5,1.5) 7.10 (1 H, td, *J* 7.5,1.5), 6.09 (1 H, t, 10.0), 5.62 (1 H, s), 5.36 (1 H, dd, *J* 10.0, 4.0), 5.25 (1 H, d, *J* 4.0), 4.41 (1 H, dd, *J* 10.5, 5.0), 4.10 (1 H, m), 3.94 (1 H, t, *J* 10.0), 3.89 (1 H, t, *J* 10.5), 3.47 (3 H, s); δ_C (100 MHz; $CDCl_3$) 165.7, 165.4, 141.6, 141.2, 136.9, 135.0, 133.4, 133.0, 132.9, 132.0, 131.0, 129.1, 128.3, 128.2, 128.0, 126.2, 101.4, 97.6, 94.9, 94.1, 79.1, 72.6, 70.3, 68.9, 62.5, 55.7; HRMS found ESI $[M+Na]^+$ 764.9458, $[C_{28}H_{24}NaI_2O_8]^+$ requires 764.9440.

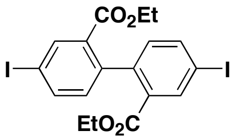


General Procedure for the intermolecular biaryl bond-forming reaction: *i*PrMgCl (1 mmol, 0.5 mL of a 2 M solution in THF) was added to a solution of an aryl iodide (1 mmol) in THF (3 mL) at –20 °C. After addition the reaction mixture was stirred for 10 min at –20 °C and then transferred *via* cannula onto solid copper(I) bromide-dimethyl sulfide complex (0.103 g, 0.5 mmol). A solution of **3** (0.294 g, 1 mmol) in THF (3 mL) was then added and the solution allowed to warm to 20 °C. The reaction mixture was filtered through a plug of silica eluting with hexane-EtOAc (1:1). The filtrate was concentrated under reduced pressure and the residue purified by flash column chromatography on silica gel.

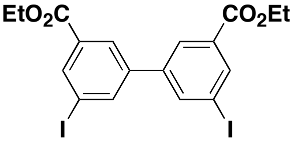
2b: mp 53-54 °C (lit.[5] 53.7-54.7 °C); ν_{max}(film)/cm^{-1} 2980, 1707, 1283, 1264, 1176, 1138, 1101, 1024, 759; δ_H (500 MHz; CDCl$_3$) 7.85 (2 H, dd, *J* 8.0, 0.5), 7.43 (2 H, dd, *J* 8.0, 0.5), 7.34 (2 H, t, *J* 8.0), 4.00 (4 H, q, *J* 7.0), 1.94 (6 H, s), 0.97 (6 H, t, *J* 7.0); δ_C (125 MHz; CDCl$_3$) 167.5, 140.9, 136.7, 133.3, 130.1, 127.7, 126.9, 60.4, 20.1, 13.7; HRMS found ESI [M+H]$^+$ 327.1592, [C$_{20}$H$_{23}$O$_4$]$^+$ requires 327.1591.



2g: mp 143-144 °C; ν_{max}(film)/cm^{-1} 1714, 1289, 1273, 1252, 1234, 1152, 1078, 1020, 999, 826, 785; δ_H (500 MHz; CDCl$_3$) 8.09 (2 H, d, *J* 2.0), 7.70 (2 H, dd, *J* 8.5, 2.0), 7.46 (2 H, d, *J* 8.5), 4.42 (4 H, q, *J* 7.0), 1.43 (6 H, t, *J* 7.0); δ_C (125 MHz; CDCl$_3$) 165.1, 142.7, 141.4, 139.5, 137.2, 93.3, 93.0, 62.1, 14.2; HRMS found ESI [M+Na]$^+$ 572.9052, [C$_{18}$H$_{16}$NaI$_2$O$_4$]$^+$ requires 572.9030.

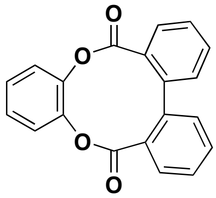


2h: mp 139-141 °C; ν_{max}(film)/cm^{-1} 1716, 1556, 1253, 1129, 1108, 1077, 1017, 877, 763, 722; δ_H (500 MHz; CDCl$_3$) 8.41 (2 H, t, *J* 1.5), 8.20 (2 H, t, *J* 1.5), 8.10 (2 H, t, *J* 1.5), 4.44 (4 H, q, *J* 7.0), 1.44 (6 H, t, *J* 7.0); δ_C (125 MHz; CDCl$_3$) 164.8, 140.9, 140.0, 138.0, 132.9, 127.6, 94.3, 61.7, 14.3; HRMS found ESI [M+Na]$^+$ 572.9058, [C$_{18}$H$_{16}$NaI$_2$O$_4$]$^+$ requires 572.9030.

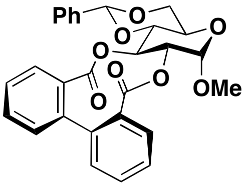


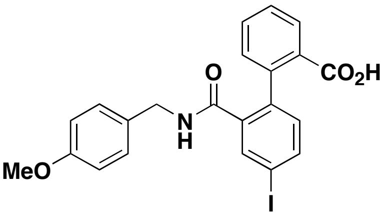
General Procedure for the intramolecular biaryl bond-forming reaction: *i*PrMgCl (2 mmol, 1.0 mL of a 2 M solution in THF) was added to a solution of an aryl iodide (1 mmol) in THF (3 mL) at –20 °C. After addition the reaction mixture was stirred for 10 min at –20 °C and then transferred *via* cannula onto solid copper(I) bromide-dimethyl sulfide complex (0.206 g, 1.0 mmol). A solution of **3** (0.294 g, 1 mmol) in THF (3 mL) was then added and the solution allowed to warm to 20 °C. The reaction mixture was filtered through a plug of silica eluting with hexane-EtOAc (1:1). The filtrate was concentrated under reduced pressure and the residue purified by flash column chromatography on silica gel.

2j: mp 169-171 °C; ν_{max}(film)/cm^{-1} 1725, 1488, 1246, 1225, 1057, 1022, 750, 739; δ_H (400 MHz; CDCl$_3$) 7.61 (4 H, m), 7.53 (2 H, dd, *J* 8.0, 1.0), 7.35 (2 H, t, *J* 8.0), 7.25-7.19 (4 H, m); δ_C (125 MHz; CDCl$_3$) 165.7, 142.1, 140.0, 132.4, 131.1, 130.3, 128.3, 127.6, 126.6, 121.9; HRMS found ESI [M+NH$_4$]$^+$ 334.1073, [C$_{20}$H$_{16}$NO$_4$]$^+$ requires 334.1074.



2m:[6] mp 139-143 °C; $[\alpha]_D^{25}$ = +63.0 (*c* = 1.0, CHCl$_3$); ν_{max}(film)/cm^{-1} 1750, 1705, 1273, 1235, 1072, 1045, 983, 746, 699; δ_H (500 MHz; CDCl$_3$) 7.60-7.57 (8 H, m), 7.46-7.38 (5 H, m), 5.78 (1 H, t, *J* 10.0), 5.61 (1 H, s), 5.38 (1 H, dd, *J* 9.5, 3.5), 5.03 (1 H, d, *J* 3.5), 4.39 (1 H, dd, *J* 10.5, 4.5), 4.04 (1 H, dd, *J* 10.0, 4.5), 3.97 (1 H, t, *J* 10.0), 3.88 (1 H, t, *J* 10.5), 3.86 (3 H, s); δ_C (125 MHz; CDCl$_3$) 169.1, 168.9, 137.4, 137.3, 136.9, 133.2, 132.8, 131.1, 131.0, 129.3, 129.2, 128.3, 127.8, 127.6, 126.4, 126.3, 126.2, 126.1, 101.9, 98.4, 78.4, 74.6, 73.7, 69.0, 63.1, 55.5; HRMS found ESI [M+Na]$^+$ 511.1369, [C$_{28}$H$_{24}$NaO$_8$]$^+$ requires 511.1365.





Synthesis of 4: *i*-PrMgCl (1.58 mmol, 0.79 mL, 2 M solution in THF) was added to a solution of **1l** (0.51 g, 0.72 mmol) in THF (3 mL) at –20 °C. After addition the reaction mixture was stirred for 10 min at –20 °C and then transferred *via* cannula onto solid copper(I) bromide-dimethyl sulfide complex (0.148 g, 0.72 mmol). A solution of **3** (0.212 g, 0.72 mmol) in THF (3 mL) was then added and the solution allowed to warm to 20 °C. The reaction mixture was filtered through a through a plug of silica eluting with hexane-EtOAc (1:1), concentrated under reduced pressure and the residue dissolved in CH_2Cl_2 (10 mL). 4-Methoxybenzylamine was added to the solution and the mixture stirred at 60 °C for 6 h, allowed to cool and added to citric acid (10 mL of a 10% aqueous solution). The solution was extracted with CH_2Cl_2 (2 × 50 mL), the organic fractions dried ($MgSO_4$) and the solvent removed under reduced pressure to give **4** (84%); mp 74-77 °C; ν_{max}(film)/cm^{-1} 1694, 1607, 1556, 1514, 1300, 1277, 1249, 1237, 822, 802, 771; δ_H (500 MHz; $CDCl_3$) 7.89 (1 H, d, *J* 2.0), 7.75 (1 H, m), 7.66 (1 H, dd, *J* 8.0, 2.0), 7.41 (2 H, t, *J* 4.0), 7.09 (1 H, m), 6.82 (1 H, b), 6.79 (1 H, d, *J* 8.0), 6.69 (2 H, d, *J* 9.0), 6.65 (2 H, d, *J* 9.0), 4.30 (1 H, dd, *J* 15.0, 6.0), 4.06 (1 H, dd, *J* 15.0, 5.0), 3.74 (3 H, s); δ_C (125 MHz; $CDCl_3$) 171.2, 168.4, 139.4, 138.7, 138.6, 136.8, 136.1, 131.6, 131.3, 131.1, 130.1, 129.7, 129.0, 128.8, 128.1, 114.0, 93.1, 55.3, 43.4; HRMS found ESI $[M+H]^+$ 488.0349, $[C_{22}H_{19}INO_4]^+$ requires 488.0359.

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