Regioselective Routes to Orthogonally-Substituted Aromatic MIDA boronates.

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General experimental methods Solvents.

Solvents and reagents were purchased from commercial suppliers and used without further purification. Reactions were heated using a CEM Discovery microwave fitted with an Explorer unit; ensure a ventilated fume hood with the sash lowered is used as these reactions are under high pressure and temperature. All thermally heated reactions were heated in a fume hood. Dry degassed solvents were only used where stated. NMR spectra were recorded on a Varian 500 MHz or 400 MHz spectrometer. Chemical shifts are reported in ppm and are referenced to the residual solvent peak or to TMS used as an internal standard; note that in some cases the C-B bond is not detectable in the ^{13}C NMR.[1] LCMS were ran with a 5 µm C18 110 Å column. Percentage purities were performed using a 30 minutes method in water/acetonitrile with 0.1% formic acid (5 min at 5%, 5%-95% over 20 min, 5 min at 95%) with the UV set to 254 nm. High resolution mass spectrometry (HRMS) was done either internally or by the National Mass Spectrometry Facility, University of Swansea on a LTQ Orbitrap XL.

General procedure for MIDA boronate formation with PEG 300[2]

The boronic acid (1 mmol) was added to a 10 mL microwave vial equipped with a magnetic stirrer, and then PEG 300 (1 mL) was added followed by methyliminodiacetic acid (MIDA) (147 mg, 1 mmol). The Teflon cap was added and the reaction was heated using the dynamic heating method, with max power set to 40 W, max pressure 250 psi, max temperature 130 ˚C, high stirring throughout and power max turned off. This method was used to hold the reaction mixture at 130 ºC for 5 min. After cooling, the mixture was added to water (9 mL). This mixture was stirred forming a white precipitate, then cooled in an ice bath allowing flocculation, then collected by filtration and washed with cold water (5 mL). The precipitate was allowed to dry in an oven set to 100˚C, giving pure product as a white precipitate (if not otherwise quoted).

Notes: The 5 mmol scale reaction was performed using a 35 mL microwave vial and the 10 mmol scale was carried out using a 100 mL round bottomed flask with a small air condenser attached with the open vessel

attenuator installed. The heating parameters were kept the same but the hold time was changed to 7.5 min for the 5 mmol scale and 10 min for the 10 mmol scale reactions.

2-Fluoro-4-(trifluoromethyl)phenyl MIDA boronate (1d). Yield: 1.36 g (85%). 5 mmol scale. ^{1}H NMR (500 MHz, DMSO-d6) δ 7.78 – 7.68 (m, 1H), 7.64 – 7.52 (m, 2H), 4.50 – 4.43 (m, 2H), 4.19 – 4.10 (m, 2H), 2.67 (d, J = 2.6 Hz, 3H). ^{13}C NMR (126 MHz, DMSO-d6) δ 169.2, 165.7 (d, $^{1}J_{CF}$ = 243.7 Hz), 136.7 (d, $^{3}J_{CF}$ = 9.5 Hz), 132.5 (qd, $^{2}J_{CF}$ = 32.5, $^{3}J_{CF}$ = 9.0 Hz), 123.6 (qd, $^{1}J_{CF}$ = 272.2, $^{4}J_{CF}$ = 2.9 Hz), 121.3 – 121.2 (m), 112.7 (dq, $^{3}J_{CF}$ = 29.0, $^{4}J_{CF}$ = 3.8 Hz), 63.0, 48.0. ^{19}F NMR (376 MHz, DMSO-d6) δ -61.46 , -103.26 – -103.40 (m). ^{11}B NMR (128 MHz, DMSO-d6) δ 11.14. LCMS purity UV >99%, Ret. time = 17.38 min. FTMS ESI (m/z) found 337.0975, calcd for $[C_{12}H_{10}BF_4NO_4NH_4]^+$ 337.0977.

2-Fluoro-4-methylphenyl MIDA boronate (1e). Yield: 1.90 g (72%). 10 mmol scale. ^{1}H NMR (500 MHz, DMSO-d6) δ 7.37 (pt, $^{3}J_{HH,}$ $^{4}J_{HF}$ = 6.9 Hz, 1H), 7.02 (d, $^{3}J_{HH}$ = 7.5 Hz, 1H), 6.95 (d, $^{3}J_{HF}$ = 11.1 Hz, 1H), 4.40 (d, J = 17.2 Hz, 2H), 4.08 (d, J = 17.2 Hz, 2H), 2.61 (s, 3H), 2.32 (s, 3H). ^{13}C NMR (126 MHz, DMSO-d6) δ 169.4, 166.0 (d, $^{1}J_{CF}$ = 240.5 Hz), 142.3 (d, $^{3}J_{CF}$ = 8.7 Hz), 135.0 (d, $^{3}J_{CF}$ = 9.8 Hz), 125.3 (d, $^{4}J_{CF}$ = 2.3 Hz), 115.8 (d, $^{2}J_{CF}$ = 24.5 Hz), 62.8, 47.9, 21.1. ^{19}F NMR (376 MHz, DMSO-d6) δ -106.68 (dd, J = 11.2, 7.2 Hz). ^{11}B NMR (128 MHz, DMSO-d6) δ 11.07. LCMS purity UV >99%, Ret. time = 15.90 min. HRMS-ESI (m/z) found 288.0814, calcd for $[C_{12}H_{13}{}^{10}BFNO_4Na]^+$ 288.0814.

Electrophilic aromatic substitution

Nitration

5-Fluoro-4-formyl-2-nitrophenyl boronic acid (2a). 3-Fluoro-4-formylphenyl boronic acid (2.02 g, 12 mmol) was dissolved in sulphuric acid (98%, 12 mL) at rt then cooled to 0 ^{0}C. Nitric acid (70%, 1.46 mL, 22 mmol) in sulphuric acid 98% (15 mL) was added drop-wise over 20 minutes and maintained at 0 ^{0}C. The mixture was allowed to warm to RT and left overnight. The mixture was poured on to ice (150g) then was allowed to warm to RT and extracted with diethyl ether (3 x 50 mL). The combined organic layers were washed with brine. The pH of the brine washings was monitored until they were no longer acidic and reached pH 7. The organic layer was then dried ($MgSO_4$) and evaporated under reduced pressure to give the title compound as a light yellow powder. Yield: 2.26 g (88%). Mpt: decomposes at 135 ^{o}C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.20 (s, 1H), 8.54 (d, $^{4}J_{FH}$ = 5.7 Hz, 1H), 8.46 (s, 2H), 7.61 (d, $^{3}J_{FH}$ = 9.8 Hz, 1H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 186.8 (d, $^{3}J_{FC}$ = 2.1 Hz), 165.3 (d, $^{1}J_{FC}$ = 268.4 Hz), 146.3 (d, $^{4}J_{FC}$ = 1.8 Hz), 145.1, 124.7 (d, $^{3}J_{FC}$ = 2.2 Hz), 123.7 (d, $^{2}J_{FC}$ = 11.1 Hz), 120.7 (d, $^{2}J_{FC}$ = 21.4 Hz). ^{19}F NMR (376 MHz, DMSO-d_6) δ -111.7 (dd, $^{3}J_{FH}$ = 9.8, $^{4}J_{FH}$ = 5.7 Hz). ^{11}B NMR (128 MHz, DMSO-d_6) δ 27.8. Elemental analysis CHN (%) found C: 39.36, H: 2.50, N: 6.39, calcd for $C_7H_5BFNO_5$ C: 39.49, H: 2.37, N: 6.58. HRMS-ES (m/z) found 238.0430, calcd for (ethlyglycol)$[C_9H_7O_5N_1B_1F_1]$+ 238.0432.

5-Fluoro-4-formyl-2-nitrophenyl MIDA boronate (2b). 3-Fluoro-4-formylphenyl MIDA boronate (250 mg, 1 mmol) was dissolved in sulphuric acid (98%, 1.5 mL) at rt then cooled to 0 ^{0}C. Nitric acid (70%, 0.5 mL, 7.7 mmol) in sulphuric acid (98% 1.5 mL) was added drop-wise over 20 minutes and the reaction temperature was maintained at 0 °C. The mixture was allowed to warm to RT and was left to stir overnight. The mixture was poured on to ice (8 g); this then formed a precipitate which was filtered under reduced pressure. The filtrate was then washed with water (3 x 10 mL) and then cold diethyl ether (3 x 5 mL). This was then oven dried (100 °C) to afford pure product as a light yellow powder. Yield: 275 mg (85%). TLC (diethyl ether:MeCN 7:3) R_f = 0.47. ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.17 (s, 1H), 8.23 (d, $^{4}J_{FH}$ = 5.6 Hz, 1H), 7.67 (d, $^{3}J_{FH}$ = 10.9 Hz, 1H), 4.46 (d, J = 17.5 Hz, 2H), 4.25 (d, J = 17.5 Hz, 2H), 2.89 (s, 3H).^{13}C NMR (126 MHz, DMSO-d_6) δ 187.0 (d, $^{3}J_{FC}$ = 3.4 Hz), 169.2, 163.4 (d, $^{1}J_{FC}$ = 264.7 Hz), 151.4 (d, $^{4}J_{FC}$ = 2.5 Hz), 125.6 (d, $^{3}J_{FC}$ = 3.0 Hz), 125.2 (d, $^{2}J_{FC}$ = 11.0 Hz), 125.0 (d, $^{2}J_{FC}$ = 21.7 Hz), 64.8, 49.9.^{19}F NMR (376 MHz, DMSO-d_6) δ -114.38

(dd, $^{3}J_{FH}$ = 11.1, $^{4}J_{FH}$ = 5.9 Hz). ^{11}B NMR (128 MHz, DMSO-d_6) δ 10.1. LCMS purity >95% (UV), Ret. time = 11.09 min. FTMS APCI (m/z) found 325.0638, calcd for $[C_{12}H_{10}BFN_2O_7H]^+$ 325.0638.

4-Fluoro-3-formyl-5-nitrophenyl MIDA boronate (2c). 4-Fluoro-3-formylphenyl MIDA boronate (250 mg, 1 mmol) was dissolved in sulphuric acid (98%, 1.5 mL) at rt then cooled to 0 °C. Nitric acid (70 %, 0.5 mL, 7.7 mmol) in sulphuric acid (98 %, 1.5 mL) was added drop-wise over 20 minutes and maintained at 0 °C. The mixture was allowed to warm to RT and left overnight. The mixture was poured on to ice (8 g); this then formed a precipitate which was collected by vacuum filtration. The filtrate was then washed with water (3 x 10 mL) and then cold diethyl ether (3 x 5 mL). This was then oven dried (100 °C) to give pure product as a light yellow powder. Yield: 105 mg (32%). TLC (diethyl ether:MeCN 7:3) R_f = 0.44. ^{1}H NMR (399 MHz, DMSO-d_6) δ 10.28 (s, 1H), 8.44 (d, $^{4}J_{FH}$ = 6.8 Hz, 1H), 8.27 (d, $^{4}J_{FH}$ = 6.3 Hz, 1H), 4.40 (d, J = 17.2 Hz, 2H), 4.19 (d, J = 17.2 Hz, 2H), 2.62 (s, 3H).

^{13}C NMR (126 MHz, DMSO-d_6) δ 187.4 (d, $^{3}J_{FC}$ = 5.4 Hz), 169.5, 156.9 (d, $^{1}J_{FC}$ = 275.5 Hz), 139.7 (d, $^{3}J_{FC}$ = 2.4 Hz), 137.7 (d, $^{2}J_{FC}$ = 6.6 Hz), 135.7, 125.5 (d, $^{2}J_{FC}$ = 7.0 Hz), 62.9, 48.5. ^{19}F NMR (376 MHz, DMSO-d_6) δ -128.36. ^{11}B NMR (128 MHz, DMSO-d_6) δ 10.3. LCMS purity >99% (UV), Ret. time = 10.43 min. FTMS APCI (m/z) found 325.0638, calcd for $[C_{12}H_{10}BFN_2O_7H]^+$ 325.0638.

2-Fluoro-5-nitro-4-(trifluoromethyl)phenyl MIDA boronate (2d). 2-Fluoro-(trifluoromethyl)phenyl MIDA boronate (321 mg, 1 mmol) was dissolved in sulphuric acid (98%, 2 mL) and cooled to 0 °C. Nitric acid (70%, 315 µL, 22 mmol) was added to the mixture at 0 °C, which was allowed to warm to RT and left overnight. The mixture was poured onto ice (20 g) and then was allowed to warm to RT forming a precipitate, which was collected by filtration, washed with water (3 x 50 mL) and then diethyl ether (10 mL). This was then dried overnight in a vacuum desiccator over $CaCl_2$ giving title compound as a bright yellow powder. Yield: 344 mg (92%). Mpt: decomposes at 232-234 ˚C. ^{1}H NMR (500 MHz, MeCN-d_3) δ 8.20 (d, J = 5.4 Hz, 1H), 7.65 (d, J = 9.4 Hz, 1H), 4.20 (d, J = 17.3 Hz, 2H), 4.01 (d, J = 17.3 Hz, 2H), 2.72 (s, 3H). ^{13}C NMR (126 MHz, MeCN-d_3) δ 168.8, 167.8 ($^{1}J_{FC}$ = 251.3 Hz), 145.0, 134.0 (d, $^{1}J_{FC}$ = 11.3 Hz), 127.4 (qd, $^{2}J_{FC}$ = 34.8, $^{3}J_{FC}$ = 10.0 Hz), 122.7 (qd, $^{1}J_{FC}$ = 272.6, $^{4}J_{FC}$ 2.1 Hz), 117.2 (dq, $^{2}J_{FC}$ = 32.3, $^{3}J_{FC}$ =5.5 Hz), 63.9(s), 48.8.^{19}F NMR (376 MHz, MeCN-d_3) δ -61.03 (s), -97.13 (dd, $^{3}J_{FH}$ = 9.4, $^{4}J_{FH}$ =5.4 Hz). ^{11}B NMR (128 MHz, MeCN-d_3) δ 10.13. Elemental analysis CHN (%) found C: 39.49, H: 2.47, N: 7.68, calcd for $C_{12}H_9BF_4N_2O_6$ C: 39.59, H: 2.49, N: 7.70. FTMS (m/z) found 381.0865, calcd for $[C_{12}H_9BF_4N_2O_6NH_4]^+$ 381.0864.

2-Fluoro-4-methyl-5-nitrophenyl MIDA boronate (2e). 2-Fluoro-4-methylphenyl MIDA boronate (530 mg, 2 mmol) was dissolved in sulphuric acid (98%, 6 mL) and cooled to 0 °C. Nitric acid (70%, 126 µL, 2.04 mmol) was added to the mixture at 0 °C, which was allowed to warm to RT and left overnight. The mixture was poured onto ice (10 g) and this was allowed to warm to RT forming a precipitate, which was collected by filtration, washed with water (3 x 50 mL) and then diethyl ether (10 mL). This was then dried overnight in a vacuum desiccator over $CaCl_2$ giving title compound as a white powder. Yield: 242 mg (39%). TLC (DCM:MeCN 7:3) R_f = 0.80. ^{1}H NMR (399 MHz, DMSO-d_6) δ 8.11 (d, $^{4}J_{FH}$ = 5.9 Hz, 1H), 7.35 (d, $^{3}J_{FH}$ = 10.1 Hz, 1H), 4.45 (d, J = 17.3 Hz, 2H), 4.13 (d, J = 17.3 Hz, 2H), 2.68 (s, 3H), 2.56 (s, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 168.7, 166.9 (d, $^{1}J_{FC}$ = 250.9 Hz), 145.1, 138.2 (d, $^{3}J_{FC}$ = 11.0 Hz), 131.8 (d, $^{3}J_{FC}$ = 11.8 Hz), 119.2 (d, $^{2}J_{FC}$ = 27.4 Hz), 62.5, 47.6, 19.7. ^{19}F NMR (376 MHz, DMSO-d_6) δ -98.29 (dd, $^{4}J_{FH}$ = 10.1, $^{3}J_{FH}$ = 5.9 Hz). ^{11}B NMR (128 MHz, DMSO-d_6) δ 10.47. LCMS purity 95% (UV), Ret. time = 16.29 min. FTMS APCI MS m/z found 381.0865, calcd for $[C_{12}H_{12}BFN_2O_6H]^+$ 311.0845.

Bromination

2-Bromo-5-fluoro-4-formylphenyl MIDA boronate (3b). 3-Fluoro-4-formylphenyl MIDA boronate (279 mg, 1 mmol) was dissolved in sulphuric acid (98%, 4 mL) and the temperature was then increased to 60 °C.

N-Bromosuccinimide (214 mg, 1.2 mmol) was added in three portions at 15 min intervals. After a further 1.5 h, the cooled reaction mixture was poured onto crushed ice (20 g). This resulted in a white precipitate, which was collected by vacuum filtration. The resulting powder was purified by flash chromatography on silica gel (DCM:MeCN 7:3) to afford the title compound as a white powder. Yield: 93 mg (54%). Mpt: decomposes at 232-234 ˚C. TLC (DCM:MeCN 7:3) R_f = 0.53. ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.15 (s, 1H), 7.97 (d, $^4J_{FH}$ = 6.2 Hz, 1H), 7.50 (d, $^3J_{FH}$ = 11.5 Hz, 1H), 4.46 (d, J = 17.4 Hz, 2H), 4.20 (d, J = 17.4 Hz, 2H), 2.75 (s, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 187.0 (d, $^3J_{FC}$ = 3.7 Hz), 169.0, 161.2 (d, $^1J_{FC}$ = 258.8 Hz), 133.6 (d, $^3J_{FC}$ = 1.6 Hz), 125.5 (d, $^2J_{FC}$ = 9.9 Hz), 124.5 (d, $^2J_{FC}$ = 20.7 Hz), 121.9 (d, $^4J_{FC}$ = 2.8 Hz), 64.2, 48.4. ^{19}F NMR (376 MHz, DMSO-d_6) δ -123.4 (dd, $^3J_{FH}$ = 11.5, $^4J_{FH}$ = 6.2 Hz). ^{11}B NMR (128 MHz, DMSO-d_6) δ 10.4. Elemental analysis CHN (%) found C: 40.31, H: 2.81, N: 4.04, calcd for $C_{12}H_{10}BBrFNO_5$ C: 40.27, H: 2.82, N: 3.91. FTMS (m/z) found 356.9928, calcd for $[C_{12}H_{10}BBrFNO_5H:]^+$ 356.9929.

5-Bromo-2-fluoro-4-(trifluoromethyl)phenyl MIDA boronate (3d). 2-Fluoro-4-(trifluoromethyl)phenyl MIDA boronate (321 mg, 2 mmol) was dissolved in sulphuric acid (98%, 8 mL). The temperature was increased to 30 °C and then *N*-bromosuccinimide (427 mg, 2.4 mmol) was added in three portions at 15 min intervals. After a further 4 h the cooled reaction mixture was poured on to crushed ice (20 g) resulting in a white precipitate, which was filtered under vacuum. This resulting white powder required no further purification giving the tile compound. Yield: 787 mg (99%).

TLC (DCM:MeCN 7:3) R_f = 0.72. Mpt: decomposes at 232-234 °C. ^{1}H NMR (500 MHz, MeCN-d_3) δ 7.93 (d, $^4J_{FH}$ = 5.8 Hz, 1H), 7.51 (d, $^3J_{FH}$ = 9.8 Hz, 1H), 4.16 (d, J = 17.2 Hz, 2H), 3.98 (d, J = 17.3 Hz, 2H), 2.70 (s, 3H). ^{13}C NMR (126 MHz, MeCN-d_3) δ 168.8, 165.5 (d, $^1J_{FC}$ = 243.6 Hz), 142.4 (d, $^3J_{FC}$ = 9.3 Hz), 133.0 (dq, $^2J_{FC}$ = 32.3 Hz, $^3J_{FC}$ = 9.0 Hz), 123.4 (dq, $^1J_{FC}$ = 272.5, $^4J_{FC}$ = 2.5 Hz), 116.8 (dq, $^2J_{FC}$ = 31.5, $^3J_{FC}$ = 5.8 Hz), 115.0, 63.8, 48.7. ^{19}F NMR (376 MHz, MeCN-d_3) δ -63.7 (s), -107.3 (dd, $^3J_{FH}$ =9.8, $^4J_{FH}$ =5.8 Hz). ^{11}B NMR (128 MHz, MeCN-d_3) δ 10.3 (s). Elemental analysis CHN (%) found C: 36.18, H: 2.30, N: 3.61, calcd for $C_{12}H_9BBrF_4NO_4$: 36.22, H: 2.28, N: 3.52. FTMS APCI MS m/z found 397.9818, calcd for $[C_{12}H_9BBrF_4NO_4H]^+$ 397.9817.

5-Bromo-2-fluoro-4-methylphenyl MIDA boronate (3e). 2-Fluoro-4-methylphenyl MIDA boronate (3.69 g, 13.9 mmol) was dissolved in acetonitrile (70 mL), and sulphuric acid (98%, 13.9 mmol, 778 µL) was added to this mixture and it was then heated to 70 °C. *N*-Bromosuccinimide (2.72 g, 15.3 mmol) was added in three portions at 15 min intervals and the reaction was left to stir overnight. The reaction mixture was evaporated directly to dryness under reduced pressure. Water (100 mL) was added, and this aqueous layer was extracted with 50 % ethyl acetate in acetone (3 x 150 mL). The combined organic layers were washed with brine (3 x 100 mL), then dried with $MgSO_4$ and evaporated under reduced pressure. The resulting powder was dissolved in the minimum amount of DMSO and loaded on to a reversed phase flash chromatography column. A 0.1 % formic acid modifier was used throughout the column chromatography; 5 column volumes at 100 % water (removing the DMSO) then a gradient of 20 %-90 % acetonitrile in water was used to elute the desired product. The desired samples were dried by lyophilisation to afford the title compound as a white powder. Yield: 3.457 mg (72%). TLC (diethyl ether:MeCN 7:3) R_f = 0.69. ^{1}H NMR (500 MHz, DMSO-d6) δ 7.58 (d, $^4J_{FH}$ = 6.1 Hz, 1H), 7.20 (d, $^3J_{FH}$ = 10.1 Hz, 1H), 4.41 (d, J = 17.3 Hz, 2H), 4.09 (d, J = 17.2 Hz, 2H), 2.66 (s, 3H), 2.35 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d6) δ 169.3, 164.9 (d, $^1J_{FC}$ = 241.7 Hz), 141.5 (d, $^3J_{FC}$ = 9.3 Hz), 138.0 (d, $^3J_{FC}$ = 9.8 Hz), 119.4 (d, $^4J_{FC}$ = 2.6 Hz), 118.3 (d, $^2J_{FC}$ = 26.7 Hz), 62.9, 48.1, 22.8. ^{19}F NMR (376 MHz, DMSO-d_6) δ -108.43 (dd, $^3J_{FH}$ = 10.1, $^4J_{FH}$ =6.1 Hz). ^{11}B NMR (128 MHz, DMSO-d_6) δ 10.5. LCMS purity >99% (UV), Ret. time = 16.21 min. (FTMS m/z) found 342.0141, calcd for $[C_{12}H_{12}BBrFNO_4H]^+$ 342.0143.

2-Bromo-5-hydroxyphenyl MIDA boronate (3g). 3-Hydroxyphenyl MIDA boronate (498 mg, 2 mmol) was dissolved in acetonitrile (40 mL), and sulphuric acid (98%, 1 mmol, 55 µL) was added to this mixture.

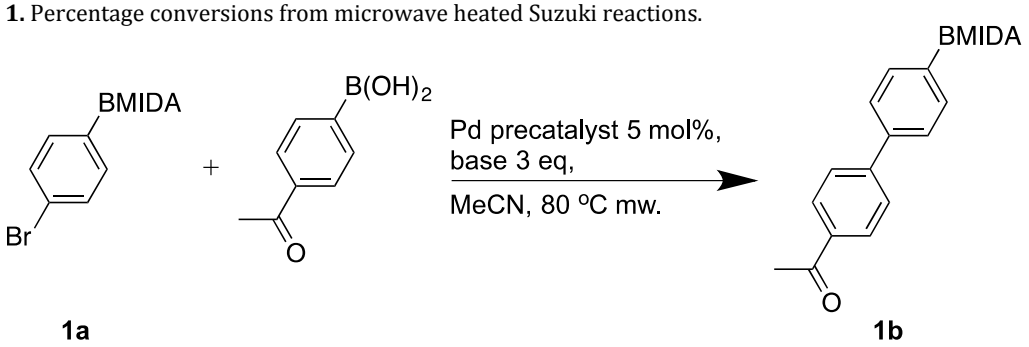
N-Bromosuccinimide (356 mg, 2 mmol) was added in three portions at 15 min intervals and the reaction was left to stir overnight at RT. The reaction mixture was evaporated directly on to Celite. The resulting powder was purified by flash chromatography on silica gel (acetonitrile: diethyl ether 10%: 30%) to afford the title compound as a white powder. Yield: 501 mg (76%). TLC (diethyl ether:MeCN 7:3) R_f = 0.78. ^{1}H NMR (500 MHz, Acetonitrile-d_3) δ 7.41 (d, *J* = 8.6 Hz, 1H), 7.14 (d, *J* = 3.2 Hz, 1H), 7.02 (s, 1H), 6.75 (dd, *J* = 8.6, 3.2 Hz, 1H), 4.11 (d, *J* = 17.4 Hz, 2H), 4.01 (d, *J* = 17.4 Hz, 2H), 2.73 (s, 3H). ^{13}C NMR (126 MHz, Acetonitrile-d3) δ 169.5, 157.0, 135.6, 124.1, 119.2, 117.8, 65.2, 49.5. Elemental analysis CHN (%) found C: 40.18, H: 3.31 N: 4.46, calcd for $C_{11}H_{11}BBrF_4NO_5$: 40.29, H: 3.38, N: 4.40. (FTMS m/z) found 327.0023, calcd for $[C_{11}H_{11}BBrNO_5H]^+$ 327.9986 .

5-Bromo-2-methoxyphenyl MIDA boronate (3h). 2-Methoxyphenyl MIDA boronate (263 mg, 1 mmol) was dissolved in acetonitrile (40 mL), and sulphuric acid (98%, 0.5 mmol, 28 µL) was added to this mixture. *N*-Bromosuccinimide (178 mg, 1 mmol) was added in three portions at 15 min intervals and the reaction was left to stir overnight at RT. The reaction mixture was evaporated directly onto celite. The resulting powder was purified by flash chromatography on silica gel (acetonitrile: diethyl ether 10%: 30%) to afford the title compound as a white powder. Yield: 298 mg (87%). TLC (diethyl ether:MeCN 7:3) R_f = 0.82. ^{1}H NMR (399 MHz, DMSO-d6) δ 7.50 – 7.45 (m, 2H), 6.91 (d, J = 9.4 Hz, 1H), 4.33 (d, J = 17.1 Hz, 2H), 3.99 (d, J = 17.1 Hz, 2H), 3.69 (s, 3H), 2.59 (s, 3H). 13C NMR (100 MHz, DMSO-d6) δ 169.6, 161.7, 136.6, 133.5, 113.4, 112.8, 63.7, 55.8, 47.8. ^{13}C NMR (100 MHz, DMSO-d6) δ 169.6, 161.7, 136.6, 133.5, 113.4, 112.8, 63.7, 55.8, 47.8. ^{11}B NMR (128 MHz, DMSO-d6) δ 11.1. Elemental analysis CHN (%) found C: 40.25, H: 3.88 N: 4.15, calcd for $C_{12}H_{13}BBrF_4NO_5$: 40.15, H: 3.83, N: 4.10. FTMS APCI MS m/z found 346.0080, calcd for $[C_{12}H_{13}BBrFNO_5H]^+$ 346.0079.

5-Acetamido-2-bromophenyl MIDA boronate (3j). 3-Acetamidophenyl MIDA boronate (290 mg, 1 mmol) was dissolved in acetonitrile (4 mL), and *p*-toluenesulfonic acid (0.5 mmol, 95 mg) was added to this mixture. *N*-bromosuccinimide (185 mg, 1.04 mmol) was added in three portions at 15 min intervals and the reaction was left to stir overnight at RT. The reaction mixture was evaporated directly on to celite. The resulting powder was purified by flash chromatography on silica gel (acetonitrile: DCM 0 %: 40 %) to afford the title compound as a white powder. Yield: 222 mg (60%). TLC (DCM:MeCN 7:3) R_f = 0.57. ^{1}H NMR (399 MHz, DMSO-d_6) δ 10.03 (s, 1H), 7.78 (dd, *J* = 8.6, 2.8 Hz, 1H), 7.52 (d, *J* = 2.8 Hz, 1H), 7.46 (d, *J* = 8.6 Hz, 1H), 4.39 (d, *J* = 17.5 Hz, 2H), 4.14 (d, *J* = 17.4 Hz, 2H), 2.66 (s, 3H), 1.99 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 169.5, 168.8, 138.7, 134.0, 127.0, 122.1, 120.7, 64.3, 48.9. ^{11}B NMR (128 MHz, DMSO-d_6) δ 11.0. LCMS purity >99% (UV), Ret. time = 13.13 min. (FTMS m/z) found 371.0233, calcd for $[C_{13}H_{14}BBrN_2O_5H]^+$ 371.0232. (FTMS m/z) found 371.0233, calcd for $[C_{13}H_{14}BBrN_2O_5H]^+$ 371.0232.

Anhydrous Suzuki cross-couplings.

Table 1. Percentage conversions from microwave heated Suzuki reactions.



Entry	Catalyst	Base	Time (min)	Conversion (%)[a]
1	XPHOS Pd G2	K_3PO_4	30	47
2	XPHOS Pd G2	K_3PO_4	60	49
3	SPHOS Pd G2	K_3PO_4	30	35
4	SPHOS Pd G2	K_3PO_4	60	56
5	PEPPIS iPr	K_3PO_4	30	33
6	PEPPSI-iPr	K_3PO_4	60	40
7	Pd 118	K_3PO_4	30	38
8	Pd 118	K_3PO_4	60	61
9	Pd 118	KF	60	35
10	Pd 118	Cs_2CO_3	60	50
11	Pd 118	MeONa	60	52

[a] Calculated by LCMS. Reactions performed with the bromide (0.25 mmol, 78 mg), boronic acid (1.1 eq, 28 mmol, 45mg) all other solid components were added to a microwave vial sealed, degassed and purged with nitrogen then dry MeCN (1 mL) was added to the mixture.

The Table 1 shows the percentage conversions from the microwave reactions in which a variety of catalyst we trailed *i.e.* Buchwald's second generation precatalysts XPhos and SPhos, PEPPIS-*i*Pr and Pd 118. The low yields were where discussed in the main text.

Figure 1 shows the that microwave continued to heat to almost 90 °C after the irradiation was removed overshooting the maximum temperature of 80 °C. This suggest that the internal temperature must have been much higher as over heating is cased by the internal heat dissipating to the outer surface of the reaction vessel to where the external IR thermometer monitors the temperature. This is caused by the lack of stirring as discussed in the main text.

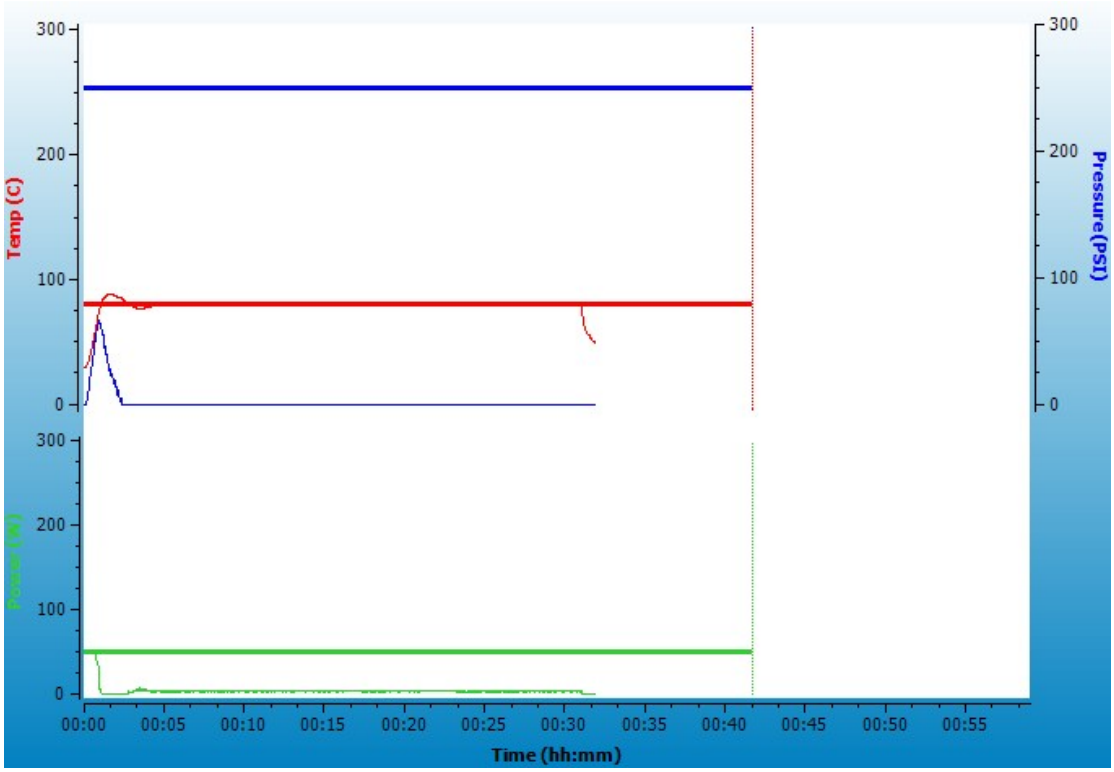


Figure 1. Temperature, pressure and power reading from entry 8, Table 1.

General procedure for anhydrous Suzuki cross-couplings on a 1 mmol scale. A bromophenyl MIDA boronate (1 mmol), potassium phosphate (5 mmol, 1.06 g), Pd 118 (5 mol %, 33 mg) and an aromatic boronic acid (1.1 mmol) were loaded into a reaction tube and sealed. This mixture was placed under vacuum and purged with argon 3 times. Then dry degassed acetonitrile (5 mL) was added to this mixture to form a yellow suspension, this stirred mixture was then heated to 80 °C and monitored via LCMS. After completion of the reaction the mixture was cooled filtered through a pad of celite, which was then washed though with dry acetonitrile (40 mL). The combined filtrates were then evaporated under reduced pressure to yield crude product. Specific examples of purification are given below.

4'-Acetyl-[1,1'-biphenyl]-4-yl MIDA boronate (4a). The reaction was followed by LCMS and after 1h 50 min it had gone to completion. The crude material was triturated with ethyl acetate, and then this solid was washed with 5 mL of cold ethyl acetate, to give the title compound as a light brown powder.

Yield: 231 mg (68%). ^{1}H NMR (400 MHz, DMSO-d6) δ 8.04 (d, J = 8.3 Hz, 2H), 7.85 (d, J = 8.3 Hz, 2H), 7.75 (d, J = 8.0 Hz, 2H), 7.58 (d, J = 8.0 Hz, 2H), 4.37 (d, J = 17.2 Hz, 2H), 4.15 (d, J = 17.2 Hz, 2H), 2.61 (s, 3H), 2.57 (s, 3H). ^{13}C NMR (101 MHz, DMSO) δ 197.4, 169.2, 144.4, 139.1, 135.6, 133.1, 128.8, 126.7, 126.1, 61.8, 47.6, 26.7. ^{11}B NMR (128 MHz, Acetonitrile-d3) δ 11.21. LCMS purity 95% (UV), Ret. time = 16.59 min. (TOFMS EI^{+}) found 350.1193, calcd for $[C_{19}H_{17}BNO_5]^{-}$ 350.1200.

5-Fluoro-4-formyl-2-(thiophen-3-yl)phenyl MIDA boronate (4b). The reaction was followed by LCMS and after 12 hours it had gone to completion. The crude material was triturated with ethyl acetate, and then this solid was then washed with 5 mL of cold ethyl acetate. This was then absorbed on to silica and loaded onto a silica column washed with a solution of 1.5% methanol in diethyl ether. The compound was then eluted with 100% THF, and then evaporated to give the title compound. Yield: 223 mg (62%). ^{1}H NMR (500 MHz, Acetonitrile-d3) δ 10.32 (s, 1H), 7.65 (d, $^{3}J_{FH}$ = 12.2 Hz, 1H), 7.61 (d, $^{4}J_{FH}$ = 6.8 Hz, 1H), 7.45 (dd, J = 4.9, 3.0 Hz, 1H), 7.34 (dd, J = 3.0, 1.3 Hz, 1H), 7.11 (dd, J = 4.9, 1.3 Hz, 1H), 3.88 (d, J = 17.1 Hz, 2H), 3.39 (d, J = 17.1 Hz, 2H), 2.54 (s, 3H). ^{13}C NMR (126 MHz, Acetonitrile-d3) δ 187.6 (d, $^{3}J_{FC}$ = 4.9 Hz), 167.6, 162.7 (d, $^{1}J_{FC}$

= 258.2 Hz), 141.5, 139.0 (d, $^4J_{FC}$ = 3.8 Hz), 131.5, 130.0, 125.8, 124.5, 123.8 (d, $^3J_{FC}$ = 8.8 Hz), 122.2 (d, $^4J_{FC}$ = 19.7 Hz), 62.8, 47.8. ^{19}F NMR (376 MHz, Acetonitrile-d3) δ -125.61 (dd, J = 12.2, 6.8 Hz). ^{11}B NMR (128 MHz, Acetonitrile-d3) δ 10.84. LCMS purity 90% (UV), Ret. time = 16.65 min. (TOFMS EI+) found 379.0930, calcd for $[C_{16}H_{13}BFNO_5SNH_4]^-$ 379.0930.

4'-Acetyl-4-fluoro-6-(trifluoromethyl)-[1,1'-biphenyl]-3-yl MIDA boronate (4c). The reaction was followed by LCMS and after 2 hours the reaction had gone to completion. The crude material was absorbed on to silica and then loaded onto a silica column. This was washed with 1.5% methanol in diethyl ether and then the compound was then eluted with 100% THF and then evaporated to give the title compound as a light brown solid. Yield: 411 mg (94%). ^{1}H NMR (500 MHz, Acetonitrile-d3) δ 8.08 – 8.02 (m, 2H), 7.59 – 7.54 (m, 2H), 7.53 – 7.48 (m, 2H), 4.20 (d, J = 17.1 Hz, 2H), 4.02 (d, J = 17.1 Hz, 2H), 2.75 (s, 3H), 2.64 (s, 3H). ^{13}C NMR (100 MHz, Acetonitrile-d3) δ 198.6, 169.0, 166.0 (d, $^1J_{FC}$ 243.3 Hz), 144.7, 139.9 (d, $^3J_{FC}$ = 9.5 Hz), 137.6, 136.9 (dd, $^3J_{FC}$ = 3.8, $^4J_{FC}$ = 2.1 Hz), 131.5 (dd, $^2J_{FC}$ = 31.1, $^3J_{FC}$ = 8.9 Hz), 130.5 (d, $^5J_{FC}$ = 1.1 Hz), 128.9, 124.5 (dd, $^1J_{FC}$ = 273.4, $^4J_{FC}$ =2.6 Hz), 114.4 (dq, $^2J_{FC}$ = 29.9, $^3J_{FC}$ = 5.3 Hz), 63.8, 48.7, 27.1. ^{19}F NMR (376 MHz, Acetonitrile-d3) δ -57.91, -107.07 – -107.16 (m). ^{11}B NMR (128 MHz, Acetonitrile-d3) δ 10.72. LCMS purity 94% (UV), Ret. time = 18.50 min. (FTMS m/z) found 436.0977, calcd for $[C_{20}H_{15}BF_4NO_5]^-$ 436.0985.

4-Fluoro-2'-methoxy-6-(trifluoromethyl)-[1,1'-biphenyl]-3-yl MIDA boronate (4d). The reaction was done on a 0.86 mmol scale and had gone to completion after 2 hours. The crude material was absorbed on to silica and then loaded onto a silica column. This was washed with 1.5 % methanol in diethyl ether and then the compound was then eluted off the column with 100 % ethyl acetate and then was evaporated to give the title compound as a light white solid. Yield: 234 mg (64%). ^{1}H NMR (500 MHz, Acetonitrile-d3) δ 7.44 (d, $^4J_{FH}$ = 6.4 Hz, 1H), 7.37 (d, $^3J_{FH}$ = 10.0 Hz, 1H), 7.32 – 7.25 (m, 1H), 7.05 – 7.02 (m, 1H), 6.98 – 6.95 (m, 1H), 6.91 – 6.85 (m, 1H), 4.36 (d, J = 17.2 Hz, 2H), 4.11 (d, J = 17.2 Hz, 2H), 3.61 (s, 3H), 2.88 (s, 3H). ^{13}C NMR (126 MHz, Acetonitrile-d3) δ 167.6, 164.6 (d, $^1J_{FC}$ = 242.6 Hz), 157.0, 139.5 (d, $^3J_{FC}$ = 9.3 Hz), 133.4, 131.4 (dd, $^2J_{FC}$ = 30.7, $^3J_{FC}$ = 8.6 Hz), 130.5, 129.5, 127.6, 123.4 (dd, $^1J_{FC}$ = 273.9, $^4J_{FC}$ = 2.1 Hz), 119.6, 112.6 (dq, $^2J_{FC}$ =$^2J_{FC}$ = 29.4 29.4, $^3J_{FC}$ = 5.3 Hz), 110.7, 62.7, 54.8, 47.5. ^{19}F NMR (376 MHz, Acetonitrile-d3) δ -60.32, -107.91 (dd, $^3J_{FH}$ = 10.0, $^4J_{FH}$ = 6.4 Hz). ^{11}B NMR (128 MHz, Acetonitrile-d3) δ 10.80. LCMS purity >99% (UV), Ret. time = 19.23 min. (TOFMS EI$^+$) found 448.0942, calcd for $[C_{19}H_{16}BNO_5F_4Na]^+$ 448.0942.

2-Fluoro-5-(thiophen-3-yl)-4-(trifluoromethyl)phenyl MIDA boronate (4e). The reaction was followed by LCMS and, after 1 hour, had gone to completion. The crude material was triturated with ethyl acetate, and then this solid was then washed with 2.5 mL of cold ethyl acetate, to give the title compound as a white solid. Yield: 105 mg (52%). ^{1}H NMR (399 MHz, Acetonitrile-d3) δ 7.60 (d, $^4J_{FH}$ = 6.4 Hz, 1H), 7.51 (d, $^3J_{FH}$ = 10.2 Hz, 1H), 7.48 (dd, $^3J_{HH}$ = 5, $^4J_{HH}$ = 3 Hz, 1H), 7.41 (d, $^4J_{FH}$ = 3 Hz, 1H), 7.18 (d, $^3J_{HH}$ = 5 Hz, 1H), 4.16 (d, J = 17 Hz, 2H), 3.98 (d, J = 17 Hz, 2H), 2.71 (s, 3H). ^{13}C NMR (100 MHz, Acetonitrile-d3) δ 169.0, 165.7 (d, $^1J_{FC}$ = = 242.8 Hz), 140.3 (d, $^3J_{FC}$ = 9.3 Hz), 139.6, 133.0 – 132.8 (m), 131.6 (qd, $^2J_{FC}$ = 30.8, $^3J_{FC}$ = 9.0 Hz), 130.1 (d, $^6J_{FC}$ = 1.9 Hz), 126.5, 125.31 (d, $^5J_{FC}$ = 2.1 Hz), 124.5 (dd, $^1J_{FC}$ = 273.2, $^4J_{FC}$ = 2.8 Hz), 114.4 (dq, $^2J_{FC}$ = 29.7, $^3J_{FC}$ = 5.6 Hz), 63.8, 48.7. ^{19}F NMR (376 MHz, Acetonitrile-d3) δ -58.84, -107.68 (dd, $^3J_{FH}$ = 10.2, $^4J_{FH}$ = 6.4 Hz). ^{11}B NMR (128 MHz, Acetonitrile-d3) δ 10.81. LCMS purity > 99% (UV), Ret. time = 19.39 min. (TOFMS EI$^+$) found 402.0590, calcd for $[C_{16}H_{13}{}^{11}BNO_4F_4S]^+$ 402.0594.

2-Fluoro-4-methyl-5-(thiophen-3-yl)phenyl MIDA boronate (4f). This was followed by LCMS and after 30 minutes the reaction had gone to completion. The crude material was triturated with ethyl acetate, and then this solid was then washed with 5 mL of cold ethyl acetate, to give the title compound as a yellow solid. Yield: 202 mg (58%).

^{1}H NMR (400 MHz, DMSO-d6) δ 7.62 (dd, J = 4.9, 3.0 Hz, 1H), 7.51 (dd, J = 3.0, 1.3 Hz, 1H), 7.36 (d, $^4J_{FH}$ = 7.0 Hz, 1H), 7.23 (dd, J = 4.9, 1.3 Hz, 1H), 7.07 (d, $^3J_{FH}$ = 10.9 Hz, 1H), 4.39 (d, J = 17.9 Hz, 2H), 4.08 (d, J = 17.3 Hz,

2H), 2.66 (s, 3H), 2.31 (s, 3H). ^{13}C NMR (101 MHz, DMSO-d6) δ 168.9, 164.5 (d, $^{1}J_{FC}$ = 241.4 Hz), 140.7, 139.2 (d, $^{3}J_{FC}$ = 8.9 Hz), 135.8 (d, $^{2}J_{FC}$ = 9.8 Hz), 132.0 (d, $^{4}J_{FC}$ = 2.7 Hz), 128.9, 125.8, 123.1, 116.5 (d, $^{2}J_{FC}$ = 24.9 Hz), 62.3, 47.6, 20.3. ^{19}F NMR (376 MHz, DMSO-d6) δ -109.15 – -109.25 (m). ^{11}B NMR (128 MHz, DMSO-d6) δ 10.59. LCMS purity >99% (UV), Ret. time = 18.52 min. (TOFMS EI^{+}) found 347.0792, calcd for $[C_{16}H_{15}{}^{11}BNO_4FS]^{+}$ 347.0799.

2',4-Dimethoxy-[1,1'-biphenyl]-3-yl MIDA boronate (4g). The reaction was followed by LCMS and after 2 hours, had gone to completion. The crude material was triturated with ethyl acetate, and then this solid was washed with 5 mL of cold ethyl acetate, to give the title compound as a white solid. Yield: 285 mg (56%). ^{1}H NMR (600 MHz, Acetonitrile-d3) δ 7.66 (s, 1H), 7.61 – 7.55 (m, 1H), 7.36 – 7.29 (m, 2H), 7.11 – 6.97 (m, 3H), 4.10 (d, J = 17.0 Hz, 2H), 3.99 (d, J = 17.0 Hz, 2H), 3.83 (s, 3H), 3.81 (s, 3H), 2.68 (s, 3H). ^{13}C NMR (100 MHz, Acetonitrile-d3) δ 168.7, 161.5, 156.5, 135.5, 132.0, 130.7, 130.4, 128.3, 120.8, 111.6, 109.8, 63.5, 55.2, 54.8, 47.3. ^{11}B NMR (128 MHz, Acetonitrile-d3) δ 11.95. LCMS purity >99% (UV), Ret. time = 17.69 min. (TOFMS EI^{+}) found 408.1028, calcd for $[C_{20}H_{20}{}^{11}BNO_6K]^{+}$ 408.1021

4'-Acetyl-4-methoxy-[1,1'-biphenyl]-3-yl MIDA boronate (4h). The reaction was followed by LCMS and after 2 hours, had gone to completion. The crude material was triturated with ethyl acetate, and then this solid was then washed with 5 mL of cold ethyl acetate, to give the title compound as a white solid. Yield: 214 mg (56%). ^{1}H NMR (500 MHz, Acetonitrile-d3) δ 8.06 – 8.00 (m, 2H), 7.92 – 7.89 (m, 1H), 7.79 – 7.73 (m, 3H), 7.10 – 7.06 (m, 1H), 4.10 (d, J = 17.1 Hz, 2H), 3.99 (d, J = 17.0 Hz, 2H), 3.83 (s, 3H), 2.67 (s, 3H), 2.59 (s, 3H). ^{13}C NMR (126 MHz, Acetonitrile-d3) δ 198.5, 169.7, 163.9, 146.3, 136.5, 134.4, 130.8, 129.9, 127.5, 111.9, 111.0, 64.6, 56.0, 48.4, 27.0. ^{11}B NMR (128 MHz, Acetonitrile-d3) δ 12.00. LCMS purity > 99% (UV), Ret. time = 16.46 min. (FTMS m/z) found 380.1307, calcd for $[C_{20}H_{19}BNO_6]^{-}$ 380.1311.

General procedure for one-pot MIDA deprotection Suzuki cross-couplings.

The phenyl MIDA analogue (0.20 mmol), aryl bromide (0.22 mmol), potassium phosphate (1.00 mmol, 212 mg) and Pd-118 (0.004 mmol, 6.5 mg) were added to a 10mL microwave vial equipped with a magnetic stirrer and a Teflon cap. Then this mixture was placed under vacuum and purged with argon 3 times. Next, dry degassed THF (1 mL), followed by degassed water (0.4 mL) were added to this mixture to form a yellow solution. This reaction mixture was heated using the dynamic heating method, with the power set to 150 W, max pressure 300 psi, max temperature 80 °C, high stirring throughout and power max turned off. This method was used to hold the reaction mixture at 80 °C for 15 min. After cooling, sodium hydroxide solution was added (5 mL, 2 M), this aqueous phase was then extracted with ethyl acetate (3 x 10 mL). The combined organic layers were washed with brine (3 x 10 mL) and then dried with $MgSO_4$ and evaporated under reduced pressure. This crude material was then absorbed on to silica and purified by flash chromatography. Specific examples of flash chromatography mobile phases are given below.

2-(2-Fluoro-4-methyl-5-(thiophen-3-yl)phenyl)pyridine (5b). This was purified by flash chromatography on silica gel, 10% ethyl acetate in hexane. Yield: 26 mg (48%). TLC (hexane 90 %: ethyl acetate, 10 %) R_f = 0.48. ^{1}H NMR (500 MHz, Acetone-d6) δ 8.70 – 8.67 (m, 1H), 8.02 (d, $^{3}J_{FH}$ = 8.3 Hz, 1H), 7.88 – 7.85 (m, 2H), 7.57 (dd, J = 4.9, 2.9 Hz, 1H), 7.47 (d, J = 2.9 Hz, 1H), 7.36 – 7.32 (m, 1H), 7.26 (dd, J = 4.9, 1.3 Hz, 1H), 7.18 (d, $^{4}J_{FH}$ = 12.4 Hz, 1H), 2.39 (s, 3H). ^{13}C NMR (126 MHz, Acetone-d6) δ 160.4 (d, $^{1}J_{FC}$ = 248.6 Hz), 153.8 (d, $^{3}J_{FC}$ = 3.3 Hz), 150.7, 141.9, 139.9 (d, $^{3}J_{FC}$ = 8.5 Hz), 137.4, 134.2 (d, $^{4}J_{FC}$ = 3.4 Hz), 132.9 (d, $^{3}J_{FC}$ = 3.6 Hz), 129.7, 126.4, 125.6 (d, $^{2}J_{FC}$ = 11.8 Hz), 124.9 (d, $^{4}J_{FC}$ = 10.1 Hz), 124.0, 123.4, 118.6 (d, $^{2}J_{FC}$ = 23.5 Hz), 20.7. ^{19}F NMR (376 MHz, Acetone-d6) δ -121.13 (dd, $^{3}J_{FH}$ = 12.4, $^{3}J_{FH}$ = 8.3 Hz). LCMS purity >99% (UV), Ret. time = 22.27 min. (TOFMS EI^{+}) found 270.0748, calcd for $[C_{16}H_{13}NFS]^{+}$ 270.0753.

2-Fluoro-4-(pyridin-2-yl)-5-(thiophen-3-yl)benzaldehyde (5c). This was purified by flash chromatography on silica gel on a gradient of 0-20% ethyl acetate in hexane. Yield: 9 mg (16%). ^{1}H NMR (500 MHz, Acetone-d6) δ 10.39 (s, 1H), 8.68 – 8.64 (m, 1H), 7.94 (d, $^{4}J_{FH}$ = 7.0 Hz, 1H), 7.68 – 7.62 (m, 1H), 7.57 (d, $^{3}J_{FH}$ = 11.3 Hz, 1H), 7.40 – 7.36 (m, 1H), 7.36 – 7.32 (m, 1H), 7.32 – 7.30 (m, 1H), 7.16 – 7.10 (m, 1H), 6.78 – 6.73 (m, 1H). ^{13}C NMR (126 MHz, Acetone-d6) δ 186.4 (d, $^{3}J_{FC}$ = 5.0 Hz), 162.9 (d, $^{1}J_{FC}$ = 257.8 Hz), 156.7, 149.7, 147.3 (d, $^{2}J_{FC}$ = 8.6 Hz), 139.7, 135.9, 132.4 (d, $^{3}J_{FC}$ = 3.7 Hz), 130.7 (d, $^{3}J_{FC}$ = 2.3 Hz), 128.5, 125.7, 124.5, 123.8, 122.9, 118.3 (d, $^{2}J_{FC}$ = 21.9 Hz). ^{19}F NMR (376 MHz, Benzene-d6) δ -120.15 (dd, $^{3}J_{FH}$ = 11.3, $^{4}J_{FH}$ = 7.0 Hz). LCMS purity >99% (UV), Ret. time = 19.75 min. (TOFMS EI^{+}) found 284.0551, calcd for $[C_{16}H_{11}NOFS]^{+}$ 284.0545.

5-Fluoro-2'-methoxy-2-(thiophen-3-yl)-[1,1'-biphenyl]-4-carbaldehyde (5d). This was purified by flash chromatography on silica gel on a gradient of 0-3% diethyl ether in hexane. Yield: 20 mg (32%).
^{1}H NMR (500 MHz, Chloroform-d) δ 10.41 (s, 1H), 7.96 (d, $^{4}J_{FH}$ = 7.1 Hz, 1H), 7.36 – 7.29 (m, 1H), 7.18 (d, $^{3}J_{FH}$ = 10.9 Hz, 1H), 7.18 – 7.11 (m, 1H), 7.13 – 7.10 (m, 1H), 7.00 – 6.95 (m, 1H), 6.94 – 6.89 (m, 1H), 6.84 – 6.78 (m, 1H), 6.78 – 6.75 (m, 1H), 3.46 (s, 3H). ^{13}C NMR (126 MHz, Chloroform-d) δ 186.8 (d, $^{3}J_{FC}$ = 5.8 Hz), 163.3 (d, $^{1}J_{FC}$ = 259.0 Hz), 156.1, 146.1 (d, $^{2}J_{FC}$ = 9.1 Hz), 140.2, 133.5 (d, $^{3}J_{FC}$ = 3.5 Hz), 130.6, 129.9, 129.1 (d, $^{4}J_{FC}$ = 2.3 Hz), 128.7, 128.0, 124.5, 122.9 (d, $^{3}J_{FC}$ = 8.4 Hz), 122.6, 120.7, 118.9 (d, $^{2}J_{FC}$ = 20.8 Hz), 111.1, 55.2. ^{19}F NMR (376 MHz, Chloroform-d) δ -125.16 (dd, $^{3}J_{FH}$ = 10.9, $^{4}J_{FH}$ = 7.1 Hz). LCMS purity >99% (UV), Ret. time = 23.46 min. (FTMS m/z) found 313.0690, calcd for $[C_{18}H_{13}FO_2SH]^{+}$ 313.0693.

2-Fluoro-4-(1*H*-indol-5-yl)-5-(thiophen-3-yl)benzaldehyde (5e). This was purified by flash chromatography on silica gel on a gradient of 0-10% DCM in hexane. Yield: 17 mg (26%). ^{1}H NMR (500 MHz, Acetone-d6) δ 10.36 (s, 1H), 10.35 (bs, 1H), 7.93 (d, $^{4}J_{FH}$ = 7.2 Hz, 1H), 7.55 – 7.52 (m, 1H), 7.39 – 7.33 (m, 3H), 7.31 – 7.27 (m, 1H), 7.26 – 7.21 (m, 1H), 6.95 – 6.90 (m, 1H), 6.71 – 6.67 (m, 1H), 6.49 – 6.45 (m, 1H). ^{13}C NMR (126 MHz, Acetone-d6) δ 187.3 (d, $^{3}J_{FC}$ = 5.0 Hz), 163.8 (d, $^{1}J_{FC}$ = 257.8 Hz), 151.5 (d, $^{2}J_{FC}$ = 9.1 Hz), 141.5, 137.0, 133.4 (d, $^{3}J_{FC}$ = 3.4 Hz), 131.5, 131.3 (d, $^{4}J_{FC}$ = 2.6 Hz), 129.6, 129.2, 127.0, 126.0, 124.4, 123.6, 123.4 (d, $^{3}J_{FC}$ = 8.9 Hz), 122.1, 119.4 (d, $^{2}J_{FC}$ = 20.8 Hz), 112.0, 103.0. ^{19}F NMR (376 MHz, Acetone-d6) δ -125.64 (dd, $^{3}J_{FH}$ = 11.6, $^{4}J_{FH}$ = 7.2 Hz).
LCMS purity 96% (UV), Ret. time = 17.28 min. (TOFMS EI^{+}) found 344.0505, calcd for $[C_{19}H_{12}NOFSNa]^{+}$ 344.0521.

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