Supporting Information

One-pot Coupling-Cyclization-Alkylation Synthesis of 1,2,5-Trisubstituted 7-Azaindoles in a Consecutive Three-component Fashion

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General procedure (GP) for the consecutive three-component synthesis of 1,2,5-trisubstituted 7-azaindoles 4

In a dry screw-cap Schlenk tube with a magnetic stir bar were placed the corresponding bromide 1 (2.00 mmol), Pd(PPh<sub>3</sub>)<sub>2</sub>Cl<sub>2</sub> (34.8 mg, 50.0 μmol), and (1-Ad)<sub>2</sub>PBN·HBr (47.2 mg, 100 μmol) and the vessel was evacuated (For experimental details see Table SI-1). After flushing the vessel with nitrogen dry DMSO (3.00 mL), the corresponding alkyne 2 (2.40 mmol) and DBU (914 mg, 6.00 mmol) were added and the reaction mixture was stirred at 100 °C under nitrogen for 1 h until the bromide was completely consumed (monitored by TLC). After cooling to room temp KOt-Bu (1.01 g, 9.00 mmol) and DMSO (2.00 mL) were added to the reaction mixture and the mixture was stirred at 100 °C under nitrogen for 0.25 h. After cooling to room temp the electrophile 3 (4.00 to 8.00 mmol) was added to the reaction mixture, which was stirred at room temp for 5 min. Then, deionized water or brine was added to the mixture. And the aqueous layer was extracted several times with ethyl acetate or dichloromethane. The combined organic phases were dried (anhydrous sodium sulfate) and after filtration the solvents were removed in vacuo. The residue was adsorbed on silica and chromatographed on silica gel (SNAP cartridge 100 g, hexanes/ethyl acetate) using a Biotage SP-1 flash chromatography purification system to give the analytically pure 1,2,5-trisubstituted 7-azaindoles 4.

Table SI-1. Experimental details of the three-component synthesis of 1,2,5-trisubstituted 7-azaindoles 4.

<table>
<thead>
<tr>
<th>entry</th>
<th>bromide 1 [mg] (mmol)</th>
<th>alkyne 2 [mg] (mmol)</th>
<th>electrophile 3 [mg] (mmol)</th>
<th>1,2,5-trisubstituted 7-azaindoles 4 [mg] (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>187 (1.00) of 2-amino-3-bromo-5-methyl pyridine (1a)</td>
<td>122 (1.20) of phenyl acetylene (2a)</td>
<td>173 (2.00) of benzyl bromide (3a)</td>
<td>94 (32) of 4a</td>
</tr>
<tr>
<td>2</td>
<td>93 (0.50) of 1a</td>
<td>61 (0.60) of 2a</td>
<td>142 (1.00) of methyl iodide (3b)</td>
<td>72 (65) of 4b</td>
</tr>
<tr>
<td>3</td>
<td>374 (2.00 mmol) of 1a</td>
<td>244 (2.40) of 2a</td>
<td>1510 (8.00) of m-fluoro benzy l bromide (3c)</td>
<td>328 (52) of 4c</td>
</tr>
<tr>
<td>4</td>
<td>374 (2.00 mmol) of 1a</td>
<td>244 (2.40) of 2a</td>
<td>2000 (8.00) of p-bromo benzy l bromide (3d)</td>
<td>373 (49) of 4d</td>
</tr>
<tr>
<td>5</td>
<td>374 (2.00 mmol) of 1a</td>
<td>244 (2.40) of 2a</td>
<td>1480 (8.00) of o-methyl benzyl bromide (3e)</td>
<td>166 (27) of 4e</td>
</tr>
<tr>
<td>6</td>
<td>374 (2.00 mmol) of 1a</td>
<td>244 (2.40) of 2a</td>
<td>1910 (8.00) of m-trifluoromethyl benzyl bromide (3f)</td>
<td>157 (21) of 4f</td>
</tr>
<tr>
<td>7</td>
<td>94 (0.50) of 1a</td>
<td>61 (0.60) of 2a</td>
<td>207 (1.50) of 3,5-difluorobenzyl bromide (3g)</td>
<td>110 (66) of 4g</td>
</tr>
<tr>
<td>8&lt;sup&gt;a,b&lt;/sup&gt;</td>
<td>1730 (10.0) of 2-amino-3-bromo pyridine (1b)</td>
<td>1220 (12.0) of 2a</td>
<td>5680 (40.0) of 3b</td>
<td>1190 (57) of 4h</td>
</tr>
<tr>
<td>9</td>
<td>187 (1.00 mmol) of 1a</td>
<td>122 (1.20) of 2a</td>
<td>363 (3.00) of allyl bromide (3h)</td>
<td>85 (34) of 4i</td>
</tr>
</tbody>
</table>

<sup>a</sup> Using allyl bromide (3h) as electrophile

<sup>b</sup> Using 1,2-dibromoethane as electrophile
<table>
<thead>
<tr>
<th>entry</th>
<th>bromide 1 [mg (mmol)]</th>
<th>alkyne 2 [mg (mmol)]</th>
<th>electrophile 3 [mg (mmol)]</th>
<th>1,2,5-trisubstituted 7-azaindoles 4 [mg (%)]</th>
</tr>
</thead>
<tbody>
<tr>
<td>10°</td>
<td>374 (2.00 mmol) of 1a</td>
<td>244 (2.40) of 2a</td>
<td>1350 (8.00) of 2-bromo-1,1-dimethoxyethane (3i) 1.05 (8.00) of 1-bromo-2-methoxyethane (3j)</td>
<td>199 (34) of 4j</td>
</tr>
<tr>
<td>11</td>
<td>374 (2.00 mmol) of 1a</td>
<td>244 (2.40) of 2a</td>
<td>1510 (8.00) of 3c</td>
<td>204 (38) of 4k</td>
</tr>
<tr>
<td>12</td>
<td>374 (2.00 mmol) of 1a</td>
<td>159 (2.40) of ethynyl cyclopropane (2b) 198 (2.40) of 1-hexyne (2c)</td>
<td>1510 (8.00) of 3c</td>
<td>240 (43) of 4l</td>
</tr>
<tr>
<td>13</td>
<td>374 (2.00 mmol) of 1a</td>
<td>416 (2.00) of 2-amino-3-bromo-5-chloropyridine (1c)</td>
<td>1510 (8.00) of 3c</td>
<td>166 (28) of 4m</td>
</tr>
<tr>
<td>14</td>
<td>244 (2.40) of 2a</td>
<td></td>
<td></td>
<td>412 (61) of 4n</td>
</tr>
</tbody>
</table>

The reaction was performed on a 10 mmol scale using Pd(PPh₃)₂Cl₂ (175 mg, 0.20 mmol), (1-Ad)₂PBn·HBr (95 mg, 0.50 mmol), and DMSO (15 mL). After addition of the electrophile the mixture was stirred at room temp for 2.5 h. After addition of electrophile 3i the reaction mixture was stirred at 100 °C for 23 h.

1-Benzyl-5-methyl-2-phenyl-1H-pyrrolo[2,3-b]pyridine (4a)

According to the general procedure and after automated flash chromatography with a 2→5% ethyl acetate/n-hexane gradient compound 4a (94 mg, 32%) was obtained as a yellow solid. Mp 69 °C. ¹H NMR (600 MHz, CDCl₃): δ 2.44 (s, 3 H), 5.55 (s, 2 H), 6.48 (s, 1 H), 6.94 (m, 2 H), 7.15-7.19 (m, 3 H), 7.36-7.39 (m, 5 H), 7.73 (d, J = 1.0 Hz, 1 H), 8.18 (s, 1 H). ¹³C NMR (150 MHz, CDCl₃): δ 18.7 (CH₃), 46.2 (CH₂), 99.9 (CH), 120.7 (Cquat), 125.5 (Cquat), 126.6 (CH), 127.1 (CH), 128.4 (CH), 128.5 (CH), 128.6 (CH), 128.6 (CH), 129.3 (CH), 132.6 (Cquat), 138.7 (Cquat), 142.2 (Cquat), 143.9 (CH), 148.0 (Cquat). EI MS (70 eV, m/z (%)): 299 (18), 298 ([M⁺], 92), 297 (100), 283 ([M-CH₃]⁺, 7), 282 (6), 222 (11), 221 ([M-C₆H₅]⁺, 60), 219 (6), 192 (5), 152 (6), 110 (5), 91 (36), 65 (7), 56 (5). IR (ATR): ν [cm⁻¹]: 3059 (w), 3030 (w), 2916 (w), 2860 (w), 1603 (w), 1537 (w), 1495 (w), 1474 (w), 1452 (w), 1443 (w), 1431 (w), 1404 (w), 1389 (w), 1362 (w), 1348 (w), 1295 (w), 1246 (w), 1223 (w), 1202 (w), 1180 (w), 1144 (w), 1074 (w), 1051 (w), 1030 (w), 1001 (w), 966 (w), 958 (w), 920 (w), 883 (w), 839 (w), 818 (w), 772 (w), 752 (m), 698 (s), 677 (w), 665 (w), 623 (w), 615 (w). Anal. calcd. for C₂₁H₁₈N₂ (298.4): C 84.53, H 6.08, N 9.39; Found: C 84.60, H 6.28, N 9.13.

1,5-Dimethyl-2-phenyl-1H-pyrrolo[2,3-b]pyridine (4b)

According to the general procedure and after automated flash chromatography with a 12→85% ethyl acetate/n-hexane gradient compound 4b (72 mg, 65%) was obtained as a yellow solid. Mp 65 °C. ¹H NMR (300 MHz, CDCl₃): δ 2.45 (s, 3 H), 3.86 (s, 3 H), 6.44 (s, 1 H), 7.42-7.52 (m, 5 H), 7.70-7.71 (m, 1 H), 8.19 (m, 1 H). ¹³C NMR (75 MHz, CDCl₃): δ 18.7 (CH₃), 30.1 (CH₃), 99.0 (CH), 120.7 (Cquat), 125.1 (Cquat), 128.3 (CH), 128.4 (CH), 128.7 (CH), 129.2 (CH), 132.6 (Cquat), 142.1 (Cquat), 143.5 (CH), 148.1 (Cquat). EI MS (70 eV, m/z (%)): 223 (15), 219 (10), 192 (7), 180 (6), 179 (5), 145 (5), 139 (5), 131 (4), 128 (3), 120 (3), 115 (3), 114 (3), 105 (2), 102 (2), 91 (2), 89 (2), 80 (2), 73 (2), 66 (2), 65 (2), 56 (2), 42 (2), 33 (2), 28 (2), 23 (2). Anal. calcd. for C₂₁H₁₆N₂ (292.4): C 84.15, H 6.12, N 9.52; Found: C 84.09, H 6.28, N 9.13.
222 ([M]+, 100), 221 (84), 220 (5), 205 (6), 152 (5), 145 ([M-C₆H₅]+, 17), 111 (7), 110 (11). IR (ATR): $\tilde{\nu}$ [cm⁻¹]: 3119 (w), 3078 (w), 3055 (w), 3005 (w), 2980 (w), 2945 (w), 2916 (w), 1599 (w), 1566 (w), 1532 (w), 1485 (m), 1296 (m), 748 (s), 694 (m). Anal. calcd. for C₃₃H₂₄N₂ (222.3): C 81.05, H 6.35, N 12.60; Found: C 80.92, H 6.07, N 12.40.

1-(3-Fluorobenzyl)-5-methyl-2-phenyl-1H-pyrrolo[2,3-b]pyridine (4c)

According to the general procedure and after automated flash chromatography with a 5→10% ethyl acetate/n-hexane gradient compound 4c (328 mg, 52%) was obtained as a yellow solid.

Mp 83 °C. ¹H NMR (600 MHz, CDCl₃): $\delta$ 2.45 (s, 3 H), 5.52 (s, 2 H), 6.49 (s, 1 H), 6.63-6.65 (m, 1 H), 6.73-6.74 (m, 1 H), 6.84-6.87 (m, 1 H), 7.13-7.17 (m, 1 H), 7.38 (s, 5 H), 7.73-7.74 (m, 1 H), 8.17-8.18 (m, 1 H). ¹³C NMR (150 MHz, CDCl₃): $\delta$ 18.7 (CH₃), 45.7 (CH₂), 100.1 (CH), 114.1 (d, $J_{CF} = 22.2$ Hz, CH), 114.1 (d, $J_{CF} = 21.2$ Hz, CH), 120.6 (C_quat), 122.2 (d, $J_{CF} = 2.8$ Hz, CH), 125.8 (C_quat), 128.5 (CH), 128.5 (CH), 128.7 (CH), 128.7 (CH), 129.3 (CH), 130.1 (d, $J_{CF} = 8.2$ Hz, CH), 132.5 (C_quat), 141.4 (d, $J_{CF} = 7.0$ Hz, C_quat), 142.0 (C_quat), 144.2 (CH), 148.1 (C_quat), 163.1 (d, $J_{CF} = 245.9$ Hz, C_quat). EI MS (70 eV, m/z (%)): 317 (20), 316 ([M]+, 100), 315 (90), 301 ([M-CH₃]+, 5), 300 (5), 239 ([M-C₆H₅]+, 26), 222 (8), 221 ([M-C₆H₄F]+, 47), 219 (5), 205 (6), 192 (10), 180 (5), 158 (8), 152 (8), 151 (5), 110 (7), 109 (20), 83 (5). IR (ATR): $\tilde{\nu}$ [cm⁻¹]: 3055 (w), 3007 (w), 2916 (w), 2951 (w), 2862 (w), 1616 (w), 1589 (w), 1544 (w), 1445 (w), 1425 (w), 1406 (m), 1393 (w), 1348 (w), 1300 (w), 1273 (w), 1246 (m), 1219 (w), 1202 (w), 1128 (w), 1096 (w), 1065 (w), 1001 (w), 972 (w), 961 (w), 922 (w), 893 (w), 876 (m), 833 (w), 797 (w), 775 (s), 760 (s), 743 (w), 727 (w), 698 (s), 683 (m), 667 (w), 635 (w). Anal. calcd. for C₂₁H₁₇FN₂ (316.4): C 79.72, H 5.42, N 8.85; Found: C 79.76, H 5.57, N 8.56.

1-(4-Bromobenzyl)-5-methyl-2-phenyl-1H-pyrrolo[2,3-b]pyridine (4d)

According to the general procedure and after automated flash chromatography with a 3→5→10% ethyl acetate/n-hexane gradient compound 4d (373 mg, 49%) was obtained as a yellow solid.

Mp 83 °C. ¹H NMR (600 MHz, CDCl₃): $\delta$ 2.44 (s, 3 H), 5.47 (s, 2 H), 6.47 (s, 1 H), 6.81-6.82 (m, 2 H), 7.29-7.31 (m, 2 H), 7.35-7.39 (m, 5 H), 7.72-7.73 (m, 1 H), 8.17 (m, 1 H). ¹³C NMR (150 MHz, CDCl₃): $\delta$ 18.7 (CH₃), 45.6 (CH₂), 100.1 (CH), 120.7 (C_quat), 121.0 (C_quat), 125.7 (C_quat), 128.5 (CH), 128.5 (CH), 128.5 (CH), 128.7 (CH), 129.3 (CH), 131.7 (CH), 132.5 (C_quat), 133.8 (C_quat), 141.9 (C_quat), 144.1 (CH), 148.0 (C_quat). EI MS (70 eV, m/z (%)): 379 (19), 378 ([M⁻¹Br]+, 84), 377 ([M]+, 100), 376 ([M⁻¹Br]+, 85), 375 (87), 301 ([M⁺¹Br]-C₆H₅]+, 25), 299 ([M⁺¹Br]-C₆H₅]+, 26), 297 ([M-Br]+, 11), 296 (10), 295 (9), 282 (6), 281 (6), 222 (14), 221 ([M-C₆H₄Br]+, 79), 220 (6), 219 (10), 206 (5), 205 (10), 193 (5), 192 (13), 180 (7), 178 (5), 171 (38), 169 (40), 165 (6), 152 (12), 151 (7), 148 (47), 147 (7), 140 (7), 127 (5), 110 (6), 90 (22), 89 (15), 77 (5). IR (ATR): $\tilde{\nu}$ [cm⁻¹]: 3077 (w), 3063 (w), 3026 (w), 2951 (w), 2911 (w),
5-Methyl-1-(2-methylbenzyl)-2-phenyl-1\textsubscript{H}-pyrrolo[2,3-b]pyridine (4e)

According to the general procedure and after automated flash chromatography with a 3→5→10% ethyl acetate/n-hexane gradient compound 4e (166 mg, 27%) was obtained as a yellow solid.

Mp 147 °C. \textsuperscript{1}H NMR (600 MHz, CDCl\textsubscript{3}): \(\delta\) 2.25 (s, 3 H), 2.45 (s, 3 H), 5.46 (s, 2 H), 6.46 (d, \(J = 7.7\) Hz, 1 H), 6.54 (s, 1 H), 6.96-6.98 (m, 1 H), 7.08-7.13 (m, 2 H), 7.76 (s, 1 H), 8.16 (s, 1 H). \textsuperscript{13}C NMR (150 MHz, CDCl\textsubscript{3}): \(\delta\) 18.7 (CH\textsubscript{3}), 44.3 (CH\textsubscript{2}), 99.7 (CH), 120.5 (C\textsubscript{quat}), 125.6 (CH), 126.4 (CH), 126.9 (CH), 128.4 (CH), 128.4 (C\textsubscript{quat}), 128.7 (CH), 129.0 (CH), 130.2 (CH), 132.6 (C\textsubscript{quat}), 134.4 (C\textsubscript{quat}), 136.8 (C\textsubscript{quat}), 142.2 (C\textsubscript{quat}), 144.2 (CH), 148.2 (C\textsubscript{quat}). EI MS (70 eV, \textit{m/z} (%)): 313 (24), 312 ([M\textsuperscript{+}], 100), 311 (45), 298 (14), 297 ([M-CH\textsubscript{3}\textsuperscript{+}], 57), 296 (6), 294 (5), 235 ([M-C\textsubscript{6}H\textsubscript{5}\textsuperscript{+}], 21), 221 ([M-C\textsubscript{7}H\textsubscript{4}F\textsubscript{3}\textsuperscript{+}], 19), 209 (13), 208 (79), 207 ([M-C\textsubscript{8}H\textsubscript{9}\textsuperscript{+}], 14), 192 (5), 156 (6), 152 (5), 105 (31), 104 (6), 103 (10), 79 (12), 77 (13). IR (ATR): \(\tilde{\nu} [\text{cm}^{-1}]\): 2986 (w), 2972 (w), 2943 (w), 2901 (w), 1603 (w), 1568 (w), 1541 (w), 1527 (m), 1513 (w), 1500 (m), 1477 (w), 1458 (w), 1449 (w), 1427 (w), 1405 (m), 1395 (w), 1379 (w), 1352 (w), 1339 (w), 1302 (w), 1294 (w), 1262 (w), 1229 (w), 1202 (w), 1177 (w), 1159 (w), 1148 (w), 1103 (w), 1072 (w), 1068 (w), 1053 (w), 1028 (w), 986 (w), 964 (w), 920 (w), 841 (w), 772 (m), 752 (s), 735 (s), 723 (w), 700 (s), 671 (w), 617 (w). Anal. calcd. for C\textsubscript{21}H\textsubscript{17}BrN\textsubscript{2} (377.3): C 66.85, H 4.54, N 7.43; Found: C 66.80, H 4.61, N 7.22.

5-Methyl-2-phenyl-1-(3-(trifluoromethyl)benzyl)-1\textsubscript{H}-pyrrolo[2,3-b]pyridine (4f)

According to the general procedure and after automated flash chromatography with a 3→5→10→15% ethyl acetate/n-hexane gradient compound 4f (157 mg, 21%) was obtained as a beige solid.

Mp 87 °C. \textsuperscript{1}H NMR (300 MHz, CDCl\textsubscript{3}): \(\delta\) 2.45 (s, 3 H), 5.57 (s, 2 H), 6.49 (s, 1 H), 7.11-7.13 (m, 1 H), 7.20 (s, 1 H), 7.28-7.43 (m, 7 H), 7.74-7.75 (m, 1 H), 8.18 (m, 1 H). \textsuperscript{13}C NMR (75 MHz, CDCl\textsubscript{3}): \(\delta\) 18.7 (CH\textsubscript{3}), 45.8 (CH\textsubscript{2}), 100.3 (CH), 120.6 (C\textsubscript{quat}), 123.8 (q, \textit{J}\textsubscript{CF} = 3.8 Hz, CH), 124.1 (q, \textit{J}\textsubscript{CF} = 3.8 Hz, CH), 124.1 (q, \textit{J}\textsubscript{CF} = 272.5 Hz, C\textsubscript{quat}), 125.9 (C\textsubscript{quat}), 128.7 (CH), 128.8 (CH), 129.1 (CH), 129.3 (CH), 130.2 (CH), 130.2 (CH), 130.8 (q, \textit{J}\textsubscript{CF} = 32.2 Hz, C\textsubscript{quat}), 132.4 (C\textsubscript{quat}), 139.7 (C\textsubscript{quat}), 142.0 (C\textsubscript{quat}), 144.1 (CH), 147.9 (C\textsubscript{quat}). EI MS (70 eV, \textit{m/z} (%)): 367 (23), 366 ([M\textsuperscript{+}], 100), 365 (76), 347 (5), 345 (8), 290 (6), 289 ([M-C\textsubscript{6}H\textsubscript{5}\textsuperscript{+}], 34), 222 (9), 221 ([M-C\textsubscript{7}H\textsubscript{4}F\textsubscript{3}\textsuperscript{+}], 52), 206 (6), 205 (7), 192 (12), 191 (10), 189 (8), 183 (6), 180 (7), 159 (11), 152 (8), 110 (6), 109 (8). IR (ATR): \(\tilde{\nu} [\text{cm}^{-1}]\): 3061 (w), 3033 (w), 2958 (w), 2925 (w), 1478
1-(3,5-Difluorobenzyl)-5-methyl-2-phenyl-1H-pyrrolo[2,3-b]pyridine (4g)

According to the general procedure and after automated flash chromatography with a 9% ethyl acetate/n-hexane gradient compound 4g (110 mg, 66%) was obtained as a yellow solid. An analytic sample was obtained after recrystallization from pentane.

Mp 106 °C. 1H NMR (500 MHz, CDCl₃): δ 2.45 (s, 3 H), 5.52 (s, 2 H), 6.47 (m, 2 H), 6.76 (s, 1 H), 6.17 (d, J = 1.6 Hz, 1 H). 13C NMR (125 MHz, CDCl₃): δ 18.7 (CH₃), 45.6 (CH₂), 100.5 (CH), 102.7 (t, J_CF = 25.6 Hz, CH), 109.7 (dd, J_CF = 19.6 Hz, 6.1 Hz, CH), 120.9 (C_quat), 126.0 (C_quat), 128.2 (CH), 128.9 (CH), 129.3 (CH), 132.3 (C_quat), 142.0 (C_quat), 142.8 (t, J_CF = 8.1 Hz, CH), 144.0 (C_quat), 147.8 (C_quat), 163.3 (dd, J_CF = 249.7 Hz, 12.6 Hz, C_quat). EI MS (70 eV, m/z (%)): 335 (21), 334 ([M]+, 100), 333 (83), 319 ([M-CH₃]+, 5), 318 (5), 258 (5), 257 ([M-C₆H₅]+, 29), 222 (10), 221 ([M-C₆H₅F₂]+, 59), 206 (6), 205 (8), 192 (14), 180 (8), 167 (9), 165 (5), 153 (4), 152 (10), 151 (5), 127 (11), 110 (6), 77 (5). IR (ATR): v [cm⁻¹]: 3051 (w), 3026 (w), 2918 (w), 1626 (m), 1595 (w), 1568 (w), 1541 (w), 1481 (m), 1452 (w), 1443 (m), 1408 (m), 1393 (w), 1348 (w), 1317 (w), 1296 (w), 1254 (w), 1231 (w), 1202 (w), 1188 (w), 1123 (s), 1078 (w), 1049 (w), 1032 (w), 990 (w), 966 (m), 914 (w), 880 (m), 855 (m), 824 (w), 785 (w), 772 (m), 743 (s), 729 (m), 691 (m), 675 (m), 652 (w), 611 (m). Anal. calcd. for C₂₁H₁₆N₂F₂ (334.4): C 75.43, H 4.82, N 8.38; Found: C 75.20, H 4.90, N 8.12.

1-Methyl-2-phenyl-1H-pyrrolo[2,3-b]pyridine (4h)

According to the general procedure and after automated flash chromatography with a 5−10% ethyl acetate/n-hexane gradient compound 4h (1190 mg, 57%) was obtained as a yellow solid.

Mp 33 °C. 1H NMR (300 MHz, CDCl₃): δ 3.88 (s, 3 H), 6.52 (s, 1 H), 7.09 (dd, J = 7.8 Hz, 4.8 Hz, 1 H), 7.39-7.57 (m, 5 H), 7.91 (dd, J = 7.8 Hz, 1.6 Hz, 1 H), 8.35 (dd, J = 4.8 Hz, 1.6 Hz, 1 H). 13C NMR (75 MHz, CDCl₃): δ 30.1 (CH₃), 99.6 (CH), 116.2 (CH), 120.8 (C_quat), 128.4 (CH), 128.5 (CH), 128.8 (CH), 129.3 (CH), 132.5 (C_quat), 142.1 (C_quat), 142.6 (CH), 149.3 (C_quat). EI MS (70 eV, m/z (%)): 209 (15), 208 ([M]+, 98), 207 (100), 206 (17), 205 (12), 180 (9), 152 (10), 151 (5), 139 (5), 131 ([M-C₆H₅]+, 23), 104 (10), 103 (17), 102 (5), 77 (5). IR (ATR): v [cm⁻¹]: 3053 (w), 2947 (w), 2918 (w), 1593 (w), 1568 (w), 1541 (w), 1481 (m), 1452 (m), 1439 (w), 1402 (w), 1370 (m), 1317 (m), 1294 (m), 1275 (w), 1225 (m), 1161 (w), 1130 (w), 1107 (w), 1074 (w), 1034 (w), 1011 (w), 961 (w), 918 (w), 905 (w), 802 (m), 772 (s), 754 (w).
1-Allyl-5-methyl-2-phenyl-1H-pyrrolo[2,3-b]pyridine (4i)

According to the general procedure and after automated flash chromatography with a 3→5→8% ethyl acetate/n-hexane gradient compound 4i (85 mg, 34%) was obtained as a yellow solid.

Mp 34 °C. 1H NMR (600 MHz, CDCl3): δ 2.36 (s, 3 H), 4.70-4.74 (m, 1 H), 4.84-4.85 (m, 2 H), 5.02-5.04 (m, 1 H), 5.91-5.96 (m, 1 H), 6.38 (s, 1 H), 7.33-7.39 (m, 3 H), 7.47-7.48 (m, 2 H), 7.64 (m, 1 H), 8.11 (m, 1 H). 13C NMR (150 MHz, CDCl3): δ 18.7 (CH3), 45.0 (CH2), 99.5 (CH), 116.1 (CH2), 120.6 (Cquat), 125.4 (Cquat), 128.4 (CH), 128.7 (CH), 129.2 (CH), 130.4 (CH), 132.7 (Cquat), 134.5 (CH), 142.1 (Cquat), 143.8 (CH), 147.7 (Cquat). EI MS (70 eV, m/z (%)): 288 (9), 287 (6), 249 (16), 248 ([M]+, 91), 247 (100), 233 ([M-CH3]+, 8), 232 (10), 221 ([M-C2H3]+, 14), 220 (16), 219 (5), 208 (9), 207 ([M-C3H5]+, 6), 206 (5), 205 (7), 192 (7), 171 ([M-C6H5]+, 5), 152 (6). IR (ATR): ν [cm⁻¹]: 3059 (w), 3005 (w), 2982 (w), 2920 (w), 2862 (w), 1647 (w), 1601 (w), 1570 (w), 1533 (w), 1506 (m), 1485 (m), 1475 (m), 1466 (m), 1456 (m), 1436 (m), 1425 (m), 1406 (m), 1396 (m), 1358 (m), 1338 (m), 1300 (m), 1254 (w), 1225 (w), 1204 (w), 1155 (w), 1126 (w), 1074 (w), 1044 (w), 1028 (w), 1001 (w), 964 (w), 943 (m), 922 (m), 912 (h), 874 (m), 855 (w), 841 (w), 791 (w), 774 (m), 747 (s), 725 (m), 696 (s), 679 (w), 638 (m). Anal. calcd. for C17H16N2 (248.3): C 82.22, H 6.49, N 11.28; Found: C 82.05, H 6.43, N 11.00.

1-(2,2-Dimethoxyethyl)-5-methyl-2-phenyl-1H-pyrrolo[2,3-b]pyridine (4j)

According to the general procedure and after automated flash chromatography with a 3→5→8→12→20→30% ethyl acetate/n-hexane gradient compound 4j (199 mg, 34%) was obtained as an orange solid.

Mp 65 °C. 1H NMR (600 MHz, CDCl3): δ 2.44 (s, 3 H), 3.19 (s, 6 H), 4.42 (d, J = 5.6 Hz, 2 H), 4.85 (t, J = 5.6 Hz, 1 H), 6.41 (s 1 H), 7.39-7.41 (m, 1 H), 7.45-7.47 (m, 2 H), 7.61-7.62 (m, 2 H), 7.69 (m, 1 H), 8.17 (m, 1 H). 13C NMR (150 MHz, CDCl3): δ 18.7 (CH3), 45.0 (CH2), 54.8 (CH3), 99.9 (CH), 102.7 (CH), 120.5 (Cquat), 125.4 (Cquat), 128.3 (CH), 128.3 (CH), 128.7 (CH), 129.7 (CH), 132.8 (Cquat), 142.4 (Cquat), 143.7 (CH), 148.2 (Cquat). EI MS (70 eV, m/z (%)): 297 (5), 296 ([M]+, 24), 281 ([M-CH3]+, 21), 265 (8), 235 (5), 222 (5), 221 ([M-C2H3O2]+, 22), 220 (8), 219 ([M-C6H5]+, 8), 209 (7), 208 (41), 207 ([M-C4H9O2]+, 5), 206 (7), 205 (9), 152 (5), 116 (5), 75 (100), 47 (6). IR (ATR): ν [cm⁻¹]: 3009 (w), 2972 (w), 2928 (w), 2860 (w), 2826 (w), 1603 (w), 1568 (w), 1558 (w), 1541 (w), 1506 (w), 1472 (m), 1445 (m), 1429 (m), 1406 (m), 1393 (m), 1364 (w), 1356 (w), 1327 (w), 1307 (w), 1296 (m), 1263 (w), 1244 (w), 1217 (w), 1198 (m), 1159 (w), 1153 (w), 1130 (m), 1096 (m), 1067 (s), 1044 (m), 1032 (m), 1013 (m), 999 (w), 974 (m), 920 (w), 880 (s), 851 (w), 828 (w), 801 (w), 781 (w), 774 (m), 747 (s), 725 (m), 696 (s), 679 (w), 638 (m). Anal. calcd. for C17H18N2 (248.3): C 82.22, H 6.49, N 11.28; Found: C 82.05, H 6.43, N 11.00.
1-(2-Methoxyethyl)-5-methyl-2-phenyl-1H-pyrrolo[2,3-b]pyridine (4k)

According to the general procedure and after automated flash chromatography with a 5→30% ethyl acetate/n-hexane gradient compound 4k (204 mg, 38%) was obtained as a yellow solid.

Mp 55 °C. $^1$H NMR (600 MHz, CDCl$_3$): $\delta$ 2.43 (s, 3 H), 3.17 (s, 3 H), 3.70 (t, $J = 6.1$ Hz, 2 H), 4.49 (t, $J = 6.1$ Hz, 2 H), 6.40 (s, 1 H), 7.40-7.42 (m, 1 H), 7.45-7.48 (m, 2 H), 7.58-7.60 (m, 2 H), 7.69 (m, 1 H), 8.16 (m, 1 H). $^{13}$C NMR (150 MHz, CDCl$_3$): $\delta$ 18.7 (CH$_3$), 42.4 (CH$_2$), 58.9 (CH$_3$), 71.0 (CH$_2$), 99.7 (CH), 120.7 (Cquat), 125.3 (Cquat), 128.3 (CH), 128.4 (CH), 128.7 (CH), 129.6 (CH), 132.8 (Cquat), 142.3 (Cquat), 143.6 (CH), 148.0 (Cquat). EI MS (70 eV, m/z (%)): 266 ([M$^+$], 22), 259 (8), 257 (8), 251 ([M-CH$_3$]$^+$), 235 ([M-CH$_2$O]$^+$), 222 (5), 221 ([M-CH$_2$H$_5$O]$^+$), 204 (5), 220 (13), 219 (10), 208 (16), 208 (100), 207 ([M-C$_3$H$_7$O]$^+$), 206 (13), 205 (11), 152 (5). IR (ATR): $\tilde{\nu}$ [cm$^{-1}$]: 3030 (w), 2976 (w), 2922 (w), 2878 (w), 2859 (w), 2824 (w), 1599 (w), 1566 (w), 1541 (w), 1474 (m), 1443 (w), 1408 (m), 1393 (w), 1379 (m), 1358 (m), 1302 (m), 1275 (m), 1242 (w), 1217 (w), 1194 (w), 1150 (w), 1117 (m), 1098 (m), 1072 (w), 1045 (w), 1026 (w), 1009 (m), 997 (w), 970 (w), 926 (w), 920 (w), 880 (m), 866 (w), 814 (w), 801 (w), 775 (m), 756 (s), 706 (s), 692 (m), 673 (w), 665 (w), 619 (w). Anal. calcd. for C$_{18}$H$_{20}$N$_2$O$_2$ (296.4): C 72.95, H 6.80, N 9.45; Found: C 73.04, H 6.54, N 9.40.

2-Cyclopropyl-1-(3-fluorobenzyl)-5-methyl-1H-pyrrolo[2,3-b]pyridine (4l)

According to the general procedure and after automated flash chromatography with a 3→5→10% ethyl acetate/n-hexane gradient compound 4l (240 mg, 43%) was obtained as a yellow oil.

$^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 0.65-0.70 (m, 2 H), 0.84-0.91 (m, 2 H), 1.86-1.74 (m, 1 H), 2.40 (s, 3 H), 5.61 (s, 2 H), 6.02 (d, $J = 1.0$ Hz, 1 H), 6.73-6.78 (m, 1 H), 7.17-7.24 (m, 1 H), 7.61 (m, 1 H), 8.08 (d, $J = 1.7$ Hz, 1 H). $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ 6.8 (CH$_2$), 16.8 (CH$_3$), 44.7 (d, $J_{CF} = 1.7$ Hz, CH$_2$), 95.4 (CH), 113.7 (d, $J_{CF} = 22.0$ Hz, CH), 114.1 (d, $J_{CF} = 21.2$ Hz, CH), 120.2 (Cquat), 122.3 (d, $J_{CF} = 2.9$ Hz, CH), 125.1 (Cquat), 127.9 (CH), 130.2 (d, $J_{CF} = 8.3$ Hz, CH), 141.4 (d, $J_{CF} = 7.0$ Hz, Cquat), 142.9 (CH), 143.8 (Cquat), 147.4 (Cquat), 163.2 (d, $J_{CF} = 246.0$ Hz, Cquat). EI MS (70 eV, m/z (%)): 281 (18), 280 ([M$^+$], 100), 279 (52), 266 (8), 265 ([M-CH$_3$]$^+$), 253 (15), 252 (6), 251 (17), 250 (8), 239 ([M-C$_3$H$_5$F]$^+$), 185 ([M-C$_3$H$_5$F]$^+$), 172 (5), 171 ([M-C$_3$H$_5$F]$^+$), 170 (13), 169 (10), 158 (7), 156 (11), 155 (9), 145 (12), 144 (6), 133 (5), 132 (6), 115 (5), 109 (29), 83 (8). IR (ATR): $\tilde{\nu}$ [cm$^{-1}$]: 3086 (w), 3011 (w), 2922 (w), 2860 (w), 1614 (m), 1591 (m), 1574 (w), 1549 (w), 1485 (s), 1449 (m), 1435 (m), 1416 (s), 1367 (w), 1350 (m), 1335 (w), 1292 (m), 1269 (m), 1248 (s), 1211 (w), 1171 (w), 1153 (w), 1138 (m), 1126 (w), 1096 (w), 1076 (w), 1053 (w), 1026 (w), 1009 (m), 970 (w), 926 (w), 920 (w), 880 (m), 866 (w), 814 (w), 801 (w), 775 (m), 756 (s), 706 (s), 692 (m), 673 (w), 665 (w), 619 (w). Anal. calcd. for C$_{17}$H$_{18}$N$_2$O (266.3): C 76.66, H 6.81, N 10.52; Found: C 76.50, H 6.76, N 10.24.
2-Butyl-1-(3-fluorobenzyl)-5-methyl-1H-pyrrolo[2,3-b]pyridine (4m)

According to the general procedure and after automated flash chromatography with a 3→5→10% ethyl acetate/n-hexane gradient compound 4m (166 mg, 28%) was obtained as an orange solid.

Mp 56 °C. 1H NMR (300 MHz, CDCl3): δ 0.89 (t, J = 7.3 Hz, 3 H), 1.34-1.41 (m, 2 H), 1.58-1.68 (m, 2 H), 2.42 (s, 3 H), 2.58-2.63 (m, 2 H), 5.49 (s, 2 H), 6.19 (m, 1 H), 6.65-6.68 (m, 1 H), 6.86-6.91 (m, 1 H), 6.78-6.81 (m, 1 H), 7.16-7.24 (m, 1 H), 7.63-7.64 (m, 1 H), 8.07 (m, 1 H). 13C NMR (75 MHz, CDCl3): δ 14.0 (CH3), 18.7 (CH3), 22.6 (CH2), 26.7 (CH2), 30.2 (CH2), 44.4 (d, JCF = 1.7 Hz, CH2), 97.0 (CH), 113.5 (d, JCF = 22.1 Hz, CH), 114.2 (d, JCF = 21.2 Hz, CH), 120.5 (Cquat), 122.0 (d, JCF = 2.9 Hz, CH), 125.1 (Cquat), 127.7 (CH), 130.3 (d, JCF = 8.3 Hz, CH), 141.2 (d, JCF = 7.0 Hz, Cquat), 142.1 (Cquat), 142.7 (CH), 147.4 (Cquat), 163.2 (d, JCF = 246.2 Hz, Cquat). El MS (70 eV, m/z (%)): 297 (9), 296 ([M]+, 45), 267 ([M-C2H5]+, 10), 255 (15), 254 (91), 253 ([M-C2H3]+, 100), 252 (5), 251 (17), 239 ([M-C6H5]+, 22), 237 (5), 159 (16), 145 (27), 127 (10), 109 (37), 83 (7). IR (ATR): ν[cm⁻¹]: 3061 (w), 3026 (w), 2959 (w), 2878 (w), 2859 (w), 1616 (w), 1574 (w), 1559 (w), 1537 (m), 1487 (m), 1466 (m), 1449 (s), 1429 (m), 1415 (m), 1404 (m), 1383 (w), 1350 (m), 1292 (m), 1271 (m), 1257 (w), 1236 (m), 1206 (w), 1173 (w), 1157 (w), 1134 (w), 1123 (w), 1018 (w), 100 (w), 1003 (w), 943 (m), 876 (s), 793 (s), 762 (m), 745 (s), 731 (m), 710 (w), 679 (s), 638 (w), 615 (w). Anal. calcd. for C19H21FN2 (296.4): C 77.00, H 7.14, N 9.45; Found: C 76.83, H 7.12, N 9.32.

5-Chloro-1-(3-fluorobenzyl)-2-phenyl-1H-pyrrolo[2,3-b]pyridine (4n)

According to the general procedure and after automated flash chromatography with a 3→5→5% ethyl acetate/n-hexane gradient compound 4n (412 mg, 61%) was obtained as an orange solid.

Mp 46 °C. 1H NMR (300 MHz, CDCl3): δ 5.50 (s, 2 H), 6.51 (s, 1 H), 6.61-6.65 (m, 1 H), 6.70-6.73 (m, 1 H), 6.84-6.90 (m, 1 H), 7.13-7.20 (m, 1 H), 7.35-7.42 (m, 5 H), 7.90 (d, J = 2.3 Hz, 1 H), 8.26 (d, J = 2.3 Hz, 1 H). 13C NMR (75 MHz, CDCl3): δ 45.8 (d, JCF = 1.8 Hz, CH2), 100.2 (CH), 113.7 (d, JCF = 22.2 Hz, CH), 114.3 (d, JCF = 21.2 Hz, CH), 121.4 (Cquat), 122.2 (d, JCF = 2.9 Hz, CH), 124.6 (Cquat), 127.6 (CH), 128.8 (CH), 129.0 (CH), 129.3 (CH), 130.2 (d, JCF = 8.3 Hz, CH), 131.8 (Cquat), 140.8 (d, JCF = 7.0 Hz, Cquat), 141.8 (CH), 143.5 (Cquat), 147.5 (Cquat), 163.1 (d, JCF = 246.3 Hz, Cquat). El MS (70 eV, m/z (%)): 339 (6), 338 ([M37Cl]+, 32), 337 (45), 336 ([M35Cl]+, 100), 335 (81), 301 ([M-Cl]+, 9), 300 (11), 299 (5), 261 ([M37Cl]-C6H5]+, 7), 259 ([M35Cl]-C6H5]+, 22), 243 ([M37Cl]-C6H4F]+, 13), 242 (6), 241
(\([\text{M}^{35}\text{Cl}]-\text{C}_6\text{H}_4\text{F}\]^\text{+}, 39), 200 (5), 192 (8), 168 (6), 165 (8), 164 (8), 151 (5), 150 (5), 140 (5), 110 (5), 109 (60), 83 (14). \text{IR (ATR): } \tilde{\nu}[^\text{cm}^{-1}]: 3059 (\text{w}), 3034 (\text{w}), 2947 (\text{w}), 2928 (\text{w}), 2853 (\text{w}), 1616 (\text{w}), 1591 (\text{m}), 1560 (\text{w}), 1541 (\text{w}), 1485 (\text{m}), 1464 (\text{m}), 1451 (\text{m}), 1443 (\text{m}), 1433 (\text{w}), 1410 (\text{m}), 1391 (\text{w}), 1354 (\text{m}), 1294 (\text{m}), 1271 (\text{w}), 1252 (\text{m}), 1236 (\text{w}), 1221 (\text{w}), 1169 (\text{m}), 1152 (\text{w}), 1132 (\text{w}), 1086 (\text{m}), 1028 (\text{w}), 1000 (\text{w}), 966 (\text{w}), 932 (\text{m}), 883 (\text{m}), 860 (\text{w}), 826 (\text{w}), 772 (\text{s}), 750 (\text{s}), 698 (\text{s}), 677 (\text{m}), 667 (\text{w}), 615 (\text{w}). \text{Anal. calcd. for } C_{20}H_{14}ClFN_2 (336.8): C 71.32, H 4.19, N 8.32; Found: C 71.21, H 4.47, N 8.14.

2 3-Iodo-1-methyl-2-phenyl-1H-pyrrolo[2,3-b]pyridine (5) by consecutive four-component reaction

In a dry screw-cap Schlenk tube with a magnetic stir bar were placed the corresponding \(\alpha\)-amino-3-bromopyridine (1b) (173 mg, 1.00 mmol), \(\text{Pd(PPh}_3\text{)}_2\text{Cl}_2\) (17.5 mg, 25.0 \(\mu\text{mol})), and \((1\text{-Ad})_2\text{PBn-HBr}\) (23.6 mg, 50.0 \(\mu\text{mol}) and the vessel was evacuated. After flushing the vessel with nitrogen dry DMSO (1.50 mL), phenylacetylene (2a) (122 mg, 1.20 mmol), and DBU (457 mg, 3.00 mmol) were added and the reaction mixture was stirred at 100 °C under nitrogen for 1 h. After cooling to room temp KOt-Bu (505 mg, 4.50 mmol) and DMSO (1.50 mL) were added to the reaction mixture and the mixture was stirred at 100 °C under nitrogen for 0.25 h. After cooling to room temp \(N\)-iodosuccinimide (338 mg, 3.00 mmol) and DMSO (1.00 mL) were added and the mixture was stirred at room temp for 5 h. Then, methyl iodide (2b) (639 mg, 4.50 mmol) was added and the reaction mixture was stirred at room temp for 5 min. Then, deionized water was added to the mixture and the aqueous layer was extracted several times with ethyl acetate. The combined organic phases were dried (anhydrous sodium sulfate) and after filtration the solvents were removed in vacuo. The residue was adsorbed on silica and purified by automated flash chromatography on silica gel (SNAP cartridge 100 g, hexanes/ethyl acetate 5→10→20%) to give the analytically pure 3-iodo-1-methyl-2-phenyl-1H-pyrrolo[2,3-b]pyridine (5) (186 mg, 56%) as an orange solid. Mp 85 °C. \(\text{H NMR (300 MHz, CDCl}_3\text{): } ^\text{H} \text{NMR (300 MHz, CDCl}_3\text{): } ^\text{H} \text{NMR (300 MHz, CDCl}_3\text{): } ^\text{H} \text{NMR (300 MHz, CDCl}_3\text{): } ^\text{H} \text{NMR (300 MHz, CDCl}_3\text{): } ^\text{H} \text{NMR (300 MHz, CDCl}_3\text{): } \delta 3.80 (\text{s, 3 H}), 7.17 (\text{dd, } J = 7.9 \text{ Hz, 4.8 Hz, 1 H}), 7.47-7.56 (\text{m, 5 H}), 7.76 (\text{dd, } J = 7.9 \text{ Hz, 1.5 Hz, 1 H}), 8.37 (\text{dd, } J = 4.8 \text{ Hz, 1.5 Hz, 1 H}). \text{C NMR (75 MHz, CDCl}_3\text{): } ^\text{C} \text{NMR (75 MHz, CDCl}_3\text{): } ^\text{C} \text{NMR (75 MHz, CDCl}_3\text{): } ^\text{C} \text{NMR (75 MHz, CDCl}_3\text{): } ^\text{C} \text{NMR (75 MHz, CDCl}_3\text{): } \delta 30.8 (\text{CH}_3), 56.6 (\text{C}_\text{quat}), 117.0 (\text{CH}), 123.9 (\text{C}_\text{quat}), 128.7 (\text{CH}), 129.3 (\text{CH}), 129.5 (\text{CH}), 130.8 (\text{CH}), 131.2 (\text{C}_\text{quat}), 142.3 (\text{C}_\text{quat}), 143.9 (\text{CH}), 148.7 (\text{C}_\text{quat}). \text{El MS (70 eV, } m/z (\%)): 335 (15), 334 ([M]^+, 100), 333 (20), 207 ([M-I]^+, 14), 206 (43), 205 (35), 180 (9), 178 (6), 167 (5), 164 (5), 152 (8), 151 (7), 139 (5), 103 (18), 89 (5), 77 (5). \text{IR (ATR): } \tilde{\nu}[^\text{cm}^{-1}]: 3065 (\text{w}), 3050 (\text{w}), 3021 (\text{w}), 2976 (\text{w}), 2943 (\text{w}), 2878 (\text{w}), 1593 (\text{w}), 1566 (\text{m}), 1476 (\text{w}), 1451 (\text{w}), 1435 (\text{w}), 1400 (\text{m}), 1362 (\text{w}), 1314 (\text{m}), 1279 (\text{w}), 1130 (\text{w}), 1114 (\text{m}), 1078 (\text{w}), 1020 (\text{w}), 936 (\text{m}), 924 (\text{w}), 833 (\text{w}), 787 (\text{m}), 754 (\text{s}), 698 (\text{s}), 669 (\text{m}), 637 (\text{m}). \text{Anal. calcd. for } C_{14}H_{11}IN_2 (334.2): C 50.32, H 3.32, N 8.38; Found: C 50.30, H 3.20, N 8.27.
1-(6,7-Dimethoxy-3,4-dihydroisoquinolin-2(1H)-yl)prop-2-ene-1-one (6)\(^1\)

In a dry screw-cap Schlenk tube with a magnetic stir bar were placed 6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline hydrochloride (1.00 g, 4.40 mmol) and dry dichloromethane (50.0 mL). The suspension was cooled to 0 °C (ice bath) and triethylamine (1.80 mL, 13.0 mmol) was added. After removal of the ice bath the mixture was allowed to come to room temp and it was stirred at room temp for 30 min. Then the reaction mixture was cooled to 0 °C (ice bath) again and acryloyl chloride (380 μL, 4.70 mmol) was added dropwise and then stirred at 0 °C for 1 h. After removal of the ice bath the mixture was allowed to come to room temp and it was stirred at room temp for 2 h min. Then, saturated aqueous ammonium chloride solution was added to the mixture and the aqueous layer was extracted several times with dichloromethane. The combined organic phases were washed with brine, dried (anhydrous sodium sulfate) and after filtration the solvents were removed in vacuo. The residue was adsorbed on silica and purified by automated flash chromatography on silica gel (SNAP cartridge 100 g, ethyl acetate/n-hexanes 50→83%) to give the analytically pure acryloyl isoquinoline 6 (750 mg, 69%) as a colorless solid.

Mp 104 °C. \(^1\)H NMR (300 MHz, CDCl\(_3\)) (two rotamers in a ratio of 1.3:1): \(\delta\) 2.83 (m, 2 H), 3.77-3.86 (m, 8 H), 4.67-4.71 (m, 2 H), 5.71 (d, \(J = 2.0\) Hz, 0.48 H), 5.74 (d, \(J = 2.0\) Hz, 0.52 H), 6.30 (d, \(J = 2.0\) Hz, 0.41 H), 6.36 (d, \(J = 2.0\) Hz, 0.59 H), 6.61-6.70 (m, 3 H). \(^{13}\)C NMR (75 MHz, CDCl\(_3\)): \(\delta\) 28.1 (CH\(_2\)), 29.2 (CH\(_2\)), 40.1 (CH\(_2\)), 43.7 (CH\(_2\)), 44.3 (CH\(_2\)), 47.3 (CH\(_2\)), 56.1 (CH\(_3\)), 109.2 (CH), 109.7 (CH), 111.6 (CH), 111.9 (CH), 124.3 (C\(_{\text{quat}}\)), 125.4 (C\(_{\text{quat}}\)), 125.9 (C\(_{\text{quat}}\)), 127.1 (C\(_{\text{quat}}\)), 127.6 (CH\(_2\)), 128.0 (CH), 128.2 (CH), 148.0 (C\(_{\text{quat}}\)), 148.1 (C\(_{\text{quat}}\)), 165.7 (C\(_{\text{quat}}\)), 165.8 (C\(_{\text{quat}}\)). El MS (70 eV, m/z (%)): 248 (15), 247 ([M\(^+\)], 100), 246 (77), 232 ([M – CH\(_3\)\(^+\)], 12), 219 (5), 215 (5), 204 (6), 193 (5), 192 ([M – C\(_3\)H\(_2\)O\(^+\)], 37), 191 (42), 190 (19), 178 (19), 177 (30), 176 (35), 165 (11), 164 (43), 162 (12), 161 (16), 160 (6), 151 (10), 150 (12), 149 (21), 148 (7), 147 (7), 146 (18), 133 (7), 131 (6), 121 (17), 119 (5), 105 (6), 91 (11), 78 (5), 77 (11), 55 (25), 43 (9). IR (ATR): \(\tilde{\nu}\) [cm\(^{-1}\)]: 2996 (w), 2961 (w), 2941 (w), 2870 (w), 2841 (w), 1651 (m), 1611 (m), 1578 (w), 1518 (s), 1505 (w), 1460 (m), 1431 (m), 1381 (w), 1364 (w), 1348 (m), 1329 (w), 1287 (m), 1273 (m), 1246 (w), 1229 (m), 1209 (s), 1202 (s), 1159 (w), 1121 (s), 1061 (w), 1051 (w), 1036 (w), 1017 (m), 986 (w), 970 (w), 947 (m), 928 (w), 885 (m), 856 (m), 833 (w), 789 (m), 743 (w). Anal. calcd. for C\(_{14}\)H\(_{17}\)NO\(_3\) (247.3): C 68.00, H 6.93, N 5.66. Found: C 67.78, H 6.87, N 5.50.

4 (\(E\))-1-(6,7-Dimethoxy-3,4-dihydroisoquinolin-2(1H)-yl)-3-(1-methyl-2-phenyl-1H-pyrrolo[2,3-b]-pyridin-3-yl)prop-2-en-1-one (SIS3)\(^2\)

In a dry 8 mL microwave vessel with septum and magnetic stir bar were placed acrylamide 6 (167 mg, 0.50 mmol), tetra"butylammonium chloride (139 mg, 500 μmol), sodium carbonate (53.0 mg, 500 μmol), and palladium acetate (5.60 mg, 25.0 μmol). The vessel was
evacuated, flushed with dry argon and dry DMF (2.50 mL) were added by syringe. Then the suspension was degassed with dry argon for 5 min. The vessel was placed in the microwave cavity and heated at 200 °C for 7 min. After cooling to room temp deionized water was added and the aqueous layer was extracted with ethyl acetate and diethyl ether until no products were detected in the extract by TLC. The combined organic phases were subsequently washed with deionized water, saturated aqueous sodium bicarbonate solution, as well as with brine, and then dried (anhydrous sodium sulfate). After filtration the solvents were removed in vacuo. The residue was adsorbed on silica and purified by automated flash chromatography on silica gel (SNAP cartridge 100 g, ethyl acetate/ n-hexanes 50→75%) to give SIS3 (7) (123 mg, 54%) as a yellow solid.

Mp 78 °C. \(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta\) 2.81 (br, 2 H), 3.75 (s, 3 H), 3.85 (m, 8 H), 4.71 (m, 2 H), 6.63 (m, 2 H), 6.86 (d, \(J = 15.4\) Hz, 1 H), 7.21-7.26 (m, 1 H), 7.42-7.47 (m, 2 H), 7.49-7.56 (m, 3 H), 7.73-7.79 (m, 1 H), 8.23 (m, 1 H), 8.42 (dd, \(J = 4.7\) Hz, 1.3 Hz, 1 H). \(^{13}\)C NMR (75 MHz, CDCl\(_3\)) (two rotamers): \(\delta\) 28.3 (CH\(_2\)), 29.2 (CH\(_2\)), 29.9 (CH\(_3\)), 40.2 (CH\(_2\)), 43.8 (CH\(_2\)), 44.4 (CH\(_2\)), 47.3 (CH\(_2\)), 56.1 (CH\(_3\)), 109.2 (CH), 109.5 (CH), 111.3 (CH), 111.7 (CH), 113.6 (CH), 113.8 (CH), 117.2 (CH), 118.6 (C\(_{\text{quat}}\)), 124.5 (C\(_{\text{quat}}\)), 125.9 (C\(_{\text{quat}}\)), 127.4 (C\(_{\text{quat}}\)), 127.9 (C\(_{\text{quat}}\)), 128.3 (CH), 128.9 (CH), 129.5 (CH), 130.0 (C\(_{\text{quat}}\)), 130.8 (CH), 136.1 (CH), 143.7 (CH), 144.5 (C\(_{\text{quat}}\)), 147.9 (C\(_{\text{quat}}\)), 149.0 (C\(_{\text{quat}}\)), 166.9 (C\(_{\text{quat}}\)). El MS (70 eV, m/z (%)): 453 ([M]+, 3), 262 (32), 261 ([M – C\(_{11}\)H\(_{14}\)NO\(_2\)]+, 51), 246 ([C\(_{14}\)H\(_{16}\)NO\(_3\)]+, 6), 245 (16), 235 (7), 234 (42), 233 ([M – C\(_{13}\)H\(_{14}\)NO\(_3\)]+, 78), 232 (9), 231 (19), 221 (7), 219 (12), 218 (40), 217 (5), 209 (8), 208 (15), 207 ([M – C\(_{14}\)H\(_{16}\)NO\(_3\)]+, 17), 192 ([C\(_{11}\)H\(_{14}\)NO\(_2\)]+, 14), 191 (11), 190 (11), 178 (9), 177 (6), 176 (7), 164 (5), 44 (100), 43 (6). IR (ATR): \(\tilde{\nu}\) [cm\(^{-1}\)]: 2990 (w), 2953 (w), 2930 (w), 2909 (w), 2835 (w), 1636 (m), 1589 (m), 1570 (m), 1559 (m), 1516 (s), 1460 (s), 1437 (s), 1410 (s), 1397 (s), 1362 (m), 1350 (m), 1333 (w), 1267 (s), 1257 (s), 1219 (s), 1206 (s), 1152 (m), 1111 (s), 1057 (w), 1018 (m), 972 (m), 930 (w), 839 (s), 810 (w), 768 (s), 708 (s), 689 (w), 652 (w).
5. 1H and 13C NMR spectra of compounds 4, 5, 6, and 7
5.1 1-Benzyl-5-methyl-2-phenyl-1H-pyrrolo[2,3-b]pyridine (4a)

$^1$H NMR spectrum of 4a (CDCl$_3$, 600 MHz, 293 K).

$^{13}$C NMR spectrum of 4a (CDCl$_3$, 150 MHz, 293 K).
135DEPT NMR spectrum of 4a (CDCl$_3$, 293 K).

5.2 1,5-Dimethyl-2-phenyl-1H-pyrrolo[2,3-b]pyridine (4b)

$^1$H NMR spectrum of 4b (CDCl$_3$, 300 MHz, 293 K).
$^{13}$C NMR spectrum of 4b (CDCl$_3$, 75 MHz, 293 K).

135DEPT NMR spectrum of 4b (CDCl$_3$, 293 K).
5.3 1-(3-Fluorobenzyl)-5-methyl-2-phenyl-1H-pyrrolo[2,3-b]pyridine (4c)

$^1$H NMR spectrum of 4c (CDCl$_3$, 600 MHz, 293 K).

$^{13}$C NMR spectrum of 4c (CDCl$_3$, 150 MHz, 293 K).
135DEPT NMR spectrum of 4c (CDCl₃, 293 K).

5.4 1-(4-Bromobenzyl)-5-methyl-2-phenyl-1H-pyrrolo[2,3-b]pyridine (4d)

¹H NMR spectrum of 4d (CDCl₃, 600 MHz, 293 K).
$^{13}$C NMR spectrum of 4d (CDCl$_3$, 150 MHz, 293 K).

135DEPT NMR spectrum of 4d (CDCl$_3$, 293 K).
5.5  5-Methyl-1-(2-methylbenzyl)-2-phenyl-1H-pyrrolo[2,3-b]pyridine (4e)

$^1$H NMR spectrum of 4e (CDCl$_3$, 600 MHz, 293 K).

$^{13}$C NMR spectrum of 4e (CDCl$_3$, 150 MHz, 293 K).
135DEPT NMR spectrum of 4e (CDCl₃, 293 K).

5.6 5-Methyl-2-phenyl-1-(3-(trifluoromethyl)benzyl)-1H-pyrrolo[2,3-b]pyridine (4f)

¹H NMR spectrum of 4f (CDCl₃, 300 MHz, 293 K).
$^{13}$C NMR spectrum of 4f (CDCl$_3$, 75 MHz, 293 K).

135DEPT NMR spectrum of 4f (CDCl$_3$, 293 K).
5.7 1-(3,5-Difluorobenzyl)-5-methyl-2-phenyl-1H-pyrrolo[2,3-b]pyridine (4g)

$^1$H NMR spectrum of 4g (CDCl$_3$, 500 MHz, 293 K).

$^{13}$C NMR spectrum of 4g (CDCl$_3$, 125 MHz, 293 K).
135DEPT NMR spectrum of 4g (CDCl₃, 293 K).

5.8 1-Methyl-2-phenyl-1H-pyrrolo[2,3-b]pyridine (4h)

¹H NMR spectrum of 4h (CDCl₃, 300 MHz, 293 K).
$^{13}$C NMR spectrum of 4h (CDCl$_3$, 75 MHz, 293 K).

135DEPT NMR spectrum of 4h (CDCl$_3$, 293 K).
5.9 1-Allyl-5-methyl-2-phenyl-1H-pyrrolo[2,3-b]pyridine (4i)

$^1$H NMR spectrum of 4i (CDCl$_3$, 600 MHz, 293 K).

$^{13}$C NMR spectrum of 4i (CDCl$_3$, 150 MHz, 293 K).
135DEPT NMR spectrum of 4i (CDCl₃, 293 K).

5.10 1-(2,2-Dimethoxyethyl)-5-methyl-2-phenyl-1H-pyrrolo[2,3-b]pyridine (4j)

¹H NMR spectrum of 4j (CDCl₃, 600 MHz, 293 K).
$^{13}$C NMR spectrum of 4j (CDCl$_3$, 150 MHz, 293 K).

135DEPT NMR spectrum of 4j (CDCl$_3$, 293 K).
5.11 1-(2-Methoxyethyl)-5-methyl-2-phenyl-1H-pyrrolo[2,3-b]pyridine (4k)

1H NMR spectrum of 4k (CDCl₃, 600 MHz, 293 K).

13C NMR spectrum of 4k (CDCl₃, 150 MHz, 293 K).
135DEPT NMR spectrum of 4k (CDCl$_3$, 293 K).

5.12 2-Cyclopropyl-1-(3-fluorobenzyl)-5-methyl-1H-pyrrolo[2,3-b]pyridine (4l)

$^1$H NMR spectrum of 4l (CDCl$_3$, 300 MHz, 293 K).
$^{13}$C NMR spectrum of 4I (CDCl$_3$, 75 MHz, 293 K).

135DEPT NMR spectrum of 4I (CDCl$_3$, 293 K).
5.13 2-Butyl-1-(3-fluorobenzyl)-5-methyl-1H-pyrrolo[2,3-b]pyridine (4m)

$^1$H NMR spectrum of 4m (CDCl$_3$, 300 MHz, 293 K).

$^{13}$C NMR spectrum of 4m (CDCl$_3$, 75 MHz, 293 K).
135DEPT NMR spectrum of 4m (CDCl₃, 293 K).

5.14 5-Chloro-1-(3-fluorobenzyl)-2-phenyl-1H-pyrrolo[2,3-b]pyridine (4n)

¹H NMR spectrum of 4n (CDCl₃, 300 MHz, 293 K).
$^{13}$C NMR spectrum of 4n (CDCl$_3$, 75 MHz, 293 K).

$^{135}$DEPT NMR spectrum of 4n (CDCl$_3$, 293 K).
5.15  3-ido-1-methyl-2-phenyl-1H-pyrrol[2,3-b]pyridine (5)

$^1$H NMR spectrum of 5 (CDCl$_3$, 300 MHz, 293 K).

$^{13}$C NMR spectrum of 5 (CDCl$_3$, 75 MHz, 293 K).
135DEPT NMR spectrum of 5 (CDCl₃, 293 K).

5.16 1-(6,7-Dimethoxy-3,4-dihydroisoquinolin-2(1H)-yl)prop-2-ene-1-one (6)

¹H NMR spectrum of 6 (CDCl₃, 300 MHz, 293 K).
$^{13}$C NMR spectrum of 6 (CDCl$_3$, 75 MHz, 293 K).

135DEPT NMR spectrum of 6 (CDCl$_3$, 293 K).
5.17  (E)-1-(6,7-Dimethoxy-3,4-dihydroisoquinolin-2(1H)-yl)-3-(1-methyl-2-phenyl-1H-pyrrolo[2,3-b]-pyridin-3-yl)prop-2-en-1-one (SIS3) (7)

\[ \text{\textsuperscript{1}H NMR spectrum of 7 (CDCl\textsubscript{3}, 300 MHz, 293 K).} \]

\[ \text{\textsuperscript{13}C NMR spectrum of 7 (CDCl\textsubscript{3}, 75 MHz, 293 K).} \]
135DEPT NMR spectrum of 7 (CDCl₃, 293 K).
