Copper-catalyzed [4+1]-annulation of 2-alkenylnidoles with diazoacetates: a facile access to dihydrocyclopenta[b]indoles

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General Information

All reactions were performed in 10 ml oven-dried glassware under atmosphere of argon. Solvents were dried and distilled by following the standard methods before using. Analytical thin-layer chromatography was performed using glass plates pre-coated with 200-300 mesh silica gel impregnated with a fluorescent indicator (254 nm). Flash column chromatography was performed using silica gel (300-400 mesh). $^1$H NMR and $^{13}$C NMR spectra were recorded in CDCl$_3$ on a 400 MHz spectrometer; chemical shifts are reported in ppm with the solvent signals as reference and coupling constants ($J$) are given in Hertz. The peak information is described as: br = broad, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, comp = composite. Enantioselectivity was determined on HPLC using Chiralpak IC-3. High-resolution mass spectra (HRMS) were recorded on a commercial apparatus (ESI Source) and (CI Source). Starting materials 1$^1$ and 2$^2$ were prepared according to the reported reference.

Condition Optimization

The initial exploration was carried out with 2-alkenyindole 1a and methyl phenyldiazoacetate 2a as model substrates in dichloromethane (DCM) at 25 °C (Table S1). Instead of giving the annulation product 3a, only decomposition of 2a was observed when the reaction was catalyzed by Rh-, Pd-, or Ag-catalysts (entries 1-4), and most of the material 1a remained intact. The desired product 3a was obtained in moderate to high yields contaminated with C-H insertion product 4a when the copper-catalysts were explored (entries 5-14), and Cu(CH$_3$CN)$_4$PF$_6$ gave the superior results in terms of both the yield and selectivity (entry 12, 85% yield, 3a:4a = 91:9). Control experiment in the presence of Lewis acid, such as Sc(OTf)$_3$, was conducted and no reaction occurred (entry 15). Further optimization of solvents, reaction temperature, and the concentration of reaction mixture showed that only trace amount of 3a was formed when the reaction was conducted in tetrahydrofuran (entry 18) or acetonitrile (entry 19), and the best results were obtained by conducting the reaction...
in DCM at 35 °C, giving 3a as a single product in 86% yield (entry 21).

Table S1  Condition optimization

<table>
<thead>
<tr>
<th>Entry</th>
<th>Cat (x mol %)</th>
<th>Solvent</th>
<th>Yield (3a+4a)</th>
<th>Ratio 3a:4a</th>
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<tr>
<td>1&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Rh&lt;sub&gt;2&lt;/sub&gt;(OAc)&lt;sub&gt;4&lt;/sub&gt; (1.0)</td>
<td>DCM</td>
<td>-</td>
<td>-</td>
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<tr>
<td>2&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Rh&lt;sub&gt;2&lt;/sub&gt;(esp)&lt;sub&gt;2&lt;/sub&gt; (1.0)</td>
<td>DCM</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>3&lt;sup&gt;a&lt;/sup&gt;</td>
<td>[PdCl(η&lt;sup&gt;3&lt;/sup&gt;-C&lt;sub&gt;8&lt;/sub&gt;H&lt;sub&gt;8&lt;/sub&gt;)]&lt;sub&gt;2&lt;/sub&gt; (5.0)</td>
<td>DCM</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>4&lt;sup&gt;a&lt;/sup&gt;</td>
<td>AgOTf (5.0)</td>
<td>DCM</td>
<td>-</td>
<td>-</td>
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<td>5</td>
<td>Cu(OTf)&lt;sub&gt;2&lt;/sub&gt; (5.0)</td>
<td>DCM</td>
<td>61</td>
<td>83:17</td>
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<td>6</td>
<td>Cu(hfacac)&lt;sub&gt;2&lt;/sub&gt; (5.0)</td>
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<td>48</td>
<td>67:33</td>
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<td>7</td>
<td>CuBr&lt;sub&gt;2&lt;/sub&gt; (5.0)</td>
<td>DCM</td>
<td>37</td>
<td>71:29</td>
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<td>8</td>
<td>Cu(CH&lt;sub&gt;3&lt;/sub&gt;CN)&lt;sub&gt;2&lt;/sub&gt;BF&lt;sub&gt;4&lt;/sub&gt; (5.0)</td>
<td>DCM</td>
<td>78</td>
<td>85:15</td>
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<td>61</td>
<td>54:46</td>
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<td>CuTC (5.0)</td>
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<td>55</td>
<td>73:27</td>
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<td>Cu(CH&lt;sub&gt;3&lt;/sub&gt;CN)&lt;sub&gt;2&lt;/sub&gt;PF&lt;sub&gt;6&lt;/sub&gt; (5.0)</td>
<td>DCM</td>
<td>85</td>
<td>91:9</td>
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<td>13</td>
<td>[CuOTf]&lt;sub&gt;2&lt;/sub&gt;, benzene (5.0)</td>
<td>DCM</td>
<td>60</td>
<td>63:37</td>
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<td>14</td>
<td>Cu(acac)&lt;sub&gt;2&lt;/sub&gt; (5.0)</td>
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<td>49</td>
<td>77:23</td>
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<td>15</td>
<td>Sc(OTf)&lt;sub&gt;3&lt;/sub&gt; (5.0)</td>
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<td>NR</td>
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<td>Cu(CH&lt;sub&gt;3&lt;/sub&gt;CN)&lt;sub&gt;2&lt;/sub&gt;PF&lt;sub&gt;6&lt;/sub&gt; (5.0)</td>
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<td>81:13</td>
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<td>84</td>
<td>71:29</td>
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<td>18&lt;sup&gt;a&lt;/sup&gt;</td>
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<td>THF</td>
<td>&lt;5</td>
<td>-</td>
</tr>
<tr>
<td>19&lt;sup&gt;a&lt;/sup&gt;</td>
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<td>CH&lt;sub&gt;3&lt;/sub&gt;CN</td>
<td>&lt;5</td>
<td>-</td>
</tr>
<tr>
<td>20</td>
<td>Cu(CH&lt;sub&gt;3&lt;/sub&gt;CN)&lt;sub&gt;2&lt;/sub&gt;PF&lt;sub&gt;6&lt;/sub&gt; (5.0)</td>
<td>TBME</td>
<td>43</td>
<td>55:45</td>
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<tr>
<td>21&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Cu(CH&lt;sub&gt;3&lt;/sub&gt;CN)&lt;sub&gt;2&lt;/sub&gt;PF&lt;sub&gt;6&lt;/sub&gt; (5.0)</td>
<td>DCM</td>
<td>86</td>
<td>&gt;95:5</td>
</tr>
</tbody>
</table>

<sup>a</sup> Reaction conditions: to the catalyst and 1a (30.0 mg, 0.1 mmol) in 1.0 mL of solvent, was added 2a (35.0 mg, 0.2 mmol) in 1.0 mL of the same solvent via syringe pump over 2 h under argon atmosphere at 25 °C. <sup>b</sup> Isolated yields. <sup>c</sup> The ratio was determined by proton NMR of the crude reaction mixture. <sup>d</sup> Most of material 1a was recovered and 2a was decomposed. <sup>e</sup> The reaction was carried out at 35 °C in 3.0 mL DCM. CuTC = Copper(I) thiophene-2-carboxylate.
General Procedure for the Preparation of 2-Alkenylindoles 1

2-Alkenylindoles 1 were prepared according to the reported reference.¹

![Structure of Diethyl 2-[(1-methyl-1H-indol-2-yl)methylene]malonate (1a)](image)

Diethyl 2-[(1-methyl-1H-indol-2-yl)methylene]malonate (1a)

¹H NMR (400 MHz, CDCl₃) (δ, ppm) 7.82 (s, 1H), 7.61 (d, J = 8.0 Hz, 1H), 7.32 – 7.27 (m, 2H), 7.14 – 7.10 (m, 1H), 6.96 (s, 1H), 4.43 (q, J = 7.1 Hz, 2H), 4.34 (q, J = 7.1 Hz, 2H), 3.80 (s, 3H), 1.36 (comp, 6H); ¹³C NMR (100 MHz, CDCl₃) (δ, ppm) 166.8, 164.2, 138.8, 131.9, 129.4, 127.6, 124.8, 124.4, 121.9, 120.6, 109.8, 106.5, 61.9, 61.7, 29.9, 14.3, 14.0; HRMS (TOF MS ESI⁺) calculated for C₁₇H₁₉NNaO₄ [M + Na]⁺, 324.1206; found, 324.1201.

![Structure of Diethyl 2-((4-chloro-1-methyl-1H-indol-2-yl)methylene)malonate (1n)](image)

Diethyl 2-((4-chloro-1-methyl-1H-indol-2-yl)methylene)malonate (1n)

¹H NMR (400 MHz, CDCl₃) (δ, ppm) δ 7.76 (s, 1H), 7.22 – 7.13 (m, 2H), 7.12 – 7.07 (m, 1H), 6.98 (s, 1H), 4.44 (q, J = 7.1 Hz, 2H), 4.33 (q, J = 7.1 Hz, 2H), 3.79 (s, 3H), 1.37 (dt, J = 16.7, 7.1 Hz, 6H); ¹³C NMR (100 MHz, CDCl₃) (δ, ppm) δ 166.5, 164.0, 139.3, 132.5, 128.7, 127.1, 126.6, 126.1, 124.7, 120.3, 108.5, 104.7, 62.2, 61.9, 30.4, 14.3, 14.1; HRMS (TOF MS ESI⁺) calculated for C₁₇H₁₉ClNNaO₄ [M + Na]⁺, 358.0817; found, 358.0825.
**Diethyl 2-[(5-chloro-1-methyl-1H-indol-2-yl)methylene]malonate (1o)**

$^1$H NMR (400 MHz, CDCl$_3$) (δ, ppm) δ 7.75 (s, 1H), 7.54 (t, J = 1.2 Hz, 1H), 7.20 (d, J = 1.2 Hz, 2H), 6.83 (s, 1H), 4.41 (q, J = 7.1 Hz, 2H), 4.32 (q, J = 7.1 Hz, 2H), 3.77 (s, 3H), 1.34 (td, J = 7.1, 1.8 Hz, 6H); $^{13}$C NMR (100 MHz, CDCl$_3$) (δ, ppm) δ 166.6, 164.0, 137.1, 133.1, 128.9, 128.4, 126.3, 125.9, 124.7, 121.0, 110.9, 105.6, 62.1, 61.9, 30.2, 14.3, 14.1; HRMS (TOF MS ESI$^+$) calculated for C$_{17}$H$_{18}$ClINaO$_4$ [M + Na]$^+$, 358.0817; found, 358.0813.

**Diethyl 2-[(6-chloro-1-methyl-1H-indol-2-yl)methylene]malonate (1p)**

$^1$H NMR (400 MHz, CDCl$_3$) (δ, ppm) δ 7.74 (s, 1H), 7.48 (s, 1H), 7.28 (d, J = 8.5 Hz, 1H), 7.28 (d, J = 0.7 Hz, 1H), 7.08 – 7.03 (m, 1H), 6.89 (s, 1H), 4.41 (q, J = 7.1 Hz, 2H), 4.32 (q, J = 7.1 Hz, 2H), 3.74 (s, 3H), 1.34 (td, J = 7.1, 2.8 Hz, 6H); $^{13}$C NMR (100 MHz, CDCl$_3$) (δ, ppm) δ 166.7, 164.0, 139.1, 132.7, 130.4, 128.8, 126.1, 125.4, 122.8, 121.5, 109.8, 106.4, 62.0, 61.8, 30.0, 14.2, 14.1; HRMS (TOF MS ESI$^+$) calculated for C$_{17}$H$_{18}$ClINaO$_4$ [M + Na]$^+$, 358.0817; found, 358.0809.

**Diethyl 2-[(1-benzyl-1H-indol-2-yl)methylene]malonate (1q)**

$^1$H NMR (400 MHz, CDCl$_3$) (δ, ppm) δ 7.78 (s, 1H), 7.69 – 7.64 (m, 1H), 7.33 – 7.23 (comp, 5H), 7.18 – 7.12 (m, 1H), 7.08 – 7.01 (comp, 3H), 5.45 (s, 2H), 4.44 (q, J = 7.1 Hz, 2H), 4.29 (q, J = 7.1 Hz, 2H), 1.37 (t, J = 7.1 Hz, 3H), 1.32 (t, J = 7.1 Hz, 3H);
$^{13}$C NMR (100 MHz, CDCl$_3$) (δ, ppm) δ 166.6, 164.0, 138.6, 137.1, 131.9, 129.5, 129.0, 127.84, 127.77, 126.2, 125.3, 124.7, 122.0, 120.9, 110.2, 107.0, 61.9, 61.6, 46.9, 14.2, 14.0; HRMS (TOF MS ESI$^+$) calculated for C$_{23}$H$_{23}$NNaO$_4$ [M + Na$^+$], 400.1519; found, 400.1528.

Diethyl 2-[(1-allyl-1H-indol-2-yl)methylene]malonate (1r)

$^1$H NMR (400 MHz, CDCl$_3$) (δ, ppm) δ 7.75 (s, 1H), 7.62 (d, $J$ = 8.0 Hz, 1H), 7.30 – 7.25 (m, 2H), 7.15 – 7.09 (m, 1H), 6.98 (s, 1H), 6.02 – 5.90 (m, 1H), 5.17 (dd, $J$ = 10.4, 0.7 Hz, 1H), 4.90 (dd, $J$ = 17.1, 0.6 Hz, 1H), 4.85 – 4.79 (m, 1H), 4.17 (dd, $J$ = 10.4, 0.7 Hz, 1H), 4.32 (q, $J$ = 7.1 Hz, 2H), 1.35 (td, $J$ = 7.1, 4.0 Hz, 6H); $^{13}$C NMR (100 MHz, CDCl$_3$) (δ, ppm) δ 166.8, 164.1, 138.3, 132.8, 131.7, 129.5, 127.8, 125.1, 124.5, 122.0, 120.8, 117.1, 110.0, 106.8, 62.0, 61.7, 45.5, 14.3, 14.1; HRMS (TOF MS ESI$^+$) calculated for C$_{19}$H$_{21}$NNaO$_4$ [M + Na$^+$], 350.1363; found, 350.1347.

3-[(1-Methyl-1H-indol-2-yl)methylene]pentane-2,4-dione (1s)

$^1$H NMR (400 MHz, CDCl$_3$) (δ, ppm) δ 7.60 – 7.55 (comp, 2H), 7.31 – 7.30 (m, 2H), 7.14 – 7.11 (m, 1H), 6.79 (s, 1H), 3.81 (s, 3H), 2.41 (s, 3H), 2.40 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) (δ, ppm) δ 205.8, 195.0, 141.1, 139.2, 131.6, 127.6, 126.7, 124.8, 122.0, 120.9, 109.8, 107.9, 77.5, 77.2, 76.8, 62.0, 61.7, 45.5, 14.3, 14.1; HRMS (TOF MS ESI$^+$) calculated for C$_{15}$H$_{15}$NNaO$_2$ [M + Na$^+$], 264.0995; found, 264.1007.
Diethyl 2-{{1-(tert-butoxycarbonyl)-1H-indol-2-yl}methylene}malonate (1t)

$^1$H NMR (400 MHz, CDCl$_3$) (δ, ppm) δ 8.26 – 8.16 (comp, 2H), 7.56 (d, $J = 7.7$ Hz, 1H), 7.43 – 7.35 (m, 1H), 7.29 – 7.22 (m, 1H), 6.96 (s, 1H), 4.33 (qd, $J = 7.1$, 5.8 Hz, 4H), 1.71 (s, 9H), 1.36 (t, $J = 7.1$ Hz, 3H), 7.43 – 7.35 (m, 1H), 7.29 – 7.22 (m, 1H), 6.96  (s, 1H), 4.33 (qd, $J = 7.1$, 5.8 Hz, 4H), 1.71 (s, 9H), 1.36 (t, $J = 7.1$ Hz, 3H), 1.28 (t, $J = 7.1$ Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) (δ, ppm) δ 166.5, 163.9, 150.0, 137.4, 134.1, 132.9, 128.8, 126.2, 125.7, 123.5, 121.6, 115.8, 113.1, 85.2, 61.8, 61.7, 28.3, 14.3, 14.0; HRMS (TOF MS ESI$^+$) calculated for C$_{21}$H$_{25}$NO$_6$ [M + Na]$^+$, 387.1682; found, 387.1689.

Ethyl (Z)-2-{{1-methyl-1H-indol-2-yl}methylene}-3-oxobutanoate (Z-1u)

$^1$H NMR (400 MHz, CDCl$_3$) (δ, ppm) δ 7.74 (s, 1H), 7.48 (d, $J = 8.5$ Hz, 1H), 7.28 (d, $J = 0.7$ Hz, 1H), 7.08 – 7.03 (m, 1H), 6.89 (s, 1H), 4.41 (q, $J = 7.1$ Hz, 2H), 4.32 (q, $J = 7.1$ Hz, 2H), 3.83 (s, 3H), 2.46 (s, 3H), 1.35 (td, $J = 7.1$, 0.5 Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) (δ, ppm) δ 166.7, 164.0, 139.1, 132.7, 130.4, 128.8, 126.1, 125.4, 122.8, 121.5, 109.8, 106.4, 62.0, 61.8, 30.0, 14.2, 14.1; HRMS (TOF MS ESI$^+$) calculated for C$_{16}$H$_{17}$NNaO$_3$ [M + Na]$^+$, 294.1101; found, 294.1092.

Ethyl (E)-2-{{1-methyl-1H-indol-2-yl}methylene}-3-oxobutanoate (E-1u)

$^1$H NMR (400 MHz, CDCl$_3$) (δ, ppm) δ 7.67 (s, 1H), 7.60 (d, $J = 8.0$ Hz, 1H), 7.32 – 7.27 (m, 2H), 7.15 – 7.08 (m, 1H), 6.96 (s, 1H), 4.44 (q, $J = 7.1$ Hz, 2H), 3.78 (s, 3H), 2.41 (s, 3H), 1.37 (t, $J = 7.2$ Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) (δ, ppm) δ 193.4,
168.3, 139.1, 132.4, 128.2, 127.6, 124.7, 122.0, 120.7, 109.8, 107.0, 62.0, 29.8, 26.9, 14.0; HRMS (TOF MS ESI\(^+\)) calculated for C\(_{16}\)H\(_{17}\)NNaO\(_3\) [M + Na]\(^+\), 294.1101; found, 294.1110.

**General Procedure for [4 + 1]-Annulation Reaction**

To a 10-mL oven-dried vial containing a magnetic stirring bar, Cu(CH\(_3\)CN)\(_4\)PF\(_6\) (1.9 mg, 5.0 mol %), compound 1 (0.1 mmol) in DCM (2.0 mL), diazo compound 1 (0.2 mmol) in DCM (1.0 mL) was added as a solution via a syringe pump over 2 h under argon atmosphere at 35 °C. After addition, the reaction mixture was stirred overnight under these conditions until consumption of the material (monitored by TLC). Then the reaction mixture was purified by column chromatography on silica gel without any additional treatment (Hexanes : EtOAc = 15:1 to 10:1) to give the pure products 3.

![2,2-Diethyl 1-methyl 4-methyl-1-phenyl-3,4-dihydrocyclopenta[b]indole-1,2,2 (1H)-tricarboxylate (3a)](image)

2,2-Diethyl 1-methyl 4-methyl-1-phenyl-3,4-dihydrocyclopenta[b]indole-1,2,2 (1H)-tricarboxylate (3a)

White solid, 38.6 mg, 86% yield, mp: 134.5-135.9 °C; \(^1\)H NMR (400 MHz, CDCl\(_3\)) (δ, ppm) δ 7.66 (d, \(J = 3.4\) Hz, 2H), 7.30 (t, \(J = 6.9\) Hz, 4H), 7.20 – 7.12 (m, 2H), 7.02 (t, \(J = 7.5\) Hz, 1H), 4.40 – 4.28 (m, 2H), 3.82 (d, \(J = 15.5\) Hz, 1H), 3.78 (s, 3H), 3.65 (d, \(J = 15.5\) Hz, 1H), 3.62 – 3.56 (m, 1H), 3.55 (s, 3H), 3.32 – 3.18 (m, 1H), 1.37 (t, \(J = 7.1\) Hz, 3H), 0.73 (t, \(J = 7.1\) Hz, 3H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) (δ, ppm) δ 173.4, 170.4, 169.6, 145.6, 141.4, 136.7, 130.8, 127.7, 127.3, 123.7, 120.9, 119.9, 119.2, 114.6, 109.8, 74.1, 66.2, 61.8, 61.7, 52.3, 34.3, 31.1, 14.2, 13.4; HRMS (TOF MS ESI\(^+\)) calculated for C\(_{26}\)H\(_{27}\)NNaO\(_6\) [M + Na]\(^+\), 472.1731; found, 472.1743.
2,2-Diethyl 1-methyl 4-methyl-1-(p-tolyl)-3,4-dihydrocyclopenta[b]indole-1,2,2(1H)-tricarboxylate (3b)

White solid, 41.7 mg, 90% yield, mp: 111.2-113.0 °C; ¹H NMR (400 MHz, CDCl₃) (δ, ppm) δ 7.53 (d, J = 8.0 Hz, 2H), 7.32 – 7.27 (m, 1H), 7.19 – 7.13 (m, 2H), 7.09 (d, J = 8.0 Hz, 2H), 7.04 – 6.97 (m, 1H), 4.40 – 4.26 (m, 2H), 3.80 (d, J = 15.5 Hz, 1H), 3.77 (s, 3H), 3.63 (d, J = 15.5 Hz, 1H), 3.61 – 3.56 (m, 1H), 3.54 (s, 3H), 3.38 – 3.24 (m, 1H), 2.34 (s, 3H), 1.36 (t, J = 7.1 Hz, 3H), 0.74 (t, J = 7.1 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) (δ, ppm) δ 173.5, 170.4, 169.7, 145.6, 141.4, 137.3, 133.7, 130.7, 128.0, 123.8, 120.8, 119.8, 119.2, 114.8, 109.8, 74.2, 67.0, 61.8, 61.6, 52.3, 34.3, 31.1, 21.2, 14.2, 13.3; HRMS (TOF MS ESI⁺) calculated for C₂₇H₂₉NNaO₆ [M + Na]⁺, 486.1887; found, 486.1893.

2,2-Diethyl 1-methyl 1-(4-methoxyphenyl)-4-methyl-3,4-dihydrocyclopenta[b]indole-1,2,2(1H)-tricarboxylate (3c)

White solid, 35.0 mg, 73% yield, mp: 159.2-161.3 °C; ¹H NMR (400 MHz, CDCl₃) (δ, ppm) δ 7.56 (d, J = 8.3 Hz, 2H), 7.29 (d, J = 8.5 Hz, 1H), 7.20 – 7.11 (m, 2H), 7.01 (t, J = 7.5 Hz, 1H), 6.81 (d, J = 8.6 Hz, 2H), 4.38 – 4.26 (m, 2H), 3.84 – 3.77 (comp, 4H), 3.77 (s, 3H), 3.65 – 3.57 (m, 2H), 3.53 (s, 3H), 3.39 – 3.28 (m, 1H), 1.36 (t, J = 7.1 Hz, 3H), 0.77 (t, J = 7.1 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) (δ, ppm) δ 173.6, 170.5, 169.8, 159.2, 145.5, 141.4, 132.1, 128.8, 123.8, 120.8, 119.9, 119.2, 114.9,
112.6, 109.8, 74.2, 65.7, 61.8, 61.7, 55.4, 52.4, 34.3, 31.1, 14.2, 13.5; HRMS (TOF MS ESI\(^+\)) calculated for C\(_{27}\)H\(_{29}\)NNaO\(_7\) [M + Na]\(^+\), 502.1836; found, 502.1831.

\[ \text{2,2-Diethyl 1-methyl 1-(4-fluorophenyl)-4-methyl-3,4-dihydrocyclopenta[b] indole-1,2,2(1H)-tricarboxylate (3d)} \]

White solid, 40.2 mg, 86% yield, mp: 116.2-117.5 °C; \(^1\)H NMR (400 MHz, CDCl\(_3\)) (\(\delta\), ppm) \(\delta\) 7.70 – 7.60 (m, 2H), 7.31 (d, \(J = 8.2\) Hz, 1H), 7.21 – 7.15 (m, 1H), 7.13 (d, \(J = 7.8\) Hz, 1H), 7.07 – 6.93 (m, 3H), 4.40 – 4.25 (m, 2H), 3.81 (d, \(J = 15.5\) Hz, 1H), 3.77 (s, 3H), 3.67 – 3.58 (m, 2H), 3.54 (s, 3H), 3.40 – 3.25 (m, 1H), 1.36 (t, \(J = 7.1\) Hz, 3H), 0.79 (t, \(J = 7.1\) Hz, 3H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) (\(\delta\), ppm) \(\delta\) 173.2, 170.3, 169.6, 162.5 (d, \(J = 246.5\) Hz), 145.6, 141.4, 132.8 (d, \(J = 8.0\) Hz), 132.5 (d, \(J = 3.2\) Hz), 123.5, 121.0, 120.0, 119.0, 114.5, 114.1 (d, \(J = 21.1\) Hz), 110.0, 74.1, 65.5, 61.9, 61.8, 52.4, 34.3, 31.1, 14.2, 13.5; \(^{19}\)F NMR (376 MHz, CDCl\(_3\)) (\(\delta\), ppm) \(\delta\) -115.2; HRMS (TOF MS ESI\(^+\)) calculated for C\(_{26}\)H\(_{26}\)FNNaO\(_6\) [M + Na]\(^+\), 490.1636; found, 490.1641.

\[ \text{2,2-Diethyl 1-methyl 1-(4-chlorophenyl)-4-methyl-3,4-dihydrocyclopenta[b] indole-1,2,2(1H)-tricarboxylate (3e)} \]

White solid, 39.2 mg, 81% yield, mp: 171.6-172.9 °C; \(^1\)H NMR (400 MHz, CDCl\(_3\)) (\(\delta\), ppm) \(\delta\) 7.61 (d, \(J = 8.2\) Hz, 2H), 7.31 (d, \(J = 8.2\) Hz, 1H), 7.28 – 7.25 (m, 2H), 7.21 –
7.15 (m, 1H), 7.11 (d, \(J = 7.8\) Hz, 1H), 7.02 (t, \(J = 7.2\) Hz, 1H), 4.39 – 4.26 (m, 2H), 3.80 (d, \(J = 15.6\) Hz, 1H), 3.77 (s, 3H), 3.67 – 3.58 (m, 2H), 3.54 (s, 3H), 3.40 – 3.30 (m, 1H), 1.36 (t, \(J = 7.1\) Hz, 3H), 0.78 (t, \(J = 7.1\) Hz, 3H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) (\(\delta, \text{ppm}\)) \(\delta 173.0, 170.2, 169.5, 145.7, 141.4, 135.4, 133.7, 132.4, 127.4, 123.5, 121.0, 120.1, 119.0, 114.2, 109.9, 77.5, 77.2, 76.8, 74.1, 65.6, 62.0, 61.8, 52.4, 34.3, 31.2, 14.2, 13.4; HRMS (TOF MS ESI\(^+\)) calculated for C\(_{26}\)H\(_{26}\)ClNNaO\(_6\) [M + Na]\(^+\), 506.1341; found, 506.1333.

![Chemical Structure](image)

2,2-Diethyl 1-methyl 4-methyl-1-(4-(trifluoromethyl)phenyl)-3,4-dihydrocyclopenta[b]indole-1,2,2(1\(H\))-tricarboxylate (3f)

Yellow oil, 41.4 mg, 80% yield, \(^1\)H NMR (400 MHz, CDCl\(_3\)) (\(\delta, \text{ppm}\)) \(\delta 7.84 (d, \(J = 7.9\) Hz, 2H), 7.58 (d, \(J = 8.3\) Hz, 2H), 7.35 (d, \(J = 8.3\) Hz, 1H), 7.24 – 7.19 (m, 1H), 7.14 – 7.02 (m, 2H), 4.41 – 4.29 (m, 2H), 3.85 (d, \(J = 15.5\) Hz, 1H), 3.81 (s, 3H), 3.68 (d, \(J = 15.5\) Hz, 1H), 3.65 – 3.58 (m, 1H), 3.58 (s, 3H), 3.34 – 3.21 (m, 1H), 1.38 (t, \(J = 7.1\) Hz, 3H), 0.72 (t, \(J = 7.1\) Hz, 3H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) (\(\delta, \text{ppm}\)) \(\delta 172.8, 170.1, 169.4, 145.8, 141.5, 141.0, 131.4, 129.9 (q, \(J = 32.3\) Hz), 124.2 (q, \(J = 241.6\) Hz), 124.2 (q, \(J = 3.7\) Hz), 123.4, 121.1, 120.2, 118.9, 113.9, 110.0, 74.1, 65.8, 62.0, 61.9, 52.5, 34.4, 31.2, 14.2, 13.2; \(^{19}\)F NMR (376 MHz, CDCl\(_3\)) (\(\delta, \text{ppm}\)) \(\delta -62.6;\) HRMS (TOF MS ESI\(^+\)) calculated for C\(_{27}\)H\(_{26}\)F\(_3\)NNaO\(_6\) [M + Na]\(^+\), 540.1604; found, 540.1618.
2,2-Diethyl 1-methyl 1-(4-bromophenyl)-4-methyl-3,4-dihydrocyclopenta[\(b\)] indole-1,2,2(1\(H\))-tricarboxylate (3g)

White solid, 43.9 mg, 83% yield, mp: 199.2-200.3 °C; \(^1\)H NMR (400 MHz, CDCl\(_3\)) (δ, ppm) δ 7.55 (d, \(J = 8.2\) Hz, 2H), 7.41 (d, \(J = 8.7\) Hz, 2H), 7.31 (d, \(J = 8.2\) Hz, 1H), 7.18 (t, \(J = 7.6\) Hz, 1H), 7.11 (d, \(J = 7.8\) Hz, 1H), 7.02 (t, \(J = 7.4\) Hz, 1H), 4.40 – 4.26 (m, 2H), 3.80 (d, \(J = 15.6\) Hz, 1H), 3.77 (s, 3H), 3.67 – 3.58 (m, 2H), 3.54 (s, 3H), 3.41 – 3.30 (m, 1H), 1.35 (t, \(J = 7.1\) Hz, 3H), 0.78 (t, \(J = 7.1\) Hz, 3H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) (δ, ppm) δ 172.9, 170.2, 169.5, 145.7, 141.4, 135.9, 132.8, 130.4, 123.5, 122.1, 121.0, 120.1, 119.0, 114.1, 109.9, 74.0, 65.6, 62.0, 61.8, 52.4, 34.3, 31.2, 14.2, 13.4; HRMS (TOF MS ESI\(^+\)) calculated for C\(_{26}\)H\(_{26}\)BrNNaO\(_6\) [M + Na]\(^+\), 550.0836; found, 550.0829.

2,2-Diethyl 1-methyl 1-(3-fluorophenyl)-4-methyl-3,4-dihydrocyclopenta[\(b\)] indole-1,2,2(1\(H\))-tricarboxylate (3h)

White solid, 37.0 mg, 79% yield, mp: 184.1-185.9 °C; \(^1\)H NMR (400 MHz, CDCl\(_3\)) (δ, ppm) δ 7.54 – 7.36 (m, 2H), 7.31 (d, \(J = 8.2\) Hz, 1H), 7.26 – 7.10 (m, 3H), 7.07 – 6.93 (m, 2H), 4.40 – 4.26 (m, 2H), 3.85 – 3.75 (comp, 4H), 3.68 – 3.59 (m, 2H), 3.54 (s, 3H), 3.39 – 3.27 (m, 1H), 1.37 (t, \(J = 7.1\) Hz, 3H), 0.78 (t, \(J = 7.1\) Hz, 3H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) (δ, ppm) δ 172.9, 169.8, 169.5, 145.7, 141.4, 139.5 (d, \(J = 7.1\) Hz, 3H), 0.78 (d, \(J = 7.1\) Hz, 3H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) (δ, ppm) δ 172.9, 169.8 (d, \(J = 71.5\) Hz), 162.2 (d, \(J = 243.6\) Hz), 145.7, 141.4, 139.5 (d, \(J = 7.5\) Hz), 128.6 (d, \(J = 8.0\) Hz), 126.4, 123.5, 121.0, 120.1,
119.0, 118.3 (d, $J = 23.1$ Hz), 114.8, 114.6, 114.2, 109.9, 74.1, 65.8 (d, $J = 1.8$ Hz), 62.0, 61.9, 52.5, 34.4, 31.2, 14.2, 13.4; $^{19}$F NMR (376 MHz, CDCl$_3$) ($\delta$, ppm) $\delta$ -114.4; HRMS (TOF MS ESI$^+$) calculated for C$_{26}$H$_{26}$FNO$_6$ [M + H]$^+$, 468.1817; found, 468.1797.

2,2-Diethyl 1-methyl 1-(2-fluorophenyl)-4-methyl-3,4-dihydrocyclopenta[b]indole-1,2,2(1H)-tricarboxylate (3i)

White solid, 34.6 mg, 74% yield, mp: 170.4-171.8 °C; $^1$H NMR (400 MHz, CDCl$_3$) ($\delta$, ppm) $\delta$ 7.35 – 7.29 (m, 2H), 7.24 – 7.09 (comp, 3H), 7.05 – 6.93 (comp, 3H), 4.39 – 4.22 (m, 2H), 3.85 – 3.78 (comp, 4H), 3.75 – 3.64 (comp, 2H), 3.59 (s, 3H), 3.41 – 3.30 (m, 1H), 1.33 (td, $J = 7.1$, 0.5 Hz, 3H), 0.81 – 0.68 (m, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) ($\delta$, ppm) $\delta$ 171.6, 169.5 (d, $J = 3.2$ Hz), 161.5 (d, $J = 252.4$ Hz), 145.7, 141.4, 131.8 (d, $J = 3.3$ Hz), 129.9 (d, $J = 8.8$ Hz), 124.9 (d, $J = 12.3$ Hz), 123.5, 123.1 (d, $J = 3.4$ Hz), 120.8, 119.9, 119.0, 116.4, 116.1, 114.0, 109.9, 74.3, 62.8, 61.9, 61.5, 52.4, 33.6, 31.1, 14.0, 13.4; $^{19}$F NMR (376 MHz, CDCl$_3$) ($\delta$, ppm) $\delta$ -104.8; HRMS (TOF MS ESI$^+$) calculated for C$_{26}$H$_{26}$FNNaO$_6$ [M + Na]$^+$, 490.1636; found, 490.1646.

Triethyl 4-methyl-1-phenyl-3,4-dihydrocyclopenta[b]indole-1,2,2(1H)-tricarboxylate (3j)

Yellow oil, 40.8 mg, 88% yield; $^1$H NMR (400 MHz, CDCl$_3$) ($\delta$, ppm) 7.70 – 7.59 (m, 2H), 7.32 – 7.26 (comp, 4H), 7.18 – 7.11 (m, 2H), 7.03 – 6.97 (m, 1H), 4.38 – 4.27 (m,
2H), 4.01 (q, J = 7.1 Hz, 2H), 3.81 (d, J = 15.5 Hz, 1H), 3.77 (s, 3H), 3.64 (d, J = 15.5 Hz, 1H), 3.61 – 3.53 (m, 1H), 3.30 – 3.17 (m, 1H), 1.36 (t, J = 7.1 Hz, 3H), 1.03 (t, J = 7.1 Hz, 3H), 0.72 (t, J = 7.1 Hz, 3H); 13C NMR (100 MHz, CDCl3) (δ, ppm) δ 172.7, 170.4, 169.7, 145.6, 141.4, 136.8, 130.9, 127.6, 127.2, 123.8, 120.8, 119.8, 119.3, 114.8, 109.8, 74.1, 66.3, 61.8, 61.6, 61.3, 34.4, 31.1, 14.2, 14.1, 13.4; HRMS (TOF MS ESI+) calculated for C27H29NNaO6 [M + Na]+, 486.1887; found, 486.1878.

![Structural diagram](image)

2,2-Diethyl 1-[2-(tosyloxy)ethyl] 4-methyl-1-phenyl-3,4-dihydrocyclopenta[b]indole-1,2,2(1H)-tricarboxylate (3k)

White solid, 52.6 mg, 83% yield, mp: 161.3-162.8 °C; 1H NMR (400 MHz, CDCl3) (δ, ppm) 7.69 – 7.62 (m, 2H), 7.59 (d, J = 8.3 Hz, 2H), 7.37 – 7.30 (comp, 4H), 7.26 (s, 2H), 7.21 – 7.15 (m, 1H), 6.99 – 6.92 (m, 2H), 4.40 – 4.31 (m, 2H), 4.17 – 4.09 (m, 1H), 4.05 – 3.98 (m, 1H), 3.95 (t, J = 4.6 Hz, 2H), 3.84 – 3.75 (m, 4H), 3.68 (d, J = 15.6 Hz, 1H), 3.65 – 3.57 (m, 1H), 3.29 – 3.18 (m, 1H), 2.45 (s, 3H), 1.37 (t, J = 7.1 Hz, 3H), 0.75 (t, J = 7.1 Hz, 3H); 13C NMR (100 MHz, CDCl3) (δ, ppm) δ 172.2, 170.2, 169.5, 146.0, 145.0, 141.4, 136.3, 132.6, 130.9, 130.0, 128.0, 127.8, 127.3, 123.5, 120.9, 119.9, 119.0, 114.1, 109.9, 74.2, 67.5, 65.8, 62.2, 61.9, 61.8, 34.3, 31.1, 21.8, 14.2, 13.4; HRMS (TOF MS ESI+) calculated for C34H35NNaO6S [M + Na]+, 656.1925; found, 656.1929.
2,2-Diethyl 1-[(1R, 2R, 5S)-2-Isopropyl-5-methylocyclohexyl] (S)-4-methyl-1-phenyl-3,4-dihydrocyclopenta[b]indole-1,2,2(1H)-tricarboxylate (3l)

White oil, 39.0 mg, 68% yield; \(^1\)H NMR (400 MHz, CDCl\(_3\)) (\(\delta\), ppm) 7.64 (d, \(J = 3.0\) Hz, 2H), 7.27 – 7.30 (comp, 3H), 7.22 – 7.26 (m, 1H), 7.14 – 7.07 (m, 2H), 7.00 – 6.93 (m, 1H), 4.58 – 4.51 (m, 1H), 4.36 – 4.26 (m, 2H), 3.81 (d, \(J = 15.4\) Hz, 1H), 3.76 (s, 3H), 3.68 – 3.55 (m, 3H), 3.21 – 3.51 (m, 1H), 1.76 (d, \(J = 11.4\) Hz, 1H), 1.51 – 1.44 (m, 1H), 1.36 – 1.31 (m, 3H), 1.12 – 1.05 (m, 1H), 0.94 – 0.83 (m, 2H), 0.80 (d, \(J = 6.6\) Hz, 4H), 0.77 – 0.67 (m, 5H), 0.46 (d, \(J = 7.0\) Hz, 3H), 0.27 (d, \(J = 6.9\) Hz, 3H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) (\(\delta\), ppm) \(\delta\) 172.8, 170.4, 169.8, 169.8, 145.6, 141.4, 136.9, 131.0, 127.5, 127.1, 123.8, 120.7, 119.6, 119.5, 115.0, 115.6, 75.7, 74.2, 66.7, 61.7, 61.5, 46.9, 40.4, 34.3, 34.2, 31.4, 31.1, 25.0, 22.6, 22.1, 20.8, 15.3, 14.2, 13.4; HRMS (TOF MS ESI\(^+\)) calculated for C\(_{35}\)H\(_{43}\)NNaO\(_6\) [M + Na]\(^+\), 596.2983; found, 596.2989.

1-[(3R, 9R, 10S, 13S, 14R)-10,13-Dimethyl-17-((S)-6-methylheptan-2-yl)-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1H-cyclopenta[a]phenanthren-3-yl] 2,2-diethyl (1S)-4-methyl-1-phenyl-
3,4-dihydrocyclopenta[b]indole-1,2,2(1H)-tricarboxylate (3m)

White oil, 34.5 mg, 43% yield; $^1$H NMR (400 MHz, CDCl$_3$) of the two isomers ($\delta$, ppm) 7.68-7.51 (m, 2H), 7.35-7.31 (comp, 3H), 7.30 – 7.24 (m, 2H), 7.20 (m, 1H), 7.04 (t, $J = 7.5$ Hz, 1H), 5.44 – 5.17 (m, 1H), 4.48-4.74 (m, 1H), 4.43 – 4.15 (m, 2H), 3.89 – 3.51 (m, 2H), 3.68 – 3.51 (m, 2H), 3.31 – 3. 25 (m, 1H), 2.45 – 2.13 (m, 2H), 2.06 – 1.94 (m, 2H), 1.73 – 1.52 (m, 6H), 1.48 – 1.36 (m, 8H), 1.33 – 1.25 (m, 4H), 1.18 – 1.09 (m, 6H), 1.06 – 1.01 (m, 3H), 0.96 – 0. 85 (m, 11H), 0.81 – 0.74 (m, 2H), 0.73 – 0.64 (m, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$) of the two isomers ($\delta$, ppm) 172.4, 172.1, 172.0, 169.8, 168.7, 145.6, 141.4, 139.8, 139.6, 139.6, 138.9, 137.0, 136.9, 134.7, 130.9, 128.39, 128.37, 128.3, 127.6, 127.2, 126.7, 126.6, 123.8, 123.77, 122.7, 122.66, 122.6, 121.6, 121.5, 121.4, 120.8, 120.75, 119.7, 119.68, 119.5, 119.4, 115.0, 109.8, 109.1, 75.2, 75.1, 74.9, 74.02, 74.00, 66.59, 66.55, 62.0, 61.9, 61.8, 61.6, 56.81, 56.78, 56.75, 56.3, 52.4, 50.1, 50.06, 50.03, 48.8, 48.7, 42.44, 42.41, 39.9, 39.8, 39.7, 38.0, 37.8, 37.1, 37.06, 37.00, 36.9, 36.7, 36.6, 36.3, 35.9, 34.4, 34.3, 32.0, 31.9, 31.1, 30.1, 28.4, 28.2, 24.4, 24.0, 23.7, 23.0, 22.7, 21.2, 21.1, 21.1, 19.5, 19.4, 18.9, 18.8, 14.2, 14.1, 14.0, 13.4, 11.99, 11.97; HRMS (TOF MS ESI$^+$) calculated for C$_{52}$H$_{69}$NNaO$_6$ [M + Na]$^+$, 826.5017; found, 826.5029.

![Chemical Structure Image]

2,2-Diethyl 1-methyl 8-chloro-4-methyl-1-phenyl-3,4-dihydrocyclopenta[b]indole-1,2,2(1H)-tricarboxylate (3n)

White solid, 34.4 mg, 71% yield, mp: 121.4-122.8 °C; $^1$H NMR (400 MHz, CDCl$_3$) ($\delta$, ppm) $\delta$ 7.58-7.69 (m, 2H), 7.25 – 7.15 (m, 4H), 7.08 – 6.96 (m, 2H), 4.35 – 4.25 (m, 2H), 3.85 – 3.73 (m, 4H), 3.68 – 3.53 (m, 5H), 3.17 – 3.07 (m, 1H), 1.35 (td, $J = 7.1$, 1.6 Hz, 3H), 0.75 (td, $J = 7.1$, 1.5 Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) ($\delta$, ppm) $\delta$ 173.6, 170.4, 169.8, 147.2, 142.3, 138.1, 131.3, 127.5, 126.7, 125.1, 122.5, 121.6, 121.2, 114.6, 108.2, 75.1, 66.3, 62.0, 61.8, 52.4, 34.1, 31.4, 14.2, 13.4; HRMS (TOF
MS ESI\textsuperscript{+}) calculated for C\textsubscript{26}H\textsubscript{26}ClINaO\textsubscript{6} [M + Na]\textsuperscript{+}, 506.1341, found, 506.1334.

\[
\text{2,2-Diethyl 1-methyl 7-chloro-4-methyl-1-phenyl-3,4-dihydrocyclopenta[\textit{b}]indole -1,2,2(1\textit{H})-tricarboxylate (3o)}
\]
White solid, 38.2 mg, 79\% yield, mp: 144.1-142.2 °C; \textit{\textit{\textit{1}}}H NMR (400 MHz, CDCl\textsubscript{3}) (δ, ppm) δ 7.62 – 7.55 (m, 2H), 7.33 – 7.27 (m, 3H), 7.19 (d, J = 9.3 Hz, 1H), 7.12 – 7.08 (m, 2H), 4.37 – 4.27 (m, 2H), 3.78 (d, J = 15.7 Hz, 1H), 3.75 (s, 3H), 3.64 (d, J = 7.3 Hz, 1H), 3.61 – 3.57 (m, 1H), 3.56 (s, 3H), 3.28 – 3.17 (m, 1H), 1.35 (t, J = 7.1 Hz, 3H), 0.72 (t, J = 7.1 Hz, 3H); \textit{\textit{\textit{1}}}C NMR (100 MHz, CDCl\textsubscript{3}) (δ, ppm) δ 173.2, 170.2, 169.5, 146.4, 141.8, 136.4, 130.7, 127.9, 127.4, 127.0, 122.2, 120.6, 119.9, 115.0, 110.1, 74.1, 66.1, 61.9, 61.8, 52.4, 34.3, 31.3, 14.2, 13.4; HRMS (TOF MS ESI\textsuperscript{+}) calculated for C\textsubscript{26}H\textsubscript{26}ClINaO\textsubscript{6} [M + Na]\textsuperscript{+}, 506.1341, found, 506.1347.

\[
\text{2,2-Diethyl 1-methyl 6-chloro-4-methyl-1-phenyl-3,4-dihydrocyclopenta[\textit{b}]indole -1,2,2(1\textit{H})-tricarboxylate (3p)}
\]
White solid, 36.3 mg, 75\% yield, mp: 163.3-164.5 °C; \textit{\textit{\textit{1}}}H NMR (400 MHz, CDCl\textsubscript{3}) (δ, ppm) δ 7.63 – 7.55 (m, 2H), 7.33 – 7.26 (m, 4H), 7.07 – 6.95 (m, 2H), 4.39 – 4.25 (m, 2H), 3.78 (d, J = 15.7 Hz, 1H), 3.74 (s, 3H), 3.63 (d, J = 15.5 Hz, 1H), 3.60 – 3.55 (m, 1H), 3.54 (s, 3H), 3.29 – 3.17 (m, 1H), 1.35 (t, J = 7.1 Hz, 3H), 0.72 (t, J = 7.1 Hz, 3H); \textit{\textit{\textit{1}}}C NMR (100 MHz, CDCl\textsubscript{3}) (δ, ppm) δ 173.2, 170.2, 169.5, 146.4, 141.8, 136.4, 130.7, 127.9, 127.4, 127.0, 122.2, 120.6, 119.9, 115.0, 110.1, 74.1, 66.1, 61.9, 61.8, 52.4, 34.3, 31.3, 14.2, 13.4; HRMS (TOF MS ESI\textsuperscript{+}) calculated for C\textsubscript{26}H\textsubscript{26}ClINaO\textsubscript{6} [M + Na]\textsuperscript{+}, 506.1341, found, 506.1347.
2,2-Diethyl 1-methyl 4-benzyl-1-phenyl-3,4-dihydrocyclopenta[b]indole-1,2,2(1H)-tricarboxylate (3q)

White solid, 43.6 mg, 83% yield; \(^1\)H NMR (400 MHz, CDCl\(_3\)) (\(\delta\), ppm) \(\delta\) 7.73 – 7.63 (m, 2H), 7.36 – 7.28 (comp, 5H), 7.26 – 7.21 (m, 2H), 7.18 (d, \(J = 7.4\) Hz, 3H), 7.10 (t, \(J = 7.4\) Hz, 1H), 7.01 (t, \(J = 7.4\) Hz, 1H), 5.40 – 5.26 (m, 2H), 4.31 (q, \(J = 7.1\) Hz, 2H), 3.77 (d, \(J = 15.6\) Hz, 1H), 3.62 – 3.55 (comp, 4H), 3.54 – 3.47 (m, 1H), 3.35 – 3.23 (m, 1H), 1.34 (t, \(J = 7.1\) Hz, 3H), 0.74 (t, \(J = 7.1\) Hz, 3H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) (\(\delta\), ppm) \(\delta\) 173.3, 170.4, 169.6, 145.6, 140.8, 137.3, 136.6, 130.9, 129.0, 127.8, 127.7, 127.3, 126.7, 124.0, 121.1, 120.2, 119.4, 115.5, 110.5, 74.3, 66.1, 61.8, 61.7, 52.4, 48.6, 34.6, 14.2, 13.5; HRMS (TOF MS ESI\(^+\)) calculated for C\(_{32}\)H\(_{31}\)NO\(_6\) [M + H]\(^+\), 525.2151; found, 525.2147.

2,2-Diethyl 1-methyl 4-allyl-1-phenyl-3,4-dihydrocyclopenta[b]indole-1,2,2(1H)-tricarboxylate (3r)

White oil, 40.0 mg, 89% yield; \(^1\)H NMR (400 MHz, CDCl\(_3\)) (\(\delta\), ppm) \(\delta\) 7.70 – 7.62 (m, 2H), 7.34 – 7.27 (comp, 4H), 7.15 (t, \(J = 8.4\) Hz, 2H), 7.02 (t, \(J = 7.5\) Hz, 1H), 6.13 – 5.97 (m, 1H), 5.22 (dd, \(J = 10.3\), 1.0 Hz, 1H), 5.07 (dd, \(J = 17.1\), 1.0 Hz, 1H), 4.84 – 4.66 (m, 2H), 4.33 (q, \(J = 7.1\) Hz, 2H), 3.79 (d, \(J = 15.6\) Hz, 1H), 3.61 (d, \(J = 15.6\) Hz, 1H), 3.58 – 3.49 (comp, 4H), 3.33 – 3.23 (m, 1H), 1.36 (t, \(J = 7.1\) Hz, 3H), 0.74 (t, \(J = 7.1\) Hz, 3H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) (\(\delta\), ppm) \(\delta\) 173.3, 170.4, 169.6, 145.5,
140.7, 136.6, 133.1, 130.9, 127.8, 127.3, 123.8, 121.0, 120.0, 119.3, 117.1, 115.3, 110.2, 74.3, 66.0, 61.8, 61.7, 52.3, 47.1, 34.5, 14.2, 13.4; HRMS (TOF MS ESI\(^{+}\)) calculated for C\(_{28}\)H\(_{29}\)NNaO\(_6\) [M + Na]\(^{+}\), 498.1887, found, 498.1892.

![Methyl 2,2-diacetyl-4-methyl-1-phenyl-1,2,3,4-tetrahydrocyclopenta[\(b\)]indole-1-carboxylate (3s)](image)

White solid, 32.3 mg, 83% yield, mp: 163.3-164.5 °C; \(^1\)H NMR (400 MHz, CDCl\(_3\)) (\(\delta\), ppm) \(\delta\) 7.54 – 7.47 (m, 2H), 7.34 – 7.26 (m, 4H), 7.22 – 7.15 (m, 2H), 7.02 (t, \(J = 7.5\) Hz, 1H), 3.83 – 3.73 (comp, 4H), 3.64 – 3.52 (comp, 4H), 2.27 (s, 3H), 1.51 (s, 3H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) (\(\delta\), ppm) \(\delta\) 206.2, 203.9, 174.0, 144.4, 141.6, 136.8, 130.6, 128.1, 128.0, 123.6, 121.2, 120.1, 119.6, 115.5, 109.9, 85.2, 66.5, 52.5, 32.3, 31.2, 29.3, 27.9; HRMS (TOF MS ESI\(^{+}\)) calculated for C\(_{24}\)H\(_{23}\)NNaO\(_4\) [M + Na]\(^{+}\), 412.1519, found, 412.1523.

![Diethyl 1-cyano-4-methyl-1-phenyl-3,4-dihydrocyclopenta[\(b\)]indole-2,2(1H)-dicarboxylate (3ao)](image)

36.0 mg, 87% yield; \(^1\)H NMR (500 MHz, CDCl\(_3\)) (\(\delta\), ppm) 7.71 – 7.54 (m, 2H), 7.43 – 7.30 (comp, 4H), 7.21 (t, \(J = 7.6\) Hz, 1H), 7.10 (d, \(J = 7.8\) Hz, 1H), 7.04 (t, \(J = 7.5\) Hz, 1H), 4.51 – 4.25 (m, 2H), 3.88 – 3.67 (comp, 5H), 3.57 (d, \(J = 16.0\) Hz, 1H), 3.36 – 3.33 (m, 1H), 1.36 (t, \(J = 7.1\) Hz, 3H), 0.79 (t, \(J = 7.2\) Hz, 3H); \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) (\(\delta\), ppm) 168.4, 167.6, 144.0, 141.7, 134.9, 128.9, 128.7, 128.3, 122.6, 121.8, 120.5, 120.3, 118.8, 113.2, 110.1, 74.7, 62.5, 62.3, 53.7, 32.8, 31.2, 14.108, 13.4. HRMS (TOF MS ESI\(^{+}\)) calculated for C\(_{25}\)H\(_{25}\)N\(_2\)O\(_4\) [M + H]\(^{+}\),
417.1809; found, 417.1810.

Diethyl 2-[[3-(2-methoxy-2-oxo-1-phenylethyl)-1-methyl-1H-indol-2-yl]methylene]malonate 4a

Yellow solid, mp: 121.1-122.4 °C; $^1$H NMR (400 MHz, CDCl$_3$) ($\delta$, ppm) $\delta$ 7.79 (s, 1H), 7.51 (d, $J = 8.1$ Hz, 1H), 7.30 – 7.21 (comp, 7H), 7.10 – 7.02 (m, 1H), 5.31 (s, 1H), 4.39 – 4.26 (m, 2H), 3.93 – 3.84 (m, 1H), 3.74 (t, $J = 3.5$ Hz, 1H), 3.70 (s, 3H), 3.65 (s, 3H), 1.35 (t, $J = 7.1$ Hz, 3H), 0.93 (t, $J = 7.1$ Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) ($\delta$, ppm) $\delta$ 173.0, 164.8, 163.6, 138.8, 138.0, 134.1, 132.0, 131.9, 128.6, 128.4, 127.1, 126.8, 123.5, 121.7, 120.3, 113.1, 109.7, 62.1, 61.6, 52.4, 48.6, 31.5, 14.2, 13.8; HRMS (TOF MS ESI$^+$) calculated for C$_{26}$H$_{27}$NNaO$_6$ [M + Na]$^+$, 472.1731; found, 472.1743.

Diethyl 2-((3-(1-(4-fluorophenyl)-2-oxopropyl)-1-methyl-1H-indol-2-yl)methylene)malonate (4an). 29.2 mg, 65% yield; $^1$H NMR (400 MHz, CDCl$_3$) ($\delta$, ppm) 7.79 (s, 1H), 7.39 – 7.26 (comp, 3H), 7.15 – 7.05 (comp, 3H), 6.99 – 6.91 (m, 2H), 5.24 (s, 1H), 4.37 – 4.31 (m, 2H), 3.91 – 4.83 (m, 1H), 3.74 – 3.66 (comp, 4H), 2.12 (s, 3H), 1.35 (t, $J = 7.1$ Hz, 3H), 0.97 (t, $J = 7.1$ Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) ($\delta$, ppm) 206.1, 164.8, 163.5, 163.1, 160.7, 139.0, 133.4, 132.4, 132.3, 130.9, 130.8, 126.5, 123.8, 121.0 (d, $J = 32.5$ Hz), 115.1 (d, $J = 21.2$ Hz), 112.4, 110.0, 62.3, 61.7, 55.8, 31.6, 29.4, 14.2, 13.9; $^{19}$F NMR (376 MHz, CDCl$_3$) ($\delta$, ppm) -116.10. HRMS
(TOF MS ESI^+) calculated for C_{26}H_{26}FNNaO_{5} [M + Na]^+, 474.1687; found, 474.1670.

**Ethyl (E)-3-(3-(2-methoxy-2-oxo-1-phenylethyl)-1-methyl-1H-indol-2-yl)acrylate (4ha).** 30.6 mg, 81% yield; ^1H NMR (500 MHz, CDCl_3) (δ, ppm) 7.88 (d, J = 16.2 Hz, 1H), 7.55 (d, J = 8.1 Hz, 1H), 7.41 – 7.20 (comp, 6H), 7.09 – 7.05 (m, 1H), 6.27 (d, J = 16.2 Hz, 1H), 5.49 (s, 1H), 4.28 (q, J = 7.1 Hz, 2H). 3.84 (s, 3H), 3.74 (s, 3H), 1.35 (t, J = 7.1 Hz, 3H); ^13C NMR (100 MHz, CDCl_3) (δ, ppm) 173.1, 166.8, 138.9, 138.3, 133.0, 132.3, 128.6, 128.5, 127.2, 126.6, 124.1, 121.6, 121.2, 120.5, 115.2, 109.7, 60.9, 52.5, 48.6, 31.5, 14.5. HRMS (TOF MS ESI^+) calculated for C_{23}H_{24}NO_{4} [M + H]^+, 378.1700; found, 378.1717.

**Methyl (E)-2-(2-(2-cyanovinyl)-1-methyl-1H-indol-3-yl)-2-phenylacetate (4ia).** 22.2 mg, 67% yield; ^1H NMR (500 MHz, CDCl_3) (δ, ppm) 7.56 – 7.54 (m, 1H), 7.51 (d, J = 16.7 Hz, 1H), 7.35 – 7.27 (comp, 5H), 7.23 – 7.17 (m, 2H), 7.12 – 7.08 (m, 1H), 5.68 (d, J = 16.7 Hz, 1H), 5.40 (s, 1H), 3.81 (s, 3H), 3.74 (s, 3H); ^13C NMR (100 MHz, CDCl_3) (δ, ppm) 172.7, 138.9, 138.2, 137.7, 132.1, 128.8, 128.3, 127.5, 126.7, 124.9, 121.6, 121.0, 118.2, 115.9, 109.9, 99.1, 52.7, 48.5, 31.4. HRMS (TOF MS ESI^+) calculated for C_{21}H_{19}N_{2}O_{2} [M + H]^+, 331.1441; found, 331.1449.
Methyl (E)-2-(1-methyl-2-(3-oxobut-1-en-1-yl)-1H-indol-3-yl)-2-phenylacetate (4ja) and Methyl 2-acetyl-4-methyl-1-phenyl-1,2,3,4-tetrahydrocyclopenta[b]-indole-1-carboxylate (3ja). 27.1 mg, 4xa : 3xa = 4.8 : 1, 78% total yield; 4xa: ¹H NMR (500 MHz, CDCl₃) (δ, ppm) 7.74 (d, J = 16.4 Hz, 1H), 7.66 – 7.56 (m, 1H), 7.38 – 7.26 (comp, 7H), 7.16 – 7.08 (m, 1H), 6.56 (d, J = 16.4 Hz, 1H), 5.56 (s, 1H), 3.83 (s, 3H), 3.76 (s, 3H), 2.33 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) (δ, ppm) 197.6, 172.9, 139.1, 138.2, 132.8, 131.0, 128.8, 128.5, 128.3, 127.2, 126.7, 124.3, 121.0, 120.5, 116.0, 109.8, 52.4, 48.4, 31.5, 28.0. 3xa: ¹H NMR (500 MHz, CDCl₃) (δ, ppm) 7.54 – 7.49 (m, 2H), 7.41 – 7.28 (comp, 3H), 7.25 – 7.17 (m, 3H), 7.07 – 7.03 (m, 1H), 3.85 – 3.81 (m, 1H), 3.74 (s, 3H), 3.64 (s, 3H), 3.53 (dd, J = 15.3, 8.4 Hz, 1H), 3.24 (dd, J = 15.3, 8.4 Hz, 1H), 2.22 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) (δ, ppm) 205.9, 173.6, 144.2, 142.3, 141.3, 128.2, 128.1, 127.2, 123.6, 120.9, 119.8, 119.5, 116.9, 109.6, 69.6, 62.8, 52.1, 30.8, 29.6, 27.3. HRMS (TOF MS ESI⁺) calculated for C₂₂H₂₁NNaO₃ [M + Na]⁺, 370.1414; found, 370.1400.

2-Ethyl 1-methyl (1S*, 2R*)-2-acetyl-4-methyl-1-phenyl-1,2,3,4-tetrahydrocyclopenta[b]indole-1,2-dicarboxylate (7)

Yellow solid, 32.3 mg, 77% yield, mp: 133.7-134.5 °C; ¹H NMR (400 MHz, CDCl₃) (δ, ppm) δ 7.61 – 7.54 (m, 2H), 7.34 – 7.28 (comp, 4H), 7.20 – 7.10 (m, 2H), 7.03 – 6.98 (m, 1H), 4.40 – 4.28 (m, 2H), 3.78 (d, J = 4.9 Hz, 3H), 3.70 (d, J = 15.8 Hz, 1H), 3.58 – 3.51 (comp, 4H), 1.47 (s, 3H), 1.38 (t, J = 7.1 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) (δ, ppm) δ 202.7, 173.5, 172.0, 145.8, 141.5, 136.3, 130.8, 128.1, 128.0,
123.7, 121.0, 120.0, 119.3, 114.4, 109.9, 78.9, 66.4, 61.8, 52.4, 32.9, 31.2, 27.7, 14.2; HRMS (TOF MS ESI⁺) calculated for C₂₅H₂₇NNaO₅ [M + Na]⁺, 442.1625, found, 442.1629.

2-Ethyl 1-methyl (1S*, 2S*)-2-acetyl-4-methyl-1-phenyl-1,2,3,4-tetrahydrocyclopenta[b]indole-1,2-dicarboxylate (8)

Yellow solid, 33.1 mg, 79% yield, mp: 133.7-134.5 °C; ¹H NMR (400 MHz, CDCl₃) (δ, ppm) δ 7.63 – 7.54 (m, 2H), 7.32 – 7.27 (m, 2H), 7.26 (d, J = 1.6 Hz, 2H), 7.19 – 7.12 (m, 2H), 7.04 – 6.97 (m, 1H), 3.79 (s, 3H), 3.76 – 3.66 (m, 2H), 3.65 – 3.58 (m, 1H), 3.55 (s, 3H), 3.26 – 3.15 (m, 1H), 2.30 (s, 3H), 0.74 (t, J = 7.1 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) (δ, ppm) δ 202.1, 173.7, 169.7, 144.4, 141.5, 137.1, 130.8, 127.6, 127.5, 123.7, 121.0, 120.0, 119.4, 115.4, 109.8, 80.3, 65.6, 62.0, 52.4, 33.7, 31.2, 28.5, 13.4; HRMS (TOF MS ESI⁺) calculated for C₂₅H₂₇NNaO₅ [M + Na]⁺, 442.1625, found, 442.1626.

General Procedure of the Scale Up and Synthesis of 5 and 6.

General Procedure of the Scale Up:

To a 50-mL oven-dried vial containing a magnetic stirring bar, Cu(CH₃CN)₄PF₆ (74.5 mg, 5.0 mol %), compound 1a (1.20 g, 4.0 mmol) in DCM (20.0 mL), diazo
compound 2a (1.41 g, 8.0 mmol) in DCM (10.0 mL) was added as a solution via a syringe pump over 2 h under argon atmosphere at 35 °C. After addition, the reaction mixture was stirred overnight under these conditions until consumption of the material (monitored by TLC). Then the reaction mixture was purified by column chromatography on silica gel after evaporate most of the solvent in vacuo (Hexanes : EtOAc = 15:1 to 10:1) to give the pure products 1.40 g of 3 (78% yield).

Synthesis of 5.

To a 10-mL oven-dried vial containing a magnetic stirring bar, 3q (52.6 mg, 0.1 mmol), Pd/C (1.1 mg, 0.01 mmol, 0.1 equiv), was added MeOH (3.0 mL) under H₂ atmosphere. Then the reaction mixture was stirred at 50 °C for 2 h with a H₂ balloon. After the reaction was complete, the reaction mixture was cooled to room temperature and concentrated under reduced pressure. The obtained residue was purified by flash column chromatography on silica gel (Hexanes: EtOAc = 15:1) to give 44.3 mg pure product 5 as white solid (84% yield). mp: 137.2-138.9 °C, ¹H NMR (400 MHz, CDCl₃) (δ, ppm) 7.49 (d, J = 7.9 Hz, 1H), 7.30 – 7.26 (comp, 3H), 7.26 – 7.18 (comp, 6H), 7.15 – 7.09 (m, 1H), 7.06 – 6.99 (m, 1H), 6.97 – 6.91 (m, 2H), 5.45 (s, 2H), 5.42 (s, 1H), 4.21 – 4.05 (m, 2H), 4.00 – 3.84 (m, 2H), 3.73 (s, 3H), 3.56 (t, J = 7.3 Hz, 1H), 3.42 (d, J = 7.0 Hz, 2H), 1.19 (t, J = 7.1 Hz, 3H), 1.11 (t, J = 7.1 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) (δ, ppm) δ 173.6, 168.7, 168.6, 138.6, 137.7, 137.3, 134.8, 129.0, 128.5, 128.4, 127.5, 126.9, 126.0, 122.0, 121.1, 120.0, 110.4, 109.9, 61.9, 61.8, 52.3, 52.3, 48.2, 46.8, 29.9, 23.8, 14.07, 14.0. HRMS (TOF MS ESI⁺) calculated for C₃₂H₃₃NNaO₆ [M + Na]⁺, 550.2200; found, 550.2196.
Synthesis of 6.\textsuperscript{4}

To a 10-mL oven-dried vial containing a magnetic stirring bar, 3g (52.8 mg, 0.1 mmol), Phenylacetylene (15.3 mg, 0.15 mmol, 1.5 equiv), Et\textsubscript{3}N (30.3 mg, 0.3 mmol, 3.0 equiv), Pd(PPh\textsubscript{3})\textsubscript{2}Cl\textsubscript{2} (1.4 mg, 2.0 mol%), and CuI (0.4 mg, 2.0 mol%), was added DMF (2.0 mL) under argon atmosphere. Then the reaction mixture was stirred at 80 °C for 12 h. After the reaction was complete, the reaction mixture was cooled to room temperature and quenched with water (10 mL) and extracted with EtOAc (10 mL). The organic layer was dried over anhydrous Na\textsubscript{2}SO\textsubscript{4} and concentrated under reduced pressure after filtration. The obtained residue was purified by flash column chromatography on silica gel (Hexanes: EtOAc = 10:1) to give 50.6 mg pure product 6 as yellow solid (92% yield). mp: 178.8-179.3 °C, \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}) (δ, ppm) δ 7.66 (d, J = 8.0 Hz, 2H), 7.57 – 7.51 (m, 2H), 7.46 (d, J = 8.7 Hz, 2H), 7.38 – 7.29 (comp, 4H), 7.21 – 7.11 (m, 2H), 7.06 – 6.99 (m, 1H), 4.42 – 4.27 (m, 2H), 3.85 – 3.73 (comp, 4H), 3.69 – 3.58 (comp, 2H), 3.55 (s, 3H), 3.40 – 3.27 (m, 1H), 1.37 (t, J = 7.1 Hz, 3H), 0.79 (t, J = 7.1 Hz, 3H); \textsuperscript{13}C NMR (100 MHz, CDCl\textsubscript{3}) (δ, ppm) δ 173.1, 170.3, 169.5, 145.7, 141.4, 137.1, 131.7, 130.9, 130.5, 128.5, 128.3, 123.6, 123.5, 122.6, 121.0, 120.0, 119.1, 114.3, 109.9, 89.7, 89.6, 74.2, 66.0, 62.0, 61.8, 52.4, 34.3, 31.2, 14.2, 13.5; HRMS (TOF MS ESI\textsuperscript{+}) calculated for C\textsubscript{34}H\textsubscript{31}NNaO\textsubscript{6} [M + Na]\textsuperscript{+}, 572.2044; found, 572.2048.
1D-Noe Study of 8

References


Datablock: s180711a

Bond precision: C-C = 0.0037 Å  Wavelength=0.71073

Cell: a=9.936(7)  b=11.476(9)  c=12.791(10)
alpha=112.481(8)  beta=91.011(11)  gamma=111.954(8)

Temperature: 293 K

Calculated  Reported
Volume  1224.6(16)  1224.58(10)
Space group  P 1  P 1
Hall group  -P 1  -P 1
Molality formula  C26 H26 F N O6  ?
Sum formula  C26 H26 F N O6  C26 H26 F N O6
Mr  467.48  467.48
Dx.g/cm³  1.268  1.268
Z  2  2
µ (mm⁻¹)  0.095  0.095
F(000)  492.0  492.0
F(000)'  492.28
h,k,lmax  15,18,20  15,18,19
Nref  10657  9038
Tmin,Tmax

Correction method: Not given

Data completeness  0.848  Theta(max) = 34.830
R(reflections)  0.0933( 6826)  wR2(reflections)  0.2820( 9035)

S = 1.152  Npar= 311

The following ALERTS were generated. Each ALERT has the format:
test-name ALERT alert-type alert-level.
Click on the hyperlinks for more details of the test.