Supporting Information
for
Scope and limitations of a DMF bio-alternative within Sonogashira cross-coupling and Cacchi-type annulation

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Experimental procedures, analytical data, copies of NMR spectra, and single X-ray crystal diffraction data of 4b
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1. General
All reagents and solvents were obtained from commercial suppliers and were used without further purification unless otherwise stated. Purification was carried out according to standard laboratory methods.¹

1.1 Purification of solvents
Cyrene was supplied directly by Circa and used as obtained. DMF was dried by heating to reflux over previously activated 4 Å molecular sieves and distilling under vacuum before being purged with, and stored under N₂ in a septum-sealed oven-dried flask over previously activated 4 Å molecular sieves. THF was obtained from a PureSolv SPS-400-5 solvent purification system and transferred to and stored in a septum-sealed oven-dried flask over previously activated 4 Å molecular sieves.

THF was obtained from a PureSolv SPS-400-5 solvent purification system and transferred to and stored in a septum-sealed oven-dried flask over previously activated 4 Å molecular sieves and purged with and stored under N₂. CH₂Cl₂, Et₂O, EtOAc, MeCN, and petroleum ether 40–60 °C for purification purposes were used as obtained from suppliers without further purification.

1.2 Purification and drying of bases
Et₃N was dried by heating to reflux over previously activated 4 Å molecular sieves and distilling under vacuum before being purged with, and stored under N₂ in a septum-sealed oven-dried flask over previously activated 4 Å molecular sieves. Inorganic bases were dried in a Heraeus Vacutherm oven at 60 °C under vacuum for a minimum of 24 h before use.

1.3 Experimental details
Reactions were carried out using conventional glassware (preparation of S1 and S2) or in sealed 5 mL microwave vials (optimization reactions and reactions for Schemes 2 and 3). The glassware was oven-dried (150 °C) and purged with N₂ before use. Purging refers to a vacuum/nitrogen-refilling procedure. Room temperature was generally ca. 18 °C. Reactions were carried out at elevated temperatures using a temperature-regulated hotplate/stirrer.

1.4 Purification of products
Thin layer chromatography was carried out using Merck silica plates coated with fluorescent indicator UV254. These were analyzed under 254 nm UV light or developed using a vanillin solution. Normal phase flash chromatography was carried out using ZEOprep 60 HYD 40–63 µm silica gel. Reverse phase flash chromatography was carried out using IST Isolute C18 cartridges. Strong cation-exchange purification was carried out using an SCX cartridge.

1.5 Analysis of products
Fourier transformed infrared (FTIR) spectra were obtained on a Shimadzu IRAffinity-1 machine. ¹H, ¹³C, ¹⁹F and ¹¹B NMR spectra were obtained on a Bruker DRX 500 spectrometer (Avance III HD console, Ascend 500 MHz magnet, BBO smart probe) at 500 MHz, 126 MHz, 471 MHz and 160 MHz, respectively. ¹H NMR for the evaluation of the base sensitivity were obtained on a Bruker AV 400 at 400 MHz. Chemical shifts are reported in ppm and coupling constants are reported in Hz with CDCl₃ referenced at 7.26 (¹H) and 77.0 ppm (¹³C) and DMSO-d₆ referenced at 2.50 (¹H) and 39.5 (¹³C). High-resolution mass spectra were obtained through analysis at the EPSRC UK National Mass Spectrometry Facility at Swansea University or at Glasgow University’s School of Chemistry Mass Spectrometry Service. Crystal data was obtained at 123(2) K using an Oxford Diffraction Gemini instrument and monochromatic Mo radiation.
2. General experimental procedures

General Procedure A: Optimized conditions

For example, synthesis of 1,2-diphenylethyne, 3a.

To an oven-dried 5 mL microwave vessel was added Pd(PPh₃)₂Cl₂ (3.5 mg, 0.005 mmol, 2 mol %) and CuI (1.9 mg, 0.01 mmol, 4 mol %). The vessel was then capped and purged with N₂ before addition of Cyrene (0.5 mL, 0.5 M), Et₃N (38 µL, 0.275 mmol, 1.1 equiv), iodobenzene (27.9 µL, 0.25 mmol, 1 equiv), and phenylacetylene (28.8 µL, 0.263 mmol, 1.05 equiv). The reaction mixture was heated to 30 °C and maintained at this temperature with stirring for 1 h before the vessel was vented, and decapped. The solution was then diluted with EtOAc (10 mL), and washed with water (2 × 20 mL) and brine (2 × 20 mL). The organics were then passed through a hydrophobic frit and concentrated under reduced pressure to give a yellow oil, which was purified by flash chromatography (silica gel, 0–5% Et₂O in petroleum ether) to afford the title compound as a white solid (44.5 mg, quant.).

νₘₐₓ (solid): 3068, 1603, 1495, 1446 cm⁻¹.

¹H NMR (CDCl₃, 500 MHz): δ 7.55 (dd, J = 7.2, 1.9 Hz, 4H), 7.36 (m, 6H).

¹³C NMR (CDCl₃, 126 MHz): δ 131.6, 128.4, 128.3, 123.3, 89.4.

HRMS: exact mass calculated for [M] (C₁₈H₁₀) requires m/z 178.0782, found m/z 178.0784.

Characterisation data is consistent with literature reported values.²

General Procedure B: Synthesis of indoles and benzofuran

For example, synthesis of 2-phenyl-1-tosyl-1H-indole (7a).

To an oven-dried 5 mL microwave vessel was added Pd(PPh₃)₂Cl₂ (3.5 mg, 0.005 mmol, 2 mol %), CuI (1.9 mg, 0.01 mmol, 4 mol %), and N-(2-iodophenyl)-4-methylbenzenesulfonylamide (93 mg, 0.25 mmol, 1 equiv). The vessel was then capped and purged with N₂ before addition of Cyrene (0.5 mL, 0.5 M), Et₃N (104 µL, 0.75 mmol, 3 equiv), and phenylacetylene (28.8 µL, 0.263 mmol, 1.05 equiv). The reaction mixture was heated to 30 °C and maintained at this temperature with stirring for 1 h. The reaction was subsequently heated to 60 °C and maintained at this temperature for 6 h before the vessel was vented and decapped. The solution was then diluted with EtOAc (10 mL), and washed with water (2 × 20 mL) and brine (2 × 20 mL). The organics were then passed through a hydrophobic frit and concentrated under reduced pressure to give a yellow oil, which was purified by flash chromatography (silica gel, 0–15% EtOAc in petroleum ether) to afford the title compound as a white solid (78.4 mg, 90%).

νₘₐₓ (solid): 3073, 1368, 1169 cm⁻¹.

¹H NMR (CDCl₃, 500 MHz): δ 8.33 (d, J = 8.4 Hz, 1H), 7.54–7.50 (m, 2H), 7.45 (t, J = 8.2 Hz, 2H), 7.38 (t, J = 7.4 Hz, 1H), 7.31–7.28 (m, 3H), 7.06 (d, J = 8.1 Hz, 2H), 6.56 (s, 1H), 2.31 (s, 3H).


HRMS: exact mass calculated for [M+H]⁺ (C₂₁H₁₈NO₅S) requires m/z 348.1058, found m/z 348.1061.

Characterisation data is consistent with literature reported values.³
3. Reaction optimization data

3.1. Variation of concentration
Reactions were carried out according to General Procedure A using Pd(PPh₃)₂Cl₂ (3.5 mg, 0.005 mmol, 2 mol %), CuI (1.9 mg, 0.01 mmol, 4 mol %), Cyrene (X M), Et₃N (104 µL, 0.75 mmol, 3 equiv), iodobenzene (27.9 µL, 0.25 mmol, 1 equiv), and phenylacetylene (28.8 µL, 0.263 mmol, 1.05 equiv). After stirring at 20 °C for 5 h, the reaction was subjected to the purification outlined in the General Procedure (silica gel, 0–5% Et₂O in petroleum ether) to afford the desired compound as a white solid.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Concentration (M)</th>
<th>Volume (mL)</th>
<th>Isolated yield (%)</th>
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<td>0.83</td>
<td>98</td>
</tr>
<tr>
<td>2</td>
<td>0.1</td>
<td>2.5</td>
<td>94</td>
</tr>
<tr>
<td>3</td>
<td>0.5</td>
<td>0.5</td>
<td>100</td>
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</tbody>
</table>

3.2. Variation of the base
Reactions were carried out according to General Procedure A using Pd(PPh₃)₂Cl₂ (3.5 mg, 0.005 mmol, 2 mol %), CuI (1.9 mg, 0.01 mmol, 4 mol %), Cyrene (0.5 mL, 0.5 M), Base (X equiv), iodobenzene (27.9 µL, 0.25 mmol, 1 equiv), and phenylacetylene (28.8 µL, 0.263 mmol, 1.05 equiv). After stirring at 20 °C for 5 h, the reaction was subjected to the purification outlined in the General Procedure (silica gel, 0–5% Et₂O in petroleum ether) to afford the desired compound as a white solid.

<table>
<thead>
<tr>
<th>Entry</th>
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<th>Equiv</th>
<th>Isolated yield (%)</th>
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<tbody>
<tr>
<td>1*</td>
<td>K₃PO₄ (159 mg)</td>
<td>3</td>
<td>-</td>
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<tr>
<td>2*</td>
<td>Cs₂CO₃ (245 mg)</td>
<td>3</td>
<td>-</td>
</tr>
<tr>
<td>3</td>
<td>DIPEA (97 mg)</td>
<td>3</td>
<td>85</td>
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<tr>
<td>4</td>
<td>Pyridine (59 mg)</td>
<td>3</td>
<td>0</td>
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<tr>
<td>5</td>
<td>Et₃N (28 mg)</td>
<td>1.1</td>
<td>98</td>
</tr>
<tr>
<td>6</td>
<td>Et₃N (38 mg)</td>
<td>1.5</td>
<td>94</td>
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<tr>
<td>7</td>
<td>Et₃N (51 mg)</td>
<td>2</td>
<td>92</td>
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</table>

* Formation of solid Cyrene dimer – product was not isolated

3.3. Variation of time and temperature
Reactions were carried out according to General Procedure A using Pd(PPh₃)₂Cl₂ (3.5 mg, 0.005 mmol, 2 mol %), CuI (1.9 mg, 0.01 mmol, 4 mol %), Cyrene (0.5 mL, 0.5 M), Et₃N (38 µL, 0.275 mmol, 1.1 equiv), iodobenzene (27.9 µL, 0.25 mmol, 1 equiv), and phenylacetylene (28.8 µL, 0.263 mmol, 1.05 equiv). After stirring at X °C for X h, the reaction was subjected to the purification outlined in the General Procedure (silica gel, 0–5% Et₂O in petroleum ether) to afford the desired compound as a white solid.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Temp. (°C)</th>
<th>Time (h)</th>
<th>Isolated yield (%)</th>
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<td>20</td>
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<tr>
<td>5</td>
<td>30</td>
<td>1</td>
<td>96</td>
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3.4. Variation of solvent
Reactions were carried out according to General Procedure A using Pd(PPh$_3$)$_2$Cl$_2$ (3.5 mg, 0.005 mmol, 2 mol %), CuI (1.9 mg, 0.01 mmol, 4 mol %), solvent (0.5 mL, 0.5 M), Et$_3$N (38 µL, 0.275 mmol, 1.1 equiv), iodobenzene (27.9 µL, 0.25 mmol, 1 equiv), and phenylacetylene (28.8 µL, 0.263 mmol, 1.05 equiv). After stirring at 30 °C for 1 h, the reaction was subjected to the purification outlined in the General Procedure (silica gel, 0–5% Et$_2$O in petroleum ether) to afford the desired compound as a white solid.

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<th>Entry</th>
<th>Solvent</th>
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<tr>
<td>3</td>
<td>DMF</td>
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4. Base sensitivity study
Base (0.07 mmol) was added to a test tube and Cyrene (0.5 mL) was added. The tube was then capped and the mixture stirred at X °C. After 24 h the reaction mixture was sampled and analysed by TLC (60% EtOAc in petroleum ether) and $^1$H NMR and the resulting spectrum compared with that of Cyrene.

<table>
<thead>
<tr>
<th>Base</th>
<th>Mass (mg)</th>
<th>Temperature (°C)</th>
<th>Reaction (Y/N)</th>
<th>Solid Formation</th>
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<td>50 N</td>
<td>x</td>
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<tr>
<td></td>
<td></td>
<td>100 N</td>
<td>x</td>
<td></td>
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<tr>
<td>Pyridine</td>
<td>6</td>
<td>25 N</td>
<td>x</td>
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<tr>
<td></td>
<td></td>
<td>50 N</td>
<td>x</td>
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<td></td>
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<td>100 N</td>
<td>x</td>
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<td>K$_2$CO$_3$</td>
<td>10</td>
<td>25 N</td>
<td>x</td>
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<tr>
<td></td>
<td></td>
<td>50 N</td>
<td>x</td>
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<tr>
<td></td>
<td></td>
<td>100 Y</td>
<td>√</td>
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<tr>
<td>DIPEA</td>
<td>9</td>
<td>25 N</td>
<td>x</td>
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<tr>
<td></td>
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<td>50 N</td>
<td>x</td>
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<tr>
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<td>25 Y</td>
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<td>x</td>
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<tr>
<td></td>
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<td>KOH</td>
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5. Compound characterisation data
5.1. Preparation of intermediates

**S1: N-(5-Chloro-2-iodophenyl)-4-methylbenzenesulfonamide**

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<table>
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<th>5.1. Preparation of intermediates</th>
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<tbody>
<tr>
<td><strong>S1</strong>: N-(5-Chloro-2-iodophenyl)-4-methylbenzenesulfonamide</td>
</tr>
</tbody>
</table>

To a round-bottomed flask charged with 5-chloro-2-iodoaniline (1 g, 3.95 mmol, 1 equiv) was added a solution of 1:1 pyridine in CH₂Cl₂ (0.7 M, 40 mL) and the reaction mixture was cooled to 0 °C. 4-Methylbenzenesulfonyl chloride (750 mg, 3.95 mmol, 1 equiv) was added portionwise, and the reaction mixture was allowed to slowly warm to room temperature and then stirred for 24 h. Upon completion of the reaction, water (80 mL) and CH₂Cl₂ (80 mL) were added. The reaction mixture was separated and the organics were washed with 1 N NaOH (2 × 40 mL), 1 N HCl (2×40 mL), and brine (2 × 40 mL). The organics were then passed through a hydrophobic frit and concentrated under reduced pressure to give a crude residue, which was purified by flash chromatography (silica gel, 0–12% EtOAc in petroleum ether) to afford the title compound as an off white solid (890 mg, 52%).

³H NMR (CDCl₃, 500 MHz): δ 7.72–7.65 (m, 3H), 7.57 (d, J = 8.5 Hz, 1H), 7.27 (d, J = 8.0 Hz, 2H), 6.88–6.80 (m, 2H), 2.42 (s, 3H).

¹³C NMR (CDCl₃, 126 MHz): δ 144.1, 139.1, 138.1, 135.1, 135.1, 129.4, 127.0, 126.4, 121.4, 88.3, 21.2.

Characterisation data is consistent with literature reported values.¹

**S2: N-(3-Iodo-5-nitropyridin-2-yl)-4-methylbenzenesulfonamide**

Prepared in two steps from 3-iodo-5-nitropyridin-2-amine:

**Step 1**: To a 25 mL three-necked flask charged with 5-nitropyridin-2-amine (1 g, 7.1 mmol, 1 equiv), was added concentrated sulfuric acid (12 mL, 0.6 M) and potassium iodate (653 mg, 2.8 mmol, 0.4 equiv) portionwise, before subsequent heating to 200 °C. Potassium iodide (1.18 g, 7.1 mmol, 1 equiv) was then added dropwise as an aqueous solution (4 mL), and the reaction mixture was stirred at 200 °C for 1.5 h. Upon completion, the reaction mixture was allowed to cool to room temperature before the slow addition of saturated sodium bicarbonate solution (20 mL) and EtOAc (20 mL). The reaction mixture was separated and the organics were washed with an aqueous solution of saturated Na₂S₂O₃ (2 × 30 mL). The organics were then passed through a hydrophobic frit and concentrated under reduced pressure to give a yellow solid, 3-iodo-5-nitropyridin-2-amine, which was used without further purification (1.64 g, 87%).

**Step 2**: To a 100 mL round-bottomed flask charged with 3-iodo-5-nitropyridin-2-amine (1.29 g, 4.86 mmol, 1 equiv) was added THF (40 mL, 0.13 M) and the reaction mixture was cooled to 0 °C.
Sodium hydride (224 mg, 9.72 mmol, 2 equiv) was added portionwise and the reaction mixture was stirred at 0 °C for 20 minutes. 4-Methylbenzenesulfonyl chloride (1.09 g, 4.86 mmol, 1 equiv) was added portion wise, and the reaction mixture was allowed to slowly warm to room temperature and was stirred for 18 h. Upon completion of the reaction, water (50 mL) and CH₂Cl₂ (50 mL) were added and the reaction mixture was separated and the organics washed with 1 M NaOH (2 × 50 mL), 1 M HCl (2 × 50 mL), and brine (2 × 50 mL). The organics were passed through a hydrophobic frit and concentrated under reduced pressure to give a crude residue, which was purified by flash chromatography (silica gel, 0–30% EtOAc in petroleum ether) to afford the title compound as a yellow solid (1.43 g, 70%).

υₘₐₓ (solid): 3581, 3268, 3064, 2919, 1571, 1444, 1320 cm⁻¹.

¹H NMR (DMSO-d₆, 500 MHz): δ 8.66 (d, J = 2.6 Hz, 1H), 8.40 (d, J = 2.5 Hz, 1H), 7.74 (d, J = 8.1 Hz, 2H), 7.21 (d, J = 8.0 Hz, 2H), 3.35 (bs, 1H), 2.32 (s, 3H).

¹³C NMR (DMSO-d₆, 126 MHz): δ 161.9, 145.0, 142.3, 140.9, 140.7, 134.7, 128.9, 127.4, 86.7, 21.4.

HRMS: exact mass calculated for [M+H]⁺ (C₁₀H₁₁N₅O₂S) requires m/z 419.9509, found m/z 419.9510.

Characterisation data is consistent with literature reported values.⁴

5.2. Products from Table 1

3a: 1,2-Diphenylethyne

Prepared according to General Procedure A using Pd(PPh₃)₂Cl₂ (3.5 mg, 0.005 mmol, 2 mol %), CuI (1.9 mg, 0.01 mmol, 4 mol %), Cyrene (0.5 mL, 0.5 M), Et₃N (38 µL, 0.275 mmol, 1.1 equiv), iodobenzene (27.9 µL, 0.25 mmol, 1 equiv), and phenylacetylene (28.8 µL, 0.263 mmol, 1.05 equiv). After 1 h, the reaction mixture was subjected to the purification method outlined in the General Procedure (silica gel, 0–5% Et₂O in petroleum ether) to afford the title compound as a white solid (44.5 mg, quan.).

υₘₐₓ (solid): 3068, 1603, 1495, 1446 cm⁻¹.

¹H NMR (CDCl₃, 500 MHz): δ 7.55 (dd, J = 7.2, 1.9 Hz, 4H), 7.36 (m, 6H).

¹³C NMR (CDCl₃, 126 MHz): δ 131.6, 128.9, 127.3, 89.4.

HRMS: exact mass calculated for [M]⁺ (C₁₄H₁₀) requires m/z 178.0782, found m/z 178.0784.

Characterisation data is consistent with literature reported values.²

5.3. Products from Scheme 2a

3b: 1-Fluoro-4-(phenylethynyl)benzene

Prepared according to General Procedure A using Pd(PPh₃)₂Cl₂ (3.5 mg, 0.005 mmol, 2 mol %), CuI (1.9 mg, 0.01 mmol, 4 mol %), Cyrene (0.5 mL, 0.5 M), Et₃N (38 µL, 0.275 mmol, 1.1 equiv), 4-fluoroiodobenzene (28.8 µL, 0.25 mmol, 1 equiv), and phenylacetylene (28.8 µL, 0.263 mmol, 1.05 equiv). After 1 h, the reaction mixture was subjected to the purification method outlined in the General Procedure (silica gel, 0–5% Et₂O in petroleum ether) to afford the title compound as a white solid (48.8 mg, quan.).

Prepared according to General Procedure A using Pd(PPh₃)₂Cl₂ (3.5 mg, 0.005 mmol, 2 mol %), CuI (1.9 mg, 0.01 mmol, 4 mol %), DMF (0.5 mL, 0.5 M), Et₃N (38 µL, 0.275 mmol, 1.1 equiv), 4-fluoroiodobenzene (28.8 µL, 0.25 mmol, 1 equiv), and phenylacetylene (28.8 µL, 0.263 mmol, 1.05 equiv).
After 1 h, the reaction mixture was subjected to the purification method outlined in the General Procedure (silica gel, 0–5% Et₂O in petroleum ether) to afford the title compound as a white solid (46.9 mg, 96%).

υ₉₉₅ (solid): 2921, 1595, 1508, 1217 cm⁻¹.

¹H NMR (CDCl₃, 500 MHz): δ 7.55–7.50 (m, 4H), 7.38–7.33 (m, 3H), 7.05 (t, J = 8.7 Hz, 2H).

¹³C NMR (CDCl₃, 126 MHz): δ 162.5 (d, ¹JC = 249.6 Hz), 133.5 (d, ¹JC = 8.2 Hz), 131.6, 128.4, 128.4, 123.3, 119.4 (d, ¹JC = 3.4 Hz), 115.7 (d, ¹JC = 22.4 Hz), 89.1, 88.3.

¹⁹F NMR (CDCl₃, 471 MHz): δ -110.98.

HRMS: exact mass calculated for [M] (C₁₄H₉F) requires m/z 196.0688, found m/z 196.0689.
Characterisation data is consistent with literature reported values.

3e: 1-Nitro-4-(phenylethynyl)benzene

\[
\begin{array}{c}
\text{O}_2\text{N} & \equiv & \equiv \\
\text{H} & \equiv & \equiv \\
\text{H} & \equiv & \equiv \\
\end{array}
\]

Prepared according to General Procedure A using Pd(PPh₃)₂Cl₂ (3.5 mg, 0.005 mmol, 2 mol %), CuI (1.9 mg, 0.01 mmol, 4 mol %), Cyrene (0.5 mL, 0.5 M), Et₃N (38 µL, 0.275 mmol, 1.1 equiv), 4-nitro-iodobenzene (62.3 mg, 0.25 mmol, 1 equiv), and phenylacetylene (28.8 µL, 0.263 mmol, 1.05 equiv). After 1 h, the reaction mixture was subjected to the purification method outlined in the General Procedure (silica gel, 0–5% Et₂O in petroleum ether) to afford the title compound as an off white solid (48.8 mg, quant.).

Prepared according to General Procedure A using Pd(PPh₃)₂Cl₂ (3.5 mg, 0.005 mmol, 2 mol %), CuI (1.9 mg, 0.01 mmol, 4 mol %), Cyrene (0.5 mL, 0.5 M), Et₃N (38 µL, 0.275 mmol, 1.1 equiv), 4-nitro-bromobenzene (50.5 mg, 0.25 mmol, 1 equiv), and phenylacetylene (28.8 µL, 0.263 mmol, 1.05 equiv). After 1 h, the reaction mixture was subjected to the purification method outlined in the General Procedure (silica gel, 0–5% Et₂O in petroleum ether) to afford the title compound as an off white solid (14.6 mg, 28%).

υ₉₉₅ (solid): 3107, 2926, 2217, 1593, 1511 cm⁻¹.

¹H NMR (CDCl₃, 500 MHz): δ 8.22 (d, J = 8.9 Hz, 2H), 7.67 (d, J = 8.9 Hz, 2H), 7.58–7.54 (m, 2H), 7.39 (dd, J = 5.3, 1.8 Hz, 3H).

¹³C NMR (CDCl₃, 126 MHz): δ 147.0, 132.3, 131.9, 130.4, 129.3, 132.8, 123.7, 122.1, 94.7, 87.6.

HRMS: exact mass calculated for [M⁺H]⁺ (C₁₄H₁₀NO₂) requires m/z 224.0712, found m/z 224.0714.
Characterisation data is consistent with literature reported values.

3d: 1-Methoxy-4-(phenylethynyl)benzene

\[
\begin{array}{c}
\text{MeO} & \equiv & \equiv \\
\text{MeO} & \equiv & \equiv \\
\text{MeO} & \equiv & \equiv \\
\end{array}
\]

Prepared according to General Procedure A using Pd(PPh₃)₂Cl₂ (3.5 mg, 0.005 mmol, 2 mol %), CuI (1.9 mg, 0.01 mmol, 4 mol %), Cyrene (0.5 mL, 0.5 M), Et₃N (38 µL, 0.275 mmol, 1.1 equiv), 4-iodoanisole (58.5 mg, 0.25 mmol, 1 equiv), and phenylacetylene (28.8 µL, 0.263 mmol, 1.05 equiv). After 1 h, the reaction mixture was subjected to the purification method outlined in the General Procedure (silica gel, 0–15% Et₂O in petroleum ether) to afford the title compound as an off white solid (51.9 mg, quant.).

υ₉₉₅ (solid): 3014, 2841, 2217, 1509 cm⁻¹.

¹H NMR (CDCl₃, 500 MHz): δ 7.51 (dt, J = 3.9, 2.1 Hz, 2H), 7.49–7.46 (m, 2H), 7.36–7.29 (m, 3H), 6.88 (d, J = 8.8 Hz, 2H), 3.83 (s, 3H).
$^{13}$C NMR (CDCl$_3$, 126 MHz): $\delta$ 159.6, 133.1, 131.5, 128.3, 127.9, 123.6, 115.4, 114.0, 89.4, 88.1, 55.3.

HRMS: exact mass calculated for [2M+H]$^+$ (C$_{30}$H$_{25}$O$_2$) requires $m/z$ 417.1855, found $m/z$ 417.1847. Characterisation data is consistent with literature reported values.$^5$

3e: 4-(Phenylethynyl)phenol

![4-(Phenylethynyl)phenol](image)

Prepared according to General Procedure A using Pd(PPh$_3$)$_2$Cl$_2$ (3.5 mg, 0.005 mmol, 2 mol %), CuI (1.9 mg, 0.01 mmol, 4 mol %), Cyrene (0.5 mL, 0.5 M), Et$_3$N (70 µL, 0.5 mmol, 2 equiv), 4-iodophenol (55 mg, 0.25 mmol, 1 equiv), and phenylacetylene (28.8 µL, 0.263 mmol, 1.05 equiv). After 1 h, the reaction mixture was subjected to the purification method outlined in the General Procedure (silica gel, 0–10% Et$_2$O in petroleum ether) to afford the title compound as an off white solid (32.6 mg, 68%).

$\nu$$_{max}$ (solid): 3412, 3059, 1513, 1254 cm$^{-1}$.

$^1$H NMR (CDCl$_3$, 500 MHz): $\delta$ 7.51 (dd, $J$ = 7.7, 1.4 Hz, 2H), 7.43 (d, $J$ = 8.6 Hz, 2H), 7.33 (m, 3H), 6.81 (d, $J$ = 8.6 Hz, 2H).

$^{13}$C NMR (CDCl$_3$, 126 MHz): $\delta$ 155.7, 133.3, 131.5, 128.3, 127.9, 123.6, 115.7, 115.5, 89.2, 88.1.

HRMS: exact mass calculated for [M+H]$^+$ (C$_{15}$H$_{13}$O) requires $m/z$ 209.0966, found $m/z$ 209.1008. Characterisation data is consistent with literature reported values.$^6$

3f: 1-Methoxy-3-(phenylethynyl)benzene

![1-Methoxy-3-(phenylethynyl)benzene](image)

Prepared according to General Procedure A using Pd(PPh$_3$)$_2$Cl$_2$ (3.5 mg, 0.005 mmol, 2 mol %), CuI (1.9 mg, 0.01 mmol, 4 mol %), Cyrene (0.5 mL, 0.5 M), Et$_3$N (38 µL, 0.275 mmol, 1.1 equiv), 3-iodoanisole (29.8 µL, 0.25 mmol, 1 equiv), and phenylacetylene (28.8 µL, 0.263 mmol, 1.05 equiv). After 1 h, the reaction mixture was subjected to the purification method outlined in the General Procedure (silica gel, 0–5% Et$_2$O in petroleum ether) to afford the title compound as a yellow oil (51.4 mg, 99%).

$\nu$$_{max}$ (liquid film): 2937, 2838 cm$^{-1}$.

$^1$H NMR (CDCl$_3$, 500 MHz): $\delta$ 7.57–7.53 (m, 2H), 7.35 (dd, $J$ = 4.9, 2.4 Hz, 3H), 7.27 (t, $J$ = 7.9 Hz, 1H), 7.15 (d, $J$ = 7.6 Hz, 1H), 7.08 (s, 1H), 6.91 (dd, $J$ = 8.3, 2.0 Hz, 1H), 3.83 (s, 3H).

$^{13}$C NMR (CDCl$_3$, 126 MHz): $\delta$ 159.4, 131.7, 129.4, 128.4, 128.3, 124.3, 124.2, 123.2, 116.4, 114.9, 89.3, 89.2, 55.3.

HRMS: exact mass calculated for [M+Na]$^+$ (C$_{14}$H$_{11}$O) requires $m/z$ 195.0810, found $m/z$ 195.0813. Characterisation data is consistent with literature reported values.$^2$

3g: 1-Chloro-3-(phenylethynyl)benzene

![1-Chloro-3-(phenylethynyl)benzene](image)

Prepared according to General Procedure A using Pd(PPh$_3$)$_2$Cl$_2$ (3.5 mg, 0.005 mmol, 2 mol %), CuI (1.9 mg, 0.01 mmol, 4 mol %), Cyrene (0.5 mL, 0.5 M), Et$_3$N (38 µL, 0.275 mmol, 1.1 equiv), 3-
chloro-iodobenzene (30.9 µL, 0.25 mmol, 1 equiv), and phenylacetylene (28.8 µL, 0.263 mmol, 1.05 equiv). After 1 h, the reaction mixture was subjected to the purification method outlined in the General Procedure (silica gel, 0–5% Et₂O in petroleum ether) to afford the title compound as a yellow oil (53.5 mg, 82%).

ν_max (liquid film): 3064, 2224, 884 cm⁻¹.

1H NMR (CDCl₃, 500 MHz): δ 7.55–7.51 (m, 3H), 7.41 (dt, J = 7.3, 1.4 Hz, 1H), 7.36 (dd, J = 4.9, 1.7 Hz, 3H), 7.31 (dt, J = 8.0, 1.5 Hz, 1H), 7.29 (d, J = 7.5 Hz, 1H).

13C NMR (CDCl₃, 126 MHz): δ 134.4, 131.9, 131.6, 129.9, 129.8, 128.8, 128.7, 128.6, 125.2, 122.9, 90.7, 88.1.

HRMS: exact mass calculated for [M] (C₁₄H₉Cl) requires m/z 212.0393, found m/z 212.0395.

Characterisation data is consistent with literature reported values.

3h: 1-Nitro-3-(phenylethynyl)benzene

Prepared according to General Procedure A using Pd(PPh₃)₂Cl₂ (3.5 mg, 0.005 mmol, 2 mol %), CuI (1.9 mg, 0.01 mmol, 4 mol %), Cyrene (0.5 mL, 0.5 M), Et₃N (38 µL, 0.275 mmol, 1.1 equiv), 3-nitro-iodobenzene (62.3 mg, 0.25 mmol, 1 equiv), and phenylacetylene (28.8 µL, 0.263 mmol, 1.05 equiv). After 1 h, the reaction mixture was subjected to the purification method outlined in the General Procedure (silica gel, 0–5% Et₂O in petroleum ether) to afford the title compound as a white solid (55.2 mg, 99%).

ν_max (solid): 3083, 2213, 1517, 1349 cm⁻¹.

1H NMR (CDCl₃, 500 MHz): δ 8.40–8.37 (m, 1H), 8.19 (m, 1H), 7.83 (d, J = 7.7 Hz, 1H), 7.56 (m, 3H), 7.40 (m, 3H).

13C NMR (CDCl₃, 126 MHz): δ 148.2, 137.2, 131.8, 129.4, 129.1, 129.8, 125.2, 122.9, 122.2, 91.9, 86.9.

HRMS: exact mass calculated for [M+H]^+ (C₁₄H₁₀NO₂) requires m/z 224.0712, found m/z 224.0710.

Characterisation data is consistent with literature reported values.

3i: 1-Methyl-2-(phenylethynyl)benzene

Prepared according to General Procedure A using Pd(PPh₃)₂Cl₂ (3.5 mg, 0.005 mmol, 2 mol %), CuI (1.9 mg, 0.01 mmol, 4 mol %), Cyrene (0.5 mL, 0.5 M), Et₃N (38 µL, 0.275 mmol, 1.1 equiv), 2-iodotoluene (31.8 µL, 0.25 mmol, 1 equiv), and phenylacetylene (28.8 µL, 0.263 mmol, 1.05 equiv). After 24 h, the reaction mixture was subjected to purification by reverse phase chromatography (C18 cartridge, 20–65% MeCN in water) to afford the title compound as a yellow oil (40 mg, 83%).

ν_max (liquid film): 3023, 2924, 2855, 2217, 1496 cm⁻¹.

1H NMR (CDCl₃, 500 MHz): δ 7.56–7.53 (m, 2H), 7.50 (d, J = 7.5 Hz, 1H), 7.35 (m, 3H), 7.24 (d, J = 3.9 Hz, 2H), 7.17 (m, 1H), 2.52 (s, 3H).

13C NMR (CDCl₃, 126 MHz): δ 140.3, 131.9, 131.7, 129.6, 128.5, 128.3, 125.7, 123.7, 123.2, 93.5, 88.5, 20.9.

HRMS: exact mass calculated for [M] (C₁₅H₁₂) requires m/z 192.0939, found m/z 192.0935.

Characterisation data is consistent with literature reported values.
3j: 1-Chloro-2-(phenylethynyl)benzene

Prepared according to General Procedure A using Pd(PPh₃)₂Cl₂ (3.5 mg, 0.005 mmol, 2 mol %), CuI (1.9 mg, 0.01 mmol, 4 mol %), Cyrene (0.5 mL, 0.5 M), Et₃N (38 µL, 0.275 mmol, 1.1 equiv), 2-chloro-iodobenzene (30.5 µL, 0.25 mmol, 1 equiv), and phenylacetylene (28.8 µL, 0.263 mmol, 1.05 equiv). After 24 h, the reaction mixture was subjected to purification by reverse phase chromatography (C18 cartridge, 20–65% MeCN in water) to afford the title compound as a yellow oil (54.9 mg, quant.).

υmax (liquid film): 3060, 2926, 2224, 1495 cm⁻¹.
¹H NMR (DMSO-d₆, 500 MHz): δ 7.69 (dd, J = 7.5, 1.7 Hz, 1H), 7.62–7.58 (m, 3H), 7.48–7.41 (m, 5H).
¹³C NMR (DMSO-d₆, 126 MHz): δ 135.1, 133.8, 131.9, 130.9, 129.9, 129.8, 129.3, 127.9, 122.4, 122.3, 94.8, 86.4.
HRMS: exact mass calculated for [M+] (C₁₄H₉Cl) requires m/z 212.0393, found m/z 212.0385.
Characterisation data is consistent with literature reported values.

3k: 2-(Phenylethynyl)thiophene

Prepared according to General Procedure A using Pd(PPh₃)₂Cl₂ (3.5 mg, 0.005 mmol, 2 mol %), CuI (1.9 mg, 0.01 mmol, 4 mol %), Cyrene (0.5 mL, 0.5 M), Et₃N (38 µL, 0.275 mmol, 1.1 equiv), 2-iodothiophene (27.6 µL, 0.25 mmol, 1 equiv), and phenylacetylene (28.8 µL, 0.263 mmol, 1.05 equiv). After 1 h, the reaction mixture was subjected to the purification method outlined in the General Procedure (silica gel, 0–5% Et₂O in petroleum ether) to afford the title compound as an off white solid (41.4 mg, 92%).

υmax (liquid film): 3088, 2204 cm⁻¹.
¹H NMR (CDCl₃, 500 MHz): δ 7.54–7.50 (m, 2H), 7.35 (dd, J = 5.2, 1.9 Hz, 3H), 7.31–7.28 (m, 2H), 7.02 (dd, J = 5.0, 3.8 Hz, 1H).
¹³C NMR (CDCl₃, 126 MHz): δ 131.9, 131.4, 128.4, 128.4, 127.3, 127.1, 123.4, 122.9, 93.0, 82.6.
HRMS: exact mass calculated for [M+] (C₁₂H₈S) requires m/z 184.0347, found m/z 184.0348.
Characterisation data is consistent with literature reported values.

3l: 2-Nitro-5-(phenylethynyl)pyridine

Prepared according to General Procedure A using Pd(PPh₃)₂Cl₂ (3.5 mg, 0.005 mmol, 2 mol %), CuI (1.9 mg, 0.01 mmol, 4 mol %), Cyrene (0.5 mL, 0.5 M), Et₃N (38 µL, 0.275 mmol, 1.1 equiv), 5-bromo-2-nitropyridine (50.8 mg, 0.25 mmol, 1 equiv), and phenylacetylene (28.8 µL, 0.263 mmol, 1.05 equiv). After 1 h, the reaction mixture was subjected to the purification method outlined in the General Procedure (silica gel, 0–15% Et₂O in petroleum ether) to afford the title compound as a white solid (51.4 mg, 92%).

υmax (solid): 3058, 2219, 1532, 1348 cm⁻¹.
¹H NMR (CDCl₃, 500 MHz): δ 8.73 (d, J = 1.6 Hz, 1H), 8.26 (d, J = 8.4 Hz, 1H), 8.10 (dd, J = 8.4, 2.0 Hz, 1H), 7.58 (dd, J = 7.7, 1.4 Hz, 2H), 7.44–7.38 (m, 3H).
13C NMR (CDCl3, 126 MHz): δ 154.8, 151.1, 141.8, 131.9, 129.8, 128.7, 126.7, 121.4, 117.7, 97.9, 84.2.

HRMS: exact mass calculated for [M+H]+ (C13H9N2O2) requires m/z 225.0664, found m/z 225.0670.

3m: 5-Chloro-2-(phenylethynyl)pyridine

Prepared according to General Procedure A using Pd(PPh3)2Cl2 (3.5 mg, 0.005 mmol, 2 mol %), CuI (1.9 mg, 0.01 mmol, 4 mol %), Cyrene (0.5 mL, 0.5 M), Et3N (38 µL, 0.275 mmol, 1.1 equiv), 3-chloro-6-iodopyridine (59.8 mg, 0.25 mmol, 1 equiv), and phenylacetylene (28.8 µL, 0.263 mmol, 1.05 equiv). After 1 h, the reaction mixture was subjected to the purification method outlined in the General Procedure (silica gel, 0–5% Et2O in petroleum ether) to afford the title compound as a white solid (54.5 mg, quant.).

υmax (solid): 3040, 2221, 1493, 1459 cm⁻¹.

1H NMR (CDCl3, 500 MHz): δ 8.58 (d, J = 1.8 Hz, 1H), 7.67 (dd, J = 8.4, 2.4 Hz, 1H), 7.60 (dd, J = 7.5, 1.9 Hz, 2H), 7.48 (d, J = 8.4 Hz, 1H), 7.40–7.36 (m, 3H).

13C NMR (CDCl3, 126 MHz): δ 149.1, 141.5, 136.0, 132.1, 131.3, 129.2, 128.5, 127.7, 121.9, 90.4, 87.6.

HRMS: exact mass calculated for [M+H]+ (C13H9NCl) requires m/z 214.0418, found m/z 214.0421.

3n: 2-(Phenylethynyl)-1,8-naphthyridine

Prepared according to General Procedure A using Pd(PPh3)2Cl2 (3.5 mg, 0.005 mmol, 2 mol %), CuI (1.9 mg, 0.01 mmol, 4 mol %), Cyrene (0.5 mL, 0.5 M), Et3N (38 µL, 0.275 mmol, 1.1 equiv), 2-bromo-1,8-naphthyridine (52.3 mg, 0.25 mmol, 1 equiv), and phenylacetylene (28.8 µL, 0.263 mmol, 1.05 equiv). After 1 h, the reaction mixture was subjected to the purification method outlined in the General Procedure (silica gel, 0–65% Et2O in petroleum ether) to afford the title compound as a white solid (54.3 mg, 94%).

υmax (solid): 3049, 3008, 2211, 1601, 1498 cm⁻¹.

1H NMR (CDCl3, 500 MHz): δ 9.15 (s, 1H), 8.17 (d, J = 8.2 Hz, 2H), 7.69–7.64 (m, 3H), 7.43–7.37 (m, 3H).

13C NMR (CDCl3, 126 MHz): δ 156.1, 154.3, 146.9, 137.2, 136.6, 132.4, 129.5, 128.5, 125.4, 122.3, 121.9, 91.6, 89.3. Quaternary carbon at ring junction not observed.

HRMS: exact mass calculated for [M+H]+ (C16H11N2) requires m/z 231.0922, found m/z 231.0923.

3o: 2-Chloro-6-(phenylethynyl)pyridine

Prepared according to General Procedure A using Pd(PPh3)2Cl2 (3.5 mg, 0.005 mmol, 2 mol %), CuI (1.9 mg, 0.01 mmol, 4 mol %), Cyrene (0.5 mL, 0.5 M), Et3N (38 µL, 0.5 mmol, 1.1 equiv), 2-bromo-6-chloropyridine (48 mg, 0.25 mmol, 1 equiv), and phenylacetylene (28.8 µL, 0.263 mmol, 1.05 equiv). After 1 h, the reaction mixture was subjected to the purification method outlined in the
General Procedure (silica gel, 0–10% Et₂O in petroleum ether) to afford the title compound as an off white solid (52.3 mg, quant.).

ν₉₅ₕₗ (solid): 3059, 2960, 2226, 1577, 1435 cm⁻¹.

¹H NMR (CDCl₃, 500 MHz): δ 7.63 (t, J = 7.8 Hz, 1H), 7.60–7.56 (m, 2H), 7.44 (d, J = 7.6 Hz, 1H), 7.37 (q, J = 5.7 Hz, 3H), 7.28 (d, J = 8.0 Hz, 1H).

¹³C NMR (CDCl₃, 126 MHz): δ 151.4, 143.6, 138.7, 132.1, 129.3, 128.5, 125.7, 123.6, 121.8, 90.7, 87.5.

HRMS: exact mass calculated for [M+H]⁺ (C₁₃H₉NCl) requires m/z 214.0424, found m/z 214.0427.

¹H NMR and HRMS data is consistent with literature reported values.¹

5.4. Products from Scheme 2b

3p: 1-Methyl-5-(phenylethynyl)-1H-indole

Prepared according to General Procedure A using Pd(PPh₃)₂Cl₂ (2.6 mg, 0.004 mmol, 2 mol %), CuI (1.4 mg, 0.007 mmol, 4 mol %), Cyrene (0.5 mL, 0.5 M), Et₃N (28 µL, 0.20 mmol, 1.1 equiv), 5-iodo-1-methyl-1H-indole (47 mg, 0.18 mmol, 1 equiv), and phenylacetylene (21 µL, 0.19 mmol, 1.05 equiv). After 1 h, the reaction mixture was subjected to the purification method outlined in the General Procedure (silica gel, 0–10% Et₂O in petroleum ether) to afford the title compound as a off white solid (27.7 mg, 67%).

ν₉₅ₕₗ (solid): 3051, 2926, 2208, 1597, 1496 cm⁻¹.

¹H NMR (CDCl₃, 500 MHz): δ 7.85 (s, 1H), 7.57–7.54 (m, 2H), 7.41 (dd, J = 8.5, 1.2 Hz, 1H), 7.35 (t, J = 7.2 Hz, 2H), 7.30 (t, J = 8.7 Hz, 2H), 7.08 (d, J = 3.1 Hz, 1H), 6.49 (d, J = 2.7 Hz, 1H), 3.80 (s, 3H).

¹³C NMR (CDCl₃, 126 MHz): δ 136.4, 131.5, 129.8, 128.4, 128.3, 127.7, 125.2, 124.8, 124.1, 113.8, 109.3, 101.3, 91.2, 87.0, 32.9.

HRMS: exact mass calculated for [M] (C₁₇H₁₃N) requires m/z 231.1048, found m/z 231.1057.

Characterisation data is consistent with literature reported values.⁹

3q: Phenylethynylboronic acid, MIDA ester

Prepared according to General Procedure A using Pd(PPh₃)₂Cl₂ (3.5 mg, 0.005 mmol, 2 mol %), CuI (1.9 mg, 0.01 mmol, 4 mol %), Cyrene (0.5 mL, 0.5 M), Et₃N (38 µL, 0.275 mmol, 1.1 equiv), iodobenzene (27.9 µL, 0.25 mmol, 1 equiv), and ethynyl boronic acid, MIDA ester (47.5 mg, 0.263 mmol, 1.05 equiv). After 1 h, the reaction mixture was subjected to the purification method outlined in the General Procedure (silica gel, 0–60% EtOAc in petroleum ether) to afford the title compound as an off white solid (61.3 mg, 95%).
in the General Procedure (silica gel, 0-60% EtOAc in petroleum ether) to afford the title compound as an off white solid (61.2 mg, 95%).

$\nu_{\text{max}}$ (solid): 3025, 2198, 1768, 1493 cm$^{-1}$.

$^1$H NMR (DMSO-$d_6$, 500 MHz): $\delta$ 7.51–7.48 (m, 2H), 7.42–7.37 (m, 3H), 4.32 (d, $J = 17.1$ Hz, 2H), 4.15 (d, $J = 17.1$ Hz, 2H), 3.08 (s, 3H).

$^{13}$C NMR (DMSO-$d_6$, 126 MHz): $\delta$ 169.1, 132.0, 129.4, 129.1, 122.9, 99.9, 61.9, 48.4. Carbon bearing boron not observed.

$^{11}$B NMR (DMSO-$d_6$, 160 MHz): $\delta$ 6.24.

HRMS: exact mass calculated for [M+NH$_4$]$^+$ (C$_{13}$H$_{16}$BN$_2$O$_4$) requires m/z 275.1202, found m/z 275.1198.

Characterisation data is consistent with literature reported values.$^{10}$

3r: Trimethyl(phenylethynyl)silane

Prepared according to General Procedure A using Pd(PPh$_3$)$_2$Cl$_2$ (3.5 mg, 0.005 mmol, 2 mol %), CuI (1.9 mg, 0.01 mmol, 4 mol %), Cyrene (0.5 mL, 0.5 M), Et$_3$N (38 $\mu$L, 0.275 mmol, 1.1 equiv), 2-iodobenzene (27.9 $\mu$L, 0.25 mmol, 1 equiv), and ethynyltrimethylsilane (37 $\mu$L, 0.263 mmol, 1.05 equiv). After 1 h, the reaction mixture was subjected to the purification method outlined in the General Procedure (silica gel, 0–1% Et$_2$O in petroleum ether) to afford the title compound as a colourless oil (44 mg, quant.).

$\nu_{\text{max}}$ (liquid film): 2962, 2161, 1491, 1251 cm$^{-1}$.

$^1$H NMR (CDCl$_3$, 500 MHz): $\delta$ 7.50–7.47 (m, 2H), 7.34–7.29 (m, 3H), 0.27 (s, 9H).

$^{13}$C NMR (CDCl$_3$, 126 MHz): $\delta$ 131.9, 128.5, 128.2, 123.1, 105.1, 94.1, -0.01.

HRMS: exact mass calculated for [M] (C$_{11}$H$_{14}$Si) requires m/z 174.0865, found m/z 174.0866.

Characterisation data is consistent with literature reported values.$^{11}$

3s: 4-Phenylbut-3-yn-1-yl 4-methylbenzenesulfonate

Prepared according to General Procedure A using Pd(PPh$_3$)$_2$Cl$_2$ (3.5 mg, 0.005 mmol, 2 mol %), CuI (1.9 mg, 0.01 mmol, 4 mol %), Cyrene (0.5 mL, 0.5 M), Et$_3$N (38 $\mu$L, 0.275 mmol, 1.1 equiv), 2-iodobenzene (27.9 $\mu$L, 0.25 mmol, 1 equiv), and 3-butylnyl-4-toluenesulfonate (46.3 $\mu$L, 0.263 mmol, 1.05 equiv). After 1 h, the reaction mixture was subjected to the purification method outlined in the General Procedure (silica gel, 0–30% EtOAc in petroleum ether) to afford the title compound as a colourless oil (60.7 mg, 81%).

$\nu_{\text{max}}$ (liquid film): 2924, 2980, 1493, 1361, 1176 cm$^{-1}$.

$^1$H NMR (CDCl$_3$, 500 MHz): $\delta$ 7.79 (d, $J = 8.3$ Hz, 2H), 7.32–7.28 (m, 3H), 7.28–7.23 (m, 4H), 4.16 (t, $J = 7.0$ Hz, 2H), 2.75 (t, $J = 7.0$ Hz, 2H), 2.39 (s, 3H).

$^{13}$C NMR (CDCl$_3$, 126 MHz): $\delta$ 144.9, 132.9, 131.7, 129.9, 128.2, 128.2, 127.9, 122.9, 83.8, 82.7, 67.8, 21.6, 20.4.

HRMS: exact mass calculated for [M+Na]$^+$ (C$_{17}$H$_{16}$O$_3$SNa) requires m/z 323.0712, found m/z 323.0702.

Characterisation data is consistent with literature reported values.$^{12}$

3t: N,N-Dimethyl-3-phenylprop-2-yn-1-amine
Prepared according to General Procedure A using Pd(PPh₃)₂Cl₂ (3.5 mg, 0.005 mmol, 2 mol %), CuI (1.9 mg, 0.01 mmol, 4 mol %), Cyrene (0.5 mL, 0.5 M), Et₃N (38 µL, 0.275 mmol, 1.1 equiv), 2-iodobenzene (27.9 µL, 0.25 mmol, 1 equiv), and dimethyl(prop-2-ynyl)amine (28 µL, 0.263 mmol, 1.05 equiv). After 1 h, the reaction mixture was subjected to purification by SCX (MeOH in 3M ammonium MeOH) to afford the title compound as a yellow oil (23.6 mg, 60%).

νmax (liquid film): 3058, 2941, 2824, 2775, 1690, 1493 cm⁻¹.

1H NMR (CDCl₃, 500 MHz): δ 7.46–7.42 (m, 2H), 7.32–7.28 (m, 3H), 3.49 (s, 2H), 2.39 (s, 6H).

13C NMR (CDCl₃, 126 MHz): δ 131.7, 128.3, 128.1, 123.2, 85.4, 84.4, 48.6, 44.2.

HRMS: exact mass calculated for [M+H]⁺ (C₁₁H₁₄N) requires m/z 160.1126, found m/z 160.1125. Characterisation data is consistent with literature reported values.

3u: Pent-1-yn-1-ylbenzene

Prepared according to General Procedure A using Pd(PPh₃)₂Cl₂ (3.5 mg, 0.005 mmol, 2 mol %), CuI (1.9 mg, 0.01 mmol, 4 mol %), Cyrene (0.5 mL, 0.5 M), Et₃N (38 µL, 0.275 mmol, 1.1 equiv), 2-iodobenzene (27.9 µL, 0.25 mmol, 1 equiv), and 1-pentyne (25.8 µL, 0.263 mmol, 1.05 equiv). After 1 h, the reaction mixture was subjected to the purification method outlined in the General Procedure (silica gel, 0–1% Et₂O in petroleum ether) to afford the title compound as a yellow oil (34.5 mg, 96%).

νmax (liquid film): 3058, 2963, 2934, 2872, 2237, 1601, 1491 cm⁻¹.

1H NMR (CDCl₃, 500 MHz): δ 7.32 (dd, J = 7.5, 1.9 Hz, 2H), 7.22–7.17 (m, 3H), 2.31 (t, J = 7.0 Hz, 2H), 1.56 (h, J = 7.3 Hz, 2H), 0.98 (t, J = 7.4 Hz, 3H).


HRMS: exact mass calculated for [M+H]⁺ (C₁₁H₁₂) requires m/z 144.0939, found m/z 144.0941. Characterisation data is consistent with literature reported values.

3v: (Cyclopropylethynyl)benzene

Prepared according to General Procedure A using Pd(PPh₃)₂Cl₂ (3.5 mg, 0.005 mmol, 2 mol %), CuI (1.9 mg, 0.01 mmol, 4 mol %), Cyrene (0.5 mL, 0.5 M), Et₃N (38 µL, 0.275 mmol, 1.1 equiv), 2-iodobenzene (27.9 µL, 0.25 mmol, 1 equiv), and ethynylcyclopropane (22 µL, 0.263 mmol, 1.05 equiv). After 1 h, the reaction mixture was subjected to the purification method outlined in the General Procedure (silica gel, 0–1% Et₂O in petroleum ether) to afford the title compound as a colourless oil (30.3 mg, 85%).

νmax (liquid film): 3034, 2924, 2219, 1597, 1513 cm⁻¹.

1H NMR (CDCl₃, 500 MHz): δ 7.42–7.38 (m, 2H), 7.30–7.26 (m, 3H), 1.47 (m, 1H), 0.91–0.87 (m, 2H), 0.83 (m, 2H).

13C NMR (CDCl₃, 126 MHz): δ 131.6, 128.1, 127.4, 123.9, 93.4, 75.8, 86.0, 0.1.

Characterisation data is consistent with values reported in the literature.
3w: Prop-1-yne-1,3-diyl dibenzene

Prepared according to General Procedure A using Pd(PPh₃)₂Cl₂ (3.5 mg, 0.005 mmol, 2 mol %), CuI (1.9 mg, 0.01 mmol, 4 mol %), Cyrene (0.5 mL, 0.5 M), Et₃N (38 µL, 0.275 mmol, 1.1 equiv), 2-iodobenzene (27.9 µL, 0.25 mmol, 1 equiv), and 3-phenyl-1-propyne (32.6 µL, 0.263 mmol, 1.05 equiv). After 1 h, the reaction mixture was subjected to the purification method outlined in the General Procedure (silica gel, 0–1% Et₂O in petroleum ether) to afford the title compound as a colourless oil (38.7 mg, 81%).

υ max (liquid film): 3064, 3032, 2924, 1601, 1493 cm⁻¹.

¹ H NMR (CDCl₃, 500 MHz): δ 7.46 (dd, J = 6.5, 3.0 Hz, 2H), 7.44 (d, J = 7.4 Hz, 2H), 7.36 (t, J = 7.6 Hz, 2H), 7.32–7.29 (m, 3H), 7.26 (dd, J = 8.8, 5.8 Hz, 1H), 3.85 (s, 2H).

¹³ C NMR (CDCl₃, 126 MHz): δ 136.8, 131.7, 128.6, 128.3, 127.9, 127.8, 126.7, 123.7, 87.5, 82.7, 25.8.

HRMS: exact mass calculated for [M] (C₁₅H₁₂) requires m/z 192.0939, found m/z 192.0932.

Characterisation data is consistent with literature reported values.

3x: (Cyclohex-1-en-1-ylethynyl)benzene

Prepared according to General Procedure A using Pd(PPh₃)₂Cl₂ (3.5 mg, 0.005 mmol, 2 mol %), CuI (1.9 mg, 0.01 mmol, 4 mol %), Cyrene (0.5 mL, 0.5 M), Et₃N (38 µL, 0.275 mmol, 1.1 equiv), 2-iodobenzene (27.9 µL, 0.25 mmol, 1 equiv), and 1-ethynylcyclohexene (30.8 µL, 0.263 mmol, 1.05 equiv). After 1 h, the reaction mixture was subjected to the purification method outlined in the General Procedure (silica gel, 0–1% Et₂O in petroleum ether) to afford the title compound as an off white solid (46.3 mg, quant.).

υ max (liquid film): 3064, 2924, 1601, 1493 cm⁻¹.

¹ H NMR (CDCl₃, 500 MHz): δ 7.46 (dd, J = 6.5, 3.0 Hz, 2H), 7.44 (d, J = 7.4 Hz, 2H), 7.36 (t, J = 7.6 Hz, 2H), 7.32–7.29 (m, 3H), 7.26 (dd, J = 8.8, 5.8 Hz, 1H), 3.85 (s, 2H).

¹³ C NMR (CDCl₃, 126 MHz): δ 136.8, 131.7, 128.6, 128.3, 127.9, 127.8, 126.7, 123.7, 87.5, 82.7, 25.8.

HRMS: exact mass calculated for [M] (C₁₄H₁₄) requires m/z 182.1095, found m/z 182.1102.

Characterisation data is consistent with literature reported values.

3y: 1-Methyl-4-(phenylethynyl)benzene

Prepared according to General Procedure A using Pd(PPh₃)₂Cl₂ (3.5 mg, 0.005 mmol, 2 mol %), CuI (1.9 mg, 0.01 mmol, 4 mol %), Cyrene (0.5 mL, 0.5 M), Et₃N (38 µL, 0.275 mmol, 1.1 equiv), 2-iodobenzene (27.9 µL, 0.25 mmol, 1 equiv), and p-tolylacetylene (33.2 µL, 0.263 mmol, 1.05 equiv). After 1 h, the reaction mixture was subjected to the purification method outlined in the General
Procedure (silica gel, 0–1% Et<sub>2</sub>O in petroleum ether) to afford the title compound as an off white solid (46.9 mg, 98%).

ν<sub>max</sub> (liquid film): 3032, 2921, 2219, 1597, 1511 cm<sup>-1</sup>.

1<sup>H</sup> NMR (CDCl<sub>3</sub>, 500 MHz): δ 7.53 (dd, J = 7.7, 1.5 Hz, 2H), 7.44 (d, J = 8.0 Hz, 2H), 7.34 (d, J = 7.3 Hz, 3H), 7.16 (d, J = 7.9 Hz, 2H), 2.38 (s, 3H).

13<sup>C</sup> NMR (CDCl<sub>3</sub>, 126 MHz): δ 138.4, 131.6, 131.5, 129.1, 128.3, 128.1, 123.5, 120.2, 89.6, 88.7, 21.5.

HRMS: exact mass calculated for [M] (C<sub>15</sub>H<sub>12</sub>) requires m/z 192.0939, found m/z 192.0942.

Characterisation data is consistent with literature reported values.

3z: 1-(Phenylethynyl)-2-(trifluoromethyl)benzene

![Chemical structure](image)

Prepared according to General Procedure A using Pd(PPh<sub>3</sub>)<sub>2</sub>Cl<sub>2</sub> (3.5 mg, 0.005 mmol, 2 mol %), CuI (1.9 mg, 0.01 mmol, 4 mol %), Cyrene (0.5 mL, 0.5 M), Et<sub>3</sub>N (38 μL, 0.275 mmol, 1.1 equiv), 2-iodobenzene (27.9 µL, 0.25 mmol, 1 equiv), and 2-ethynyltrifluorotoluene (36.5 µL, 0.263 mmol, 1.05 equiv). After 1 h, the reaction mixture was subjected to the purification method outlined in the General Procedure (silica gel, 0–1% Et<sub>2</sub>O in petroleum ether) to afford the title compound as a yellow oil (53 mg, 86%).

ν<sub>max</sub> (liquid film): 3066, 2224, 1312 cm<sup>-1</sup>.

1<sup>H</sup> NMR (CDCl<sub>3</sub>, 500 MHz): δ 7.69 (t, J = 8.3 Hz, 2H), 7.57 (dd, J = 6.5, 3.0 Hz, 2H), 7.53 (t, J = 7.5 Hz, 1H), 7.43 (t, J = 7.7 Hz, 1H), 7.40–7.35 (m, 3H).

13<sup>C</sup> NMR (CDCl<sub>3</sub>, 126 MHz): δ 133.7, 131.7, 131.4, 128.8, 128.4, 127.9, 125.9 (q, 3<sup>J</sup><sub>CF</sub> = 5.2 Hz), 123.6 (q, 1<sup>J</sup><sub>CF</sub> = 273.5 Hz), 122.8, 121.6, 94.9, 85.4. Carbon bearing trifluoromethyl group not observed.

19<sup>F</sup> NMR (CDCl<sub>3</sub>, 471 MHz): δ -62.35.

HRMS: exact mass calculated for [M+Na]<sup>+</sup> (C<sub>15</sub>H<sub>9</sub>F<sub>3</sub>) requires m/z 246.0656, found m/z 246.0654.

Characterisation data is consistent with literature reported values.

3aa: 2-(Phenylethynyl)pyridine

![Chemical structure](image)

Prepared according to General Procedure A using Pd(PPh<sub>3</sub>)<sub>2</sub>Cl<sub>2</sub> (3.5 mg, 0.005 mmol, 2 mol %), CuI (1.9 mg, 0.01 mmol, 4 mol %), Cyrene (0.5 mL, 0.5 M), Et<sub>3</sub>N (38 µL, 0.275 mmol, 1.1 equiv), 2-iodobenzene (27.9 µL, 0.25 mmol, 1 equiv), and 2-ethynylpyridine (26.5 µL, 0.263 mmol, 1.05 equiv). After 1 h, the reaction mixture was subjected to the purification method outlined in the General Procedure (silica gel, 0–15% EtOAc in petroleum ether) to afford the title compound as a yellow oil (43.3 mg, 97%).

υ<sub>max</sub> (liquid film): 3053, 2224, 1582, 1493, 1463 cm<sup>-1</sup>.

1<sup>H</sup> NMR (CDCl<sub>3</sub>, 500 MHz): δ 8.62 (d, J = 4.4 Hz, 1H), 7.67 (td, J = 7.7, 1.7 Hz, 1H), 7.60 (dd, J = 6.5, 3.1 Hz, 2H), 7.52 (d, J = 7.8 Hz, 1H), 7.38–7.35 (m, 3H), 7.26–7.22 (m, 1H).

13<sup>C</sup> NMR (CDCl<sub>3</sub>, 126 MHz): δ 150.1, 143.5, 136.2, 132.1, 128.9, 128.4, 127.2, 122.8, 122.3, 89.2, 88.6.

HRMS: exact mass calculated for [M+Na]<sup>+</sup> (C<sub>21</sub>H<sub>18</sub>BF<sub>3</sub>N<sub>2</sub>O<sub>6</sub>Na) requires m/z 179.0735, found m/z 179.0731.

s18
Characterisation data is consistent with literature reported values.²

3ab: 2-(Phenylethynyl)thiophene

Prepared according to General Procedure A using Pd(PPh₃)₂Cl₂ (3.5 mg, 0.005 mmol, 2 mol %), CuI (1.9 mg, 0.01 mmol, 4 mol %), Cyrene (0.5 mL, 0.5 M), Et₃N (38 µL, 0.275 mmol, 1.1 equiv), 2-iodobenzene (27.9 µL, 0.25 mmol, 1 equiv), and 2-ethynylthiophene (24.9 µL, 0.263 mmol, 1.05 equiv). After 1 h, the reaction mixture was subjected to the purification method outlined in the General Procedure (silica gel, 0–1% Et₂O in petroleum ether) to afford the title compound as an off white solid (42.4 mg, 92%).

νmax (liquid film): 3088, 2204 cm⁻¹.

¹H NMR (CDCl₃, 500 MHz): δ 7.54–7.50 (m, 2H), 7.35 (m, 3H), 7.31–7.28 (m, 2H), 7.02 (t, J = 4.4 Hz, 1H).

¹³C NMR (CDCl₃, 126 MHz): δ 131.9, 131.4, 128.4, 128.4, 127.3, 127.1, 123.4, 122.9, 93.0, 82.6.

HRMS: exact mass calculated for [M] (C₁₂H₈S) requires m/z 184.0347, found m/z 184.0349.

Characterisation data is consistent with literature reported values.²

5.5. Products from Scheme 2c

3ac: 2-Acetyl phenylethynylboronic acid, MIDA ester

Prepared according to General Procedure A using Pd(PPh₃)₂Cl₂ (3.5 mg, 0.005 mmol, 2 mol %), CuI (1.9 mg, 0.01 mmol, 4 mol %), Cyrene (0.5 mL, 0.5 M), Et₃N (38 µL, 0.275 mmol, 1.1 equiv), 2-iodoacetophenone (35.8 µL, 0.25 mmol, 1 equiv), and ethynyl boronic acid, MIDA ester (47.5 mg, 0.263 mmol, 1.05 equiv). After 1 h, the reaction mixture was subjected to the purification method outlined in the General Procedure (silica gel, 0–100% EtOAc in petroleum ether) to afford the title compound as an off white solid (66.5 mg, 89%).

νmax (solid): 2960, 2193, 1770, 1684 cm⁻¹.

¹H NMR (DMSO-d₆, 500 MHz): δ 7.79 (dd, J = 7.7, 0.9 Hz, 1H), 7.63 (dd, J = 7.6, 0.9 Hz, 1H), 7.57 (td, J = 7.5, 1.3 Hz, 1H), 7.52 (td, J = 7.6, 1.3 Hz, 1H), 4.34 (d, J = 17.1 Hz, 2H), 4.13 (d, J = 17.1 Hz, 2H), 3.11 (s, 3H), 2.63 (s, 3H).

¹³C NMR (DMSO-d₆, 126 MHz): δ 200.1, 169.1, 141.2, 134.6, 131.9, 129.4, 129.2, 120.7, 98.6, 61.9, 48.4, 29.9. Carbon bearing boron not observed.

¹¹B NMR (DMSO-d₆, 160 MHz): δ 6.23.

HRMS: exact mass calculated for [M+NH₄]⁺ (C₁₅H₁₆BN₂O₅) requires m/z 317.1305, found m/z 317.1303.

3ad: 2-Methyl-phenylethynylboronic acid, MIDA ester
Prepared according to General Procedure A using Pd(PPh₃)₂Cl₂ (3.5 mg, 0.005 mmol, 2 mol %), CuI (1.9 mg, 0.01 mmol, 4 mol %), Cyrene (0.5 mL, 0.5 M), Et₃N (38 µL, 0.275 mmol, 1.1 equiv), 2-iodotoluene (31.8 µL, 0.25 mmol, 1 equiv), and ethynyl boronic acid, MIDA ester (47.5 mg, 0.263 mmol, 1.05 equiv). After 1 h, the reaction mixture was subjected to the purification method outlined in the General Procedure (silica gel, 0–60% EtOAc in petroleum ether) to afford the title compound as an off white solid (62.9 mg, 93%).

Prepared according to General Procedure A using Pd(PPh₃)₂Cl₂ (3.5 mg, 0.005 mmol, 2 mol %), CuI (1.9 mg, 0.01 mmol, 4 mol %), DMF (0.5 mL, 0.5 M), Et₃N (38 µL, 0.275 mmol, 1.1 equiv), 2-iodotoluene (31.8 µL, 0.25 mmol, 1 equiv), and ethynyl boronic acid, MIDA ester (47.5 mg, 0.263 mmol, 1.05 equiv). After 1 h, the reaction mixture was subjected to the purification method outlined in the General Procedure (silica gel, 0–60% EtOAc in petroleum ether) to afford the title compound as an off white solid (62.3 mg, 92%).

νmax (solid): 3019, 2911, 1770, 1290, 1247 cm⁻¹.

1H NMR (DMSO-d₆, 500 MHz): δ 7.45 (d, J = 7.4 Hz, 1H), 7.31–7.27 (m, 2H), 7.22–7.18 (m, 1H), 4.33 (d, J = 17.1 Hz, 2H), 4.15 (d, J = 17.1 Hz, 2H), 3.09 (s, 3H), 2.40 (s, 3H).


11B NMR (DMSO-d₆, 160 MHz): δ 6.37.

HRMS: exact mass calculated for [M+NH₄]⁺ (C₁₄H₁₂BF₃NO₄) requires m/z 289.1355, found m/z 289.1354.

Characterisation data is consistent with literature reported values.¹⁷

3ae: 2-Trifluoromethoxy-phenylethynylboron acid, MIDA ester

\[
\begin{align*}
\text{OCF}_3 & \equiv \text{B} \quad \text{MIDA} \\
\end{align*}
\]

Prepared according to General Procedure A using Pd(PPh₃)₂Cl₂ (3.5 mg, 0.005 mmol, 2 mol %), CuI (1.9 mg, 0.01 mmol, 4 mol %), Cyrene (0.5 mL, 0.5 M), Et₃N (38 µL, 0.275 mmol, 1.1 equiv), 2-(trifluoromethoxy)iodobenzene (38.8 µL, 0.25 mmol, 1 equiv), and ethynyl boronic acid, MIDA ester (47.5 mg, 0.263 mmol, 1.05 equiv). After 1 h, the reaction mixture was subjected to the purification method outlined in the General Procedure (silica gel, 0–60% EtOAc in petroleum ether) to afford the title compound as an off white solid (71.8 mg, 85%).

νmax (solid): 3016, 2922, 2965, 2198, 1772, 1217, 1024 cm⁻¹.

1H NMR (DMSO-d₆, 500 MHz): δ 7.69 (d, J = 7.5 Hz, 1H), 7.55 (t, J = 7.4 Hz, 1H), 7.45 (dd, J = 16.7, 8.6 Hz, 2H), 4.35 (d, J = 17.2 Hz, 2H), 4.15 (d, J = 17.2 Hz, 2H), 3.09 (s, 3H).

13C NMR (DMSO-d₆, 126 MHz): δ 169.0, 148.9, 134.5, 131.3, 128.3, 121.9, 120.6 (q, 1JCF = 257.4 Hz), 117.3, 93.5, 62.1, 48.3. Carbon bearing boron not observed.

11B NMR (DMSO-d₆, 160 MHz): δ 6.29.

19F NMR (DMSO-d₆, 471 MHz): δ -56.54.

HRMS: exact mass calculated for [M+H]⁺ (C₁₄H₁₂BF₃NO₄) requires m/z 342.0763, found m/z 342.0767.
3af: Triisopropyl(2-(trifluoromethoxy)phenyl)ethynyl)silane

![Chemical structure of 3af]

Prepared according to General Procedure A using Pd(PPh₃)₂Cl₂ (3.5 mg, 0.005 mmol, 2 mol %), CuI (1.9 mg, 0.01 mmol, 4 mol %), Cyrene (0.5 mL, 0.5 M), Et₃N (38 µL, 0.275 mmol, 1.1 equiv), 2-(trifluoromethoxy)iodobenzene (38.8 µL, 0.25 mmol, 1 equiv), and (triisopropylsilyl)acetylene (58.9 µL, 0.263 mmol, 1.05 equiv). After 1 h, the reaction mixture was subjected to the purification method outlined in the General Procedure (silica gel, 0–1% Et₂O in petroleum ether) to afford the title compound as a colourless oil (58.3 mg, 68%).

ν_max (liquid film): 2947, 2868, 2167, 1491, 1258, 1219, 1169 cm⁻¹.

¹H NMR (CDCl₃, 500 MHz): δ 7.47 (dd, J = 7.6, 1.3 Hz, 1H), 7.28–7.24 (m, 1H), 7.19–7.14 (m, 2H), 1.06 (s, 21H).

¹³C NMR (CDCl₃, 126 MHz): δ 149.8, 134.1, 129.4, 126.6, 121.2, 120.6 (q, ¹JC₁F = 258.1 Hz), 118.3, 100.4, 97.1, 18.5, 11.2.

¹⁹F NMR (471 MHz, CDCl₃): δ -57.50.

HRMS: exact mass calculated for [M] (C₁₈H₂₅F₃SiO) requires m/z 342.1627, found m/z 342.1626.

Characterisation data is consistent with literature reported values.

3ag: 2-((Triisopropylsilyl)ethynyl)aniline

![Chemical structure of 3ag]

Prepared according to General Procedure A using Pd(PPh₃)₂Cl₂ (3.5 mg, 0.005 mmol, 2 mol %), CuI (1.9 mg, 0.01 mmol, 4 mol %), Cyrene (0.5 mL, 0.5 M), Et₃N (38 µL, 0.275 mmol, 1.1 equiv), 2-iodoaniline (54.8 mg, 0.25 mmol, 1 equiv), and (triisopropylsilyl)acetylene (58.9 µL, 0.263 mmol, 1.05 equiv). After 1 h, the reaction mixture was subjected to the purification method outlined in the General Procedure (silica gel, 0–10% Et₂O in petroleum ether) to afford the title compound as a yellow oil (45.3 mg, 66%).

ν_max (liquid film): 3487, 3388, 2945, 2867, 2146, 1616, 1318 cm⁻¹.

¹H NMR (CDCl₃, 500 MHz): δ 7.31 (dd, J = 7.7, 1.1 Hz, 1H), 7.14–7.09 (m, 1H), 6.71–6.64 (m, 2H), 4.25 (s, 2H), 1.14 (s, 21H).

¹³C NMR (CDCl₃, 126 MHz): δ 148.3, 132.4, 129.7, 117.7, 114.1, 108.3, 103.7, 95.9, 18.7, 11.3.

HRMS: exact mass calculated for [M+H]+ (C₁₇H₂₇NSi) requires m/z 274.1986, found m/z 274.1986.

Characterisation data is consistent with literature reported values.

3ah: ((2-Chlorophenyl)ethynyl)triisopropylsilane

![Chemical structure of 3ah]

Prepared according to General Procedure A using Pd(PPh₃)₂Cl₂ (3.5 mg, 0.005 mmol, 2 mol %), CuI (1.9 mg, 0.01 mmol, 4 mol %), Cyrene (0.5 mL, 0.5 M), Et₃N (38 µL, 0.275 mmol, 1.1 equiv), 2-chloro-iodobenzene (30.5 µL, 0.25 mmol, 1 equiv), and (triisopropylsilyl)acetylene (58.9 µL, 0.263 mmol, 1.05 equiv). After 1 h, the reaction mixture was subjected to purification by reverse phase chromatography (C18 cartridge, 20–100% MeCN in water) to afford the title compound as a yellow oil (47.7 mg, 65%).
5.6. Cyrene homo-aldol adducts, 4a and 4b

To a stirred solution of Cyrene (256 mg, 2.0 mmol, 1 equiv) was added DBU (30 mg, 0.2 mmol, 0.1 equiv) and the mixture heated to 100 °C for 10 minutes. The resulting mixture was cooled to 20 °C for 10 minutes and then kept at 20 °C for 72 hours over which time the mixture began to crystallise. The mixture was then purified by flash chromatography (30% EtOAc/hexanes to EtOAc) to give 4a as a colourless oil (40 mg, 16%).

\[
\nu_{\text{max}} \text{ (neat): } 3470, 2962, 2895, 1731 \text{ cm}^{-1}.
\]

\[\text{1H NMR (CDCl}_3, 500 \text{ MHz): } \delta 5.71 \text{ (s, 1H), 5.04 (s, 1H), 4.73-4.70 (m, 1H), 4.44-4.41 (m, 1H), 4.01 (br d, } J = 7.4 \text{ Hz, 1H), 3.91 (dd, } J = 7.4, 4.9, 1.6 \text{ Hz, 1H), 3.83 (d, } J = 7.1 \text{ Hz, 1H), 3.76 (dd, } J = 7.1, 5.1, 0.9 \text{ Hz, 1H), 3.55 (dd, } J = 12.0, 7.4 \text{ Hz, 1H), 2.72 (s, 1H), 2.27 (dd, } J = 13.3, 12.0, 3.7, 1.8 \text{ Hz, 1H), 1.96 (dd, } J = 13.3, 7.4, 1.6 \text{ Hz, 1H), 1.64-1.59 (m, 3H), 1.50-1.46 (m, 1H).\]

\[\text{13C NMR (CDCl}_3, 126 \text{ MHz): } \delta 203.7, 102.9, 101.6, 73.6, 73.2, 72.9, 68.4, 67.9, 42.7, 32.6, 26.7, 25.1.\]

ESI-MS: \text{m/z} 257 (50, [M+H]+), 279 (100, [M+Na]).

To an oven-dried 5 mL microwave vessel was added K$_3$PO$_4$ (637 mg, 3 mmol, 3 equiv). The vessel was then capped and purged with N$_2$ before addition of THF (4 mL, 0.25 M), and Cyrene (123 μL, 1 mmol, 1 equiv). The reaction mixture was heated to 70 °C and maintained at this temperature with stirring for 8 h before the vessel was vented, and decapped. The solution was then diluted with EtOAc (20 mL), and washed with water (2 × 20 mL) and brine (2 × 20 mL). The organics were then passed through a hydrophobic frit and concentrated under reduced pressure to give an off white solid, which was purified by flash chromatography (silica gel, 0–50% EtOAc in petroleum ether) to afford the title compound as a white solid (105 mg, 88%).

\[
\nu_{\text{max}} \text{ (solid): } 2898, 1703, 1621, 1098 \text{ cm}^{-1}.
\]

\[\text{1H NMR (CDCl}_3, 500 \text{ MHz): } \delta 6.76 \text{ (s, 1H), 5.18 (s, 1H), 4.79 (t, } J = 5.1 \text{ Hz, 1H), 4.60 (t, } J = 4.0 \text{ Hz, 1H), 3.94 – 3.83 (m, 4H), 2.78 (dd, } J = 16.3, 2.6 \text{ Hz, 1H), 2.56 (d, } J = 16.3 \text{ Hz, 1H), 2.41-2.24 (m, 2H), 2.14-2.07 (m, 1H), 1.75 (dd, } J = 13.5, 6.5 \text{ Hz, 1H).}\]

s22
\[ ^{13}C \text{ NMR (CDCl}_3, 126 \text{ MHz}): \delta 190.7, 151.0, 123.4, 101.5, 97.2, 72.6, 72.5, 68.7, 67.8, 34.1, 28.8, 20.4. \]

HRMS: exact mass calculated for [M] (C_{12}H_{14}) requires \textit{m/z} 238.0841, found \textit{m/z} 238.0839.

## 5.7. Products from Scheme 3

### 7a: 2-Phenyl-1-tosyl-1H-indole

Prepared according to General Procedure B using Pd(PPh\(_3\))\(_2\)Cl\(_2\) (3.5 mg, 0.005 mmol, 2 mol %), CuI (1.9 mg, 0.01 mmol, 4 mol %), Cyrene (0.5 mL, 0.5 M), Et\(_3\)N (104 \(\mu\)L, 0.75 mmol, 3 equiv), \(N\)-(2-iodophenyl)-4-methylbenzenesulfonamide (93 mg, 0.25 mmol, 1 equiv), and phenylacetylene (28.8 \(\mu\)L, 0.263 mmol, 1.05 equiv). After 7 h, the reaction mixture was subjected to the purification method outlined in the General Procedure (silica gel, 0–15% EtOAc in petroleum ether) to afford the title compound as a white solid (78.4 mg, 90%).

Prepared according to General Procedure B using Pd(PPh\(_3\))\(_2\)Cl\(_2\) (3.5 mg, 0.005 mmol, 2 mol %), CuI (1.9 mg, 0.01 mmol, 4 mol %), DMF (0.5 mL, 0.5 M), Et\(_3\)N (104 \(\mu\)L, 0.75 mmol, 3 equiv), \(N\)-(2-iodophenyl)-4-methylbenzenesulfonamide (93 mg, 0.25 mmol, 1 equiv), and phenylacetylene (28.8 \(\mu\)L, 0.263 mmol, 1.05 equiv). After 7 h, the reaction mixture was subjected to the purification method outlined in the General Procedure (silica gel, 0–15% EtOAc in petroleum ether) to afford the title compound as a white solid (78.6 mg, 91%).

### 7b: 5-Nitro-2-phenyl-1-tosyl-1H-pyrrolo[2,3-b]pyridine

Prepared according to General Procedure B using Pd(PPh\(_3\))\(_2\)Cl\(_2\) (3.5 mg, 0.005 mmol, 2 mol %), CuI (1.9 mg, 0.01 mmol, 4 mol %), Cyrene (0.5 mL, 0.5 M), Et\(_3\)N (104 \(\mu\)L, 0.75 mmol, 3 equiv), \(N\)-(3-iodo-5-nitropyridin-2-yl)-4-methylbenzenesulfonamide (104 mg, 0.25 mmol, 1 equiv), and phenylacetylene (28.8 \(\mu\)L, 0.263 mmol, 1.05 equiv). After 7 h, the reaction mixture was subjected to the purification method outlined in the General Procedure (silica gel, 0–30% EtOAc in petroleum ether) to afford the title compound as an off white solid (71.4 mg, 73%).

\[ \nu_{\text{max}} \text{(solid): 3070, 2935, 1593, 1517, 1394, 1346, 1184 cm}^{-1}. \]

\[ ^{1}H \text{ NMR (CDCl}_3, 500 \text{ MHz}): \delta 9.32 \text{ (d, } J = 2.4 \text{ Hz, 1H)}, 8.61 \text{ (d, } J = 2.4 \text{ Hz, 1H)}, 7.85 \text{ (d, } J = 8.3 \text{ Hz, 2H)}, 7.55 – 7.48 \text{ (m, 5H)}, 7.24 \text{ (d, } J = 8.1 \text{ Hz, 2H)}, 6.63 \text{ (s, 1H)}, 2.37 \text{ (s, 3H)}. \]

\[ ^{13}C \text{ NMR (CDCl}_3, 126 \text{ MHz): } \delta 151.3, 145.8, 145.8, 141.4, 140.3, 135.3, 135.5, 131.5, 129.9, 129.6, 129.6, 128.2, 127.9, 124.3, 121.4, 108.3, 21.7. \]

HRMS: exact mass calculated for [M+H]\(^{+}\) (C\(_{29}\)H\(_{16}\)N\(_3\)O\(_5\)S) requires \textit{m/z} 394.0862, found \textit{m/z} 394.0869.
7c: 2-Phenylbenzofuran

Prepared according to General Procedure B using Pd(PPh$_3$)$_2$Cl$_2$ (3.5 mg, 0.005 mmol, 2 mol %), CuI (1.9 mg, 0.01 mmol, 4 mol %), Cyrene (0.5 mL, 0.5 M), Et$_3$N (104 µL, 0.75 mmol, 3 equiv), 2-iodophenol (55 mg, 0.25 mmol, 1 equiv), and phenylacetylene (28.8 µL, 0.263 mmol, 1.05 equiv). After 7 h, the reaction mixture was subjected to the purification method outlined in the General Procedure (silica gel, 0–1% EtOAc in petroleum ether) to afford the title compound as a white solid (43.3 mg, 89%).

ν$_{\text{max}}$ (solid): 3038, 2924, 2855 cm$^{-1}$.

$^1$H NMR (CDCl$_3$, 500 MHz): δ 7.88 (d, $J =$ 7.4 Hz, 2H), 7.59 (d, $J =$ 7.5 Hz, 1H), 7.53 (d, $J =$ 8.1 Hz, 1H), 7.46 (t, $J =$ 7.7 Hz, 2H), 7.36 (t, $J =$ 7.4 Hz, 1H), 7.29 (t, $J =$ 7.7 Hz, 1H), 7.23 (t, $J =$ 7.4 Hz, 1H), 7.03 (s, 1H).

$^{13}$C NMR (CDCl$_3$, 126 MHz): δ 155.9, 154.9, 130.5, 129.2, 128.8, 124.9, 124.3, 122.9, 120.9, 111.2, 101.3

HRMS: exact mass calculated for [M]$^+$ (C$_{14}$H$_{10}$O) requires m/z 194.0732, found m/z 194.0737.

Characterization data is consistent with literature reported values.

7d: (1-Tosyl-1H-indol-2-yl)boronic acid, MIDA ester

Prepared according to General Procedure B using Pd(PPh$_3$)$_2$Cl$_2$ (3.5 mg, 0.005 mmol, 2 mol %), CuI (1.9 mg, 0.01 mmol, 4 mol %), Cyrene (0.5 mL, 0.5 M), Et$_3$N (104 µL, 0.75 mmol, 3 equiv), N-(2-iodophenyl)-4-methylbenzenesulfonamide (93 mg, 0.25 mmol, 1 equiv), and ethynyl boronic acid, MIDA ester (47.5 mg, 0.263 mmol, 1.05 equiv). After 7 h, the reaction mixture was subjected to the purification method outlined in the General Procedure (silica gel, 0–80% EtOAc in petroleum ether) to afford the title compound as a white solid (87.4 mg, 82%).

ν$_{\text{max}}$ (solid): 2928, 1763, 1450, 1176, 1038 cm$^{-1}$.

$^1$H NMR (DMSO-d$_6$, 500 MHz): δ 8.12 (d, $J =$ 8.4 Hz, 1H), 7.91 (d, $J =$ 8.2 Hz, 2H), 7.63 (d, $J =$ 7.7 Hz, 1H), 7.37 (dd, $J =$ 13.1, 8.0 Hz, 3H), 7.25 (t, $J =$ 7.4 Hz, 1H), 7.06 (s, 1H), 4.47 (d, $J =$ 17.5 Hz, 2H), 4.23 (d, $J =$ 17.4 Hz, 2H), 2.96 (s, 3H), 2.32 (s, 3H).

$^{13}$C NMR (DMSO-d$_6$, 126 MHz): δ 169.6, 145.72, 138.9, 135.5, 130.4, 130.1, 127.08, 125.7, 123.9, 122.2, 122.0, 114.7, 64.8, 49.9, 21.5. Carbon bearing boron not observed.

$^{11}$B NMR (DMSO-d$_6$, 160 MHz): δ 10.28.

HRMS: exact mass calculated for [M+H]$^+$ (C$_{20}$H$_{20}$BN$_2$O$_6$S) requires m/z 427.1139, found m/z 427.1139.

Characterization data is consistent with literature reported values.

7e: (5-Fluoro-1-tosyl-1H-indol-2-yl)boronic acid, MIDA ester

Prepared according to General Procedure B using Pd(PPh$_3$)$_2$Cl$_2$ (3.5 mg, 0.005 mmol, 2 mol %), CuI (1.9 mg, 0.01 mmol, 4 mol %), Cyrene (0.5 mL, 0.5 M), Et$_3$N (104 µL, 0.75 mmol, 3 equiv), N-(4-fluoro-2-iodophenyl)-4-methylbenzenesulfonamide (98 mg, 0.25 mmol, 1 equiv), and ethynyl boronic acid, MIDA ester (47.5 mg, 0.263 mmol, 1.05 equiv). After 7 h, the reaction mixture was subjected to the purification method outlined in the General Procedure (silica gel, 0–80% EtOAc in petroleum ether) to afford the title compound as a white solid (87.4 mg, 82%).

ν$_{\text{max}}$ (solid): 2928, 1763, 1450, 1176, 1038 cm$^{-1}$.

$^1$H NMR (DMSO-d$_6$, 500 MHz): δ 8.12 (d, $J =$ 8.4 Hz, 1H), 7.91 (d, $J =$ 8.2 Hz, 2H), 7.63 (d, $J =$ 7.7 Hz, 1H), 7.37 (dd, $J =$ 13.1, 8.0 Hz, 3H), 7.25 (t, $J =$ 7.4 Hz, 1H), 7.06 (s, 1H), 4.47 (d, $J =$ 17.5 Hz, 2H), 4.23 (d, $J =$ 17.4 Hz, 2H), 2.96 (s, 3H), 2.32 (s, 3H).

$^{13}$C NMR (DMSO-d$_6$, 126 MHz): δ 169.6, 145.72, 138.9, 135.5, 130.4, 130.1, 127.08, 125.7, 123.9, 122.2, 122.0, 114.7, 64.8, 49.9, 21.5. Carbon bearing boron not observed.

HRMS: exact mass calculated for [M+H]$^+$ (C$_{20}$H$_{20}$BN$_2$O$_6$S) requires m/z 427.1139, found m/z 427.1139.

Characterization data is consistent with literature reported values.
acid, MIDA ester (47.5 mg, 0.263 mmol, 1.05 equiv). After 7 h, the reaction mixture was subjected to the purification method outlined in the General Procedure (silica gel, 0–80% EtOAc in petroleum ether) to afford the title compound as a white solid (98 mg, 88%).

\[ \nu_{\text{max}} \text{ (solid): } 2930, 1750, 1305, 1174, 1040 \text{ cm}^{-1}. \]

$^1$H NMR (DMSO-$d_6$, 500 MHz): \( \delta 8.13 \) (dd, \( J = 9.2, 4.3 \text{ Hz}, 1\text{H} \)), 7.91 (dd, \( J = 8.8, 2.6 \text{ Hz}, 1\text{H} \)), 7.40 (dd, \( J = 8.2, 2.6 \text{ Hz}, 2\text{H} \)), 7.22 (td, \( J = 9.2, 2.6 \text{ Hz}, 1\text{H} \)), 7.06 (s, 1H), 4.48 (d, \( J = 17.5 \text{ Hz}, 2\text{H} \)), 4.24 (d, \( J = 17.5 \text{ Hz}, 2\text{H} \)), 2.96 (s, 3H), 2.33 (s, 3H).

$^{13}$C NMR (DMSO-$d_6$, 126 MHz): \( \delta 169.6, 159.3 \) (d, \( J_{\text{CF}} = 238.2 \text{ Hz} \)), 145.9, 135.4, 135.3, 131.2 (d, \( J_{\text{CF}} = 10.4 \text{ Hz} \)), 130.5, 127.1, 121.9, 116.1 (d, \( J_{\text{CF}} = 9.4 \text{ Hz} \)), 113.5 (d, \( J_{\text{CF}} = 25.5 \text{ Hz} \)), 107.1 (d, \( J_{\text{CF}} = 23.5 \text{ Hz} \)), 64.8, 49.9, 21.5. Carbon bearing boron not observed.

$^{11}$B NMR (DMSO-$d_6$, 160 MHz): \( \delta 10.09 \).

$^{19}$F NMR (DMSO-$d_6$, 471 MHz): \( \delta -120.04 \).

HRMS: exact mass calculated for [M] \((C_{21}H_{18}BF_3N_2O_5SNa)\) requires \( m/z \) 444.2966, found \( m/z \) 444.0951.

Characterization data is consistent with literature reported values.$^4$

7f: (6-Chloro-1-tosyl-1H-indol-2-yl)boronic acid, MIDA ester

![MIDA ester](image)

Prepared according to General Procedure B using Pd(PPh$_3$)$_2$Cl$_2$ (3.5 mg, 0.005 mmol, 2 mol %), Cul (1.9 mg, 0.01 mmol, 4 mol %), Cyrene (0.5 mL, 0.5 M), Et$_3$N (104 µL, 0.75 mmol, 3 equiv), N-(4-chloro-2-iodophenyl)-4-methylbenzenesulfonylamine (102 mg, 0.25 mmol, 1 equiv), and ethynyl boronic acid, MIDA ester (47.5 mg, 0.263 mmol, 1.05 equiv). After 7 h, the reaction mixture was subjected to the purification method outlined in the General Procedure (silica gel, 0–80% EtOAc in petroleum ether) to afford the title compound as a white solid (116 mg, quant.).

\[ \nu_{\text{max}} \text{ (solid): } 2922, 1763, 1455, 1267, 1173, 1038 \text{ cm}^{-1}. \]

$^1$H NMR (DMSO-$d_6$, 500 MHz): \( \delta 8.11 \) (s, 1H), 7.90 (d, \( J = 8.4 \text{ Hz}, 2\text{H} \)), 7.69 (d, \( J = 8.4 \text{ Hz}, 1\text{H} \)), 7.42 (d, \( J = 8.2 \text{ Hz}, 2\text{H} \)), 7.34 (dd, \( J = 8.4, 1.7 \text{ Hz}, 1\text{H} \)), 7.09 (s, 1H), 4.48 (d, \( J = 17.5 \text{ Hz}, 2\text{H} \)), 4.23 (d, \( J = 17.4 \text{ Hz}, 2\text{H} \)), 2.94 (s, 3H), 2.34 (s, 3H).

$^{13}$C NMR (DMSO-$d_6$, 126 MHz): \( \delta 169.6, 146.1, 139.3, 135.2, 130.6, 130.4, 128.9, 127.0, 124.4, 123.4, 121.9, 114.4, 64.7, 49.9, 21.5 \). Carbon bearing boron not observed.

$^{11}$B NMR (DMSO-$d_6$, 160 MHz): \( \delta 10.21 \).

HRMS: exact mass calculated for [M]+ \((C_{20}H_{16}ClN_2O_6SB)\) requires \( m/z \) 460.0671, found \( m/z \) 460.0658.

Characterization data is consistent with literature reported values.$^4$

6. Crystallographic Data for Compound 4b

Single crystal diffraction measurements were made with an Oxford Diffraction Gemini S instrument. Refinement was to convergence against $F^2$ and used all unique reflections. Programs used were from the SHELX suite.$^{20}$ Non-hydrogen atoms were refined anisotropically whereas hydrogen atoms were placed in idealized positions and refined in riding modes. Selected crystallographic and refinement parameters are given in Table 1. CCDC reference number CCDC 1485168 contains the supplementary crystallographic data for this paper. This data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.
### Table S1 Selected crystallographic data and refinement parameters for compound 4b.

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<tr>
<th>Compound</th>
<th>4</th>
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<tr>
<td>Formula</td>
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<td>M_r (g mol⁻¹)</td>
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<tr>
<td>(a) (Å)</td>
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<td>(b) (Å)</td>
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<td>(c) (Å)</td>
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<tr>
<td>(β) (°)</td>
<td>96.341(3)</td>
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<tr>
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<td>(μ) (mm⁻¹)</td>
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<tr>
<td>(θ_{max}) (°)</td>
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<td>(R) [on (F), obs rflns only]</td>
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<tr>
<td>(wR) [on (F^2), all data]</td>
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<td>Largest diff. peak/hole/e Å⁻³</td>
<td>0.242/−0.191</td>
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### References

8. NMR spectra for intermediates and products

$^1$H NMR of S1
$^{13}$C NMR of S1

$^1$H NMR of S2
$^{13}$C NMR of S2

$^1$H NMR of 3a
$^{13}$C NMR of 3a

$^1$H NMR of 3b
$^{13}$C NMR of 3b

$^{19}$F NMR of 3b
$^1$H NMR 3c

\[
\begin{array}{c}
\text{Chemical Structure}
\end{array}
\]

\[
\begin{array}{c}
\text{NMR Spectrum}
\end{array}
\]
$^{13}$C NMR 3e

$^1$H NMR 3f
$^{13}$C NMR 3g

$^1$H NMR 3h
\[ ^{13}\text{C NMR 3h} \]

\[ ^{1}\text{H NMR 3i} \]
$^{13}$C NMR 3o

$^1$H NMR 3p
$^1$H NMR 3r

$^{13}$C NMR 3r
$^1$H NMR 3s

$^{13}$C NMR 3s
$^1$H NMR 3u

$^{13}$C NMR 3u
$^1$H NMR 3z

$^{13}$C NMR 3z
$^{19}\text{F NMR 3z}$

$^{1}\text{H NMR 3aa}$
$^{13}$C NMR 3aa

$^1$H NMR 3ab
$^{13}$C NMR 3ac

$^{11}$B NMR 3ac
$^1$H NMR

$^{13}$C NMR

s61
$^{11}$B NMR 3ad

$^1$H NMR 3ae
$^{13}$C NMR 3ae

\[ \text{BMIDA} \]
\[ \text{OCF}_3 \]

$^{11}$B NMR 3ae

\[ \text{BMIDA} \]
\[ \text{OCF}_3 \]
$^{19}\text{F NMR 3ae}$

$^1\text{H NMR 3af}$
$^{1}H$ NMR 3ag

$^{13}C$ NMR 3ag
$^1$H NMR of 4a

$^{13}$C NMR of 4a
$^1$H NMR 7a

$^{13}$C NMR 7a
$^1$H NMR 7b

O$_2$N

$^{13}$C NMR 7b

O$_2$N
$^1$H NMR 7d

$^{13}$C NMR 7d
$^{11}$B NMR 7d

$^1$H NMR 7e
$^{13}$C NMR 7e

$^{11}$B NMR 7e
$^{19}$F NMR 7e

$^{1}$H NMR 7f
$^{13}$C NMR 7f

$^{11}$B NMR 7f
9. $^1$H NMR Evidence for the Evaluation of the Base Sensitivity
Cyrene $^1$H NMR

KOAc 25 °C

KOAc 25°C
Pyridine 25 °C

Pyridine 50 °C
Pyridine 100 °C

K₂CO₃ 25 °C
DIPEA 100 °C

Cs₂CO₃ 25 °C
$\text{Cs}_2\text{CO}_3 \text{ 50 °C}$

$\text{Cs}_2\text{CO}_3 \text{ 100 °C}$
$\text{Et}_3\text{N} \ 25 ^\circ \text{C}$

$\text{Et}_3\text{N} \ 50 ^\circ \text{C}$
$\text{Et}_3\text{N} \ 100 \ ^\circ\text{C}$

$\text{K}_3\text{PO}_4 \ 25 \ ^\circ\text{C}$
$t$-BuOK $25^\circ$C

$t$-BuOK $50^\circ$C
$t$-BuOK $100\,^\circ\text{C}$

$NaH\,25\,^\circ\text{C}$
NaH 50 °C

NaH 100 °C