Supporting Information
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Synthesis of Oxindoles and Benzofuranones via Oxidation of 2-Heterocyclic BMIDAs
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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

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. Acetone, MeOH, CH₂Cl₂, Et₂O, EtOAc, MeCN, and petroleum ether 40-60° for purification purposes were used as obtained from suppliers without further purification.

1.3 Experimental Details

Reactions were carried out using conventional glassware (preparation of intermediates) or in capped 5 mL microwave vials. 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 potassium permanganate solution. Normal phase flash chromatography was carried out using ZEOprep 60 HYD 40-63 µm silica gel.

1.5 Analysis of Products

Fourier Transformed Infra-Red (FTIR) spectra were obtained on a Shimadzu IRAffinity-1 machine. ¹⁹F NMR spectra were obtained on a Bruker AV 400 spectrometer at 376 MHz. ¹¹B NMR spectra were obtained on a Bruker AV 400 spectrometer at 128 MHz. ¹H and ¹³C NMR spectra were obtained on either a Bruker AV 400 at 400 MHz and 125 MHz, respectively, or Bruker DRX 500 at 500 MHz and 126 MHz, respectively. 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). ¹¹B NMR spectra are referenced to BF₃•Et₂O. High-resolution mass spectra were obtained through analysis at the EPSRC UK National Mass Spectrometry Facility at Swansea University. Reversed phase HPLC data was obtained on an Agilent 1200 series HPLC using a Machery-Nagel Nucleodur C18 column. Analysis was performed using a gradient method, eluting with 5–80% MeCN/H₂O over 16 minutes at a flow rate of 2 mL/min. Samples for HPLC analysis were prepared through the addition of 2 mL of caffeine standard in MeCN to the completed reaction mixture. The resulting solution was then stirred before the removal of a 200 μL aliquot. The aliquot was diluted to 1 mL with MeCN. A 200 μL aliquot of the diluted solution was then filtered through cotton wool and further diluted with 800 μL MeCN and 500 μL H₂O for HPLC analysis against established conversion factors.
2. Optimization of Hydrolysis/Oxidation procedure

2.1 General procedure for optimization reactions.
A 10 mL microwave vial was charged with N-tosylindole-2-BMIDA (43 mg, 0.1 mmol, 1 equiv) before the addition of solvent (0.4 mL, 0.25 M) and base (x equiv). To the resulting solution was added oxidant (x equiv). The reaction mixture was stirred at X °C for X h before being quenched with sodium metabisulfite (10 mg). The reaction mixtures were then analyzed by reverse phase HPLC against established conversion factors.

2.2 H2O2 optimization
Carried out according to the general procedure using 30% w/v H2O2 (0.2 mL, 2.5 mmol, 25 equiv) for 1 hr.

<table>
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<th>Entry</th>
<th>Base (vol/mass)</th>
<th>Base equiv</th>
<th>Solvent</th>
<th>Temp (°C)</th>
<th>Conversion %</th>
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<td>MeCN</td>
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<tr>
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2.3 Oxone optimization
Carried out according to the general procedure for 24 hr.

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<th>K3PO4 equiv (mass)</th>
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<th>Solvent</th>
<th>Conversion %</th>
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<td>THF</td>
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</tr>
<tr>
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<td>3 (64 mg)</td>
<td>60</td>
<td>THF</td>
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</tr>
<tr>
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<td>70</td>
<td>THF</td>
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<tr>
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<td>3 (64 mg)</td>
<td>60</td>
<td>MeCN</td>
<td>0</td>
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<tr>
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<td>2.5 (77 mg)</td>
<td>3 (64 mg)</td>
<td>70</td>
<td>MeCN</td>
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<tr>
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<td>MeCN</td>
<td>16</td>
</tr>
<tr>
<td>8</td>
<td>10 (307 mg)*</td>
<td>-</td>
<td>50</td>
<td>THF</td>
<td>11</td>
</tr>
<tr>
<td>9</td>
<td>10 (307 mg)*</td>
<td>-</td>
<td>60</td>
<td>THF</td>
<td>11</td>
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<tr>
<td>10</td>
<td>10 (307 mg)*</td>
<td>-</td>
<td>70</td>
<td>THF</td>
<td>4</td>
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</tbody>
</table>

* Oxone was added to the reaction as a solution in 2 mL H2O
4. Compound characterization data

Synthesis of starting materials.
Compounds 1a, b, c, f, g, h, i, and l were synthesized according to ref 7. Compounds 1d and j were purchased from commercial suppliers and used as received.

Synthesis of (5-chloro-1-tosyl-1H-indol-2-yl)boronic acid, MIDA ester 1e

To an oven dried 50 mL flask was added N-(2-iodo-4-chlorophenyl)-4-methylbenzenesulfonamide (1.02 g, 2.5 mmol, 1 equiv), ethynyl boronic acid, MIDA ester (540 mg, 3 mmol, 1.2 equiv), Pd(PPh₃)₂Cl₂ (35 mg, 0.05 mmol, 2 mol%), CuI (48 mg, 0.25 mmol, 10 mol%), Cu(OAc)₂ (136 mg, 0.75 mmol, 30 mol%), and K₃PO₄ (530 mg, 2.5 mmol, 1 equiv). The flask was then sealed and purged with N₂ before addition of DMF (20 mL, 0.125 M). The reaction mixture was then heated to 30 °C for 4 h before being heated to 55 °C for a further 14 h. The reaction mixture was allowed to cool to room temperature before the solution was then dried and concentrated under reduced pressure before being diluted with EtOAc (10 mL) and washed with water (2 × 20 mL) and brine (2 × 20 mL). The organics were then dried and concentrated under reduced pressure to give a yellow oil, which was purified by flash chromatography (silica gel, 40-70% EtOAc/petroleum ether) to afford the title compound as an off-white solid (790 mg, 69%).

υₘₐₓ (solid): 2972, 1763, 1599, 1526, 1448, 1340, 1295 cm⁻¹.

¹H NMR (DMSO-d₆, 400 MHz): δ 8.12 (d, J = 9.0 Hz, 1H), 7.90 (d, J = 8.3 Hz, 2H), 7.74 (d, J = 1.7 Hz, 1H), 7.44 – 7.32 (m, 3H), 7.05 (s, 1H), 4.47 (d, J = 17.5 Hz, 2H), 4.23 (d, J = 17.5 Hz, 2H), 2.95 (s, 3H), 2.33 (s, 3H).

¹³C NMR (DMSO-d₆, 101 MHz): δ 169.1, 145.5, 136.9, 134.7, 131.1, 130.0, 128.0, 126.0, 125.0, 120.9, 115.8, 64.3, 49.4, 21.0. Carbon bearing boron not observed.

¹¹B NMR (DMSO-d₆, 128 MHz): δ 10.38.

HRMS: exact mass calculated for [M+H]⁺ (C₂₀H₁₉ClN₂O₆SB) requires m/z 461.0749, found m/z 461.0766.

Synthesis of (5-methoxy-1-tosyl-1H-indol-2-yl)boronic acid, MIDA ester 1g

To an oven dried 5 mL microwave vessel was added N-(2-iodo-4-methoxyphenyl)-4-methylbenzenesulfonamide (202 mg, 0.5 mmol, 1 equiv), ethynyl boronic acid, MIDA ester (109 mg, 0.6 mmol, 1.2 equiv), Pd(PPh₃)₂Cl₂ (7 mg, 0.01 mmol, 2 mol%), CuI (9.5 mg, 0.05 mmol, 10 mol%), Cu(OAc)₂ (27.2 mg, 0.15 mmol, 30 mol%), and K₃PO₄ (106 mg, 0.5 mmol, 1 equiv). The vessel was then capped and purged with N₂ before addition of DMF (4 mL, 0.125 M). The reaction mixture was then heated to 30 °C in a sand bath for 4 h before being heated to 55 °C for a further 14 h. The vessel was allowed to cool to room temperature, vented, and decapped. The solution was then dried and concentrated under reduced pressure before being diluted with EtOAc (20 mL) and washed with water (2 × 40 mL) and brine (2 × 40 mL). The organics were then dried and concentrated under reduced pressure to give a yellow oil, which was purified by flash chromatography (silica gel, 40-70% EtOAc/petroleum ether) to afford the title compound as a white solid (150 mg, 66%).
$\nu_{\text{max}}$ (solid): 2960, 2926, 2855, 1763, 1617, 1532, 1464, 1340, 1299 cm$^{-1}$.

$^1$H NMR (DMSO-$d_6$, 400 MHz): $\delta$ 8.01 (d, $J = 9.1$ Hz, 1H), 7.86 (d, $J = 8.4$ Hz, 2H), 7.38 (d, $J = 8.2$ Hz, 2H), 7.15 (d, $J = 2.5$ Hz, 1H), 7.00–6.94 (m, 2H), 4.46 (d, $J = 17.5$ Hz, 2H), 4.23 (d, $J = 17.4$ Hz, 2H), 3.76 (s, 3H), 2.96 (s, 3H), 2.33 (s, 3H).

$^{13}$C NMR (DMSO-$d_6$, 101 MHz): $\delta$ 168.9, 155.8, 144.9, 134.8, 132.9, 130.5, 129.6, 126.3, 121.6, 114.9, 114.0, 103.3, 64.0, 55.2, 49.2, 20.8. Carbon bearing boron not observed.

$^{11}$B NMR (DMSO-$d_6$, 128 MHz): $\delta$ 10.33.

HRMS: exact mass calculated for [M+NH$_4$]$^+$ (C$_{21}$H$_{25}$BN$_3$O$_7$S) requires $m/z$ 474.1505, found $m/z$ 474.1497.

5. References
6. NMR and HRMS spectra for intermediates and products

$^1$H NMR of 1e

$^{13}$C NMR of 1e
$^{11}$B NMR of 1e

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

$^{11}$B NMR of 1g
$^1$H NMR of 3a

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

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

$^{13}$C NMR of 3c
$^1$H NMR of 3d

$^{13}$C NMR of 3d
$^{19}$F NMR of 3d

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

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

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

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

$^{19}$F NMR of 3h
$^1$H NMR of 3i

$^{13}$C NMR of 3i
Crude $^1$H NMR of 3j

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

$^1$H NMR of 3l

3l
$^{13}$C NMR of 3l

$^{19}$F NMR of 3l
$^1$H NMR of 6

$^{13}$C NMR of 6
$^1$H NMR of semaxanib

$^{13}$C NMR of semaxanib
$^1$H NMR of 8

$^{13}$C NMR of 8
$^1$H NMR of (±) coerulescine

(±) coerulescine

$^{13}$C NMR of (±) coerulescine
$^1$H NMR of 9

$^{13}$C NMR of 9
$^1$H NMR of tenidap

$^{13}$C NMR of tenidap