Direct carboxamidation of indoles by palladium-catalyzed C–H activation and isocyanide insertion

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I. General information

All reagents were purchased without further purification unless otherwise noted. Reactions were monitored using thin-layer chromatography (TLC) on commercial silica gel plates (GF254). Visualization of the developed plates was performed under UV light (254 nm). Flash column chromatography was performed on silica gel (200-300 mesh). $^1$H and $^{13}$C NMR spectra were recorded on a 400 or 500 MHz spectrometer. Chemical shifts (δ) are reported in ppm referenced to an internal tetramethylsilane standard or the DMSO-d$_6$ residual peak (δ 2.50) for $^1$H NMR. Chemical shifts of $^{13}$C NMR are reported relative to CDCl$_3$ (δ 77.0) or DMSO-d$_6$ (δ 39.5). The following abbreviations were used to describe peak splitting patterns when appropriate: br = broad, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet. Coupling constants, $J$, were reported in Hertz unit (Hz). High resolution mass spectra (HRMS) were obtained on an ESI-LC-MS/MS spectrometer.

II. Screening of the reaction conditions

<table>
<thead>
<tr>
<th>entry</th>
<th>oxidant (equiv)</th>
<th>additive (equiv)</th>
<th>solvent</th>
<th>T/°C</th>
<th>yield (%)</th>
<th>3a</th>
<th>4a</th>
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<tr>
<td>1</td>
<td>Cu(OAc)$_2$ (1)</td>
<td>--</td>
<td>AcOH</td>
<td>110</td>
<td>54</td>
<td>n.d.</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Cu(OAc)$_2$ (1)</td>
<td>--</td>
<td>Toluene</td>
<td>110</td>
<td>n.d.</td>
<td>67</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Cu(OAc)$_2$ (1)</td>
<td>--</td>
<td>THF</td>
<td>110</td>
<td>4</td>
<td>82</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>AgOAc (1)</td>
<td>--</td>
<td>AcOH</td>
<td>110</td>
<td>37</td>
<td>n.d.</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>CuO (1)</td>
<td>--</td>
<td>AcOH</td>
<td>110</td>
<td>n.r.</td>
<td>n.r.</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>O$_2$</td>
<td>--</td>
<td>AcOH</td>
<td>110</td>
<td>10$^c$</td>
<td>n.d.</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>BQ (1)</td>
<td>--</td>
<td>AcOH</td>
<td>110</td>
<td>26</td>
<td>n.d.</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>K$_2$S$_2$O$_8$ (1)</td>
<td>--</td>
<td>AcOH</td>
<td>110</td>
<td>19</td>
<td>n.d.</td>
<td></td>
</tr>
</tbody>
</table>
III. General procedures and characterization of the products

General procedures

General procedure for the synthesis of 3

A mixture of substrate 1 (0.4 mmol), isocyanide 2 (0.48 mmol, 1.2 equiv), Pd(OAc)$_2$ (4.5 mg, 0.02 mmol, 5 mol %), Cu(OAc)$_2$ (73.2 mg, 0.4 mmol, 1 equiv), TFA (0.48 mmol, 1.2 equiv), H$_2$O (36 mg, 2 mmol, 5 equiv) in THF (2.0 mL) was stirred in a sealed tube under air atmosphere at 70 °C. The reaction was cooled down to room temperature after complete consumption of the starting material as being monitored by TLC. Saturated NH$_4$OH (10 mL) and EtOAc (10 mL) were added to the reaction mixture successively. The organic phase was separated, and the aqueous phase was further extracted with EtOAc (2 × 10 mL). The combined organic layers were dried over anhydrous Na$_2$SO$_4$ and concentrated. The residue was purified by flash chromatography to provide the desired product 3.

General procedure for the synthesis of 4

A mixture of substrate 1 (0.4 mmol), isocyanide 2 (0.48 mmol, 1.2 equiv), Pd(OAc)$_2$ (9 mg, 0.04 mmol, 10 mol %), Cu(OAc)$_2$ (73.2 mg, 0.4 mmol, 1 equiv), in
THF (2.0 mL) was stirred in a sealed tube under air atmosphere at 90 °C. The reaction was cooled down to room temperature after complete consumption of the starting material as being monitored by TLC. Saturated aqueous NH₄OH (10 mL) and EtOAc (10 mL) were added to the reaction mixture successively. The organic phase was separated, and the aqueous phase was further extracted with EtOAc (2 × 10 mL). The combined organic layers were dried over anhydrous Na₂SO₄ and concentrated. The residue was purified by flash chromatography to provide the products 4 (major) and 3 (minor).

Characterization of the products

**N-tert-butyl-1-methyl-1H-indole-3-carboxamide (3a)**

![Chemical Structure]

1H NMR (400 MHz, CDCl₃) δ 7.87-7.89 (m, 1H), 7.61 (s, 1H), 7.34 (d, J = 7.2 Hz, 1H), 7.23-7.32 (m, 1H), 5.88 (br, 1H), 3.78 (s, 1H), 1.51 (s, 9H); 13C NMR (125 MHz, CDCl₃) δ 164.6, 137.2, 132.2, 125.1, 122.3, 121.2, 119.7, 112.1, 110.0, 51.3, 33.1, 29.2; HRMS (ESI): Exact mass calcd for C₁₄H₁₉N₂O [M+H]+ 231.1492, Found 231.1495.

**N-tert-butyl-1H-indole-3-carboxamide (3b)**

![Chemical Structure]

1H NMR (400 MHz, CDCl₃) δ 10.24 (br, 1H), 7.83-7.85 (m, 1H), 7.62 (d, J = 2.8 Hz, 1H), 7.42-7.44 (m, 1H), 7.20-7.23 (m, 2H), 5.79 (s, 1H), 1.55 (s, 9H); 13C NMR (125 MHz, CDCl₃) δ 165.7, 136.7, 128.6, 124.3, 122.5, 121.2, 119.0, 112.8, 112.5, 51.5, 29.3; HRMS (ESI): Exact mass calcd for C₁₃H₁₇N₂O [M+H]+ 217.1335, Found 217.1337.

**N-tert-butyl-5-methyl-1H-indole-3-carboxamide (3c)**

![Chemical Structure]

1H NMR (400 MHz, CDCl₃) δ 10.13 (br, 1H), 7.65 (s, 1H), 7.54 (d, J = 2.8 Hz, 1H), 7.29 (d, J = 8 Hz 1H), 7.02 (dd, J = 8, 0.8 Hz, 1H), 5.94 (br, 1H), 2.45 (s, 3H), 1.54 (s, 9H); 13C NMR (125 MHz, CDCl₃) δ 165.8, 135.0, 130.5, 128.4, 124.6, 118.9, 112.1, 51.4, 29.2; HRMS (ESI): Exact mass
calcld for C_{14}H_{18}N_{2}O_{2}Na \[M+Na\]^+ 253.1311, Found 253.1313.

*N-tert*-butyl-5-methoxy-1H-indole-3-carboxamide (3d)

![Structure of 3d](image)

$^1$H NMR (400 MHz, DMSO-d$_6$) $\delta$ 11.33 (br, 1H), 8.02 (d, $J = 2.8$ Hz, 1H), 7.65 (d, $J = 2.4$ Hz, 1H), 7.28 (d, $J = 8.8$ Hz, 1H), 7.09 (br, 1H), 6.76 (dd, $J = 8.8, 2.4$ Hz, 1H), 3.76 (s, 3H), 1.40 (s, 9H); $^{13}$C NMR (125 MHz, DMSO-d$_6$) $\delta$ 164.6, 154.1, 130.1, 127.8, 126.8, 112.0, 111.7, 111.1, 102.7, 55.1, 50.0, 28.9; HRMS (ESI): Exact mass calcld for C$_{14}$H$_{19}$N$_{2}$O$_{2}$ [M+H]$^+$ 247.1441, Found 247.1440.

*N-tert*-butyl-5-(benzyloxy)-1H-indole-3-carboxamide (3e)

![Structure of 3e](image)

$^1$H NMR (400 MHz, DMSO-d$_6$) $\delta$ 11.38 (br, 1H), 8.05 (d, $J = 2.8$ Hz, 1H), 7.77 (d, $J = 2.0$ Hz, 1H), 7.48 (d, $J = 7.6$ Hz, 2H), 7.39 (t, $J = 7.2$ Hz, 2H), 7.32 (t, $J = 8.8$ Hz, 2H), 7.12 (s, 1H), 6.85 (dd, $J = 8.8, 2.0$ Hz, 1H), 5.09 (s, 1H), 1.40 (s, 9H); $^{13}$C NMR (125 MHz, DMSO-d$_6$) $\delta$ 164.6, 153.2, 137.6, 131.2, 128.1, 127.9, 127.3, 126.8, 112.3, 112.1, 111.2, 104.3, 69.7, 50.0, 28.9; HRMS (ESI): Exact mass calcld for C$_{20}$H$_{23}$N$_{2}$O$_{2}$ [M+H]$^+$ 323.1754, Found 323.1756.

*N-tert*-butyl-5-hydroxy-1H-indole-3-carboxamide (3f)

![Structure of 3f](image)

$^1$H NMR (400 MHz, DMSO-d$_6$) $\delta$ 11.12 (br, 1H), 8.37 (s, 1H), 7.92 (d, $J = 3.2$ Hz, 1H), 7.49 (d, $J = 2.4$ Hz, 1H), 7.17 (d, $J = 8.8$ Hz, 1H), 6.98 (br, 1H), 6.62 (dd, $J = 8.4, 2.4$ Hz, 1H ), 1.38 (s, 9H); $^{13}$C NMR (125 MHz, DMSO-d$_6$) $\delta$ 164.8, 151.6, 130.4, 127.8, 127.2, 111.9, 111.8, 110.7, 105.2, 50.1, 29.1; HRMS (ESI): Exact mass calcld for C$_{13}$H$_{17}$N$_{2}$O$_{2}$ [M+H]$^+$ 233.1285, Found 233.1286.

*N-tert*-butyl-5-fluoro-1H-indole-3-carboxamide (3g)

![Structure of 3g](image)

$^1$H NMR (400 MHz, DMSO-d$_6$) $\delta$ 11.60 (br, 1H), 8.16 (d, $J = 2.8$ Hz), 7.82 (dd, $J = 10.4, 2.4$ Hz,
1H), 7.40 (dd, \( J = 8.8, 4.4 \) Hz, 1H), 7.22 (br, 1H), 6.95-7.00 (m, 1H), 1.39 (s, 9H); \(^{13}\)C NMR (125 MHz, DMSO-\(d_6\)) \( \delta \) 164.2, 158.7, 156.4, 132.6, 129.2, 126.8, 126.7, 112.5, 112.4, 11.6, 111.6, 109.8, 109.5, 105.7, 105.4, 50.1, 28.9; HRMS (ESI): Exact mass calcd for C\(_{13}\)H\(_{15}\)FN\(_2\)ONa [M+Na]\(^+\) 257.1061, Found 257.1062.

**N-tert-butyl-5-chloro-1H-indole-3-carboxamide (3h)**

\( ^1\)H NMR (400 MHz, DMSO-\(d_6\)) \( \delta \) 11.67 (br, 1H), 8.14 (d, \( J = 8.8 \) Hz, 1H), 8.13 (d, \( J = 2.0 \) Hz, 1H), 7.41 (d, \( J = 8.8 \) Hz, 1H), 7.26 (br, 1H), 7.13 (dd, \( J = 8.4, 2.0 \) Hz, 1H), 1.39, (s, 9H); \(^{13}\)C NMR (125 MHz, DMSO-\(d_6\)) \( \delta \) 164.0, 134.4, 128.9, 127.4, 124.8, 121.5, 120.1, 113.0, 111.2, 50.1, 28.8; HRMS (ESI): Exact mass calcd for C\(_{13}\)H\(_{16}\)ClN\(_2\)O [M+H]\(^+\) 251.0946, Found 251.0945.

**N-tert-butyl-5-bromo-1H-indole-3-carboxamide (3i)**

\( ^1\)H NMR (400 MHz, DMSO-\(d_6\)) \( \delta \) 11.67 (br, 1H), 8.29 (d, 1.6 Hz, 1H), 8.12 (d, \( J = 2.8 \) Hz, 1H), 7.37 (d, \( J = 8.8 \) Hz, 1H), 7.23-7.26 (m, 2H), 1.39 (s, 9H); \(^{13}\)C NMR (125 MHz, DMSO-\(d_6\)) \( \delta \) 164.0, 134.6, 128.7, 128.1, 124.0, 123.2, 113.5, 112.8, 111.0, 50.1, 40.1, 28.8; HRMS (ESI): Exact mass calcd for C\(_{13}\)H\(_{16}\)BrN\(_2\)O [M+H]\(^+\) 295.0441, Found 295.0442.

**N-tert-butyl-5-iodo-1H-indole-3-carboxamide (3j)**

\( ^1\)H NMR (400 MHz, DMSO-D\(_6\)) \( \delta \) 11.64 (br, 1H), 8.50 (d, \( J = 2.8 \) Hz, 1H), 8.07 (d, \( J = 2.4 \) Hz, 1H), 7.39 (dd, \( J = 8.4, 2.0 \) Hz, 1H), 7.24-7.27 (m, 2H), 1.39 (s, 9H); \(^{13}\)C NMR (125 MHz, DMSO-\(d_6\)) \( \delta \) 164.0, 135.0, 129.5, 129.4, 128.2, 113.9, 110.7, 84.1, 50.1, 40.1, 28.8; HRMS (ESI): Exact mass calcd for C\(_{13}\)H\(_{16}\)IN\(_2\)O [M+H]\(^+\) 343.0302, Found 343.0301.

**N-tert-butyl-5-cyano-1H-indole-3-carboxamide (3k)**

Electronic Supplementary Material (ESI) for Chemical Communications
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1H NMR (400 MHz, DMSO-d$_6$) δ 12.02 (br, 1H), 8.54 (d, $J = 0.8$ Hz, 1H), 8.28 (d, $J = 2.4$ Hz), 7.58 (d, $J = 8.4$ Hz, 1H), 7.48 (dd, $J = 8.4$, 1.6 Hz, 1H), 7.40 (br, 1H), 1.40 (s, 9H); 13C NMR (125 MHz, DMSO-d$_6$) δ 164.2, 138.3, 130.5, 127.0, 126.7, 124.9, 120.9, 112.6, 112.2, 103.0, 50.9, 29.4; HRMS (ESI): Exact mass calcd for C$_{14}$H$_{15}$N$_3$ONa [M+Na]$^+$ 264.1107, Found 264.1108.

*N*-tert-butyl-5-formyl-1H-indole-3-carboxamide (3l)

methyl 3-(tert-butylcarbamoyl)-1H-indole-5-carboxylate (3m)

*N*-tert-butyl-5-nitro-1H-indole-3-carboxamide (3n)

*N*-tert-butyl-6-chloro-1H-indole-3-carboxamide (3o)
$^1$H NMR (400 MHz, DMSO-d$_6$) $\delta$ 11.58 (br, 1H), 8.09-8.12 (m, 1H), 7.45 (d, $J = 1.6$ Hz, 1H), 7.23 (br, 1H), 7.08 (dd, $J = 8.4$, 1.6 Hz, 1H), 1.39 (s, 9H); $^{13}$C NMR (125 MHz, DMSO-d$_6$) $\delta$ 164.0, 136.3, 128.3, 126.2, 125.0, 122.2, 120.2 11.7, 111.1, 50.1, 40.1, 28.8; HRMS (ESI): Exact mass calcd for C$_{13}$H$_{16}$ClN$_2$O [M+H]$^+$ 251.0947, Found 251.0946.

**N-tert-butyl-6-bromo-1H-indole-3-carboxamide (3p)**

$^1$H NMR (400 MHz, DMSO-d$_6$) $\delta$ 11.59 (br, 1H), 8.09 (d, $J = 2.8$ Hz, 1H ), 8.08 (d, $J = 8.8$ Hz, 1H), 7.60 (d, $J = 1.6$ Hz, 1H), 7.25 (s, 1H), 7.22 (dd, $J = 8.8$, 1.6 Hz, 1H), 3.34 (s, 1H), 1.39 (s, 9H); $^{13}$C NMR (125 MHz, DMSO-d$_6$) $\delta$ 164.1, 136.9, 128.5, 125.4, 123.0, 122.9, 114.4, 114.2, 111.7, 50.3, 29.0; HRMS (ESI): Exact mass calcd for C$_{13}$H$_{16}$BrN$_2$O [M+H]$^+$ 295.0441, Found 295.0444.

**N-tert-butyl-7-methyl-1H-indole-3-carboxamide (3q)**

$^1$H NMR (400 MHz, DMSO-d$_6$) $\delta$ 11.43 (br, 1H), 8.06 (d, $J = 2.8$ Hz, 1H), 7.94 (d, $J = 7.6$ Hz, 1H), 7.12 (br, 1H), 6.97 (t, $J = 8.0$ Hz, 1H), 6.91 (d, $J = 6.8$ Hz, 1H), 2.46 (s, 3H), 1.39 (s, 9H); $^{13}$C NMR (100 MHz, DMSO-d$_6$) $\delta$ 164.5, 135.4, 127.2, 125.8, 121.9, 120.5, 120.1, 118.5, 111.9, 50.0, 28.9, 16.4; HRMS (ESI): Exact mass calcd for C$_{14}$H$_{19}$N$_2$O [M+H]$^+$ 231.1492, Found 231.1492.

**N-tert-butyl-7-ethyl-1H-indole-3-carboxamide (3r)**

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 10.09 (br, 1H), 7.69 (d, $J = 2.8$ Hz, 1H), 7.56 (d, $J = 4.0$ Hz, 1H), 7.19 (t, $J = 7.6$ Hz, 1H), 7.07 (d, $J = 7.2$ Hz, 1H), 5.98 (br, 1H), 2.91 (dd, $J = 14.8$, 7.2 Hz, 2H), 1.53 (s, 9H), 1.32 (t, $J = 7.2$ Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 165.6, 135.5, 128.4, 124.0,
121.6, 121.1, 116.6, 113.5, 51.4, 29.2, 23.9, 13.9; HRMS (ESI): Exact mass calcd for C\textsubscript{12}H\textsubscript{21}N\textsubscript{2}O [M+H]\textsuperscript{+} 245.1648, Found 245.1649.

\textit{N-tert-butyl-1-ethyl-1H-indole-3-carboxamide (3s)}\textsuperscript{2}

\[
\begin{align*}
\text{1H NMR (400 MHz, DMSO-d\textsubscript{6})} & \delta 8.13 (d, J = 8.0 \text{ Hz}, 1H), 8.10 (s, 1H), 7.76(dd, J = 8.4, 1.6 \text{ Hz}, 1H), 7.49(d, J = 8.8 \text{ Hz}, 1H), 7.31 (br, 1H), 3.86 (s, 3H), 1.41 (s, 9H); ^{13}C \text{ NMR (125 MHz, DMSO-d\textsubscript{6})} \delta 164.1, 135.6, 129.8, 126.6, 121.5, 120.1, 110.7, 109.8, 50.1, 28.9, 14.9; HRMS (ESI): Exact mass calcd for C\textsubscript{15}H\textsubscript{21}N\textsubscript{2}O [M+H]\textsuperscript{+} 245.1648, Found 245.1649.
\end{align*}
\]

\textit{N-tert-butyl-1-allyl-1H-indole-3-carboxamide (3t)}

\[
\begin{align*}
\text{1H NMR (400 MHz, CDCl\textsubscript{3})} & \delta 7.88-7.90 (m, 1H), 7.66 (s, 1H), 7.33-7.36 (m, 1H), 7.23-7.28(m, 2H), 5.93-6.02 (m, 1H), 5.83 (br, 1H), 5.24 (dd, J = 10.4, 1.2 \text{ Hz}, 1H ), 5.13 (dd, J = 16.8, 1.2 \text{ Hz}, 1H ) 4.74 (t, J = 1.6 \text{ Hz}, 1H), 1.52 (s, 9H); ^{13}C \text{ NMR (100 MHz, CDCl\textsubscript{3})} \delta 164.6, 136.6, 132.3, 131.2, 125.3, 122.2, 121.3, 119.9, 118.2, 112.5, 110.5, 51.3, 49.1, 29.3; HRMS (ESI): Exact mass calcd for C\textsubscript{16}H\textsubscript{20}N\textsubscript{2}ONa [M+Na]\textsuperscript{+} 279.1468, Found 279.1466.
\end{align*}
\]

\textit{N-tert-butyl-1-benzyl-1H-indole-3-carboxamide (3u)}

\[
\begin{align*}
\text{1H NMR (400 MHz, DMSO-d\textsubscript{6})} & \delta 8.13 (d, J = 8.0 \text{ Hz}, 1H), 8.10 (s, 1H), 7.76(dd, J = 8.4, 1.6 \text{ Hz}, 1H), 7.49(d, J = 8.8 \text{ Hz}, 1H), 7.31 (br, 1H), 3.86 (s, 3H), 1.41 (s, 9H); ^{13}C \text{ NMR (100 MHz, DMSO-d\textsubscript{6})} \delta 164.2, 137.6, 136.0, 131.1, 128.6, 127.5, 127.0, 126.8, 121.9, 121.4, 120.5, 111.2, 110.4, 50.3, 49.4, 29.0; HRMS (ESI): Exact mass calcd for C\textsubscript{20}H\textsubscript{22}N\textsubscript{2}ONa [M+Na]\textsuperscript{+} 329.1624, Found 329.1627.
\end{align*}
\]

\textit{N-isopropyl-1H-indole-3-carboxamide (3v)}
$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 9.74 (br, 1H), 7.89-7.91 (m, 1H), 7.65 (d, $J$ = 2.8 Hz, 1H), 7.41-7.43 (m, 1H), 7.20-7.26 (m, 2H), 5.90 (d, $J$ = 3.6 Hz, 1H), 4.34-4.42 (m, 1H), 1.30 (d, $J$ = 2.8 Hz, 6H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 165.1, 136.6, 128.3, 122.7, 121.4, 119.5, 112.3, 112.2, 41.4, 23.1; HRMS (ESI): Exact mass calcd for C$_{12}$H$_{14}$N$_2$ONa [M+Na]$^+$ 225.0998, Found 225.0998.

**N-cyclohexyl-1H-indole-3-carboxamide (3w)**

$\ce{\text{O}}$  
$\text{N}$  
$\text{CH}_2$  
$\text{N}$

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 9.31 (br, 1H), 7.88-7.91 (m, 1H), 7.69 (d, $J$ = 2.8 Hz, 1H), 7.41-7.43 (m, 1H), 7.23-7.25 (m, 2H), 5.91 (d, $J$ = 8.0 Hz, 1H), 4.04-4.11 (m, 1H), 2.05-2.10 (m, 2H), 1.74-1.79 (m, 2H), 1.63-1.67 (m, 1H), 1.40-1.50 (m, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 164.5, 136.4, 127.8, 124.6, 122.9, 121.5, 119.7, 113.1, 112.0, 48.1, 33.5, 25.7, 24.9; HRMS (ESI): Exact mass calcd for C$_{15}$H$_{19}$N$_2$O [M+H]$^+$ 243.1492, Found 243.1493.

**N-(2, 6-dimethylphenyl)-1H-indole-3-carboxamide (3x)**

$\text{HN}$  
$\text{O}$  
$\text{N}$  
$\text{CH}_2$

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 11.66 (br, 1H), 9.20 (br, 1H), 8.24 (d, $J$ = 2.4 Hz, 1H), 8.16 (d, $J$ = 8.0 Hz, 1H), 7.47 (d, $J$ = 8.0 Hz, 1H), 7.11-7.20 (m, 5H), 2.22 (s, 6H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 163.1, 136.2, 135.9, 135.7, 128.2, 128.1, 127.6, 127.6, 126.3, 126.2, 122.0, 121.1, 121.0, 120.4, 111.8, 110.3, 18.2; HRMS (ESI): Exact mass calcd for C$_{17}$H$_{16}$N$_2$O [M+Na]$^+$ 287.1155, Found 287.1154.

**N- (1-Ad)-1H-indole-3-carboxamide (3y)**
$^1$H NMR (400 MHz, CDCl$_3$) δ 9.82 (br, 1H), 7.84-7.87 (m, 1H), 7.62 (d, $J = 4.0$ Hz, 1H), 7.40-7.44 (m, 1H), 7.19-7.24 (m, 2H), 5.81 (br, 1H), 2.20-2.21 (m, 6H), 2.14 (s, 3H), 1.75-1.78 (m, 6H); $^{13}$C NMR (125 MHz, CDCl$_3$) δ 165.1, 136.6, 128.3, 124.4, 122.5, 121.3, 119.3, 113.2, 112.3, 50.2, 42.2, 36.5, 29.6; HRMS (ESI): Exact mass calcd for C$_{19}$H$_{22}$N$_2$ONa [$M+Na]^+$ 317.1624, Found 317.1623.

**N-tert-butyl-3-methyl-1H-indole-2-carboxamide (3z)**

$^1$H NMR (400 MHz, CDCl$_3$) δ 9.45 (br, 1H), 7.61 (d, $J = 8.0$ Hz, 1H), 7.40 (d, $J = 8.0$ Hz, 1H), 7.25-7.29 (m, 1H), 7.11-7.15 (m, 1H), 5.95 (br, 1H), 2.55 (s, 3H), 1.54 (s, 9H); $^{13}$C NMR (125 MHz, CDCl$_3$) δ 162.0, 135.0, 128.7, 128.4, 124.3, 119.8, 119.6, 111.7, 110.5, 51.7, 29.1, 10.2; HRMS (ESI): Exact mass calcd for C$_{14}$H$_{18}$N$_2$ONa [$M+Na]^+$ 253.1311, Found 253.1312.

**N-tert-butyl-2-methyl-1H-indole-3-carboxamide (3aa)**

$^1$H NMR (400 MHz, DMSO-d$_6$) δ 11.32 (br, 1H), 7.66-7.68 (m, 1H), 7.29-7.32 (m, 1H), 7.02-7.08 (m, 2H), 6.78 (s, 1H), 2.55 (s, 3H), 1.41 (s, 9H); $^{13}$C NMR (125 MHz, DMSO-d$_6$) δ 165.2, 138.5, 134.5, 126.3, 120.8, 119.7, 110.8, 109.1, 50.3, 28.9, 13.1; HRMS (ESI): Exact mass calcd for C$_{14}$H$_{19}$N$_2$O [$M+H]^+$ 231.1492, Found 231.1493.

**N-tert-butyl-2-phenyl-1H-indole-3-carboxamide (3ab)**

$^1$H NMR (400 MHz, CDCl$_3$) δ 8.64 (br, 1H), 8.12-8.14 (m, 1H), 7.59-7.61 (m, 1H), 7.42-7.47 (m, 3H), 7.18-7.24 (m, 2H), 5.38 (br, 1H), 1.28 (s, 9H); $^{13}$C NMR (125 MHz, CDCl$_3$) δ 164.8, 137.9, 135.3, 121.7, 129.3, 128.9, 127.8, 123.1, 121.5, 121.4, 110.8, 51.0, 28.8; HRMS (ESI): Exact mass
calcd for C_{19}H_{20}N_{2}O_{2}Na [M\text{+Na}]^{+} 315.1468, Found 315.1466.

\textit{N-acetyl-N-tert-butyl-1-methyl-1H-indole-3-carboxamide (4a)}

\begin{tikzpicture}
  \node at (0,0) {\textbf{N}};
  \node at (1,0) {O};
  \node at (2,0) {O};
  \node at (1,-1) {N};
  \node at (1,-2) {\textbf{N}};
  \node at (2,-2) {\textbf{N}};
\end{tikzpicture}

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.29-8.31 (m, 1H), 7.86 (s, 1H), 7.36-7.41 (m, 3H), 3.89 (s, 3H), 1.99 (s, 3H), 1.54 (s, 9H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 170.5, 169.0, 138.0, 137.9, 126.5, 124.1, 123.3, 122.0, 115.2, 110.2, 57.7, 33.8, 25.5, 25.3; HRMS (ESI): Exact mass calcd for C$_{16}$H$_{20}$N$_{2}$O$_{2}$Na [M\text{+Na}]^{+} 295.1417, Found 295.1420.

\textit{N-acetyl-N-tert-butyl-1H-indole-3-carboxamide (4b)}

\begin{tikzpicture}
  \node at (0,0) {\textbf{N}};
  \node at (1,0) {O};
  \node at (2,0) {O};
  \node at (1,-1) {N};
  \node at (1,-2) {H};
\end{tikzpicture}

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 10.81 (br, 1H), 8.31-8.33 (m, 1H), 7.87 (d, $J = 3.2$ Hz, 1H), 7.52-7.55 (m, 1H), 7.34-7.39 (m, 2H), 2.07 (s, 3H), 1.59 (s, 9H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 170.6, 169.7, 137.3, 134.8, 125.8, 124.4, 123.2, 121.6, 116.1, 112.3, 58.0, 25.5, 25.3; HRMS (ESI): Exact mass calcd for C$_{15}$H$_{18}$N$_{2}$O$_{2}$Na [M\text{+Na}]^{+} 281.1260, Found 281.1261.

\textit{N-acetyl-N-tert-butyl-5-methyl-1H-indole-3-carboxamide (4c)}

\begin{tikzpicture}
  \node at (0,0) {\textbf{N}};
  \node at (1,0) {O};
  \node at (2,0) {O};
  \node at (0,-1) {H};
\end{tikzpicture}

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 10.26 (br, 1H), 8.13 (s, 1H), 7.78 (d, $J = 3.2$ Hz, 1H), 7.39 (d, $J = 8.0$ Hz, 1H), 2.50 (s, 3H), 2.04 (s, 3H), 1.57 (s, 9H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 170.6, 169.6, 135.4, 134.6, 133.1, 126.0, 126.0, 121.4, 111.8, 57.9, 28.5, 25.3, 21.6; HRMS (ESI): Exact mass calcd for C$_{16}$H$_{20}$N$_{2}$O$_{2}$Na [M\text{+Na}]^{+} 295.1417, Found 295.1413.

\textit{N-acetyl-N-tert-butyl-5-methoxy-1H-indole-3-carboxamide (4d)}

\begin{tikzpicture}
  \node at (0,0) {\textbf{O}};
  \node at (1,0) {\textbf{O}};
  \node at (0,-1) {H};
\end{tikzpicture}
$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 10.39 (br, 1H), 7.77-7.79 (m, 2H), 7.79 (d, $J = 8.8$ Hz, 1H), 6.98 (dd, $J = 8.8$, 2.4 Hz, 1H), 3.90 (s, 3H), 2.04 (s, 3H), 1.57 (s, 9H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 170.6, 169.6, 156.8, 134.6, 131.9, 126.7, 116.0, 114.9, 113.1, 120.9, 57.9, 55.7, 28.4, 25.3; HRMS (ESI): Exact mass calcd for C$_{16}$H$_{20}$N$_2$O$_3$Na $[M+Na]^+$ 311.1366, Found 311.1369.

$N$-acetyl-$N$-tert-butyl-2-methyl-$1H$-indole-3-carboxamide (4aa)

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 12.31 (br, 1H), 7.83-7.85 (m, 1H), 7.42-7.44 (m, 1H), 7.18-7.23(m, 2H), 2.69 (s, 3H), 1.81 (s, 3H), 1.43 (s, 9H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 170.9, 169.4, 135.8, 133.8, 127.6, 125.6, 123.6, 123.2, 119.5, 117.1, 57.9, 28.5, 25.4, 23.9, 10.0; HRMS (ESI): Exact mass calcd for C$_{16}$H$_{20}$N$_2$O$_2$Na $[M+Na]^+$ 295.1417, Found 295.1418.

$N$-acetyl-$N$-(2, 6-dimethylphenyl)-$1H$-indole-3-carboxamide (4x)

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.62 (br, 1H), 8.42 (d, $J = 8.0$ Hz, 1H), 7.19-7.31(m, 4H), 7.11 (d, $J = 7.6$ Hz, 2H), 6.25 (d, $J = 3.2$ Hz, 1H), 2.68 (s, 3H), 2.17 (s, 6H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 174.2, 166.5, 138.4, 136.8, 135.3, 130.0, 129.0, 128.8, 127.6, 123.6, 122.5, 122.2, 111.4, 110.5, 26.6, 18.2; HRMS (ESI): Exact mass calcd for C$_{19}$H$_{18}$N$_2$O$_2$ $[M+Na]^+$ 329.1260, Found 329.1260.

IV. X-ray Structures of 4a and 3a

4a: The deposition number at the Cambridge Crystallographic Data Centre is CCDC 858032.
3a: The deposition number at the Cambridge Crystallographic Data Centre is CCDC 862590.

V. References


VI. Copies of $^1$H NMR and $^{13}$C NMR Spectra
3a
015112

--- Bruker Spectrometer Output ---

**Spectrum: 3b**

- **1H NMR**
  - **Solvent**: DMSO-d6
  - **Temperature**: 298 K
  - **Field Strength**: 500 MHz
  - **Chemical Shifts**:
    - 0.80 ppm (9H, s)
    - 1.30 ppm (3H, t)
    - 1.30 ppm (3H, m)
    - 2.00 ppm (2H, q)
    - 2.40 ppm (2H, t)
    - 3.50 ppm (2H, q)
    - 4.00 ppm (1H, q)
    - 7.00 ppm (3H, m)

--- Additional Data ---

**Elemental Analysis**

- **Calculated**
  - C: 70.82%
  - H: 6.17%
  - N: 13.51%

- **Found**
  - C: 70.42%
  - H: 6.10%
  - N: 13.47%

--- References ---

This spectrum was generated using Bruker NMR equipment and processed with Bruker Topspin software.