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SUPPORTING INFORMATION

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General Experimental Considerations

All commercial reagents, unless otherwise stated, were used as received (Aldrich, VWR or Fischer Scientific Ltd.). Dichloromethane and acetonitrile were distilled from CaH₂ under nitrogen. Tetrahydrofuran and diethyl ether were distilled from sodium and benzophenone under nitrogen. FT-IR spectra were obtained on a Shimadzu FTIR-8400S, with samples loaded as a film onto NaCl plates. ¹H and ¹³C NMR were obtained on Varian 300 or Varian 400 or Bruker 400 or Agilent 500 spectrometers as solutions in CDCl₃ with TMS and referenced to the TMS peak. For spectra taken in other NMR solvents, CD₃OD or CD₂Cl₂ or DMSO d-6, the ¹H spectra were referenced to the solvent residual protoisomers, and ¹³C spectra (including CDCl₃ with TMS) referenced as to the NMR solvent.¹ Chemical shifts are expressed in parts per million values and coupling constants (J) are reported in Hertz (Hz) and rounded to the nearest 0.5 Hz. The following abbreviations are used to indicate multiplicities: s, singlet; d, doublet; dd, doublet of doublets; ddd, doublet of doublet of doublets; t, triplets; q, quartets; m, multiplet. High Resolution Mass Spectra (HRMS) were recorded on a time-of-flight JMS-T1000LC spectrometer with a DART ion source. Melting points were obtained on a Fisher-Johns melting point apparatus and are uncorrected. Flash column chromatography on silica gel (60 Å, 230–400 mesh, low acidity, obtained from Silicycle Inc.) was performed using reagent grade solvents, as were filtrations through Alumina (neutral, Brockmann grade I). Analytical thin-layer chromatography (TLC) was performed on pre-coated aluminium-backed silica gel plates (Alugram SIL/G/UV254 purchased from Silicycle Inc.), visualized with a UV lamp (254 nm) or potassium molybdic acid solution in ethanol or aq. KMnO₄ or aq. p-anisaldehyde or aq. vanillin. Optical rotations were taken in a 25 °C chamber.

Preparation of phenyl 5-ethyl-3,6-dihydropyridine-1(2H)-carboxylate (13)

A solution of 11 (7.428 g, 26.7 mmol)\(^2\) in EtOH (50 mL) was added to a solution of NaBH\(_4\) (4.0 g, 110 mmol) in EtOH (60 mL) dropwise at 0 °C. The reaction mixture was allowed to warm to rt, and stirred for 22 h. The reaction mixture was diluted with CH\(_2\)Cl\(_2\) (50 mL) and washed with water (50 mL). The aqueous phase was further extracted with CH\(_2\)Cl\(_2\) (2 x 50 mL). The organic phases were combined, dried (MgSO\(_4\)), and concentrated in vacuo. The crude residue was dissolved in toluene (25 mL). Phenylchloroformate (7.5 mL, 60 mmol) was added to the stirred reaction solution, dropwise, and the reaction mixture was then stirred for 16 h. The reaction mixture was concentrated in vacuo, and the residue was purified by flash chromatography (SiO\(_2\), 0-20%, EtOAc:hex, gradient elution) yielding the title compound 13 (5.36 g, 87% over two steps) as an orange oil. \(R_t = 0.60\) (20%, EtOAc:Hexanes); \(^1\)H NMR (500 MHz, CDCl\(_3\))\(^3\) \(\delta\) 7.33-7.24 (2H, m), 7.15-7.09 (1H, m), 7.07-7.00 (2H, m), 5.56-5.46 (1H, m), 3.96 (1H, s), 3.86 (1H, s), 3.61 (1H, app t, \(J = 5.5\) Hz), 3.52 (1H, app t, \(J = 5.6\) Hz), 2.14 (2H, br s), 1.95 (2H, q, \(J = 7.0\) Hz), 0.99 (3H, q, \(J = 7.5\) Hz); \(^{13}\)C NMR (125 MHz, CDCl\(_3\))\(^3\) \(\delta\) 154.1, 153.9, 151.6, 137.1, 136.4, 129.3, 125.3, 121.9, 118.3, 117.8, 46.5, 46.4, 41.5, 40.8, 27.5, 25.2, 24.7, 12.3; IR (neat, cm\(^{-1}\)) ν 2967, 1724, 1420, 1204, 845, 752; HRMS (m/z): [M+H]\(^+\) for C\(_{14}\)H\(_{17}\)NO\(_2\), calcd, 232.13375; found, 232.13414.

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\(^3\) Compound 13 is a 1:1 mixture of rotamers, confirmed by a NOESY NMR spectrum, NMR spectra shown for 13 are from an analytical sample obtained by HPLC.
Preparation of (±)-phenyl (3S*,4S*)-3,4-dibromo-3-ethylpiperidine-1-carboxylate (14)

To a stirred solution of 13 (0.5456 g, 2.356 mmol) in CH₂Cl₂ (8 mL) was added Br₂ (0.130 mL, 2.56 mmol) dropwise, until a red color persisted. The reaction mixture was diluted with sat. aq. Na₂S₂O₃ (5 mL) and stirred for an additional 15 mins. The reaction mixture was diluted with brine (25 mL) and extracted with CH₂Cl₂ (3 x 25 mL). The organic phases were combined, dried (MgSO₄), and concentrated in vacuo to yield the title compound 14 as a clear oil (0.903 g, 98%). ¹H NMR (500 MHz, CDCl₃) δ 7.29 (2H, t, J = 8.0 Hz), 7.13 (1H, t, J = 7.5 Hz), 7.06 (2H, d, J = 8.0 Hz), 4.60 (1H, s), 4.30-4.12 (2H, m), 3.54 (0.6H, d, J = 15.0 Hz), 3.48 (0.4H, t, J = 14.5 Hz), 3.38 (0.4H, d, J = 14.5 Hz), 3.32 (0.6H, t, J = 14.5 Hz), 2.94-2.66 (1H, m), 2.08-1.84 (3H, m), 1.11 (3H, t, J = 7.0 Hz); ¹³C NMR (125 MHz, CD₂Cl₂) δ 153.9, 151.5, 129.4, 125.6, 125.5, 121.9, 121.8, 71.8, 71.4, 55.8, 51.4, 50.8, 40.2, 39.6, 34.2, 34.0, 31.6, 31.2, 29.9, 8.7; IR (neat, cm⁻¹) ν 3349, 2970, 1724, 1708, 1593, 1489, 1427, 1288, 1235, 1180, 1069, 1003, 845, 753, 691; ESI-LRMS (m/z): [M+H]⁺ for C₁₄H₁₇Br₂NO₂, found, 391.0.

Preparation of (+)-phenyl (1S,4S,7S)-7-formyl-2-azabicyclo[2.2.2]oct-5-ene-2-carboxylate (20)

To a round bottom flask with 18 (11.098 g, 55.152 mmol) dissolved in MeCN:H₂O (114 mL:6 mL) was added acrolein (10.0 mL, 172 mmol). (S)-2-amino-3-methyl-1,1-diphenylbutan-1-ol·TFA (1.4493 g, 3.9236 mmol) was added, and the vessel was then

(4) Compound 14 is a 0.6:0.4 ratio of rotamers, NMR spectra shown for 14 are from an analytical sample obtained by HPLC
submerged in a 1-2 °C bath (temperature varied by depth), and then stirred for 28 h. The reaction mixture was diluted with H₂O (500 mL) and extracted with EtOAc (3 x 500 mL). The organic phases were combined, washed with brine (100 mL), dried (MgSO₄), and concentrated in vacuo. The residue was purified by flash chromatography (SiO₂, 0-100%, EtOAc:hex, gradient elution) yielding the title compound 20 (10.022 g, 71%) as a white solid. Rᵥ = 0.50 (50%, EtOAc:Hexanes); crude dr ≥ 98:2 (¹H NMR); product dr (after chromatography) = 30:1 (¹H NMR); m.p. = 93-94 °C; [α]D²⁵ = +89.0° (c 1.2, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 9.52 (0.6H, s), 9.49 (0.4H, s), 7.40-7.32 (2H, m), 7.23-7.16 (1H, m), 7.15-7.02 (2H, m), 6.52 (1H, dtd, J = 8.0, 7.0, 1.5 Hz), 6.39 (1H, dddd, J = 10.0, 8.0, 6.0, 1.5 Hz), 5.30 (1H, dddd, J = 6.0, 4.5, 3.0, 1.5 Hz), 3.54 (0.6H, dd, J = 10.5, 2.0 Hz), 3.40 (0.4H, dd, J = 10.5, 2.0 Hz), 3.24-3.15 (1.6H, m), 3.09 (0.4H, d, J = 10.5 Hz), 3.00-2.92 (1H, m), 1.98 (0.6H, dt, J = 13.0, 4.5, 3.0 Hz), 1.93 (0.8H, ddd, J = 7.0, 3.0, 2.0 Hz), 1.86 (0.6, ddd, J = 13.0, 9.5, 2.5 Hz); ¹³C NMR (125 MHz, CDCl₃) δ 200.8, 200.3, 153.7, 153.0, 151.3 (2 peaks), 136.4, 136.2, 130.5, 130.3, 129.4, 129.4, 125.5, 125.4, 121.8, 52.4, 52.2, 48.0 (2 peaks), 46.6, 45.8, 30.9, 30.5, 23.6, 23.5; IR (neat, cm⁻¹) ν 2878, 1714, 1494, 1401, 1343, 1301, 1273, 1207, 1159, 1064, 731, 722, 692. HRMS (m/z): [M+H]⁺ for C₁₅H₁₅NO₃, calcd, 258.1117; found, 258.1130.

Preparation of (+)-phenyl (1S,4S)-7-oxo-2-azabicyclo[2.2.2]oct-5-ene-2-carboxylate (21).

A 250 mL round bottomed flask was charged with 20 (1.785 g, 6.938 mmol), SiO₂ (21.164 g), Ru(bpy)₃Cl₂·(H₂O)₆ (0.260 g), MeCN (90 mL), piperidine (0.69 mL, 21 mmol), and AcOH (0.59 mL, 10.4 mmol). The flask was affixed with a septum, and sparged with O₂ under sonication for 20 mins. The flask was then affixed with a strip of Blue LED lights (0.96 W, a Blue LED light strip containing 12 SMD LED 3528-type modules purchased from Walmart, 10 cm long strip), and the flask with lights was enclosed in aluminum foil. The reaction mixture was stirred for 14 h with the lights on. The reaction mixture was diluted with water (100 mL), and the biphasic solution was

(6) 20 is a 0.6:0.4 ratio of rotamers
extracted with EtOAc (3 x 100 mL). The organic phases were combined, washed with sat. aq. NaCl (100 mL), dried (MgSO₄), and concentrated in vacuo. The residue was purified by flash chromatography (SiO₂, 0-100%, EtOAc:hex, gradient elution) yielding the title compound 21 (1.402 g, 83%) as a white solid. R_f = 0.33 (50%, EtOAc:Hexanes); m.p. = 135-136 °C (CH₂Cl₂); [α]D²⁵ = +135.4° (c 0.99, CHCl₃, lit = +132.8 for 92% ee); **¹H NMR** (500 MHz, CDCl₃) δ 7.40-7.27 (2H, m), 7.21-7.02 (3H, m), 6.70 (1H, dt, J = 15.0, 7.0 Hz), 6.48 (1H, ddd, J = 8.0, 6.5, 2.0 Hz), 5.06 (1H, dd, J = 12.5, 6.5 Hz), 3.68 (0.5H, dd, J = 10.0, 2.5 Hz), 3.56 (0.5H, dd, J = 10.5, 2.5 Hz), 3.39 (0.5H, d, J = 10.0 Hz), 3.26 (0.5H, d, J = 10.5 Hz), 3.23-3.12 (1H, m), 2.26 (2H, dd, J = 3.0, 1.5 Hz); **¹³C NMR** (125 MHz, CDCl₃) δ 202.6, 153.5, 153.1, 151.1, 150.9, 140.0, 139.4, 129.3, 128.4, 127.8, 125.6, 121.7 (2 peaks), 58.5, 57.6, 46.8, 46.7, 36.7, 36.5, 32.4, 32.1; **IR** (neat, cm⁻¹) ν 2952, 1721, 1595, 1493, 1392, 1332, 1282, 1208, 1182, 1164, 1065, 840, 746, 693; **HRMS** (m/z): [M+H]^+ for C₁₄H₁₃NO₃, calcd, 244.09737; found, 244.09729.

Preparation of (+)-2-(1H-indol-3-yl)-1-((1S,4S)-6-azaspiro[bicyclo[2.2.2]octane-2,2'-[1,3]dioxolan]-7-en-6-yl)ethan-1-one (24)

A solution of 21 (0.0550 g, 0.226 mmol) in toluene (2.5 mL) was added to pTsOH·H₂O (0.0010 g, 0.0053 mmol) and MgSO₄ (0.2 g). Ethylene glycol (0.2 mL) was added to the reaction mixture, and the solution heated at 140 °C for 20 h. MgSO₄ (0.2 g) and pTsOH·H₂O (0.0040 g, 0.021 mmol) were then added and the solution was stirred for 14 h. The reaction mixture was then diluted with sat. aq. NaHCO₃ (10 mL), and extracted with CH₂Cl₂ (3 x 15 mL). The combined organic phases were dried (MgSO₄), and concentrated in vacuo. The residue was dissolved in DMSO/H₂O (1/1, 2 mL) and KOH (0.300 g, 5.35 mmol) was added. The reaction mixture was stirred for 36 h at 130 °C. The reaction solution was diluted with sat. aq. NH₄Cl (25mL) and then extracted with

(8) Compound 21 is a 0.5:0.5 ratio of rotamers
CH₂Cl₂ (3 x 25 mL). The combined organic solutions were washed with sat. aq. NaCl (25 mL), dried (MgSO₄), and concentrated in vacuo. The crude residue of 23 was dissolved in CH₂Cl₂ (4 mL). NEt₃ (0.070 mL, 0.50 mmol), EDCI (0.080 g, 0.42 mmol) were then added, followed by 3-indoleacetic acid (0.080 g, 0.46 mmol). The reaction mixture was then stirred for 39 h, and then was diluted with CH₂Cl₂ (25 mL) and washed with water (25 mL). The aqueous phase was further extracted with CH₂Cl₂ (2 x 25 mL). The combined organic phases were dried (MgSO₄), and concentrated in vacuo. The residue was purified by flash chromatography (SiO₂, 0-10%, MeOH:CH₂Cl₂, gradient elution) yielding the known title compound 24 (0.0383 g, 52%) as a white solid. Rᵣ = 0.30 (5%, MeOH:CH₂Cl₂); m.p. = 73-74 °C; [α]D²⁵ = 29.9° (c = 1.4, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 8.43 (0.3H, s), 8.35 (0.7H, s), 7.64-7.49 (1H, m), 7.32 (1H, d, J = 8.0 Hz), 7.26 (0.3H, d, J = 2.0 Hz), 7.20-7.07 (2.4H, m), 7.01 (0.3H, s), 6.47 (0.9H, t, J = 7.0 Hz), 6.38 (0.3H, t, J = 7.0 Hz), 6.17 (0.3H, t, J = 7.0), 5.35-5.23 (1H, m), 4.28 (0.3H, d, J = 2.0 Hz), 4.12 (0.7H, dt, J = 9.1, 4.5 Hz), 4.01 (1H, m), 3.98-3.60 (4H, m), 3.57-3.40 (1H, m), 3.19-3.10 (1H, m), 2.88 (0.3H, s), 2.82 (0.7H, s), 1.96-1.72 (2H, m); ¹³C NMR (100 MHz, CDCl₃) δ 170.9, 136.4, 136.3, 135.6, 130.9, 129.9, 127.6, 127.3, 122.8, 122.2, 122.1, 119.6, 119.5, 118.7, 118.5, 111.4, 111.3, 111.2, 111.1, 109.4, 108.9, 65.1, 65.0, 64.8, 64.4, 54.2, 47.8, 47.1, 46.4, 38.7, 37.8, 32.0, 31.8, 31.3, 31.1; IR (neat, cm⁻¹) ν 3280 (br), 2968, 2931, 1624, 1459, 1420, 1341, 1270, 1229, 1124, 1011, 949, 744; HRMS (m/z): [M+H]+ for C₁₉H₂₀N₂O₃, calcd, 325.1547; found, 325.1551.

Preparation of (-)-5,6,6a,9,10,13-hexahydro-12H-6,9-methanopyrido[1',2':1,2]azepino[4,5-b]indole-7,12(8H)-dione (26).

To a vial (10 mL) containing PdCl₂(MeCN)₂ (0.150, 0.578 mmol), AgBF₄ (0.160 g, 0.822 mmol), and 25 (0.1206 g, 0.430 mmol) was added MeCN (5.0 mL). The reaction mixture was then stirred for 25 h at 85 °C. Then, the reaction mixture was cooled to 0 °C, diluted with MeOH (1 mL), followed by addition of NaBH₄ (0.046 g). The black

(10) Known compound 24 is a 0.7:0.3 ratio of rotamers
reaction mixture was filtered over Celite, then concentrated in vacuo. The residue was purified by flash chromatography (SiO$_2$, 0-10%, MeOH:CH$_2$Cl$_2$, gradient elution) to yield known title compound 26 (0.0300 g, 25%) as a white solid. Characterization data is shown below.


To a stirred solution of PdCl$_2$(MeCN)$_2$ (0.348 g, 1.34 mmol), AgBF$_4$ (0.280 g, 1.44 mmol) in MeCN (20 mL) was added 24 (0.3484 g, 1.07 mmol) in MeCN (25 mL). The reaction mixture was then stirred for 18 h at 75 °C. Then, the reaction mixture was cooled to 0 °C, then diluted with MeOH (12 mL), followed by portionwise addition of NaBH$_4$ (0.15 g). The black reaction mixture was filtered over Celite, then concentrated in vacuo. The residue was purified by flash chromatography (SiO$_2$, 0-100%, EtOAc:hexanes, gradient elution) to yield the title compound 27 (0.2215 g, 64%) as a white solid (contaminated with 0.15 equivalents of CH$_2$Cl$_2$, and an unidentified inseparable impurity), which was used for the deprotection attempts, vide supra. R$_f$ = 0.4 (5%, MeOH:CH$_2$Cl$_2$); m.p. = 300 °C (decomposition); [α]$_D^{25}$ = -35.9° (c 0.68, CH$_2$Cl$_2$); $^1$H NMR (500 MHz, DMSO-d6) δ 10.95 (s, 1H), 7.46 (1H, d, J = 7.5 Hz), 7.27 (1H, d, J = 8.0 Hz), 7.03 (1H, ddd, J = 8.0, 7.0, 1.5 Hz), 6.97 (1H, ddd, J = 8.0, 7.0, 1.0 Hz), 4.19-3.83 (m, 6H), 3.67 (1H, ddd, J = 11.5, 4.0, 2.5 Hz), 3.46 (1H, d, J = 15.5 Hz), 3.31-3.23 (1H, m), 2.96 (1H, d, J = 11.5 Hz), 2.21-2.11 (2H, m), 2.03-1.82 (2H, m), 1.13 (1H, ddd, J = 11.5, 6.5, 2.5 Hz); $^{13}$C NMR (125 MHz, DMSO-d6) δ 174.0, 139.1, 134.9, 127.4, 120.6, 118.6, 117.4, 110.7, 107.7, 100.87, 64.3, 63.9, 52.9, 47.7, 38.1, 32.2, 31.8, 31.1, 27.0; IR (neat, cm$^{-1}$) ν 2926, 2855, 1653, 1464, 1346, 1325, 1265, 1227, 1188, 1125, 1018, 980, 945; HRMS (m/z): [M+H]$^+$ for C$_{19}$H$_{20}$N$_2$O$_3$, calcd, 325.15522; found, 325.15484.
Attempted deprotection of compound 27.

![Chemical structure]

**Table A1: Ketal Deprotection Attempts**

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<th>Conditions</th>
<th>Result</th>
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<td>pTsOH, acetone/water 10:1, rt</td>
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</tr>
<tr>
<td>2</td>
<td>pTsOH, acetone/water 10:1, reflux</td>
<td>no conversion</td>
</tr>
<tr>
<td>3</td>
<td>NaI (cat.), CeCl₃·(H₂O)₇, MeCN, 70 °C</td>
<td>no conversion</td>
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<tr>
<td>4</td>
<td>1N HCl/THF 1:1, rt</td>
<td>no conversion</td>
</tr>
<tr>
<td>5</td>
<td>1N HCl/THF 1:1, 75 °C</td>
<td>decomposition</td>
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**Preparation of (+)-phenyl (1S,4S)-6-azaspiro[bicyclo[2.2.2]octane-2,2'-[1,3]dioxan]-7-ene-6-carboxylate (28).**

A round-bottomed flask charged with 21 (1.3023 g, 5.3535 mmol), benzene (80 mL), 1,3-propanediol (4.25 mL, 39.7 mmol) and pTsOH·H₂O (0.100 mg, 0.526 mmol) was affixed with a Dean Stark apparatus. The setup was purged with argon, and the solution was stirred under reflux for 42 h. K₂CO₃ (2 g) was added and the reaction mixture was stirred for 0.5 h. The solution was diluted with H₂O (30 mL) and extracted with EtOAc (3 x 75 mL). The organic phases were combined, dried (MgSO₄), and concentrated *in vacuo*. The residue was purified by flash chromatography (SiO₂, 0-
100%, EtOAc:hexanes, gradient elution) to yield the title compound 28 (1.5503 g, 96%) as a white solid. \( R_f = 0.50 \) (50%, EtOAc:hex); \textit{m.p.} = 103-104 °C; [\( \alpha \)]\(_{D}^{25} \) = 33.5° (c 1.63, CHCl\(_{3} \)); \textbf{\textit{1H NMR}} (500 MHz, CDCl\(_{3}\))\(^{(11)} \) \( \delta \) 7.41-7.29 (2H, m), 7.23-7.14 (1H, m), 7.16-7.10 (2H, m), 6.55-6.37 (2H, m), 5.55 (0.65H, dd, J = 6.5, 1.0 Hz), 5.38 (0.35H, d, J = 6.3 Hz), 4.34 (0.65H, td, J = 11.8, 3.1 Hz), 4.22 (0.35H, ddd, J = 12.0, 9.5, 3.5 Hz), 4.00 (0.65H, td, J = 11.5, 3.0 Hz), 3.99-3.88 (0.7H, m), 3.90-3.80 (1.65H, m), 3.54 (0.65H, dd, J = 10.1, 2.2 Hz), 3.41 (0.35H, dd, J = 10.5, 2.0 Hz), 3.22 (0.65H, dt, J = 10.0, 2.5 Hz), 3.09 (0.35H, dt, J = 10.5, 2.5 Hz), 2.91-2.81 (1H, m), 2.06-1.94 (0.65H, m), 1.89 (0.35H, ddd, J = 18.5, 9.5, 4.5 Hz), 1.81 (1H, ddd, J = 13.5, 9.0, 2.5 Hz), 1.74 (1H, tdd, J = 13.5, 3.5, 2.5 Hz), 1.60 (0.35H, dddd, J = 13.5, 4.5, 3.5, 1.0 Hz), 1.48 (0.65H, dp, J = 13.5, 3.0 Hz); \textbf{\textit{13C NMR}} (125 MHz, CDCl\(_{3}\))\(^{(11)} \) \( \delta \) 154.3, 153.6, 151.6, 135.4, 135.1, 130.2, 129.8, 129.4, 129.3, 125.4, 125.3, 122.0, 121.8, 102.6, 102.5, 61.3, 61.1 (2 peaks), 60.8, 49.2, 47.0, 46.9, 46.8, 40.7, 39.2, 31.5, 31.2, 25.0, 24.8; IR (neat, cm\(^{-1}\)) ν 2963, 2878, 1717, 1404, 1335, 1296, 1204, 1138, 1069, 988, 849, 748, 698; HRMS (m/z): [M+H]\(^{+}\) for C\(_{17}\)H\(_{19}\)NO\(_{4}\), calcd, 302.13923; found, 302.13836.

**Preparation of (+)-2-(1H-indol-3-yl)-1-(((1S,4S)-6-azaspiro[2.2.2]octane-2,2'-[1,3]dioxan]-7-en-6-yl)ethan-1-one (30).**

![Structure of compound 30](image)

To a solution of 28 (1.5503 g, 5.1447 mmol), NH\(_{2}\)NH\(_{2}\)H\(_{2}\)O (9.50 mL, 184 mmol) in MeOH:H\(_{2}\)O (30 mL:11 mL) was added KOH (9.13 g, 163 mmol). The mixture was sparged with argon under sonication for 0.5 h. The reaction mixture was then stirred under reflux for 61 h. The reaction mixture was then diluted with H\(_{2}\)O (150 mL) and then extracted with CH\(_{2}\)Cl\(_{2}\) (3 x 75 mL). The combined organic layers were washed with sat. aq. NaCl (75 mL), then dried (MgSO\(_{4}\)), and concentrated \textit{in vacuo}. The crude residue 29 was dissolved in CH\(_{2}\)Cl\(_{2}\) (100 mL), and then NE\(_{3}\) (2.0 mL, 14 mmol), 3-indoleaceticacid (0.990 g, 5.65 mmol), EDC (1.083 g, 5.649 mmol) were added sequentially as the solution was stirred. The reaction mixture was stirred for 21 h, then

\(^{(11)}\) Compound 28 is a 0.65:0.35 ratio of rotamers, confirmed by a NOESY NMR spectrum, NMR spectra shown for 28 are from an analytical sample obtained by HPLC
concentrated in vacuo. The residue was purified by flash chromatography (SiO$_2$, 0-100%, EtOAc:hexanes, gradient elution) to yield the title compound 30 (1.0895 g, 63%) as a clear oil which foams under vacuum. $R_f = 0.40$ (100%, EtOAc:hex); $[\alpha]_D^{25} = 38.7^\circ$ (c 0.99, CHCl$_3$); $^1$H NMR (600 MHz, CDCl$_3$) $\delta$ 8.29 (1H, s), 7.63 (0.2H, d, $J = 8.0$ Hz), 7.57 (0.8H, d, $J = 8.0$ Hz), 7.33 (1H, dt, $J = 8.0, 1.0$ Hz), 7.21-7.15 (1H, m), 7.13-7.08 (1.8H, m), 7.03-7.00 (0.2H, m), 6.44 (1H, ddd, $J = 7.5, 6.5, 1.0$ Hz), 6.38 (1H, ddd, $J = 8.0, 6.5, 1.5$ Hz), 6.15 (0.8H, dd, $J = 6.5, 1.0$ Hz), 6.12 (0.2H, ddd, $J = 8.0, 6.0, 1.5$ Hz), 4.55 (0.2H, d, $J = 5.5$ Hz), 4.44 (0.8H, td, $J = 12.0, 3.0$ Hz), 4.05 (0.8H, td, $J = 11.5, 3.0$ Hz), 4.01 (0.2H, d, $J = 16.0$ Hz), 3.90 (0.2H, dddd, $J = 11.5, 4.5, 3.0, 1.5$ Hz), 3.87-3.78 (2H, m), 3.74 (0.9H, dd, $J = 15.5, 1.0$ Hz), 3.71 (0.9H, dd, $J = 15.5, 1.0$ Hz), 3.45 (0.8H, dd, $J = 9.5, 2.0$ Hz), 3.42 (0.2H, d, $J = 11.5$ Hz), 3.18 (0.8H, d, $J = 9.5$ Hz), 3.11 (0.2H, dt, $J = 11.5, 2.5$ Hz), 2.93-2.87 (0.2H, m), 2.80-2.74 (0.8H, m), 2.05-1.91 (1H, m), 1.85-1.78 (0.4H, m), 1.69 (1.6H, d, $J = 3.0$ Hz), 1.45 (1H, dq, $J = 13.5, 2.5$ Hz); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 171.2, 170.6, 136.4, 135.3, 134.9, 130.3, 129.8, 127.6, 122.8, 122.6, 122.2, 122.1, 119.5 (2 peaks), 119.0, 118.7, 111.3, 111.2, 109.8, 109.1, 102.6, 102.1, 61.5, 61.3, 61.1, 60.0, 55.9, 47.3, 46.2, 44.4, 41.1, 34.5, 32.0, 31.6, 31.3, 31.1, 25.5, 24.7; IR (neat, cm$^{-1}$) ν 3283 (br s), 2963, 2870, 1628, 1427, 1346, 1134, 1096, 1053, 980, 799, 741, 702; HRMS (m/z): [M+H]$^+$ for C$_{20}$H$_{22}$N$_2$O$_3$, calcd, 339.17087; found, 339.17101.


PdCl$_2$(MeCN)$_2$ (0.493, 1.90 mmol) was added to a solution of AgBF$_4$ (0.398 g, 2.05 mmol) in MeCN (20 mL). The solution was stirred for 1 h, then 30 (0.4948 g, 1.462 mmol) in MeCN (40 mL) was added. The reaction mixture was then stirred for 24.5 h at 75 °C. Then, the reaction mixture was cooled to 0 °C, then diluted with MeOH (20 mL), followed by portionwise addition of NaBH$_4$ (0.30 g). The black reaction mixture was

(12) Compound 30 is a 0.8:0.2 ratio of rotamers, confirmed by a NOESY NMR spectrum.
filtered over Celite, then concentrated \textit{in vacuo}. The residue was purified by flash chromatography (SiO\textsubscript{2}, 0-100\%, EtOAc:hexanes, gradient elution) to yield the known title compound \textbf{31} (0.2934 g, 59\%) as a white which foams under vacuum. \textbf{R}_f = 0.40 (100\%, EtOAc:hex), \textbf{m.p.} = 300 °C, \textbf{[a]}\textsubscript{D}\textsuperscript{25} = 42.3° (c 0.86, 1:1 MeOH:CH\textsubscript{2}Cl\textsubscript{2}); \textbf{\textsuperscript{1}H NMR} (400 MHz, CD\textsubscript{2}Cl\textsubscript{2}) \delta 8.43 (1H, s), 7.48 (1H, d, \textbf{J} = 7.5 Hz), 7.27 (1H, d, \textbf{J} = 7.0 Hz), 7.09 (2H, pd, \textbf{J} = 7.0, 1.5 Hz), 4.53 (1H, s), 4.14-3.83 (5H, m), 3.77 (1H, dt, \textbf{J} = 11.5, 3.0 Hz), 3.69 (1H, d, \textbf{J} = 15.5 Hz), 3.42-3.30 (1H, m), 3.11 (1H, d, \textbf{J} = 11.4 Hz), 2.21-2.03 (3H, m), 1.83-1.72 (3H, m), 1.38-1.29 (1H, m); \textbf{\textsuperscript{13}C NMR} (100 MHz, CD\textsubscript{2}Cl\textsubscript{2}) \delta 174.9, 139.2, 135.6, 128.1, 121.9, 119.9, 118.1, 110.9, 102.4, 99.1, 60.9, 60.3, 53.5, 48.4, 37.7, 33.1, 32.4, 31.3, 28.1, 25.7; \textbf{IR} (neat, cm\textsuperscript{-1}) \nu 3256, 2932, 2870, 1636, 1458, 1427, 1350, 1246, 1142, 1111, 1096, 1053, 988, 972, 930, 737, 698; \textbf{HRMS (m/z)}: [M+H]\textsuperscript{+} for C\textsubscript{20}H\textsubscript{22}N\textsubscript{2}O\textsubscript{3}, calcd, 339.17087; found, 339.17057.

\textbf{Preparation of (-)-5,6,6a,9,10,13-hexahydro-12H-6,9-methanopyrido[1',2':1,2]azepino[4,5-b]indole-7,12(8H)-dione (26).}

\begin{center}
\includegraphics[width=0.4\textwidth]{image.png}
\end{center}

To a vial (20 mL) containing \textbf{31} (0.0968 g, 0.286 mmol), pTsOH·H\textsubscript{2}O (0.030 g, 0.16 mmol), was added acetone:H\textsubscript{2}O (7 mL:1.4 mL). The reaction mixture was then stirred for 171 h at 60 °C. Then, NaHCO\textsubscript{3} (0.1 g) was added to the solution. The reaction mixture was then concentrated \textit{in vacuo}. Then, the residue was diluted with water (10 mL). The biphasic solution was extracted with CH\textsubscript{2}Cl\textsubscript{2} (3 x 15 mL). The organic phases were combined, washed with sat. aq. NaCl (10 mL), dried (MgSO\textsubscript{4}), and concentrated \textit{in vacuo}. The residue was purified by flash chromatography (SiO\textsubscript{2}, 0-100\%, EtOAc:hex, gradient elution) yielding the known title compound \textbf{26} (0.068 g, 85\%) as a white solid.\textsuperscript{9} \textbf{R}_f = 0.4 (100\%, EtOAc:hex); \textbf{m.p.} = 286-287 °C; \textbf{[a]}\textsubscript{D}\textsuperscript{25} = -102.2° (c 0.59, 1:1 MeOH:CH\textsubscript{2}Cl\textsubscript{2}); \textbf{\textsuperscript{1}H NMR} (500 MHz, DMSO-d\textsubscript{6}) \delta 11.08 (1H, s), 7.48 (1H, d, \textbf{J} = 8.0 Hz), 7.29 (1H, d, \textbf{J} = 8.0 Hz), 7.05 (1H, ddd, \textbf{J} = 8.0, 7.0, 1.5 Hz), 6.99 (1H, ddd, \textbf{J} = 8.0, 7.0, 1.0 Hz), 4.58 (1H, s), 4.14 (1H, dd, \textbf{J} = 15.5, 1.5 Hz), 3.82 (1H, dt, \textbf{J} = 12.0, 3.5 Hz), 3.51 (1H, d, \textbf{J} = 15.5 Hz), 3.41 (1H, dd, \textbf{J} = 10.5, 6.0 Hz), 3.12 (1H, d, \textbf{J} = 12.5 Hz), 2.71 (1H, dt, \textbf{J} = 19.0, 2.5 Hz), 2.54-2.47 (1H, m), 2.44 (1H, s), 2.35 (2H, tdd, \textbf{J} =
Preparation of (-)-7-ethyl-7-hydroxy-5,6,6a,7,8,9,10,13-octahydro-12H-6,9-methanopyrido[1’,2’:1,2]azepino[4,5-b]indol-12-one (10).

Ethynyl magnesium bromide (0.5 M, 1.0 mL, 0.50 mmol) was added to a stirred solution of 26 (0.0199 g, 0.0710 mmol) and THF (1 mL), at 0 °C. The reaction mixture was stirred for 3 h at 0 °C. The reaction was quenched with sat. aq. NH₄Cl (10 mL), then extracted with CH₂Cl₂ (3 x 10 mL). The combined organic layers were washed with sat. aq. NaCl (10 mL), then dried (MgSO₄), and concentrated in vacuo. PtO₂ (0.5 mg, 0.002 mmol) was added to the residue, and the round-bottomed flask was purged with N₂, then MeOH (2.5 mL) was added. The flask was purged with a H₂, and then the solution was stirred for 16 h under a H₂ atmosphere. Then, the reaction solution was filtered over Celite, and concentrated in vacuo. The residue was purified by flash chromatography (SiO₂, 0-10%, MeOH:CH₂Cl₂, gradient elution) yielding the title compound 10 (0.0176 mg, 80%) as a white solid. Rₚ = 0.25 (5%, MeOH:CH₂Cl₂); m.p. = decomposition at 250-255 °C, [α]b²⁵ = -38° (c 0.70, EtOH); ¹³C NMR (500 MHz, DMSO-d₆) δ 10.96 (1H, s), 7.45 (1H, d, J = 7.5), 7.27 (1H, dt, J = 8.0, 1.0 Hz), 7.10-6.89 (2H, m), 4.70 (1H, s), 3.96 (1H, dd, J = 15.0, 2.0 Hz), 3.89 (1H, s), 3.61 (1H, dd, J = 10.5, 6.5 Hz), 3.53 (1H, dddd, J = 11.5, 4.0, 2.5 Hz), 3.49 (1H, dd, J = 15.5 Hz), 2.94 (1H, d, J = 12.0 Hz), 2.16 (1H, dddd, J = 13.0, 10.5, 4.0, 2.0 Hz), 1.98 (1H, s), 1.75 (1H, ddd, J = 13.5, 4.5, 2.5 Hz), 1.67-1.51 (3H, m), 1.16 (1H, ddt, J = 13.0, 6.5, 2.0 Hz), 0.95 (3H, t, J = 7.5 Hz); ¹³C NMR (125 MHz, DMSO-d₆) δ 174.4, 140.3, 135.0, 127.4, 120.5, 118.5, 117.4, 110.6, 100.4, 71.1, 55.8, 48.1, 39.1, 34.0, 32.4, 32.3, 29.4, 27.1, 7.2; IR (neat, cm⁻¹) ν 3295, 2932, 1636, 1458, 1420, 1339, 1277, 1150, 1134, 976, 957, 741; HRMS (m/z): [M+H]⁺ for C₁₉H₂₂N₂O₂, calcd, 311.17595; found, 311.17539.
Preparation of (+)-phenyl (1S,4S)-7,7-diethoxy-2-azabicyclo[2.2.2]oct-5-ene-2-carboxylate (33)

A vial was charged with 21 (0.1918 g, 0.7885 mmol), EtOH (1.5 mL), triethylorthoformate (3.0 mL), and pTsOH-H2O (0.0300 mg, 0.158 mmol). The vial was purged with argon, and the solution was stirred at 70 °C for 20 h. K2CO3 (0.2 g) was added and the reaction mixture was stirred for 0.5 h. The solution was diluted with H2O (10 mL) and extracted with CH2Cl2 (3 x 10 mL). The organic phases were combined, dried (MgSO4), and concentrated in vacuo. The residue was purified by flash chromatography (neutral alumina Brockmann grade 1, 0-100%, EtOAc:hexanes, gradient elution) to yield 33 (0.2263 g, 90%) as a clear oil. Rf = 0.37 (20%, EtOAc:hex); [α]D25 = + 51.5° (c 0.90, CHCl3); 1H NMR (500 MHz, CDCl3) δ 7.38-7.30 (2H, m), 7.17 (1H, tdt, J = 7.5, 6.5, 1.0 Hz), 7.13-7.08 (2H, m), 6.51-6.37 (2H, m), 4.96-4.94 (0.4H, m), 4.92 (0.6H, dd, J = 6.0, 1.5 Hz), 3.75-3.61 (1H, m), 3.59-3.36 (4H, m), 3.22 (0.6H, dt, J = 10.0, 2.5 Hz), 3.09 (0.4H, dt, J = 10.5, 2.0 Hz), 2.85 (1H, qq, J = 5.5, 2.5 Hz), 1.82 (0.6H, dt, J = 13.0, 3.0 Hz), 1.77-1.69 (0.8H, m), 1.66 (0.6H, dd, J = 13.0, 2.5 Hz), 1.22 (1.2H, t, J = 7.0 Hz), 1.18 (1.8H, t, J = 7.0 Hz), 1.15 (3H, td, J = 7.0, 1.0 Hz); 13C NMR (125 MHz, CDCl3) δ 154.0, 153.5, 151.6, 134.6, 133.9, 131.6, 130.7, 129.3 (2 peaks), 125.2, 125.1, 121.8, 104.8, 104.5, 56.9, 56.7, 56.0, 55.8, 51.8, 50.6, 46.7, 46.4, 36.7, 36.5, 31.6, 31.2, 15.5 (2 peaks), 15.3 (2 peaks); IR (neat, cm⁻¹) ν 2974, 2734, 2884, 1721, 1495, 1402, 1335, 1296, 1269, 1207, 1163, 1126, 1055, 991, 966, 839, 750, 723; HRMS (m/z): [M+H]+ for C18H23NO4, calcd, 318.17053; found, 318.17138.

(13) Compound 33 is a 0.6:0.4 ratio of rotamers, confirmed by a NOESY NMR spectrum, NMR spectra shown for 33 are from an analytical sample obtained by HPLC

S14
Preparation of (+)-(1S,4S)-7,7-diethoxy-2-azabicyclo[2.2.2]oct-5-ene (34)

To a solution of 33 (0.0278 g, 0.0876 mmol), NH₂NH₂·H₂O (0.10 mL, 2.1 mmol) in MeOH:H₂O (0.75 mL:0.25 mL) was added KOH (0.1007 g, 1.795 mmol). The reaction vessel was purged with argon. The reaction mixture was then subjected to microwave irradiation to maintain a temperature of 140 °C for 1 h 10 mins. The reaction mixture was concentrated in vacuo. The residue was purified by flash chromatography (neutral alumina Brockmann grade 1, 0-20%, MeOH:CH₂Cl₂, gradient elution) to yield 34 (0.0070 g, 41%) as a clear oil. Rf = 0.075 (10%, MeOH:CH₂Cl₂), [α]D²⁵ = -27.3° (c 0.70, MeOH); ¹H NMR (500 MHz, CD₃OD) δ 6.70 (1H, t, J = 7.5 Hz), 6.32 (1H, ddd, J = 7.5, 6.0, 1.5 Hz), 4.29 (1H, dd, J = 6.0, 1.0 Hz), 3.70-3.39 (4H, m), 3.14 (1H, dd, J = 11.0, 2.0 Hz), 3.03 (1H, s), 2.74 (1H, dt, J = 11.0, 2.5 Hz), 1.96 (1H, dd, J = 13.5, 3.0 Hz), 1.60 (1H, dt, J = 13.4, 3.1 Hz), 1.25 (3H, t, J = 7.1 Hz), 1.13 (3H, t, J = 7.1 Hz); ¹³C NMR (150 MHz, CD₃OD) δ 139.2, 127.5, 102.6, 58.5, 57.7, 52.5, 49.0, 43.4, 36.3, 30.8, 15.4; IR (neat, cm⁻¹) 3200 (br), 3063, 2926, 1603, 1497, 1481, 1396, 1260, 1125, 1099, 1053, 964, 802, 752; HRMS (m/z): [M+H]+ for C₁₁H₁₉N₁O₂, calcd, 198.14940; found, 198.15036.

Preparation of (±)-phenyl (1S*,4S*,7S*)-7-(hydroxymethyl)-2-azabicyclo[2.2.2]oct-5-ene-2-carboxylate ((±)-35).

To a stirred solution of 18 (0.110 g, 0.547 mmol) in MeCN:H₂O (1.2 mL:0.05 mL) was added acrolein (0.10 mL, 1.6 mmol). Then, (±)-2-amino-3-methyl-1,1-diphenylbutan-1-ol·TFA (0.0202 g, 0.0547 mmol) was added. The reaction mixture was purified by flash chromatography (neutral alumina Brockmann grade 1, 0-20%, MeOH:CH₂Cl₂, gradient elution) to yield 35 (0.0360 g, 46%) as a clear oil. Rf = 0.125 (10%, MeOH:CH₂Cl₂), [α]D²⁵ = -22.6° (c 0.70, MeOH); ¹H NMR (500 MHz, CD₃OD) δ 7.36 (5H, m), 7.16 (2H, d, J = 15.4 Hz), 7.13 (2H, d, J = 15.4 Hz), 4.39 (1H, dd, J = 15.4, 15.4 Hz), 3.68 (2H, m), 3.39 (2H, m), 3.04 (1H, s), 2.77 (1H, dt, J = 11.0, 2.5 Hz), 1.96 (1H, dd, J = 13.5, 3.0 Hz), 1.60 (1H, dt, J = 13.4, 3.1 Hz), 1.28 (3H, t, J = 7.1 Hz), 1.16 (3H, t, J = 7.1 Hz); ¹³C NMR (150 MHz, CD₃OD) δ 139.2, 127.5, 102.6, 58.5, 57.7, 52.5, 49.0, 43.4, 36.3, 30.8, 15.4; IR (neat, cm⁻¹) 3200 (br), 3063, 2926, 1603, 1497, 1481, 1396, 1260, 1125, 1099, 1053, 964, 82, 802, 752; HRMS (m/z): [M+H]+ for C₁₁H₁₉N₁O₂, calcd, 198.14940; found, 198.15036.

was stirred for 30 h at 0 °C, diluted with \( \text{H}_2\text{O} \) (10 mL), and then extracted with \( \text{Et}_2\text{O} \) (3 x 10 mL). The organic phases were combined, dried (MgSO\(_4\)), and concentrated \textit{in vacuo}. The crude residue was diluted with \( \text{EtOH} \) (20 mL), and then cooled to 0 °C. NaBH\(_4\) (100 mg, 2.6 mmol) was added, and the reaction mixture was stirred for 1 h. The reaction mixture was concentrated \textit{in vacuo}. The crude residue was diluted with \( \text{H}_2\text{O} \) (10 mL) and extracted with \( \text{CH}_2\text{Cl}_2 \) (3 x 10 mL). The organic phases were combined, dried (MgSO\(_4\)), and concentrated \textit{in vacuo}. The residue was purified by flash chromatography (SiO\(_2\), 0-100%, EtOAc:hex, gradient elution) yielding the known title compound \( \text{35} \) (0.0372 g, 26%) as a viscous clear oil. Characterization data are shown below.

**Preparation of (+)-phenyl (1S,4S,7S)-7-(hydroxymethyl)-2-azabicyclo[2.2.2]oct-5-ene-2-carboxylate ((+)-35).**

![Chemical Structure](image)

A portion of crude \( \text{20} \) (200 mg, from the above preparation) was diluted with \( \text{EtOH} \) (20 mL), and then cooled to 0 °C. NaBH\(_4\) (50 mg, 1.3 mmol) was added to the solution. The reaction mixture was stirred for 1 h. The reaction mixture was concentrated \textit{in vacuo}. The crude residue was diluted with \( \text{H}_2\text{O} \) (10 mL) and extracted with \( \text{CH}_2\text{Cl}_2 \) (3 x 10 mL). The organic phases were combined, dried (MgSO\(_4\)), and concentrated \textit{in vacuo}. The residue was purified by flash chromatography (SiO\(_2\), 0-100%, EtOAc:hex, gradient elution) yielding the known compound \((+)-\text{35}\) (0.0863 g)\(^1\) as a viscous clear oil. The enantiomeric excess (ee) was determined by HPLC (DAICEL Chiralcel AD-H), 0.5 mL/min, n-hexane:2-propanol 9:1 to 1:9 gradient over 60 min, 94% ee; \([\alpha]_D^{25}\) = +87.5° (\(c = 1.10, \text{CHCl}_3\), lit = +95.0 for > 95% ee/21°C)\(^2\); \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 7.34 (2H, ddd, \(J = 8.5, 7.5, 2.5\) Hz), 7.17 (1H, td, \(J = 7.5, 1.0\) Hz), 7.14-7.01 (2H, m), 6.46 (1H, dddd, \(J = 8.0, 6.0, 4.0, 1.5\) Hz), 6.38 (1H, dddd, \(J = 8.0, 5.5, 4.0, 1.5\) Hz), 5.02-4.96 (0.4H, m), 4.91 (0.6H, ddt, \(J = 6.0, 3.0, 1.5\) Hz), 3.47 (0.6H, dd, \(J = 10.5, 2.0\) Hz), 3.36-3.26 (1.5H, m), 3.18 (1.5H, ddd, \(J = 10.5, 6.5, 4.0\) Hz), 3.07 (0.4H,

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\(^{(17)}\) Compound \((+)-\text{35}\) is a 0.6:0.4 ratio of rotamers.
Preparation of phenyl (1S,4S,7R)-7-(benzoyloxy)-7-formyl-2-azabicyclo[2.2.2]oct-5-ene-2-carboxylate and phenyl (1S,4S,7S)-7-(benzoyloxy)-7-formyl-2-azabicyclo[2.2.2]oct-5-ene-2-carboxylate (36)).

O-benzoylhydroxylamine (1.050 g, 3.83 mmol)\(^{18}\) was added to a stirred solution of 20 (0.984 g, 3.82 mmol) in CH\(_2\)Cl\(_2\) (10 mL). The reaction mixture was stirred for 17.5 h and then diluted with water (50 mL). The biphasic solution was extracted with CH\(_2\)Cl\(_2\) (3 x 50 mL). The organic phases were combined, dried (MgSO\(_4\)), and concentrated in vacuo. The residue was purified by flash chromatography (SiO\(_2\), 0–100\%, EtOAc:hex, gradient elution) yielding 36 as an inseparable mixture of diastereomers (1.027 g, 71\%) as an orange oil. \(R_f = 0.33\) (33\%, EtOAc:Hexanes); \(^1\)H NMR (500 MHz, CDCl\(_3\))\(^{19}\) \(\delta\) 10.3-9.06 (m, 1H), 8.20-6.97 (m, 11H), 6.81-5.16 (m, 2H), 4.67-3.95 (m, 1H), 3.91-2.82 (m, 2H), 2.72-1.03 (m, 2H); \(^1\)C NMR (125 MHz, CDCl\(_3\))\(^{19}\) \(\delta\) 197.7, 197.2, 195.4, 195.3, 192.1, 170.6, 166.2, 166.1, 165.1, 154.8, 154.5, 153.3, 153.2, 151.3, 151.1, 150.9, 150.8, 139.4, 137.8 (2 peaks), 136.8, 135.7, 135.6, 133.9 (2 peaks), 133.7, 133.6, 133.4, 133.3, 130.2, 130.1, 130.0, 129.7 (2 peaks), 129.5 (2 peaks), 129.4 (2 peaks), 129.3 (3 peaks), 129.2 (2 peaks), 128.8, 128.7, 128.7, 128.6 (2 peaks), 128.5 (2 peaks), 128.4 (2 peaks), 127.9, 127.5, 125.8, 125.6, 125.5 (2 peaks), 125.4, 125.3, 124.3, 124.1, 121.7 (2 peaks), 121.5 (3 peaks), 121.4, 116.0, 86.6, 86.2, 68.5, 68.2, 67.2, 67.1, 53.5, 53.1, 50.2, 49.4, 47.0, 46.9, 46.8, 44.7, 35.0, 34.4, 33.8, 33.7, 32.5, 32.0, 30.9, 30.5; IR (neat, cm\(^{-1}\)) \(\nu\) 2067, 2959, 2884, 1720, 1600, 1563, 1493, 1451, 1393, 1342, 1267, 1205, 1104, 1025, 750, 712; HRMS (m/z): [M+H]\(^+\) for C\(_{22}\)H\(_{19}\)NO\(_5\), calcld, 378.13415; found, 378.13413.


\(^{19}\) The 5:4 mixture of diastereomers of 36 are both rotameric, 3 and 2 rotamers respectively.
in CD$_3$OD
Racemic 35

Retention time endo enantiomer A: 29.3
Retention time endo enantiomer B: 31.0
Ratio (enantiomer A):(enantiomer B) = 1.0:1.0

Retention time exo enantiomer A: 20.4
Retention time exo enantiomer B: 24.9
Ratio (enantiomer A):(enantiomer B) = 1.05:1.0
Enantioenriched 35

Retention time major enantiomer: 29.3

Retention time minor enantiomer: 31.0

Ratio (major enantiomer):(minor enantiomer) = 97:3
Table A2. Crystal data and structure refinement for 21

Identification code       d16137_a         
Empirical formula        C14 H13 N O3   
Formula weight           243.25        
Temperature              150(2) K      
Wavelength               1.54178 Å      
Crystal system           Monoclinic     
Space group              P21           
Unit cell dimensions     

Volume                   1171.23(12) Å³   
Z                        4                  
Density (calculated)     1.380 Mg/m³     
Absorption coefficient   0.803 mm⁻¹      
F(000)                   512               
Crystal size             0.260 x 0.240 x 0.090 mm³
Theta range for data collection 3.919 to 67.218°. 
Index ranges            -11<=h<=10, -12<=k<=12, -14<=l<=14 
Reflections collected    17855            
Independent reflections   4105 [R(int) = 0.0404] 
Completeness to theta = 67.219°  98.9 %
Absorption correction    Semi-empirical from equivalents  
Max. and min. transmission 0.7529 and 0.6786   
Refinement method        Full-matrix least-squares on F²  
Data / restraints / parameters 4105 / 1 / 325  
Goodness-of-fit on F²    1.090            
Final R indices [I>2sigma(I)] R1 = 0.0276, wR2 = 0.0695  
R indices (all data)     R1 = 0.0278, wR2 = 0.0697  
Absolute structure parameter 0.08(4)    
Extinction coefficient   n/a              
Largest diff. peak and hole 0.161 and -0.253 e.Å⁻³