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Supporting Information

Ruthenium/Iridium-Catalyzed C-2 Activation of Indoles with Bicyclic Olefins: An Easy Access to Functionalized Heterocyclic Motifs

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General Methods

All chemicals were of the best grade commercially available and are used without further purification. All solvents were purified according to standard procedure; dry solvents were obtained according to the literature methods and stored over molecular sieves. Thin layer chromatography was performed on TLC Silica gel 60 F254 aluminium sheets purchased from Merck Pvt Ltd. Gravity column chromatography was performed using silica gel and alumina, and mixtures of hexane-ethyl acetate were used for elution. Melting points were determined on a Buchi melting point apparatus and are uncorrected. Proton nuclear magnetic resonance spectra (1H NMR) were recorded on a Bruker AMX 500 spectrophotometer [acetone-d6, CD3CN, CDCl3 or CDCl3/CCl4 (7:3 mixture) as solvents]. Chemical shifts for 1H NMR spectra are reported as δ in units of parts per million (ppm) downfield from SiMe4 (δ 0.0) and relative to the signals of chloroform-d (δ 7.25, singlet), acetone –d6 (δ 2.05, quintet), and acetonitrile-d3 (δ 1.93, quintet) respectively. Multiplicities were given as: s (singlet); brs (broad singlet); d (doublet); t (triplet); m (multiplet). Coupling constants are reported as J value in Hz. Carbon nuclear magnetic resonance spectra (13C NMR) are reported as δ in units of parts per million (ppm) downfield from SiMe4 (δ 0.0) and relative to the signals of chloroform-d (δ 77.03, triplet), acetone –d6 (δ 29.97, septet; 206.68, singlet), and acetonitrile-d3 (δ 1.39, septet; 118.69, singlet) respectively. Mass spectra were recorded under ESI/HRMS at 60,000 resolution using Thermo Scientific Exactive mass spectrometer. IR spectra were recorded on Bruker FT-IR spectrometer.

General Procedure for the Ruthenium catalyzed regiospecific cyclopentenylation of suitably protected indoles with bicyclic hydrazines:-

A mixture of diazabicyclic olefin (60 mg, 0.2497 mmol, 1.5 equiv.), indole (42 mg, 0.1665 mmol, 1.0 equiv.), [RuCl2(p-cymene)]2 (3 mg, 0.0050 mmol, 3 mol%) and Cu(OAc)2.H2O (7 mg, 0.0333 mmol, 20 mol%) were weighed in a schlenk tube and degassed for 10 minutes. Dry toluene (2 mL) was added and the reaction mixture was purged with argon and allowed to stir at 110 °C for 12 hours. The crude reaction mixture on silica gel (100-200 mesh) column chromatography using ethyl acetate/hexane mixture yielded cyclopentene substituted indoles.
General Procedure for the Iridium catalyzed hydroheteroarylation of bicyclic olefins:-

A mixture of bicyclic alkene (80 mg, 0.3329 mmoles, 1.0 equiv.), indole (35 mg, 0.2996 mmoles, 0.9 equiv.), [Ir(1,5-cod)Cl]₂ (11 mg, 0.0166 mmoles, 5 mol%) and dppe (13 mg, 0.0333 mmoles, 10 mol%) were weighed in a schlenk tube and degassed for 10 minutes. Dry toluene (2 mL) was added and the reaction mixture was purged with argon and allowed to stir at 110 °C for 16 hours. The crude reaction mixture on alumina column chromatography using ethyl acetate/hexane mixture yielded hydroheteroarylated bicyclic olefins.

Table 3. Optimization studies for desymmetrization of diazabicyclic olefins

<table>
<thead>
<tr>
<th>entry</th>
<th>catalyst</th>
<th>acetate source</th>
<th>solvent</th>
<th>temp (°C)</th>
<th>yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>[RuCl₂(p-cymene)]₂</td>
<td>Cu(OAc)₂.H₂O</td>
<td>toluene</td>
<td>80</td>
<td>56</td>
</tr>
<tr>
<td>2</td>
<td>[RuCl₂(p-cymene)]₂</td>
<td>Cu(OAc)₂.H₂O</td>
<td>toluene</td>
<td>110</td>
<td>80</td>
</tr>
<tr>
<td>3</td>
<td>[RuCl₂(p-cymene)]₂</td>
<td>Cu(OAc)₂.H₂O</td>
<td>xylene</td>
<td>110</td>
<td>40</td>
</tr>
<tr>
<td>4</td>
<td>[RuCl₂(p-cymene)]₂</td>
<td>Cu(OAc)₂.H₂O</td>
<td>dioxane</td>
<td>110</td>
<td>NR</td>
</tr>
<tr>
<td>5</td>
<td>[RuCl₂(p-cymene)]₂</td>
<td>Cu(OAc)₂.H₂O</td>
<td>DMF</td>
<td>110</td>
<td>NR</td>
</tr>
<tr>
<td>6</td>
<td>[RuCl₂(p-cymene)]₂</td>
<td>Cu(OAc)₂.H₂O</td>
<td>t-amyl alcohol</td>
<td>110</td>
<td>NR</td>
</tr>
<tr>
<td>7</td>
<td>[RuCl₂(p-cymene)]₂</td>
<td>AgOAc</td>
<td>toluene</td>
<td>110</td>
<td>20</td>
</tr>
<tr>
<td>8</td>
<td>[RuCl₂(p-cymene)]₂</td>
<td>CoOAc</td>
<td>toluene</td>
<td>110</td>
<td>22</td>
</tr>
<tr>
<td>9</td>
<td>[RuCl₂(p-cymene)]₂</td>
<td>NaOAc</td>
<td>toluene</td>
<td>110</td>
<td>48</td>
</tr>
<tr>
<td>10</td>
<td>[RhCp*Cl₂]₂</td>
<td>Cu(OAc)₂.H₂O</td>
<td>toluene</td>
<td>110</td>
<td>51</td>
</tr>
<tr>
<td>11*</td>
<td>[RuCl₂(p-cymene)]₂</td>
<td>Cu(OAc)₂.H₂O</td>
<td>toluene</td>
<td>110</td>
<td>0</td>
</tr>
</tbody>
</table>

Reaction Conditions : 1a (1.5 equiv.), 2a (1 equiv.), catalyst (3 mol%), acetate source (20 mol%), solvent (2 mL), 12 h.*with 4a

The yield of the reaction was found to increase dramatically when the reaction temperature was changed to 110 °C. Changing the catalyst system to [RhCp*Cl₂]₂ furnished the product in 51% yield only. Toluene was chosen as the optimal solvent for the transformation, and the reaction was futile with other solvents like xylene, dioxane, DMF and t-amyl alcohol. Among
the different acetate sources tested, NaOAc provided a moderate yield of 48% (Table 4, entry 9). The reaction was futile with N-free indoles.

Table 4. Optimization studies for hydroheteroarylation of bicyclic olefins

<table>
<thead>
<tr>
<th>entry</th>
<th>catalyst</th>
<th>ligand</th>
<th>solvent</th>
<th>yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>[Ir(1,5-cod)Cl]_2</td>
<td>dppp</td>
<td>toluene</td>
<td>54</td>
</tr>
<tr>
<td>2</td>
<td>[Ir(OMe)(1,5-cod)]_2</td>
<td>dppp</td>
<td>toluene</td>
<td>trace</td>
</tr>
<tr>
<td>3</td>
<td>[IrCl(CO)(PPh_3)_2]</td>
<td>dppp</td>
<td>toluene</td>
<td>nr</td>
</tr>
<tr>
<td>4</td>
<td>[Ir(1,5-cod)Cl]_2</td>
<td>dppe</td>
<td>toluene</td>
<td>64</td>
</tr>
<tr>
<td>5</td>
<td>[Ir(1,5-cod)Cl]_2</td>
<td>dpff</td>
<td>toluene</td>
<td>trace</td>
</tr>
<tr>
<td>6</td>
<td>[Ir(1,5-cod)Cl]_2</td>
<td>(rac)-binap</td>
<td>toluene</td>
<td>20</td>
</tr>
<tr>
<td>7</td>
<td>[Ir(1,5-cod)Cl]_2</td>
<td>PPh_3</td>
<td>toluene</td>
<td>nr</td>
</tr>
<tr>
<td>8</td>
<td>[Ir(1,5-cod)Cl]_2</td>
<td>dppe</td>
<td>DMF</td>
<td>nr</td>
</tr>
<tr>
<td>9</td>
<td>[Ir(1,5-cod)Cl]_2</td>
<td>dppe</td>
<td>CH_3CN</td>
<td>nr</td>
</tr>
<tr>
<td>10</td>
<td>[Ir(1,5-cod)Cl]_2</td>
<td>dppe</td>
<td>DMSO</td>
<td>nr</td>
</tr>
<tr>
<td>11*</td>
<td>[Ir(1,5-cod)Cl]_2</td>
<td>dppe</td>
<td>toluene</td>
<td>nr</td>
</tr>
</tbody>
</table>

Reaction conditions: adduct (1 equiv.), indole (0.9 equiv.), [Ir(1,5-cod)Cl]_2 (5 mol%), dppe (10 mol%), toluene (2 mL), 110 °C, 16 h. *with 2a

Detailed optimization studies revealed that the reaction did not proceed well with other catalysts like [Ir(OMe)(1,5-cod)]_2 and [IrCl(CO)(PPh_3)_2]. Among the ligands screened, dppe gave a better yield of 64%. Best solvent for this transformation was found to be toluene, and the reaction was futile with other solvents like DMF, DMSO and CH_3CN. The reaction with 2a didn’t give any satisfactory results.
Characterization of the Products

The synthesized products were characterized based on various spectroscopic techniques like IR, $^1$H NMR, $^{13}$C NMR and HRMS analysis. The synthesized diazabicyclic olefin derivatives bear hydrazine moiety, and the proton NMR signals of these compounds are broadened due to rotational isomerism exhibited by the hydrazine group.1

diethyl-1-(2-(1H-indol-2-yl)cyclopent-3-enyl)hydrazine-1,2-dicarboxylate (3a)

Yield: 48 mg, 80% as colourless viscous liquid. $R_f$: 0.85 (7:3 hexane/ethyl acetate). IR (neat) $\nu_{max}$: 3289, 2919, 1716, 1606, 1532, 1419, 1262, 1172, 1096, 1061, 758 cm$^{-1}$. $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 9.99 (brs, 1 H), 7.49 (d, $J = 8$ Hz, 1 H), 7.34 (d, $J = 8$ Hz, 1 H), 7.08 (t, $J = 7$ Hz, 1 H), 7.01 (t, $J = 7.5$ Hz, 1 H), 6.57 (brs, 1 H), 6.19 (s, 1 H), 5.94 (s, 1 H), 5.88 (s, 1 H), 4.76 (brs, 1 H), 4.63-3.99 (m, 5 H), 2.57 (brs, 2 H), 1.37-1.25 (m, 4 H), 0.89-0.85 (m, 2 H). $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 155.7, 138.8, 130.8, 128.1, 127.5, 120.9, 119.7, 118.8, 110.5, 99.7, 62.5, 34.7, 29.5, 14.4. HRMS (ESI): m/z calcd for C$_{19}$H$_{23}$N$_3$O$_4$Na: 380.15863; Found: 380.15851.

diisopropyl-1-(2-(1H-indol-2-yl)cyclopent-3-enyl)hydrazine-1,2-dicarboxylate (3b)

Yield: 37 mg, 65% as yellow viscous liquid. $R_f$: 0.67 (7:3 hexane/ethyl acetate). IR (neat) $\nu_{max}$: 3308, 2982, 2935, 1696, 1518, 1459, 1381, 1255, 1106, 953, 746 cm$^{-1}$. $^1$H NMR (500 MHz, Acetone-d$_6$): $\delta$ 10.29 (brs, 1 H), 8.63-8.34 (m, 1 H), 7.46 (d, $J = 12$ Hz, 1 H), 7.31 (d, $J = 12$ Hz, 1 H), 7.02 (t, $J = 7.5$ Hz, 1 H), 6.95 (t, $J = 7.5$ Hz, 1 H), 6.21 (brs, 1 H), 5.90 (brs, 2 H), 5.03-4.79 (m, 3 H), 4.16 (brs, 1 H), 2.60 (brs, 2 H), 1.29-1.22 (m, 12 H). $^{13}$C NMR (125 MHz, Acetone-d$_6$): $\delta$ 158.7, 156.3, 129.1, 121.32, 119.9, 119.4, 111.3, 101.1, 96.9, 70.2, 69.9, 58.7, 48.0, 35.7, 21.7. HRMS (ESI): m/z calcd for C$_{21}$H$_{27}$N$_3$O$_4$Na: 408.18993; Found: 408.18799.

di-tert-butyl-1-(2-(1H-indol-2-yl)cyclopent-3-enyl)hydrazine-1,2-dicarboxylate (3c)

Yield: 35 mg, 58% as colourless liquid. $R_f$: 0.78 (7.3 hexane/ethyl acetate). IR (neat) $\nu_{max}$: 3386, 2984, 1701, 1586, 1212, 1113, 1109, 1016 cm$^{-1}$. $^1$H NMR (500 MHz, Acetone-d$_6$): $\delta$ 10.26-9.88 (m, 1 H), 8.36-8.12 (m, 1 H), 7.32 (d, $J = 8$ Hz, 1 H), 7.16 (brs, 1 H), 6.89 (t, $J = 7$ Hz, 1 H), 6.81 (t, $J = 7$ Hz, 1 H), 6.06 (brs, 1 H), 5.81-5.77 (m, 2 H), 4.76-4.63 (m,
1H), 4.11-3.97 (m, 1 H), 2.49-2.42 (m, 2 H), 1.39-1.16 (m, 18 H). 13C NMR (125 MHz, Acetone-d6): δ 158.1, 155.2, 143.2, 137.2, 131.6, 129.8, 128.9, 120.2, 119.4, 114.4, 100.9, 97.3, 81.4, 65.2, 46.1, 35.4, 28.3. HRMS (ESI): m/z calcd for C_{23}H_{31}N_{3}O_{4}Na: 436.22123; Found: 436.21901.

dibenzyl-1-(2-(1H-indol-2-yl)cyclopent-3-enyl)hydrazine-1,2-dicarboxylate (3d)

Yield: 12 mg, 22% as yellow viscous liquid. R_f: 0.50 (7:3 hexane/ethyl acetate). IR (neat) ν_{max}: 3298, 3034, 2950, 1709, 1499, 1454, 1386, 1217, 1171, 1108, 1022, 916, 740, 698 cm^{-1}. 1H NMR (500 MHz, Acetone-d6): δ 10.22-9.99 (m, 1 H), 8.98-8.81 (m, 1 H), 7.47-7.31 (m, 12 H), 7.05-6.98 (m, 2 H), 6.24 (s, 1 H), 5.89 (s, 2 H), 5.30-4.97 (m, 5 H), 4.26 (brs, 2 H). 13C NMR (125 MHz, Acetone-d6): δ 156.1, 136.9, 129.3, 128.5, 121.3, 120.2, 119.4, 115.5, 100.9, 97.6, 68.2, 68.1, 48.9, 35.4. HRMS (ESI): m/z calcd for C_{29}H_{27}N_{3}O_{4}Na: 504.18993; Found: 504.18736.

diisopropyl-1-(5-isopropyl-9-oxo-2,3,3a,9-tetrahydrocyclopenta[b]chromen-2-yl)hydrazine-1,2-dicarboxylate (3e)

Yield: 29 mg, 34% as colourless viscous liquid. R_f: 0.55 (7:3 hexane/ethyl acetate). IR (neat) ν_{max}: 3317, 2981, 2923, 1700, 1612, 1414, 1297, 1244, 1061, 967 cm^{-1}. 1H NMR (500 MHz, Acetone-d6): δ 10.04-9.96 (m, 1 H), 8.43-8.29 (m, 1 H), 7.33 (d, J = 7 Hz, 1 H), 7.21 (d, J = 8 Hz, 1 H), 6.89 (t, J = 7 Hz, 1 H), 6.83-6.81 (m, 1 H), 6.10 (brs, 1 H), 5.71 (d, J = 5 Hz, 1 H), 5.37 (d, J = 8 Hz, 1 H), 4.74 (brs, 1 H), 4.32 (brs, 1 H), 4.09-3.94 (m, 4 H), 1.15-0.94 (m, 6 H), 0.74-0.53 (m, 4 H). 13C NMR (125 MHz, Acetone-d6): δ 158.1, 156.0, 138.7, 137.7, 129.9, 121.5, 120.7, 119.9, 100.9, 62.4, 60.6, 44.9, 14.9, 10.5. HRMS (ESI): m/z calcd for C_{21}H_{25}N_{3}O_{4}Na: 406.17515; Found: 406.17436.

diethyl-1-(2-(1-(benzylcarbamoyl)-1H-indol-3-yl)cyclopent-3-enyl)hydrazine-1,2-dicarboxylate (3f)

Yield: 22 mg, 40% as colourless viscous liquid. R_f: 0.75 (7:3 hexane/ethyl acetate). IR (neat) ν_{max}: 3302, 3056, 2958, 2919, 1699, 1615, 1494, 1381, 1296, 1251, 1106 cm^{-1}. 1H NMR (500 MHz, Acetone-d6): δ 10.06-10.01 (m, 1 H), 8.32-8.19 (m, 1 H), 7.33 (d, J = 8 Hz, 1 H), 6.89 (t, J = 7 Hz, 1 H), 6.82 (t, J = 7.5 Hz, 1 H), 6.09 (s, 1 H), 5.72 (d, J = 6 Hz, 1 H), 5.37-5.35 (m, 2 H), 4.86-4.65 (m, 2 H), 1.15-0.88 (m, 12 H), 0.74-0.53 (m, 4 H). 13C NMR (125 MHz,
Acetone-\textit{d}_6): \delta 156.5, 155.9, 138.4, 138.3, 137.2, 135.2, 129.7, 121.5, 120.5, 119.8, 111.5, 100.9, 98.3, 70.4, 47.6, 31.9, 21.9, 12.8, 10.7. HRMS (ESI): \textit{m}/\textit{z} caleed for \textit{C}_{23}\text{H}_{29}\text{N}_3\text{O}_4\text{Na}: 434.20558; Found: 434.20396.

diisopropyl-1-(2-(1-(benzylcarbamoyl)-1H-indol-3-yl)cyclopent-3-enyl)hydrazine-1,2-dicarboxylate (3g)

Yield: 13 mg, 34% as colourless viscous liquid. \(R_f\) : 0.85 (7:3 hexane/ethyl acetate). IR (\textit{neat}) \textit{v}_{\text{max}}: 3315, 3057, 2997, 1698, 1523, 1393, 1250, 1155, 1059 cm\(^{-1}\). \(^1\)H NMR (500 MHz, \textit{CD}_3\text{CN}): 9.90 (brs, 1 H), 7.64-7.61 (m, 1 H), 7.50 (d, \textit{J} = 8 Hz, 1 H), 7.44 (d, \textit{J} = 7 Hz, 1 H), 7.09 (t, \textit{J} = 7 Hz, 1 H), 7.02 (t, \textit{J} = 7.5 Hz, 1 H), 6.23 (s, 1 H), 5.86 (s, 1 H), 5.49 (s, 1 H), 4.76-4.59 (m, 1 H), 4.58-4.32 (m, 1 H), 1.53-1.29 (m, 18 H), 0.91-0.64 (m, 4 H). \(^{13}\)C NMR (125 MHz, \textit{CD}_3\text{CN}): \delta 157.9, 156.2, 129.8, 128.4, 124.9, 123.1, 121.6, 120.5, 120.2, 116.2, 111.8, 110.8, 106.4, 81.6, 45.1, 44.9, 28.6, 12.7, 10.6. HRMS (ESI): \textit{m}/\textit{z} caleed for \textit{C}_{25}\text{H}_{33}\text{N}_3\text{O}_4\text{Na}: 462.23688; Found: 462.23740.

diethyl-1-(2-(4-methoxy-1H-indol-2-yl)cyclopent-3-enyl)hydrazine-1,2-dicarboxylate (3h)

Yield: 43 mg, 66% as yellow viscous liquid. \(R_f\) : 0.65 (7:3 hexane/ethyl acetate). IR (\textit{neat}) \textit{v}_{\text{max}}: 3301, 2981, 2935, 1707, 1615, 1511, 1465, 1414, 1375, 1249, 1174, 1102, 1058, 866, 766 cm\(^{-1}\). \(^1\)H NMR (500 MHz, Acetone-\textit{d}_6): \delta 10.29-9.99 (m, 1 H), 8.78-8.40 (m, 1 H), 6.97-6.93 (m, 2 H), 6.47 (d, \textit{J} = 8Hz, 1 H), 6.28 (s, 1 H), 5.89 (s, 2 H), 4.93 (brs, 1 H), 4.23-3.94 (m, 5 H), 3.88 (s, 3 H), 2.62 (brs, 2 H), 1.28-1.04 (m, 6 H). \(^{13}\)C NMR (125 MHz, Acetone-\textit{d}_6): \delta 156.3, 153.9, 138.7, 131.3, 130.6, 128.7, 127.2, 122.4, 119.8, 104.8, 99.5, 62.6, 54.8, 48.5, 35.6, 14.8. HRMS (ESI): \textit{m}/\textit{z} caleed for \textit{C}_{20}\text{H}_{25}\text{N}_3\text{O}_5\text{Na}: 410.16919; Found: 410.16772.

diethyl-1-(2-(5-methoxy-1H-indol-2-yl)cyclopent-3-enyl)hydrazine-1,2-dicarboxylate (3i)

Yield: 41 mg, 63% as yellow viscous liquid. \(R_f\) : 0.20 (7:3 hexane/ethyl acetate). IR (\textit{neat}) \textit{v}_{\text{max}}: 3302, 2983, 2937, 1712, 1625, 1588, 1486, 1450, 1413, 1376, 1254, 1217, 1171, 1124, 1058, 1030, 950, 842, 767 cm\(^{-1}\). \(^1\)H NMR (500 MHz, Acetone-\textit{d}_6): \delta 9.95 (brs, 1 H), 8.52-8.26 (m, 1 H), 7.07 (d, \textit{J} = 9 Hz, 1 H), 6.84 (d, \textit{J} = 2 Hz, 1 H), 6.55 (dd, \textit{J}_1 = 8.5 Hz, \textit{J}_2 = 2.5 Hz, 1 H), 6.01 (s, 1 H), 5.75 (s, 2 H), 4.11-3.98 (m, 6 H), 3.63 (s, 3 H), 2.48 (brs, 2 H), 1.14-1.08 (m, 6 H). \(^{13}\)C NMR (125 MHz, Acetone-\textit{d}_6): \delta 157.1, 155.1, 131.7, 129.9, 121.2, 112.2, 111.6, 102.6, 62.6, 55.9, 48.7, 35.7, 14.8. HRMS (ESI): \textit{m}/\textit{z} caleed for \textit{C}_{20}\text{H}_{25}\text{N}_3\text{O}_5\text{Na}: 410.16919;
Found: 410.16773.

diisopropyl-1-(2-(5-methoxy-1H-indol-2-yl)cyclopent-3-enyl)hydrazine-1,2-dicarboxylate (3j)

**Yield:** 38 mg, 61% as colourless viscous liquid. $R_f : 0.25$ (7:3 hexane/ethyl acetate). 

**IR (neat)** $\nu_{\text{max}}$: 3325, 2918, 1716, 1589, 1466, 1157, 1061, 966 cm$^{-1}$. H NMR (500 MHz, Acetone-$d_6$): $\delta$ 10.14 (brs, 1 H), 8.58-8.42 (m, 1 H), 7.19 (d, $J = 8.5$ Hz, 1 H), 6.98 (d, $J = 5$ Hz, 1 H), 6.68 (dd, $J_1 = 9$ Hz, $J_2 = 2.5$ Hz, 1 H), 6.14 (s, 1 H), 5.89 (s, 2 H), 5.17-4.94 (m, 1 H), 4.93-4.87 (m, 2 H), 4.13 (brs, 3 H), 3.77 (s, 3 H), 2.61 (brs, 2 H), 1.35-1.09 (m, 12 H).

**13C NMR** (125 MHz, Acetone-$d_6$): $\delta$ 155.1, 131.7, 130.5, 129.7, 128.5, 126.7, 112.3, 110.8, 100.9, 70.8, 55.7, 48.4, 22.4.

**HRMS (ESI):** $m/z$ calcd for C$_{22}$H$_{29}$N$_3$O$_5$Na: 438.20049; Found: 438.19815.

**di-tert-butyl-1-(2-(5-methoxy-1H-indol-2-yl)cyclopent-3-enyl)hydrazine-1,2-dicarboxylate (3k)**

**Yield:** 36 mg, 60% as yellow viscous liquid. $R_f : 0.70$ (7:3 hexane/ethyl acetate).

**IR (neat)** $\nu_{\text{max}}$: 3381, 2977, 2933, 1712, 1588, 1454, 1252, 1112, 965 cm$^{-1}$. H NMR (500 MHz, CDCl$_3$): $\delta$ 9.91 (brs, 1 H), 7.25-7.22 (m, 1 H), 7.01 (s, 1 H), 6.76 (d, $J = 9$ Hz, 1 H), 6.38 (s, 1 H), 6.13 (s, 1 H), 5.92-5.85 (m, 2 H), 4.62 (s, 1 H), 4.05 (s, 1 H), 3.83 (s, 3 H), 2.53 (brs, 2 H), 1.54-1.43 (m, 18 H).

**13C NMR** (125 MHz, CDCl$_3$): $\delta$ 155.6, 153.7, 128.9, 124.3, 114.8, 113.5, 107.1, 103.0, 81.7, 55.8, 47.6, 31.0.

**HRMS (ESI):** $m/z$ calcd for C$_{24}$H$_{33}$N$_3$O$_5$Na: 466.23179; Found: 466.23260.

**diethyl-1-(2-(5-methyl-1H-indol-2-yl)cyclopent-3-enyl)hydrazine-1,2-dicarboxylate (3l)**

**Yield:** 44 mg, 71% as yellow viscous liquid. $R_f : 0.53$ (7:3 hexane/ethyl acetate). 

**IR (neat)** $\nu_{\text{max}}$: 3299, 2983, 2934, 2864, 1699, 1589, 1489, 1452, 1416, 1325, 1270, 1127, 1066, 952 cm$^{-1}$. H NMR (500 MHz, Acetone-$d_6$): $\delta$ 10.15-9.84 (m, 1 H), 8.76-8.40 (m, 1 H), 7.21 (d, $J = 8$ Hz, 1 H), 6.87 (d, $J = 8.5$ Hz, 1 H), 6.14 (s, 1 H), 5.89 (s, 2 H), 4.93 (brs, 1 H), 4.24-3.96 (m, 5 H), 2.63 (brs, 2 H), 2.37 (s, 3 H), 1.29-0.82 (m, 6 H).

**13C NMR** (125 MHz, Acetone-$d_6$): $\delta$ 156.5, 131.6, 130.7, 128.1, 122.9, 120.0, 111.1, 62.8, 46.7, 35.6, 21.4, 14.7.

**HRMS (ESI):** $m/z$ calcd for C$_{20}$H$_{25}$N$_3$O$_5$Na: 394.17428; Found: 394.17253.

**diisopropyl-1-(2-(5-methyl-1H-indol-2-yl)cyclopent-3-enyl)hydrazine-1,2-dicarboxylate (3m)**

**Yield:** 43 mg, 73% as yellow viscous liquid. $R_f : 0.53$ (7:3 hexane/ethyl acetate).

**IR (neat)** $\nu_{\text{max}}$: 3325, 2918, 1716, 1589, 1466, 1157, 1061, 966 cm$^{-1}$. H NMR (500 MHz, Acetone-$d_6$): $\delta$ 10.14 (brs, 1 H), 8.58-8.42 (m, 1 H), 7.19 (d, $J = 8.5$ Hz, 1 H), 6.98 (d, $J = 5$ Hz, 1 H), 6.68 (dd, $J_1 = 9$ Hz, $J_2 = 2.5$ Hz, 1 H), 6.14 (s, 1 H), 5.89 (s, 2 H), 5.17-4.94 (m, 1 H), 4.93-4.87 (m, 2 H), 4.13 (brs, 3 H), 3.77 (s, 3 H), 2.61 (brs, 2 H), 1.35-1.09 (m, 12 H).

**13C NMR** (125 MHz, Acetone-$d_6$): $\delta$ 155.1, 131.7, 130.5, 129.7, 128.5, 126.7, 112.3, 110.8, 100.9, 70.8, 55.7, 48.4, 22.4.

**HRMS (ESI):** $m/z$ calcd for C$_{22}$H$_{29}$N$_3$O$_5$Na: 438.20049; Found: 438.19815.
acetate). IR (neat) $\nu_{\text{max}}$: 3301, 2982, 1713, 1592, 1496, 1409, 1179, 1143, 1108, 1042 cm$^{-1}$. $^1$H NMR (500 MHz, CD$_3$CN): $\delta$ 9.97-9.95 (m, 1 H), 7.52 (brs, 1 H), 7.29 (s, 1 H), 7.26-7.7.15 (m, 1 H), 6.89 (d, $J = 8$ Hz, 1 H), 6.11 (s, 1 H), 5.88 (s, 1 H), 5.24-4.76 (m, 5 H), 4.06 (brs, 1 H), 2.63-2.53 (m, 2 H), 2.37 (s, 3 H), 1.28-1.21 (m, 6 H). $^{13}$C NMR (125 MHz, CD$_3$CN): $\delta$ 156.3, 154.7, 130.0, 127.9, 126.7, 128.8, 121.8, 117.0, 109.9, 99.5, 69.6, 43.5, 34.3, 20.9. HRMS (ESI): $m/z$ calced for C$_{22}$H$_{29}$N$_3$O$_4$Na: 422.20558; Found: 422.20508.

diethyl-1-(2-(5-fluoro-1H-indol-2-yl)cyclopent-3-enyl)hydrazine-1,2-dicarboxylate (3n)

Yield: 46 mg, 74% as yellow viscous liquid. $R_f$: 0.48 (7:3 hexane/ethyl acetate). IR (neat) $\nu_{\text{max}}$: 3289, 2983, 1714, 1533, 1254, 1062, 1016, 966 cm$^{-1}$. $^1$H NMR (500 MHz, CD$_3$CN): $\delta$ 10.35 (brs, 1 H), 8.77 (brs, 1 H), 7.34-7.29 (m, 1 H), 7.18-7.15 (m, 1 H), 6.83 (dt, $J_1 = 9.5$ Hz, $J_2 = 2.5$ Hz, 1 H), 6.24 (s, 1 H), 5.91 (s, 2 H), 4.93 (brs, 1 H), 4.24-4.04 (m, 5 H), 2.63 (brs, 2 H), 1.29-1.19 (m, 6 H). $^{13}$C NMR (125 MHz, CD$_3$CN): $\delta$ 159.2, 157.5, 133.7, 131.1, 129.9, 128.8, 125.9, 112.3, 109.1, 105.0, 62.7, 46.7, 35.7, 14.8. HRMS (ESI): $m/z$ calced for C$_{19}$H$_{22}$FN$_3$O$_4$Na: 398.14920; Found: 398.14769.

diisopropyl-1-(2-(5-fluoro-1H-indol-2-yl)cyclopent-3-enyl)hydrazine-1,2-dicarboxylate (3o)

Yield: 42 mg, 60% as yellow viscous liquid. $R_f$: 0.70 (7:3 hexane/ethyl acetate). IR (neat) $\nu_{\text{max}}$: 3314, 2981, 2922, 2851, 1716, 1485, 1381, 1287, 1230, 1164, 1132, 1059, 1032, 870, 761 cm$^{-1}$. $^1$H NMR (500 MHz, CD$_3$CN): $\delta$ 10.16 (brs, 1 H), 7.64 (s, 1 H), 7.27 (d, $J = 8.5$ Hz, 1 H), 6.51 (brs, 1 H), 6.21 (s, 1 H), 5.90-5.87 (m, 1 H), 4.08 (brs, 1 H), 2.53 (brs, 2 H), 1.29-1.17 (m, 6 H). $^{13}$C NMR (125 MHz, CD$_3$CN): $\delta$ 156.2, 131.2, 130.1, 129.7, 129.2, 128.4, 118.3, 112.3, 109.2, 105.1, 70.9, 46.4, 35.3, 21.9. HRMS (ESI): $m/z$ calced for C$_{21}$H$_{26}$FN$_3$O$_4$Na: 426.18050; Found: 426.18013.

diethyl-1-(2-(5-bromo-1H-indol-2-yl)cyclopent-3-enyl)hydrazine-1,2-dicarboxylate (3p)

Yield: 54 mg, 60% as yellow viscous liquid. $R_f$: 0.73 (7:3 hexane/ethyl acetate). IR (neat) $\nu_{\text{max}}$: 3229, 2983, 1711, 1576, 1469, 1404, 1376, 1115, 1057, 1018 cm$^{-1}$. $^1$H NMR (500 MHz, CD$_3$CN): $\delta$ 10.18 (brs, 1 H), 7.64 (s, 1 H), 7.27 (d, $J = 8.5$ Hz, 1 H), 7.16 (d, $J = 10.8$ Hz, 1 H), 6.51 (brs, 1 H), 6.21 (s, 1 H), 5.90-5.87 (m, 2 H), 4.85-4.77 (m, 1 H), 4.21-4.08 (m, 5 H), 2.55 (brs, 2 H), 1.28-1.21 (m, 6 H). $^{13}$C NMR (125 MHz, CD$_3$CN): $\delta$
diisopropyl-1-(2-(3-methyl-1H-indol-2-yl)cyclopent-3-enyl)hydrazine-1,2-dicarboxylate (3q)

Yield: 36 mg, 60% as yellow viscous liquid. Rf: 0.55 (7:3 hexane/ethyl acetate). IR (neat) νmax: 3296, 2977, 2929, 1706, 1584, 1521, 1455, 1392, 1368, 1253, 1156, 1052, 854, 755 cm\(^{-1}\). \(^1\)H NMR (500 MHz, Acetone-\(d_6\)):\ δ 9.80 (brs, 1 H), 8.17 (brs, 1 H), 7.44 (d, \(J = 7.5\) Hz, 1 H), 7.23-7.22 (m, 1 H), 6.57 (s, 1 H), 5.88-5.79 (m, 2 H), 5.10-4.86 (m, 2 H), 4.29 (s, 1 H), 2.6 (brs, 2 H), 2.28 (s, 3 H), 1.49-1.29 (m, 12 H). \(^13\)C NMR (125 MHz, Acetone-\(d_6\)):\ δ 155.2, 129.7, 129.1, 126.2, 121.3, 118.9, 111.1, 100.4, 70.5, 65.6, 48.2, 35.7, 21.9, 9.0. HRMS (ESI): \(m/z\) calcd for C\(_{22}\)H\(_{29}\)N\(_3\)O\(_4\)Na: 422.20558; Found: 422.20510.

diisopropyl-1-(2-(3-formyl-1H-indol-2-yl)cyclopent-3-enyl)hydrazine-1,2-dicarboxylate (3r)

Yield: 41 mg, 67% as yellow viscous liquid. Rf: 0.30 (7:3 hexane/ethyl acetate). IR (neat) νmax: 3299, 2983, 2934, 2864, 1699, 1589, 1489, 1452, 1325, 1270, 1127, 1066, 952 cm\(^{-1}\). \(^1\)H NMR (500 MHz, CDCl\(_3\)):\ δ 11.06, 10.04 (s, 1 H), 9.29 (s, 1 H), 8.31-8.29 (m, 1 H), 7.44-7.42 (m, 1 H), 7.31-7.29 (m, 2 H), 6.69 (s, 1 H), 6.09 (t, \(J = 3\) Hz, 1 H), 5.87-5.86 (m, 1 H), 5.49 (d, \(J = 7.5\) Hz, 1 H), 5.00-4.45 (m, 2 H), 4.55 (brs, 1 H), 2.69-2.56 (m, 2 H), 1.29-1.25 (m, 12 H). \(^13\)C NMR (125 MHz, CDCl\(_3\)):\ δ 184.9, 155.2, 135.2, 127.9, 124.5, 124.1, 122.7, 121.7, 119.5, 111.5, 99.8, 57.9, 30.6, 29.8, 21.9. HRMS (ESI): \(m/z\) calcd for C\(_{22}\)H\(_{27}\)N\(_3\)O\(_5\)Na: 436.18484; Found: 436.18499.

diethyl-5-(1H-indol-2-yl)-2,3-diazabicyclo[2.2.1]heptane-2,3-dicarboxylate (5a)

Yield: 76 mg, 64% as reddish brown viscous liquid; Rf: 0.28 (hexane/ethyl acetate = 7:3). IR (neat) νmax: 3333, 3054, 2982, 2911, 1713, 1618, 1459, 1402, 1374, 1323, 1171 cm\(^{-1}\). \(^1\)H NMR (500 MHz, CDCl\(_3\)):\ δ 8.88-8.41 (m, 1 H), 7.53 (d, \(J = 8.0\) Hz, 1 H), 7.33 (d, \(J = 8.0\) Hz, 1 H), 7.15 (t, \(J = 7.0\) Hz, 1 H), 7.07 (t, \(J = 7.0\) Hz, 1 H), 6.21 (s, 1 H), 4.73-4.61 (m, 2 H), 4.27 (m, 4 H), 3.40 (brs, 1 H), 2.36-2.26 (m, 1 H), 2.11 (brs, 1 H), 1.92-1.90 (m, 1 H), 1.72 (brs, 1 H), 1.33-1.24 (m, 6 H). \(^13\)C NMR (125 MHz, CDCl\(_3\)):\ δ 157.7, 139.3, 136.4, 128.1, 121.8, 120.0, 119.8, 110.8, 99.2, 64.4, 62.8, 60.2, 39.5, 35.6, 14.5. HRMS (ESI): \(m/z\) calcd for C\(_{19}\)H\(_{23}\)N\(_3\)O\(_4\)Na: 380.15863; Found: 380.16012.
diisopropyl-5-(1H-indol-2-yl)-2,3-diazabicyclo[2.2.1]heptane-2,3-dicarboxylate (5b)

Yield: 67 mg, 58% as pale brown viscous liquid; Rf: 0.42 (hexane/ethyl acetate = 7:3). 1H NMR (500 MHz, CDCl3): δ 9.30-8.75 (m, 1 H), 7.48 (d, J = 8.0 Hz, 1 H), 7.30 (s, 1 H), 7.10 (t, J = 7.5 Hz, 1 H), 7.03 (t, J = 7.5 Hz, 1 H), 6.15 (s, 1 H), 5.03 (brs, 2 H), 4.72 (brs, 1 H), 4.56 (brs, 1 H), 3.52-3.39 (m, 1 H), 2.34-2.14 (m, 2 H), 1.90-1.88 (m, 1 H), 1.67-1.60 (m, 1 H), 1.31-1.17 (m, 12 H). 13C NMR (125 MHz, CDCl3): δ 157.3, 139.6, 136.5, 128.1, 121.6, 119.9, 119.7, 111.0, 98.7, 70.5, 64.9, 64.3, 59.9, 39.1, 35.6, 22.1, 21.9. HRMS (ESI): m/z calcd for C21H27N3O4Na: 408.18993; Found: 408.18894.

di-tert-butyl-5-(1H-indol-2-yl)-2,3-diazabicyclo[2.2.1]heptane-2,3-dicarboxylate (5c)

Yield: 57 mg, 51% as pale brown viscous liquid; Rf: 0.50 (hexane/ethyl acetate = 7:3). 1H NMR (500 MHz, CDCl3): δ 9.37-8.27 (m, 1 H), 7.49 (d, J = 7.5 Hz, 1 H), 7.34-7.28 (m, 1 H), 7.11 (t, J = 7.5 Hz, 1 H), 7.03 (t, J = 7.5 Hz, 1 H), 6.16 (s, 1 H), 4.72-4.66 (m, 1 H), 4.51 (brs, 1 H), 3.53-3.44 (m, 1 H), 2.39-2.16 (m, 2 H), 1.85 (brs, 1 H), 1.64 (brs, 1 H), 1.55-1.47 (m, 15 H), 1.29-1.26 (m, 3 H). 13C NMR (125 MHz, CDCl3): δ 156.8, 139.7, 136.5, 129.0, 128.2, 125.3, 121.7, 120.0, 119.7, 110.7, 99.7, 81.6, 64.8, 64.1, 60.0, 39.2, 35.4, 28.4, 28.2. HRMS (ESI): m/z calcd for C23H31N3O4Na: 436.22123; Found: 436.22126.

dibenzyl-5-(1H-indol-2-yl)-2,3-diazabicyclo[2.2.1]heptane-2,3-dicarboxylate (5d)

Yield: 52 mg, 49% as pale yellow viscous liquid; Rf: 0.50 (hexane/ethyl acetate = 7:3). 1H NMR (500 MHz, CDCl3): δ 8.81-8.36 (m, 1 H), 7.47 (d, J = 7.5 Hz, 1 H), 7.30 (m, 11 H), 7.09 (t, J = 7.0 Hz, 1 H), 7.03 (t, J = 7.0 Hz, 1 H), 6.11 (s, 1 H), 5.18-5.07 (m, 4 H), 4.69-4.59 (m, 2 H), 3.47-3.29 (m, 1 H), 2.26-2.21 (m, 1 H), 2.03 (brs, 1 H), 1.86-1.84 (m, 1 H), 1.66 (brs, 1 H). 13C NMR (125 MHz, CDCl3): δ 157.5, 138.9, 135.8, 128.6, 128.3, 128.1, 121.8, 120.0, 119.8, 110.8, 99.1, 68.2, 65.1, 60.3, 39.4, 35.6. HRMS (ESI): m/z calcd for C29H27N3O4Na: 504.18909; Found: 504.18909.
2,4-bis(benzyloxy)-6-(1H-indol-2-yl)-2,4-diazabicyclo[3.2.1]octan-3-one (5e)

Yield: 86 mg, 80% as colourless viscous liquid; Rf: 0.42 (hexane/ethyl acetate = 3:2). IR (neat) νmax: 3296, 3032, 2979, 2945, 1699, 1545, 1456, 1371, 1274, 1214, 1170, 1078, 1029, 990, 911, 786, 749 cm⁻¹. 1H NMR (500 MHz, CDCl3): δ 8.70-8.65 (m, 1 H), 7.44-7.38 (m, 5 H), 7.33-7.30 (m, 7 H), 7.11-7.08 (m, 1 H), 7.02 (t, J = 7.5 Hz, 1 H), 5.95 (s, 1 H), 5.02-5.00 (m, 2 H), 4.89-4.84 (m, 2 H), 3.77 (s, 1 H), 3.70 (t, J = 4.0 Hz, 1 H), 3.57 (d, J = 4.0 Hz, 1 H), 2.72-2.67 (m, 1 H), 2.06-2.03 (m, 1 H), 1.89-1.86 (m, 1 H), 1.84-1.79 (m, 1 H). 13C NMR (125 MHz, CDCl3): δ 160.8, 140.8, 136.2, 136.1, 136.0, 129.7, 129.6, 128.4, 121.5, 119.8, 119.6, 110.8, 97.6, 77.9, 77.8, 67.9, 62.6, 40.9, 36.4, 32.0. HRMS (ESI): m/z calcd for C28H27N3O3Na: 476.19501; Found: 476.19604.

2,4-bis(benzyloxy)-6-(4-methoxy-1H-indol-2-yl)-2,4-diazabicyclo[3.2.1]octan-3-one (5f)

Yield: 66 mg, 57% as colourless solid (m.p. = 192-194 °C); Rf: 0.36 (hexane/ethyl acetate = 3:2). IR (neat) νmax: 3389, 1649, 1453, 1428, 1391, 1360, 1268, 1241, 1168, 1093, 997, 910, 738, 697 cm⁻¹. 1H NMR (500 MHz, CDCl3): δ 8.42 (s, 1 H), 7.44-7.40 (m, 4 H), 7.34-7.32 (m, 6 H), 7.02 (t, J = 8.0 Hz, 1 H), 6.93 (d, J = 8.5 Hz, 1 H), 6.45 (d, J = 8.0 Hz, 1 H), 6.08 (d, J = 2.0 Hz, 1 H), 5.03-5.01 (m, 2 H), 4.89-4.84 (m, 2 H), 3.90 (s, 3 H), 3.73-3.69 (m, 2 H), 3.55 (d, J = 4.5 Hz, 1 H), 2.71-2.66 (m, 1 H), 2.04-2.01 (m, 1 H), 1.92-1.82 (m, 2 H). 13C NMR (125 MHz, CDCl3): δ 160.7, 152.7, 139.2, 137.4, 136.3, 136.0, 129.7, 129.6, 128.6, 128.5, 128.4, 122.3, 118.6, 104.3, 99.4, 95.0, 77.9, 77.8, 68.0, 62.6, 55.1, 40.9, 36.3, 31.9. HRMS (ESI): m/z calcd for C29H30N3O4: 484.22363; Found: 484.22456.

2,4-bis(benzyloxy)-6-(5-methoxy-1H-indol-2-yl)-2,4-diazabicyclo[3.2.1]octan-3-one (5g)

Yield: 76 mg, 66% as yellow viscous liquid; Rf: 0.37 (hexane/ethyl acetate = 3:2). IR (neat) νmax: 3303, 3063, 3033, 2944, 1697, 1598, 1488, 1455, 1372, 1326, 1268, 1209, 1169, 1030, 912, 739, 700 cm⁻¹. 1H NMR (500 MHz, CDCl3): δ 8.36 (brs, 1 H), 7.36-7.32 (m, 4 H), 7.12 (d, J = 9.0 Hz, 1 H), 6.86 (d, J = 2.5 Hz, 1 H), 6.70 (dd, J1 = 8.5 Hz, J2 = 7.5 Hz, 1 H), 5.84 (t, J = 1.0 Hz, 1 H), 4.95-4.93 (m, 2 H), 4.82-4.77 (m, 2 H), 3.72 (s, 3 H), 3.66-3.63 (m, 2 H), 3.49 (d, J = 4.0 Hz, 1 H), 2.63-2.58 (m, 1 H), 1.98-1.96 (m, 1 H), 1.82-1.72 (m, 2 H). 13C NMR (125 MHz, CDCl3): δ 159.7, 153.1, 140.5, 135.2, 134.9, 130.2, 128.6, 128.5, 127.5, 127.4, 110.5, 100.9, 96.5, 76.9, 76.8, 66.9, 61.5, 54.9, 40.0, 35.3, 31.0. HRMS (ESI): m/z calcd for C29H30N3O4: 484.22363; Found: 484.22291.

S12
2,4-bis(benzyloxy)-6-(5-methyl-1H-indol-2-yl)-2,4-diazabicyclo[3.2.1]octan-3-one (5h)

Yield: 79 mg, 71% as brownish viscous liquid; Rf: 0.45 (hexane/ethyl acetate = 3:2). IR (neat) $\nu_{max}$: 3391, 2929, 2864, 1691, 1455, 1372, 1319, 1267, 1213, 1170, 1028, 992, 911, 784, 740, 700 cm$^{-1}$. $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 8.48 (brs, 1 H), 7.34-7.30 (m, 4 H), 7.25-7.22 (m, 6 H), 7.14-7.11 (m, 2 H), 6.84 (d, $J = 8.0$ Hz, 1 H), 5.79-5.78 (m, 1 H), 4.93-4.91 (m, 2 H), 4.80-4.75 (m, 2 H), 3.68-3.65 (m, 1 H), 3.60 (t, $J = 4.0$ Hz, 1 H), 3.47 (d, $J = 4.0$ Hz, 1 H), 2.62-2.57 (m, 1 H), 2.32 (s, 3 H), 1.96-1.94 (m, 1 H), 1.81-1.76 (m, 1 H), 1.74-1.69 (m, 1 H). $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 160.9, 141.0, 136.3, 136.0, 134.5, 129.7, 129.6, 128.5, 128.4, 128.3, 123.0, 119.5, 110.5, 97.1, 77.9, 77.8, 67.9, 62.7, 41.0, 36.5, 32.1, 21.5. HRMS (ESI): m/z calcd for C$_{29}$H$_{30}$N$_3$O$_3$: 468.22872; Found: 468.22867.

2,4-bis(benzyloxy)-3-oxo-2,4-diazabicyclo[3.2.1]octan-6-yl)-1H-indole-5-carbaldehyde (5i)

Yield: 78 mg, 68% as reddish brown viscous liquid; Rf: 0.34 (hexane/ethyl acetate = 1:1). IR (neat) $\nu_{max}$: 3409, 1677, 1615, 1549, 1488, 1455, 1428, 1374, 1331, 1306, 1267, 1221, 1163, 1114, 1078, 1029, 998, 909, 786, 741, 701 cm$^{-1}$. $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 10.30 (s, 1 H), 9.97 (s, 1 H), 7.97 (s, 1 H), 6.80 (dd, $J_1 = 8.5$ Hz, $J_2 = 1.5$ Hz, 1 H), 7.47 (d, $J = 8.5$ Hz, 1 H), 7.37-7.35 (m, 2 H), 7.31-7.29 (m, 3 H), 7.28-7.26 (m, 2 H), 7.23-7.17 (m, 3 H), 6.04-6.03 (m, 1 H), 4.98-4.96 (m, 1 H), 4.92-4.87 (m, 2 H), 4.82-4.80 (m, 1 H), 3.90 (dd, $J_1 = 9.0$ Hz, $J_2 = 6.0$ Hz, 1 H), 3.79 (s, 1 H), 3.70 (t, $J = 4.0$ Hz, 1 H), 3.62 (d, $J = 4.5$ Hz, 1 H), 2.74-2.69 (m, 1 H), 2.15-2.12 (m, 1 H), 1.97-1.93 (m, 1 H), 1.77-1.72 (m, 1 H). $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 192.5, 161.4, 143.5, 140.0, 135.7, 129.5, 129.4, 128.6, 128.5, 128.4, 128.2, 124.8, 122.2, 111.7, 98.5, 77.8, 77.8, 67.4, 62.8, 40.8, 37.2, 32.4. HRMS (ESI): m/z calcd for C$_{29}$H$_{27}$N$_3$NaO$_4$: 504.18993; Found: 504.19184.

2,4-bis(benzyloxy)-6-(5-fluoro-1H-indol-2-yl)-2,4-diazabicyclo[3.2.1]octan-3-one (5j)

Yield: 78 mg, 70% as reddish brown viscous liquid; Rf: 0.39 (hexane/ethyl acetate = 3:2). IR (neat) $\nu_{max}$: 3433, 1650, 1490, 1454, 1375, 1326, 1269, 1211, 1176, 1113, 1029, 995, 959, 911, 852, 747, 699 cm$^{-1}$. $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 9.24 (brs, 1 H), 7.39-7.37 (m, 2 H), 7.33-7.31 (m, 5 H), 7.26-7.23 (m, 4 H), 7.08-7.06 (m, 1 H), 6.84 (td, $J_1 = 9.0$ Hz, $J_2 = 2.5$ Hz, 1 H), 5.88 (t, $J = 1.0$ Hz, 1 H), 4.99-4.93 (m, 2 H), 4.88-4.80 (m, 2 H), 3.79 (s, 1 H), 3.70 (t, $J = 4.0$ Hz, 1 H), 5.80 (d, $J = 4.0$ Hz, 1 H), 2.70-2.65 (m, 1 H), 2.09-2.06 (m, 1 H), 1.92-1.88 (m, 1 H), 1.92-1.88 (m, 1 H).
1.78-1.73 (m, 1 H). \(^{13}\)C NMR (125 MHz, CDCl \(_3\)): \(\delta\) 161.2, 158.8, 156.9, 142.9, 135.9, 135.8, 132.7, 129.6, 129.5, 128.6, 128.5, 128.4, 128.4, 111.6, 111.5, 109.6, 109.4, 104.6, 104.5, 97.3, 77.8, 67.7, 62.7, 40.9, 36.9, 32.3. HRMS (ESI): m/z calcd for C\(_{28}\)H\(_{26}\)FN\(_3\)NaO\(_3\): 494.18559; Found: 494.18571.

2,4-bis(benzyloxy)-6-(5-chloro-1H-indol-2-yl)-2,4-diazabicyclo[3.2.1]octan-3-one (5k)

Yield: 86 mg, 74% as brownish viscous liquid; R\(_f\): 0.45 (hexane/ethyl acetate = 3:2). IR (neat) \(\nu_{\text{max}}\): 3301, 1696, 1580, 1542, 1496, 1453, 1368, 1315, 1267, 1218, 1169, 1062, 1029, 992, 915, 867, 779, 740, 699 cm\(^{-1}\). \(\text{H NMR (500 MHz, CDCl}_3\): \(\delta\) 9.30 (s, 1 H), 7.41-7.38 (m, 3 H), 7.33-7.31 (m, 5 H), 7.28-7.23 (m, 4 H), 7.06 (dd, \(J_1 = 8.5\) Hz, \(J_2 = 2.0\) Hz, 1 H), 5.88-5.87 (m, 1 H), 4.99-4.93 (m, 2 H), 4.89-4.80 (m, 2 H), 3.80 (dd, \(J_1 = 8.5\) Hz, \(J_2 = 6.0\) Hz, 1 H), 3.72 (t, \(J = 4.0\) Hz, 1 H), 3.57 (d, \(J = 4.5\) Hz, 1 H), 2.70-2.65 (m, 1 H), 2.10-2.07 (m, 1 H), 1.91-1.87 (m, 1 H), 1.78-1.73 (m, 1 H). \(^{13}\)C NMR (125 MHz, CDCl \(_3\)): \(\delta\) 161.1, 142.7, 135.9, 134.5, 129.6, 129.5, 129.3, 128.6, 128.5, 128.5, 112.0, 97.0, 77.9, 77.8, 67.7, 62.7, 40.9, 36.9, 32.2. HRMS (ESI): m/z calcd for C\(_{28}\)H\(_{27}\)ClN\(_3\)O\(_3\): 488.17409; Found: 488.17340.

2,4-bis(benzyloxy)-6-(5-bromo-1H-indol-2-yl)-2,4-diazabicyclo[3.2.1]octan-3-one (5l)

Yield: 99 mg, 78% as brownish viscous liquid; R\(_f\): 0.37 (hexane/ethyl acetate = 3:2). IR (neat) \(\nu_{\text{max}}\): 3279, 3032, 2979, 2944, 1696, 1577, 1540, 1495, 1456, 1373, 1313, 1268, 1214, 1169, 1111, 1078, 1029, 991, 905, 827, 780, 738, 699 cm\(^{-1}\). \(\text{H NMR (500 MHz, CDCl}_3\): \(\delta\) 9.35 (s, 1 H), 7.49 (d, \(J = 2.0\) Hz, 1 H), 7.31-7.29 (m, 2 H), 7.27-7.22 (m, 5 H), 7.19-7.15 (m, 4 H), 7.11-7.09 (m, 1 H), 5.79 (t, \(J = 1.0\) Hz, 1 H), 4.91-4.84 (m, 2 H), 4.80-4.72 (m, 2 H), 3.72 (dd, \(J_1 = 9.0\) Hz, \(J_2 = 6.0\) Hz, 1 H), 3.63 (t, \(J = 4.0\) Hz, 1 H), 3.49 (d, \(J = 4.0\) Hz, 1 H), 2.62-2.57 (m, 1 H), 2.02-1.99 (m, 1 H), 1.83-1.77 (m, 1 H), 1.68-1.64 (m, 1 H). \(^{13}\)C NMR (125 MHz, CDCl \(_3\)): \(\delta\) 161.1, 142.6, 135.9, 134.8, 130.0, 129.6, 129.5, 128.6, 128.6, 128.5, 128.5, 122.0, 112.6, 112.5, 96.8, 77.9, 77.8, 67.6, 62.7, 40.9, 36.9, 32.3. HRMS (ESI): m/z calcd for C\(_{28}\)H\(_{26}\)BrN\(_3\)O\(_3\): 554.10552; Found: 554.10531.

2-(-2,4-bis(benzyloxy)-3-oxo-2,4-diazabicyclo[3.2.1]octan-6-yl)-1H-indole-5-carbonitrile (5m)

Yield: 77 mg, 68% as pale yellow viscous liquid; R\(_f\): 0.39 (hexane/ethyl acetate = 1:1). IR (neat) \(\nu_{\text{max}}\): 3303, 1645, 1455, 1372, 1321, 1268, 1214,
2,4-bis(benzyloxy)-6-(5-nitro-1H-indol-2-yl)-2,4-diazabicyclo[3.2.1]octan-3-one (5n)

Yield: 89 mg, 75% as pale yellow solid (m.p. = 185-187 °C); \( R_f \): 0.43 (hexane/ethyl acetate = 1:1). \(^1\)H NMR (500 MHz, CDCl\(_3\)): \( \delta 10.04 \) (brs, 1 H), 7.71 (s, 1 H), 7.36-7.34 (m, 1 H), 7.30-7.22 (m, 6 H), 7.21-7.19 (m, 2 H), 7.17-7.12 (m, 3 H), 5.90 (s, 1 H), 4.91-4.89 (m, 1 H), 4.85-4.80 (m, 2 H), 4.75-4.72 (m, 1 H), 3.80 (dd, \( J_1 = 8.5 \text{ Hz}, J_2 = 6.0 \text{ Hz}, 1 \text{ H} \)), 3.67 (t, \( J = 4.0 \text{ Hz}, 1 \text{ H} \)), 3.52 (d, \( J = 4.5 \text{ Hz}, 1 \text{ H} \)), 2.67-2.61 (m, 1 H), 2.08-2.06 (m, 1 H), 1.88-1.84 (m, 1 H), 1.69-1.64 (m, 1 H). \(^{13}\)C NMR (125 MHz, CDCl\(_3\)): \( \delta 160.3, 142.7, 137.0, 134.5, 128.4, 128.3, 127.6, 127.5, 127.4, 127.0, 124.1, 123.3, 119.8, 110.9, 101.4, 96.5, 76.8, 66.3, 61.6, 39.7, 36.2, 31.3. \)

HRMS (ESI): \( m/z \) calcd for C\(_{29}\)H\(_{26}\)N\(_4\)NaO\(_3\): 501.19026; Found: 501.19153.

2,4-bis(benzyloxy)-6-(5-hydroxy-1H-indol-2-yl)-2,4-diazabicyclo[3.2.1]octan-3-one (5o)

Yield: 45 mg, 40% as light brown viscous liquid; \( R_f \): 0.29 (hexane/ethyl acetate = 1:1). \(^1\)H NMR (500 MHz, CDCl\(_3\)): \( \delta 7.97 \) (brs, 1 H), 7.44-7.43 (m, 4 H), 7.37-7.34 (m, 6 H), 7.08 (d, \( J = 8.5 \text{ Hz}, 1 \text{ H} \)), 6.85 (d, \( J = 2.5 \text{ Hz}, 1 \text{ H} \)), 6.67 (dd, \( J_1 = 9.0 \text{ Hz}, J_2 = 2.5 \text{ Hz}, 1 \text{ H} \)), 5.85 (s, 1 H), 5.07-5.01 (m, 2 H), 4.89-4.86 (m, 2 H), 3.69 (t, \( J = 4.0 \text{ Hz}, 1 \text{ H} \)), 3.65 (d, \( J = 9.0 \text{ Hz}, J_2 = 6.0 \text{ Hz}, 1 \text{ H} \)), 3.54 (d, \( J = 4.5 \text{ Hz}, 1 \text{ H} \)), 2.70-2.64 (m, 1 H), 2.04-2.01 (m, 1 H), 1.86-1.80 (m, 2 H). \(^{13}\)C NMR (125 MHz, CDCl\(_3\)): \( \delta 160.6, 149.7, 141.4, 136.3, 136.0, 131.2, 129.7, 129.6, 128.6, 128.5, 129.4, 129.3, 128.7, 128.6, 128.4, 128.7, 117.1, 116.9, 110.9, 99.0, 77.9, 77.8, 67.3, 62.7, 40.8, 37.3, 32.4. \)

HRMS (ESI): \( m/z \) calcd for C\(_{28}\)H\(_{27}\)N\(_3\)O\(_4\)Na: 492.18993; Found: 492.19013.
6-(5-amino-1H-indol-2-yl)-2,4-bis(benzyloxy)-2,4-diazabicyclo[3.2.1]octan-3-one (5p)

Yield: 61 mg, 55% as brownish viscous liquid; Rf: 0.29 (hexane/ethyl acetate = 3:7). IR (neat) νmax: 3617, 3248, 1651, 1425, 1266, 1027, 781, 732 cm⁻¹. ¹H NMR (500 MHz, CDCl₃): δ 8.10 (s, 1 H), 7.45-7.43 (m, 4 H), 7.36-7.34 (m, 6 H), 7.06 (d, J = 8.5 Hz, 1 H), 6.79 (d, J = 2.0 Hz, 1 H), 5.80 (dd, J₁ = 8.5 Hz, J₂ = 2.0 Hz, 1 H), 5.82 (t, J = 1.0 Hz, 1 H), 5.06-5.01 (m, 2 H), 4.89-4.86 (m, 2 H), 3.71 (t, J = 4.0 Hz, 1 H), 3.66 (dd, J₁ = 8.5 Hz, J₂ = 5.5 Hz, 1 H), 3.55 (dd, J = 9.0 Hz, 1 H), 3.25 (brs, 2 H), 2.69-2.63 (m, 1 H), 2.04-2.02 (m, 1 H), 1.87-1.80 (m, 2 H).

¹³C NMR (125 MHz, CDCl₃): δ 160.6, 150.4, 141.2, 138.7, 136.3, 136.0, 131.0, 129.7, 129.6, 129.0, 128.6, 128.4, 112.6, 111.2, 105.5, 97.2, 78.0, 77.9, 68.0, 62.5, 41.1, 36.1, 32.0. HRMS (ESI): m/z calcld for C₂₈H₂₉N₄O₃: 469.22397; Found: 469.22344.

6-(benzofuran-2-yl)-2,4-bis(benzyloxy)-2,4-diazabicyclo[3.2.1]octan-3-one (5q)

Yield: 52 mg, 48% as pale yellow viscous liquid; Rf: 0.50 (hexane/ethyl acetate = 3:2). IR (neat) νmax: 2923, 2851, 1643, 1457, 1364, 1266, 1210, 1166, 914, 749, 702 cm⁻¹. ¹H NMR (500 MHz, CDCl₃): δ 7.47-7.42 (m, 5 H), 7.38-7.31 (m, 7 H), 7.21-7.13 (m, 2 H), 6.31 (s, 1 H), 5.08-5.03 (m, 2 H), 4.90-4.86 (m, 2 H), 3.87 (dd, J₁ = 9.0 Hz, J₂ = 5.5 Hz, 1 H), 3.72-3.70 (m, 2 H), 2.71-2.66 (m, 1 H), 2.12-2.09 (m, 1 H), 2.04-1.99 (m, 1 H), 1.94-1.89 (m, 1 H).

¹³C NMR (125 MHz, CDCl₃): δ 160.6, 158.6, 154.7, 136.2, 136.1, 129.6, 129.4, 128.4, 128.4, 123.8, 122.7, 120.5, 110.9, 102.2, 77.8, 77.8, 67.0, 62.7, 40.9, 34.9, 32.6. HRMS (ESI): m/z calcld for C₂₈H₂₆N₂NaO₄: 477.17903; Found: 477.17776.

2,4-bis(benzyloxy)-6-(1H-pyrrol-2-yl)-2,4-diazabicyclo[3.2.1]octan-3-one (5r)

Yield: 51 mg, 53% as light brown viscous liquid; Rf: 0.39 (hexane/ethyl acetate = 3:2). IR (neat) νmax: 3272, 1653, 1498, 1454, 1374, 1264, 1214, 1166, 1028, 784, 728 cm⁻¹. ¹H NMR (500 MHz, CDCl₃): δ 8.25 (brs, 1 H), 7.35-7.34 (m, 4 H), 7.29-7.23 (m, 6 H), 6.53-6.52 (m, 1 H), 5.93 (q, J = 3.0 Hz, 1 H), 5.59 (s, 1 H), 4.95-4.91 (m, 2 H), 4.79-4.75 (m, 2 H), 3.59 (t, J = 4.0 Hz, 1 H), 3.55-3.52 (m, 1 H), 3.39 (dd, J = 4.5 Hz, 1 H), 2.59-2.54 (m, 1 H), 1.93-1.91 (m, 1 H), 1.78-1.74 (m, 1 H), 1.69-1.64 (m, 1 H).

¹³C NMR (125 MHz, CDCl₃): δ 160.7, 136.3, 136.1, 133.7, 129.6, 129.5, 128.5, 128.4, 117.1, 108.0, 103.6, 77.8, 77.8, 68.2, 62.5, 40.5, 36.4, 31.8. HRMS (ESI): m/z calcld for C₂₄H₂₅N₃NaO₃: 426.17936; Found: 426.17895.
References

1H NMR of 3a

13C NMR of 3a
$^1$H NMR of 3c

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

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

$^{13}$C NMR of 3f
\[ \text{\(1^H\) NMR of 3h} \]

\[ \text{\(13^C\) NMR of 3h} \]
$^1$H NMR of 3i

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

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

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

$^{13}$C NMR of 3m
\textbf{\textsuperscript{1}H NMR of 3n}

\textbf{\textsuperscript{13}C NMR of 3n}
$^{1}H$ NMR of 3o

$^{13}C$ NMR of 3o
$^1$H NMR of 3q

$^{13}$C NMR of 3q
$^1$H NMR of 3r

$^{13}$C NMR of 3r
$^{1}$H NMR of compound 5a

$^{13}$C NMR of compound 5a
\[ 1^H \text{ NMR of compound 5b} \]

\[ 13^C \text{ NMR of compound 5b} \]

S37
$^1$H NMR of compound 5c

$^{13}$C NMR of compound 5c
$^{1}H$ NMR of compound 5d

$^{13}C$ NMR of compound 5d
$^1$H NMR of compound 5e

$^{13}$C NMR of compound 5e
$^{1}$H NMR of compound 5f

$^{13}$C NMR of compound 5f
$^{1}H$ NMR of compound 5g

$^{13}C$ NMR of compound 5g
$\text{H NMR of compound 5h}$

$\text{13C NMR of compound 5h}$
$^1$H NMR of compound 5i

$^{13}$C NMR of compound 5i
$^{1}H$ NMR of compound 5j

$^{13}C$ NMR of compound 5j
$^{1}$H NMR of compound 5k

$^{13}$C NMR of compound 5k
$^1$H NMR of compound 5l

$^{13}$C NMR of compound 5l
\[ \text{\textsuperscript{1}H NMR of compound 5m} \]

\[
\begin{align*}
\text{\textsuperscript{13}C NMR of compound 5m}
\end{align*}
\]
$\text{O}_2\text{N}$

\begin{align*}
\text{O}_2\text{N} & \quad \text{OBn} \\
\text{BnO} & \quad \text{N} \\
\text{H} & \quad \text{O}_2\text{N}
\end{align*}

$5n$

**$^1H$ NMR of compound $5n$**

**$^{13}C$ NMR of compound $5n$**

549
$^{1}\text{H NMR of compound 5o}$

$^{13}\text{C NMR of compound 5o}$
\(^1\)H NMR of compound 5p

\(^{13}\)C NMR of compound 5p
$^1$H NMR of compound 5q

$^{13}$C NMR of compound 5q
$^1$H NMR of compound 5r

$^{13}$C NMR of compound 5r
Single Crystal X-ray Structure of 5n