Supporting Information

C3-Hetero-functionalization of Indole Derivatives via Facilitated Indolyl 1,3-Heteroatom Transposition
Yujin Lee, Yun Seung Nam, Soo Young Kim, Jeong Eun Ki and Hong Geun Lee*

Department of Chemistry, College of Natural Science, Seoul National University,1 Gwanak-ro, Gwanak-gu, Seoul 08826, Republic of Korea
*hglee@snu.ac.kr

Table of Contents

1. General Information ................................................................................................................................. 4
2. Preparation of Starting Materials ............................................................................................................... 6
  2.1. Preparation of Indole Derivatives ......................................................................................................... 7
  2.2. Preparation of Indoline Derivatives ................................................................................................... 12
  2.3. Preparation of N-Hydroxyindole Derivatives .................................................................................... 27
3. Mechanistic Investigations ......................................................................................................................... 40
  3.1. Identification of 2'-Substituent Effect in the Facilitated IHT Reaction (Scheme 1) .................. 40
  3.2. 18O Isotope Experiment (Figure 3) .................................................................................................. 45
    3.2.1. Preparation of 18O Labeled Compounds ...................................................................................... 46
    3.2.1.1. Benzoyl substituent .................................................................................................................. 46
    3.2.1.2. 3-Bromo-4-fluorobenzoyl substituent ...................................................................................... 51
    3.2.1.3. Pentafluorobenzoyl substituent ............................................................................................... 58
    3.2.1.4. Bromotryptamine with benzoyl substituent ........................................................................... 63
    3.2.1.5. Bromotryptamine with 3-bromo-4-fluorobenzoyl substituent ............................................ 67
    3.2.2. Determination of 18O Saturation ................................................................................................. 72
    3.2.3. Quantitative Analysis of 18O-Labeling Experiment Results (Figures 4 and 5) .................. 96
      3.2.3.1. Dependence of the electronic properties (Figure 4) ............................................................ 96
      3.2.3.2. The influence of electronic properties of the indole backbone (Figure 5) ...................... 101
3.3. Crossover Experiment (Figure 6A) ........................................................................................................104
  3.3.1. Preparation of Compound 2b-Int and 2b'-Int ..................................................................................104
  3.3.2. Preparation of Crossover Products .................................................................................................106
  3.3.3. Crossover Experiment .....................................................................................................................108
  3.3.4. Analysis of Crossover Experiment Results .....................................................................................110
    3.3.4.1. TLC analysis of the crossover experiment .................................................................................110
    3.3.4.2. HRMS/HPLC analysis of the crossover experiment .................................................................111
3.4. Radical-trapping Experiment (Figure 6B) ..........................................................................................113
  3.4.1. Radical-trapping Experiment with Indolyl N-Carboxylate 2b-Int ..................................................113
    3.4.1.1. HRMS results using TEMPO as a radical scavenger ..............................................................114
    3.4.1.2. HRMS results using 1,1-diphenylethylene as a radical scavenger ........................................115
  3.4.2. Radical-trapping Experiment with Electron-deficient Indolyl N-Carboxylate ..............................116
    3.4.2.1. Instability of 1a in the presence of TEMPO .............................................................................117
    3.4.2.2. HRMS results using 1,1-diphenylethylene as a radical scavenger ........................................118
3.5. IHT Reaction of Indolyl N-Carbamates (Figure 7) ..........................................................................119
  3.5.1. Preparation of Indolyl N-Carbamates ............................................................................................119
  3.5.2. IHT Reaction of Indolyl N-Carbamate 2g-Int ...............................................................................120
4. C–O Bond Formation via Indolyl 1,3-Heteroatom Transposition (IHT) ..........................................121
  4.1. Optimization of the C3-Acylxylation Conditions ............................................................................121
  4.2. General Procedures for C3-Acylxylation of Indole Derivatives (Scheme 2) .................................122
5. C–N Bond Formation via Indolyl 1,3-Heteroatom Transposition (IHT) ..........................................131
  5.1. Optimization of the C3-Amidation Reaction Conditions .................................................................131
  5.2. Preparation of Trifluoroacetimidoyl Chlorides ................................................................................135
  5.3. General Procedure for C3-Amidation of Indole Derivatives (Scheme 3) .......................................136
  5.4. Evaluation of Practicality and Versatility of the C3-Amidation (Scheme 4) ....................................157
<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>5.4.1. Gram-scale Reaction</td>
<td>157</td>
</tr>
<tr>
<td>5.4.2. Conversion to the 3-Aminopyrroloindoline</td>
<td>158</td>
</tr>
<tr>
<td>5.4.3. Formal Synthesis of Psychotriasine</td>
<td>159</td>
</tr>
<tr>
<td>6. Abbreviations</td>
<td>162</td>
</tr>
<tr>
<td>7. References</td>
<td>164</td>
</tr>
<tr>
<td>8. NMR Spectra</td>
<td>165</td>
</tr>
</tbody>
</table>
1. General Information

Reactions were performed in oven-dried or flame-dried glassware under N\textsubscript{2} atmosphere with dry solvents under anhydrous conditions, unless otherwise stated. Tetrahydrofuran (THF) and dichloromethane (CH\textsubscript{2}Cl\textsubscript{2}) were initially degassed by sonication, and subsequently dried by passing them through a PureSolv solvent purification system and toluene was dried over CaH\textsubscript{2} and distilled under N\textsubscript{2} atmosphere. N,N-Dimethylformamide (DMF), dimethyl sulfoxide (DMSO), 1,2-dichloroethane (DCE), acetonitrile (MeCN), and 1,4-dioxane were purchased in anhydrous form from a commercial source (Sigma-Aldrich). Nitromethane was dried over molecular sieves (4 Å) and degassed prior to use. Acetone, ethyl acetate (EtOAc), diethyl ether (Et\textsubscript{2}O), CH\textsubscript{2}Cl\textsubscript{2}, hexanes, and water (H\textsubscript{2}O) were purchased from a commercial source (Samchun Chemical) and used without further purification. H\textsubscript{2}\textsuperscript{18}O (97 atom\% \textsuperscript{18}O) was purchased from Sigma-Aldrich and used as received. Other reagents were purchased from commercial sources (Sigma-Aldrich, Alfa Aesar, Acros Organics, and TCI) and used as received. Yields refer to chromatographically and spectroscopically (\textsuperscript{1}H NMR) homogeneous materials, unless otherwise stated. Reactions were monitored by thin-layers chromatography (TLC) using 0.25 mm E. Merck silica gel plates (60 F\textsubscript{254}) and the developed chromatogram was visualized by using UV light or an acidic ethanolic anisaldehyde or potassium permanganate (KMnO\textsubscript{4}) stain with heating. Intertec Silica gel (60, particle size 60–200 μm) was used for flash column chromatography. \textsuperscript{1}H, \textsuperscript{13}C and \textsuperscript{19}F NMR spectra were recorded on an Agilent 400-MR DD2 Magnetic Resonance System, Varian/Oxford As-500 instrument, or Bruker 500 MHz instrument and calibrated using residual un-deuterated solvent signal (CHCl\textsubscript{3} in CDCl\textsubscript{3}: δ 7.26 ppm for \textsuperscript{1}H, δ 77.16 ppm for \textsuperscript{13}C; CH\textsubscript{3}OH in MeOD: δ 3.31 ppm for \textsuperscript{1}H, δ 49.00 ppm for \textsuperscript{13}C) as the internal reference. \textsuperscript{19}F NMR spectra were calibrated to an external standard of neat PhCF\textsubscript{3} (δ –63.72 ppm). Data for NMR spectra were reported as follows: chemical shift (multiplicities, coupling constant (Hz), and integration) and chemical shifts are reported in ppm. The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, qui = quintet, h = heptet, dd = doublet of doublets, dq = doublet of quartets, dm = doublet of multiplets, td = triplet of doublets, tt = triplet of triplets, qd = quartet of doublets, ddd = doublet of doublet of doublets, dddd = doublet of doublet of doublet of doublets, dtt = doublet of triplet of triplets, tdd = triplet of doublet of doublets, m = multiplet, br = broad. High-resolution mass spectrometry (HRMS) was performed using a HRMS-ESI Q-TOF 5600 spectrometer at National Instrumentation.
Center for Environmental Management (NICEM) in Seoul National University, Ultra High Resolution ESI Q-TOF mass spectrometer (Bruker compact) at the Organic Chemistry Research Center in Sogang University, or ThermoFisher Scientific mass spectrometer (Orbitrap Exploris 120) at Department of Chemistry in Seoul National University.
2. Preparation of Starting Materials

**Scheme S1.** Synthetic scheme for the preparation of $N$-hydroxyindole 1.

The synthetic scheme for the preparation of $N$-hydroxyindole 1, the substrate of indolyl 1,3-heteroatom transposition (IHT) reaction, is depicted in Scheme S1. The two-step sequence, reduction of indole S1 followed by tungstate-catalyzed oxidation, was utilized to provide a series of $N$-hydroxyindole 1.[1] Detailed information on the preparation and characterization of S1, S2 and 1 is described in Section 2.1, 2.2 and 2.3, respectively.
2.1. Preparation of Indole Derivatives

**Figure S1.** List of indole derivatives categorized by methods of preparation.

The spectral data matched to those reported in the literature: S1a[2], S1b[2], S1f[2], S1g[3], S1j[3], S1l[2], S1m[4], S1n[5], S1o, S1p[6], S1r[6], S1t[7], S1u[7], S1v[8], S1w[9], S1a[10].
General procedure A

![Chemical Structure](image)

To an oven-dried round-bottom flask equipped with a stir bar and septum were added tryptamine (1.0 equiv) and EtOAc:1 N NaOH (1:1, 0.2 M in tryptamine) at 23 °C, followed by methyl chloroformate (1.1 equiv). The resulting mixture was stirred for 16 h, before it was quenched with H₂O. The layers were separated and the aqueous layer was extracted with CH₂Cl₂ three times. The combined organic layer was washed with brine, dried over anhydrous MgSO₄, filtered, and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography to afford the desired product.

Methyl (2-(5-phenyl-1H-indol-3-yl)ethyl)carbamate (S1c)

Following the general procedure A, 5-phenyl tryptamine (0.580 g, 1.97 mmol) afforded tryptamine S1c (465 mg, 80%) as a pale yellow oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 7:3).

**Rf**=0.40 (silica gel, hexanes:EtOAc = 1:1); **¹H NMR** (400 MHz, CDCl₃): δ 8.42 (br s, 1H), 7.84 (s, 1H), 7.71 (d, J = 7.6 Hz, 2H), 7.51 – 7.47 (m, 3H), 7.42 (d, J = 8.4 Hz, 1H), 7.37 (t, J = 7.4 Hz, 1H), 7.06 – 6.96 (m, 1H), 4.94 (br s, 1H), 3.70 (s, 3H), 3.60 – 3.55 (m, 2H), 3.03 (t, J = 6.8 Hz, 2H); **¹³C NMR** (101 MHz, CDCl₃): δ 157.3, 142.5, 135.9, 132.8, 128.7, 127.8, 127.3, 126.3, 123.0, 121.7, 117.0, 112.9, 111.6, 52.0, 41.5, 25.6; **HRMS** calcd. for C₁₉H₁₈N₂O₂⁺ [M + H]⁺ 295.1441, found 295.1438.
Methyl (2-(5-(naphthalen-2-yl)-1H-indol-3-yl)ethyl)carbamate (S1d)

Following the general procedure A, 5-(naphthalen-2-yl)-tryptamine (0.490 g, 1.71 mmol) afforded tryptamine S1d (0.340 g, 58%) as a pale yellow amorphous solid after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 7:3).

Rf=0.40 (silica gel, hexanes:EtOAc = 7:3); ¹H NMR (400 MHz, CDCl₃): δ 8.11 (br s, 1H), 8.09 (s, 1H), 7.94 – 7.90 (m, 3H), 7.88 – 7.83 (m, 2H), 7.60 (d, J = 8.3 Hz, 1H), 7.53 – 7.45 (m, 3H), 7.09 (s, 1H), 4.80 (s, 1H), 3.67 (s, 3H), 3.58 (br q, J = 6.5 Hz, 2H), 3.05 (t, J = 6.8 Hz, 2H); ¹³C NMR (101 MHz, CDCl₃): δ 157.2, 139.9, 136.1, 134.0, 133.1, 132.3, 128.4, 128.1, 128.1, 127.8, 126.4, 126.3, 125.7, 125.6, 123.0, 122.4, 117.7, 113.5, 111.7, 52.2, 41.5, 25.9; HRMS calcd. for C₂₂H₂₁N₂O₂⁺ [M + H]⁺ 345.1598, found 345.1591.

Methyl (2-(5-(4-methoxyphenyl)-1H-indol-3-yl)ethyl)carbamate (S1e)

Following the general procedure A, 5-(4-methoxyphenyl)-tryptamine (0.750 g, 2.82 mmol) afforded tryptamine S1e (0.630 g, 69%) as a pale yellow oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 7:3).

Rf=0.27 (silica gel, hexanes:EtOAc = 1:1); ¹H NMR (500 MHz, CDCl₃): δ 8.15 (br s, 1H), 7.74 (s, 1H), 7.58 (d, J = 8.6 Hz, 1H), 7.44 – 7.38 (m, 2H), 7.04 (s, 1H), 7.00 (d, J = 8.6 Hz, 2H), 4.81 (br s, 1H), 3.87 (s, 3H), 3.67 (s, 3H), 3.57 – 3.53 (m, 2H), 3.01 (t, J = 6.8 Hz, 2H); ¹³C NMR (126 MHz, CDCl₃): δ 158.6, 157.2, 135.7, 135.3, 133.0, 128.5, 128.0, 122.9, 12.0, 116.9, 114.3, 113.4, 111.5, 55.5, 52.2, 41.5, 25.9; HRMS calcd. for C₁₉H₂₁N₂O₃⁺ [M + H]⁺ 325.1547, found 325.1556.
Methyl 3-(2-((methoxycarbonyl)amino)ethyl)-1H-indole-5-carboxylate (S1h)

Following the general procedure A, Methyl tryptamine-5-carboxylate (0.300 g, 1.36 mmol) afforded tryptamine S1h (0.210 g, 56%) as a pale yellow amorphous solid after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 6:4).

\[ R_f = 0.40 \] (silica gel, hexanes:EtOAc = 4:6); \[ ^1H\text{ NMR} \] (400 MHz, CDCl\(_3\)): \[ \delta \ 8.78 \text{ (br s, 1H), 8.35 (s, 1H), 7.89 (d, } J = 8.6 \text{ Hz, 1H), 7.35 (d, } J = 8.5 \text{ Hz, 1H), 7.06 (s, 1H), 4.88 (br s, 1H), 3.93 (s, 3H), 3.65 (s, 3H), 3.53 – 3.48 (m, 2H), 2.97 (t, } J = 6.5 \text{ Hz, 2H); } ^{13}C\text{ NMR} \] (101 MHz, CDCl\(_3\)): \[ \delta \ 168.4, 157.3, 139.1, 127.0, 123.6, 123.5, 121.7, 121.4, 114.3, 111.1, 52.2, 52.0, 41.4, 25.7; \text{ HRMS calcd. for } C_{14}H_{17}N_2O_4^+ [M + H]^+ 277.1187, \text{ found 277.1182.} \]

Methyl (2-(5-cyano-1H-indol-3-yl)ethyl)carbamate (S1i)

Following the general procedure A, 5-cyanotryptamine (352 mg, 1.88 mmol) afforded tryptamine S1i (0.250 g, 55%) as a pale yellow oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 6:4).

\[ R_f = 0.20 \] (silica gel, hexanes:EtOAc = 4:6); \[ ^1H\text{ NMR} \] (400 MHz, CDCl\(_3\)): \[ \delta \ 8.58 \text{ (br s, 1H), 7.94 (s, 1H), 7.42 (s, 2H), 7.16 (s, 1H), 4.81 (br s, 1H), 3.67 (s, 3H), 3.53 – 3.48 (m, 2H), 2.97 (t, } J = 6.5 \text{ Hz, 2H); } ^{13}C\text{ NMR} \] (101 MHz, CDCl\(_3\)): \[ \delta \ 157.2, 138.1, 127.4, 125.2, 124.6, 124.3, 120.9, 114.2, 112.3, 102.7, 52.3, 41.4, 25.7; \text{ HRMS calcd. for } C_{13}H_{14}N_3O_2^+ [M + H]^+ 244.1076, \text{ found 244.1081.} \]
Methyl (2-(1,6,7,8-tetrahydrocyclopenta[g]indol-3-yl)ethyl)carbamate (S1k)

Following the general procedure A, 2-(1,6,7,8-tetrahydrocyclopenta[g]indol-3-yl)ethan-1-amine (0.230 g, 1.14 mmol) afforded tryptamine S1k (191 mg, 65%) as a pale yellow oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 7:3).

$R_f$ = 0.60 (silica gel, hexanes:EtOAc = 6:4); $^1$H NMR (400 MHz, CDCl$_3$): δ 7.93 (br s, 1H), 7.42 (d, $J = 8.1$ Hz, 1H), 7.07 (d, $J = 8.0$ Hz, 1H), 6.97 (s, 1H), 4.77 (br s, 1H), 3.66 (s, 3H), 3.52 (d, $J = 6.6$ Hz, 2H), 3.05 (q, $J = 8.0$ Hz, 4H), 2.97 (t, $J = 6.9$ Hz, 2H), 2.22 (p, $J = 7.3$ Hz, 2H); $^{13}$C NMR (101 MHz, CDCl$_3$): δ 157.2, 138.9, 133.7, 126.0, 125.7, 121.4, 116.9, 116.6, 113.6, 52.1, 41.4, 33.2, 29.9, 26.1, 25.5; HRMS calcd. for C$_{15}$H$_{20}$N$_2$O$_2$ $^{+}$ [M + H]$^+$ 259.1441, found 259.1439.
2.2. Preparation of Indoline Derivatives

![Diagram of indoline derivatives]

**Figure S2.** List of indoline derivatives categorized by methods of preparation.

The spectral data matched to those reported in the literature: S2p[11], S2q[11], S2t[12], S2u[11], S2l[11], S2u[13], S2x[1]
General procedure B

To an oven-dried round-bottom flask equipped with a stir bar and septum were added indole S1 (1.0 equiv) and TFA (0.3 M in S1) at 23 °C, followed by Et3SiH (3.0 equiv). The resulting mixture was heated to 65 °C in a pre-heated oil bath and stirred for 3 h, before it was cooled to 23 °C and directly concentrated under reduced pressure to remove most of TFA. The crude product was re-dissolved in CH2Cl2 and basified to pH 9–10 using NH3·H2O (25.0–30.0 wt% in H2O). The layers were separated and the aqueous layer was extracted with CH2Cl2 three times. The combined organic layer was washed with brine, dried over anhydrous MgSO4, filtered, and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography to afford indoline S2.

General procedure C

To an oven-dried round-bottom flask equipped with a stir bar and septum were added indole S1 (1.0 equiv) and AcOH (0.1 M in S1) at 23 °C. The resulting solution was cooled to 0 °C, and NaBH3CN (2.0 equiv) was added to the solution. The reaction mixture was warmed up to 23 °C and stirred while the reaction was monitored by TLC. After completion of reaction (1–2 h), the reaction mixture was directly concentrated under reduced pressure. The crude product was re-dissolved in CH2Cl2 and basified to pH 9–10 using NH3·H2O (25.0–30.0 wt% in H2O). The layers were separated and the aqueous layer was extracted with CH2Cl2 three times. The combined organic layer was washed with brine, dried over anhydrous MgSO4, filtered, and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography to afford indoline S2.
Methyl (2-(indolin-3-yl)ethyl)carbamate (S2a)

Following the **general procedure B**, tryptamine S1a (3.50 g, 16.0 mmol) afforded indoline S2a (3.30 g, 94%) as a pale yellow amorphous solid after purification by flash column chromatography (silica gel, hexanes:EtOAc = 8:2 → 6:4).

$R_f=0.20$ (silica gel, hexanes:EtOAc = 1:1); $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 7.08 (d, $J=7.3$ Hz, 1H), 7.03 (t, $J=7.6$ Hz, 1H), 6.72 (t, $J=7.4$ Hz, 1H), 6.64 (d, $J=7.7$ Hz, 1H), 5.03 (s, 1H), 3.78–3.62 (m, 5H), 3.35–3.26 (m, 2H), 2.04–1.93 (m, 1H), 1.73 (m, 1H); $^{13}$C NMR (126 MHz, CDCl$_3$): $\delta$ 157.2, 151.3, 132.1, 127.7, 123.9, 118.8, 109.7, 53.3, 52.1, 39.6, 39.1, 34.5; HRMS calcd. for C$_{12}$H$_{17}$N$_2$O$_2$+ [M + H]$^+$ 221.1285, found 221.1278.

Methyl (2-(5-methylindolin-3-yl)ethyl)carbamate (S2b)

Following the **general procedure B**, tryptamine S1b (0.100 g, 0.431 mmol) afforded indoline S2b (75.0 mg, 74%) as a pale yellow oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 8:2 → 6:4).

$R_f=0.34$ (silica gel, hexanes:EtOAc = 4:6); $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 6.91 (s, 1H), 6.85 (d, $J=7.9$ Hz, 1H), 6.57 (d, $J=7.8$ Hz, 1H), 4.86 (br s, 1H), 3.68 (t, $J=7.3$ Hz, 2H), 3.66 (s, 3H), 3.35–3.18 (m, 4H), 2.26 (s, 3H), 2.04–1.95 (m, 1H), 1.78–1.69 (m, 1H); $^{13}$C NMR (101 MHz, CDCl$_3$): $\delta$ 157.2, 148.8, 132.5, 132.1, 128.1, 127.9, 124.5, 109.7, 53.4, 51.9, 39.5, 39.0, 34.3, 20.8; HRMS calcd. for C$_{13}$H$_{19}$N$_2$O$_2$+ [M + H]$^+$ 235.1442, found 235.1441.

Methyl (2-(5-phenylindolin-3-yl)ethyl)carbamate (S2c)
Following the general procedure B, tryptamine S1c (0.300 g, 1.02 mmol) afforded indoline S2c (0.265 g, 88%) as a pale yellow amorphous solid after purification by flash column chromatography (silica gel, hexanes:EtOAc = 8:2 → 6:4).

Rf=0.30 (silica gel, hexanes:EtOAc = 4:6); \(^1\)H NMR (500 MHz, CDCl\(_3\)): \(\delta\) 7.54 (d, \(J = 7.7\) Hz, 2H), 7.41 (t, \(J = 7.6\) Hz, 2H), 7.34 (s, 1H), 7.33 – 7.27 (m, 2H), 6.71 (d, \(J = 8.0\) Hz, 1H), 5.01 (br s, 1H), 3.75 (t, \(J = 8.7\) Hz, 1H), 3.68 (s, 3H), 3.41 – 3.35 (m, 1H), 3.33 – 3.24 (m, 3H), 2.09 – 2.03 (m, 1H), 1.79 (dt, \(J = 14.2, 7.1\) Hz, 1H); \(^{13}\)C NMR (126 MHz, CDCl\(_3\)): \(\delta\) 157.2, 150.7, 141.6, 132.9, 132.2, 128.7, 126.8, 126.6, 126.2, 122.8, 109.8, 53.5, 52.1, 39.5, 39.1, 34.6; HRMS calcd. for C\(_{18}\)H\(_{21}\)N\(_2\)O\(_2\) \([M + H]^+\) 297.1592, found 297.1598.

Methyl (2-(5-(naphthalen-2-yl)indolin-3-yl)ethyl)carbamate (S2d)

Following the general procedure B, tryptamine S1d (0.450 g, 1.31 mmol) afforded indoline S2d (0.330 g, 73%) as a pale yellow amorphous solid after purification by flash column chromatography (silica gel, hexanes:EtOAc = 8:2 → 6:4).

Rf=0.33 (silica gel, hexanes:EtOAc = 4:6); \(^1\)H NMR (500 MHz, CDCl\(_3\)): \(\delta\) 7.97 (s, 1H), 7.87 (d, \(J = 8.2\) Hz, 2H), 7.84 (d, \(J = 8.0\) Hz, 1H), 7.71 (dd, \(J = 8.5, 1.8\) Hz, 1H), 7.52 – 7.40 (m, 4H), 6.74 (d, \(J = 8.0\) Hz, 1H), 4.92 (s, 1H), 3.77 (t, \(J = 8.7\) Hz, 1H), 3.68 (s, 3H), 3.45 – 3.37 (m, 1H), 3.37 – 3.24 (m, 3H), 2.15 – 2.03 (m, 1H), 1.88 – 1.76 (m, 1H); \(^{13}\)C NMR (126 MHz, CDCl\(_3\)): \(\delta\) 157.3, 150.9, 139.1, 134.0, 133.0, 132.2, 132.0, 128.3, 128.0, 127.7, 127.2, 126.2, 125.6, 125.5, 124.6, 123.1, 109.9, 53.5, 52.2, 39.7, 39.2, 34.7; HRMS calcd. for C\(_{22}\)H\(_{23}\)N\(_2\)O\(_2\) \([M + H]^+\) 347.1754, found 347.1748.

Methyl (2-(5-(4-methoxyphenyl)indolin-3-yl)ethyl)carbamate (S2e)

Following the general procedure B, tryptamine S1e (0.370 g, 1.14 mmol) afforded indoline S2e (0.280 g, 75%)
as a pale yellow oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 8:2 → 6:4). $R_f=0.10$ (silica gel, hexanes:EtOAc = 1:1); $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 7.44 (d, $J = 8.3$ Hz, 2H), 7.21 (d, $J = 6.5$ Hz, 1H), 6.92 (d, $J = 8.2$ Hz, 2H), 6.61 (d, $J = 8.0$ Hz, 1H), 5.33 (br s, 1H), 3.85 (s, 1H), 3.77 (s, 3H), 3.64 (s, 3H), 3.32 – 3.12 (m, 4H), 2.02 – 1.96 (m, 1H), 1.73 – 166 (m, 1H); $^{13}$C NMR (126 MHz, CDCl$_3$): $\delta$ 158.1, 157.1, 150.2, 134.1, 132.7, 131.3, 127.2, 126.0, 122.1, 113.9, 109.5, 55.1, 53.2, 51.8, 39.3, 38.9, 34.2; HRMS calcd. for C$_{19}$H$_{23}$N$_2$O$_3$ $[M + H]^+$ 327.1701, found 327.1703.

Methyl (2-(5-fluorindolin-3-yl)ethyl)carbamate (S2f)

Following the general procedure B, tryptamine S1f (1.80 g, 7.62 mmol) afforded indoline S2f (1.30 g, 72%) as a brown oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 8:2 → 1:1). $R_f=0.28$ (silica gel, hexanes:EtOAc = 2:8); $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 6.81 (d, $J = 8.3$ Hz, 1H), 6.73 (t, $J = 8.8$ Hz, 1H), 6.54 (dd, $J = 8.5$, 4.3 Hz, 1H), 4.88 (br s, 1H), 3.71 (t, $J = 8.0$ Hz, 2H), 3.66 (s, 3H), 3.35 – 3.17 (m, 4H), 2.03 – 1.90 (m, 1H), 1.79 – 1.68 (m, 1H); $^{13}$C NMR (101 MHz, CDCl$_3$): $\delta$ 157.2 (d, $J = 235.6$ Hz), 157.2, 147.3 (d, $J = 1.4$ Hz), 134.0 (d, $J = 6.1$ Hz), 113.8 (d, $J = 23.4$ Hz), 111.4 (d, $J = 23.9$ Hz), 110.0 (d, $J = 8.2$ Hz), 53.9, 52.2, 40.0, 39.0, 34.4; $^{19}$F NMR (376 MHz, CDCl$_3$): $\delta$ ~126.1; HRMS calcd. for C$_{12}$H$_{16}$FN$_2$O$_2$ $[M + H]^+$ 239.1188, found 239.1190.

Methyl (2-(5-bromoindolin-3-yl)ethyl)carbamate (S2g)

Following the general procedure B, tryptamine S1g (0.500 g, 1.68 mmol) afforded indoline S2g (0.400 g, 80%) as a yellow oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 8:2 → 1:1).
**Methyl 3-(2-((methoxycarbonyl)amino)ethyl)indoline-5-carboxylate (S2h)**

Following the general procedure B, tryptamine S1h (0.340 g, 1.23 mmol) afforded indoline S2h (0.212 g, 76%) as a colorless oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 8:2 → 1:1).

\( R_f = 0.23 \) (silica gel, hexanes:EtOAc = 1:1); **\(^1\)H NMR** (400 MHz, CDCl\(_3\)): \( \delta 7.16\) (s, 1H), 7.12 (d, \( J = 7.9\) Hz, 1H), 6.50 (d, \( J = 8.2\) Hz, 1H), 4.80 (br s, 1H), 3.75 – 3.65 (m, 4H), 3.36 – 3.20 (m, 4H), 2.01 – 1.93 (s, 1H), 1.80 – 1.69 (m, 1H); **\(^{13}\)C NMR** (101 MHz, CDCl\(_3\)) \( \delta 157.2, 150.4, 134.6, 130.4, 127.0, 110.9, 110.3, 53.5, 52.2, 39.6, 39.0, 34.5\); **HRMS** calcd. for \( \text{C}_{12}\text{H}_{16}\text{BrN}_{2}\text{O}_{2}^{+} \) [M + H]\(^+\) 299.0390, found 299.0390.

**Methyl (2-(5-cyanoindolin-3-yl)ethyl)carbamate (S2i)**

Following the general procedure B, tryptamine S1i (0.900 g, 3.70 mmol) afforded indoline S2i (0.700 g, 77%) as a pale yellow amorphous solid after purification by flash column chromatography (silica gel, hexanes:EtOAc = 8:2 → 1:1).

\( R_f = 0.34 \) (silica gel, hexanes:EtOAc = 2:8); **\(^1\)H NMR** (400 MHz, CDCl\(_3\)): \( \delta 7.33 – 7.26\) (m, 2H), 6.54 (d, \( J = 8.2\) Hz, 1H), 3.79 – 3.72 (m, 1H), 3.63 (s, 3H), 3.35 – 3.27 (m, 2H), 3.19 (t, \( J = 7.6\) Hz, 2H), 1.97 – 1.90 (m, 1H), 1.75 – 1.65 (m, 1H); **\(^{13}\)C NMR** (101 MHz, CDCl\(_3\)): \( \delta 157.3, 155.1, 133.5, 133.5, 132.6, 127.6, 120.8, 108.4, 99.7, 53.0, 52.3, 38.8, 38.7, 34.8\); **HRMS** calcd. for \( \text{C}_{13}\text{H}_{16}\text{N}_{2}\text{O}_{2}^{+} \) [M + H]\(^+\) 246.1234, found 246.1237.
Methyl (2-(7-methylindolin-3-yl)ethyl)carbamate (S2j)

Following the general procedure B, tryptamine S1j (0.450 g, 1.94 mmol) afforded indoline S2j (0.345 g, 76%) as a pale yellow amorphous solid after purification by flash column chromatography (silica gel, hexanes:EtOAc = 8:2 → 6:4).

\[ R_f = 0.34 \text{ (silica gel, hexanes:EtOAc = 2:8)} \]

\[ ^1H \text{ NMR (400 MHz, CDCl}_3\text{): } \delta 6.96 (d, J = 7.4 \text{ Hz}, 1H), 6.89 (d, J = 7.5 \text{ Hz}, 1H), 4.91 (br s, 1H), 3.76 – 3.69 (m, 2H), 3.67 (s, 2H), 3.39 – 3.30 (m, 1H), 2.13 (s, 3H), 2.06 – 1.93 (m, 1H), 1.81 – 1.68 (m, 1H); ^13C \text{ NMR (101 MHz, CDCl}_3\text{): } \delta 157.2, 149.8, 131.5, 128.7, 121.5, 119.3, 119.1, 53.2, 52.2, 40.0, 39.2, 34.7, 16.9; \text{ HRMS calcd. for C}_{13}\text{H}_{19}\text{N}_{2}\text{O}_{2}^+ [M + H]^+ 235.1441, found 235.1441. \]

Methyl (2-(1,2,3,6,7,8-hexahydrocyclopenta[g]indol-3-yl)ethyl)carbamate (S2k)

Following the general procedure B, tryptamine S1k (0.230 g, 0.891 mmol) afforded indoline S2k (0.210 g, 91%) as a pale yellow oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 8:2 → 6:4).

\[ R_f = 0.24 \text{ (silica gel, hexanes:EtOAc = 7:3)} \]

\[ ^1H \text{ NMR (500 MHz, CDCl}_3\text{): } \delta 6.91 (d, J = 7.4 \text{ Hz}, 1H), 6.66 (d, J = 7.4 \text{ Hz}, 1H), 4.83 (br s, 1H), 3.73 (t, J = 8.2 \text{ Hz}, 1H), 3.67 (s, 3H), 3.57 (s, 1H), 3.37 – 3.15 (m, 4H), 2.86 (t, J = 7.5 \text{ Hz}, 2H), 2.70 (t, J = 7.3 \text{ Hz}, 2H), 2.17 (s, 1H), 2.08 (p, J = 7.5 \text{ Hz}, 2H), 1.99 (dq, J = 13.9, 7.0 \text{ Hz}, 1H), 1.74 (dq, J = 14.4, 7.6 \text{ Hz}, 1H); ^13C \text{ NMR (126 MHz, CDCl}_3\text{): } \delta 157.2, 147.3, 144.8, 129.7, 125.2, 121.9, 114.8, 77.4, 77.2, 76.9, 53.9, 52.2, 39.7, 39.3, 34.9, 32.9, 31.1, 29.5, 25.6; \text{ HRMS calcd. for C}_{15}\text{H}_{21}\text{N}_{2}\text{O}_{2}^+ [M + H]^+ 261.1598, found 261.1590. \]
Methyl (2-(4-chloroindolin-3-yl)ethyl)carbamate (S2l)

Following the general procedure B, tryptamine S11 (0.100 g, 0.396 mmol) afforded indoline S21 (80.0 mg, 89%) as a pale yellow oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 8:2 → 1:1). 

$R_f=0.34$ (silica gel, hexanes:EtOAc = 2:8); $^1H$ NMR (400 MHz, CDCl$_3$) : $\delta$ 6.95 (t, $J = 7.9$ Hz, 1H), 6.65 (d, $J = 8.0$ Hz, 1H), 6.50 (d, $J = 7.8$ Hz, 1H), 4.97 (s, 1H), 3.87 (s, 1H), 3.68 (d, $J = 8.8$ Hz, 1H), 3.65 (s, 3H), 3.51 – 3.34 (m, 2H), 3.31 – 3.07 (m, 2H), 2.00 – 1.81 (m, 2H); $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 157.2, 152.8, 130.8, 129.6, 129.4, 119.1, 107.9, 77.5, 77.2, 76.8, 52.2, 52.1, 39.3, 38.7, 32.6; HRMS calcd. for C$_{12}$H$_{16}$ClN$_2$O$_2$ $[M + H]^+$ 255.0895, found 255.0892.

Methyl (2-(2-methylindolin-3-yl)ethyl)carbamate (S2m)

Following the general procedure C for 1 h, tryptamine S1m (0.500 g, 2.15 mmol) afforded indoline S2m (0.430 g, 85%) as a pale yellow oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 8:2 → 1:1). 

$R_f=0.48$ (silica gel, hexanes:EtOAc = 2:8); $^1H$ NMR (400 MHz, CDCl$_3$) : $\delta$ 7.09 – 7.04 (m, 1H), 7.02 (t, $J = 7.6$ Hz, 1H), 6.70 (q, $J = 6.9$ Hz, 1H), 6.59 (t, $J = 8.7$ Hz, 1H), 5.09 (br s, 1H), 3.95 and 3.59 (t, $J = 6.1$ Hz, 1H), 3.80 – 3.70 (m, 1H), 3.65 (s, 3H), 3.23 – 3.18 (m, 2H), 3.10 and 2.84 (q, $J = 6.2$ Hz, 1H), 1.91 – 1.73 (m, 2H), 1.22 and 1.16 (d, $J = 6.4$ Hz, 3H); $^{13}$C NMR (101 MHz, CDCl$_3$) : $\delta$ 157.2, 150.4, 150.0, 131.8, 131.3, 127.7, 127.5, 124.3, 124.3, 118.5, 118.6, 109.6, 109.4, 60.4, 58.3, 52.0, 47.1, 42.2, 39.3, 38.7, 34.3, 28.4, 22.2, 16.0; HRMS calcd. for C$_{13}$H$_{19}$N$_2$O$_2$$^+$ [M + H]$^+$ 235.1442, found 235.1441.
**N-benzyl-2-(indolin-3-yl)acetamide (S2n)**

Following the general procedure B, indole S1n (2.30 g, 8.70 mmol) afforded indoline S2n (1.37 g, 59%) as a pale yellow oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 1:1).

Rf = 0.26 (silica gel, hexanes:EtOAc = 6:4); 1H NMR (500 MHz, CDCl3): δ 7.36 – 7.27 (m, 3H), 7.26 – 7.21 (m, 2H), 7.07 (d, J = 7.6 Hz, 2H), 6.75 (t, J = 7.3 Hz, 1H), 6.67 (d, J = 7.5 Hz, 1H), 6.34 (s, 1H), 5.12 (s, 1H), 4.40 (d, J = 5.8 Hz, 2H), 3.80 – 3.74 (m, 1H), 3.70 (t, J = 9.0 Hz, 1H), 3.30 – 3.22 (m, 1H), 2.50 (ddd, J = 61.3, 14.5, 7.3 Hz, 2H); 13C NMR (126 MHz, CDCl3): δ 171.4, 150.0, 138.2, 138.2, 132.1, 132.1, 128.7, 128.1, 127.8, 127.5, 124.3, 119.7, 110.6, 110.6, 52.8, 43.6, 41.2, 38.9; HRMS calcd. for C17H19N2O+ [M + H]+ 267.1492, found 267.1491.

**Methyl (2S)-3-(indolin-3-yl)-2-((methoxycarbonyl)amino)propanoate (S2o)**

Following the general procedure B, tryptophan S1o (1.50 g, 5.43 mmol) afforded indoline S2o (1.07 g, 71%) as an inconsequential 1:1 mixture of diastereomers in the form of a pale yellow oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 1:1). The resulting diastereomeric mixture was used directly in the subsequent reaction without separation. The diastereomeric ratio was determined by 1H NMR analysis of the crude reaction mixture.

Rf = 0.25 (silica gel, hexanes:EtOAc = 1:1); 1H NMR (500 MHz, CDCl3, 50:50 mixture of diastereomers): δ 7.15 (d, J = 7.3 Hz, 0.5H), 7.05 (d, J = 7.3 Hz, 0.5H), 7.03 (t, J = 7.6 Hz, 1H), 6.74 – 6.69 (m, 1H), 6.63 (t, J = 7.2 Hz, 1H), 5.61 (br s, 1H), 4.52 – 4.43 (m, 1H), 3.80-3.70 (m, 1H), 3.72 and 3.69 (s, 6H), 3.39 – 3.33 (m, 1H), 3.28 and 3.21 (t, J = 7.4 Hz, 1H), 2.29 and 1.87 (dt, J = 13.3, 6.1 Hz, 1H), 2.10 – 2.01 (m, 1H); 13C NMR (126 MHz, CDCl3): δ 173.2, 156.9, 156.7, 151.2, 151.1, 131.4, 131.1, 131.7, 127.9, 127.8, 124.3, 123.6, 118.9, 118.7, 109.8,
21

109.7, 53.7, 52.9, 52.6, 52.5, 52.4, 38.8, 38.6, 37.2; **HRMS** calcd. for C\textsubscript{14}H\textsubscript{19}N\textsubscript{2}O\textsubscript{4} \([\text{M + H}]^+\) 279.1339, found 279.11340.

**2-Phenethylindoline (S2p)**

Following the **general procedure C** for 2 h, indole S\textsubscript{1p} (0.280 g, 1.27 mmol) afforded indoline S\textsubscript{2p} (0.230 g, 81%) as a pale yellow oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 95:5). Analytic data is in agreement with the reported literature values.[11]

\(R_f=0.24\) (silica gel, hexanes:EtOAc = 7:3); \(^1\text{H NMR}\) (400 MHz, CDCl\textsubscript{3}): \(\delta 7.39 - 7.32\) (m, 2H), 7.28 - 7.24 (m, 3H), 7.05 (d, \(J = 7.4\) Hz, 1H), 6.99 (t, \(J = 7.6\) Hz, 1H), 6.67 (t, \(J = 7.4\) Hz, 1H), 6.61 (d, \(J = 7.7\) Hz, 1H), 3.96 - 3.87 (m, 1H), 3.20 (dd, \(J = 15.4, 8.7\) Hz, 1H), 2.80 - 2.73 (m, 3H), 2.03 - 1.97 (m, 2H); \(^{13}\text{C NMR}\) (101 MHz, CDCl\textsubscript{3}): \(\delta 151.0, 141.9, 128.8, 128.6, 128.4, 127.4, 126.1, 124.8, 118.7, 109.3, 59.6, 38.6, 36.2, 33.0.

**2-((tert-Butyldimethylsilyl)oxy)methyl)indoline (S2q)**

To an oven-dried round-bottom flask equipped with a stir bar and septum were added indoline-2-carboxylic acid (2.00 g, 12.3 mmol, 1.0 equiv) and THF (30 mL) at 23 °C. The resulting solution was cooled to 0 °C, and LAH (0.412 g, 13.7 mmol, 1.11 equiv) was added to the solution. The reaction mixture was stirred for 2 h before it was quenched with brine (20 mL). The layers were separated and the aqueous layer was extracted with EtOAc (3 × 30 mL). The combined organic layer was washed with brine (3 × 20 mL), dried over anhydrous MgSO\textsubscript{4}, filtered, and concentrated under reduced pressure to afford crude indolin-2-ylmethanol, which was used directly in the subsequent reaction without further purification.

To an oven-dried round-bottom flask equipped with a stir bar and septum were added crude indolin-2-ylmethanol and DMF (20 mL) at 23 °C, followed by TBSCI (1.88 g, 12.5 mmol, 1.01 equiv) and DMAP (1.50 g, 12.3 mmol,
1.0 equiv). The resulting mixture was stirred for 16 h before it was quenched with brine (20 mL). The layers were separated and the aqueous layer was extracted with CH$_2$Cl$_2$ (3 × 20 mL). The combined organic layer was washed with brine (3 × 20 mL), dried over anhydrous MgSO$_4$, filtered, and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 95:5) to afford the product S2q (2.09 g, 73%) as a pale yellow oil. Analytic data is in agreement with the reported literature values.$^{11}$

$R_f$=0.24 (silica gel, hexanes:EtOAc = 95:5); $^1$H NMR (400 MHz, CDCl$_3$): δ 7.10 (d, $J$ = 7.3 Hz, 1H), 7.05 (t, $J$ = 7.6 Hz, 1H), 6.72 (t, $J$ = 7.4 Hz, 1H), 6.65 (d, $J$ = 7.7 Hz, 1H), 4.01 – 3.93 (m, 1H), 3.67 – 3.54 (m, 2H), 3.14 (dd, $J$ = 15.8, 9.1 Hz, 1H), 2.68 (dd, $J$ = 15.8, 5.8 Hz, 1H), 0.96 (s, 9H), 0.11 (s, 6H); $^{13}$C NMR (101 MHz, CDCl$_3$): δ 150.6, 128.2, 127.5, 124.9, 118.5, 109.4 5, 66.7, 60.5, 32.2, 26.0, 18.4, −5.2.

2-Cyclohexylindoline (S2r)

Following the general procedure C for 2 h, indole S1r (0.100 g, 0.502 mmol) afforded indoline S2r (82.0 mg, 81%) as a pale yellow oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 95:5). Analytic data is in agreement with the reported literature values.$^{12}$

$R_f$=0.24 (silica gel, hexanes:EtOAc = 7:3); $^1$H NMR (400 MHz, CDCl$_3$): δ 7.08 (d, $J$ = 7.3 Hz, 1H), 7.01 (t, $J$ = 7.6 Hz, 1H), 6.68 (t, $J$ = 7.4 Hz, 1H), 6.61 (d, $J$ = 7.7 Hz, 1H), 3.94 (br s, 1H), 3.56 (q, $J$ = 8.8 Hz, 1H), 3.07 (dd, $J$ = 15.5, 8.7 Hz, 1H), 2.75 (dd, $J$ = 15.5, 9.8 Hz, 1H), 1.89 (d, $J$ = 12.3 Hz, 1H), 1.51 – 1.41 (m, 1H), 1.34 – 1.13 (m, 3H), 1.06 – 0.94 (m, 2H); $^{13}$C NMR (101 MHz, CDCl$_3$): δ 151.3, 129.2, 127.3, 124.6, 118.5, 109.0, 65.7, 44.0, 34.3, 30.3, 29.7, 26.6, 26.2, 26.1.
2,3,4,4a,9,9a-Hexahydro-1H-carbazole (S2s)

Following the general procedure C for 1 h, 1,2,3,4-tetrahydrocarbazole (3.00 g, 17.5 mmol) afforded indoline S2s (2.37 g, 78%) as a white amorphous solid after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 95:5). Analytic data is in agreement with the reported literature values.[11]

R_f=0.68 (silica gel, hexanes:EtOAc = 9:1); \(^1\)H NMR (300 MHz, CDCl\(_3\)): δ 7.10 (d, \(J = 7.3\) Hz, 1H), 7.04 (t, \(J = 7.6\) Hz, 1H), 6.69 (d, \(J = 7.7\) Hz, 1H), 3.74 (q, \(J = 6.1\) Hz, 1H), 1.72 – 1.65 (m, 1H), 1.62 – 1.53 (m, 2H), 1.58 (dq, \(J = 12.5, 7.0, 5.5\) Hz, 2H), 1.48 – 1.32 (m, 3H); \(^{13}\)C NMR (75 MHz, CDCl\(_3\)): δ 150.9, 133.9, 127.1, 123.3, 118.9, 110.3, 59.8, 41.1, 29.3, 27.1, 22.7, 21.8.

5,5a,6,7,8,9,10,10a-Octahydrocyclohepta[b]indole (S2t)

Following the general procedure C for 1 h, indole S1t (0.300 g, 1.62 mmol) afforded indoline S2t (0.280 g, 92%) as a white amorphous solid after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 95:5). Analytic data is in agreement with the reported literature values.[11]

R_f=0.68 (silica gel, hexanes:EtOAc = 9:1); \(^1\)H NMR (400 MHz, CDCl\(_3\)): δ 7.01 – 6.93 (m, 2H), 6.68(t, \(J = 7.3\) Hz, 1H), 6.55 (d, \(J = 7.6\) Hz, 1H), 4.07 – 4.01 (m, 1H), 3.47 (td, \(J = 10.4, 3.9\) Hz, 1H), 2.00 – 1.93 (m, 1H), 1.89 – 1.69 (m, 6H), 1.44 – 1.32 (m, 3H); \(^{13}\)C NMR (101 MHz, CDCl\(_3\)): δ 150.3, 133.7, 127.5, 124.3, 118.3, 108.6, 63.6, 47.5, 33.7, 31.5, 30.0, 26.2.

5a,6,7,8,9,10,11a-Octahydro-5H-cycloocta[b]indole (S2u)

Following the general procedure C for 1 h, indole S1u (0.250 g, 1.25 mmol) afforded indoline S2u (0.221 g,
88%) as a pale yellow oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 95:5). Analytic data is in agreement with the reported literature values.\[^{13}\]

\( R_f = 0.68 \) (silica gel, hexanes:EtOAc = 9:1); \(^1\)H NMR (500 MHz, CDCl\(_3\)): \( \delta \) 7.07 (d, \( J = 7.4 \) Hz, 1H), 7.01 (t, \( J = 7.6 \) Hz, 1H), 6.71 (t, \( J = 7.4 \) Hz, 1H), 6.57 (d, \( J = 7.7 \) Hz, 1H), 3.88 (t, \( J = 9.9 \) Hz, 1H), 3.21 (t, \( J = 9.7 \) Hz, 1H), 2.01 (dq, \( J = 45.0, 12.4, 11.5 \) Hz, 2H), 1.78 – 1.50 (m, 10H); \(^{13}\)C NMR (126 MHz, CDCl\(_3\)): \( \delta \) 149.5, 135.4, 127.3, 124.3, 118.6, 108.6, 63.9, 46.2, 30.3, 30.1, 28.8, 27.7, 25.9, 25.5.

\textit{tert}-Butyl 1,3,4,4a,5,9b-hexahydro-2H-pyrido[4,3-b]indole-2-carboxylate (S2v)

Following the \textbf{general procedure C} for 2 h, indole S1v (0.200 g, 0.734 mmol) afforded indoline S2v (0.127 g, 63%) as a pale yellow oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 7:3).

\( R_f = 0.24 \) (silica gel, hexanes:EtOAc = 7:3); \(^1\)H NMR (400 MHz, CDCl\(_3\)): \( \delta \) 7.12 (d, \( J = 7.1 \) Hz, 1H), 7.05 (td, \( J = 7.7, 1.3 \) Hz, 1H), 6.73 (td, \( J = 7.4, 1.0 \) Hz, 1H), 6.66 (d, \( J = 7.8 \) Hz, 1H), 3.97 (dt, \( J = 7.4, 5.0 \) Hz, 1H), 3.45 – 3.27 (m, 5H), 1.93 – 1.84 (m, 1H), 1.77 – 1.71 (m, 1H), 1.45 (s, 9H); \(^{13}\)C NMR (101 MHz, CDCl\(_3\)): \( \delta \) 155.1, 151.0, 128.1, 124.4, 119.1, 110.1, 79.6, 57.6, 43.9, 41.2, 40.1, 39.5, 28.6, 28.2; HRMS calcd. for C\(_{16}\)H\(_{23}\)N\(_2\)O\(_2\) [M + H]\(^+\) 275.1754, found 275.1759.

Methyl 1,3,4,4a,9,9a-hexahydro-2H-pyrido[3,4-b]indole-2-carboxylate (S2w)

Following the \textbf{general procedure C} for 1 h, indole S1w (0.500 g, 1.84 mmol) afforded indoline S2w (0.262 g, 52%) as a white amorphous solid after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 7:3).

\( R_f = 0.24 \) (silica gel, hexanes:EtOAc = 7:3); \(^1\)H NMR (400 MHz, CDCl\(_3\)): \( \delta \) 7.07 – 7.01 (m, 2H), 6.73 (t, \( J = 7.4 \) Hz, 1H), 6.62 (d, \( J = 7.7 \) Hz, 1H), 3.97 – 3.86 (m, 2H), 3.68 (s, 3H), 3.58 – 3.53 (m, 1H), 3.39 – 3.34 (m, 3H), 2.01 (dq, \( J = 45.0, 12.4, 11.5 \) Hz, 2H), 1.78 – 1.50 (m, 10H); \(^{13}\)C NMR (126 MHz, CDCl\(_3\)): \( \delta \) 149.5, 135.4, 127.3, 124.3, 118.6, 108.6, 63.9, 46.2, 30.3, 30.1, 28.8, 27.7, 25.9, 25.5.

24
Methyl (1R,2S,4aR,13bS,14aS)-2-hydroxy-1,2,3,4,4a,5,7,8,8a,13,13a,13b,14,14a-tetradecahydroindolo[2′,3′:3,4]pyrido[1,2-b]isoquinoline-1-carboxylate (S2x)

To an oven-dried round-bottom flask equipped with a stir bar and septum were added yohimbine hydrochloride (0.100 g, 0.256 mmol, 1.0 equiv) and TFA (5 mL) at 23 °C. The resulting solution was cooled to 0 °C, and NaBH₃CN (48.2 mg, 0.767 mmol, 3.0 equiv) was added to the solution. The reaction mixture was stirred for 1 h before it was directly concentrated under reduced pressure. The crude product was re-dissolved in CH₂Cl₂ (20 mL) and basified to pH 9–10 using NH₃·H₂O (25.0–30.0 wt% in H₂O). The layers were separated and the aqueous layer was extracted with CH₂Cl₂ (3 × 30 mL). The combined organic layer was washed with brine (1 × 20 mL), dried over anhydrous MgSO₄, filtered, and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography (silica gel, CH₂Cl₂:MeOH = 1:0 → 9:1) to afford indoline S2x (83.0 mg, 91%) as a pale yellow viscous oil as a single diastereomer, which is consistent with the literature observations.[1]

Rᶠ=0.31 (silica gel, CH₂Cl₂:MeOH = 9:1); ¹H NMR (500 MHz, MeOD): δ 7.05 (d, J = 7.2 Hz, 1H), 6.97 (t, J = 7.7 Hz, 1H), 6.67 – 6.64 (m, 2H), 4.25 (s, 1H), 3.69 (s, 3H), 3.55 (d, J = 4.8 Hz, 1H), 2.99 (dt, J = 12.5, 6.6 Hz, 1H), 2.88 (d, J = 11.4 Hz, 1H), 2.83 (d, J = 11.8 Hz, 1H), 2.51 (d, J = 11.6 Hz, 1H), 2.35 – 2.27 (m, 2H), 2.13 (t, J = 10.3 Hz, 1H), 1.91 – 1.89 (m, 3H), 1.79 (dd, J = 14.1, 6.3 Hz, 1H), 1.65 (t, J = 12.6 Hz, 1H), 1.55 – 1.43 (m, 3H), 1.38 – 1.28 (m, 2H); ¹³C NMR (126 MHz, MeOD): δ 175.0, 151.5, 135.6, 128.5, 124.1, 119.8, 111.5, 68.4, 64.2, 64.0, 62.4, 54.7, 53.7, 52.0, 49.8, 41.0, 40.6, 37.1, 35.0, 33.3, 30.1, 24.0; HRMS calcd. for C₂₁H₂₀N₂O₃⁺ [M + H]⁺ 357.2173, found 357.2180.
Benzyl (2-(indolin-3-yl)ethyl)carbamate (S2a')

Following the general procedure B, tryptamine S1a' (3.50 g, 16.0 mmol) afforded indoline S2a' (3.30 g, 94%) as a pale yellow oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 6:4). 

$R_f = 0.18$ (silica gel, hexanes:EtOAc = 6:4); $^1$H NMR (500 MHz, CDCl$_3$): 7.36 (d, $J = 4.3$ Hz, 4H), 7.34 – 7.28 (m, 1H), 7.10 (d, $J = 7.3$ Hz, 1H), 7.05 (t, $J = 7.6$ Hz, 1H), 6.74 (t, $J = 7.5$ Hz, 1H), 6.68 (d, $J = 7.8$ Hz, 1H), 5.10 (s, 2H), 4.89 (s, 1H), 3.71 (t, $J = 8.7$ Hz, 1H), 3.33 (q, $J = 7.2$ Hz, 1H), 3.27 (t, $J = 7.4$ Hz, 1H), 2.01 (dq, $J = 13.2$, 6.3 Hz, 1H), 1.77 (dt, $J = 13.8$, 7.0 Hz, 1H); $^{13}$C NMR (126 MHz, CDCl$_3$): $\delta$ 156.5, 151.2, 136.6, 132.0, 128.4, 128.0, 127.6, 123.8, 118.6, 109.6, 66.5, 53.1, 39.4, 39.0, 34.3; HRMS calcd. for C$_{12}$H$_{17}$N$_2$O$_2$ $^{[M + H]}$ 221.1285, found 221.1278.
2.3. Preparation of N-Hydroxyindole Derivatives

General procedure D

The compounds were synthesized according to a known literature procedure.[14] To an oven-dried round-bottom flask equipped with a stir bar and septum were added indoline S2 (1.0 equiv) and MeOH (0.1 M in S2) at 23 °C. The resulting solution was cooled to 0 °C, and sodium tungstate dihydrate (0.05 equiv) and H₂O₂ (30 wt% in H₂O, 10.0 equiv) were successively added to the solution. The reaction mixture was stirred while the reaction was monitored by TLC. After completion of reaction, the reaction mixture was quenched with H₂O. The layers were separated and the aqueous layer was extracted with CH₂Cl₂ three times. The combined organic layer was washed with H₂O three times, dried over anhydrous MgSO₄, filtered, and concentrated under reduced pressure to afford N-hydroxyindole 1. The resulting crude product was used directly for the subsequent reaction without further purification.

*note:* In most cases, N-hydroxyindoles are unstable and slowly undergo decomposition, thus was unable to be stored for an extended period of time. However, most of N-hydroxyindoles could be obtained in excellent state which are clean enough to be characterized without purification. N-hydroxyindoles enlisted in this section were characterized without further purification (1a–1o, 1s, 1x) or otherwise protected with TBS group (1p', 1q', 1r', 1v', 1w', 1a'') for characterization. In case of the N-hydroxyindoles 1t and 1u, the products could be obtained in affordable quality. However, they could not be fully characterized due to their fast decomposition.

**Determination of the reaction yield for the preparation of N-hydroxyindoles:** The crude product was dissolved in CH₂Cl₂ to provide a solution with a total volume of 10.0 mL. 1.0 mL of the resulting solution was syringed out and dried separately in a 4 mL vial. To the 4 mL vial containing the separated sample was added 10.0 µL of 1,1,2,2-tetrachloroethane (TCE) as an internal standard and the resulting mixture was dissolved entirely in d4-methanol. The yield of product was determined by the integration of peaks from the ¹H NMR spectra relative to the internal standard, TCE. The calculated amount of the product in the sample (A) was then multiplied by 10 to
provide the total mass of the N-hydroxyindole product. The remaining 9.0 mL of the stock solution was dried under reduced pressure and used directly for the next step. The calculated amount of the product in the sample (A) was multiplied by 9 to provide the quantity of the starting material for the next reaction.
General Procedure E

For compounds \(1p', 1q', 1r', 1v', 1w', 1a''\):

To an oven-dried round-bottom flask equipped with a stir bar and septum were added crude \(N\)-hydroxyindole \(1\) (1.0 equiv) and \(\text{CH}_2\text{Cl}_2\) (0.2 M in \(1\)) at 23 °C, followed by TBSCI (2.0 equiv) and imidazole (3.0 equiv). The resulting mixture was stirred for 16 h before it was quenched with \(\text{H}_2\text{O}\). The layers were separated and the aqueous layer was extracted with \(\text{CH}_2\text{Cl}_2\) three times. The combined organic layer was dried over anhydrous MgSO\(_4\), filtered, and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography to afford TBS protected \(N\)-hydroxyindole.

**Methyl (2-(1-hydroxy-1H-indol-3-yl)ethyl)carbamate (1a)**

Following the general procedure D for 2 h, indoline \(S2a\) (0.120 g, 0.545 mmol) afforded \(N\)-hydroxyindole \(1a\) (93.0 mg, 73%) as a yellow oil and was used directly in the subsequent reaction without further purification.

\[ R_f = 0.45 \text{ (silica gel, hexanes:EtOAc = 1:1); } \]  \(\text{H NMR} \) (500 MHz, MeOD): \(\delta 7.53 \text{ (d, } J = 8.1 \text{ Hz, } 1\text{H}), 7.34 \text{ (d, } J = 8.2 \text{ Hz, } 1\text{H}), 7.13 \text{ (t, } J = 7.7 \text{ Hz, } 1\text{H}), 7.10 \text{ (s, } 1\text{H}), 6.99 \text{ (t, } J = 7.5 \text{ Hz, } 1\text{H}), 3.62 \text{ (s, } 3\text{H}), 3.36 \text{ (t, } J = 7.5 \text{ Hz, } 2\text{H}), 2.89 \text{ (t, } J = 7.7 \text{ Hz, } 2\text{H}); \] \(\text{C NMR} \) (126 MHz, MeOD): \(\delta 159.6, 135.7, 125.0, 124.4, 122.7, 119.7, 119.5, 109.2, 108.8, 75.8, 52.4, 42.8, 26.6; \) HRMS calcd. for \(\text{C}_{12}\text{H}_{15}\text{N}_2\text{O}_3^+ \) [M + H\(^+\)] 235.1077, found 235.1077.

**Methyl (2-(1-hydroxy-5-methyl-1H-indol-3-yl)ethyl)carbamate (1b)**

Following the general procedure D for 2 h, indoline \(S2b\) (75.0 mg, 0.320 mmol) afforded \(N\)-hydroxyindole \(1b\)
(48.0 mg, 60%) as a pale yellow oil and was used directly in the subsequent reaction without further purification.

\[ R_f = 0.24 \] (silica gel, hexanes:EtOAc = 7:3); \[ ^1H \text{NMR (500 MHz, MeOD): } \delta 7.32 (s, 1H), 7.23 (d, J = 8.3 Hz, 1H), 7.04 (s, 1H), 6.97 (dd, J = 8.4, 1.6 Hz, 1H), 3.62 (s, 3H), 3.34 (t, J = 7.4 Hz, 2H), 2.85 (t, J = 7.4 Hz, 2H), 2.41 (s, 3H); \]

\[ ^{13}C \text{NMR (126 MHz, MeOD): } \delta 159.6, 134.3, 128.8, 125.3, 124.5, 124.3, 119.1, 109.0, 108.2, 52.4, 42.8, 26.6, 21.6; \]

HRMS calcd. for C\textsubscript{13}H\textsubscript{17}N\textsubscript{2}O\textsubscript{3} \[ [M + H]^+ \] 249.1234, found 249.1233.

Methyl (2-(1-hydroxy-5-phenyl-1H-indol-3-yl)ethyl)carbamate (1c)

Following the general procedure D for 2 h, indoline S\textsubscript{2c} (60.0 mg, 0.202 mmol) afforded \( N \)-hydroxyindole 1c (29.0 mg, 47%) as a pale yellow oil and was used directly in the subsequent reaction without further purification.

\[ R_f = 0.40 \] (silica gel, hexanes:EtOAc = 1:1); \[ ^1H \text{NMR (500 MHz, MeOD): } \delta 7.76 (s, 1H), 7.64 (d, J = 7.7 Hz, 2H), 7.44 – 7.37 (m, 4H), 7.26 (t, J = 7.4 Hz, 1H), 7.14 (s, 1H), 3.60 (s, 3H), 3.39 (t, J = 7.3 Hz, 2H), 2.94 (t, J = 7.4 Hz, 2H); \]

\[ ^{13}C \text{NMR (126 MHz, MeOD): } \delta 159.6, 144.0, 135.1, 133.6, 129.6, 128.1, 127.2, 125.6, 125.1, 122.4, 118.0, 109.6, 109.4, 52.4, 43.0, 26.6; \]

HRMS calcd. for C\textsubscript{18}H\textsubscript{17}N\textsubscript{2}O\textsubscript{3} – \[ [M - H]^− \] 309.1245, found 309.1241.

Methyl (2-(1-hydroxy-5-(naphthalen-2-yl)-1H-indol-3-yl)ethyl)carbamate (1d)

Following the general procedure D for 4 h, indoline S\textsubscript{2d} (75.0 mg, 0.216 mmol) afforded \( N \)-hydroxyindole 1d (56.0 mg, 72%) as a brown oil and was used directly in the subsequent reaction without further purification.

\[ R_f = 0.24 \] (silica gel, hexanes:EtOAc = 7:3); \[ ^1H \text{NMR (400 MHz, MeOD): } \delta 8.10 (s, 1H), 7.91 (d, J = 7.8 Hz, 3H), 7.87 – 7.83 (m, 2H), 7.59 (dd, J = 8.5, 1.7 Hz, 1H), 7.50 – 7.42 (m, 3H), 7.17 (s, 1H), 3.61 (s, 3H), 3.42 (t, J = 7.3 Hz, 2H), 2.97 (t, J = 7.3 Hz, 2H); \]

\[ ^{13}C \text{NMR (126 MHz, MeOD): } \delta 159.7, 141.4, 135.1, 133.6, 129.6, 128.1, 127.2, 125.6, 125.1, 122.4, 118.0, 109.6, 109.4, 52.4, 43.0, 26.6; \]

HRMS calcd. for C\textsubscript{22}H\textsubscript{21}N\textsubscript{2}O\textsubscript{3} \[ [M + H]^+ \] 361.1547, found 361.1545.
Methyl (2-(1-hydroxy-5-(4-methoxyphenyl)-1H-indol-3-yl)ethyl)carbamate (1e)

Following the general procedure D for 2 h, indoline S2e (75.0 mg, 0.230 mmol) afforded N-hydroxyindole 1e (44.6 mg, 57%) as a pale yellow oil and was used directly in the subsequent reaction without further purification.

\[ R_f = 0.27 \] (silica gel, hexanes:EtOAc = 1:1); \( ^1H \) NMR (500 MHz, MeOD): \( \delta \) 7.70 (s, 1H), 7.55 (d, \( J = 8.7 \) Hz, 2H), 7.38 (s, 2H), 7.12 (s, 1H), 6.97 (d, \( J = 8.7 \) Hz, 2H), 3.81 (s, 3H), 3.60 (s, 3H), 3.38 (t, \( J = 7.3 \) Hz, 2H), 2.92 (t, \( J = 7.4 \) Hz, 2H); \( ^13C \) NMR (126 MHz, MeOD): \( \delta \) 159.9, 159.6, 136.6, 134.9, 133.3, 129.1, 125.6, 125.0, 122.2, 117.4, 115.1, 109.5, 109.3, 55.7, 52.4, 43.0, 26.6; HRMS calcd. for C_{19}H_{21}N_{2}O_{4} \([M + H]^+\) 341.1496, found 341.1504.

Methyl (2-(5-fluoro-1-hydroxy-1H-indol-3-yl)ethyl)carbamate (1f)

Following the general procedure D for 4 h, indoline S2f (50.0 mg, 0.210 mmol) afforded N-hydroxyindole 1f (34.0 mg, 64%) as a pale yellow oil and was used directly in the subsequent reaction without further purification.

\[ R_f = 0.27 \] (silica gel, hexanes:EtOAc = 1:1); \( ^1H \) NMR (500 MHz, MeOD): \( \delta \) 7.31 (dd, \( J = 8.9, 4.5 \) Hz, 1H), 7.22 (dd, \( J = 9.9, 2.4 \) Hz, 1H), 7.17 (s, 1H), 6.91 (td, \( J = 9.1, 2.4 \) Hz, 1H), 3.62 (s, 3H), 3.35 (t, \( J = 8.0 \) Hz, 2H), 2.85 (t, \( J = 7.4 \) Hz, 2H); \( ^13C \) NMR (126 MHz, MeOD): \( \delta \) 159.9, 159.6, 136.9, 134.9, 133.3, 129.1, 125.6, 125.0, 122.2, 117.4, 115.1, 109.5, 109.3, 55.7, 52.4, 43.0, 26.6; HRMS calcd. for C_{12}H_{12}FN_{2}O_{3} \([M - H]^−\) 251.0837, found 251.0832.

Methyl (2-(5-bromo-1-hydroxy-1H-indol-3-yl)ethyl)carbamate (1g)
Following the general procedure D for 2.5 h, indoline S2g (0.100 g, 0.334 mmol) afforded N-hydroxyindole 1g (57.0 mg, 54%) as a pale yellow oil and was used directly in the subsequent reaction without further purification. 

\[ R_f = 0.41 \] (silica gel, hexanes:EtOAc = 1:1); \[ ^{1}H \text{ NMR} (500 \text{ MHz, MeOD}): \delta 7.68 (s, 1H), 7.26 (d, \text{ } J = 8.7 \text{ Hz, 1H}), 7.21 (dd, \text{ } J = 8.7, 1.8 \text{ Hz, 1H}), 7.14 (s, 1H), 3.61 (s, 3H), 3.33 (t, \text{ } J = 7.3 \text{ Hz, 2H}), 2.84 (t, \text{ } J = 7.3 \text{ Hz, 2H}); \] 13C NMR (126 MHz, MeOD): \( \delta 159.6, 134.1, 126.7, 125.7, 125.4, 122.1, 112.8, 110.9, 108.6, 52.4, 42.8, 26.3; \) HRMS calcd. for C_{12}H_{12}BrN_{2}O_{3}^{−} [M − H]^{−} 311.0037, found 311.0033.

**Methyl 1-hydroxy-3-(2-((methoxycarbonyl)amino)ethyl)-1H-indole-5-carboxylate (1h)**

![Methyl 1-hydroxy-3-(2-((methoxycarbonyl)amino)ethyl)-1H-indole-5-carboxylate (1h)](image)

Following the general procedure D for 6 h, indoline S2h (70.0 mg, 0.252 mmol) afforded N-hydroxyindole 1h (45.0 mg, 61%) as a pale yellow oil and was used directly in the subsequent reaction without further purification. 

\[ R_f = 0.24 \] (silica gel, hexanes:EtOAc = 7:3); \[ ^{1}H \text{ NMR} (500 \text{ MHz, MeOD}): \delta 8.32 (s, 1H), 7.83 (dd, \text{ } J = 8.7, 1.4 \text{ Hz, 1H}), 7.39 (d, \text{ } J = 8.7 \text{ Hz, 1H}), 7.23 (s, 1H), 3.90 (s, 3H), 3.62 (s, 3H), 3.37 (t, \text{ } J = 7.2 \text{ Hz, 2H}), 2.94 (t, \text{ } J = 7.2 \text{ Hz, 2H}); \] 13C NMR (126 MHz, MeOD): \( \delta 170.0, 159.6, 137.4, 126.1, 124.5, 123.9, 121.9, 110.9, 109.0, 52.4, 52.3, 42.8, 26.3; \) HRMS calcd. for C_{14}H_{15}N_{2}O_{5}^{−} [M − H]^{−} 291.0987, found 291.0985.

**Methyl (2-(5-cyano-1-hydroxy-1H-indol-3-yl)ethyl)carbamate (1i)**

![Methyl (2-(5-cyano-1-hydroxy-1H-indol-3-yl)ethyl)carbamate (1i)](image)

Following the general procedure D for 6 h, indoline S2i (25.3 mg, 0.103 mmol) afforded N-hydroxyindole 1i (17.1 mg, 64%) as a pale yellow oil and was used directly in the subsequent reaction without further purification. 

\[ R_f = 0.24 \] (silica gel, hexanes:EtOAc = 7:3); \[ ^{1}H \text{ NMR} (500 \text{ MHz, MeOD}): \delta 8.02 (s, 1H), 7.49 (d, \text{ } J = 8.5 \text{ Hz, 1H}), 7.41 (dd, \text{ } J = 8.4, 1.5 \text{ Hz, 1H}), 7.31 (s, 1H), 3.61 (s, 3H), 3.36 (t, \text{ } J = 7.2 \text{ Hz, 3H}), 2.92 (t, \text{ } J = 7.2 \text{ Hz, 3H}); \] 13C NMR (126 MHz, MeOD): \( \delta 159.6, 136.4, 126.9, 125.8, 125.3, 124.8, 121.8, 110.5, 110.3, 102.2, 52.4, 42.7, 26.2; \) HRMS calcd. for C_{13}H_{14}N_{3}O_{4}^{−} [M + H]^{+} 260.1030, found 260.1024.
Methyl (2-(1-hydroxy-7-methyl-1H-indol-3-yl)ethyl)carbamate (1j)

Following the general procedure D for 2 h, indoline S2j (80.0 mg, 0.341 mmol) afforded N-hydroxyindole 1j (39.6 mg, 47%) as a pale yellow oil and was used directly in the subsequent reaction without further purification. 

$R_f=0.24$ (silica gel, hexanes:EtOAc = 7:3); $^1H$ NMR (400 MHz, MeOD): $\delta$ 7.33 (d, $J=7.6$ Hz, 1H), 7.03 (s, 1H), 6.90 – 6.80 (m, 2H), 3.62 (s, 3H), 3.35 (t, $J=7.5$ Hz, 2H), 2.85 (t, $J=7.4$ Hz, 2H), 2.67 (s, 3H); $^{13}$C NMR (101 MHz, MeOD): $\delta$ 159.6, 134.3, 125.7, 125.3, 124.7, 121.7, 120.0, 117.2, 108.8, 52.4, 42.7, 26.6, 18.3; HRMS calcd. for C$_{13}$H$_{17}$N$_2$O$_3$ $[M + H]^+$ 249.1234, found 249.1234.

Methyl (2-(1-hydroxy-1,6,7,8-tetrahydrocyclopenta[g]indol-3-yl)ethyl)carbamate (1k)

Following the general procedure D for 2 h, indoline S2k (50.0 mg, 0.192 mmol) afforded N-hydroxyindole 1k (40.5 mg, 77%) as a pale yellow oil and was used directly in the subsequent reaction without further purification. 

$R_f=0.24$ (silica gel, hexanes:EtOAc = 7:3); $^1H$ NMR (500 MHz, MeOD): $\delta$ 7.29 (d, $J=8.1$ Hz, 1H), 6.97 (s, 1H), 6.88 (d, $J=8.1$ Hz, 1H), 3.61 (s, 3H), 3.35 – 3.27 (m, 4H), 2.94 (t, $J=7.4$ Hz, 2H), 2.84 (t, $J=7.5$ Hz, 2H), 2.14 (qui, $J=7.4$ Hz, 2H); $^{13}$C NMR (126 MHz, MeOD): $\delta$ 159.6, 139.6, 132.9, 125.4, 124.1, 123.9, 117.6, 116.7, 109.2, 52.4, 42.7, 33.6, 31.4, 26.8, 26.5; HRMS calcd. for C$_{15}$H$_{19}$N$_2$O$_3$ $[M + H]^+$ 275.1390, found 275.1389.

Methyl (2-(4-chloro-1-hydroxy-1H-indol-3-yl)ethyl)carbamate (1l)

Following the general procedure D for 5 h, indoline S2l (50.0 mg, 0.196 mmol) afforded N-hydroxyindole 1l (37.1 mg, 70%) as a pale yellow oil and was used directly in the subsequent reaction without further purification.
$R_f=0.24$ (silica gel, hexanes:EtOAc = 7:3); $^1$H NMR (500 MHz, MeOD): $\delta$ 7.30 (dd, $J = 8.2$, 0.7 Hz, 1H), 7.17 (s, 1H), 7.05 (t, $J = 7.9$ Hz, 1H), 6.96 (d, $J = 7.5$ Hz, 1H), 3.61 (s, 3H), 3.40 (t, $J = 7.3$ Hz, 2H), 3.12 (t, $J = 7.3$ Hz, 2H); $^{13}$C NMR (126 MHz, MeOD): $\delta$ 159.6, 137.0, 127.1, 126.1, 123.1, 121.3, 120.6, 108.8, 108.3, 52.4, 43.8, 27.5; HRMS calcd. for C$_{12}$H$_{14}$ClN$_2$O$_3$ [M + H]$^+$ 269.0688, found 269.0685.

Methyl (2-(1-hydroxy-2-methyl-1H-indol-3-yl)ethyl)carbamate (1m)

Following the general procedure D for 2 h, indoline S$2_m$ (33.6 mg, 0.143 mmol) afforded N-hydroxyindole 1m (23.7 mg, 67%) as a pale yellow oil and was used directly in the subsequent reaction without further purification.

$R_f=0.60$ (silica gel, hexanes:EtOAc = 1:1); $^1$H NMR (500 MHz, MeOD): $\delta$ 7.46 (d, $J = 7.4$ Hz, 1H), 7.30 (d, $J = 8.1$ Hz, 1H), 7.06 (t, $J = 7.6$ Hz, 1H), 6.96 (t, $J = 7.4$ Hz, 1H), 3.62 (s, 1H), 3.27 (t, $J = 7.3$ Hz, 2H), 2.87 (t, $J = 7.2$ Hz, 2H), 2.36 (s, 3H); $^{13}$C NMR (126 MHz, MeOD): $\delta$ 159.6, 135.3, 133.1, 124.9, 121.6, 119.7, 118.4, 108.6, 104.6, 52.3, 42.8, 25.8, 8.9; HRMS calcd. for C$_{13}$H$_{17}$N$_2$O$_3$ [M + H]$^+$ 249.1234, found 249.1233.

$N$-Benzyl-2-(1-hydroxy-1H-indol-3-yl)acetamide (1n)

Following the general procedure D for 1.5 h, indoline S$2_n$ (40.8 mg, 0.153 mmol) afforded N-hydroxyindole 1n (23.2 mg, 54%) as a pale yellow oil and was used directly in the subsequent reaction without further purification.

$R_f=0.58$ (silica gel, hexanes:EtOAc = 1:1); $^1$H NMR (500 MHz, MeOD): $\delta$ 7.52 (dt, $J = 8.0$, 1.0 Hz, 1H), 7.37 (dt, $J = 8.2$, 1.0 Hz, 1H), 7.26 – 7.18 (m, 6H), 7.16 (ddd, $J = 8.2$, 7.0, 1.1 Hz, 1H), 7.00 (ddd, $J = 8.0$, 6.9, 1.0 Hz, 1H), 4.35 (s, 2H), 3.66 (s, 2H); $^{13}$C NMR (126 MHz, MeOD): $\delta$ 174.6, 139.9, 135.6, 129.4, 128.5, 128.1, 125.6, 124.8, 122.9, 120.0, 119.7, 109.3, 104.8, 44.2, 33.7; HRMS calcd. for C$_{17}$H$_{17}$N$_2$O$_2$ [M + H]$^+$ 281.1285, found 281.1282.
Methyl (S)-3-(1-hydroxy-1H-indol-3-yl)-2-((methoxycarbonyl)amino)propanoate (1o)

Following the general procedure D for 2 h, indoline S2o (70.0 mg, 0.252 mmol) afforded N-hydroxyindole 1o (48.5 mg, 66%) as a pale yellow oil and was used directly in the subsequent reaction without further purification. 

RF=0.44 (silica gel, hexanes:EtOAc = 1:1); \(^1\)H NMR (400 MHz, MeOD): δ 7.50 (d, \(J = 7.9\) Hz, 1H), 7.36 (d, \(J = 8.1\) Hz, 1H), 7.17 – 7.12 (m, 2H), 7.01 (t, \(J = 7.5\) Hz, 1H), 4.47 (t, \(J = 6.7\) Hz, 1H) 3.64 (s, 3H), 3.59 (s, 3H), 3.25 (dd, \(J = 14.6, 5.7\) Hz, 1H), 3.10 (dd, \(J = 14.6, 7.9\) Hz, 1H); \(^{13}\)C NMR (101 MHz, MeOD): δ 174.3, 159.0, 135.4, 125.2, 124.9, 122.8, 119.9, 119.3, 109.3, 106.1, 56.5, 52.7, 28.4; HRMS calcd. for C_{14}H_{17}N_{2}O_{5}^[M + H]^+ 293.1132, found 293.1138.

1-((tert-Butyldimethylsilyl)oxy)-2-phenethyl-1H-indole (1p')

Following the general procedure D for 1.5 h, indoline S2p (30.0 mg, 0.134 mmol) afforded N-hydroxyindole 1p as a pale yellow oil and was used directly in the subsequent reaction without further purification. For characterization, crude N-hydroxyindole 1p underwent TBS protection following the general procedure E to afford TBS-protected N-hydroxyindole 1p' (27.4 mg, 0.0781 mmol, 58% for 2 steps) as a colorless oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 1:1). 

RF=0.24 (silica gel, hexanes:EtOAc = 7:3); \(^1\)H NMR (400 MHz, CDCl₃): δ 7.49 (d, \(J = 7.8\) Hz, 1H), 7.34 – 7.30 (m, 3H), 7.26 – 7.21 (m, 3H), 7.14 (t, \(J = 7.5\) Hz, 1H), 7.05 (t, \(J = 7.4\) Hz, 1H), 6.16 (s, 1H), 3.06 (s, 4H), 1.14 (s, 9H), 0.27 (s, 6H); \(^{13}\)C NMR (126 MHz, CDCl₃): δ 141.5, 139.2, 134.8, 128.6, 128.5, 126.2, 124.1, 121.0, 120.0, 119.6, 109.0, 95.5, 34.6, 27.9, 26.1, 18.4, –3.7; HRMS calcd. for C_{22}H_{30}NOSi^[M + H]^+ 352.2091, found 352.2091.
1-((tert-Butyldimethylsilyl)oxy)-2-(((tert-butyldimethylsilyl)oxy)methyl)-1H-indole (1q')

Following the general procedure D for 1.5 h, indoline S2q (70.0 mg, 0.266 mmol) afforded N-hydroxyindole 1q as a pale yellow oil and was used directly in the subsequent reaction without further purification. For characterization, crude N-hydroxyindole 1q underwent TBS protection following the general procedure E to afford TBS-protected N-hydroxyindole 1q' (71.9 mg, 0.190 mmol, 72% for 2 steps) as a colorless oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 1:1).

\[ R_f = 0.24 \] (silica gel, hexanes:EtOAc = 7:3); \[ ^{1}H\ NMR \] (400 MHz, CDCl\textsubscript{3}): \[ \delta 7.53 \ (d, \ J = 7.8 \ Hz, 1H), 7.32 \ (d, \ J = 8.2 \ Hz, 1H), 7.16 \ (t, \ J = 7.6 \ Hz, 1H), 7.06 \ (t, \ J = 7.4 \ Hz, 1H), 6.33 \ (s, 1H), 4.84 \ (s, 2H), 1.14 \ (s, 9H), 0.95 \ (s, 9H), 0.29 \ (s, 6H), 0.11 \ (s, 6H); \[ ^{13}C\ NMR \] (126 MHz, CDCl\textsubscript{3}): \[ \delta 138.9, 135.3, 124.1, 121.5, 120.6, 119.8, 109.2, 96.9, 57.3, 26.1, 18.5, 18.5, -4.0, -5.1; \ HRMS \] calcd. for C\textsubscript{21}H\textsubscript{38}NO\textsubscript{2}Si\textsubscript{2}+ [M + H]\textsuperscript{+} 392.2436, found 392.2435.

1-((tert-Butyldimethylsilyl)oxy)-2-cyclohexyl-1H-indole (1r')

Following the general procedure D for 1.5 h, indoline S2r (20.0 mg, 0.0993 mmol) afforded N-hydroxyindole 1r as a pale yellow oil and was used directly in the subsequent reaction without further purification. For characterization, crude N-hydroxyindole 1r underwent TBS protection following the general procedure E to afford TBS-protected N-hydroxyindole 1r' (18.4 g, 0.0558 mmol, 56% for 2 steps) as a colorless oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 1:1).

\[ R_f = 0.24 \] (silica gel, hexanes:EtOAc = 7:3); \[ ^{1}H\ NMR \] (500 MHz, CDCl\textsubscript{3}): \[ \delta 7.48 \ (d, \ J = 7.8 \ Hz, 1H), 7.28 \ (d, \ J = 8.2 \ Hz, 1H), 7.10 \ (td, \ J = 7.1, 0.9 \ Hz, 1H), 7.02 \ (td, \ J = 7.5, 0.8 \ Hz, 1H), 6.08 \ (s, 1H), 2.81 – 2.75 \ (m, 1H), 2.08 \ (d, \ J = 8.4 \ Hz, 2H), 1.86 – 1.84 \ (m, 2H), 1.76 \ (d, \ J = 11.7 \ Hz, 1H), 1.42 – 1.24 \ (m, 6H), 1.14 \ (s, 9H), 0.24 \ (s, 6H); \[ ^{13}C\ NMR \] (126 MHz, CDCl\textsubscript{3}): \[ \delta 145.0, 134.1, 124.0, 120.6, 120.0, 119.3, 108.9, 92.8, 35.1, 32.8, 26.7, 26.3, 26.1, 18.4, -3.8; \ HRMS \] calcd. for C\textsubscript{20}H\textsubscript{32}NO\textsubscript{5}Si\textsubscript{2}+ [M + H]\textsuperscript{+} 330.2248, found 330.2246.
1,2,3,4-Tetrahydro-9H-carbazol-9-ol (1s)

Following the general procedure D for 1.5 h, indoline S2s (30.0 mg, 0.173 mmol) afforded N-hydroxyindole 1s (25.0 mg, 77%) as a pale yellow oil and was used directly in the subsequent reaction without further purification. 

\[ R_f = 0.65 \] (silica gel, hexanes:EtOAc = 9:1); \(^1\)H NMR (400 MHz, MeOD): \( \delta \) 7.30 (dd, \( J = 14.5, 7.9 \) Hz, 2H), 7.04 (t, \( J = 7.6 \) Hz, 1H), 6.92 (t, \( J = 7.4 \) Hz, 1H), 2.69 (dt, \( J = 36.8, 4.8 \) Hz, 4H), 1.91 – 1.82 (m, 4H); \(^13\)C NMR (101 MHz, MeOD): \( \delta \) 135.9, 135.15, 124.6, 121.5, 119.4, 118.3, 108.6, 105.9, 24.5, 24.0, 21.9, 21.8; HRMS calcd. for C\(_{12}\)H\(_{14}\)NO\(^+\) [M + H\(^+\)]\(^+\) 188.1070, found 188.1067.

tert-Butyl 5-((tert-butyldimethylsilyl)oxy)-1,3,4,5-tetrahydro-2H-pyrido[4,3-b]indole-2-carboxylate (1v)

Following the general procedure D for 2 h, indoline S2v (50.0 mg, 0.182 mmol) afforded N-hydroxyindole 1v as a pale yellow oil and was used directly in the subsequent reaction without further purification. For characterization, N-hydroxyindole 1v underwent TBS protection following the general procedure E to afford TBS-protected N-hydroxyindole 1v' (55.6 mg, 0.138 mmol, 76% for 2 steps) as a colorless oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 7:3).

\[ R_f = 0.24 \] (silica gel, hexanes:EtOAc = 7:3); \(^1\)H NMR (400 MHz, CDCl\(_3\)): \( \delta \) 7.40 (d, \( J = 7.8 \) Hz, 1H), 7.29 (d, \( J = 8.2 \) Hz, 1H), 7.17 (t, \( J = 7.6 \) Hz, 1H), 7.09 (d, \( J = 7.5 \) Hz, 1H), 4.61 (br s, 2H), 3.78 (br s, 2H), 2.79 (br s, 2H), 1.51 (s, 9H), 1.11 (s, 9H), 0.29 (s, 6H); \(^13\)C NMR (126 MHz, CDCl\(_3\)): \( \delta \) 136.6, 121.7, 119.9, 117.7, 109.5, 80.1, 41.4, 40.6, 28.7, 26.0, 22.7, 18.3, –4.0; HRMS calcd. for C\(_{23}\)H\(_{35}\)N\(_2\)O\(_3\)Si\(^+\) [M + H\(^+\)]\(^+\) 403.2412, found 403.2412.
Methyl 9-((tert-butyldimethylsilyl)oxy)-1,3,4,9-tetrahydro-2H-pyrido[3,4-b]indole-2-carboxylate (1w')

Following the general procedure D for 2 h, indoline S2w (50.0 mg, 0.215 mmol) afforded N-hydroxyindole 1w as a pale yellow oil and was used directly in the subsequent reaction without further purification. For characterization, N-hydroxyindole 1w underwent TBS protection following the general procedure E to afford TBS-protected N-hydroxyindole 1w' (55.8 mg, 0.155 mmol, 72% for 2 steps) as a colorless oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 1:1).

Analytic data is in agreement with the reported literature values. [1]
Benzyl (2-(1-((tert-butyldimethylsilyl)oxy)-1H-indol-3-yl)ethyl)carbamate (1a’’)

Following the general procedure D for 2 h, indoline S2a’ (70.0 mg, 0.236 mmol) afforded N-hydroxyindole 1a’ as a pale yellow oil and was used directly in the subsequent reaction without further purification. For characterization, N-hydroxyindole 1a’ underwent TBS protection following the general procedure E to afford TBS-protected N-hydroxyindole 1a’’ (66.2 mg, 0.156 mmol, 66% for 2 steps) as a colorless oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 7:3).

\[ R_f = 0.63 \] (silica gel, hexanes:EtOAc = 7:3); \[ ^1H \text{ NMR} \] (500 MHz, MeOD): \( \delta 7.56 \) (d, \( J = 8.0 \) Hz, 1H), 7.35 – 7.26 (m, 5H), 7.26 (d, \( J = 8.2 \) Hz, 1H), 7.15 (t, \( J = 7.5 \) Hz, 1H), 7.07 (s, 1H), 7.01 (t, \( J = 7.5 \) Hz, 1H), 5.06 (s, 2H), 3.39 (t, \( J = 7.1 \) Hz, 2H), 2.91 (t, \( J = 7.1 \) Hz, 2H), 1.10 (s, 9H), 0.22 (s, 6H); \[ ^13C \text{ NMR} \] (126 MHz, MeOD): \( \delta 158.9, 138.5, 136.0, 129.5, 128.9, 128.7, 125.1, 124.9, 123.1, 122.6, 120.2, 119.8, 110.0, 109.8, 67.3, 42.7, 26.4, 26.2, 18.8, -4.7; \[ \text{HRMS} \] calcd. for C_{24}H_{33}N_2O_3Si^+ [M + H]^+ 425.2255, found 425.2269.
3. Mechanistic Investigations

3.1. Identification of 2'-Substituent Effect in the Facilitated IHT Reaction (Scheme 1)

Table S1. Evaluation of 2'-substituents.\textsuperscript{a}

<table>
<thead>
<tr>
<th>entry</th>
<th>2'-substituent ((\bullet))</th>
<th>yield of 2-Int (%)</th>
<th>yield of 2 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>(\bullet) \text{\textit{n}Pent}</td>
<td>62%</td>
<td>0%</td>
</tr>
<tr>
<td>2</td>
<td>(\bullet) (\bullet) (\bullet) (\bullet)</td>
<td>65%</td>
<td>0%</td>
</tr>
<tr>
<td>3</td>
<td>(\bullet) (\text{CF}_3) (\text{CF}_3)</td>
<td>60%\textsuperscript{b}</td>
<td>5%\textsuperscript{b}</td>
</tr>
<tr>
<td>4</td>
<td>(\bullet) (\text{CF}_3) (\text{CF}_3) (\text{CF}_3) (\text{CF}_3)</td>
<td>30%\textsuperscript{b}</td>
<td>30%\textsuperscript{b}</td>
</tr>
<tr>
<td>5</td>
<td>(\bullet) (\text{CF}_3) (\text{CF}_3) (\text{CF}_3) (\text{CF}_3) (\text{CF}_3) (\text{CF}_3)</td>
<td>9%\textsuperscript{b}</td>
<td>39%\textsuperscript{b}</td>
</tr>
<tr>
<td>6</td>
<td>(\bullet) (\bullet) (\bullet) (\bullet) (\bullet) (\bullet) (\bullet) (\bullet) (\bullet) (\bullet) (\bullet) (\bullet) (\bullet)</td>
<td>0%</td>
<td>53%</td>
</tr>
</tbody>
</table>

\textsuperscript{a}Reactions performed with benzoyl chloride (1.1 equiv) and Et\(_3\)N (1.2 equiv) in CH\(_2\)Cl\(_2\) (0.05 M) at 0 to 23 °C for 2 h on 0.201 mmol scale. 
\textsuperscript{b}2-Int and 2 were co-eluted from silica gel chromatography. The ratio between 2-Int and 2 were determined by \(^1\text{H}\) NMR analysis of the mixture.

For characterization, the mixture obtained in entries 3, 4 and 5 was converted to pyrroloindoline 2 under separately performed thermal conditions since indolyl N-benzoate 2-Int and pyrroloindoline 2 co-eluted under the various solvent systems.
Methyl 3a-(hexanoyloxy)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate (2a-Int)

![Methyl 3a-(hexanoyloxy)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate (2a-Int)](image)

Purified by silica gel column chromatography (silica gel, hexanes:EtOAc = 1:0 → 7:3) to indolyl N-carboxylate 2a-Int (41.1 mg, 62%) as a pale yellow oil.

$R_f=0.60$ (silica gel, hexanes:EtOAc = 6:4); $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.58 (d, $J = 7.9$ Hz, 1H), 7.28 – 7.22 (m, 1H), 7.19 – 7.13 (m, 2H), 6.98 (br s, 1H), 4.83 (s, 1H), 3.66 (s, 3H), 3.51 (q, $J = 6.7$ Hz, 2H), 2.94 (t, $J = 6.8$ Hz, 2H), 2.63 (t, $J = 7.5$ Hz, 2H), 1.82 (p, $J = 7.4$ Hz, 2H), 1.50 – 1.35 (m, 4H), 0.95 (t, $J = 6.9$ Hz, 3H); $^{13}$C NMR (101 MHz, CDCl$_3$): $\delta$ 171.8, 157.2, 135.4, 124.7, 123.9, 123.5, 120.8, 119.3, 111.5, 108.9, 52.2, 41.1, 31.7, 31.3, 25.8, 24.7, 22.4; HRMS calcd. for C$_{18}$H$_{25}$N$_2$O$_4$ $[M + H]^+$ 333.1809, found 333.1810.

3-(2-((Methoxycarbonyl)amino)ethyl)-1H-indol-1-yl benzoate (2b-Int)

![3-(2-((Methoxycarbonyl)amino)ethyl)-1H-indol-1-yl benzoate (2b-Int)](image)

Purified by silica gel column chromatography (silica gel, hexanes:EtOAc = 1:0 → 7:3) to indolyl N-carboxylate 2b-Int (44.2 mg, 65%) as a pale yellow oil.

$R_f=0.31$ (silica gel, hexanes:EtOAc = 7:3); $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 8.22 (d, $J = 7.2$ Hz, 2H), 7.72 (t, $J = 7.5$ Hz, 1H), 7.62 (d, $J = 7.8$ Hz, 1H), 7.57 (t, $J = 7.8$ Hz, 2H), 7.26 (d, $J = 3.5$ Hz, 2H), 7.18 (ddd, $J = 8.1$, 4.6, 3.5 Hz, 1H), 7.10 (s, 1H), 4.83 (s, 1H), 3.67 (s, 3H), 3.55 (q, $J = 6.6$ Hz, 2H), 2.98 (t, $J = 6.8$ Hz, 2H); $^{13}$C NMR (126 MHz, CDCl$_3$): $\delta$ 164.9, 157.2, 135.9, 134.7, 130.4, 129.1, 126.6, 125.0, 124.2, 123.7, 121.1, 119.4, 112.0, 109.2, 52.2, 41.1, 25.9; HRMS calcd. for C$_{19}$H$_{23}$N$_2$O$_4$ $[M + H]^+$ 339.1339, found 339.1338.

Methyl 3a-((4-(trifluoromethyl)benzoyl)oxy)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate (2c)

41
Purified by silica gel column chromatography (silica gel, hexanes:EtOAc = 1:0 → 7:3) to an inseparable mixture of indolyl N-carboxylate 2c-Int and pyrroloindoline 2c (53.1 mg, 12:1, overall 65%) as a pale yellow oil. For characterization, the pure sample of 2c was obtained as a sole product by the reaction of 1a at 90 °C (general procedure H, Section 3.3).

\[ R_f = 0.63 \] (silica gel, hexanes:EtOAc = 1:1); \^H NMR (500 MHz, CDCl\textsubscript{3}, 60:40 mixture of rotamers): \( \delta 8.10 \ (d, J = 8.1 \text{ Hz}, 2H), 7.67 \ (d, J = 7.6 \text{ Hz}, 1H), 7.61 \text{ and } 7.55 \ (d, J = 7.6 \text{ Hz}, 1H), 7.21 \ (t, J = 7.7 \text{ Hz}, 1H), 6.81 \ (q, J = 6.9 \text{ Hz}, 1H), 6.69 \ (d, J = 7.9 \text{ Hz}, 1H), 5.77 \ (s, 1H), 3.94 \text{ and } 3.82 \ (t, J = 9.6 \text{ Hz}, 1H), 3.80 \text{ and } 3.73 \ (s, 3H), 3.26 \text{ – } 3.20 \ (m, 1H), 3.09 \text{ and } 2.99 \ (d, J = 12.6, 5.9 \text{ Hz}, 1H), 2.71 \ (q, J = 11.2 \text{ Hz}, 1H); ^{13}C NMR (126 MHz, CDCl\textsubscript{3}): \( \delta 164.3, 155.7, 154.9, 151.1, 150.9, 134.8 \ (q, J = 32.5 \text{ Hz}), 133.5, 131.4, 130.3, 126.7, 126.2, 125.5 \ (q, J = 4.2 \text{ Hz}), 123.5 \ (q, J = 272.7 \text{ Hz}), 119.8, 119.6, 110.6, 110.4, 95.1, 93.8, 80.4, 79.6, 53.0, 52.7, 45.6, 35.8, 35.7; ^{19}F NMR (471 MHz, CDCl\textsubscript{3}): \( \delta -63.2; \) HRMS calcd. for C\textsubscript{20}H\textsubscript{18}F\textsubscript{3}N\textsubscript{2}O\textsubscript{4} \[ [M + H]^+ \text{ 407.1213} \], found 407.1206.

Methyl 3a-((2-(trifluoromethyl)benzoyl)oxy)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate (2d)

Purified by silica gel column chromatography (silica gel, hexanes:EtOAc = 1:0 → 7:3) to an inseparable mixture of indolyl N-carboxylate 2d-Int and pyrroloindoline 2d (49.0 mg, 1:1, overall 60%) as a pale yellow oil. For characterization, the pure sample of 2d was obtained as a sole product by the reaction of 1a at 90 °C (general procedure H, Section 3.3).

\[ R_f = 0.50 \] (silica gel, hexanes:EtOAc = 1:1); \^H NMR (500 MHz, CDCl\textsubscript{3}, 60:40 mixture of rotamers): \( \delta 7.74 – 7.68 \ (m, 2H), 7.62 \text{ and } 7.58 \ (d, J = 7.5 \text{ Hz}, 1H), 7.60 – 7.54 \ (m, 2H), 7.21 \ (t, J = 7.8 \text{ Hz}, 1H), 6.82 \ (q, J = 7.2 \text{ Hz}, 1H), 6.69 \ (d, J = 8 \text{ Hz}, 1H), 6.65 \ (t, J = 8 \text{ Hz}, 1H), 6.13 \ (q, J = 27 \text{ Hz}, 1H); ^{19}F NMR (471 MHz, CDCl\textsubscript{3}): \( \delta -63.2; \) HRMS calcd. for C\textsubscript{20}H\textsubscript{18}F\textsubscript{3}N\textsubscript{2}O\textsubscript{4} \[ [M + H]^+ \text{ 407.1213} \], found 407.1206.
6.68 (d, \( J = 7.9 \) Hz, 1H), 5.71 and 5.70 (s, 1H), 3.92 and 3.81 (t, \( J = 9.8 \) Hz, 1H), 3.80 and 3.73 (s, 3H), 3.25–3.19 (m, 1H), 3.05 and 2.96 (dd, \( J = 12.9, 6.3 \) Hz, 1H), 2.78–2.69 (m, 1H); \(^{13}\)C NMR (126 MHz, CDCl\(_3\)): \( \delta \) 165.6, 155.7, 154.9, 151.1, 150.8, 131.9, 131.5, 131.3, 131.2, 130.7, 128.7 (q, \( J = 32.6 \) Hz), 126.8 (q, \( J = 5.6 \) Hz), 126.6, 126.2, 125.5, 125.4, 123.5 (q, \( J = 272.7 \) Hz), 119.8, 119.5, 110.5, 110.4, 95.5, 94.3, 80.0, 79.3, 53.0, 52.7, 45.6, 35.2, 35.1; \(^{19}\)F NMR (471 MHz, CDCl\(_3\)): \( \delta \) –58.9; HRMS calcd. for C\(_{20}\)H\(_{18}\)F\(_3\)N\(_2\)O\(_4\)\([M + H]\)\(^+\) 407.1213, found 407.1204.

Methyl 3a-((3,5-bis(trifluoromethyl)benzoyl)oxy)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate (2e)

Purified by silica gel column chromatography (silica gel, hexanes:EtOAc = 1:0 \( \rightarrow \) 7:3) to an inseparable mixture of indolyl N-carboxylate 2e-Int and pyrroloindoline 2e (45.8 mg, 1:4, overall 48%) as a pale yellow oil. For characterization, the pure sample of 2e was obtained as a sole product by the reaction of 1a at 90 °C (general procedure H, Section 3.3).

\( R_f = 0.70 \) (silica gel, hexanes:EtOAc = 1:1); \(^1\)H NMR (500 MHz, CDCl\(_3\), 60:40 mixture of rotamers): \( \delta \) 8.54 and 8.42 (s, 2H), 8.11 and 8.05 (s, 1H), 7.60 (dd, \( J = 20.2, 7.6 \) Hz, 1H), 7.22 (t, \( J = 7.7 \) Hz, 1H), 6.82 (q, \( J = 7.0 \) Hz, 1H), 6.71 (d, \( J = 7.9 \) Hz, 1H), 5.80 and 5.77 (s, 1H), 5.78 (d, \( J = 13.8 \) Hz, 1H), 3.96 and 3.86 (t, \( J = 9.5 \) Hz, 1H), 3.82 and 3.74 (s, 3H), 3.24 (tt, \( J = 11.5, 6.0 \) Hz, 1H), 3.13 and 3.07 (dd, \( J = 12.7, 6.2 \) Hz, 1H), 2.77–2.65 (m, 1H); \(^{13}\)C NMR (126 MHz, CDCl\(_3\)): \( \delta \) 162.8, 155.7, 154.8, 151.2, 151.0, 132.7, 132.4, 132.35 (q, \( J = 26.0 \) Hz), 131.7, 130.4, 130.0, 127.0, 126.8, 126.7, 126.4, 125.0, 125.0, 122.93 (q, \( J = 272.9 \) Hz), 120.0, 119.7, 110.6, 110.5, 95.8, 94.6, 80.4, 79.7, 53.1, 52.8, 45.7, 35.7; \(^{19}\)F NMR (471 MHz, CDCl\(_3\)): \( \delta \) –63.0; –63.0; HRMS calcd. for C\(_{21}\)H\(_{17}\)F\(_3\)N\(_2\)O\(_4\)\([M + H]\)\(^+\) 475.1087, found 475.1077.

Methyl 3a-((perfluorobenzoyl)oxy)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate (2f)

43
Purified by silica gel column chromatography (silica gel, hexanes:EtOAc = 1:0 → 7:3) to pyrroloindoline 2f (45.6 mg, 53%) as a pale yellow oil.

R_f = 0.56 (silica gel, hexanes:EtOAc = 1:1); ^1H NMR (400 MHz, CDCl_3, 60:40 mixture of rotamers): δ 7.56 and 7.53 (d, J = 8.7 Hz, 1H), 7.22 (t, J = 7.7 Hz, 1H), 6.83 (q, J = 7.2, 6.7 Hz, 1H), 6.69 (d, J = 8.0 Hz, 1H), 5.71 (d, J = 3.3 Hz, 1H), 3.92 and 3.82 (t, J = 9.7 Hz, 1H), 3.80 and 3.73 (s, 3H), 3.25 – 3.16 (m, 1H), 3.03 and 2.96 (dd, J = 12.6, 6.2 Hz, 1H), 2.70 (q, J = 10.7 Hz, 1H); ^13C NMR (101 MHz, CDCl_3): δ 157.8, 155.6, 154.8, 151.2, 151.0, 147.2 – 144.0 (dm, J = 262.7 Hz), 145.1 – 141.9 (dm, J = 260.2 Hz), 139.5 – 136.1 (dm, J = 257.6 Hz), 131.7, 126.4, 126.1, 124.8, 124.7, 122.6, 120.5, 120.0, 119.7, 110.7, 110.5, 108.2 (t, J = 15.7 Hz), 96.6, 95.4, 80.1, 79.4, 53.0, 52.8, 45.5, 35.7, 35.6; ^19F NMR (376 MHz, CDCl_3): δ –139.6 (dp, J = 17.0, 5.8 Hz), –149.6 (dt, J = 57.4, 20.7, 4.8 Hz), –161.8 – –162.0 (m); HRMS calcd. for C_{19}H_{14}F_5N_2O_4 [M + H]^+ 429.0868, found 429.0873.
3.2. $^{18}$O Isotope Experiment (Figure 3)

Scheme S2. Overview of the $^{18}$O labeling experiment.

The general method for measuring $^{18}$O saturation is as follows: First, $^{18}$O enriched acyl chlorides were prepared according to the literature procedures.$^{[15]}$ Indolyl N-carboxylates, $^{18}$O-1-A and $^{18}$O-1-B, were synthesized using the prepared $^{18}$O-enriched acyl chlorides. These precursors were subsequently subjected to IHT reaction conditions to provide $^{18}$O-2-A and $^{18}$O-2-B respectively. In the case of $^{18}$O-1-C, upon acylation, the intermediate immediately underwent the desired IHT reaction to provide $^{18}$O-2-C. Independent HRMS analyses of acylation products of methanol with acyl chlorides used for the preparation of $^{18}$O-1-A and $^{18}$O-1-B had shown that the level of $^{18}$O enrichment in the acyl chloride is directly reflected the acylation products. Also, it was shown that the level of $^{18}$O enrichment for $^{18}$O-1-A and $^{18}$O-1-B remained unchanged after IHT reaction to provide $^{18}$O-2-A and $^{18}$O-2-B respectively. Therefore, the level of $^{18}$O enrichment for $^{18}$O-1-C was estimated to be identical to that of $^{18}$O-2-C.

Detailed synthetic schemes for preparation of compounds are presented below.
3.2.1. Preparation of $^{18}$O Labeled Compounds

3.2.1.1. Benzoyl substituent

$^{18}$O-Benzoic acid

\[ \text{CCl}_3 \xrightarrow{\text{H}_2^{18}\text{O}} \text{HO}^{18}\text{O} \]

To an oven-dried heavy-wall pressure tube equipped with a stir bar and rubber septum were added α,α,α-trichlorotoluene (1.40 mL, 10.0 mmol, 1.0 equiv) and H$_2^{18}$O (1.00 mL, 50.0 mmol, 5.0 equiv) at 23 °C. The rubber septum was replaced with a Teflon screw cap under N$_2$ and the resulting mixture was heated to 120 °C in a preheated oil bath and stirred for 24 h. After the reaction mixture was cooled to 23 °C, the white solid was formed and precipitate was collected by filtration. The resulting filter cake was washed with H$_2$O (1 × 3 mL), and the solid was dried in vacuo, to afford $^{18}$O-benzoic acid (1.16 g, 92%) as a white solid. The resulting residue was used directly in the subsequent reaction without further purification. Analytic data is in agreement with the reported literature values.$^{[16]}$

$R_f$=0.24 (silica gel, hexanes:EtOAc = 7:3); $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 8.14 (dd, $J$ = 8.3, 1.5 Hz, 2H), 7.63 (t, $J$ = 7.5 Hz, 1H), 7.49 (t, $J$ = 7.8 Hz, 2H); $^{13}$C NMR (126 MHz, CDCl$_3$): $\delta$ 172.3, 134.0, 130.4, 129.5, 128.7; HRMS calcd. for C$_7$H$_5^{18}$O$_2$ $[\text{M} - \text{H}]^-$ 125.0380, found 125.0380; Isotopic Incorporation: [M+4] 96.8%, [M+2] 3.1%, [M+0] 0.1%.
3-(2-((Methoxycarbonyl)amino)ethyl)-1H-indol-1-yl benzoate (18O-1-A)

To an oven-dried two-neck round-bottom flask equipped with a stir bar, septum, and condenser were added 18O-benzoic acid (126 mg, 1.00 mmol, 1.0 equiv), DMF (a few drops) and CH2Cl2 (3 mL) at 23 °C. The resulting solution was cooled to 0 °C and oxalyl chloride (126 µL, 1.47 mmol, 1.5 equiv) was added dropwise. The reaction mixture was stirred for 4 h at 23 °C, before it was directly concentrated under reduced pressure. The resulting 18O-benzoic acid was used directly in the subsequent reaction without further purification.

To an oven-dried round-bottom flask equipped with a stir bar and septum were added N-hydroxyindole 1a (0.230 g, 0.982 mmol, 1.0 equiv) and CH2Cl2 (10 mL) at 23 °C, followed by the crude benzoic acid and Et3N (0.178 mL, 1.28 mmol, 1.3 equiv). The resulting mixture was stirred for 2 h, before it was quenched with H2O (10 mL). The layers were separated, and the aqueous layer was extracted with CH2Cl2 (3 × 20 mL). The combined organic layer was washed with brine (1 × 20 mL), dried over anhydrous MgSO4, filtered, and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography (silica gel, hexanes:EtOAc = 7:3) to afford the product (237 mg, 71%) as a pale yellow oil. The spectral data matched to those of compound 2b-Int (See section 3.1).

Rf=0.65 (silica gel, hexanes:EtOAc = 1:1); 1H NMR (500 MHz, CDCl3): δ 8.22 (d, J = 6.9 Hz, 2H), 7.72 (t, J = 7.5 Hz, 1H), 7.62 (d, J = 7.9 Hz, 1H), 7.57 (t, J = 7.8 Hz, 2H), 7.27 – 7.25 (m, 2H), 7.18 (ddd, J = 8.1, 4.7, 3.5 Hz, 1H), 7.10 (s, 1H), 4.83 (s, 1H), 3.67 (s, 3H), 3.55 (q, J = 6.6 Hz, 2H), 2.98 (t, J = 6.9 Hz, 2H); 13C NMR (126 MHz, CDCl3): δ 164.9, 157.2, 135.9, 134.7, 130.4, 129.1, 126.6, 125.0, 124.2, 123.7, 121.1, 119.4, 112.0, 109.2, 52.2, 41.1, 25.9; HRMS calcd. for C19H18N2O318ONa+ [M + Na]+ 363.1201, found 363.1192; Isotopic Incorporation: [M+2] 91.5%, [M+0] 8.5%.
Methyl 3a-(benzoyloxy)-3,3a,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate (18O-2-A)

To an oven-dried round-bottom flask equipped with a stir bar and septum were added \( ^{18}\text{O}-1\text{-A} \) (155 mg, 0.455 mmol, 1.0 equiv) and toluene (9 mL) at 23 °C. The resulting mixture was heated to 90 °C in a pre-heated oil bath and stirred for 16 h, before it was cooled to 23 °C and directly concentrated under reduced pressure. The resulting residue was purified by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 7:3) to afford the product (98.3 mg, 63%) as a pale yellow oil. 

\( R_f = 0.65 \) (silica gel, hexanes:EtOAc = 1:1); \(^1\)H NMR (500 MHz, CDCl\(_3\), 55:45 mixture of rotamers): \( \delta 7.99 \) (d, \( J = 7.7 \) Hz, 2H), 7.63 and 7.42 (d, \( J = 7.6 \) Hz, 1H), 7.54 (br t, \( J = 8.3 \) Hz, 1H), 7.41 (t, \( J = 7.6 \) Hz, 2H), 7.19 (t, \( J = 7.8 \) Hz, 1H), 6.80 (q, \( J = 6.9 \) Hz, 1H), 6.68 (d, \( J = 7.9 \) Hz, 1H), 5.78 (s, 1H), 3.93 and 3.80 (t, \( J = 9.7 \) Hz, 1H), 3.80 and 3.73 (s, 3H), 3.27 – 3.20 (m, 1H), 3.07 and 2.96 (dd, \( J = 12.9, 6.3 \) Hz, 1H), 2.78 – 2.64 (m, 1H); \(^{13}\)C NMR (126 MHz, CDCl\(_3\)): \( \delta 165.3, 155.6, 154.8, 151.0, 150.7, 133.2, 131.0, 130.2, 129.8, 129.1, 128.4, 126.5, 126.3, 126.0, 119.6, 119.3, 110.3, 110.2, 94.5, 93.3, 80.4, 79.6, 52.8, 52.5, 45.5, 35.9, 35.8; \) HRMS calcd. for \( C_{19}H_{19}N_2O_3^{18}\text{O}^+ \) [M + H]\(^+\) 341.1382, found 341.1373; Isotopic Incorporation: [M+2] 91.6%, [M+0] 8.4%.
Methyl 3a-(benzoyloxy)-8-(3-methylbut-2-en-1-yl)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate (18O-3-A)

To an oven-dried round-bottom flask equipped with a stir bar and septum were added 18O-2-A (98.3 mg, 0.289 mmol, 1.0 equiv) and acetone (7 mL) at 23 °C, followed by 1-bromo-3-methyl-2-buten (50 μL, 0.434 mmol, 1.5 equiv) and K2CO3 (0.120 g, 0.867 mmol, 3.0 equiv). The resulting mixture was stirred for 16 h, before it was directly concentrated under reduced pressure and re-dissolved in CH2Cl2 (10 mL) and H2O (10 mL). The layers were separated, and the aqueous layer was extracted with CH2Cl2 (3 × 10 mL). The combined organic layer was washed with brine (1 × 10 mL), dried over anhydrous MgSO4, filtered, and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 8:2) to afford the product (99.0 mg, 84%) as a pale yellow oil.

Rf = 0.38 (silica gel, hexanes:EtOAc = 7:3); 1H NMR (400 MHz, CDCl3, 50:50 mixture of rotamers): δ 7.98 (d, J = 7.7 Hz, 2H), 7.54 (br t, J = 7.3 Hz, 1H), 7.53 and 7.46 (d, J = 7.2 Hz, 1H), 7.41 (t, J = 7.6 Hz, 2H), 7.20 (t, J = 7.7 Hz, 2H), 6.71 (t, J = 7.5 Hz, 2H), 6.53 (t, J = 8.5 Hz, 1H), 5.89 and 5.83 (s, 1H), 5.24 (s, 1H), 4.28 and 4.10 (dd, J = 16.3, 7.5 Hz, 1H), 4.07 (br t, J = 11.9, 10.4 Hz, 1H), 4.07 and 3.93 (br t, J = 9.8 Hz, 1H), 3.78 and 3.75 (s, 3H), 3.23 – 3.10 (m, 1H), 2.93 – 2.79 (m, 1H), 2.68 (t, J = 10.9 Hz, 1H), 1.78 (d, J = 14.6 Hz, 3H), 1.71 (s, 3H); 13C NMR (101 MHz, CDCl3): 165.2, 155.9, 155.1, 152.1, 134.8, 134.4, 133.2, 131.1, 130.4, 129.8, 128.4, 127.0, 126.8, 126.0, 125.5, 121.3, 121.0, 118.2, 108.5, 108.0, 94.6, 93.7, 85.0, 84.4, 52.8, 45.6, 45.5, 45.3, 45.0, 37.6, 25.9, 18.3, 18.2; HRMS calcld. for C24H27N2O318O+ [M + H]+ 409.2008, found 409.2003; Isotopic Incorporation: [M+2] 91.6%, [M+0] 8.4%.
Methyl 3a-hydroxy-8-(3-methylbut-2-en-1-yl)-3,3a,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate ([\(^{18}\text{O}-4\)-A]

\[ \begin{array}{c}
\text{O} \quad \text{KOH} \\
\text{EtOH: } \text{H}_2\text{O} = 5:1, 60 \degree \text{C, 3 h} \\
\end{array} \]

\[ \begin{array}{c}
\text{H}^{18}\text{O} \quad \text{NCO}_2\text{Me} \\
\text{Me} \quad \text{Me} \\
\end{array} \]

\[ \begin{array}{c}
\text{H}^{18}\text{O} \quad \text{NCO}_2\text{Me} \\
\text{Me} \quad \text{Me} \\
\end{array} \]

To an oven-dried round-bottom flask equipped with a stir bar and septum were added \(^{18}\text{O}-3\)-A (99.0 mg, 0.242 mmol, 1.0 equiv) and EtOH: H\(_2\)O (5:1, 6 mL) at 23 \degree C, followed by KOH (20.4 mg, 0.363 mmol, 1.5 equiv). The resulting mixture was heated to 60 \degree C in a pre-heated oil bath and stirred for 3 h, before it was cooled to 23 \degree C and re-dissolved with CH\(_2\)Cl\(_2\) (10 mL) and H\(_2\)O (5 mL). The layers were separated, and the aqueous layer was extracted with CH\(_2\)Cl\(_2\) (3 × 10 mL). The combined organic layer was washed with brine (1 × 10 mL), dried over anhydrous MgSO\(_4\), filtered, and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 7:3) to afford the product (57.2 mg, 78%) as a pale yellow oil.

\( R_f = 0.45 \) (silica gel, hexanes:EtOAc = 1:1); \(^1\)H NMR (400 MHz, CDCl\(_3\), 50:50 mixture of rotamers): \( \delta \) 7.25 (d, \( J = 8.4 \) Hz, 1H), 7.20 (t, \( J = 7.8 \) Hz, 1H), 6.74 (t, \( J = 7.4 \) Hz, 1H), 6.49 (s, 1H), 5.38 and 5.30 (s, 1H), 5.16 (s, 1H), 4.22 – 4.08 and 4.07 – 3.93 (m, 1H), 3.96 (br s, 1H), 3.96 and 3.83 (br s, 1H), 3.73 (s, 3H), 3.23 – 3.04 (m, 2H), 2.41 – 2.23 (m, 2H), 1.75 (d, \( J = 11.7 \) Hz, 3H), 1.69 (s, 3H); \(^{13}\)C NMR (101 MHz, CDCl\(_3\)): \( \delta \) 150.4, 135.2, 130.8, 130.7, 130.5, 123.4, 123.2, 120.4, 120.3, 118.2, 108.4, 108.0, 87.7, 87.5, 86.9, 52.7, 45.8, 44.9, 44.4, 38.4, 25.9, 18.3; HRMS calcd. for C\(_{17}\)H\(_{21}\)N\(_2\)O\(_2\)\(^{18}\)O\(^+\) [M + H]\(^+\) 305.1746, found 305.1740; Isotopic Incorporation: [M+2] 80.0%, [M+0] 20.0%.
3.2.1.2. 3-Bromo-4-fluorobenzoyl substituent

2-Bromo-1-fluoro-4-(trichloromethyl)benzene

\[
\begin{array}{c}
\text{CF}_{3} \\
\text{F} \\
\text{Br}
\end{array}
\xrightarrow{\text{AlCl}_{3}}
\begin{array}{c}
\text{CCl}_{3} \\
\text{F} \\
\text{Br}
\end{array}
\]

To an oven-dried round-bottom flask equipped with a stir bar, septum, and condenser were added AlCl₃ (1.73 g, 13.0 mmol, 1.3 equiv) and CH₂Cl₂ (30 mL) at 23 °C. To a stirred mixture was added 3-bromo-4-fluorobenzotrifluoride (1.42 mL, 10.0 mmol, 1.0 equiv) dropwise via syringe. The reaction mixture was then heated to reflux in a pre-heated oil bath and stirred for 2 h, before it was cooled to 23 °C and quenched with iced water (15 mL). The layers were separated, and the aqueous layer was extracted with CH₂Cl₂ (3 × 5 mL). The combined organic layer was washed with brine (1 × 5 mL), dried over anhydrous MgSO₄, filtered, and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 9:1) to afford 3-bromo-4-fluorobenzotrichloride (1.75 g, 60%) as a pale yellow liquid. Analytic data is in agreement with the reported literature values.

\( R_f = 0.75 \) (silica gel, hexanes:EtOAc = 9:1); \(^1\)H NMR (400 MHz, CDCl₃): \( \delta 8.15 \) (dd, \( J = 6.2, 2.7 \) Hz, 1H), 7.87 (ddd, \( J = 9.1, 4.4, 2.5 \) Hz, 1H), 7.17 (ddd, \( J = 9.5, 7.8, 1.9 \) Hz, 1H); \(^13\)C NMR (126 MHz, CDCl₃): \( \delta 160.0 \) (d, \( J = 253.1 \) Hz), 141.6 (d, \( J = 3.8 \) Hz), 131.4, 126.8 (d, \( J = 8.1 \) Hz), 116.3 (d, \( J = 23.3 \) Hz), 109.1 (d, \( J = 22.0 \) Hz), 95.6; \(^19\)F NMR (376 MHz, CDCl₃): \( \delta -103.7 \) – –104.3 (m); HRMS calcd. for C₇H₄BrClF\(^+\) [M + H]\(^+\) 290.8541, found 290.8541.
**18**O-3-Bromo-4-fluorobenzoic acid

![Chemical Structure]

To an oven-dried heavy-wall pressure tube equipped with a stir bar and rubber septum were added 3-bromo-4-fluorobenzotrichloride (0.230 g, 0.787 mmol, 1.0 equiv) and H$_2^{18}$O (160 µL, 7.99 mmol, 10.2 equiv) at 23 °C. The rubber septum was replaced with a Teflon screw cap under N$_2$ and the resulting mixture was heated to 120 °C in a pre-heated oil bath and stirred for 24 h. After the reaction mixture was cooled to 23 °C, the white solid was formed and precipitate was collected by filtration. The resulting filter cake was washed with H$_2$O (1 × 3 mL), and the solid was dried in vacuo, to afford $^{18}$O-3-bromo-4-fluorobenzoic acid (70.8 mg, 40%) as a white solid. The resulting residue was used directly in the subsequent reaction without further purification. Analytic data is in agreement with the reported literature values.

$R_f$=0.24 (silica gel, hexanes:EtOAc = 7:3); $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 8.35 (dd, $J = 6.6, 2.1$ Hz, 1H), 8.07 (ddd, $J = 8.6, 4.7, 2.1$ Hz, 1H), 7.22 (t, $J = 8.3$ Hz, 1H); $^{13}$C NMR (126 MHz, CDCl$_3$): $\delta$ 169.9, 162.8 (d, $J = 256.3$ Hz), 136.2 (d, $J = 1.8$ Hz), 131.7 (d, $J = 8.7$ Hz), 126.8 (d, $J = 3.6$ Hz), 116.9 (d, $J = 23.1$ Hz), 109.7 (d, $J = 21.8$ Hz); $^{19}$F NMR (471 MHz, CDCl$_3$): $\delta$ $-98.1$ (dd, $J = 12.4, 6.7$ Hz); HRMS calcd. for C$_7$H$_3$BrF$^{18}$O$_2$ $^\text{[M-H]}$ 220.9391, found 220.9391; Isotopic Incorporation: [M+4] 96.6%, [M+2] 3.4%, [M+0] 0.0%.
To an oven-dried two-neck round-bottom flask equipped with a stir bar, septum, and condenser were added \(^{18}\)O-3-bromo-4-fluorobenzoic acid (70.8 mg, 0.317 mmol, 1.0 equiv) and CH\(_2\)Cl\(_2\) (3 mL) at 23 °C, followed by DMF (a few drops) and oxalyl chloride (136 \(\mu\)L, 1.59 mmol, 5.0 equiv). The reaction mixture was stirred for 2 h at 23 °C, then heated to reflux in a pre-heated oil bath and stirred for additional 5 min before it was directly concentrated under reduced pressure. The resulting \(^{18}\)O-benzoyl chloride was used directly in the subsequent reaction without further purification.

To an oven-dried round-bottom flask equipped with a stir bar and septum were added \(N\)-hydroxyindole 1a (72.9 mg, 0.311 mmol, 1.0 equiv) and CH\(_2\)Cl\(_2\) (10 mL) at 23 °C, followed by the crude benzoyl chloride and Et\(_3\)N (56 \(\mu\)L, 0.402 mmol, 1.3 equiv). The resulting mixture was stirred for 2 h, before it was cooled to 23 °C and quenched with H\(_2\)O (10 mL). The layers were separated, and the aqueous layer was extracted with CH\(_2\)Cl\(_2\) (3 \(\times\) 10 mL). The combined organic layer was washed with brine (1 \(\times\) 10 mL), dried over anhydrous MgSO\(_4\), filtered, and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 \(\rightarrow\) 7:3) to afford the product (107 mg, 79%) as a pale pink oil.

\(R_f\) = 0.70 (silica gel, hexanes:EtOAc = 1:1); \(^1\)H NMR (500 MHz, CDCl\(_3\)): \(\delta\) 8.47 (dd, \(J = 6.5, 2.2\) Hz, 1H), 8.18 (ddd, \(J = 8.7, 4.7, 2.2\) Hz, 1H), 7.64 (d, \(J = 7.8\) Hz, 1H), 7.35 – 7.20 (m, 5H), 7.10 (s, 1H), 4.89 (s, 1H), 3.70 (s, 3H), 3.56 (q, \(J = 6.7\) Hz, 2H), 2.99 (t, \(J = 6.9\) Hz, 2H); \(^{13}\)C NMR (126 MHz, CDCl\(_3\)): \(\delta\) 163.2 (d, \(J = 257.8\) Hz), 162.9, 157.2, 136.2, 136.1 (d, \(J = 2.1\) Hz), 131.6 (d, \(J = 8.8\) Hz), 125.2, 124.3, 124.1 (d, \(J = 3.7\) Hz), 123.8, 121.4, 119.5, 117.3 (d, \(J = 23.1\) Hz), 112.8, 110.3 (d, \(J = 21.9\) Hz), 109.3, 52.2, 41.0, 25.9; \(^{19}\)F NMR (471 MHz, CDCl\(_3\)): \(\delta\) –98.1; HRMS calcd. for C\(_{19}\)H\(_{17}\)BrFN\(_2\)O\(_3\)\(^{18}\)O\(^{\pm}\) [M + H\(^{\pm}\)] \(437.0393\), found 437.0388; Isotopic Incorporation:
[M+2] 89.5%, [M+0] 11.5%.
To an oven-dried round-bottom flask equipped with a stir bar and septum were added 18O-1-B (80.0 mg, 0.183 mmol, 1.0 equiv) and toluene (4 mL) at 23 °C. The resulting mixture was heated to 70 °C in a pre-heated oil bath and stirred for 8 h, before it was cooled to 23 °C and directly concentrated under reduced pressure. The resulting residue was purified directly by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 7:3) to afford the product (47.3 mg, 59%) as a pale pink oil.

\[ R_f = 0.70 \text{ (silica gel, hexanes:EtOAc = 1:1)} \]; \[ ^1H\text{ NMR (500 MHz, CDCl}_3\text{, 60:40 mixture of rotamers)}: \delta 8.20 \text{ (dd, } J = 6.6, 2.1 \text{ Hz, 1H}), 7.95 – 7.88 \text{ (m, 1H)}, 7.60 \text{ and 7.54 (d, } J = 7.5 \text{ Hz, 1H}), 7.20 \text{ (t, } J = 7.7 \text{ Hz, 1H}), 7.14 \text{ (t, } J = 8.3 \text{ Hz, 1H}), 6.80 \text{ (q, } J = 6.9 \text{ Hz, 1H}), 6.69 \text{ (d, } J = 7.9 \text{ Hz, 1H}), 5.75 \text{ (d, } J = 3.5 \text{ Hz, 1H}), 3.93 \text{ and 3.81 (t, } J = 9.7 \text{ Hz, 1H}), 3.80 \text{ and 3.73 (s, 2H), 3.22 (ddd, } J = 17.2, 8.5, 4.9 \text{ Hz, 1H}), 3.07 \text{ and 2.98 (dd, } J = 12.8, 6.2 \text{ Hz, 1H}), 2.69 \text{ (ddd, } J = 12.0, 8.7, 3.2 \text{ Hz, 1H)}; \]

\[ ^13C\text{ NMR (126 MHz, CDCl}_3\text{): } \delta 163.4, 163.3, 155.7, 151.1, 150.8, 135.6, 131.4, 131.1 \text{ (d, } J = 8.5 \text{ Hz), 127.9, 127.8, 126.7, 126.2, 125.5, 119.8, 119.6, 116.6 \text{ (d, } J = 23.0 \text{ Hz), 110.5, 110.4, 109.4 \text{ (d, } J = 21.7 \text{ Hz), 95.1, 93.8, 80.4, 79.6, 53.0, 52.7, 45.6, 35.8, 35.7; } \]

\[ ^19F\text{ NMR (471 MHz, CDCl}_3\text{): } \delta -99.3 \text{ (q, } J = 7.1 \text{ Hz), } -99.4 \text{ (q, } J = 7.2 \text{ Hz)}; \]

HRMS calcd. for C_{19}H_{17}BrFN_{2}O_{3}^{18O}\text{ [M + H]}^{+} 437.0393, found 437.0397; \n
**Isotopic Incorporation:** [M+2] 89.7%, [M+0] 11.3%.
Methyl 3a-((3-bromo-4-fluorobenzoyl)oxy)-8-(3-methyl-2-en-1-yl)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate (18O-3-B)

To an oven-dried round-bottom flask equipped with a stir bar and septum were added 18O-2-B (47.3 mg, 0.108 mmol, 1.0 equiv) and acetone (5 mL) at 23 °C, followed by 1-bromo-3-methyl-2-butene (19 μL, 0.162 mmol, 1.5 equiv) and K2CO3 (44.2 mg, 0.320 mmol, 3.0 equiv). The resulting mixture was stirred for 16 h, before it was directly concentrated under reduced pressure and re-dissolved in CH2Cl2 (5 mL) and H2O (5 mL). The layers were separated, and the aqueous layer was extracted with CH2Cl2 (3 × 5 mL). The combined organic layer was washed with brine (1 × 5 mL), dried over anhydrous MgSO4, filtered, and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 8:2) to afford the product (44.9 mg, 82%) as a pale pink oil.

Rf=0.50 (silica gel, hexanes:EtOAc = 7:3); 1H NMR (500 MHz, CDCl3, 55:45 mixture of rotamers): δ 8.18 (dd, J = 6.7, 2.1 Hz, 1H), 7.93 (ddd, J = 8.8, 4.8, 2.2 Hz, 1H), 7.49 and 7.44 (s, 1H), 7.21 (td, J = 7.8, 1.3 Hz, 1H), 7.14 (t, J = 8.4 Hz, 1H), 6.71 (t, J = 7.4 Hz, 1H), 6.54 (br s, 1H), 5.87 and 5.80 (s, 1H), 5.23 (t, J = 6.2 Hz, 1H), 4.29 – 4.19 (m, 1H), 4.12 – 4.00 (m, 2H), 3.97 – 3.90 (m, 1H), 3.78 and 3.75 (s, 3H), 3.16 (br s, 1H), 2.91 – 2.76 (m, 1H), 2.64 (td, J = 12.1, 8.4 Hz, 1H), 1.78 (d, J = 12.9 Hz, 3H), 1.72 (s, 3H); 13C NMR (126 MHz, CDCl3): δ 163.3, 163.2, 161.3, 155.9, 155.1, 152.1, 135.6 (d, J = 1.1 Hz), 135.0, 134.5, 131.3, 131.1 (d, J = 8.4 Hz), 128.0, 126.5, 126.3, 126.0, 125.5, 121.1, 120.8, 118.3, 116.6 (d, J = 23.0 Hz), 109.4 (d, J = 21.8 Hz), 108.4, 108.0, 95.3, 94.3, 84.9, 84.3, 52.8, 45.4, 45.2, 45.0, 37.7, 37.6, 26.0, 18.3; 19F NMR (471 MHz, CDCl3): δ −99.4, −99.5; HRMS calcd. for C29H23BrFN3O3 18O+ [M + H]+ 505.1019, found 505.1017; Isotopic Incorporation: [M+2] 89.1%, [M+0] 11.9%.
Methyl 3a-hydroxy-8-(3-methylbut-2-en-1-yl)-3,3a,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate (\(^{18}\)O-4-B)

\[
\begin{align*}
\text{O} & \quad \text{KOH} \\
\text{EtOH:H}_{2}\text{O} = 5:1 \\
60 \degree \text{C}, 3 \text{ h}
\end{align*}
\]

To an oven-dried round-bottom flask equipped with a stir bar and septum were added \(^{18}\)O-3-B (44.9 mg, 0.089 mmol, 1.0 equiv) and EtOH: H\(_2\)O (5:1, 6 mL) at 23 \degree C, followed by KOH (7.5 mg, 0.134 mmol, 1.5 equiv). The resulting mixture was heated to 60 \degree C in a pre-heated oil bath and stirred for 3 h, before it was cooled to 23 \degree C and diluted with CH\(_2\)Cl\(_2\) (5 mL) and H\(_2\)O (5 mL). The layers were separated, and the aqueous layer was extracted with CH\(_2\)Cl\(_2\) (3 \times 5 mL). The combined organic layer was washed with brine (1 \times 5 mL), dried over anhydrous MgSO\(_4\), filtered, and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 \rightarrow 7:3) to afford the product (19.1 mg, 71%) as a pale yellow oil.

\(R_f\)=0.44 (silica gel, hexanes:EtOAc = 1:1); \(^1\)H NMR (400 MHz, CDCl\(_3\), 50:50 mixture of rotamers): \(\delta\) 7.25 (d, \(J = 8.4 \text{ Hz}, 1\text{H}\)), 7.20 (t, \(J = 7.8 \text{ Hz}, 1\text{H}\)), 6.74 (t, \(J = 7.4 \text{ Hz}, 1\text{H}\)), 6.49 (s, 1\text{H}), 5.38 and 5.30 (s, 1\text{H}), 5.16 (s, 1\text{H}), 4.22 – 4.08 and 4.07 – 3.93 (m, 1\text{H}), 4.07 – 3.93 (m, 1\text{H}), 4.07 – 3.93 and 3.87 – 3.79 (m, 1\text{H}), 3.73 (s, 3\text{H}), 3.23 – 3.04 (m, 2\text{H}), 2.41 – 2.23 (m, 2\text{H}), 1.75 (d, \(J = 11.7 \text{ Hz}, 3\text{H}\)), 1.69 (s, 3\text{H}); \(^{13}\)C NMR (101 MHz, CDCl\(_3\)): \(\delta\) 150.4, 135.2, 130.8, 130.7, 130.5, 123.4, 123.2, 120.4, 120.3, 118.2, 108.4, 108.0, 87.7, 87.5, 86.9, 52.7, 45.8, 44.9, 44.4, 38.4, 25.9, 18.3; HRMS calcd. for C\(_{17}\)H\(_{21}\)N\(_2\)O\(_2\)\(^{18}\)O\(^+\) [M + H]\(^+\) 305.1746, found 305.1740; Isotopic Incorporation: [M+2] 66.9%, [M+0] 33.1%.
3.2.1.3. Pentafluorobenzoyl substituent

\(^{18}\text{O}-2,3,4,5,6\text{-Pentafluorobenzoic acid}\)

![Chemical structure diagram]

To an oven-dried heavy-wall pressure tube equipped with a stir bar and rubber septum were added 2,3,4,5,6-pentafluorobenzonitrile (965 mg, 5.00 mmol, 1.0 equiv) and sulfuric acid (0.5 mL) at 23 °C, followed by H\(^{18}\text{O}\) (500 µL, 25.0 mmol, 5.0 equiv). The rubber septum was replaced with a Teflon screw cap under N\(_2\) and the resulting mixture was heated to 100 °C in a pre-heated oil bath. The reaction mixture was stirred for 48 h and cooled to 23 °C before it was diluted with CH\(_2\)Cl\(_2\) (20 mL). The layers were separated, and the aqueous layer was extracted with CH\(_2\)Cl\(_2\) (3 × 20 mL). The combined organic layer was dried over anhydrous MgSO\(_4\), filtered, and concentrated under reduced pressure to afford \(^{18}\text{O}\)-pentafluorobenzoic acid (248 mg, 23%) as a white-beige solid.

The resulting residue was used directly in the subsequent reaction without further purification.

\(R_f=0.10\) (silica gel, hexanes:EtOAc = 9:1); \(^{13}\text{C} \text{NMR}\) (126 MHz, CDCl\(_3\)): \(\delta\) 164.0, 147.6 – 145.2 (dm, \(J = 263.1\) Hz), 145.5 – 143.0 (dm, d, \(J = 256.3\) Hz), 139.2 – 136.7 (dm, d, \(J = 256.5\) Hz), 106.8 (td, \(J = 14.4, 4.1\) Hz); \(^{19}\text{F} \text{NMR}\) (471 MHz, CDCl\(_3\)): \(\delta\) −136.2 (dt, \(J = 19.5, 5.5\) Hz), −146.1 (td, \(J = 20.9, 5.9\) Hz), −159.8 – −159.9 (m);

\(\text{HRMS}\) calcd. for C\(_7\)F\(_5\)O\(_2\) \([M - H]^-\) 214.9909, found 214.9910; \textbf{Isotopic Incorporation}: \([M+4]\) 19.5%, \([M+2]\) 49.6%, \([M+0]\) 30.9%.
Methyl 3a-((perfluorobenzoyl)oxy)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate (18O-2-C)

To an oven-dried round-bottom flask equipped with a stir bar and septum were added 18O-2,3,4,5,6-pentafluorobenzoic acid (50 mg, 0.231 mmol, 1.0 equiv) and CH₂Cl₂ (3 mL) at 23 °C. The resulting solution was cooled to 0 °C, and DMF (a few drops) and oxalyl chloride (19 µL, 0.222 mmol, 1.0 equiv) were successively added to the solution. The reaction mixture was warmed up to 23 °C and stirred for 2 h, before it was directly concentrated under reduced pressure. The resulting 18O-benzoyl chloride was used directly in the subsequent reaction without further purification.

To an oven-dried round-bottom flask equipped with a stir bar and septum were added N-hydroxyindole 1a (51.5 mg, 0.220 mmol, 1.0 equiv) and CH₂Cl₂ (5 mL) at 23 °C. The solution was then cooled to 0 °C and the crude benzoyl chloride and Et₃N (40 µL, 0.287 mmol, 1.3 equiv) was added to the solution. The reaction mixture was warmed up to 23 °C and stirred for 2 h, before it was quenched with H₂O (5 mL). The layers were separated, and the aqueous layer was extracted with CH₂Cl₂ (3 × 5 mL). The combined organic layer was washed with brine (1 × 5 mL), dried over anhydrous MgSO₄, filtered, and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 7:3) to afford the product (45.2 mg, 47%) as a pale yellow oil.

Rₓ=0.56 (silica gel, hexanes:EtOAc = 1:1); ¹H NMR (400 MHz, CDCl₃, 60:40 mixture of rotamers): δ 7.56 and 7.53 (d, J = 8.7 Hz, 1H), 7.22 (t, J = 7.7 Hz, 1H), 6.83 (q, J = 7.2, 6.7 Hz, 1H), 6.69 (d, J = 8.0 Hz, 1H), 5.71 (d, J = 3.3 Hz, 1H), 3.92 and 3.82 (t, J = 9.7 Hz, 1H), 3.80 and 3.73 (s, 3H), 3.25 – 3.16 (m, 1H), 3.03 and 2.96 (dd, J = 12.6, 6.2 Hz, 1H), 2.70 (q, J = 10.7 Hz, 1H); ¹³C NMR (101 MHz, CDCl₃): δ 157.8, 155.6, 154.8, 151.2, 151.0, 147.2 – 144.0 (dm, J = 262.7 Hz), 145.1 – 141.9 (dm, J = 260.2 Hz), 139.5 – 136.1 (dm, J = 257.6 Hz),
131.7, 126.4, 126.1, 124.8, 124.7, 122.6, 120.5, 120.0, 119.7, 110.7, 110.5, 108.2 (t, $J = 15.7$ Hz), 96.6, 95.4, 80.1, 79.4, 53.0, 52.8, 45.5, 35.7, 35.6; $^{19}$F NMR (376 MHz, CDCl$_3$): $\delta\delta$ $-139.6$ (dp, $J = 17.0, 5.8$ Hz), $-149.6$ (dtt, $J = 57.4, 20.7, 4.8$ Hz), $-161.8$ – $-162.0$ (m); HRMS calcd. for C$_{19}$H$_1_4$F$_2$N$_2$O$_3$ [M + H]$^+$ 431.0911, found 431.0907; Isotopic Incorporation: [M+2] 44.4%, [M+0] 55.6%.
Methyl 8-(3-methylbut-2-en-1-yl)-3a-((perfluorobenzoyl)oxy)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate (18O-3-C)

To an oven-dried round-bottom flask equipped with a stir bar and septum were added 18O-2-C (45.2 mg, 0.105 mmol, 1.0 equiv) and acetone (3 mL) at 23 °C, followed by 1-bromo-3-methyl-2-butene (37 μL, 0.315 mmol, 3.0 equiv) and K2CO3 (87.0 mg, 0.629 mmol, 6.0 equiv). The resulting mixture was stirred for 4 d, before it was directly concentrated under reduced pressure and re-dissolved in CH2Cl2 (5 mL) and H2O (5 mL). The layers were separated and the aqueous layer was extracted with CH2Cl2 (3 × 5 mL). The combined organic layer was washed with brine (1 × 5 mL), dried over anhydrous MgSO4, filtered, and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 8:2) to afford the product (43.1 mg, 82%) as a pale yellow oil.

Rf=0.66 (silica gel, hexanes:EtOAc = 1:1); 1H NMR (500 MHz, CDCl3, 60:40 mixture of rotamers): δ 7.46 (d, J = 7.6 Hz, 1H), 7.22 (t, J = 7.9 Hz, 1H), 6.74 (t, J = 7.5 Hz, 1H), 6.53 (d, J = 7.7 Hz, 1H), 5.83 and 5.76 (s, 1H), 5.20 (s, 1H), 4.27 – 4.23 and 4.10 – 4.08 (m, 1H), 4.05 – 3.89 (m, 3H), 3.78 and 3.75 (s, 3H), 3.26 – 3.06 (m, 1H), 2.92 – 2.75 (m, 1H), 2.72 – 2.56 (m, 1H), 1.76 (s, 3H), 1.69 (s, 3H); 13C NMR (126 MHz, CDCl3): δ 157.6, 155.8, 155.0, 152.1, 146.9 – 144.4 (dm, J = 264.7 Hz), 144.6 – 142.0 (dm, J = 260.6 Hz), 139.2 – 136.4 (dm, J = 250.5 Hz), 135.2, 134.7, 131.6, 128.2, 125.7, 125.6, 120.9, 120.5, 118.6, 108.7, 108.3, 97.0, 95.9, 84.7, 84.2, 52.9, 45.6, 45.5, 45.1, 44.9, 38.2, 37.6, 37.6, 25.8, 18.2; 19F NMR (471 MHz, CDCl3): δ −137.4 (dq, J = 17.5, 5.8 Hz), −137.8 (tdd, J = 26.9, 12.3, 7.0 Hz), −148.0 (dt, J = 43.5, 20.8 Hz), −148.2 (ddd, J = 25.5, 13.0, 4.7 Hz), −160.2 – −160.3 (m), −160.4 – −160.5 (m); HRMS calcd. for C24H22F3N2O118O+ [M + H]+ 499.1537, found 499.1535; Isotopic Incorporation: [M+2] 44.3%, [M+0] 55.7%.
Methyl 3a-hydroxy-8-(3-methylbut-2-en-1-yl)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate (18O-4-C)

To an oven-dried round-bottom flask equipped with a stir bar and septum were added 18O-3-C (43.1 mg, 0.086 mmol, 1.0 equiv) and EtOH: H₂O (5:1, 4 mL) at 23 °C, followed by KOH (7.0 mg, 0.125 mmol, 1.5 equiv). The resulting mixture was heated to 60 °C in a pre-heated oil bath and stirred for 3 h, before it was cooled to 23 °C and diluted with CH₂Cl₂ (5 mL) and H₂O (5 mL). The layers were separated, and the aqueous layer was extracted with CH₂Cl₂ (3 × 5 mL). The combined organic layer was washed with brine (1 × 5 mL), dried over anhydrous MgSO₄, filtered, and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 7:3) to afford the product (18.1 mg, 69%) as a pale yellow oil.

Rᵣ=0.45 (silica gel, hexanes:EtOAc = 1:1); ¹H NMR (400 MHz, CDCl₃, 50:50 mixture of rotamers): δ 7.25 (d, J = 8.4 Hz, 1H), 7.20 (t, J = 7.8 Hz, 1H), 6.74 (t, J = 7.4 Hz, 1H), 6.49 (s, 1H), 5.38 and 5.30 (s, 1H), 5.16 (s, 1H), 4.22 – 4.08 and 4.07 – 3.93 (m, 1H), 4.07 – 3.93 (m, 1H), 4.07 – 3.93 and 3.87 – 3.79 (m, 1H), 3.73 (s, 3H), 3.23 – 3.04 (m, 2H), 2.41 – 2.23 (m, 2H), 1.75 (d, J = 11.7 Hz, 3H), 1.69 (s, 3H); ¹³C NMR (101 MHz, CDCl₃): δ 150.4, 135.2, 130.8, 130.7, 130.5, 123.4, 123.2, 120.4, 120.3, 118.2, 108.4, 108.0, 87.7, 87.5, 86.9, 52.7, 45.8, 44.9, 44.4, 38.4, 25.9, 18.3; HRMS calcd. for C₁₇H₂₃N₂O₂ [M + H]⁺ 305.1746, found 305.1740; Isotopic Incorporation: [M+2] 27.4%, [M+0] 72.6%.
3.2.1.4. Bromotryptamine with benzoyl substituent

5-Bromo-3-(2-((methoxycarbonyl)amino)ethyl)-1H-indol-1-yl benzoate (\(^{18}O\)-1-D)

To an oven-dried two-neck round-bottom flask equipped with a stir bar, septum, and condenser were added \(^{18}O\)-benzoic acid (31.8 mg, 0.252 mmol, 1.02 equiv), DMF (a few drops) and \(\text{CH}_2\text{Cl}_2\) (3 mL) at 23 °C. The resulting solution was cooled to 0 °C and oxalyl chloride (32 \(\mu\)L, 0.371 mmol, 1.5 equiv) was added dropwise. The reaction mixture was stirred for 4 h at 23 °C, before it was directly concentrated under reduced pressure. The resulting \(^{18}O\)-benzoyl chloride was used directly in the subsequent reaction without further purification.

To an oven-dried round-bottom flask equipped with a stir bar and septum were added \(N\)-hydroxyindole \(1g\) (77.3 mg, 0.247 mmol, 1.0 equiv) and \(\text{CH}_2\text{Cl}_2\) (10 mL) at 23 °C, followed by the crude benzoyl chloride and \(\text{Et}_3\text{N}\) (44 \(\mu\)L, 0.317 mmol, 1.3 equiv). The resulting mixture was stirred for 2 h, before it was quenched with \(\text{H}_2\text{O}\) (10 mL). The layers were separated, and the aqueous layer was extracted with \(\text{CH}_2\text{Cl}_2\) (3 \(\times\) 10 mL). The combined organic layer was washed with brine (1 \(\times\) 10 mL), dried over anhydrous \(\text{MgSO}_4\), filtered, and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 \(\rightarrow\) 7:3) to afford the product (68.6 mg, 66%) as a pale yellow oil.

\(R_f=0.48\) (silica gel, hexanes:EtOAc = 6:4); \(^1\text{H NMR}\) (400 MHz, \(\text{CDCl}_3\)): \(\delta\) 8.20 (d, \(J = 8.1\) Hz, 2H), 7.76 – 7.68 (m, 1H), 7.73 (s, 1H), 7.57 (t, \(J = 7.5\) Hz, 1H), 7.13 (d, \(J = 8.6\) Hz, 2H), 7.10 (s, 1H), 3.69 (s, 3H), 3.51 (q, \(J = 6.7\) Hz, 2H), 2.94 (t, \(J = 6.8\) Hz, 2H); \(^{13}\text{C NMR}\) (126 MHz, \(\text{CDCl}_3\)): \(\delta\) 164.7, 157.2, 134.9, 134.1, 130.4, 130.3, 129.2, 128.6, 126.5, 126.2, 125.0, 122.1, 114.2, 110.6, 52.3, 41.2, 25.7; \(\text{HRMS}\) calcd. for \(\text{C}_{19}\text{H}_{18}\text{BrN}_2\text{O}_3^{18}\text{O}^+\) [M + H] \(^+\) 419.0487, found 419.0496; \textbf{Isotopic Incorporation}: [M+2] 96.8%, [M+0] 3.2%.
Methyl 3a-(benzoyloxy)-5-bromo-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate (\(^{18}\text{O}-2\)-D)

To an oven-dried round-bottom flask equipped with a stir bar and septum were added \(^{18}\text{O}-1\)-D (68.6 mg, 0.164 mmol, 1.0 equiv) and toluene (3 mL) at 23 °C. The resulting mixture was heated to 90 °C in a pre-heated oil bath and stirred for 24 h, before it was cooled to 23 °C and directly concentrated under reduced pressure. The resulting residue was purified directly by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 7:3) to afford the product (34.5 mg, 50%) as a pale yellow oil.

\(R_f=0.48\) (silica gel, hexanes:EtOAc = 6:4); \(^1\text{H NMR}\) (500 MHz, CDCl\(_3\), 60:40 mixture of rotamers): δ 7.99 (dd, \(J = 8.2, 1.4 \text{ Hz}, 2\text{H}), 7.72 \text{ and 7.63 (s, 1H)}, 7.56 (td, \(J = 7.6, 3.8 \text{ Hz}, 2\text{H}), 7.43 (td, \(J = 7.9, 2.3 \text{ Hz}, 1\text{H}), 7.30 – 7.26 (m, 1\text{H}), 6.56 (d, \(J = 8.4 \text{ Hz}, 1\text{H}), 5.77 (s, 1\text{H}), 5.25 \text{ and 4.91 (s, 1H)}, 3.93 \text{ and 3.82 (t, } J = 9.2 \text{ Hz, 1H), 3.79 and 3.73 (s, 3H), 3.24 (td, } J = 10.9, 6.4 \text{ Hz, 1H), 3.01 \text{ and 2.90 (ddd, } J = 12.9, 6.4, 1.8 \text{ Hz, 2H), 2.70 (ddd, } J = 12.9, 10.9, 8.6 \text{ Hz, 1H}); \(^{13}\text{C NMR}\) (126 MHz, CDCl\(_3\)): δ 165.4, 155.7, 154.8, 150.0, 149.7, 133.9, 133.6, 133.5, 129.9, 129.5, 128.9, 128.6, 128.3, 128.1, 111.8, 111.7, 111.2, 110.9, 94.0, 92.7, 80.7, 79.9, 53.0, 52.8, 45.5, 45.4, 36.1, 35.9; \(\text{HRMS}\) calcd. for C\(_{19}\)H\(_{18}\)BrN\(_2\)O\(_3\)^{18}\text{O}^+ [M + H]^+ 419.0487, found 419.0494; \textbf{Isotopic Incorporation}: [M+2] 97.1%, [M+0] 2.9%. 

64
Methyl 3a-(benzoyloxy)-5-bromo-8-(3-methylbut-2-en-1-yl)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate (18O-3-D)

\[
\begin{align*}
\text{Br} & \quad \text{\^{18}O} & \quad \text{NCO}_2\text{Me} \\
\text{Me} & \quad \text{Me} & \quad \text{Br} \\
\text{acetone, 23 °C, 2 d} & \quad \text{K}_2\text{CO}_3
\end{align*}
\]

To an oven-dried round-bottom flask equipped with a stir bar and septum were added 18O-2-D (34.5 mg, 0.082 mmol, 1.0 equiv) and acetone (4 mL) at 23 °C, followed by 1-bromo-3-methyl-2-butene (28 µL, 0.246 mmol, 3.0 equiv) and K2CO3 (67.7 mg, 0.490 mmol, 6.0 equiv). The resulting mixture was stirred for 2 d, before it was directly concentrated under reduced pressure and re-dissolved in CH2Cl2 (5 mL) and H2O (5 mL). The layers were separated, and the aqueous layer was extracted with CH2Cl2 (3 × 10 mL). The combined organic layer was washed with brine (1 × 10 mL), dried over anhydrous MgSO4, filtered, and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 8:2) to afford the product (29.0 mg, 73%) as a pale yellow oil.

Rf = 0.69 (silica gel, hexanes:EtOAc = 7:3); 1H NMR (500 MHz, CDCl3, 50:50 mixture of rotamers): δ 7.98 (d, J = 7.6 Hz, 1H), 7.63 – 7.48 (m, 2H), 7.42 (t, J = 7.7 Hz, 2H), 7.28 (d, J = 2.1 Hz, 2H), 6.40 and 6.39 (s, 1H), 5.90 and 5.84 (s, 1H), 5.21 (s, 1H), 4.26 – 4.21 and 4.14 – 4.07 (m, 1H), 4.04 – 3.92 (m, 2H), 3.75 (s, 3H), 3.23 – 3.08 (m, 1H), 2.87 – 2.71 (m, 1H), 2.65 (q, J = 11.2, 10.5 Hz, 1H), 1.76 (d, J = 13.0 Hz, 3H); 13C NMR (126 MHz, CDCl3): 165.2, 151.0, 133.7, 133.5, 130.1, 129.9, 129.1, 129.0, 128.5, 120.7, 120.5, 109.7, 109.5, 109.3, 93.9, 92.9, 85.2, 84.6, 52.9, 45.5, 45.2, 44.8, 37.8, 37.8, 25.9, 18.2; HRMS calcd. for C24H26BrN2O3\textsuperscript{18}O\textsuperscript{+} [M + H]\textsuperscript{+} 487.1113, found 487.1107; Isotopic Incorporation: [M+2] 97.2%, [M+0] 2.8%.
To an oven-dried round-bottom flask equipped with a stir bar and septum were added $^{18}$O-3-D (29.0 mg, 0.060 mmol, 1.0 equiv) and EtOH: H$_2$O (5:1, 3 mL) at 23 °C, followed by KOH (5.0 mg, 0.090 mmol, 1.5 equiv). The resulting mixture was heated to 60 °C in a pre-heated oil bath and stirred for 3 h, before it was cooled to 23 °C and diluted with CH$_2$Cl$_2$ (2 mL) and H$_2$O (2 mL). The layers were separated, and the aqueous layer was extracted with CH$_2$Cl$_2$ (3 × 3 mL). The combined organic layer was washed with brine (1 × 3 mL), dried over anhydrous MgSO$_4$, filtered, and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 7:3) to afford the product (15.0 mg, 65%) as a pale yellow oil.

$R_f$=0.55 (silica gel, hexanes:EtOAc = 1:1); $^1$H NMR (400 MHz, CDCl$_3$, 55:45 mixture of rotamers): $\delta$ 7.32 (d, $J$ = 2.1 Hz, 1H), 7.27 (d, $J$ = 2.1 Hz, 1H), 6.35 (t, $J$ = 8.1 Hz, 1H), 5.39 and 5.31 (s, 1H), 5.13 and 5.09 (s, 1H), 4.16 – 4.10 and 3.99 – 3.96 (m, 1H), 3.96 – 3.83 (m, 3H), 3.73 (s, 3H), 3.25 – 3.05 (m, 2H), 2.39 – 2.22 (m, 2H), 1.74 (d, $J$ = 14.0 Hz, 3H), 1.69 (s, 3H); $^{13}$C NMR (101 MHz, CDCl$_3$): $\delta$ 149.3, 135.7, 135.4, 133.4, 133.3, 126.5, 126.4, 119.9, 119.8, 109.8, 109.5, 88.3, 87.8, 87.1, 52.8, 45.8, 44.8, 44.3, 38.5, 25.9; HRMS calcd. for C$_{17}$H$_{22}$BrN$_2$O$_2$^{18}O$^+$ [M + H]$^+$ 383.0851, found 383.0838; Isotopic Incorporation: [M+2] 93.5%, [M+0] 6.5%.
3.2.1.5. Bromotryptamine with 3-bromo-4-fluorobenzoyl substituent

5-Bromo-3-(2-((methoxycarbonyl)amino)ethyl)-1H-indol-1-yl 3-bromo-4-fluorobenzoate (\(^{18}\)O-1-E)

![Chemical structure]

To an oven-dried two-neck round-bottom flask equipped with a stir bar, septum, and a reflux condenser were added \(^{18}\)O-3-bromo-4-fluorobenzoic acid (60.0 mg, 0.269 mmol, 1.04 equiv) and CH\(_2\)Cl\(_2\) (3 mL) at 23 °C, followed by DMF (a few drops) and oxalyl chloride (111 \(\mu\)L, 1.29 mmol, 5.0 equiv). The reaction mixture was stirred for 2 h at 23 °C, then heated to reflux in a pre-heated oil bath and stirred for additional 5 min before it was directly concentrated under reduced pressure. The resulting \(^{18}\)O-benzylocyl chloride was used directly in the subsequent reaction without further purification.

To an oven-dried round-bottom flask equipped with a stir bar and septum were added N-hydroxyindole 1g (80.8 mg, 0.258 mmol, 1.0 equiv) and CH\(_2\)Cl\(_2\) (10 mL) at 23 °C, followed by the crude benzylocyl chloride and Et\(_3\)N (47 \(\mu\)L, 0.337 mmol, 1.3 equiv). The resulting mixture was stirred for 2 h, before it was quenched with H\(_2\)O (10 mL). The layers were separated, and the aqueous layer was extracted with CH\(_2\)Cl\(_2\) (3 × 20 mL). The combined organic layer was dried over anhydrous MgSO\(_4\), filtered, and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 7:3) to afford the product (77.2 mg, 58%) as a pale yellow oil.

\(R_f=0.55\) (silica gel, hexanes:EtOAc = 6:4); \(^1H\) NMR (500 MHz, CDCl\(_3\)): \(\delta\) 8.43 (dd, \(J = 6.5, 2.2\) Hz, 1H), 8.16 (ddd, \(J = 8.6, 4.6, 2.2\) Hz, 1H), 7.73 (d, \(J = 1.8\) Hz, 1H), 7.34 (dd, \(J = 8.6, 1.8\) Hz, 1H), 7.34 (t, \(J = 8.3\) Hz, 1H), 7.10 (d, \(J = 8.6\) Hz, 1H), 7.08 (s, 1H), 4.80 (s, 1H), 3.68 (s, 3H), 3.51 (q, \(J = 6.8\) Hz, 2H), 2.93 (t, \(J = 6.8\) Hz, 2H); \(^13\)C NMR (126 MHz, CDCl\(_3\)): \(\delta\) 163.3 (d, \(J = 258.2\) Hz), 162.8, 157.2, 136.2, 134.4, 131.7 (d, \(J = 8.9\) Hz), 126.7, 125.1, 123.8 (d, \(J = 3.8\) Hz), 122.2, 117.5, 117.4 (d, \(J = 23.2\) Hz), 117.4, 114.5, 111.9, 110.6, 110.5, 110.3, 52.3,
41.1, 25.7; \textit{\textsuperscript{19}F NMR} (471 MHz, CDCl\textsubscript{3}): $\delta$ = 95.8 (dd, $J$ = 12.5, 5.7 Hz); \textbf{HRMS} calcd. for C\textsubscript{19}H\textsubscript{15}Br\textsubscript{2}FN\textsubscript{2}O\textsubscript{3}\textsuperscript{18}ONa\textsuperscript{+}

[M + Na]\textsuperscript{+} 536.9317, found 536.9327; \textbf{Isotopic Incorporation:} [M+2] 94.3%, [M+0] 5.7%.
Methyl 5-bromo-3a-((3-bromo-4-fluorobenzoyl)oxy)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate (18O-2-E)

To an oven-dried round-bottom flask equipped with a stir bar and septum were added 18O-1-E (77.2 mg, 0.150 mmol, 1.0 equiv) and toluene (3 mL) at 23 °C. The resulting mixture was heated to 90 °C in a pre-heated oil bath and stirred for 8 h, before it was cooled to 23 °C and directly concentrated under reduced pressure. The resulting residue was purified directly by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 7:3) to afford the product (42.6 mg, 55%) as a pale yellow oil.

\( R_f = 0.55 \) (silica gel, hexanes:EtOAc = 6:4); \(^1\)H NMR (500 MHz, CDCl\(_3\), 60:40 mixture of rotamers): \( \delta \) 8.20 (dt, \( J = 6.5, 1.8 \) Hz, 1H), 7.98 – 7.89 (m, 1H), 7.69 and 7.63 (s, 1H), 7.29 (d, \( J = 8.4 \) Hz, 1H), 7.16 (t, \( J = 8.5 \) Hz, 1H), 6.57 (dd, \( J = 8.4, 1.4 \) Hz, 1H), 5.74 (d, \( J = 1.8 \) Hz, 1H), 5.27 and 4.91 (s, 1H), 3.93 and 3.82 (t, \( J = 9.8 \) Hz, 1H), 3.79 and 3.73 (s, 3H), 3.23 (q, \( J = 11.9, 10.8 \) Hz, 1H), 3.02 and 2.93 (dd, \( J = 13.2, 6.1 \) Hz, 1H), 2.67 (q, \( J = 10.9 \) Hz, 1H); \(^{13}\)C NMR (126 MHz, CDCl\(_3\)): \( \delta \) 163.3, 162.4 (d, \( J = 254.9 \) Hz), 155.6, 154.7, 150.0, 149.8, 135.7, 134.1, 131.18 (d, \( J = 8.6 \) Hz), 129.5, 129.1, 127.7, 127.6, 127.5 (d, \( J = 3.4 \) Hz), 116.7 (d, \( J = 23.3 \) Hz), 111.9, 111.8, 111.2, 110.9, 109.6, 109.5, 94.4, 93.2, 80.6, 79.9, 53.1, 52.8, 45.5, 35.9, 35.8; \(^{19}\)F NMR (471 MHz, CDCl\(_3\)): \( \delta \) –98.9 (q, \( J = 6.8 \) Hz), –99.0 (q, \( J = 6.9 \) Hz); HRMS calcd. for C\(_{19}\)H\(_{16}\)Br\(_2\)F\(_2\)O\(_3\)\(^{18}\)O\(^+\) [M + H]\(^+\) 514.9498, found 514.9486; Isotopic Incorporation: [M+2] 94.5%, [M+0] 5.5%.
Methyl 5-bromo-3a-((3-bromo-4-fluorobenzoyl)oxy)-8-(3-methylbut-2-en-1-yl)-3,3a,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate (18O-3-E)

To an oven-dried round-bottom flask equipped with a stir bar and septum were added 18O-2-E (42.6 mg, 0.083 mmol, 1.0 equiv) and acetone (4 mL) at 23 °C, followed by 1-bromo-3-methyl-2-butene (29 µL, 0.247 mmol, 3.0 equiv) and K₂CO₃ (69.0 mg, 0.499 mmol, 6.0 equiv). The resulting mixture was stirred for 2 d, before it was directly concentrated under reduced pressure and re-dissolved in CH₂Cl₂ (5 mL) and H₂O (5 mL). The layers were separated, and the aqueous layer was extracted with CH₂Cl₂ (3 × 5 mL). The combined organic layer was washed with brine (1 × 5 mL), dried over anhydrous MgSO₄, filtered, and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 8:2) to afford the product (34.3 mg, 71%) as a pale yellow oil.

Rᵥ = 0.71 (silica gel, hexanes:EtOAc = 7:3); ¹H NMR (500 MHz, CDCl₃, 60:40 mixture of rotamers): δ 8.18 (d, J = 6.1 Hz, 1H), 7.93 (s, 1H), 7.57 and 7.50 (s, 1H), 7.28 (d, J = 8.7 Hz, 1H), 7.16 (t, J = 8.3 Hz, 1H), 6.40 and 6.39 (s, 1H), 5.88 and 5.80 (s, 1H), 5.19 (s, 1H), 4.23 and 4.04 (dd, J = 15.8, 6.8 Hz, 1H), 4.13 – 3.92 (m, 2H), 3.77 and 3.75 (s, 1H), 3.24 – 3.05 (m, 1H), 2.89 – 2.71 (m, 1H), 2.61 (q, J = 10.3 Hz, 1H), 1.77 (d, J = 10.4 Hz, 3H); ¹³C NMR (126 MHz, CDCl₃): 163.0, 162.3 (d, J = 255.6 Hz), 161.3, 150.9, 135.5, 133.8, 131.0 (d, J = 8.6 Hz), 128.5, 128.4, 127.6, 120.4, 120.3, 118.2, 116.5 (d, J = 23.1 Hz), 109.5, 109.3, 94.4, 93.4, 84.9, 84.2, 64.5, 52.7, 45.2, 44.9, 44.7, 37.8, 25.8, 18.1, 18.0; ¹⁹F NMR (471 MHz, CDCl₃): δ -99.0, -99.1; HRMS calcd. for C₂₉H₂₃Br₂FN₂O₃¹⁸O⁺ [M + H⁺]⁺ 583.0124, found 583.0116; Isotopic Incorporation: [M+2] 94.7%, [M+0] 5.3%.
Methyl 5-bromo-3a-hydroxy-8-(3-methylbut-2-en-1-yl)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate (18O-4-E)

To an oven-dried round-bottom flask equipped with a stir bar and septum were added 18O-3-E (34.2 mg, 0.059 mmol, 1.0 equiv) and EtOH: H2O (5:1, 2 mL) at 23 °C, followed by KOH (5.0 mg, 0.089 mmol, 1.5 equiv). The resulting mixture was heated to 60 °C in a pre-heated oil bath and stirred for 3 h, before it was cooled to 23 °C and diluted with CH2Cl2 (3 mL) and H2O (3 mL). The layers were separated, and the aqueous layer was extracted with CH2Cl2 (3 × 3 mL). The combined organic layer was washed with brine (1 × 3 mL), dried over anhydrous MgSO4, filtered, and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 7:3) to afford the product (15.6 mg, 69%) as a pale yellow oil.

Rf = 0.55 (silica gel, hexanes:EtOAc = 1:1); 1H NMR (400 MHz, CDCl3, 55:45 mixture of rotamers): δ 7.32 (d, J = 2.1 Hz, 1H), 7.27 (d, J = 2.1 Hz, 1H), 6.35 (t, J = 8.1 Hz, 1H), 5.39 and 5.31 (s, 1H), 5.13 and 5.09 (s, 1H), 4.16 – 4.10 and 3.99 – 3.96 (m, 1H), 3.96 – 3.83 (m, 3H), 3.73 (s, 3H), 3.25 – 3.05 (m, 2H), 2.39 – 2.22 (m, 2H), 1.74 (d, J = 14.0 Hz, 3H), 1.69 (s, 3H); 13C NMR (101 MHz, CDCl3): δ 149.3, 135.7, 135.4, 133.4, 133.3, 126.5, 126.4, 119.9, 119.8, 109.8, 109.5, 88.3, 87.8, 87.1, 52.8, 45.8, 44.8, 44.3, 38.5, 25.9; HRMS calcd. for C17H22BrN2O218O+ [M + H]+ 383.0851, found 383.0820; Isotopic Incorporation: [M+2] 90.4%, [M+0] 9.6%.

71
3.2.2. Determination of $^{18}$O Saturation

General information of HRMS

Reagents and Chemicals

MeCN (LC-MS grade), H$_2$O with 0.1% formic acid (LC-MS grade) were obtained from Samchun Chemical.

Instrumentation and Experimental

HRMS experiments were performed using a Thermo Scientific™ Orbitrap Exploris 120 equipped with a Hypersil GOLD™ C18 Selectivity HPLC column and Thermo Scientific™ mass spectrometer with Thermo Scientific™ Xcalibur™ software for instrument control and data processing. The aqueous mobile phase A is H$_2$O with 0.1% formic acid (v/v), and organic mobile phase B is MeCN with 0.1% formic acid (v/v). 20 µL of samples were injected onto the column with a flow rate of 0.4 mL/min at 40 °C. The chromatographic condition is as followed: 30 min method consisting with 5% B over 0.0–2.0 min, then a gradient of 5% B to 95% B over 2.0–20.0 min, then maintain 95% B over 20.0–24.9 min followed by a gradient of 95% B to 5% B over 24.9–25.0 min, then hold 5% B for 5 min. The eluents were monitored by a UV detector with a range of 210 nm to 400 nm, followed by HRMS detection in electrospray ionization with both positive and negative mode. The MS conditions were as followed: voltage for positive ion mode 3500 V, voltage for negative ion mode 3000 V, sheath gas flow rate 55 Arb; aux gas flow rate 15 Arb; sweep gas flow rate 1 Arb, ion transfer tube temperature 320 °C, vaporizer temperature 350 °C, orbitrap resolution 120000, m/z range 100–1000 Da.

The conditions above were used for all the HRMS analysis in mechanistic section.

The $M+2$ isotopic enrichment values ($M$ = mass of unlabeled compound), and full isotopic incorporation data were calculated using the relative abundance in mass spectra for each $M+n$ ($n = 0, 2$) peak in HRMS.
$^{18}\text{O}$-benzoic acid

HRMS result of $^{18}\text{O}$-benzoic acid
3-(2-((Methoxycarbonyl)amino)ethyl)-1H-indol-1-yl benzoate (**O-1-A)**

$\text{[M+Na]}^+$ Exact Mass: 363.12012

$\text{[M+Na]}^+$ Exact Mass: 363.1192

$\text{[M+Na]}^+$ Exact Mass: 363.11588

$\text{[M+Na]}^+$ Exact Mass: 363.12128

$\text{[M+Na]}^+$ Exact Mass: 363.1191

$18^O$ enrichment: 91.5%
Methyl 3a-(benzoyloxy)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate ($^{18}$O-2-A)

$^{18}$O enrichment: 91.6%
Methyl 3a-(benzoyloxy)-8-(3-methylbut-2-en-1-yl)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate ($^{18}$O-3-A)

$^{18}$O enrichment: 91.6%
Methyl 3a-hydroxy-8-(3-methylbut-2-en-1-yl)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate

\((^{18}\text{O}-4-\text{A})\)

\[\text{C}_{17}\text{H}_{22}\text{N}_{2}\text{O}_{4}\text{H}^{+}\]

\([\text{M+H}]^{+}\) Exact Mass: 305.1746

\({}^{18}\text{O}\) enrichment: 80.0%
$^{18}$O-3-Bromo-4-fluorobenzoic acid

Isotopic simulation of negative ion mode

HRMS result of $^{18}$O-3-bromo-4-fluorobenzoic acid
No overlap of isotopes (i.e. \( \text{C}_7\text{H}_7\text{Br}^{81}\text{O}_2 \) and \( \text{C}_7\text{H}_7\text{Br}^{79}\text{O}^{18}\text{O} \)) on HRMS was observed.
3-(2-((Methoxycarbonyl)amino)ethyl)-1H-indol-1-yl 3-bromo-4-fluorobenzoate (\(1^8\)O-1-B)

\[
\text{\[M+H]^+ Exact Mass: 437.03927}
\]

\(1^8\)O enrichment: 89.5%
Methyl 3a-((3-bromo-4-fluorobenzoyl)oxy)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate

$^{18}$O enrichment: 89.7%
Methyl 3a-((3-bromo-4-fluorobenzoyl)oxy)-8-(3-methylbut-2-en-1-yl)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate (18O-3-B)

18O enrichment: 89.1%
Methyl 3a-hydroxy-8-(3-methylbut-2-en-1-yl)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate

(\(^{18}\)O-4-B)

\[\text{\(18\)O enrichment: 66.9\%} \]
$^{18}$O-2,3,4,5,6-Pentafluorobenzoic acid

Isotopic simulation of negative ion mode

HRMS result of $^{18}$O-pentafluorobenzoic acid

<table>
<thead>
<tr>
<th>m/z</th>
<th>Intensity</th>
<th>Relative intensity</th>
</tr>
</thead>
<tbody>
<tr>
<td>210.98239</td>
<td>112405195.2</td>
<td>62.22390173</td>
</tr>
<tr>
<td>212.967136</td>
<td>180742756.6</td>
<td>100</td>
</tr>
<tr>
<td>214.990507</td>
<td>711082964</td>
<td>39.33979485</td>
</tr>
<tr>
<td>214.99089</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Methyl 3a-((perfluorobenzoyl)oxy)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate (\(^{18}\text{O}-2\text{-C})

\[
\text{NCO}_2\text{Me}
\]

\(^{18}\text{O}\) enrichment: 44.4\%
Methyl 8-(3-methylbut-2-en-1-yl)-3a-((perfluorobenzoyl)oxy)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate \((^{18}\text{O}-3\text{-C})\)

Isotopic simulation of positive ion mode

HRMS result of compound \(^{18}\text{O}-3\text{-C}\)

\(^{18}\text{O}\) enrichment: 44.3%
Methyl 3a-hydroxy-8-(3-methylbut-2-en-1-yl)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate (18O-4-C)

\[ \text{[M+H]'} \text{ Exact Mass: 305.17456} \]

\[ \text{[M+H]'} \text{ Exact Mass: 303.17032} \]

\[^{18}\text{O} \text{ enrichment: 27.4\%} \]
5-Bromo-3-(2-((methoxycarbonyl)amino)ethyl)-1H-indol-1-yl benzoate (\(^{18}\)O-1-D)

\[
\text{Isotopic simulation of positive ion mode}
\]

\[
\text{HRMS result of compound} \quad ^{18}\text{O-1-D}
\]

\(^{18}\text{O enrichment: 96.8\%}\)
Methyl 3a-(benzoyloxy)-5-bromo-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate (18O-2-D)

18O enrichment: 97.1%
Methyl 3a-(benzoyloxy)-5-bromo-8-(3-methylbut-2-en-1-yl)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate (\(^{18}\)O-3-D)

\[^{18}\text{O}\] enrichment: 97.2%
Methyl 5-bromo-3a-hydroxy-8-(3-methylbut-2-en-1-yl)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate (\(^{18}\)O-4-D)

\[
\text{[M+H]^+ Exact Mass: 383.08508}
\]

\(^{18}\)O enrichment: 93.5\%
5-Bromo-3-(2-((methoxycarbonyl)amino)ethyl)-1H-indol-1-yl 3-bromo-4-fluorobenzoate ($^{18}$O-1-E)

$^{18}$O enrichment: 94.3%
Methyl 5-bromo-3a-((3-bromo-4-fluorobenzoyl)oxy)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate (18O-2-E)

\[
\begin{align*}
\text{Isotopic simulation of positive ion mode} \\
\text{HRMS result of compound 18O-2-E} \\
\text{18O enrichment: 94.5%}
\end{align*}
\]
Methyl 5-bromo-3a-((3-bromo-4-fluorobenzoyl)oxy)-8-(3-methylbut-2-en-1-yl)-3,3a,8a-
tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate ($^{18}$O-3-E)

$^{18}$O enrichment: 94.7%
Methyl 5-bromo-3a-hydroxy-8-(3-methylbut-2-en-1-yl)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate ($^{18}$O-4-E)

$^{18}$O enrichment: 90.4%
3.2.3. Quantitative Analysis of $^{18}$O-Labeling Experiment Results (Figures 4 and 5)

3.2.3.1. Dependence of the electronic properties (Figure 4)

Assuming path b and path c are primarily operating for the IHT process, the relative contribution of each pathway could be determined. The formation of $^{18}$O-4 is attributed to the action of path b from $^{18}$O-1 in total, and half the participation of path c from the identical starting material. The other half of the involvement of path c from $^{18}$O-1, along with the rearrangement from $^{18}$O-free starting material, $^{16}$O-1, generates the unlabeled oxygenation product $^{18}$O-4.

Figure S3. Schematic explanation for the calculation of the ratio of each pathway.

Conditions: (a) For $^{18}$O-1-A: toluene, 90 °C, 16 h, for $^{18}$O-1-B: toluene, 70 °C, 8 h, for $^{18}$O-1-C: CH$_2$Cl$_2$, 0 °C, 2 h; (b) For $^{18}$O-2-A, $^{18}$O-2-B, 1-bromo-3-methyl-2-butene (1.5 equiv), K$_2$CO$_3$ (3.0 equiv), acetone, 23 °C, 16 h, for $^{18}$O-2-C: 1-bromo-3-methyl-2-butene (3.0 equiv), K$_2$CO$_3$ (6.0 equiv), acetone, 23 °C, 4 d; (c) KOH (1.5 equiv), EIOH/Et$_2$O = 5:1, 60 °C, 3 h.
The relative contribution of each pathway for the formation of the IHT product was determined based on the following premises. **path b** will exclusively produce $^{18}\text{O}\cdot-2\text{a}$ as a sole product while **path c** will form $^{18}\text{O}\cdot-2\text{a}$ and $^{18}\text{O}\cdot-2\text{b}$ in a 1:1 ratio, respectively.

The mole fraction of $^{18}\text{O}\cdot-1$ is denoted as $a$, and since the $^{18}\text{O}$ enrichment is not 100%, the mole fraction of naturally existing $^{16}\text{O}\cdot-1$ is defined as $b$. Also, the relative contribution of **path b** for the formation of the product is denoted as $x$, and the relative contribution of **path c** for the formation of the product is defined as $y$. The ratio between $^{18}\text{O}\cdot-4$ and $^{16}\text{O}\cdot-4$ is expressed as $a(x+y):\frac{1}{2}ay+b$ (Figure S3). Detailed calculation process is attached below.
(1) IHT reaction with benzoyl substituent

The system of equations is established by the two proportional expressions:

\[
\begin{align*}
    a : b &= 100:9.3 \\
    a(x + \frac{1}{2}y) : \frac{1}{2}ay + b &= 100:25.1
\end{align*}
\]

From equation 1, \( b \) can be expressed as:

\[
b = \frac{93}{1000}a
\]

Insertion of the equation 3 into equation 2 gives equation 4:

\[
a(x + \frac{1}{2}y) : \frac{1}{2}ay + \frac{93}{1000}a = 100:25.1
\]

\[
\therefore x + \frac{1}{2}y : \frac{1}{2}y + \frac{93}{1000} = 100:25.1
\]

\[
\therefore 50y + 9.3 = 25.1x + \frac{251}{20}y
\]

\[
\therefore 25.1x - \frac{749}{20}y = 9.3
\]

Since \( y \) is defined in terms of \( 1-x \), the equation 5 can be re-written as:

\[
25.1x - \frac{749}{20}(1-x) = 9.3
\]

\[
\therefore 62.6x = 46.8
\]

\[
\therefore x = 0.75
\]

\[
\therefore y = 1 - x = 0.25
\]
(2) IHT reaction with 3-bromo-4-fluorobenzoyl substituent

The system of equations is established by the two proportional expressions:

\[
\begin{align*}
\text{(1)} & \quad a : b = 100 : 11.7 \\
\text{(2)} & \quad a(x + \frac{1}{2}y) : \frac{1}{2}ay + b = 100 : 49.4
\end{align*}
\]

From equation 1, \(b\) can be expressed as:

\[
b = \frac{117}{1000}a
\]

Insertion of the equation 3 into equation 2 gives equation 4:

\[
a(x + \frac{1}{2}y) : \frac{1}{2}ay + \frac{117}{1000}a = 100 : 49.4
\]

\[
\therefore x + \frac{1}{2}y : \frac{1}{2}y + \frac{117}{1000} = 100 : 49.4
\]

\[
\therefore 50y + 11.7 = 49.4x + \frac{494}{20}y
\]

\[
\therefore 49.4x - \frac{506}{20}y = 11.7
\]

Since \(y\) is defined in terms of \(1-x\), the equation 5 can be re-written as:

\[
49.4x - \frac{506}{20}(1-x) = 11.7
\]

\[
\therefore 74.7x = 37
\]

\[
\therefore x = 0.49
\]

\[
\therefore y = 1 - x = 0.51
\]
The system of equations is established by the two proportional expressions:

\[
\begin{align*}
\begin{cases}
    a : b &= 79.8 : 100 \\
    a(x + \frac{1}{2}y) : \frac{1}{2}ay + b &= 37.8 : 100
\end{cases}
\end{align*}
\]

From equation 1, \( b \) can be expressed as:

\[
b = \frac{1000}{798}a
\]  \( (3) \)

Insertion of the equation 3 into equation 2 gives equation 4:

\[
a(x + \frac{1}{2}y) : \frac{1}{2}ay + \frac{1000}{798}a = 37.8 : 100
\]

\[
\therefore x + \frac{1}{2}y : \frac{1}{2}y + \frac{1000}{798} = 37.8 : 100
\]

\[
\therefore 37.8\left(\frac{1}{2}y + \frac{1000}{798}\right) = 100x + 50y
\]

\[
\therefore 100x + 31.1y = \frac{37800}{798} = 47.4
\]  \( (5) \)

Since \( y \) is defined in terms of \( 1-x \), the equation 5 can be re-written as:

\[
100x + 31.1(1 - x) = 47.4
\]

\[
\therefore 68.9x = 16.3
\]

\[
\therefore x = 0.24
\]  \( (6) \)

\[
\therefore y = 1 - x = 0.76
\]  \( (7) \)

100
3.2.3.2. The influence of electronic properties of the indole backbone (Figure 5)

![Chemical Structures](image)

**Figure S4.** The influence of electronic properties of the indole backbone.

The determination of the relative contribution of path b and path c in each case was carried out via analogous calculations used for section 5.1.3.2.
(1) IHT reaction with benzyol substituent

The system of equations is established by the two proportional expressions:

\[
\begin{align*}
(a): & \quad b = 100 : 3.1 \\
(b): & \quad a(x + \frac{1}{2}y) : \frac{1}{2}ay + b = 100 : 7.0
\end{align*}
\]

From equation (1), \( b \) can be expressed as:

\[ b = \frac{31}{1000}a \]  

(3)

Insertion of the equation 3 into equation 2 gives equation 4:

\[
\begin{align*}
& a(x + \frac{1}{2}y) : \frac{1}{2}ay + \frac{31}{1000}a = 100 : 7.0 \\
\therefore & \quad \frac{1}{2}x + \frac{1}{2}y : y + \frac{31}{1000} = 100 : 7.0 \\
\therefore & \quad 50y + 3.1 = 7x + 3.5y \\
\therefore & \quad 7x - 46.5y = 3.1
\end{align*}
\]

(5)

Since \( y \) is defined in terms of \( 1-x \), the equation 5 can be re-written as:

\[ 7x - 46.5(1 - x) = 3.1 \]

\[ \therefore 53.5x = 49.6 \]

\[ \therefore x = 0.93 \]  

(6)

\[ \therefore y = 1 - x = 0.7 \]  

(7)
(2) IHT reaction with 3-bromo-4-fluorobenzoyl substituent

\[
\begin{align*}
\text{IHT reaction with 3-bromo-4-fluorobenzoyl substituent} \\
103 & \text{reaction with 3-bromo-4-fluorobenzoyl substituent} \\
\text{The system of equations is established by the two proportional expressions:} \\
\begin{align*}
a : b &= 50.9 : 3.1 \\
(a + \frac{1}{2}y) : \frac{1}{2}ay + b &= 100 : 10.6
\end{align*}
\end{align*}
\]

From equation 1, \( b \) can be expressed as:

\[
b = \frac{31}{509} a
\]

Insertion of the equation 3 into equation 2 gives equation 4:

\[
a(x + \frac{1}{2}y) : \frac{1}{2}ay + \frac{31}{509} a = 100 : 10.6
\]

\[
\Rightarrow x + \frac{1}{2}y : \frac{1}{2}y + \frac{31}{509} = 100 : 10.6
\]

\[
\Rightarrow 50y + \frac{3100}{509} = 10.6x + 5.3y
\]

\[
\Rightarrow 10.6x - 44.7y = \frac{3100}{509}
\]

Since \( y \) is defined in terms of \( 1-x \), the equation 5 can be re-written as:

\[
10.6x - 44.7(1-x) = \frac{3100}{509}
\]

\[
\Rightarrow 55.3x = 50.8
\]

\[
\Rightarrow x = 0.92
\]

\[
\Rightarrow y = 1 - x = 0.08
\]
3.3. Crossover Experiment (Figure 6A)

3.3.1. Preparation of Compound 2b-Int and 2b'-Int

To an oven-dried round-bottom flask equipped with a stir bar and septum were added N-hydroxyindole 1 (1.0 equiv) and CH$_2$Cl$_2$ (0.05 M in 1) at 23 °C, followed by benzoic acid (1.1 equiv), EDC·HCl (1.1 equiv), HOBt (1.1 equiv), and Et$_3$N (2.2 equiv). The resulting mixture was stirred for 2 h, before it was quenched with H$_2$O. The layers were separated, and the aqueous layer was extracted with CH$_2$Cl$_2$ three times. The combined organic layer was washed with brine, dried over anhydrous MgSO$_4$, filtered, and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 1:1) to afford indolyl N-carboxylate 2-Int.

3-((2-(((Benzyloxy)carbonyl)amino)ethyl)-1H-indol-1-yl) 4-ethylbenzoate (2b'-Int)

$R_f=0.60$ (silica gel, hexanes:EtOAc = 7:3); $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 8.13 (d, $J=8.2$ Hz, 2H), 7.60 (d, $J=8.0$ Hz, 1H), 7.39 (d, $J=8.0$ Hz, 2H), 7.36 – 7.27 (m, 5H), 7.24 (d, $J=3.2$ Hz, 2H), 7.16 (dt, $J=8.1$, 3.8 Hz, 1H), 7.07 (s, 1H), 5.12 (s, 2H), 4.92 (s, 1H), 3.56 (q, $J=6.6$ Hz, 2H), 2.99 (t, $J=6.8$ Hz, 2H), 2.78 (q, $J=7.6$ Hz, 2H), 1.31 (td, $J=7.6$, 1.6 Hz, 3H); $^{13}$C NMR (126 MHz, CDCl$_3$): $\delta$ 164.9, 156.5, 152.0, 136.8, 135.8, 130.6, 128.6,
128.2, 128.2, 124.9, 124.2, 123.9, 123.6, 121.0, 119.4, 111.7, 109.2, 66.8, 41.2, 29.8, 29.3, 25.8, 15.3; \textbf{HRMS}

3.3.2. Preparation of Crossover Products

To an oven-dried round-bottom flask equipped with a stir bar and septum were added $N$-hydroxyindole $1$ (1.0 equiv) and CH$_2$Cl$_2$ (0.05 M in 1) at 23 °C, followed by benzoic acid (1.1 equiv), EDC·HCl (1.1 equiv), HOBt (1.1 equiv), and Et$_3$N (2.2 equiv). The resulting mixture was stirred for 2 h, before it was quenched with H$_2$O. The layers were separated, and the aqueous layer was extracted with CH$_2$Cl$_2$ three times. The combined organic layer was washed with brine, dried over anhydrous MgSO$_4$, filtered, and concentrated under reduced pressure. The resulting crude was filtered through a short pad of silica gel using CH$_2$Cl$_2$ as eluent, concentrated under reduced pressure and re-dissolved in toluene (0.05 M in 1). The resulting solution was then heated to 90 °C in a pre-heated oil bath and stirred for 16 h, before it was cooled to 23 °C and directly concentrated under reduced pressure to provide the crude product. The crude product was purified by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 7:3) to afford the product.

**Methyl 3a-((4-ethylbenzoyl)oxy)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate (crossover product 1)**
\( R_f = 0.43 \) (silica gel, hexanes:EtOAc = 7:3); \(^1\)H NMR (500 MHz, CDCl\(_3\), 60:40 mixture of rotamers): \( \delta \) 7.90 (d, \( J = 7.8 \) Hz, 2H), 7.62 and 7.54 (d, \( J = 7.6 \) Hz, 1H), 7.23 (d, \( J = 7.9 \) Hz, 2H), 7.18 (t, \( J = 7.6 \) Hz, 1H), 6.79 (q, \( J = 6.8 \) Hz, 1H), 6.68 (d, \( J = 7.9 \) Hz, 1H), 5.77 (s, 1H), 3.92 and 3.81 (t, \( J = 9.7 \) Hz, 1H), 3.79 and 3.73 (s, 3H), 3.22 (td, \( J = 10.9, 6.3 \) Hz, 1H), 3.06 (dd, \( J = 12.9, 6.3 \) Hz, 1H), 2.94 (dd, \( J = 12.8, 6.1 \) Hz, 0H), 2.75 – 2.65 (m, 3H), 1.23 (t, \( J = 7.6 \) Hz, 3H); \(^1\)C NMR (126 MHz, CDCl\(_3\)): \( \delta \) 165.5, 155.7, 154.9, 151.0, 150.8, 150.3, 131.1, 130.0, 128.0, 127.7, 126.7, 126.3, 126.1, 126.1, 119.7, 119.5, 110.4, 110.3, 94.3, 93.1, 80.5, 79.7, 52.9, 52.7, 45.6, 45.5, 36.0, 35.9, 29.1, 15.4; HRMS calcd. for C\(_{21}\)H\(_{23}\)N\(_2\)O\(_4\) \([M + H]^+\) 367.1652, found 367.1647.

**Benzy1 3a-(benzoyloxy)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate (crossover product 2)**

\( R_f = 0.56 \) (silica gel, hexanes:EtOAc = 7:3); \(^1\)H NMR (500 MHz, CDCl\(_3\), 55:45 mixture of rotamers): \( \delta \) 7.99 and 7.98 (d, \( J = 7.6 \) Hz, 2H), 7.63 and 7.55 (d, \( J = 7.5 \) Hz, 1H), 7.54 (t, \( J = 8.3 \) Hz, 1H), 7.44 – 7.28 (m, 7H), 7.19 (q, \( J = 6.7 \) Hz, 1H), 6.80 (t, \( J = 7.5 \) Hz, 2H), 6.69 and 6.63 (d, \( J = 7.9 \) Hz, 1H), 5.81 and 5.79 (s, 1H), 5.25 and 5.20 (d, \( J = 12.3 \) Hz, 1H), 5.21 and 5.12 (d, \( J = 12.3 \) Hz, 1H), 3.94 and 3.87 (t, \( J = 9.1 \) Hz, 1H), 3.32 – 3.20 (m, 1H), 3.07 and 2.98 (dd, \( J = 12.8, 5.3 \) Hz, 1H), 2.77 – 2.67 (m, 1H); \(^1\)C NMR (126 MHz, CDCl\(_3\)): \( \delta \) 165.5, 165.4, 155.1, 154.3, 151.0, 150.7, 136.4, 134.4, 133.3, 133.3, 131.2, 131.1, 130.9, 130.2, 129.9, 129.9, 128.9, 128.7, 128.5, 128.4, 128.3, 128.1, 126.7, 126.6, 126.2, 126.0, 119.7, 119.5, 110.5, 110.3, 94.4, 93.3, 80.5, 79.7, 67.6, 67.2, 45.7, 45.6, 35.9, 35.8; HRMS calcd. for C\(_{22}\)H\(_{24}\)N\(_2\)O\(_4\) \([M + H]^+\) 415.1652, found 415.1648.
3.3.3. Crossover Experiment

To a 10 mL oven-dried reaction tube equipped with a stir bar were added 2b-Int (67.6 mg, 0.200 mmol, 1.0 equiv), 2b'-Int (88.5 mg, 0.200 mmol, 1.0 equiv) and toluene (2 mL). The reaction tube was sealed under N₂ and the resulting mixture was heated to 90 °C in a pre-heated oil bath and stirred for 16 h, before it was cooled to 23 °C and directly concentrated under reduced pressure to provide the crude product. A small portion of the crude mixture was then analyzed by TLC and HRMS. The crude mixture of crossover experiment was purified by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 7:3) to afford the product 2b (41.7 mg, 62%) and 2b' (48.9 mg, 55%).

From the TLC analysis, no appreciable amount of crossover products was detected. As a result of comparing the retention times of individually synthesized compounds by HPLC analysis performed simultaneously with HRMS analysis, it was concluded that crossover product 1 and crossover product 2 were not detected.
Methyl 3a-(benzoyloxy)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate (2b)

The spectral data matched to those of compound 19O-2-A (See section 3.2.1.1). 

\[
\text{R}_f = 0.38 \text{ (silica gel, hexanes:EtOAc = 7:3);} \]

\[ ^1\text{H NMR (500 MHz, CDCl}_3\text{s):} \delta 7.99 (d, J = 7.7 \text{ Hz, 2H}), 7.63 \text{ and 7.58 (d, } J = 7.6 \text{ Hz, 1H}), 7.54 (t, J = 8.4 \text{ Hz, 1H}), 7.41 (t, J = 7.6 \text{ Hz, 2H}), 7.19 (t, J = 7.7 \text{ Hz, 1H}), 6.80 (q, J = 7.0 \text{ Hz, 1H}), 6.68 (d, J = 7.9 \text{ Hz, 1H}), 5.78 (s, 1H), 3.93 \text{ and 3.81 (t, } J = 9.7 \text{ Hz, 1H}), 3.80 \text{ and 3.73 (s, 3H), 3.26 – 3.20 (m, 1H), 3.07 and 2.96 (dd, J = 12.9, 6.1 \text{ Hz, 1H}), 2.75 – 2.69 (m, 1H); } \]

\[ ^{13}\text{C NMR (126 MHz, CDCl}_3\):} \delta 165.3, 155.6, 154.8, 151.0, 150.7, 133.2, 131.0, 130.2, 129.8, 129.1, 128.4, 126.5, 126.3, 126.1, 126.0, 119.6, 119.3, 110.3, 110.2, 94.5, 93.3, 80.4, 79.6, 52.8, 52.5, 45.5, 35.9, 35.8; HRMS calcd. for C_{19}H_{18}N_{2}O_{4}Na^{+} [M + Na]^{+} 361.1159, found 361.1160. \]

3-(2-(((Benzyloxy)carbonyl)amino)ethyl)-1H-indol-1-yl 4-ethylbenzoate (2b’)

\[
\text{R}_f = 0.76 \text{ (silica gel, hexanes:EtOAc = 1:1);} \]

\[ ^1\text{H NMR (500 MHz, CDCl}_3\):} \delta 7.89 (dd, J = 8.2, 3.8 \text{ Hz, 2H}), 7.62 and 7.54 (d, J = 7.4 \text{ Hz, 1H}), 7.42 (d, J = 6.8 \text{ Hz, 1H}), 7.36 (d, J = 4.4 \text{ Hz, 2H}), 7.40 – 7.30 (m, 2H), 7.22 (d, J = 8.0 \text{ Hz, 2H}), 7.18 (ddd, J = 7.2, 5.6, 1.3 \text{ Hz, 1H}), 6.79 (t, J = 7.5 \text{ Hz, 1H}), 6.68 \text{ and 6.63 (d, } J = 7.9 \text{ Hz, 1H}), 5.80 \text{ and 5.78 (s, 1H), 5.24 and 5.20 (d, } J = 12.2 \text{ Hz, 1H}), 5.20 \text{ and 5.12 (d, } J = 12.3 \text{ Hz, 1H}), 3.93 \text{ and 3.87 (ddd, } J = 10.6, 8.5, 1.8 \text{ Hz, 1H}), 3.30 – 3.20 (m, 1H), 3.06 \text{ and 2.96 (ddd, } J = 12.8, 6.4, 1.8 \text{ Hz, 1H}), 2.76 – 2.68 (m, 1H), 2.68 (q, J = 7.5 \text{ Hz, 2H}), 1.23 (t, J = 7.6 \text{ Hz, 3H);} \]

\[ ^{13}\text{C NMR (126 MHz, CDCl}_3\):} \delta 165.5, 155.1, 154.3, 151.0, 150.7, 150.3, 136.6, 136.5, 131.1, 130.0, 128.9, 128.8, 128.5, 128.3, 128.1, 128.0, 127.7, 127.7, 126.7, 126.2, 126.1, 119.7, 119.5, 110.4, 110.3, 94.2, 93.1, 80.5, 79.7, 67.5, 67.2, 45.7, 45.6, 35.9, 35.8, 29.1, 15.4; HRMS calcd. for C_{27}H_{27}N_{2}O_{4}^{+} [M + H]^{+} 443.1965, found 443.1964. \]
3.3.4. Analysis of Crossover Experiment Results

3.3.4.1. TLC analysis of the crossover experiment

Figure S5. TLC analysis of crossover experiment.

TLC was checked with the reference compounds, which are the pyrroloindoline 2b, 2b', crossover product 1, and crossover product 2. Each TLC sample was visualized by 254 nm UV lamp and stained with KMnO₄ stain with heating. Among the photos of the TLC plates with two differently visualized forms, the one visualized by 254 nm UV lamp is on the left and the one stained with KMnO₄ is on the right. TLC analysis indicates that no detectable spots corresponding to the crossover product 1, 2 were observed in each TLC while formation of 2b and 2b' was clearly detected.
3.3.4.2. HRMS/HPLC analysis of the crossover experiment

(1) Result of UV detection for the crude mixture of the crossover experiment and the relative location of each product

For all HRMS peaks shown below, the red arrow was used to indicate the detected mass of the desired products.

(2) Result of mass detection at peak corresponding to compound 2b

**Extracted mass detection of compound 2b**
(3) Result of mass detection at peak corresponding to compound 2b'
3.4. Radical-trapping Experiment (Figure 6B)

3.4.1. Radical-trapping Experiment with Indolyl N-Carboxylate 2b-Int

To a 10 mL oven-dried reaction tube equipped with a stir bar were added indolyl N-carboxylate 2b-Int (67.6 mg, 0.200 mmol, 1.0 equiv) and toluene (4 mL, 0.05 M in 2b-Int) at 23 °C, followed by radical-trapping reagent (2.0 equiv). The reaction tube was sealed under N₂ and the resulting mixture was heated to 90 °C in a pre-heated oil bath and stirred for 16 h, before it was cooled to 23 °C and directly concentrated under reduced pressure to provide the crude product. The crude mixture was then analyzed by HRMS. HRMS result of the resulting crude mixture indicated the formation of TEMPO-adduct or 1,1-diphenylethylene-adduct when TEMPO or 1,1-diphenylethylene were used as a radical scavenger, even though no significant yield loss was observed for 2b.

Each crude mixture of radical-trapping experiment was purified by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 1:1) to afford the product 2b (when using TEMPO: 40.3 mg, 54%, when using BHT: 44.1 mg, 65%, when using 1,1-diphenylethylene: 38.6 mg, 57%)
3.4.1.1. HRMS results using TEMPO as a radical scavenger

(1) Result of UV detection for the radical-trapping experiment and the relative location of each product detected

(2) Result of mass detection at peaks corresponding to compound 2b and TEMPO-adduct
3.4.1.2. HRMS results using 1,1-diphenylethylene as a radical scavenger

(1) Result of UV detection for the radical-trapping experiment and the relative location of each product detected

(2) Result of mass detection at peaks corresponding to compound 2b and 1,1-diphenylethylene-adduct
3.4.2. Radical-trapping Experiment with Electron-deficient Indolyl N-Carboxylate

To an oven-dried round-bottom flask equipped with a stir bar and septum were added \( \text{N-hydroxyindole } 1a \) (50.0 mg, 0.213 mmol, 1.0 equiv) and \( \text{CH}_2\text{Cl}_2 \) (4.2 mL, 0.05 M in \( 1a \)) at 23 °C. The resulting solution was cooled to 0 °C and 2,3,4,5,6-pentafluorobenzoyl chloride (1.1 equiv), \( \text{Et}_3\text{N} \) (1.1 equiv) and radical-trapping reagent (2.0 equiv) were successively added to the solution. The reaction mixture was warmed up to 23 °C and stirred for 2 h, before it was quenched with \( \text{H}_2\text{O} \) (2 mL). The layers were separated and the aqueous layer was extracted with \( \text{CH}_2\text{Cl}_2 \) (3 × 3 mL). The combined organic layer was dried over anhydrous MgSO\(_4\), filtered, and concentrated under reduced pressure to provide the crude product. The crude mixture was then analyzed by HRMS. When 1,1-diphenylethylene was used as the radical scavenger, \( 1,1\text{-diphenylethylene-adduct} \) was detected by HRMS analysis, while no significant decrease in the reaction yield was observed. On the other hand, the formation of \( 2f \) was noticeably suppressed when TEMPO was used as the radical scavenger due to the rapid decomposition of \( 1a \) induced by TEMPO. Each crude mixture of radical-trapping experiment was purified by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 1:1) to afford the product \( 2f \) (when using TEMPO: 0 mg, 0%, when using BHT: 44.7 mg, 49%, when using 1,1-diphenylethylene: 41.1 mg, 45%)
3.4.2.1. Instability of 1a in the presence of TEMPO

To confirm that the TEMPO is interacting with the \( N \)-hydroxyindole, \( N \)-hydroxyindole 1a (50.0 mg, 0.213 mmol, 1.0 equiv) and CH\(_2\)Cl\(_2\) (4.2 mL, 0.05 M in 1a) were added to an oven-dried round-bottom flask equipped with a stir bar and septum at 23 °C. The resulting solution was cooled to 0 °C, and TEMPO (2.0 equiv) was added to the solution. The reaction mixture was stirred while the reaction was monitored by TLC. TLC indicated that fast decomposition of 1a occurred immediately after TEMPO was added. This clearly indicates that the result of radical-trapping experiment with TEMPO is derived from the decomposition of 1a, not from the inhibition of the radical-involved reaction pathway.
3.4.2.2. HRMS results using 1,1-diphenylethylene as a radical scavenger

(1) Result of UV detection for the radical-trapping experiment and the relative location of each product detected

(2) Result of mass detection at peaks corresponding to compound 2f and 1,1-diphenylethylene-adduct
3.5. IHT Reaction of Indolyl N-Carbamates (Figure 7)

3.5.1. Preparation of Indolyl N-Carbamates

Methyl (2-(1-((phenylcarbamoyl)oxy)-1H-indol-3-yl)ethyl)carbamate (2g-Int)

\[
\text{NCO} \quad \text{CH}_2\text{Cl}_2, 0 \, ^\circ\text{C}, 2 \, \text{h} \quad \text{NCO}
\]

To an oven-dried round-bottom flask equipped with a stir bar and septum were added N-hydroxyindole 1a (318 mg, 1.36 mmol, 1.0 equiv) and CH\(_2\)Cl\(_2\) (14 mL, 0.1 M in 1a) at 23 °C. The resulting solution was cooled to 0 °C, and phenyl isocyanate (155 µL, 1.42 mmol, 1.04 equiv) was added to the solution. The reaction mixture was stirred for 2 h, before it was quenched with H\(_2\)O (10 mL). The layers were separated, and the aqueous layer was extracted with CH\(_2\)Cl\(_2\) (3 × 20 mL). The combined organic layer was washed with brine (1 × 20 mL), dried over anhydrous MgSO\(_4\), filtered, and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 7:3) to afford indolyl N-carboxylate 2g-Int (336 mg, 70%) as a pale yellow oil.

\( R_f = 0.47 \) (silica gel, hexanes:EtOAc = 1:1); \(^1\)H NMR (500 MHz, CDCl\(_3\)): \( \delta \) 7.59 (d, \( J = 8.1 \) Hz, 1H), 7.47 (d, \( J = 8.0 \) Hz, 2H), 7.37 (t, \( J = 7.8 \) Hz, 2H), 7.33 – 7.26 (m, 2H), 7.17 (q, \( J = 7.1 \) Hz, 2H), 7.06 (s, 1H), 4.84 (s, 1H), 3.66 (s, 3H), 3.52 (q, \( J = 6.7 \) Hz, 2H), 2.95 (t, \( J = 6.9 \) Hz, 2H); \(^{13}\)C NMR (126 MHz, CDCl\(_3\)): \( \delta \) 157.4, 151.8, 136.7, 135.7, 129.3, 124.7, 124.6, 124.0, 123.6, 122.2, 121.0, 119.3, 119.1, 111.5, 111.4, 109.0, 52.2, 41.1, 25.7; HRMS calcd. for C\(_{19}\)H\(_{20}\)N\(_3\)O\(_4\)\(^+\) [M + H]\(^+\) 354.1448, found 354.1445.
To a 10 mL oven-dried reaction tube equipped with a stir bar were added indolyl N-carboxylate 2g-Int (0.120 g, 0.340 mmol, 1.0 equiv) and toluene (7 mL, 0.05 M in 2g-Int) at 23 °C. The resulting mixture was heated to 90 °C in a pre-heated oil bath and stirred for 16 h, before it was cooled to 23 °C and directly concentrated under reduced pressure to provide the crude product. The resulting residue was purified by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 7:3) to afford the product 2g and 2h (2g: 32.4 mg, 27%, 2h: 18.9 mg, 18%) as a pale yellow oil.

2g: RF = 0.47 (silica gel, hexanes:EtOAc = 1:1); 1H NMR (500 MHz, CDCl3): δ 7.61 and 7.53 (d, J = 7.6 Hz, 1H), 7.36 – 7.26 (m, 5H), 7.19 (t, J = 7.6 Hz, 1H), 7.05 (t, J = 7.1 Hz, 1H), 6.81 (q, J = 7.4 Hz, 1H), 6.67 (d, J = 8.0 Hz, 1H), 6.65 – 6.61 (m, 1H), 5.68 and 5.63 (s, 1H), 5.21 and 4.85 (s, 1H), 3.89 and 3.79 (t, J = 9.8 Hz, 1H), 3.79 and 3.72 (s, 3H), 3.18 (t, J = 10.9, 6.3 Hz, 1H), 3.00 and 2.85 (d, J = 12.9, 6.4 Hz, 1H), 2.70 (p, J = 11.6 Hz, 2H); 13C NMR (126 MHz, CDCl3): δ 155.7, 154.9, 152.0, 151.9, 150.9, 150.6, 137.7, 137.6, 131.2, 129.2, 126.6, 126.0, 125.9, 123.8, 119.8, 119.6, 119.0, 110.5, 110.4, 94.1, 92.8, 80.4, 79.6, 52.9, 52.7, 45.8, 45.6, 35.7, 35.5; HRMS calcd. for C19H20N3O4 [M + H]+ 354.1448, found 354.1445.

2h: RF = 0.45 (silica gel, hexanes:EtOAc = 1:1); 1H NMR (500 MHz, CDCl3): δ 7.18 (d, J = 7.6 Hz, 1H), 7.15 (d, J = 7.7 Hz, 1H), 7.10 (t, J = 7.0 Hz, 2H), 6.77 (q, J = 7.1 Hz, 1H), 6.72 (t, J = 7.3 Hz, 1H), 6.64 (d, J = 7.8 Hz, 1H), 6.51 (dd, J = 11.4, 8.0 Hz, 2H), 5.73 and 5.69 (s, 1H), 5.14 and 4.80 (s, 1H), 4.05 and 4.00 (s, 1H), 3.85 and 3.74 (dd, J = 11.5, 7.7, 3.7 Hz, 1H), 3.76 and 3.73 (s, 3H), 3.27 (ddd, J = 19.8, 16.6, 9.3 Hz, 1H), 2.63 (dt, J = 30.8, 12.8, 8.5 Hz, 1H), 2.37 – 2.29 (m, 1H); 13C NMR (126 MHz, CDCl3): δ 156.0, 155.3, 149.1, 148.9, 145.10, 145.09, 129.9, 129.4, 129.3, 123.6, 123.5, 119.6, 119.4, 118.7, 118.5, 115.5, 115.2, 109.9, 109.7, 73.6, 72.4, 52.9, 52.7, 44.8, 44.6, 37.8, 37.6; HRMS calcd. for C18H20N3O2 [M + H]+ 310.1550, found 310.1546.
4. C–O Bond Formation via Indoly1,3-Heteroatom Transposition (IHT)

4.1. Optimization of the C3-Acyloxylation Conditions

Table S2. Evaluation of esterification conditions for pentafluorobenzoyl sources. 

<table>
<thead>
<tr>
<th>entry</th>
<th>benzoyl source</th>
<th>conditions</th>
<th>temperature</th>
<th>yield of 2f (%)&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>C₆F₅COOH</td>
<td>EDC·HCl (1.1 equiv), HOBt (1.1 equiv), Et₃N (2.2 equiv)</td>
<td>23 °C</td>
<td>31%</td>
</tr>
<tr>
<td>2</td>
<td>C₆F₅COOH</td>
<td>DCC (1.1 equiv), DMAP (1.1 equiv)</td>
<td>23 °C</td>
<td>27%</td>
</tr>
<tr>
<td>3</td>
<td>C₆F₅COCl</td>
<td>Et₃N (1.2 equiv)</td>
<td>23 °C</td>
<td>38%</td>
</tr>
<tr>
<td>4</td>
<td>C₆F₅COCl</td>
<td>Et₃N (1.2 equiv)</td>
<td>0 to 23 °C</td>
<td>55%</td>
</tr>
</tbody>
</table>

<sup>a</sup>Reactions performed with N-hydroxyindole 1a (1.0 equiv), benzoyl source (1.1 equiv) in CH₂Cl₂ (0.05 M) at indicated temperature on 0.5−1.0 mmol scale. <sup>b</sup>Yields determined by ¹H NMR using TCE as an internal standard.
4.2. General Procedures for C3-Acyloxylation of Indole Derivatives (Scheme 2)

**Figure S6.** List of C3-acyloxylated products categorized by methods of C3-acyloxylation.
General procedure F

To an oven-dried round-bottom flask equipped with a stir bar and septum were added \(N\)-hydroxyindole 1 (1.0 equiv) and \(\text{CH}_2\text{Cl}_2\) (0.05 M in 1) at 23 °C. The resulting solution was cooled to 0 °C, and benzylic chloride (1.1 equiv) and \(\text{Et}_3\text{N}\) (1.2 equiv) were added to the solution at the same time. The reaction mixture was warmed up to 23 °C and stirred for 2 h, before it was quenched with \(\text{H}_2\text{O}\). The layers were separated, and the aqueous layer was extracted with \(\text{CH}_2\text{Cl}_2\) three times. The combined organic layer was washed with brine, dried over anhydrous \(\text{MgSO}_4\), filtered, and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography to afford the product 2.

General procedure G

To an oven-dried round-bottom flask equipped with a stir bar and septum were added \(N\)-hydroxyindole 1 (1.0 equiv) and \(\text{CH}_2\text{Cl}_2\) (0.05 M in 1) at 23 °C. The resulting solution was cooled to 0 °C, and benzoic acid (1.1 equiv), EDC·HCl (1.1 equiv), HOBt (1.1 equiv) and \(\text{Et}_3\text{N}\) (2.2 equiv) were successively added to the solution. The reaction mixture was warmed up to 23 °C and stirred for 2 h, before it was quenched with \(\text{H}_2\text{O}\). The layers were separated and the aqueous layer was extracted with \(\text{CH}_2\text{Cl}_2\) three times. The combined organic layer was washed with brine, dried over anhydrous \(\text{MgSO}_4\), filtered, and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography to afford the product 2.
To an oven-dried round-bottom flask equipped with a stir bar and septum were added N-hydroxyindole 1 (1.0 equiv) and CH$_2$Cl$_2$ (0.05 M in 1) at 23 °C, followed by benzoyl chloride (1.1 equiv) and Et$_3$N (1.2 equiv). The resulting mixture was stirred for 2 h, before it was quenched with NaHCO$_3$ (20 mL, sat. aq.). The layers were separated and the aqueous layer was extracted with CH$_2$Cl$_2$ three times. The combined organic layer was washed with NaHCO$_3$ (sat. aq.), dried over anhydrous MgSO$_4$, filtered, and concentrated under reduced pressure. The resulting crude was filtered through a short pad of silica gel using CH$_2$Cl$_2$ as eluent, concentrated under reduced pressure and re-dissolved in toluene (0.05 M in 1). The resulting solution was then heated to 90 °C in a pre-heated oil bath and stirred while the reaction was monitored by TLC. After completion of reaction (2−16 h), the reaction mixture was cooled to 23 °C, the crude mixture was concentrated under reduced pressure and directly purified by column chromatography to afford the product 2.

1,2,3,4-Tetrahydro-4aH-carbazol-4a-yl 3,5-bis(trifluoromethyl)benzoate (2i)

Following the general procedure G, N-hydroxyindole 1s (86.6mg, 0.463 mmol) afforded indolenine 2i (85.0 mg, 43%) as a pale yellow oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 9:1).

$R_f$=0.27 (silica gel, hexanes:EtOAc = 9:1); $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 8.45 (s, 2H), 8.08 (s, 1H), 7.62 (d, $J$ = 7.7 Hz, 1H), 7.43 − 7.40 (m, 2H), 7.20 (t, $J$ = 7.5 Hz, 1H), 3.00 (d, $J$ = 15.0 Hz, 2H), 2.51 (td, $J$ = 13.2, 5.9 Hz, 1H), 2.22 (br d, $J$ = 10.9 Hz, 1H), 1.90 (tt, $J$ = 13.3, 3.5 Hz, 1H), 1.85 − 1.81 (m, 1H), 1.62 − 1.49 (m, 1H), 1.36
(td, J = 14.1, 4.1 Hz, 1H); $^{13}$C NMR (126 MHz, CDCl$_3$): δ 182.3, 161.7, 154.3, 137.2, 132.6 (q, J = 34.2 Hz), 131.7, 130.3, 130.0, 129.9, 126.9 (p, J = 3.8 Hz), 126.0, 122.9 (d, J = 273.0 Hz), 122.0, 121.2, 87.7, 38.4, 30.0, 28.6, 21.0; $^{19}$F NMR (471 MHz, CDCl$_3$): δ –63.0; HRMS calcd. for C$_{12}$H$_{16}$N$_{10}$+ [M + H]$^+$ 174.1279, found 174.1277.

1-(Methoxycarbonyl)-2,3,8a-tetrahydropyrrolo[2,3-b]indol-3a(1H)-yl methyl terephthalate (2j)

Following the general procedure G, N-hydroxyindole 1a (91.2 mg, 0.389 mmol) afforded an inseparable mixture of pyrroloindoline 2j-Int and indolyl N-carboxylate 2j (122 mg, 2.7:1, overall 79%) as a pale yellow oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 7:3). When following the general procedure H for 4 h, N-hydroxyindole 1a (71.0 mg, 0.303 mmol) afforded pyrroloindoline 2j (81.7 mg, 68%) as a sole product.

$R_f$ = 0.27 (silica gel, hexanes:EtOAc = 1:1); $^1$H NMR (400 MHz, CDCl$_3$, 60:40 mixture of rotamers): δ 8.06 (m, 1H), 7.62 and 7.56 (d, J = 7.5 Hz, 1H), 7.21 (t, J = 7.6 Hz, 1H), 6.84 – 6.76 (m, 1H), 6.70 (d, J = 8.0 Hz, 1H), 5.78 (s, 1H), 3.96 – 3.91 and 3.85 – 3.80 (m, 1H), 3.94 (s, 3H), 3.80 and 3.73 (s, 3H), 3.27 – 3.20 (m, 1H), 3.08 and 2.99 (dd, J = 12.8, 6.2 Hz, 1H), 2.72 (q, J = 10.7 Hz, 1H); $^{13}$C NMR (101 MHz, CDCl$_3$): δ 166.3, 164.7, 155.7, 154.9, 151.0, 150.7, 134.3, 134.0, 131.4, 129.9, 129.7, 126.7, 126.2, 125.8, 125.7, 122.4, 119.9, 119.7, 111.3, 110.6, 110.5, 94.9, 93.7, 80.4, 79.6, 53.0, 52.7, 52.6, 45.6, 35.8, 35.7; HRMS calcd. for C$_{21}$H$_{21}$N$_{2}$O$_6$+ [M + H]$^+$ 397.1394, found 397.1383.

Methyl 3a-((4-chlorobenzoyl)oxy)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate (2k)

Following the general procedure G, N-hydroxyindole 1a (88.0 mg, 0.376 mmol) afforded an inseparable mixture of pyrroloindoline 2k-Int and indolyl N-carboxylate 2k (109 mg, 7.7:1, overall 78%) as a pale yellow oil after
purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 7:3). When following the general procedure H for 16 h, N-hydroxyindole 1a (70.9 mg, 0.303 mmol) afforded pyrroloindoline 2k (68.8 mg, 61%) as a sole product.

\[ R_f = 0.53 \] (silica gel, hexanes:EtOAc = 1:1);

\[ ^1H \text{ NMR} \ (500 \text{ MHz, CDCl}_3, 60:40 \text{ mixture of rotamers}): \delta 7.91 \ (d, J = 8.4 \text{ Hz}, 2H), 7.61 \text{ and } 7.54 \ (d, J = 7.6 \text{ Hz}, 1H), 7.38 \ (d, J = 8.2 \text{ Hz}, 2H), 7.20 \ (t, J = 7.8 \text{ Hz}, 1H), 6.80 \ (q, J = 6.9 \text{ Hz}, 1H), 6.68 \ (d, J = 7.9 \text{ Hz}, 1H), 5.75 \ (s, 1H), 3.93 \text{ and } 3.81 \ (t, J = 9.8 \text{ Hz}, 1H), 3.79 \text{ and } 3.72 \ (s, 3H), 3.25 \text{ – } 3.19 \ (m, 1H), 3.06 \text{ and } 2.96 \ (dd, J = 13.0, 6.3 \text{ Hz}, 0H), 2.73 \text{ – } 2.65 \ (m, 1H); \]

\[ ^{13}C \text{ NMR} \ (126 \text{ MHz, CDCl}_3): \delta 164.6, 155.7, 154.9, 151.0, 150.8, 139.8, 139.8, 131.3, 128.8, 128.7, 128.0, 128.0, 126.7, 126.1, 125.9, 125.7, 119.8, 119.5, 110.5, 110.3, 94.7, 93.5, 80.4, 79.6, 52.9, 52.7, 45.6, 45.6, 35.8, 35.7; \]

HRMS calcd. for C_{19}H_{18}ClN_2O_4^+ \ [M + H]^+: 373.0950, found 373.0947.

Methyl 3a-((3,5-bis(trifluoromethyl)benzoyl)oxy)-5-fluoro-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate (2l)

Following the general procedure H for 8 h, N-hydroxyindole 1f (43.0 mg, 0.170 mmol) afforded pyrroloindoline 2l (52.8 mg, 63%) as a pale yellow oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 7:3).

\[ R_f = 0.57 \] (silica gel, hexanes:EtOAc = 1:1);

\[ ^1H \text{ NMR} \ (400 \text{ MHz, CDCl}_3, 55:45 \text{ mixture of rotamers}): \delta 8.42 \ (s, 2H), 8.06 \ (s, 1H), 7.35 \text{ and } 7.31 \ (d, J = 8.2 \text{ Hz}, 1H), 6.94 \ (t, J = 8.8 \text{ Hz}, 1H), 6.64 \text{ and } 6.62 \ (d, J = 4.2 \text{ Hz}, 1H), 5.80 \text{ and } 5.78 \ (s, 1H), 5.19 \text{ and } 4.83 \ (s, 1H), 3.97 \text{ and } 3.85 \ (t, J = 9.9 \text{ Hz}, 1H), 3.81 \text{ and } 3.74 \ (s, 3H), 3.29 \text{ – } 3.21 \ (m, 1H), 3.11 \text{ – } 3.01 \ (m, 1H), 2.73 \text{ – } 2.65 \ (m, 1H); \]

\[ ^{13}C \text{ NMR} \ (101 \text{ MHz, CDCl}_3): \delta 162.8, 157.2 \ (d, J = 237.3 \text{ Hz}), 157.1 \ (d, J = 237.0 \text{ Hz}), 155.6, 154.7, 147.3, 147.1, 132.4 \ (q, J = 34.1 \text{ Hz}), 132.2, 130.0 \ (d, J = 3.9 \text{ Hz}), 126.8, 126.1 \ (br t, J = 9.4 \text{ Hz}), 122.9 \ (q, J = 273.1 \text{ Hz}), 118.4 \ (d, J = 24.0 \text{ Hz}), 113.8 \ (d, J = 24.9 \text{ Hz}), 113.5 \ (d, J = 24.6 \text{ Hz}), 111.3 \ (d, J = 8.1 \text{ Hz}), 111.2 \ (d, J = 7.8 \text{ Hz}), 113.3, 111.4, 111.3, 111.2, 95.5, 94.3, 81.1, 80.4, 53.1, 52.8, 45.6, 45.6, 35.7, 31.0; \]

\[ ^{19}F \text{ NMR} \ (376 \text{ MHz, CDCl}_3): \delta \text{ -63.0, -124.1 (q, J = 4.5 \text{ Hz}), -124.5 (q, J = 4.5 \text{ Hz});} \]
HRMS calcd. for C_{21}H_{16}F_{7}N_{2}O_{4}^{+} [M + H]^{+} 493.0993, found 493.0990.

**Methyl 3a-((3,5-bis(trifluoromethyl)benzoyl)oxy)-5-(4-methoxyphenyl)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate (2m)**

![Chemical Structure](image1)

Following the **general procedure F**, N-hydroxyindole 1e (51.0 mg, 0.150 mmol) afforded pyrroloindoline 2m (47.8 mg, 55%) as a pale yellow oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 8:2).

$R_f$=0.43 (silica gel, hexanes:EtOAc = 1:1); $^1$H NMR (400 MHz, CDCl$_3$, 60:40 mixture of rotamers): $\delta$ 8.56 and 8.44 (s, 2H), 8.11 and 8.05 (s, 1H), 7.83 and 7.78 (s, 1H), 7.47 – 7.43 (m, 2H), 6.95 (d, $J$ = 8.4 Hz, 2H), 6.78 (d, $J$ = 8.3 Hz, 1H), 5.86 and 5.83 (s, 1H), 4.00 and 3.88 (t, $J$ = 8.2 Hz, 1H), 3.84 and 3.77 (s, 3H), 3.34 – 3.26 (m, 1H), 3.20 and 3.14 (dd, $J$ = 12.7, 6.0 Hz, 1H), 2.79 – 2.70 (m, 1H); $^{13}$C NMR (101 MHz, CDCl$_3$): $\delta$ 166.9, 162.9, 158.8, 158.8, 154.9, 150.2, 149.9, 133.7, 133.6, 133.2, 132.9, 132.8, 132.4, 132.4 (q, $J$ = 34.0 Hz), 132.3 (q, $J$ = 34.0 Hz), 130.4, 130.3, 130.2, 130.1, 130.0, 127.7, 126.7, 126.7, 126.7, 127.1 – 126.8 (m), 126.3, 125.7, 125.6, 125.0, 124.6, 123.0 (q, $J$ = 273.1 Hz), 122.91 (q, $J$ = 273.1 Hz), 115.1, 114.3, 110.9, 110.7, 95.8, 94.6, 80.7, 80.0, 55.5, 53.2, 52.9, 45.7, 35.8, 35.8; $^{19}$F NMR (376 MHz, CDCl$_3$): $\delta$ –62.9, –63.0; HRMS calcd. for C_{28}H_{23}F_{6}N_{2}O_{5}^{+} [M + H]^{+} 581.1506, found 581.1499.

**Methyl 4-chloro-3a-((perfluorobenzoyl)oxy)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate (2n)**

![Chemical Structure](image2)

Following the **general procedure F**, N-hydroxyindole 1l (75.0 mg, 0.279 mmol) afforded pyrroloindoline 2n.
(58.1 mg, 45%) as a pale yellow oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 8:2).

$R_f=0.57$ (silica gel, hexanes:EtOAc = 1:1); $^1H$ NMR (400 MHz, CDCl$_3$, 60:40 mixture of rotamers): $\delta$ 7.13 (t, $J = 7.9$ Hz, 1H), 6.73 (d, $J = 7.8$ Hz, 1H), 6.57 (d, $J = 8.0$ Hz, 1H), 5.97 and 5.91 (s, 1H), 5.30 (s, 1H), 3.92 – 3.87 and 3.83 – 3.79 (m, 1H), 3.79 and 3.75 (s, 3H), 3.32 (q, $J = 9.7$ Hz, 1H), 2.88 – 2.72 (m, 2H); $^{13}C$ NMR (101 MHz, CDCl$_3$): $\delta$ 157.7, 157.6, 155.8, 154.9, 152.2, 152.1, 145.9 (dm, $J = 257.6$ Hz), 143.6 (dm, $J = 259.0$ Hz), 137.8 (ddd, $J = 256.1$, 18.2, 12.4, 5.3 Hz), 132.5, 130.4, 121.9, 120.3, 120.0, 108.7, 108.6, 107.7 (t, $J = 14.2$ Hz), 96.7, 95.6, 79.8, 79.2, 53.0, 52.9, 44.3, 44.2, 35.8, 35.4; $^{19}F$ NMR (376 MHz, CDCl$_3$): $\delta -137.1$ (tt, $J = 20.3$, 6.0 Hz), $-147.5$ (t, $J = 20.7$ Hz), $-147.8$ (t, $J = 20.7$ Hz), $-160.2$ (dd, $J = 32.6$, 20.2, 6.2 Hz); HRMS calcd. for C$_{19}$H$_{13}$ClF$_5$N$_2$O$_4$ $^{[\text{M + H}]^+}$: 463.0479, found 463.0475.

2-Phenethyl-1H-indol-3-yl 2,3,4,5,6-pentafluorobenzoate (2o)

Following the general procedure H for 16 h, N-hydroxyindole 1p (30.0 mg, 0.126 mmol) afforded indole 2o (32.1 mg, 59%) as a pale yellow oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 95:5).

$R_f=0.24$ (silica gel, hexanes:EtOAc = 7:3); $^1H$ NMR (500 MHz, CDCl$_3$): $\delta$ 7.59 (br s, 1H), 7.45 (d, $J = 7.6$ Hz, 1H), 7.36 – 7.31 (m, 2H), 7.29 – 7.15 (m, 6H), 3.11 – 2.98 (m, 4H); $^{13}C$ NMR (126 MHz, CDCl$_3$): $\delta$ 157.6, 145.7 (dm, $J = 258.2$ Hz), 143.6 (dm, $J = 255.2$ Hz), 140.8, 138.0 (dm, $J = 255.8$ Hz), 132.8, 128.8, 128.5, 127.9, 126.6, 126.1, 122.4, 120.8, 120.5, 117.0, 111.2, 107.9 (td, $J = 16.2$, 4.1 Hz), 35.1, 27.1; $^{19}F$ NMR (471 MHz, CDCl$_3$): $\delta$ –137.3 (dp, $J = 16.9$, 5.8 Hz), –147.6 (tt, $J = 20.9$, 4.8 Hz), –159.7 – –159.8 (m); HRMS calcd. for C$_{23}$H$_{15}$F$_5$NO$_2$ $^{[\text{M + H}]^+}$: 432.1018, found 432.1021.
2-(((tert-Butyldimethylsilyl)oxy)methyl)-1H-indol-3-yl 2,3,4,5,6-pentafluorobenzoate (2p)

Following the **general procedure H** for 16 h, N-hydroxyindole 1q (51.1 mg, 0.184 mmol) afforded indole 2p (52.9 mg, 61%) as a pale yellow oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 95:5).

\[ R_f = 0.45 \text{ (silica gel, hexanes:EtOAc = 8:2); } ^1H\text{ NMR (500 MHz, CDCl}_3\text{): } \delta 8.20 \text{ (br s, 1H), 7.45 (d, } J = 7.9 \text{ Hz, 1H), 7.38 (d, } J = 8.2 \text{ Hz, 1H), 7.22 (t, } J = 7.6 \text{ Hz, 1H), 7.16 (t, } J = 7.5 \text{ Hz, 1H), 4.87 (s, 2H), 0.94 (s, 9H), 0.12 (s, 6H); } ^13C\text{ NMR (126 MHz, CDCl}_3\text{): } \delta 157.2, 145.8 \text{ (dm, } J = 244.4 \text{ Hz), 143.8 (dm, } J = 261.0 \text{ Hz), 138.0 (dm, } J = 256.0 \text{ Hz), 132.9, 127.0, 124.5, 122.8, 120.8, 120.6, 117.5, 111.6, 56.5, 26.0, −5.3; } ^{19}F\text{ NMR (471MHz, CDCl}_3\text{): } \delta −137.2 \text{ (dp, } J = 17.2, 6.0 \text{ Hz), −147.4 (tt, } J = 20.9, 4.6 \text{ Hz), −159.6 − −159.8 (m); } \text{HRMS calcd. for C}_{22}\text{H}_{23}\text{F}_{5}\text{NO}_3\text{Si}^+ [M + H]^+ 472.1362, \text{found 472.1365.}

2-Cyclohexyl-1H-indol-3-yl 2,3,4,5,6-pentafluorobenzoate (2q)

Following the **general procedure H** for 16 h, N-hydroxyindole 1r (28.8 mg, 0.134 mmol) afforded indole 2q (43.3 mg, 76%) as a pale yellow oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 95:5).

\[ R_f = 0.45 \text{ (silica gel, hexanes:EtOAc = 8:2); } ^1H\text{ NMR (400 MHz, CDCl}_3\text{): } \delta 7.83 \text{ (s, 1H), 7.40 (d, } J = 7.7 \text{ Hz, 1H), 7.29 (d, } J = 7.9 \text{ Hz, 1H), 7.18 (t, } J = 7.5 \text{ Hz, 1H), 7.14 (t, } J = 7.2 \text{ Hz, 1H), 2.85 (tt, } J = 12.0, 3.5 \text{ Hz, 1H), 2.02 (dd, } J = 12.5, 3.4 \text{ Hz, 2H), 1.88 (dt, } J = 13.1, 3.3 \text{ Hz, 2H), 1.79 (dt, } J = 13.1, 3.4 \text{ Hz, 1H), 1.54−1.37 (m, 4H), 1.29 (ddt, } J = 12.3, 8.0, 3.6 \text{ Hz, 1H); } ^13C\text{ NMR (126 MHz, CDCl}_3\text{): } \delta 157.8, 145.6 \text{ (dm, } J = 257.0 \text{ Hz), 143.6 (d, } J = 252.5 \text{ Hz), 138.0 (ddddd, } J = 250.9, 15.8, 12.6, 4.8 \text{ Hz), 133.1, 132.6, 124.8, 122.2, 121.0, 120.4, 116.9, 111.3, 129}
108.2 (t, \( J = 16.7 \) Hz), 35.3, 32.2, 26.5, 26.0; \(^{19}F\) NMR (376 MHz, CDCl\(_3\)): \( \delta -137.5 \) (dp, \( J = 16.9, 5.5, 5.1 \) Hz), 
\( -148.0 \) (tt, \( J = 21.1, 4.8 \) Hz), \( -159.7 - -159.9 \) (m); \textbf{HRMS} calcd. for C\(_{21}\)H\(_{17}\)F\(_5\)NO\(_2\)\(^+\) [M + H]\(^+\) 410.1174, found 410.1176.
5. C–N Bond Formation via Indolyl 1,3-Heteroatom Transposition (IHT)

5.1. Optimization of the C3-Amidation Reaction Conditions

Table S3. Evaluation of bases.\textsuperscript{a}

\begin{table}[h]
\centering
\begin{tabular}{lllll}
\hline
entry & base & equiv & yield of 3a (%)\textsuperscript{a} & yield of S1a (%)\textsuperscript{b} \\
\hline
1 & DIPEA & 0.1 & 51\% & 7\% \\
2 & DBU & 0.1 & 70\% & 5\% \\
3 & DABCO & 0.1 & 59\% & 6\% \\
4 & pyridine & 0.1 & <5\% & 54\% \\
5 & NaH & 1.1 & 68\% & 5\% \\
6 & Et\textsubscript{3}N & 0.1 & 75\% (71\%) & <1\% \\
7 & Et\textsubscript{3}N & 1.0 & 37\% & 21\% \\
\hline
\end{tabular}
\end{table}

\textsuperscript{a}Reactions were performed with trichloroacetonitrile (3.0 equiv) and base in CH\textsubscript{2}Cl\textsubscript{2} (0.05 M) at 0 to 23 °C on 0.3–1.2 mmol scale. \textsuperscript{b}Determined by \textsuperscript{1}H NMR analysis of the crude mixture using TCE as an internal standard and the yield of the isolated product was given in the parentheses.
**Table S4.** Optimization of the stoichiometry of trichloroacetonitrile.\textsuperscript{a}

![Chemical structure](image)

<table>
<thead>
<tr>
<th>entry</th>
<th>equiv</th>
<th>yield of 3a (%)\textsuperscript{b}</th>
<th>yield of S1a (%)\textsuperscript{b}</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1.0</td>
<td>36%</td>
<td>22%</td>
</tr>
<tr>
<td>2</td>
<td>2.0</td>
<td>55%</td>
<td>9%</td>
</tr>
<tr>
<td>3</td>
<td>3.0</td>
<td>79% (78%)</td>
<td>&lt;1%</td>
</tr>
<tr>
<td>4</td>
<td>4.0</td>
<td>48%</td>
<td>11%</td>
</tr>
</tbody>
</table>

\textsuperscript{a}Reactions performed with trichloroacetonitrile and Et\textsubscript{3}N (0.1 equiv) in CH\textsubscript{2}Cl\textsubscript{2} (0.05 M) at 0 to 23 °C on 0.3–1.2 mmol scale. \textsuperscript{b}Determined by \textsuperscript{1}H NMR analysis of the crude mixture using TCE as an internal standard and the yield of the isolated product was given in the parentheses.
<table>
<thead>
<tr>
<th>entry</th>
<th>solvent</th>
<th>temperature</th>
<th>time</th>
<th>yield of 3a (%)&lt;sup&gt;b&lt;/sup&gt;</th>
<th>yield of S1a (%)&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>THF</td>
<td>0 to 23 °C</td>
<td>3 h</td>
<td>4%</td>
<td>48%</td>
</tr>
<tr>
<td>2</td>
<td>toluene</td>
<td>0 to 23 °C</td>
<td>3 h</td>
<td>11%</td>
<td>63%</td>
</tr>
<tr>
<td>3</td>
<td>MeCN</td>
<td>0 to 23 °C</td>
<td>3 h</td>
<td>16%</td>
<td>72%</td>
</tr>
<tr>
<td>4</td>
<td>DMF</td>
<td>0 to 23 °C</td>
<td>3 h</td>
<td>&lt;5%</td>
<td>56%</td>
</tr>
<tr>
<td>5</td>
<td>CH₂Cl₂</td>
<td>0 to 23 °C</td>
<td>3 h</td>
<td>75% (73%)</td>
<td>&lt;1%</td>
</tr>
<tr>
<td>6</td>
<td>CH₂Cl₂</td>
<td>23 °C</td>
<td>3 h</td>
<td>67%</td>
<td>&lt;1%</td>
</tr>
<tr>
<td>7</td>
<td>CH₂Cl₂</td>
<td>0 °C</td>
<td>24 h</td>
<td>38%</td>
<td>33%</td>
</tr>
</tbody>
</table>

<sup>a</sup>Reactions performed with trichloroacetonitrile (3.0 equiv) and Et₃N (0.1 equiv) in solvent (0.05 M) at indicated temperature on 0.3–1.2 mmol scale.  
<sup>b</sup>Determined by <sup>1</sup>H NMR analysis of the crude mixture using TCE as an internal standard and the yield of the isolated product was given in the parentheses.
**Table S6.** Evaluation of reaction conditions using trifluoroacetimidoyl chloride.\(^a\)

\[ \text{1a} + \text{F}_3\text{C} = \text{Cl} \rightarrow \text{base} \rightarrow 3\text{y} \]

<table>
<thead>
<tr>
<th>entry</th>
<th>base (equiv)</th>
<th>equiv of R(_1)</th>
<th>solvent</th>
<th>temperature</th>
<th>time</th>
<th>yield of 3y (%)(^b)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Et(_3)N (1.1 equiv)</td>
<td>1.5</td>
<td>THF</td>
<td>0 °C</td>
<td>1 h</td>
<td>8%</td>
</tr>
<tr>
<td>2</td>
<td>LDA (1.1 equiv)</td>
<td>1.5</td>
<td>THF</td>
<td>0 °C</td>
<td>1 h</td>
<td>13%</td>
</tr>
<tr>
<td>3</td>
<td>LiHMDS (1.1 equiv)</td>
<td>1.5</td>
<td>THF</td>
<td>0 °C</td>
<td>1 h</td>
<td>17%</td>
</tr>
<tr>
<td>4</td>
<td>NaHMDS (1.1 equiv)</td>
<td>1.5</td>
<td>THF</td>
<td>0 °C</td>
<td>1 h</td>
<td>16%</td>
</tr>
<tr>
<td>5</td>
<td>NaH (1.1 equiv)</td>
<td>1.5</td>
<td>THF</td>
<td>0 °C</td>
<td>1 h</td>
<td>34% (28%)</td>
</tr>
<tr>
<td>6</td>
<td>NaH (1.1 equiv)</td>
<td>1.5</td>
<td>CH(_2)Cl(_2)</td>
<td>0 °C</td>
<td>1 h</td>
<td>26% (20%)</td>
</tr>
<tr>
<td>7</td>
<td>NaH (2.0 equiv)</td>
<td>1.5</td>
<td>THF</td>
<td>0 °C</td>
<td>1 h</td>
<td>24%</td>
</tr>
<tr>
<td>8</td>
<td>NaH (1.1 equiv)</td>
<td>3.0</td>
<td>THF</td>
<td>0 °C</td>
<td>1 h</td>
<td>21%</td>
</tr>
<tr>
<td>9</td>
<td>NaH (1.1 equiv)</td>
<td>1.5</td>
<td>THF</td>
<td>−20 °C</td>
<td>12 h</td>
<td>11%</td>
</tr>
<tr>
<td>10</td>
<td>NaH (1.1 equiv)</td>
<td>1.5</td>
<td>THF</td>
<td>−78 °C</td>
<td>24 h</td>
<td>19%</td>
</tr>
</tbody>
</table>

\(^a\)Reactions performed with imidoyl chloride and base in solvent (0.05 M) at indicated temperature on 0.3–1.2 mmol scale. \(^b\)Determined by \(^1\)H NMR analysis of the crude mixture using TCE as an internal standard and the yield of the isolated product was given in the parentheses.
5.2. Preparation of Trifluoroacetimidoyl Chlorides

Trifluoroacetimidoyl chlorides were prepared according to the literature procedure. To an oven-dried round-bottom flask equipped with a stir bar, septum, and condenser were added TFA (1.0 equiv), PPh₃ (3.0 equiv), Et₃N (1.2 equiv), and CCl₄ (5.0 equiv) at 23 °C. The resulting solution was cooled to 0 °C and stirred for 10 min before the solution of amine (1.2 equiv) in CCl₄ (5.0 equiv) was added. The reaction mixture was heated to reflux in a pre-heated oil bath and stirred for 2 h, before it was cooled to 23 °C and directly concentrated under reduced pressure. The crude product was re-dissolved in hexanes and filtered, and the filter cake was washed with hexanes three times. The resulting filtrate was concentrated under reduced pressure, and the crude product was distilled to afford the imidoyl chloride R.

![Chemical Structures](image)

**Figure S7.** List of trifluoroacetimidoyl chlorides.

**The spectral data matched to those reported in the literature:** 2,2,2-trifluoro-N-phenylacetimidoyl chloride (R1), N-(2,6-dimethylphenyl)-2,2,2-trifluoroacetimidoyl chloride (R2), 2,2,2-trifluoro-N-hexylacetimidoyl chloride (R3), N-(2-bromophenyl)-2,2,2-trifluoroacetimidoyl chloride (R4).
5.3. General Procedure for C3-Amidation of Indole Derivatives (Scheme 3)

**Method I**

- 3a (R = H)
- 3b (R = Me)
- 3e (R = 4-MeOPh)
- 3j
- 3k
- 3m
- 3n
- 3o (1:1 dr)
- 3s
- 3t
- 3u

**Method J**

- 3v
- 3w
- 3x
- 3y

**Method K**

- 3c (X = Ph)
- 3d (X = 2-Naph)
- 3f (X = F)
- 3g (X = Br)
- 3h (X = CO₂Me)
- 3i (X = CN)
- 3p
- 3q
- 3r
- 3y
- 3z (R = 2,6-Me)
- 3aa
- 3ab
- 3ac
- 3ad

*Figure S8.* List of C3-amidated products categorized by methods of C3-amidation.
**General procedure I**

To an oven-dried round-bottom flask equipped with a stir bar and septum were added *N*-hydroxyindole \( \mathbf{1} \) (1.0 equiv) and \( \text{CH}_2\text{Cl}_2 \) (0.05 M in \( \mathbf{1} \)) at 23 °C. The resulting solution was cooled to 0 °C, and trichloroacetonitrile (3.0 equiv) and \( \text{Et}_3\text{N} \) (0.1 equiv) were successively added to the solution. The reaction mixture was warmed up to 23 °C and stirred for 3 h before it was quenched with \( \text{H}_2\text{O} \). The layers were separated and the aqueous layer was extracted with \( \text{CH}_2\text{Cl}_2 \) three times. The combined organic layer was dried over anhydrous \( \text{MgSO}_4 \), filtered, and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography to afford the desired product \( \mathbf{3} \).

**General procedure J**

To an oven-dried heavy-wall pressure tube equipped with a stir bar and septum were successively added *N*-hydroxyindole \( \mathbf{1} \) (1.0 equiv) and \( \text{DCE} \) (0.05 M in \( \mathbf{1} \)) at 23 °C, followed by trichloroacetonitrile (3.0 equiv) and \( \text{Et}_3\text{N} \) (0.1 equiv). The resulting mixture was heated to 90 °C in a pre-heated oil bath and stirred for 2 h, before it was cooled to 23 °C and quenched with \( \text{H}_2\text{O} \). The layers were separated and the aqueous layer was extracted with \( \text{CH}_2\text{Cl}_2 \) three times. The combined organic layer was dried over anhydrous \( \text{MgSO}_4 \), filtered, and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography to afford the desired product \( \mathbf{3} \).
General procedure K

To an oven-dried round-bottom flask equipped with a stir bar and septum were successively added N-hydroxyindole 1 (1.0 equiv) and THF (0.05 M in 1) at 23 °C. The resulting solution was cooled to 0 °C, and NaH (60% in mineral oil, 1.1 equiv) was added to the solution. The reaction mixture was stirred for 10 min, then imidoyl chloride (1.5 equiv) was added. The resulting mixture was stirred for additional 1 h at 0 °C before it was quenched with brine. The layers were separated and the aqueous layer was extracted with EtOAc three times. The combined organic layer was washed with brine, dried over anhydrous MgSO₄, filtered, and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography to afford the desired product 3.

Methyl 3a-(2,2,2-trichloroacetamido)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate (3a)

Following the general procedure I, N-hydroxyindole 1a (133 mg, 0.568 mmol) afforded pyrroloindoline 3a (168 mg, 78%) as a pale yellow oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 7:3).

Rf=0.51 (silica gel, hexanes:EtOAc = 1:1); ¹H NMR (500 MHz, CDCl₃, 60:40 mixture of rotamers): δ 7.34 and 7.30 (d, J = 7.5 Hz, 1H), 7.23 – 7.19 (m, 1H), 6.88 – 6.80 (m, 2H), 6.68 (d, J = 7.3 Hz, 1H), 5.70 and 5.68 (s, 1H), 3.88 and 3.78 (t, J = 9.9 Hz, 1H), 3.77 and 3.70 (s, 3H), 3.16 – 3.08 (m, 1H), 3.01 – 2.91 (m, 1H), 2.50 and 2.41 (dd, J = 12.5, 6.5 Hz, 1H); ¹³C NMR (101 MHz, CDCl₃): δ 161.0, 155.5, 154.6, 149.9, 149.7, 131.1, 131.1, 127.0,
126.8, 123.8, 123.5, 120.0, 119.8, 110.5, 110.4, 92.3, 78.3, 78.2, 72.0, 70.9, 52.9, 52.6, 45.4, 45.3, 33.0; **HRMS** calcd. for C\textsubscript{14}H\textsubscript{15}Cl\textsubscript{3}N\textsubscript{3}O\textsubscript{3} \([M + H]^+\) 378.0174, found 378.0173.

**Methyl 5-methyl-3a-(2,2,2-trichloroacetamido)-3,3a,8,8a-tetrahydroppyrolo[2,3-b]indole-1(2H)-

**carboxylate (3b)**

Following the **general procedure I**, *N*-hydroxyindole 1b (72.0 mg, 0.290 mmol) afforded pyrroloindoline 3b (77.2 mg, 68%) as a pale yellow oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 7:3).

\( R_f = 0.56 \) (silica gel, hexanes:EtOAc = 1:1); \(^1\)H NMR (500 MHz, CDCl\textsubscript{3}, 55:45 mixture of rotamers): \( \delta 7.14 \) and 7.10 (s, 1H), 7.03 (d, \( J = 8.0 \) Hz, 1H), 6.80 and 6.76 (s, 1H), 6.60 (d, \( J = 8.0 \) Hz, 1H), 5.69 and 5.67 (s, 1H), 3.89 and 3.77 (t, \( J = 9.7 \) Hz, 1H), 3.77 and 3.70 (s, 3H), 3.12 (tt, \( J = 10.9, 6.8 \) Hz, 1H), 3.01 – 2.91 (m, 1H), 2.47 and 2.39 (dd, \( J = 12.4, 6.1 \) Hz, 1H), 2.30 (s, 3H); \(^{13}\)C NMR (101 MHz, CDCl\textsubscript{3}): \( \delta 161.0, 155.6, 154.7, 147.7, 147.5, 131.8, 131.7, 129.7, 129.5, 127.2, 127.0, 124.2, 123.9, 110.7, 110.5, 92.3, 78.5, 72.1, 71.0, 52.9, 52.6, 45.5, 45.3, 32.7, 32.6, 21.0; **HRMS** calcd. for C\textsubscript{15}H\textsubscript{17}Cl\textsubscript{3}N\textsubscript{3}O\textsubscript{3} \([M + H]^+\) 392.0330, found 392.0330.

**Methyl 5-phenyl-3a-(2,2,2-trichloroacetamido)-3,3a,8,8a-tetrahydroppyrolo[2,3-b]indole-1(2H)-

carboxylate (3c)**

Following the **general procedure J**, *N*-hydroxyindole 1c (35.6 mg, 0.115 mmol) afforded pyrroloindoline 3c (26.1 mg, 50%) as a pale yellow oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 7:3).
$R_f = 0.44$ (silica gel, hexanes:EtOAc = 1:1); $^1$H NMR (500 MHz, CDCl$_3$, 60:40 mixture of rotamers): $\delta$ 7.57 and 7.52 (s, 1H), 7.53 (d, $J = 7.5$ Hz, 2H), 7.48 (d, $J = 7.5$ Hz, 1H), 7.42 (t, $J = 7.5$ Hz, 2H), 7.31 (t, $J = 7.4$ Hz, 1H), 6.87 and 6.84 (s, 1H), 6.76 (d, $J = 8.1$ Hz, 1H), 5.76 and 5.74 (s, 1H), 3.94 and 3.83 (t, $J = 9.6$ Hz, 1H), 3.80 and 3.72 (s, 3H), 3.20 (tt, $J = 11.0$, 5.6 Hz, 1H), 3.00 (dq, $J = 21.9$, 10.9 Hz, 1H), 2.57 and 2.49 (dd, $J = 12.5$, 6.5 Hz, 1H); $^{13}$C NMR (126 MHz, CDCl$_3$): $\delta$ 161.2, 155.6, 154.7, 149.3, 149.2, 140.9, 140.8, 133.7, 133.5, 130.3, 130.2, 129.0, 127.9, 127.7, 126.9, 126.7, 122.5, 122.2, 110.9, 110.7, 92.3, 78.7, 72.1, 71.0, 53.0, 52.7, 45.5, 45.4, 33.0; HRMS calcd. for C$_{20}$H$_{19}$Cl$_3$N$_3$O$_3$ $[M + H]^+$ 454.0487, found 454.0487.

Methyl 5-(naphthalen-2-yl)-3a-(2,2,2-trichloroacetamido)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate (3d)

Following the general procedure J, N-hydroxyindole 1d (47.2 mg, 0.131 mmol) afforded pyrroloindoline 3d (29.7 mg, 45%) as a pale yellow oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 $\rightarrow$ 7:3).

$R_f = 0.41$ (silica gel, hexanes:EtOAc = 1:1); $^1$H NMR (500 MHz, MeOD, 60:40 mixture of rotamers): $\delta$ 7.98 (s, 1H), 7.87 (d, $J = 8.2$ Hz, 2H), 7.82 (d, $J = 8.0$ Hz, 1H), 7.76 – 7.70 (m, 2H), 7.58 (d, $J = 8.3$ Hz, 1H), 7.44 (dt, $J = 19.7$, 7.1 Hz, 2H), 6.78 (d, $J = 8.2$ Hz, 1H), 5.84 and 5.83 (s, 1H), 3.83 (t, $J = 10.3$ Hz, 1H), 3.80 and 3.74 (s, 3H), 3.22 (td, $J = 10.9$, 10.4, 6.9 Hz, 1H), 2.80 – 2.60 (m, 2H); $^{13}$C NMR (126 MHz, MeOD): $\delta$ 163.5, 157.2, 156.9, 151.4, 140.0, 135.4, 133.7, 133.5, 133.4, 130.4, 130.0, 129.9, 129.3, 129.0, 128.6, 127.2, 126.5, 126.2, 125.3, 123.7, 123.6, 111.3, 111.1, 93.9, 81.2, 80.7, 73.8, 72.8, 53.4, 53.2, 46.1, 46.0, 37.0, 36.6; HRMS calcd. for C$_{20}$H$_{19}$Cl$_3$N$_3$O$_3$ $[M + H]^+$ 504.0643, found 504.0648.
Methyl 5-(4-methoxyphenyl)-3a-(2,2,2-trichloroacetamido)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate (3e)

Following the general procedure I, N-hydroxyindole 1e (40.0 mg, 0.118 mmol) afforded pyrroloindoline 3e (37.6 mg, 68%) as a pale yellow oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 7:3).

$R_f$=0.24 (silica gel, hexanes:EtOAc = 7:3); $^1$H NMR (400 MHz, CDCl$_3$, 60:40 mixture of rotamers): $\delta$ 7.52 (s, 1H), 7.48 – 7.40 (m, 4H), 6.96 (d, $J$ = 8.2 Hz, 2H), 6.87 and 6.84 (s, 1H), 6.74 (d, $J$ = 8.2 Hz, 1H), 5.75 and 5.73 (s, 1H), 3.92 and 3.86 (t, $J$ = 8.8 Hz, 1H), 3.84 (s, 3H), 3.79 and 3.72 (s, 3H), 3.20 (td, $J$ = 10.2, 5.5 Hz, 1H), 3.00 (tt, $J$ = 19.2, 9.8 Hz, 1H), 2.56 and 2.48 (dd, $J$ = 12.4, 6.4 Hz, 1H); $^{13}$C NMR (101 MHz, CDCl$_3$): $\delta$ 161.1, 158.9, 155.6, 154.7, 148.9, 148.7, 133.5, 133.5, 133.4, 133.2, 129.8, 129.8, 128.4, 127.8, 127.7, 122.0, 121.8, 114.4, 110.9, 110.7, 92.3, 78.6, 72.1, 71.0, 55.5, 53.0, 52.7, 45.5, 45.4, 33.0; HRMS calcd. for C$_{21}$H$_{21}$Cl$_3$N$_3$O$_4$ $[M + H]^+$ 484.0592, found 484.0595.

Methyl 5-fluoro-3a-(2,2,2-trichloroacetamido)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate (3f)

Following the general procedure J, N-hydroxyindole 1f (68.4 mg, 0.271 mmol) afforded pyrroloindoline 3f (55.9 mg, 52%) as a pale yellow oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 6:4).

$R_f$=0.30 (silica gel, hexanes:EtOAc = 1:1); $^1$H NMR (500 MHz, CDCl$_3$, 60:40 mixture of rotamers): $\delta$ 7.09 and 7.04 (dd, $J$ = 7.9, 2.6 Hz, 1H), 6.94 – 6.85 (m, 2H), 6.62 (dd, $J$ = 8.9, 4.2 Hz, 1H), 5.69 and 5.66 (s, 1H), 3.89 and 3.79 (t, $J$ = 9.7 Hz, 1H), 3.77 and 3.70 (s, 3H), 3.16 (td, $J$ = 10.7, 6.4 Hz, 1H), 2.93 – 2.80 (m, 1H), 2.55 and 2.45
(dd, J = 12.7, 6.5 Hz, 1H); $^{13}$C NMR (126 MHz, CDCl$_3$): δ 161.2, 160.2, 157.4 (d, J = 238.1 Hz), 157.3 (d, J = 238.1 Hz), 157.2, 155.5, 154.7, 146.0, 145.9, 128.2 (d, J = 7.6 Hz), 128.1 (d, J = 7.5 Hz), 117.7 (d, J = 22.5 Hz), 117.6 (d, J = 22.5 Hz), 111.3, 111.2 (d, J = 24.2 Hz), 110.8 (d, J = 24.2 Hz), 92.2, 79.6, 78.6, 72.1, 71.0, 53.0, 52.7, 45.4, 45.3, 33.6, 33.5; $^{19}$F NMR (376 MHz, CDCl$_3$): δ −123.6 (q, J = 8.1 Hz), −123.9 (td, J = 8.5, 4.1 Hz); HRMS calcd. for C$_{14}$H$_{14}$Cl$_3$FN$_3$O$_3$ $[M + H]^+$ 396.0079, found 396.0081.

Methyl 5-bromo-3a-(2,2,2-trichloroacetamido)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate (3g)

Following the general procedure J, N-hydroxyindole 1g (63.1 mg, 0.201 mmol) afforded pyrroloindoline 3g (58.0 mg, 63%) as a pale yellow oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 6:4). $R_f$ = 0.35 (silica gel, hexanes:EtOAc = 1:1); $^1$H NMR (500 MHz, CDCl$_3$, 60:40 mixture of rotamers): δ 7.45 and 7.40 (s, 1H), 7.31 (d, J = 6.2 Hz, 1H), 6.82 and 6.80 (s, 1H), 6.57 (d, J = 8.3 Hz, 1H), 5.70 and 5.67 (s, 1H), 5.29 and 4.88 (s, 1H), 3.90 and 3.80 (t, J = 9.6 Hz, 1H), 3.78 and 3.71 (s, 1H), 3.16 (td, J = 10.8, 6.5 Hz, 1H), 2.91 (ddd, J = 24.2, 13.1, 9.3 Hz, 1H), 2.50 and 2.42 (dd, J = 13.0, 6.4 Hz, 1H); $^{13}$C NMR (101 MHz, CDCl$_3$): δ 161.2, 155.6, 154.6, 149.0, 134.0, 129.2, 129.0, 126.9, 126.7, 112.1, 111.9, 111.1, 92.2, 78.9, 78.0, 71.9, 70.7, 53.1, 52.8, 45.4, 45.3, 33.5, 33.4; HRMS calcd. for C$_{14}$H$_{13}$BrCl$_3$N$_3$O$_3$ $[M + H]^+$ 455.9279, found 455.9282.

Dimethyl 3a-(2,2,2-trichloroacetamido)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1,5(2H)-dicarboxylate (3h)

Following the general procedure J, N-hydroxyindole 1h (32.9 mg, 0.113 mmol) afforded pyrroloindoline 3h
(25.1 mg, 51%) as a pale yellow oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 6:4).

\( R_f = 0.30 \) (silica gel, hexanes:EtOAc = 1:1); \(^1\)H NMR (500 MHz, CDCl\(_3\), 60:40 mixture of rotamers): \( \delta \) 8.00 and 7.98 (s, 1H), 7.95 (d, \( J = 8.4 \) Hz, 1H), 6.76 (s, 1H), 6.65 (d, \( J = 8.4 \) Hz, 1H), 5.80 and 5.79 (s, 1H), 3.92 and 3.81 (t, \( J = 9.8 \) Hz, 1H), 3.88 (s, 3H), 3.79 and 3.72 (s, 3H), 3.15 (td, \( J = 10.6, 7.0 \) Hz, 1H), 30.4 – 2.90 (m, 1H), 2.48 and 2.43 (dd, \( J = 12.8, 6.9 \) Hz, 1H); \(^1\)C NMR (126 MHz, CDCl\(_3\)): \( \delta \) 166.8, 161.1, 155.6, 154.5, 153.8, 153.6, 134.0, 126.9, 126.7, 125.8, 125.6, 121.6, 121.3, 109.2, 109.0, 92.2, 78.3, 71.5, 70.4, 53.1, 52.8, 52.1, 45.3, 45.2, 33.4, 33.4; HRMS calcd. for C\(_{16}\)H\(_{17}\)Cl\(_3\)N\(_3\)O\(_5\)^+ [M + H]^+ 436.0228, found 436.0227.

\[ \text{Methyl15-cyano-3a-(2,2,2-trichloroacetamido)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate} \ (3\text{i}) \]

Following the general procedure J, N-hydroxyindole 1\( i \) (30.1 mg, 0.116 mmol) afforded pyrroloindoline 3\( i \) (25.8 mg, 55%) as a pale yellow oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 1:1).

\( R_f = 0.22 \) (silica gel, hexanes:EtOAc = 1:1); \(^1\)H NMR (500 MHz, CDCl\(_3\), 60:40 mixture of rotamers): \( \delta \) 7.61 and 7.55 (s, 1H), 7.49 (d, \( J = 8.3 \) Hz, 1H), 6.92 (s, 1H), 6.67 (d, \( J = 8.3 \) Hz, 1H), 5.78 and 5.75 (s, 1H), 3.93 and 3.83 (t, \( J = 9.8 \) Hz, 1H), 3.79 and 3.73 (s, 3H), 3.19 (td, \( J = 10.6, 6.5 \) Hz, 1H), 2.89 – 2.75 (m, 1H), 2.56 and 2.47 (dd, \( J = 12.9, 6.4 \) Hz, 1H); \(^1\)C NMR (126 MHz, CDCl\(_3\)): \( \delta \) 161.3, 155.6, 154.4, 153.1, 153.0, 136.0, 128.1, 127.9, 127.8, 119.6, 109.9, 109.7, 102.0, 101.7, 92.1, 79.2, 78.4, 71.5, 70.3, 53.2, 52.9, 45.1, 34.9, 34.7; HRMS calcd. for C\(_{13}\)H\(_{14}\)Cl\(_3\)N\(_4\)O\(_3\)^+ [M + H]^+ 403.0126, found 403.0125.
Methyl 7-methyl-3a-(2,2,2-trichloroacetamido)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-
carboxylate (3j)

Following the general procedure I, N-hydroxyindole 1j (57.0 mg, 0.230 mmol) afforded pyrroloindoline 3j (42.3 mg, 47%) as a pale yellow oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 7:3).

Rf=0.44 (silica gel, hexanes:EtOAc = 1:1); 1H NMR (400 MHz, CDCl3, 60:40 mixture of rotamers): δ 7.18 and 7.14 (d, J = 7.6 Hz, 1H), 7.05 (d, J = 7.4 Hz, 1H), 6.81 – 6.76 (m, 2H), 5.75 and 5.73 (s, 1H), 5.09 and 4.64 (s, 1H), 3.89 and 3.79 (t, J = 9.6 Hz, 1H), 3.79 and 3.71 (s, 3H), 3.13 (qd, J = 10.7, 6.3 Hz, 1H), 3.03 – 2.91 (m, 1H), 2.46 and 2.38 (dd, J = 12.2, 6.1 Hz, 1H), 2.16 and 2.15 (s, 3H); 13C NMR (101 MHz, CDCl3): δ 161.0, 155.6, 154.8, 148.6, 148.5, 132.0, 131.9, 126.4, 126.1, 121.0, 120.8, 120.3, 120.1, 119.9, 92.3, 78.1, 72.5, 71.4, 53.0, 52.6, 45.5, 45.3, 33.0, 32.9, 16.8; HRMS calcd. for C15H17Cl3N3O3 [M + H]+ 392.0330, found 392.0330.

Methyl 5b-(2,2,2-trichloroacetamido)-1,2,3,5b,6,7,8a,9-octahydro-8H-cyclopenta[g]pyrrolo[2,3-b]indole-8-
carboxylate (3k)

Following the general procedure I, N-hydroxyindole 1k (41.0 mg, 0.149 mmol) afforded pyrroloindoline 3k (34.4 mg, 55%) as a pale yellow oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 7:3).

Rf=0.48 (silica gel, hexanes:EtOAc = 1:1); 1H NMR (500 MHz, CDCl3, 60:40 mixture of rotamers): δ 7.12 and 7.09 (d, J = 7.6 Hz, 1H), 6.77 – 6.74 (m, 2H), 5.75 and 5.74 (s, 1H), 5.06 and 4.60 (s, 1H), 3.89 and 3.79 (t, J = 9.6 Hz, 1H), 3.79 and 3.71 (s, 3H), 3.19 – 3.09 (m, 1H), 3.00 (ddd, J = 20.0, 11.6, 8.6 Hz, 1H), 2.88 (m, 2H), 2.72 (m, 2H), 2.43 and 2.36 (dd, J = 12.1, 6.6 Hz, 1H), 2.11 (h, J = 7.4 Hz, 2H); 13C NMR (126 MHz, CDCl3): δ 161.0,
Following the general procedure J, N-hydroxyindole 1l (31.7 mg, 0.118 mmol) afforded pyrroloindoline 3l (27.8 mg, 57%) as a pale yellow oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 6:4).

$R_f$=0.41 (silica gel, hexanes:EtOAc = 1:1); $^1$H NMR (500 MHz, CDCl$_3$, 60:40 mixture of rotamers): $\delta$ 7.12 (t, $J$ = 8.0 Hz, 1H), 1.12 and 7.07 (s, 1H), 6.74 (dd, $J$ = 7.9, 3.6 Hz, 1H), 6.55 (d, $J$ = 8.0 Hz, 1H), 5.87 and 5.86 (s, 1H), 5.35 and 4.99 (s, 1H), 3.95 – 3.91 and 3.86 – 3.82 (m, 1H), 3.78 and 3.73 (s, 3H), 3.24 (q, $J$ = 8.4 Hz, 1H), 2.80 (dd, $J$ = 8.6, 5.9 Hz, 1H), 2.84 – 2.78 and 2.71 – 2.65 (m, 1H); $^{13}$C NMR (126 MHz, CDCl$_3$): $\delta$ 161.0, 160.8, 155.7, 154.7, 151.9, 151.8, 132.3, 130.3, 130.2, 122.9, 122.6, 120.2, 119.9, 108.7, 108.5, 92.4, 78.5, 77.9, 73.0, 71.8, 53.0, 52.8, 44.8, 33.8, 31.1; HRMS calcd. for C$_{14}$H$_{14}$Cl$_3$N$_3$O$_3$ $[M + H]^+$ 411.9784, found 411.9789.

Methyl 8a-methyl-3a-(2,2,2-trichloroacetamido)-3,3a,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate (3m)

Following the general procedure I, N-hydroxyindole 1m (27.0 mg, 0.109 mmol) afforded pyrroloindoline 3m (22.4 mg, 52%) as a pale yellow oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 7:3).
$R_f = 0.63$ (silica gel, hexanes:EtOAc = 1:1); $^1$H NMR (500 MHz, CDCl$_3$, 60:40 mixture of rotamers): $\delta$ 7.44 (d, $J$ = 7.5 Hz, 1H), 7.18 (t, $J$ = 7.7 Hz, 1H), 6.84 – 6.81 (m, 2H), 6.68 (d, $J$ = 7.9 Hz, 1H), 5.87 (s, 1H), 3.64 (s, 3H), 3.09 – 3.03 (m, 1H), 2.95 (dd, $J$ = 12.9, 6.6 Hz, 1H), 2.85 – 2.78 (m, 1H), 1.75 (s, 3H); $^{13}$C NMR (126 MHz, CDCl$_3$): $\delta$ 161.2, 154.8, 148.9, 130.7, 128.2, 124.6, 120.2, 110.8, 87.1, 71.5, 52.3, 45.5, 30.3, 19.5; HRMS calcd. for C$_{15}$H$_{17}$Cl$_3$N$_3$O$_3^+$ [M + H]$^+$ 392.0330, found 392.0333.

$N$-(1-Benzyl-2-oxo-2,3,8,8a-tetrahydropyrrolo[2,3-b]indol-3a(1H)-yl)-2,2,2-trichloroacetamide (3n)

Following the general procedure I, $N$-hydroxyindole 1n (95.1 mg, 0.339 mmol) afforded pyrroloindoline 3n (87.8 mg, 61%) as a pale yellow oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 7:3). $R_f = 0.50$ (silica gel, hexanes:EtOAc = 6:4); $^1$H NMR (400 MHz, CDCl$_3$, 60:40 mixture of rotamers): $\delta$ 7.39 – 7.27 (m, 6H), 6.96 (t, $J$ = 7.5 Hz, 1H), 6.76 (s, 1H), 6.71 (d, $J$ = 8.0 Hz, 1H), 5.43 and 5.42 (s, 1H), 4.95 (d, $J$ = 15.4 Hz, 1H), 4.38 (d, $J$ = 3.7 Hz, 1H), 4.31 (d, $J$ = 15.4 Hz, 1H), 3.51 (d, $J$ = 16.9 Hz, 1H), 3.03 (d, $J$ = 16.8 Hz, 1H); $^{13}$C NMR (101 MHz, CDCl$_3$): $\delta$ 170.6, 161.1, 148.4, 135.7, 131.6, 129.7, 129.1, 128.0, 127.8, 123.9, 121.7, 112.7, 92.0, 78.7, 65.3, 43.8, 40.1; HRMS calcd. for C$_{19}$H$_{17}$Cl$_3$N$_3$O$_2^+$ [M + H]$^+$ 424.0381, found 424.0383.

Dimethyl (2S)-3a-(2,2,2-trichloroacetamido)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1,2(2H)-dicarboxylate (3o)

Following the general procedure I, $N$-hydroxyindole 1o (108 mg, 0.369 mmol) afforded pyrroloindoline 3o (77.4 mg, 48%, 3o-1: 3o-2 = 1.3:1) as a pale yellow oil after purification by flash column chromatography (silica gel,
Both diastereomers were separated by preparative thin layer chromatography (silica gel, CH$_2$Cl$_2$:acetone = 95:5) and characterized respectively.

**Dimethyl (2S,3aR,8aS)-3a-(2,2,2-trichloroacetamido)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1,2(2H)-dicarboxylate (3o-1)**

![Structure of Dimethyl (2S,3aR,8aS)-3a-(2,2,2-trichloroacetamido)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1,2(2H)-dicarboxylate (3o-1)](structure_image)

$R_f=0.72$ (silica gel, CH$_2$Cl$_2$:acetone = 95:5); $^1$H NMR (500 MHz, CDCl$_3$, 60:40 mixture of rotamers): $\delta$ 7.39 and 7.30 (d, $J = 7.5$ Hz, 1H), 7.21 (q, $J = 7.5$ Hz, 1H), 7.05 and 6.93 (s, 1H), 6.84 (t, $J = 7.4$ Hz, 1H), 6.69 (t, $J = 8.2$ Hz, 1H), 5.86 and 5.79 (s, 1H), 5.45 and 5.00 (s, 1H), 4.37 and 4.30 (dd, $J = 8.2$, 5.8 Hz, 1H), 3.81 and 3.68 (s, 3H), 3.78 (s, 3H), 3.03 and 2.77 (dd, $J = 13.5$, 6.2 Hz, 1H), 2.96 – 2.88 (m, 1H); $^{13}$C NMR (126 MHz, CDCl$_3$): $\delta$ 172.2, 161.2, 155.3, 154.8, 148.7, 148.3, 131.0, 130.9, 127.6, 127.4, 124.0, 123.3, 120.3, 120.2, 110.9, 110.7, 92.2, 80.9, 80.5, 71.2, 69.8, 59.5, 59.1, 53.4, 53.0, 52.9, 52.9, 38.4, 37.8; HRMS calcd. for C$_{16}$H$_{17}$Cl$_3$N$_3$O$_5$ $^{[M + H]}$ 436.0228, found 436.0240.

**Dimethyl (2S,3aS,8aR)-3a-(2,2,2-trichloroacetamido)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1,2(2H)-dicarboxylate (3o-2)**

![Structure of Dimethyl (2S,3aS,8aR)-3a-(2,2,2-trichloroacetamido)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1,2(2H)-dicarboxylate (3o-2)](structure_image)

$R_f=0.70$ (silica gel, CH$_2$Cl$_2$:acetone = 95:5); $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 7.25 – 7.19 (m, 2H), 6.80 (dt, $J = 14.9$, 7.4 Hz, 1H), 6.74 – 6.65 (m, 1H), 5.77 (s, 1H), 4.75 and 4.63 (d, $J = 9.3$ Hz, 1H), 3.83 and 3.71 (s, 3H), 3.44 and 3.39 (dd, $J = 12.8$, 9.4 Hz, 1H), 3.22 and 3.21 (s, 3H), 2.79 (t, $J = 12.1$ Hz, 1H); $^{13}$C NMR (126 MHz, CDCl$_3$): $\delta$ 171.2, 171.1, 161.2, 161.2, 155.2, 154.6, 150.8, 150.5, 131.8, 131.7, 126.0, 125.9, 124.1, 124.1, 119.9, 119.6, 110.6, 92.2, 78.3, 70.9, 69.7, 59.2, 59.0, 53.3, 53.0, 52.4, 36.2, 35.7; HRMS calcd. for C$_{16}$H$_{17}$Cl$_3$N$_3$O$_5$ $^{[M + H]}$ 436.0228, found 436.0240.
2,2,2-Trichloro-N-(2-phenethyl-1H-indol-3-yl)acetamide (3p)

Following the general procedure J, N-hydroxyindole 1p (38.0 mg, 0.160 mmol) afforded indole 3p (32.4 mg, 53%) as a pale yellow oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 9:1).

$R_f=0.27$ (silica gel, hexanes:EtOAc = 9:1); $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 7.78 (br s, 1H), 7.54 (s, 1H), 7.39 (d, $J=7.8$ Hz, 1H), 7.29 – 7.22 (m, 3H), 7.17 (t, $J=7.5$ Hz, 1H), 7.14 – 7.11 (m, 3H), 3.01 (dq, $J=11.2$, 6.0 Hz, 4H); $^{13}$C NMR (126 MHz, CDCl$_3$): $\delta$ 161.5, 140.8, 134.1, 133.9, 128.9, 128.7, 126.8, 124.3, 122.5, 120.6, 117.4, 111.1, 108.7, 92.9, 35.3, 28.2; HRMS calcd. for C$_{18}$H$_{16}$Cl$_3$N$_2$O$^+$ [M + H]$^+$ 381.0323, found 381.0323.

N-(2-(((tert-Butyldimethylsilyl)oxy)methyl)-1H-indol-3-yl)-2,2,2-trichloroacetamide (3q)

Following the general procedure J, N-hydroxyindole 1q (89.8 mg, 0.324 mmol) afforded indole 3q (62.8 mg, 46%) as a pale yellow oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 9:1).

$R_f=0.25$ (silica gel, hexanes:EtOAc = 9:1); $^1$H NMR (500 MHz, MeOD): $\delta$ 7.39 (t, $J=8.3$ Hz, 2H), 7.13 (t, $J=7.6$ Hz, 1H), 7.05 (t, $J=7.5$ Hz, 1H), 4.81 (s, 2H), 0.93 (s, 9H), 0.10 (s, 6H); $^{13}$C NMR (126 MHz, MeOD): $\delta$ 164.0, 136.1, 134.0, 125.1, 123.0, 120.5, 118.6, 112.5, 109.3, 79.3, 57.9, 26.4, –5.2; HRMS calcd. for C$_{17}$H$_{24}$Cl$_3$N$_2$O$_2$Si$^+$ [M + H]$^+$ 421.0667, found 421.0682.
2,2,2-Trichloro-N-(2-cyclohexyl-1H-indol-3-yl)acetamide (3r)

Following the general procedure J, N-hydroxyindole 1r (26.2 mg, 0.122 mmol) afforded indole 3r (19.3 mg, 44%) as a pale yellow oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 9:1).

$R_f$=0.26 (silica gel, hexanes:EtOAc = 9:1); $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 7.94 (s, 1H), 7.92 (s, 1H), 7.42 (d, $J$ = 7.7 Hz, 1H), 7.31 (d, $J$ = 7.9 Hz, 1H), 7.19 – 7.12 (m, 2H), 2.82 (tt, $J$ = 11.9, 3.5 Hz, 1H), 2.04 (d, $J$ = 12.4 Hz, 2H), 1.88 (dt, $J$ = 12.8, 3.2 Hz, 2H), 1.79 (d, $J$ = 13.2 Hz, 1H), 1.51 – 1.38 (m, 4H), 1.33 – 1.24 (m, 1H); $^{13}$C NMR (126 MHz, CDCl$_3$): $\delta$ 161.6, 139.7, 133.6, 133.5, 124.7, 123.5, 122.3, 120.9, 120.6, 118.1, 117.1, 111.5, 111.2, 106.6, 56.9, 35.9, 32.4, 32.2, 26.6, 26.1, 25.6, 16.4; HRMS calcd. for C$_{16}$H$_{18}$Cl$_3$N$_2$O $[M + H]^+$ 359.0479, found 359.0480.

2,2,2-Trichloro-N-(1,2,3,4-tetrahydro-4aH-carbazol-4a-yl)acetamide (3s)

Following the general procedure I, N-hydroxyindole 1s (126 mg, 0.673 mmol) afforded indolenine 3s (129 mg, 58%) as a pale yellow oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 1:1).

$R_f$=0.29 (silica gel, hexanes:EtOAc = 1:1); $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.60 (d, $J$ = 7.7 Hz, 1H), 7.41 – 7.36 (m, 2H), 7.22 (t, $J$ = 7.4 Hz, 1H), 6.97 (s, 1H), 2.97 (d, $J$ = 12.9 Hz, 1H), 2.70 (dd, $J$ = 14.5, 2.8 Hz, 1H), 2.50 (td, $J$ = 13.1, 5.7 Hz, 1H), 2.25 – 2.20 (m, 1H), 1.80 – 1.70 (m, 3H), 1.58 – 1.47 (m, 3H), 1.35 – 1.25 (m, 1H); $^{13}$C NMR (101 MHz, CDCl$_3$): $\delta$ 182.7, 160.1, 154.3, 139.1, 129.6, 126.0, 121.4, 121.0, 92.0, 67.9, 39.0, 29.5, 28.7, 21.1; HRMS calcd. for C$_{14}$H$_{14}$Cl$_3$N$_2$O $[M + H]^+$ 331.0166, found 331.0167.
2,2,2-Trichloro-N-(7,8,9,10-tetrahydrocyclohepta[b]indol-10a(6H)-yl)acetamide (3t)

Following the general procedure I, N-hydroxyindole 1t (105 mg, 0.523 mmol) afforded indolenine 3t (136 mg, 75%) as a pale yellow oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 1:1). 

*RF*=0.25 (silica gel, hexanes:EtOAc = 1:1); 1H NMR (400 MHz, CDCl3): δ 7.48 (d, *J* = 7.7 Hz, 1H), 7.34 (t, *J* = 7.5 Hz, 1H), 7.25 – 7.17 (m, 2H), 7.11 (s, 1H), 3.09 – 3.01 (m, 1H), 2.85 (dt, *J* = 17.2, 5.2 Hz, 1H), 2.37 (dt, *J* = 14.9, 3.8 Hz, 1H), 1.97 – 1.40 (m, 7H); 13C NMR (101 MHz, CDCl3): δ 184.6, 159.7, 153.4, 139.9, 129.5, 126.2, 120.6, 120.5, 92.1, 71.8, 37.2, 32.5, 28.4, 26.0, 24.8; HRMS calcd. for C15H16Cl3N2O+ [M + H]+ 345.0323, found 345.0324.

2,2,2-Trichloro-N-(6,7,8,9,10,11-hexahydro-11aH-cycloocta[b]indol-11a-yl)acetamide (3u)

Following the general procedure I, N-hydroxyindole 1u (99.4 mg, 0.462 mmol) afforded indolenine 3u (108 mg, 65%) as a pale yellow oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 1:1). 

*RF*=0.38 (silica gel, hexanes:EtOAc = 1:1); 1H NMR (400 MHz, CDCl3): δ 7.54 (d, *J* = 7.7 Hz, 1H), 7.37 (t, *J* = 7.3 Hz, 1H), 7.26 – 7.19 (m, 2H), 6.94 (s, 1H), 2.87 – 2.80 (m, 2H), 2.65 (ddd, *J* = 13.9, 8.3, 5.5 Hz, 1H), 2.43 – 2.37 (m, 1H), 2.19 – 2.14 (m, 1H), 2.08 – 1.92 (m, 2H), 1.63 – 1.42 (m, 5H), 1.02 – 0.93 (m, 1H); 13C NMR (101 MHz, CDCl3): δ 184.8, 159.6, 154.2, 138.1, 129.7, 126.3, 121.1, 120.6, 92.0, 70.9, 34.3, 29.7, 27.4, 27.2, 24.7, 20.9; HRMS calcd. for C16H18Cl3N2O+ [M + H]+ 359.0479, found 359.0477.
tert-Butyl 9b-(2,2,2-trichloroacetamido)-1,3,4,9b-tetrahydro-2H-pyrido[4,3-b]indole-2-carboxylate (3v)

Following the general procedure I, N-hydroxyindole 1v (55.3 mg, 0.203 mmol) afforded indolenine 3v (46.6 mg, 53%) as a pale yellow oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 6:4).

$R_f$=0.36 (silica gel, hexanes:EtOAc = 1:1); $^1$H NMR (500 MHz, CDCl$_3$): δ 8.38 (br s, 1H), 7.64 (d, $J = 7.7$ Hz, 1H), 7.43 (t, $J = 7.6$ Hz, 1H), 7.38 (d, $J = 7.3$ Hz, 1H), 7.26 (t, $J = 7.4$ Hz, 1H), 5.00 (dd, $J = 14.2, 2.5$ Hz, 1H), 4.51 (dd, $J = 12.5, 5.4$ Hz, 1H), 2.94 (dd, $J = 13.3, 2.3$ Hz, 2H), 2.87 (td, $J = 12.7, 3.2$ Hz, 1H), 2.69 (td, $J = 12.4, 6.3$ Hz, 1H), 2.22 (d, $J = 14.2$ Hz, 1H), 1.54 (s, 9H); $^{13}$C NMR (126 MHz, CDCl$_3$): δ 179.0, 160.8, 157.0, 154.7, 135.1, 130.2, 126.4, 121.7, 121.5, 91.5, 82.3, 70.6, 53.9, 46.9, 30.9, 28.6; HRMS calcd. for C$_{18}$H$_{21}$Cl$_3$N$_3$O$_3$ $^+$ [M + H]$^+$ 432.0643, found 432.0641.

Methyl 4a-(2,2,2-trichloroacetamido)-1,3,4,4a,9,9a-hexahydro-2H-pyrido[3,4-b]indole-2-carboxylate (3w)

Following the general procedure I, N-hydroxyindole 1w (50.6 mg, 0.205 mmol) afforded corresponding pyrroloindoline, which was then subsequently reduced due to its lability to afford indoline 3w (32.2 mg, 40% for 2 steps) as a pale yellow oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 7:3).

$R_f$=0.25 (silica gel, hexanes:EtOAc = 1:1); $^1$H NMR (400 MHz, CDCl$_3$): δ 7.31 (d, $J = 7.6$ Hz, 1H), 7.19 (t, $J = 7.8$ Hz, 1H), 6.83 (t, $J = 7.4$ Hz, 1H), 6.72 (d, $J = 7.9$ Hz, 1H), 4.84 (s, 1H), 3.88 (d, $J = 10.4$ Hz, 1H), 3.80 (d, $J = 10.4$ Hz, 1H), 3.64 (s, 3H), 3.35 – 3.11 (m, 2H), 2.55 – 2.49 (m, 1H), 2.30 – 2.23 (m, 1H); $^{13}$C NMR (101 MHz, CDCl$_3$): δ 161.1, 157.2, 150.7, 130.3, 129.0, 123.1, 119.6, 110.9, 92.7, 65.0, 58.1, 52.3, 37.1, 36.7, 31.1; HRMS calcd. for C$_{15}$H$_{17}$Cl$_3$N$_3$O$_3$ $^+$ [M + H]$^+$ 392.0330, found 392.0325.
Methyl (1R,2S,4aR,8aS,13bS,14aS)-2-hydroxy-8a-(2,2,2-trichloroacetamido)-1,2,3,4,4a,5,7,8,8a,13b,14,14a-dodecahydroindolo[2′,3′:3,4]pyrido[1,2-b]isoquinoline-1-carboxylate (3x)

Following the general procedure I, N-hydroxyindole 1x (40.0 mg, 0.108 mmol) afforded indolenine 3x (24.5 mg, 44%) as a pale yellow oil after purification by flash column chromatography (silica gel, CHCl₃:MeOH = 1:0 → 9:1).

R_f = 0.30 (silica gel, CHCl₃:MeOH = 9:1); ¹H NMR (400 MHz, CDCl₃): δ 7.67 (d, J = 7.6 Hz, 1H), 7.43 – 7.37 (m, 2H), 7.23 (t, J = 7.4 Hz, 1H), 6.89 (s, 1H), 4.19 (s, 1H), 3.77 (s, 3H), 3.15 (s, 1H), 2.94 (ddd, J = 20.8, 10.9, 3.0 Hz, 2H), 2.83 (d, J = 12.0 Hz, 1H), 2.68 (d, J = 14.5 Hz, 1H), 2.60 (t, J = 12.9 Hz, 1H), 2.38 (d, J = 11.1 Hz, 1H), 2.18 (t, J = 10.8 Hz, 1H), 2.12 – 2.07 (m, 1H), 1.96 (ddd, J = 13.6, 10.6, 2.7 Hz, 2H), 1.93 – 1.81 (m, 2H), 1.64 – 1.35 (m, 5H); ¹³C NMR (101 MHz, CDCl₃): δ 178.7, 176.0, 160.1, 154.3, 138.7, 129.9, 126.7, 121.9, 121.7, 92.1, 66.9, 66.8, 61.6, 60.3, 52.2, 52.1, 50.1, 40.5, 36.5, 36.4, 31.4, 31.2, 23.2; HRMS calcd. for C₂₃H₂₁Cl₃N₃O₄⁺ [M + H]⁺ 514.1062, found 514.1053.

Methyl 3a-(2,2,2-trifluoro-N-phenylacetamido)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate (3y)

Following the general procedure K, N-hydroxyindole 1a (188 mg, 0.803 mmol) and imidoyl chloride R₁ (248 mg, 1.20 mmol) afforded pyrroloindoline 3y (97.7 mg, 30%) as a pale yellow oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 8:2).

R_f = 0.42 (silica gel, hexanes:EtOAc = 1:1); ¹H NMR (400 MHz, CDCl₃, 60:40 mixture of rotamers): δ 8.02 and
7.94 (s, 1H), 7.50 (d, $J = 8.3$ Hz, 2H), 7.40 – 7.36 (m, 2H), 7.10 (t, $J = 7.6$ Hz, 1H), 7.03 (t, $J = 6.6$ Hz, 1H), 6.81 – 6.73 (m, 1H), 6.68 (d, $J = 7.7$ Hz, 1H), 5.46 and 5.41 (s, 1H), 5.22 and 4.79 (s, 1H), 3.92 and 3.80 (t, $J = 9.1$ Hz, 1H), 3.79 and 3.71 (s, 3H), 3.17 (q, $J = 9.1$, 8.6 Hz, 1H), 2.66 – 2.56 (m, 2H); 13C NMR (101 MHz, CDCl3): $\delta$ 155.5, 154.9 (q, $J = 36.9$ Hz), 154.6, 149.0, 148.8, 142.1, 142.0, 134.1, 134.0, 131.9, 131.8, 129.0, 128.9, 126.9, 126.8, 124.0, 123.9, 120.9, 119.9, 119.6, 115.8 (d, $J = 288.7$ Hz), 110.3, 110.1, 82.9, 82.5, 61.2, 60.0, 52.9, 52.6, 46.5, 46.2, 36.1, 35.9; 19F NMR (376 MHz, CDCl3): $\delta$ –75.7, –75.6; HRMS calcd. for C20H19F3N3O3 [M + H]+ 406.1373, found 406.1372.

Methyl 3a-((N-(2,6-dimethylphenyl)-2,2,2-trifluoroacetamido)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate (3z)

Following the general procedure K, N-hydroxyindole 1a (150 mg, 0.642 mmol) and imidoyl chloride R2 (227 mg, 0.963 mmol) afforded pyrroloindoline 3z (47.3 mg, 17%) as a pale yellow oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 8:2).

$R_f$=0.24 (silica gel, hexanes:EtOAc = 7:3); 1H NMR (500 MHz, CDCl3, 60:40 mixture of rotamers): $\delta$ 7.42 (s, 1H), 7.12 – 7.08 (m, 3H), 7.05 ad 7.03 (d, $J = 7.4$ Hz, 1H), 6.77 (td, $J = 7.4$, 3.0 Hz, 1H), 6.67 (d, $J = 7.8$ Hz, 1H), 5.48 and 5.42 (s, 1H), 5.20 and 4.76 (s, 1H), 3.91 and 3.79 (t, $J = 8.6$ Hz, 1H), 3.79 and 3.71 (s, 3H), 3.17 – 3.09 (m, 1H), 2.63 – 2.54 (m, 2H), 2.19 (s, 6H); 13C NMR (126 MHz, CDCl3): $\delta$ 155.7 (q, $J = 36.4$ Hz), 155.5, 154.6, 149.1, 148.8, 144.3, 144.2, 135.6, 131.9, 131.8, 129.6, 128.9, 128.9, 126.1, 124.1, 124.0, 119.8, 119.5, 116.2 (q, $J = 288.8$ Hz), 110.3, 110.1, 83.0, 82.5, 61.2, 60.0, 52.9, 52.5, 46.5, 46.2, 36.5, 36.2, 18.4; 19F NMR (471 MHz, CDCl3): $\delta$ –75.3; HRMS calcd. for C22H19F3N3O3+ [M + H]+ 434.1686, found 434.1683.
Methyl 3a-(2,2,2-trifluoro-N-hexylacetamido)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate (3aa)

Following the general procedure K, N-hydroxyindole 1a (129 mg, 0.551 mmol) and imidoyl chloride R3 (178 mg, 0.825 mmol) afforded pyrroloindoline 3aa (34.5 mg, 15%) as a pale yellow oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 8:2).

$R_f=0.65$ (silica gel, hexanes:EtOAc = 1:1); $^1$H NMR (500 MHz, CDCl$_3$, 60:40 mixture of rotamers): $\delta$ 7.34 and 7.30 (d, $J = 7.4$ Hz, 1H), 7.23 – 7.19 (m, 1H), 6.83 (q, $J = 8.2$ Hz, 1H), 6.66 (d, $J = 7.9$ Hz, 1H), 5.71 and 5.70 (s, 1H), 3.92 – 3.86 and 3.80 – 3.76 (m, 1H), 3.76 and 3.68 (s, 3H), 3.29 (dq, $J = 11.2$, 6.5, 4.8 Hz, 2H), 3.11 – 2.93 (m, 2H), 2.45 – 2.42 and 2.33 – 2.28 (m, 1H), 1.39 – 1.24 (m, 2H), 1.14 – 1.07 (m, 3H), 1.04 – 0.96 (m, 3H), 0.86 (t, $J = 6.8$ Hz, 1H), 0.78 (t, $J = 7.3$ Hz, 3H); $^{13}$C NMR (126 MHz, CDCl$_3$): $\delta$ 157.6 (q, $J = 35.6$ Hz), 155.6, 154.7, 151.0, 150.9, 131.2, 131.1, 126.7, 126.6, 125.6, 125.1, 119.6, 119.3, 116.5 (q, $J = 288.4$ Hz), 110.6, 110.6, 78.3, 52.9, 52.6, 46.6, 46.5, 46.1, 45.8, 33.5, 32.6, 31.0, 30.4, 26.1, 26.0, 22.4, 14.0; $^{19}$F NMR (471 MHz, CDCl$_3$): $\delta$ –69.4; HRMS calcd. for C$_{20}$H$_{27}$F$_3$N$_3$O$_3$ $[\text{M + H}]^+$ 414.1999, found 414.1991.

Methyl 5-bromo-3a-(2,2,2-trifluoro-N-phenylacetamido)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate (3ab)

Following the general procedure K, N-hydroxyindole 1g (0.150 g, 0.479 mmol) and imidoyl chloride R1 (149 mg, 0.718 mmol) afforded pyrroloindoline 3ab (48.7 mg, 21%) as a pale yellow oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 8:2).

$R_f=0.42$ (silica gel, hexanes:EtOAc = 1:1); $^1$H NMR (500 MHz, CDCl$_3$, 60:40 mixture of rotamers): $\delta$ 7.89 (br s, 1H), 7.51 (d, $J = 8.7$ Hz, 2H), 7.39 – 7.35 (m, 2H), 7.21 – 7.17 (m, 1H), 7.10 – 7.07 (m, 1H), 6.56 (d, $J = 8.3$ Hz,
1H), 5.47 and 5.42 (s, 1H), 3.94 and 3.81 (t, \( J = 9.3 \) Hz, 1H), 3.78 and 3.72 (s, 3H), 3.17 (td, \( J = 10.8, 5.9 \) Hz, 1H), 2.67 – 2.54 (m, 2H); \(^{13}\)C NMR (126 MHz, CDCl\(_3\)): \( \delta \) 155.5, 154.9 (q, \( J = 38.7 \) Hz), 154.5, 148.1, 147.8, 141.4, 141.3, 134.5, 134.3, 134.3, 131.8, 131.7, 127.0, 126.9, 126.7, 126.7, 120.9, 115.8 (q, \( J = 288.8 \) Hz), 111.7, 111.5, 111.3, 111.0, 83.1, 82.7, 61.2, 60.0, 53.0, 52.7, 46.4, 46.1, 35.9, 35.7; \(^{19}\)F NMR (376 MHz, CDCl\(_3\)): \( \delta \) –75.7; HRMS calcd. for C\(_{20}\)H\(_{18}\)BrF\(_3\)N\(_3\)O\(_3\)\([M + H]^+\) 484.0478, found 484.0475.

2,2,2-Trifluoro-N-phenyl-N-(1,2,3,4-tetrahydro-4aH-carbazol-4a-yl)acetamide (3ac)

![Image of 2,2,2-Trifluoro-N-phenyl-N-(1,2,3,4-tetrahydro-4aH-carbazol-4a-yl)acetamide (3ac)](image)

Following the general procedure K, N-hydroxyindole 1s (72.0 mg, 0.385 mmol) and imidoyl chloride R1 (0.120 g, 0.578 mmol) afforded pyrroloindoline 3ac (43.2 mg, 31%) as a pale yellow oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 1:1). \( R_f = 0.29 \) (silica gel, hexanes:EtOAc = 1:1); \(^1\)H NMR (400 MHz, CDCl\(_3\)): \( \delta \) 7.84 (br s, 1H), 7.64 (d, \( J = 7.9 \) Hz, 1H), 7.52 (d, \( J = 8.3 \) Hz, 2H), 7.30 (td, \( J = 7.5, 1.4 \) Hz, 2H), 7.16 – 7.02 (m, 4H), 3.11 (d, \( J = 14.1 \) Hz, 1H), 2.96 (d, \( J = 13.1 \) Hz, 1H), 2.50 (td, \( J = 12.8, 5.9 \) Hz, 1H), 2.16 – 2.12 (m, 1H), 1.79 – 1.51 (m, 3H), 1.39 – 1.27 (m, 1H); \(^{13}\)C NMR (101 MHz, CDCl\(_3\)): \( \delta \) 188.6, 154.1, 147.2, 136.9, 134.1, 127.9, 127.4, 125.6, 122.4, 121.4, 120.8, 118.5 (q, \( J = 251.0 \) Hz), 62.6, 36.6, 30.7, 29.4, 22.0; \(^{19}\)F NMR (376 MHz, CDCl\(_3\)): \( \delta \) –75.7; HRMS calcd. for C\(_{20}\)H\(_{18}\)BrF\(_3\)N\(_2\)O\(_3\)\([M + H]^+\) 359.1366, found 359.1366.

N-(2-(((tert-Butyldimethylsilyl)oxy)methyl)-1H-indol-3-yl)-2,2,2-trifluoro-N-phenylacetamide (3ad)

![Image of N-(2-(((tert-Butyldimethylsilyl)oxy)methyl)-1H-indol-3-yl)-2,2,2-trifluoro-N-phenylacetamide (3ad)](image)

Following the general procedure K, N-hydroxyindole 1q (55.0 mg, 0.198 mmol) and imidoyl chloride R1 (61.7 mg, 0.297 mmol) afforded pyrroloindoline 3ad (45.3 mg, 51%) as a pale yellow oil after purification by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 95:5).
\( R_f = 0.24 \) (silica gel, hexanes:EtOAc = 7:3); \(^1\)H NMR (400 MHz, MeOD): \( \delta \) 7.90 – 7.86 (m, 1H), 7.49 – 7.43 (m, 3H), 7.38 (td, \( J = 7.4, 1.4 \) Hz, 1H), 7.19 – 7.14 (m, 2H), 7.01 (td, \( J = 7.5, 7.0, 1.1 \) Hz, 1H), 4.78 (d, \( J = 12.5 \) Hz, 1H), 4.71 (d, \( J = 12.5 \) Hz, 1H), 0.86 (s, 9H), 0.00 and –0.01 (s, 6H); \(^{13}\)C NMR (126 MHz, MeOD): \( \delta \) 154.7 (q, \( J = 37.3 \) Hz), 154.5, 136.3, 135.5, 134.1, 133.7, 131.8, 129.3, 128.6, 127.0, 126.0, 125.0, 123.1, 121.0, 119.0, 117.7, 115.7 (q, \( J = 288.8 \) Hz), 111.6, 107.0, 57.7, 26.0, 18.5, –5.4; \(^{19}\)F NMR (376 MHz, MeOD): \( \delta \) –77.5; HRMS calcd. for \( \text{C}_{23}\text{H}_{38}\text{F}_3\text{N}_2\text{O}_2\text{Si}^- \) [M – H]^- 447.1721, found 447.1719.
5.4. Evaluation of Practicality and Versatility of the C3-Amidation (Scheme 4)

5.4.1. Gram-scale Reaction

To an oven-dried round-bottom flask equipped with a stir bar and septum were added N-hydroxyindole 1a (1.01 g, 4.31 mmol, 1.0 equiv) and CH$_2$Cl$_2$ (50 mL) at 23 °C. The resulting solution was cooled to 0 °C, and trichloroacetonitrile (1.30 mL, 12.9 mmol, 3.0 equiv) and Et$_3$N (60 µL, 0.1 equiv) were successively added to the solution. The reaction mixture was warmed up to 23 °C and stirred for 3 h before it was quenched with H$_2$O (30 mL). The layers were separated and the aqueous layer was extracted with CH$_2$Cl$_2$ (3 × 20 mL). The combined organic layer was dried over anhydrous MgSO$_4$, filtered, and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 7:3) to afford pyrroloindoline 3a (1.11 g, 68%) as a pale yellow oil.
5.4.2. Conversion to the 3-Aminopyrroloindoline

To an oven-dried round-bottom flask equipped with a stir bar and septum were added 3a (0.100 g, 0.264 mmol, 1.0 equiv) and H₂O (5 mL) at 23 °C, followed by HCl (35.0–37.0 wt% in H₂O, 70 µL, 0.792 mmol, 3.0 equiv). The resulting mixture was heated to 100 °C in a pre-heated oil bath and stirred for 16 h. After the reaction mixture was cooled to 23 °C, the reaction mixture was quenched with EtOAc (5 mL) and quenched with NaHCO₃ (5 mL, sat. aq.). The layers were separated and the aqueous layer was extracted with EtOAc (3 × 20 mL). The combined organic layer was dried over anhydrous MgSO₄, filtered, and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography (silica gel, CH₂Cl₂:MeOH = 1:0 → 95:5) to afford pyrroloindoline 4a (43.0 mg, 70%) as a pale yellow oil. Analytic data is in agreement with the reported literature values.¹⁻³

_Rf_ = 0.35 (silica gel, CH₂Cl₂:MeOH = 9:1); _¹H NMR_ (500 MHz, CDCl₃, 60:40 mixture of rotamers): δ 7.24 (d, _J_ = 8.0 Hz, 1H), 7.13 (t, _J_ = 7.6 Hz, 1H), 6.82 – 6.78 (m, 1H), 6.62 (dd, _J_ = 8.0, 3.2 Hz, 1H), 5.12 and 4.71 (s, 1H), 5.09 and 5.05 (s, 1H), 3.77 and 3.69 (s, 3H), 3.67 – 3.62 (m, 1H), 3.17 – 3.09 (m, 1H), 2.40 – 2.33 (m, 1H), 2.25 – 2.16 (m, 1H); _¹³C NMR_ (126 MHz, CDCl₃): δ 155.8, 155.0, 149.1, 148.8, 131.8, 129.7, 123.3, 119.7, 119.5, 110.1, 110.0, 83.6, 83.3, 70.7, 69.6, 52.8, 52.5, 46.1, 45.7, 37.8, 37.7; _HRMS_ calcd. for C₁₂H₁₆N₃O₂⁺ [M + H]⁺ 234.1237, found 234.1238.
5.4.3. Formal Synthesis of Psychotriasine

To an oven-dried round-bottom flask equipped with a stir bar and septum were added N-hydroxyindole 1a (0.100 g, 0.427 mmol, 1.0 equiv) and THF (8 mL) at 23 °C. The resulting solution was cooled to 0 °C, and NaH (60% in mineral oil, 25.6 mg, 0.641 mmol, 1.5 equiv) was added to the solution. The reaction mixture was stirred for 10 min, then N-(2-bromophenyl)-2,2,2-trifluoroacetimidoyl chloride (0.184 g, 0.641 mmol, 1.5 equiv) was added. The resulting mixture was stirred for additional 1 h at 0 °C before it was quenched with H₂O (10 mL). The layers were separated and the aqueous layer was extracted with EtOAc (3 × 10 mL). The combined organic layer was washed with brine (1 × 10 mL), dried over anhydrous MgSO₄, filtered, and concentrated under reduced pressure.
The resulting residue was purified by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 8:2) to afford pyrroloindoline 3ae (74.0 mg, 36%) as a yellow oil.

\( R_f = 0.47 \) (silica gel, hexanes:EtOAc = 7:3); \(^1\)H NMR (400 MHz, CDCl\(_3\)): δ 8.38 (s, 1H), 8.22 (d, \( J = 8.6 \) Hz, 1H), 7.59 (dd, \( J = 7.8, 2.1 \) Hz, 1H), 7.41 – 7.38 (m, 1H), 7.12 (t, \( J = 7.5 \) Hz, 1H), 7.02 (t, \( J = 7.1 \) Hz, 1H), 6.80 – 6.76 (m, 1H), 6.69 (d, \( J = 7.8 \) Hz, 1H), 5.45 and 5.40 (s, 1H), 5.24 and 4.80 (s, 1H), 3.96 – 3.91 and 3.83 – 3.79 (m, 1H), 3.79 and 3.71 (s, 3H), 3.18 – 3.10 (m, 1H), 2.62 – 2.57 (m, 1H); 13\(^C\) NMR (101 MHz, CDCl\(_3\)): δ 155.5, 154.76 (d, \( J = 37.1 \) Hz), 154.5, 149.0, 148.7, 143.4, 143.3, 132.1, 131.2, 130.0, 129.2, 126.2, 123.9, 123.8, 122.2, 122.1, 120.0, 119.7, 115.67 (q, \( J = 288.7 \) Hz), 114.5, 110.5, 110.3, 82.8, 82.3, 60.9, 59.7, 52.9, 52.6, 46.4, 46.1, 36.0, 35.7; 19\(^F\) NMR (471 MHz, CDCl\(_3\)): δ –75.8; HRMS calcd. for C\(_{20}\)H\(_{18}\)BrF\(_3\)N\(_3\)O\(_3\)+ [M + H]+ 484.0478, found 484.0479.

Methyl 3a-((2-bromophenyl)amino)-3,3a,8,8a-tetrahydropyrrolo[2,3-b]indole-1(2H)-carboxylate (4ae)

To an oven-dried round-bottom flask equipped with a stir bar and septum were added 3ae (56.0 mg, 0.116 mmol, 1.0 equiv) and MeOH:H\(_2\)O (5:1, 3 mL) at 23 °C, followed by p-TsOH (59.9 mg, 0.348 mmol, 3.0 equiv). The resulting mixture was heated to 60 °C in a pre-heated oil bath and stirred for 3 h. After the reaction mixture was cooled to 23 °C, the reaction mixture was diluted with CH\(_2\)Cl\(_2\) (10 mL) and quenched with NaHCO\(_3\) (10 mL, sat. aq.). The layers were separated and the aqueous layer was extracted with CH\(_2\)Cl\(_2\) (3 × 10 mL). The combined organic layer was washed with brine (1 × 10 mL), dried over anhydrous MgSO\(_4\), filtered, and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography (silica gel, hexanes:EtOAc = 1:0 → 8:2) to afford pyrroloindoline 4ae (35.0 mg, 78%) as a yellow oil. Analytic data is in agreement with the reported literature values.\(^3\)

\( R_f = 0.24 \) (silica gel, hexanes:EtOAc = 7:3); \(^1\)H NMR (500 MHz, CDCl\(_3\), 50:50 mixture of rotamers): δ 7.41 (t, \( J = 8.1 \) Hz, 1H), 7.16 (t, \( J = 9.1 \) Hz, 2H), 6.98 (t, \( J = 7.9 \) Hz, 1H), 6.77 (q, \( J = 7.2 \) Hz, 1H), 6.65 (d, \( J = 7.8 \) Hz, 1H), 6.57 – 6.54 (m, 1H), 6.44 (dd, \( J = 16.5, 8.2 \) Hz, 1H), 5.73 and 5.66 (s, 1H), 5.14 and 4.82 (s, 1H), 4.81 and 4.77
(s, 1H), 3.90 – 3.85 and 3.79 – 3.75 (m, 1H), 3.77 and 3.74 (s, 3H), 3.35 – 3.28 (m, 1H), 2.65 – 2.55 (m, 1H), 2.42 – 2.36 (m, 1H); ¹³C NMR (126 MHz, CDCl₃): δ 156.1, 155.2, 149.1, 148.9, 142.2, 132.8, 132.7, 130.0, 129.1, 129.0, 128.4, 123.4, 119.8, 119.6, 119.1, 119.0, 114.3, 114.0, 111.4, 111.3, 109.8, 109.7, 78.3, 73.5, 72.3, 52.9, 52.7, 44.7, 44.5, 39.2, 38.9; HRMS calcd. for C₁₈H₁₉BrN₃O₂⁺ [M + H]⁺ 388.0655, found 388.0659.
### 6. Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>BHT</td>
<td>2,6-di-&lt;i&gt;tert&lt;/i&gt;-butyl-4-methylphenol</td>
</tr>
<tr>
<td>DABCO</td>
<td>1,4-diazabicyclo[2.2.2]octane</td>
</tr>
<tr>
<td>DBU</td>
<td>1,8-diazabicyclo(5.4.0)undec-7-ene</td>
</tr>
<tr>
<td>DCC</td>
<td>&lt;i&gt;N&lt;/i&gt;,&lt;i&gt;N&lt;/i&gt;'-dicyclohexylcarbodiimide</td>
</tr>
<tr>
<td>DCE</td>
<td>1,2-dichloroethane</td>
</tr>
<tr>
<td>DIPEA</td>
<td>&lt;i&gt;N&lt;/i&gt;,&lt;i&gt;N&lt;/i&gt;-diisopropylethylamine</td>
</tr>
<tr>
<td>DMAP</td>
<td>4-(dimethylamino)pyridine</td>
</tr>
<tr>
<td>DMF</td>
<td>&lt;i&gt;N&lt;/i&gt;,&lt;i&gt;N&lt;/i&gt;-dimethylformamide</td>
</tr>
<tr>
<td>DMSO</td>
<td>dimethyl sulfoxide</td>
</tr>
<tr>
<td>EtOAc</td>
<td>ethyl acetate</td>
</tr>
<tr>
<td>EDC·HCl</td>
<td>1-ethyl-3-(3-dimethylaminopropyl)carbodiimide</td>
</tr>
<tr>
<td>hydro-chloride</td>
<td></td>
</tr>
<tr>
<td>LC-MS</td>
<td>liquid chromatography–mass spectrometry</td>
</tr>
<tr>
<td>HOBt</td>
<td>hydroxybenzotriazole</td>
</tr>
<tr>
<td>HPLC</td>
<td>high-performance liquid chromatography</td>
</tr>
<tr>
<td>HRMS</td>
<td>high-resolution mass spectrometry</td>
</tr>
<tr>
<td>IHT</td>
<td>indoly1,3-heteroatom transposition</td>
</tr>
<tr>
<td>LAH</td>
<td>lithium aluminium hydride</td>
</tr>
<tr>
<td>LDA</td>
<td>lithium diisopropylamide</td>
</tr>
<tr>
<td>LiHMDS</td>
<td>lithium bis(trimethylsilyl)amide</td>
</tr>
</tbody>
</table>
Me  methyl

MeCN  acetonitrile

ppm  parts per million

TBSCI  tert-butyldimethylsilyl chloride

TCE  1,1,2,2-tetrachloroethane

TEMPO  (2,2,6,6-tetramethylpiperidin-1-yl)oxyl

TFA  trifluoroacetic acid

THF  tetrahydrofuran

TLC  thin-layers chromatography

$p$-TsOH  para-toluenesulfonic acid
7. References

8. NMR Spectra

\[ ^1H \text{NMR (400 MHz, CDCl}_3\]
$^{13}$C NMR (101 MHz, CDCl$_3$)

S1c
$^1$H NMR (500 MHz, CDCl$_3$)
$^{13}$C NMR (126 MHz, CDCl$_3$)

MeO

\[ \text{S1e} \]

\[
\begin{array}{c}
\text{NHCO}_2\text{Me}
\end{array}
\]
$^{1}$H NMR (400 MHz, CDCl$_3$)

MeO$_2$C

S1h
$^{13}$C NMR (101 MHz, CDCl$_3$)

MeO$_2$C

N

H

HCO$_2$Me

S1h
$^1$H NMR (400 MHz, CDCl$_3$)
$^{13}$C NMR (101 MHz, CDCl$_3$)

S1i
$^1$H NMR (400 MHz, CDCl$_3$)
$^{13}$C NMR (101 MHz, CDCl₃)

NHCO₂Me

S1k
$^1$H NMR (500 MHz, CDCl$_3$)

NHCO$_2$Me

S2a
$^{13}$C NMR (126 MHz, CDCl$_3$)

![NMR spectrum of S2a](image_url)
$^1$H NMR (400 MHz, CDCl$_3$)
$^{13}$C NMR (101 MHz, CDCl$_3$)

S2b
$^{13}$C NMR (126 MHz, CDCl$_3$)

S2c
$^{13}$C NMR (126 MHz, CDCl$_3$)

S2e
$^{13}$C NMR (101 MHz, CDCl$_3$)

S2f
$^{19}$F NMR (376 MHz, CDCl$_3$)

S2f
$^1$H NMR (400 MHz, CDCl$_3$)

Br

NHCO$_2$Me

S2g
$^{13}$C NMR (101 MHz, CDCl$_3$)

Br

NH

H

NHCO$_2$Me

S$_2$g
$^1$H NMR (400 MHz, CDCl$_3$)

Me$_2$C\[\text{N}\]\(\text{H}\)CO$_2$Me

S2h
$^{13}$C NMR (101 MHz, CDCl$_3$)

Me$_2$C

NHCO$_2$Me

S2h
$^1$H NMR (500 MHz, MeOD)

NC

NHCO$_2$Me

S2i
$^{13}$C NMR (126 MHz, CDCl$_3$)

NC$_2$H$_5$NHCO$_2$Me

S2i
$^1$H NMR (400 MHz, CDCl$_3$)

S2j
$^{13}$C NMR (101 MHz, CDCl$_3$)

\[
\begin{align*}
\text{Me} & \quad \text{NHCO}_2\text{Me} \\
\text{H} & \\
\text{Me} &
\end{align*}
\]

S2j
\(^1\)H NMR (500 MHz, CDCl\(_3\))

\[
\text{NHCO}_2\text{Me}
\]

\text{S2k}
$^{13}$C NMR (126 MHz, CDCl$_3$)

S2k
$^{1}H$ NMR (400 MHz, CDCl$_3$)
$^{13}$C NMR (101 MHz, CDCl$_3$)

![Chemical Structure](image)
$^1$H NMR (400 MHz, CDCl$_3$)
$^{13}$C NMR (101 MHz, CDCl$_3$)

![Carbon-13 NMR spectrum](image)

**S2m**
$^1$H NMR (500 MHz, CDCl$_3$)
$^{13}$C NMR (126 MHz, CDCl$_3$)

![Chemical Structure]

S2n
$^1$H NMR (500 MHz, CDCl$_3$)

NHCO$_2$Me

S2o
$^{13}$C NMR (126 MHz, CDCl$_3$)

![Chemical Structure Image]

S20
$^1$H NMR (400 MHz, CDCl$_3$)

S$_2$v
$^{13}$C NMR (101 MHz, CDCl$_3$)

S2v
$^1$H NMR (400 MHz, CDCl$_3$)

S2w
$^{13}$C NMR (101 MHz, CDCl$_3$)

$\text{NCO}_2\text{Me}$

S2w
$^1$H NMR (500 MHz, MeOD)

S2x
$^{13}$C NMR (126 MHz, MeOD)

S2x
$^1$H NMR (500 MHz, MeOD)

1a
$^{13}$C NMR (126 MHz, MeOD)

1a

\[
\begin{align*}
&\text{NHCO}_2\text{Me} \\
&\text{OH}
\end{align*}
\]
$^1$H NMR (500 MHz, MeOD)

![Diagram of molecular structure]

1b
$^{13}$C NMR (126 MHz, MeOD)

Me$_2$NCO$_2$Me

OH

1b
$^{1}H$ NMR (500 MHz, MeOD)

$\text{1c}$
$^{13}$C NMR (126 MHz, CD$_3$OD)
$^1$H NMR (400 MHz, MeOD)

1d
$^{13}$C NMR (126 MHz, MeOD)

1d

NHCO$_2$Me

OH
$^{13}$C NMR (126 MHz, MeOD)

\[ \text{MeO} \quad \text{NHCO}_2\text{Me} \]

\(1e\)
$^1$H NMR (500 MHz, MeOD)

1f
$^{13}$C NMR (126 MHz, MeOD)

![Chemical structure](image_url)

1f
$^{19}$F NMR (376 MHz, MeOD)

F
\[ \text{NHCO}_2\text{Me} \]
\[ \text{OH} \]
\[ 1f \]
$^1$H NMR (500 MHz, MeOD)
$^{13}$C NMR (126 MHz, MeOD)

$\text{Br}$

$\text{NHCO}_2\text{Me}$

$\text{OH}$

$1g$
$^1$H NMR (500 MHz, MeOD)

MeO$_2$C-\[
\begin{array}{c}
\text{N} \\
\text{MeCO}_2\text{Me}
\end{array}
\]

1h
$^{13}$C NMR (126 MHz, MeOD)

MeO$_2$C

NH

CO$_2$Me

$1h$
$^1$H NMR (500 MHz, MeOD)

1i
$^{13}$C NMR (126 MHz, MeOD)

\[
\begin{array}{c}
\text{NC} \quad \text{NHCO}_2\text{Me} \\
\text{OH} \quad \text{1i}
\end{array}
\]
$^1$H NMR (400 MHz, MeOD)

1j
$^{13}$C NMR (101 MHz, MeOD)

1j
$^1$H NMR (500 MHz, MeOD)

![NMR Spectrogram]

$1k$
$^{13}$C NMR (126 MHz, MeOD)

NHCO$_2$Me

OH

1k
$^1$H NMR (500 MHz, MeOD)
$^{13}$C NMR (126 MHz, MeOD)

![Carbon-13 NMR Spectrum](image)
$^1$H NMR (500 MHz, MeOD)

1m
$^{13}$C NMR (126 MHz, MeOD)

![NMR spectrum of compound 1m](image-url)
$^1$H NMR (500 MHz, MeOD)

$\text{1n}$
$^{13}$C NMR (126 MHz, MeOD)

![NMR spectrum of compound 1n](image-url)
$^1$H NMR (400 MHz, MeOD)
$^{13}$C NMR (101 MHz, MeOD)

\[
\text{\begin{align*}
\text{CO}_2\text{Me} \\
\text{NHCO}_2\text{Me}
\end{align*}}\]

OH

10
$^{1}$H NMR (400 MHz, CDCl$_3$)

$1p'$
$^{13}$C NMR (126 MHz, CDCl$_3$)
$^1$H NMR (400 MHz, CDCl$_3$)

1q'
$^{13}$C NMR (126 MHz, CDCl$_3$)

OTBS

1q'
$^1$H NMR (500 MHz, CDCl$_3$)

1r'

OTBS
$^{13}$C NMR (126 MHz, CDCl$_3$)

1r'

OTBS
$^1$H NMR (400 MHz, MeOD)
$^{13}$C NMR (101 MHz, MeOD)

1s
$^1$H NMR (400 MHz, CDCl$_3$)

1v'
$^1$H NMR (400 MHz, CDCl$_3$)
$^{13}$C NMR (126 MHz, CDCl$_3$)

\[ \text{NCO}_2\text{Me} \]

\[ \text{OTBS} \]

\[ 1w' \]
$^1$H NMR (500 MHz, MeOD)
$^{13}$C NMR (126 MHz, MeOD)

1x
$^1$H NMR (500 MHz, MeOD)

\[ \text{NHCbz} \]

OTBS

1a"
$^{13}$C NMR (126 MHz, MeOD)

![Chemical Structure](image)

$1a^*$
$^1$H NMR (400 MHz, CDCl$_3$)

2a-Int
$^{13}$C NMR (101 MHz, CDCl$_3$)

2a-Int
$^{1}\text{H NMR (500 MHz, CDCl}_3\text{)}$

2b-Int
$^{13}$C NMR (126 MHz, CDCl$_3$)

2b-Int
$^1$H NMR (500 MHz, CDCl$_3$)

2b'-Int
$^{13}$C NMR (126 MHz, CDCl$_3$)

2b'-Int
$^1$H NMR (500 MHz, CDCl$_3$)

2g-Int
$^{13}$C NMR (126 MHz, CDCl$_3$)

2g-Int
$^1$H NMR (500 MHz, CDCl$_3$)

$2b$
$^{13}$C NMR (126 MHz, CDCl$_3$)

2b
$^1$H NMR (500 MHz, CDCl$_3$)

2b'
$^{13}$C NMR (126 MHz, CDCl$_3$)

2b$'$
$^{13}$C NMR (126 MHz, CDCl$_3$)

![Chemical Structure](image)

2c
\[ \text{O} \quad \text{CF}_3 \]

\[ \text{O} \quad \text{NCO}_2\text{Me} \]

\[ \text{2c} \]

\[ ^{19}\text{F NMR (471 MHz, CDCl}_3) \]
$^1$H NMR (500 MHz, CDCl$_3$)
$^{13}$C NMR (126 MHz, CDCl$_3$)

![Chemical Structure]

2d
$^{19}$F NMR (471 MHz, CDCl$_3$)

2d
$^{13}$C NMR (126 MHz, CDCl$_3$)

![Chemical Structure](image_url)

2e
$^{19}$F NMR (471 MHz, CDCl$_3$)
$^1$H NMR (400 MHz, CDCl$_3$)
$^{13}$C NMR (101 MHz, CDCl$_3$)

![Chemical Structure](image)

2f
$^1$H NMR (500 MHz, CDCl$_3$)

see image for chemical structure and spectrum details
$^{13}$C NMR (126 MHz, CDCl$_3$)

2g
$^1$H NMR (500 MHz, CDCl$_3$)
$^{13}$C NMR (126 MHz, CDCl$_3$)

$2h$
$^{13}$C NMR (126 MHz, CDCl$_3$)

![Chemical Structure](image)

NMR spectrum showing various chemical shifts.
$^{13}$C NMR (101 MHz, CDCl$_3$)

2j
$^1$H NMR (500 MHz, CDCl$_3$)
$^{13}$C NMR (126 MHz, CDCl$_3$)
$^1$H NMR (400 MHz, CDCl$_3$)
\(^{13}\text{C} \text{NMR (101 MHz, CDCl}_3\text{)}\)

\[
\begin{align*}
\text{CF}_3 & \quad \text{O} \\
\text{F} & \quad \text{O} \\
\text{N} & \quad \text{NCO}_2\text{Me} \\
\text{H} & \quad \text{H}
\end{align*}
\]
$^{19}$F NMR (376 MHz, CDCl$_3$)
$^{13}$C NMR (101 MHz, CDCl$_3$)

MeO

2m
$^{19}$F NMR (376 MHz, CDCl$_3$)

2m
$^1$H NMR (400 MHz, CDCl$_3$)

![NMR spectrum](image)

$2n$
$^{13}$C NMR (101 MHz, CDCl$_3$)

2n
$^1$H NMR (500 MHz, CDCl$_3$)

![Chemical Structure Image]

2o
$^{13}$C NMR (126 MHz, CDCl$_3$)

![Chemical Structure]

2o
$^1$H NMR (500 MHz, CDCl$_3$)

![Chemical Structure](image)

**2p**
$^{13}$C NMR (126 MHz, CDCl$_3$)

2p
$^{19}$F NMR (471 MHz, CDCl$_3$)

2p
$^1$H NMR (400 MHz, CDCl$_3$)

2q
$^{13}$C NMR (126 MHz, CDCl$_3$)

![NMR Spectrum](image-url)
$^{19}$F NMR (376 MHz, CDCl$_3$)

2q
$^1$H NMR (500 MHz, CDCl$_3$)

![NMR spectrum image]

3a
$^{13}$C NMR (101 MHz, CDCl$_3$)

$^{13}$C NMR (101 MHz, CDCl$_3$)
$^1$H NMR (500 MHz, CDCl$_3$)

![NMR spectrum of compound 3b]

- 1.01 ppm
- 1.07 ppm
- 1.05 ppm
- 1.10 ppm
- 1.17 ppm
- 1.14 ppm
- 3.25 ppm
$^{13}$C NMR (101 MHz, CDCl$_3$)

![Chemical Structure](image)
$^1$H NMR (500 MHz, CDCl₃)

![NMR Spectrum](image-url)
$^{13}$C NMR (126 MHz, CDCl₃)
$^1$H NMR (500 MHz, MeOD)

![Compound 3d](image-url)
$^{13}$C NMR (126 MHz, MeOD)

3d
$^1$H NMR (400 MHz, CDCl$_3$)

3e
$^{13}\text{C NMR (101 MHz, CDCl}_3$)

3e
$^1$H NMR (500 MHz, CDCl$_3$)

![Chemical Structure Image]

3f
\[^{13}C\] NMR (126 MHz, CDCl\textsubscript{3})

\[
\begin{array}{c}
\text{O} \\
\text{CCl}_3 \\
\text{H} \\
\text{N} \\
\text{NH} \\
\text{F} \\
\text{NCO}_2\text{Me}
\end{array}
\]

3f
$^{19}$F NMR (376 MHz, CDCl$_3$)

\[
\begin{align*}
\text{O} & \quad \text{CCl}_3 \\
\text{F} & \quad \text{NCO}_2\text{Me} \\
\text{NH} & \quad \text{NH} \\
3f & 
\end{align*}
\]
$^1$H NMR (500 MHz, CDCl$_3$)
$^{13}$C NMR (101 MHz, CDCl$_3$)

![Chemical Structure](image)

3g
$^1$H NMR (500 MHz, CDCl$_3$)
$^{13}$C NMR (126 MHz, CDCl$_3$)

![Chemical Structure](image)

3h
$^{13}$C NMR (126 MHz, CDCl$_3$)

$3i$
$^1$H NMR (400 MHz, CDCl$_3$)

![NMR Spectrum](image-url)
$^{13}$C NMR (101 MHz, CDCl$_3$)

![Chemical Structure](image-url)
$^1$H NMR (500 MHz, CDCl$_3$)
$^{13}$C NMR (126 MHz, CDCl$_3$)

3k
$^1$H NMR (500 MHz, CDCl$_3$)
$^{13}$C NMR (126 MHz, CDCl$_3$)

![Carbon-13 NMR spectrum of compound 3I]
$^1$H NMR (500 MHz, CDCl$_3$)

3m
$^{13}$C NMR (126 MHz, CDCl$_3$)

![Carbon-13 NMR spectrum of compound 3m](image-url)
$^{13}$C NMR (101 MHz, CDCl$_3$)

![Chemical structure of compound 3n]
$^1$H NMR (500 MHz, CDCl$_3$)

3o-1
$^{13}$C NMR (126 MHz, CDCl$_3$)

![Chemical Structure](image)

3o-1
\[^1\text{H NMR (500 MHz, CDCl}_3\text{)}\]

![Chemical structure](image)

3o-2
$^{13}$C NMR (126 MHz, CDCl$_3$)

3o-2
$^1$H NMR (500 MHz, CDCl$_3$)
$^{13}$C NMR (126 MHz, CDCl$_3$)

3p
^1H NMR (500 MHz, MeOD)

3q
$^1^3$C NMR (126 MHz, MeOD)

![Chemical Structure](image)

3q
$^1$H NMR (500 MHz, CDCl$_3$)

3r
\[ ^{13}\text{C NMR (126 MHz, CDCl}_3) \]

\[ \text{HN} \]

\[ \text{Cl}_3 \]

\[ \text{O} \]

\[ \text{3r} \]
$^1$H NMR (400 MHz, CDCl$_3$)

3s
$^{13}$C NMR (101 MHz, CDCl$_3$)

3s
$^1$H NMR (400 MHz, CDCl$_3$)

3t

![NMR Spectrum](image-url)
$^{13}$C NMR (101 MHz, CDCl$_3$)
$^1$H NMR (400 MHz, CDCl$_3$)

3u
$^{13}$C NMR (101 MHz, CDCl$_3$)

![Chemical Structure](image)

3u
$^1$H NMR (500 MHz, CDCl$_3$)
$^{13}$C NMR (126 MHz, CDCl$_3$)

![Chemical structure](image)

3v
$^1$H NMR (400 MHz, CDCl$_3$)

![Chemical Structure](image)

3w
\(^{13}\)C NMR (101 MHz, CDCl\(_3\))

3w
$^1$H NMR (400 MHz, CDCl$_3$)

3x
$^{13}$C NMR (100 MHz, CDCl$_3$)
$^1$H NMR (400 MHz, CDCl$_3$)
$^{13}$C NMR (101 MHz, CDCl$_3$)
$^{19}$F NMR (376 MHz, CDCl$_3$)

3y
^1H NMR (500 MHz, CDCl₃)

3z (R= 2,6-Me₂)
$^{13}$C NMR (126 MHz, CDCl$_3$)

3z (R = 2,6-Me$_2$)
$^{19}$F NMR (471 MHz, CDCl$_3$)

3z (R= 2,6-Me$_2$)
$^1$H NMR (500 MHz, CDCl$_3$)

3aa
$^{13}$C NMR (126 MHz, CDCl$_3$)

![Chemical Structure](attachment:image.png)

3aa
$^{19}$F NMR (471 MHz, CDCl$_3$)

![Chemical Structure]

3aa
$^1$H NMR (500 MHz, CDCl$_3$)

3ab
$^{13}$C NMR (126 MHz, CDCl$_3$)

3ab
$^{19}\text{F NMR} \ (376 \text{ MHz, CDCl}_3)$

![Chemical structure 3ab]

- $\text{Br}$
- $\text{NCO}_2\text{Me}$
- $\text{CF}_3$
- $\text{O}$
- $\text{N}$

378
$^1$H NMR (400 MHz, CDCl$_3$)

3ac
$^{13}$C NMR (101 MHz, CDCl$_3$)

![Chemical Structure](image)

**3ac**
$^{19}$F NMR (376 MHz, CDCl$_3$)

3ac
$^1$H NMR (400 MHz, MeOD)

3ad
$^1$H NMR (400 MHz, CDCl$_3$)

3ae
$^{13}$C NMR (101 MHz, CDCl$_3$)

![NMR spectrum image]

3ae
$^{19}$F NMR (471 MHz, CDCl$_3$)

3ae
$^1$H NMR (500 MHz, CDCl$_3$)

4a
$^{13}$C NMR (126 MHz, CDCl$_3$)
$^1\text{H NMR (500 MHz, CDCl}_3$)

![Chemical Structure](image)

4ae
$^{13}$C NMR (126 MHz, CDCl$_3$)

Br
HN
NCO$_2$Me

4ae
$^1$H NMR (400 MHz, CDCl$_3$)

$^{18}$O-3-A
$^1$H NMR (400 MHz, CDCl$_3$)

$^{18}$O-4-A
$^{13}$C NMR (101 MHz, CDCl$_3$)

$^{18}$O-4-A
$^1$H NMR (400 MHz, CDCl$_3$)

2-bromo-1-fluoro-4-(trichloromethyl)benzene
$^{13}$C NMR (126 MHz, CDCl$_3$)

2-bromo-1-fluoro-4-(trichloromethyl)benzene
$^{19}\text{F NMR (376 MHz, CDCl}_3\text{)}$

2-bromo-1-fluoro-4-
(trichloromethyl)benzene
$^1\text{H NMR (500 MHz, CDCl}_3\text{)}$

$^{18}\text{O-3-Bromo-4-fluorobenzoic acid}$
$^{13}$C NMR (126 MHz, CDCl$_3$)

$^{18}$O-3-Bromo-4-fluorobenzoic acid
$^{19}$F NMR (471 MHz, CDCl$_3$)
$^{13}$C NMR (126 MHz, CDCl$_3$)

$^{18}$O-1-B

NHCO$_2$Me

F

Br
$^{19}\text{F NMR (471 MHz, CDCl}_3\text{)}$

$^{18}\text{O-1-B}$
$^1$H NMR (500 MHz, CDCl$_3$)

$^{18}$O-2-B
$^{13}$C NMR (126 MHz, CDCl$_3$)

$^{18}$O-2-B
$^{19}$F NMR (471 MHz, CDCl$_3$)

$^{18}$O-2-B
$^1$H NMR (500 MHz, CDCl$_3$)

$^{18}$O-3-B
$^{13}$C NMR (126 MHz, CDCl$_3$)

![Chemical Structure](image_url)
$^{19}$F NMR (471 MHz, CDCl$_3$)

$^{18}$O-3-B
$^{13}$C NMR (126 MHz, CDCl$_3$)

$^{18}$O-2,3,4,5,6-
Pentafluorobenzoic acid
$^{19}\text{F NMR (471 MHz, CDCl}_3\text{)}$

$^{18}\text{O-2,3,4,5,6-}
\text{Pentafluorobenzoic acid}$

\begin{center}
\begin{tabular}{c}
$\text{F} \\
$F$ \\
$\text{F} \\
$\text{F} \\
$\text{F} \\
$\text{F} \\
$^{18}\text{O} \\
$^{18}\text{O}$ \\
$\text{F} \\
$\text{F} \\
$\text{F}$ \\
$\text{F} \\
$\text{F}$ \\
$\text{F}$ \\
$\text{F}$ \\
$\text{F}$
\end{tabular}
\end{center}
$^1$H NMR (500 MHz, CDCl$_3$)

$^{18}$O-3-C
$^{13}$C NMR (126 MHz, CDCl$_3$)

$^{18}$O-3-C
$^{19}$F NMR (471 MHz, CDCl$_3$)

$^{18}$O-3-C
$^1$H NMR (500 MHz, CDCl$_3$)

$^{18}$O-2-D
$^{13}$C NMR (126 MHz, CDCl$_3$)

$^{18}$O-2-D
$^{13}$C NMR (126 MHz, CDCl$_3$)

$^{18}$O-3-D
$^1$H NMR (400 MHz, CDCl$_3$)

$^{18}$O-4-D
$^{13}$C NMR (101 MHz, CDCl$_3$)

$^{18}$O-4-D
$^{1}H$ NMR (500 MHz, CDCl$_3$)

$^{18}$O-1-E

![NMR spectrum image]
$^{13}$C NMR (126 MHz, CDCl$_3$)

$^{18}$O-1-E
$^{19}\text{F NMR (471 MHz, CDCl}_3$)
$^{1}H$ NMR (500 MHz, CDCl$_3$)

$^{18}O$-2-E
$^{13}$C NMR (126 MHz, CDCl$_3$)

$^{18}$O-2-E
$^{19}$F NMR (471 MHz, CDCl$_3$)
$^1$H NMR (500 MHz, CDCl$_3$)

$^{18}$O-3-E
$^{13}$C NMR (126 MHz, CDCl$_3$)

18O-3-E

Diagram of molecular structure with chemical shifts and spectra.
$^{19}$F NMR (471 MHz, CDCl$_3$)

$^{18}$O-3-E

![NMR spectrum graph]
$^1$H NMR (500 MHz, CDCl$_3$)

crossover product 1
$^{13}$C NMR (126 MHz, CDCl$_3$)

![Chemical Structure](image)

crossover product 1
$^1$H NMR (500 MHz, CDCl$_3$)

crossover product 2
$^{13}$C NMR (126 MHz, CDCl$_3$)

[Chemical Structure Image]

crossover product 2