Haber-Independent, Diversity-Oriented
Synthesis of Nitrogen Compounds from
Biorenewable Chitin

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Electronic Supplementary Information
Experimental section

$^1$H NMR spectrum of compound trans-3

$^{13}$C NMR spectrum of compound trans-3

$^1$H NMR spectrum of compound cis-3

$^{13}$C NMR spectrum of compound cis-3

$^1$H NMR spectrum of compound 4

$^{13}$C NMR spectrum of compound 4

$^1$H NMR spectrum of compound 5

$^{13}$C NMR spectrum of compound 5

$^1$H NMR spectrum of compound 6

$^{13}$C NMR spectrum of compound 6

$^1$H NMR spectrum of compound 7

$^{13}$C NMR spectrum of compound 7

NOESY spectrum of compound 7

$^1$H NMR spectrum of compound 8

$^{13}$C NMR spectrum of compound 8

$^1$H NMR spectrum of compound 9

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General Experimental Details

Commercially available reagents were used throughout without purification unless otherwise stated. Anhydrous solvents were used as supplied. Dichloromethane, methanol and tetrahydrofuran were dried using an LC Technology Solutions Inc. SP-1 solvent purification system under an atmosphere of dry nitrogen. All reactions were routinely carried out in oven-dried glassware under a nitrogen atmosphere unless otherwise stated. Analytical thin layer chromatography was performed using silica plates and compounds were visualized at 254 and/or 360 nm ultraviolet irradiation followed by staining ethanolic vanillin solution. Melting points were recorded on an Electrothermal melting point apparatus and are uncorrected. Infrared spectra were obtained using a Perkin Elmer spectrum One Fourier Transform Infrared spectrometer as thin films between sodium chloride plates. Absorption maxima are expressed in wavenumbers (cm⁻¹). NMR spectra were recorded on either a Bruker AV300, AVIII400 or AVIIIHD500 spectrometer operating at 300, 400, 500 MHz for ¹H nuclei respectively and 75, 100, 125 MHz for ¹³C nuclei respectively. Chemical shifts are reported in parts per million (ppm) relative to the tetramethylsilane peak recorded as δ 0.00 ppm in CDCl₃/TMS solvent, or the residual chloroform (δ 7.26 ppm), or DMSO (δ 2.50 ppm). The ¹³C NMR values were referenced to the residual chloroform (δ 77.1 ppm), DMSO (δ 39.5 ppm). ¹³C NMR values are reported as chemical shift δ and assignment. ¹H NMR shift values are reported as chemical shift δ, relative integral, multiplicity (s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet), coupling constant (J in Hz) and assignment. Assignments are made with the aid of COSY, NOESY, HMBC and edited HSQC experiments. All experiments were conducted at 298 K. Conventional NMR tubes (5 mm diameter, Norell) using a sample volume of 500 μL were used. High resolution mass spectra were obtained by electrospray ionization in positive ion mode at a nominal accelerating voltage of 70 eV on a Bruker microTOF-QII mass spectrometer.
X-ray diffraction analysis of single crystals of 3, 9, 10 and 14 were performed on a Rigaku Oxford Diffraction XtaLAB-Synergy-S single-crystal diffractometer with a PILATUS 200K hybrid pixel array detector using Cu Kα radiation (Table S1). The data were processed with the SHELX2016\(^1\) and Olex2\(^2\) software packages. All non-hydrogen atoms were refined anisotropically. Hydrogen atoms were inserted at calculated positions and refined with a riding model or without restrictions. Mercury 4.2.0\(^3\) was used to visualize the molecular structures.
(±)-Trans-N-(5-hydroxy-4-methyl-3-oxocyclopent-1-en-1-yl)acetamide (trans-3) and (±)-
cis-N-(5-hydroxy-4-methyl-3-oxocyclopent-1-en-1-yl)acetamide (cis-3)

A mixture of the furfuryl alcohol 2 (1.50 g, 8.87 mmol) and magnesium chloride hexahydrate
(7.21 g, 35.47 mmol) in water (340 mL) was stirred at 120 °C for 24 h. After completion, the
mixture was concentrated in vacuo until small amount of water was left (~30 mL) and extracted
with ethyl acetate (3 x 100 mL), washed with brine, dried (Na₂SO₄), filtered and concentrated
in vacuo. The residue was purified by flash column chromatography on silica gel eluting with
ethyl acetate to give the title compounds trans-3 (479 mg, 2.83 mmol, 32%) and cis-3 (120 mg,
0.709 mmol, 8%);

**Trans-3**: colourless solid; m.p. 136.9-138.1 °C; HRMS [ESI, (M + Na)⁺] found 192.0633,
[C₈H₁₁NO₃ + Na]⁺ requires 192.0631; ν max (neat)/cm⁻¹ 3188, 3119, 3094, 3013, 2935, 2872,
1721, 1657, 1607, 1527, 1453, 1368, 1306, 1233, 1182, 1061, 1039, 1001; δ H (400 MHz,
(CD₃)₂CO) 9.48 (1 H, br s, NH), 6.24 (1 H, s, CH), 4.82 (1 H, d, J 5.2, CH), 4.42 (1 H, br s,
OH), 2.20 -2.16 (4 H, m, CH and Me), 1.13 (3 H, d, J 7.2, Me); δ C (100 MHz, (CD₃)₂CO) 204.9
(C), 170.6 (C), 165.6 (C), 112.0 (CH), 77.5 (CH), 49.3 (CH), 24.0 (Me), 13.5 (Me).

**Cis-3**: colourless solid; m.p. 158.6-161.8 °C; HRMS [ESI, (M + Na)⁺] found 192.0638,
[C₈H₁₁NO₃ + Na]⁺ requires 192.0631; ν max (neat)/cm⁻¹ 3195, 3126, 3102, 3021, 2987, 2946,
2373, 2188, 1713, 1662, 1614, 1591, 1529, 1458, 1427, 1396, 1372, 1323, 1285, 1232, 1186,
1140, 1105, 1042, 1001; δ H (400 MHz, (CD₃)₂CO) 9.54 (1 H, br s, NH), 6.26 (1 H, s, CH), 4.88
(1 H, t, J 6.6 Hz, CH), 4.49 (1 H, d, J 6.8, OH), 2.40 (1 H, pent, J 7.6, CH), 2.19 (3 H, s, Me),
1.04 (3 H, d, J 7.6, Me); δC (100 MHz, (CD₃)₂CO) 207.4 (C), 170.5 (C), 166.3 (C), 112.1 (CH), 71.6 (CH), 44.1 (CH), 24.0 (Me), 11.0 (Me).

(±)-Trans-3-amino-4-hydroxy-5-methylcyclopent-2-en-1-one (4)

![Chemical Structure](image)

To a solution of compound 3 (400 mg, 2.36 mmol) in methanol (10 mL) was added triethylamine (1.34 mL, 9.46 mmol) at room temperature. The mixture was stirred at 65 °C for 3 h, concentrated in vacuo and the residue purified by flash column chromatography on silica gel eluting with ethyl acetate-methanol (10:1) to give the title compound 4 (279 mg, 2.19 mmol, 93%) as a colourless solid; m.p. 154.4-156.3 °C; HRMS [ESI, (M + H)+] found 128.0707, [C₆H₉NO₂ + H]+ requires 128.0706; ν max (neat)/cm⁻¹ 3298, 3134, 2981, 2968, 2860, 1674, 1644, 1623, 1534, 1416, 1371, 1332, 1236, 1198, 1089, 1066; δH (400 MHz, (CD₃)₂SO) 7.34 (1 H, br s, NHH), 6.74 (1 H, br s, NH), 5.42 (1 H, d, J 6.3, OH), 4.68 (1 H, s, CH), 4.05 (1 H, dd, J 5.4, 3.3, CH), 2.04 (1 H, dq, J 7.3, 3.3, CH), 1.02 (3 H, d, J 7.4, Me); δC (100 MHz, (CD₃)₂SO) 200.0 (C), 176.2 (C), 96.8 (CH), 75.9 (CH), 48.7 (CH), 14.0 (Me).

(±)-N-(4-methyl-3,5-dioxocyclopent-1-en-1-yl)acetamide (5)

![Chemical Structure](image)

To a solution of compound 3 (400 mg, 2.36 mmol) in ethyl acetate (20 mL) was added 2-iodoxybenzoic acid (1.32 g, 4.73 mmol) at room temperature. The mixture was stirred at 60 °C
for 24 h, then filtered and concentrated in vacuo. The residue was purified by flash chromatography on silica gel eluting with ethyl acetate-light petroleum (7:3) to give the title compound 5 (360 mg, 2.15 mmol, 91%) as a colourless solid; m.p. 158.0-159.8 °C; HRMS [ESI, (M + Na)+] found 190.0473, [C₈H₉NO₃ + Na]+ requires 190.0475; νmax (neat)/cm⁻¹ 3251, 3216, 3144, 2899, 1744, 1718, 1676, 1599, 1509, 1456, 1424, 1370, 1291, 1247, 1213, 1188, 1112, 1074, 1044, 1006; δH (400 MHz, (CD₃)₂CO) 9.48 (1 H, br s, NH), 7.22 (1 H, s, CH), 2.81 (1 H, q, J 7.5, CH), 2.29 (3 H, s, Me), 1.15 (3 H, d, J 7.8, Me); δC (100 MHz, (CD₃)₂CO) 202.4 (C), 201.4 (C), 171.0 (C), 151.8 (C), 124.1 (CH), 44.2 (CH), 24.0 (Me), 10.5 (Me).

4-Amino-2,2-dimethylcyclopent-4-ene-1,3-dione (6)

![Image of compound 6]

To a solution of compound 5 (40 mg, 0.24 mmol) in ethyl acetate (1 mL) was added iodomethane (0.044 mL, 0.72 mmol) and sodium hydroxide (19 mg, 0.48 mmol). The resulting mixture was stirred at room temperature for 5 h, then methanol (0.2 mL) was added and the mixture was stirred at 40 °C for 3 h. Water (1 mL) was added and the mixture was extracted with ethyl acetate (3 x 15 mL), washed with brine, dried (Na₂SO₄), filtered and concentrated in vacuo. The residue was purified by flash chromatography on silica gel eluting with ethyl acetate to give the title compound 6 (22 mg, 0.16 mmol, 66%) as a colourless solid; m.p. 154.0-155.5 °C; HRMS [ESI, (M + Na)+] found 162.0520, [C₇H₉NO₂ + Na]+ requires 162.0525; νmax (neat)/cm⁻¹ 3042, 3316, 3281, 3242, 3204, 2979, 1747, 1685, 1617, 1563, 1465, 1406, 1378, 1309, 1257, 1232, 1207, 1133, 1086, 1032; δH (400 MHz, (CD₃)₂CO) 6.57 (2 H, br s, NH₂), 5.75 (1 H, s, CH), 1.05 (6 H, s, 2 × Me); δC (100 MHz, (CD₃)₂CO) 205.6 (C), 202.6 (C), 158.5 (C), 109.6 (CH), 46.4 (C), 20.7 (2 × Me).
\[N-((1S^*,2S^*,3S^*)-2-hydroxy-3-methyl-4-oxocyclopentyl)acetamide \quad (7a) \quad \text{and} \quad N-((1R^*,2S^*,3S^*)-2-hydroxy-3-methyl-4-oxocyclopentyl)acetamide \quad (7b)\]

10% Pd/C (4 mg) was added to a stirred solution of compound 3 (20 mg, 0.12 mmol) in ethyl acetate (2 mL) and the mixture was stirred under an atmosphere of hydrogen for 19 h at room temperature. The mixture was filtered through Celite, then concentrated in vacuo. The residue was purified by flash column chromatography eluting with ethyl acetate to give the title compounds 7a and 7b (10:1; inseparable) (8 mg, 0.05 mmol, 40%) as a colourless oil; HRMS [ESI, (M + Na)\(^{+}\)] found 194.0792, \([C_{8}H_{13}NO_{3} + Na]^{+}\) requires 194.0788; \(\nu_{\text{max}}\) (neat)/cm\(^{-1}\) 3269, 1739, 1635, 1554, 1455, 1408, 1375, 1304, 1173, 1078; \(\delta_{H}\) (400 MHz, (CD\(_3\))\(_2\)CO)\((7a:7b, 10:1)\)

- 7.97 (1 H, br s, NH\(_{\text{minor}}\)), 7.53 (1H, br s, NH\(_{\text{major}}\)), 5.29 (1 H, d, \(J 3.0\), OH\(_{\text{major}}\)), 4.58 (1 H, d, \(J 2.9\), OH\(_{\text{minor}}\)), 4.29-4.22 (1 H, m, CH\(_{\text{minor}}\)), 4.18-4.10 (1 H, m, CH\(_{\text{major}}\)), 3.73 (1 H, ddd, \(J 10.5\), \(8.4\), \(2.6\), CH\(_{\text{major}}\)), 2.77 (1 H, ddd, \(J 10.9\), \(9.0\), \(2.0\), CH of CH\(_2\)\(_{\text{major}}\)), 2.58 (1 H, dd, \(J 18.9\), \(7.8\), CH\(_{\text{minor}}\)), 2.49-2.46 (1 H, m, CH of CH\(_2\)\(_{\text{minor}}\)), 2.33 (1 H, ddd, \(J 8.8\), \(6.9\), \(1.8\), CH\(_{\text{major}}\)), 2.28-2.20 (1 H, m, CH\(_{\text{minor}}\)), 2.14-2.08 (1 H, m, CH of CH\(_2\)\(_{\text{minor}}\)), 2.11 (1 H, dd, \(J 18.8\), \(10.4\), CH of CH\(_2\)\(_{\text{major}}\)), 1.92 (3 H, s, Me\(_{\text{major}}\)), 1.87 (3 H, s, Me\(_{\text{minor}}\)), 1.06 (3 H, d, \(J 7.0\), Me\(_{\text{major}}\)), 1.00 (3 H, d, \(J 7.3\), Me\(_{\text{minor}}\)); \(\delta_{C}\) (100 MHz, (CD\(_3\))\(_2\)CO) 212.7 (C\(_{\text{major}}\)), 172.2 (C\(_{\text{major}}\)), 162.8 (C\(_{\text{minor}}\)), 81.5 (CH\(_{\text{major}}\)), 76.7 (CH\(_{\text{minor}}\)), 54.9 (CH\(_{\text{major}}\)), 53.2 (CH\(_{\text{minor}}\)), 52.7 (CH\(_{\text{major}}\)), 47.3 (CH\(_{\text{minor}}\)), 43.0 (CH\(_2\)\(_{\text{major}}\)), 41.0 (CH\(_2\)\(_{\text{minor}}\)), 22.9 (Me\(_{\text{minor}}\)), 22.8 (Me\(_{\text{major}}\)), 11.6 (Me\(_{\text{major}}\)), 8.0 (Me\(_{\text{minor}}\)), 1C\(_{\text{minor}}\) not observed.

[Major = 7a; minor = 7b]
(±)-N-(3-methyl-4-oxocyclopent-2-en-1-yl)acetamide (8)

To a solution of compound 7 (9 mg, 0.05 mmol) in ethyl acetate (0.5 mL) was added p-toluenesulfonic acid (5 mg, 0.03 mmol) at room temperature. The mixture was stirred at 80 °C for 30 min, concentrated in vacuo and the residue was purified by flash column chromatography on silica gel eluting with ethyl acetate-methanol (10:1) to give the title compound 8 (7.5 mg, 0.05 mmol, 93%) as a colourless solid; m.p. 93.5-95.5 °C; HRMS [ESI, (M + Na)+] found 176.0683, [C8H11NO2 + Na]+ requires 176.0682; νmax (neat)/cm⁻¹ 3277, 3072, 2926, 1708, 1635, 1539, 1432, 1401, 1373, 1320, 1197, 1100, 1076; δH (400 MHz, CDCl3) 7.13-7.11 (1 H, m, CH), 6.26 (1 H, d, J 7.0, NH), 5.08-5.03 (1 H, m, CH), 2.83 (1 H, dd, J 18.8, 6.8, CH of CH₂), 2.13 (1 H, dd, J 18.8, 2.4, CH of CH₂), 1.95 (3 H, s, Me), 1.75 (3 H, t, J 1.8, Me); δC (100 MHz, CDCl₃) 206.7 (C), 170.0 (C), 155.5 (CH), 143.6 (C), 47.6 (CH), 42.1 (CH₂), 23.0 (Me), 9.9 (Me).

(±)-cis-N-(3a,7-dihydroxy-8b-methyl-1-oxo-3a,8b-dihydro-1H-cyclopenta[b]benzofuran-3-yl)acetamide (9)

To a solution of compound 5 (20 mg, 0.12 mmol) in ethanol (0.6 mL) was added p-benzoquinone (26 mg, 0.24 mmol) at room temperature. The mixture was stirred at 60 °C for 20 min, then concentrated in vacuo. The residue was purified by flash chromatography on silica gel eluting with ethyl acetate-light petroleum (1:1) to give the title compound 9 (13 mg, 0.10
mmol, 79%) as an orange solid; m.p. >200 °C (decomp.); HRMS [ESI, (M + Na)+] found 298.0677, [C\textsubscript{14}H\textsubscript{13}NO\textsubscript{5} + Na]+ requires 298.0686; ν\textsubscript{max} (neat)/cm\textsuperscript{-1} 3189, 3102, 1680, 1616, 1521, 1492, 1465, 1443, 1373, 1250, 1231, 1208, 1133, 1110, 1101, 1033; δ\textsubscript{H} (400 MHz, (CD\textsubscript{3})\textsubscript{2}SO) 10.76 (1 H, s, NH), 8.99 (1 H, s, OH), 7.97 (1 H, s, OH), 6.65 (1 H, d, J 2.4, ArH), 6.62 (1 H, d, J 8.6, ArH), 6.57 (1 H, dd, J 8.6, 2.4, ArH), 6.38 (1 H, s, CH), 2.20 (3 H, s, Me), 1.28 (3 H, s, Me); δ\textsubscript{C} (100 MHz, (CD\textsubscript{3})\textsubscript{2}SO) 202.4 (C), 171.2 (C), 160.9 (C), 152.0 (C), 148.1 (C), 128.9 (C), 115.4 (C), 113.4 (C), 110.5 (CH), 110.3 (CH), 109.7 (CH), 56.3 (C), 23.8 (Me), 16.0 (Me).

(±)-3-Amino-7a-methyl-7,7a-dihydro-1\textsubscript{H}-indene-1,5(6\textsubscript{H})-dione (10)

\begin{center}
\includegraphics[width=0.2\textwidth]{image.png}
\end{center}

To a solution of compound 5 (20 mg, 0.12 mmol) and methyl vinyl ketone (0.01 mL, 0.12 mmol) in ethyl acetate (1 mL) was added sodium hydroxide (10 mg, 0.24 mmol). The mixture was stirred at room temperature for 15 min, then filtered and concentrated \textit{in vacuo}. The residue was dissolved in methanol (0.5 mL), then sodium hydroxide (10 mg, 0.24 mmol) was added, and the mixture was stirred at room temperature for 6 h. Water was added and the mixture was extracted with ethyl acetate (3 x 20 mL), washed with brine, dried (Na\textsubscript{2}SO\textsubscript{4}), filtered and concentrated \textit{in vacuo}. The residue was purified by flash chromatography on silica gel eluting with ethyl acetate to give the title compound 10 (19 mg, 0.11 mmol, 89%) as an orange solid; m.p. 180 °C (decomp.); HRMS [ESI, (M + Na)+] found 200.0681, [C\textsubscript{10}H\textsubscript{11}NO\textsubscript{2} + Na]+ requires 200.0682; ν\textsubscript{max} (neat)/cm\textsuperscript{-1} 3391, 3211, 3037, 2930, 2871, 1719, 1642, 1616, 1548, 1467, 1448, 1412, 1377, 1347, 1308, 1261, 1220, 1198, 1102, 1078; δ\textsubscript{H} (400 MHz, (CD\textsubscript{3})\textsubscript{2}CO) 6.78 (2 H, br s, NH\textsubscript{2}), 6.13 (1 H, s, CH), 5.15 (1 H, s, CH), 2.63 (1 H, ddd, J 18.9, 13.8, 5.6, CH of CH\textsubscript{2}),
2.40 (1 H, ddt, J=18.4, 5.5, 1.2, CH of CH2), 2.02 (1 H, ddd, J=13.0, 5.5, 1.6, CH of CH2), 1.76 (1 H, dt, J=13.3, 5.4, CH of CH2), 1.31 (3 H, s, Me); δC (100 MHz, (CD3)2CO) 202.3 (C), 198.6 (C), 165.4 (C), 162.4 (C), 117.5 (CH), 103.6 (CH), 46.0 (C), 34.7 (CH2), 29.4 (CH2), 22.9 (Me).

(±)-2,5a-Dimethyl-6,7-dihydro-5H-indeno[1,2-b]pyridine-5,8(5aH)-dione (11)

A mixture of compound 10 (15 mg, 0.09 mmol), methyl vinyl ketone (0.01 mL, 0.09 mmol), potassium carbonate (47 mg, 0.34 mmol), copper bromide (5 mg, 0.04 mg) in acetonitrile (1.5 mL) was heated at 120 °C for 24 h. The mixture was filtered, concentrated in vacuo, and the residue was purified by flash chromatography on silica gel eluting with ethyl acetate-light petroleum (7:3) to give the title compound 11 (7 mg, 0.03 mmol, 36%) as a yellow solid; m.p. 103.1 – 106.3 °C; HRMS [ESI, (M + Na)+] found 250.0841, [C14H13NO2 + Na]+ requires 250.0838; νmax (neat)/cm⁻¹ 2962, 2931, 1728, 1659, 1575, 1448, 1415, 1396, 1311, 1202, 1135, 1101; δH (400 MHz, (CD3)2CO) 8.06 (1 H, d, J=8.0, ArH), 7.59 (1 H, d, J=8.0, ArH), 6.46 (1 H, s, CH), 2.85-2.75 (1 H, m, CH of CH2), 2.70 (3 H, s, Me), 2.54-2.48 (1 H, m, CH of CH2), 2.26 (1 H, ddd, J=13.2, 5.6, 1.8, CH of CH2), 2.11-2.03 (1 H, m, CH of CH2), 1.45 (3 H, s, Me); δC (100 MHz, (CD3)2CO) 202.8 (C), 198.2 (C), 168.6 (C), 163.4 (C), 161.9 (C), 133.3 (CH), 128.8 (C), 127.7 (CH), 119.6 (CH), 49.0 (C), 34.5 (CH2), 28.7 (CH2), 25.5 (Me), 22.5 (Me).
(±)-Methyl 3-(3-acetamido-1-methyl-2,5-dioxocyclopent-3-en-1-yl)propanoate (12)

A mixture of compound 5 (20 mg, 0.12 mmol) and methyl acrylate (0.06 mL, 0.60 mmol) in triethylamine (0.3 mL) was stirred at 80 °C for 1 hour. After completion, the mixture was purified by flash chromatography on silica gel eluting with ethyl acetate to give the title compound 12 (25 mg, 0.10 mmol, 82%) as a light yellow oil; HRMS [ESI, (M + Na)+] found 276.0834, [C12H15NO5 + Na]+ requires 276.0842; νmax (neat)/cm⁻¹ 3400, 1726, 1684, 1607, 1516, 1454, 1439, 1372, 1295, 1213, 1147, 1101; δH (400 MHz, CDCl3) 8.04 (1 H, br s, NH), 7.33 (1 H, s, CH), 3.62 (3 H, s, Me), 2.31-2.14 (5 H, m, CH₂ and Me), 1.99 (2 H, t, J 8.0, CH₂), 1.19 (3 H, s, Me); δC (100 MHz, CDCl₃) 204.2 (C), 203.2 (C), 172.7 (C), 168.9 (C), 148.6 (C), 123.4 (CH), 51.7 (Me), 47.8 (C), 29.09 (CH₂), 29.05 (CH₂), 24.1 (Me), 18.9 (Me).

(±)-cis-N-(4a-Methyl-2,5-dioxo-2,3,4,4a,5,7a-hexahydrocyclopenta[b]pyran-7-yl)acetamide (13)

A mixture of compound 12 (20 mg, 0.08 mmol) and zinc (10 mg, 0.16 mmol) in acetic acid (0.4 mL) was stirred at 80 °C for 24 h. After completion, the mixture was poured into saturated aqueous sodium bicarbonate solution and extracted with ethyl acetate (3 x 20 mL). The combined organic phases were washed with brine, dried (Na₂SO₄), filtered and concentrated in vacuo. The residue was purified by flash chromatography on silica gel eluting with ethyl acetate.
to give the title compound 13 (9 mg, 0.04 mmol, 51%) as a colourless solid; m.p. 203.0-205.4 °C; HRMS [ESI, (M + Na)+] found 246.0745, [C11H13NO4 + Na]+ requires 246.0737; \( \nu_{\text{max}} \) (neat)/cm\(^{-1}\) 3290, 3224, 2928, 1745, 1689, 1616, 1521, 1465, 1432, 1366, 1328, 1312, 1272, 1240, 1221, 1158, 1120; \( \delta_H \) (400 MHz, CDCl\(_3\)) 8.13 (1 H, br s, NH), 6.79 (1 H, s, CH), 5.00 (1 H, d, \( J = 0.8 \), CH), 2.52-2.45 (1 H, m, CH of CH\(_2\)), 2.24 (3 H, s, Me), 2.23-2.12 (2 H, m, CH\(_2\)), 1.77 (1 H, m, CH of CH\(_2\)), 1.31 (3 H, s, Me); \( \delta_C \) (100 MHz, CDCl\(_3\)) 205.7 (C), 170.7 (C), 169.2 (C), 159.2 (C), 115.2 (CH), 84.6 (CH), 43.4 (C), 28.4 (CH\(_2\)), 27.9 (CH\(_2\)), 24.3 (Me), 22.5 (Me).

(±)-Methyl-cis-3a-hydroxy-1-(3-methoxy-3-oxopropyl)-4,4-dimethyl-5-oxo-1,2,3,3a,4,5-hexahydrocyclopenta[b]pyrrole-3-carboxylate (14)

A mixture of compound 6 (20 mg, 0.14 mmol), cesium carbonate (187 mg, 0.58 mg), and methyl acrylate (0.4 mL) was stirred at 50 °C for 1 hour. After completion, the mixture was diluted with ethyl acetate, filtered, and concentrated in vacuo. The residue was purified by flash chromatography on silica gel eluting with ethyl acetate-methanol (10:1) to give the title compound 14 (13 mg, 0.04 mmol, 29%) as a colourless solid; m.p. 127.1-129.4 °C; HRMS [ESI, (M + Na)+] found 334.1264, [C\(_{15}\)H\(_{21}\)NO\(_6\)+Na]+ requires 334.1261; \( \nu_{\text{max}} \) (neat)/cm\(^{-1}\) 3189, 2956, 1744, 1728, 1679, 1589, 1459, 1438, 1415, 1390, 1374, 1331, 1289, 1198, 1179, 1138; \( \delta_H \) (400 MHz, CDCl\(_3\)) 4.65 (1 H, s, CH), 4.24 (1 H, t, \( J = 9.8 \), CH of CH\(_2\)), 3.77 (3 H, s, Me), 3.70 (1 H, dd, \( J = 10.3 \), 8.0, CH of CH\(_2\)), 3.68 (3 H, s, Me), 3.60 (2 H, dt, \( J = 6.6 \), 3.5, CH\(_2\)), 3.29 (1 H, dd, \( J = 9.4 \), 8.0, CH), 2.64 (2 H, t, \( J = 6.5 \), CH\(_2\)), 1.20 (3 H, s, Me), 1.14 (3 H, s, Me), OH not observed; \( \delta_C \) (100 MHz, CDCl\(_3\)) 209.2 (C), 177.0 (C), 171.4 (C), 169.7 (C), 88.9 (CH), 87.8
(C), 55.3 (CH₂), 52.19 (Me), 52.16 (Me), 51.0 (C), 46.3 (CH), 43.5 (CH₂), 31.9 (CH₂), 24.9
(Me), 16.7 (Me).

**2,6,6-Trimethyl-5H-cyclopenta[b]pyridine-5,7(6H)-dione (15)**

![](image)

A mixture of compound 6 (20 mg, 0.14 mmol), methyl vinyl ketone (0.03 mL, 0.29 mmol),
potassium carbonate (100 mg, 0.72 mmol), copper bromide (9 mg, 0.06 mg) in acetonitrile (2
mL) was heated at 80 °C for 24 h. The mixture was filtered, concentrated *in vacuo*, and the
residue was purified by flash chromatography on silica gel eluting with ethyl acetate-light
petroleum (1:1) to give the title compound 15 (9 mg, 0.05 mmol, 33%) as a yellow solid; m.p.
112.9-114.8 °C; HRMS [ESI, (M + Na)⁺] found 212.0686, [C₁₁H₁₁NO₂ + Na]⁺ requires
212.0682; ν max (neat)/cm⁻¹ 2969, 2932, 1753, 1710, 1586, 1568, 1465, 1457, 1381, 1293, 1258,
1155, 1098, 1052, 1003; δH (400 MHz, CDCl₃) 8.18 (1 H, d, J 8.1, CH), 7.59 (1 H, d, J 8.0,
CH), 2.82 (3 H, s, Me), 1.34 (6 H, s, 2 × Me); δC (100 MHz, CDCl₃) 203.7 (C), 202.2 (C),
169.2 (C), 157.3 (C), 133.8 (C), 131.9 (CH), 129.3 (CH), 50.3 (C), 25.5 (Me), 20.2 (2 × Me).

**4-(Dibenzylamino)-2,2-dimethylcyclopent-4-ene-1,3-dione (16)**

![](image)

A mixture of compound 6 (20 mg, 0.14 mmol), benzyl bromide (0.04 mL, 0.30 mmol), cesium
carbonate (94 mg, 0.29 mg) in acetonitrile (1 mL) was heated at 80 °C for 5 hours. The mixture
was diluted with ethyl acetate, filtered, and concentrated in vacuo. The residue was purified by flash chromatography on silica gel eluting with ethyl acetate-light petroleum (3:7) to give the title compound 16 (32 mg, 0.10 mmol, 70%) as a yellow oil; HRMS [ESI, (M + Na)⁺] found 342.1464, [C₂₁H₂₁NO₂ + Na]⁺ requires 342.1465; v max (neat)/cm⁻¹ 2966, 2928, 2866, 1730, 1676, 1591, 1578, 1495, 1451, 1419, 1369, 1301, 1264, 1240, 1147; δH (400 MHz, CDCl₃) 7.38-7.29 (6 H, m, 6 × ArH), 7.16 (4 H, d, J 6.9, 4 × ArH), 5.81 (1 H, s, CH), 4.73 (4 H, br s, 2 × CH₂), 1.21 (6 H, s, 2 × Me); δC (100 MHz, CDCl₃) 204.9 (C), 201.3 (C), 157.6 (C), 129.0 (6 × CH), 128.0 (4 × CH), 127.3 (2 × C), 111.9 (CH), 48.4 (C), 20.6 (2 × Me), 2 × CH₂ not observed.

2,2-Dimethyl-1H-cyclopenta[c]isoquinoline-1,3(2H)-dione (17)

A mixture of compound 16 (20 mg, 0.06 mmol), palladium (II) acetate (14 mg, 0.06 mg) in acetic acid (0.5 mL) was heated to 120 °C for 5 h. The mixture was concentrated in vacuo and diluted with ethyl acetate, filtered and the filtrate was washed with saturated aqueous sodium bicarbonate solution, brine, dried (Na₂SO₄), filtered and concentrated in vacuo. The residue was purified by flash chromatography on silica gel eluting with ethyl acetate-light petroleum (3:7) to give the title compound 17 (11 mg, 0.05 mmol, 78%) as a colourless solid; m.p. 157.7 – 161.1 °C; HRMS [ESI, (M + Na)⁺] found 248.0682, [C₁₄H₁₁NO₂ + Na]⁺ requires 248.0682; v max (neat)/cm⁻¹ 2923, 2853, 1747, 1700, 1576, 1562, 1505, 1456, 1442, 1382, 1375, 1305, 1248, 1161, 1091, 1044; δH (400 MHz, CDCl₃) 9.65 (1 H, s, ArH), 9.10 (1 H, dd, J 8.6, 0.7, ArH), 8.22 (1 H, d, J 7.3, ArH), 8.06 (1 H, ddd, J 8.4, 7.0, 1.4, ArH), 7.94 (1 H, ddd, J 8.4, 7.0,
2,2-Dimethyl-4-(phenylamino)cyclopent-4-ene-1,3-dione (18)

\[
\text{\begin{figure}[h]
\centering
\includegraphics[width=0.2\textwidth]{18.png}
\caption{2,2-Dimethyl-4-(phenylamino)cyclopent-4-ene-1,3-dione (18)}
\end{figure}}
\]

A mixture of compound 6 (20 mg, 0.14 mmol), phenylboronic acid (35 mg, 0.29 mmol), copper (II) acetate (26 mg, 0.14 mmol) in acetonitrile (1.5 mL) was heated at 80 °C for 3 h. After completion, the mixture was filtered, concentrated \textit{in vacuo}, and the residue was purified by flash chromatography on silica gel eluting with ethyl acetate-light petroleum (3:7) to give the \textit{title compound} 18 (15 mg, 0.07 mmol, 48%) as an orange oil; HRMS [ESI, (M + Na)⁺] found 238.0838, [C\textsubscript{13}H\textsubscript{13}NO\textsubscript{2} + Na]\textsuperscript{⁺} requires 238.0838; \(\nu_{\text{max}}\) (neat)/cm\textsuperscript{-1} 3244, 2970, 2927, 2854, 1745, 1674, 1593, 1520, 1493, 1446, 1378, 1306, 1199, 1144; \(\delta\text{H}\) (400 MHz, (CD\textsubscript{3})\textsubscript{2}CO) 8.45 (1 H, br s, NH), 7.48-7.41 (4 H, m, 4 × ArH), 7.20-7.16 (1 H, m, ArH), 6.32 (1 H, s, CH), 1.13 (6 H, s, 2 × Me); \(\delta\text{C}\) (100 MHz, (CD\textsubscript{3})\textsubscript{2}CO) 205.29 (C), 203.24 (C), 153.0 (C), 140.2 (C), 130.3 (2 × CH), 125.3 (CH), 121.1 (2 × CH), 109.6 (CH), 46.0 (C), 20.6 (2 × Me).
2,2-Dimethylcyclopenta[b]indole-1,3(2H,4H)-dione (19)

A mixture of compound 18 (10 mg, 0.05 mmol) and palladium (II) acetate (10 mg, 0.05 mg) in acetic acid (0.5 mL) was stirred at 110 °C for 7 h. The mixture was concentrated *in vacuo*, diluted with ethyl acetate, and filtered. The filtrate was washed with saturated aqueous sodium carbonate solution, brine, dried (Na₂SO₄), filtered and concentrated *in vacuo*. The residue was purified by flash chromatography on silica gel eluting with ethyl acetate-light petroleum (1:5) to give the *title compound* 19 (8.7 mg, 0.04 mmol, 86%) as a colourless solid; m.p. 251.3-253.5 °C (decomp.); HRMS [ESI, (M + H)+] found 214.0869, [C₁₃H₁₁NO₂ + H]+ requires 214.0863; ν<sub>max</sub> (neat)/cm⁻¹ 3251, 2988, 2971, 2933, 1722, 1665, 1620, 1578, 1507, 1481, 1455, 1440, 1406, 1372, 1354, 1160, 1142, 1059; δ<sub>H</sub> (400 MHz, (CD₃)₂CO) 11.75 (1 H, br s, NH), 7.97 (1 H, dt, J 8.1, 1.2, ArH), 7.72 (1 H, dt, J 8.5, 1.0, ArH), 7.56-7.51 (1 H, m, ArH), 7.43-7.39 (1 H, m, ArH), 1.28 (6 H, s, 2 × Me); δ<sub>C</sub> (100 MHz, (CD₃)₂CO) 196.1 (C), 195.2 (C), 148.9 (C), 145.4 (C), 128.7 (CH), 126.1 (C), 124.4 (CH), 123.4 (CH), 121.3 (C), 115.2 (CH), 56.2 (C), 20.9 (2 × Me).

SpinWorks 2.5: protonstdri Acetone /nmr/400p tpha744 42

Trans-3
AcHN

OH

Trans-3
SpinWorks 2.5: protonst dri Acetone /nmr/400p tpha744 53;

Cis-3
SpinWorks 2.5: protonstdr Acetone /nmr/400p tpha744 17

![Chemical structure](image)

PPM: 10.0 9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0

0.855 0.995 1.445 3.400 3.900
SpinWorks 2.5: protonstdri CDCl3/nmr/400p tpha744 41

\[
\begin{align*}
\text{AcHN} & \quad \text{Me} \\
\text{8} & \quad \text{O}
\end{align*}
\]
SpinWorks 2.5: protonstdri Acetone /nmr/400p tpha744 39
SpinWorks 2.5: protonstdri Acetone/nmr/400p tpha744 39

![Chemical Structure](image)
SpinWorks 2.5: carbonstdi CDCl3 /nmr/400p tpha744 10

AcHN

Me

CO₂Me

12
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MeO₂C

14
SpinWorks: protonstdri CDCl3 /nmr/400p tpha744 13

15

PPM 9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0.0
SpinWorks 2.5: carbonstdi CDCl3 /nmr/400p tpha7444

16
SpinWorks 2.5: protonstdri Acetone /nmr/400p tpha744 20

18
Crystal structure of 14. Dashed lines show the intermolecular hydrogen bonding between the different molecules in the (bc) plane.
Table S1. X-ray diffraction data for compounds 3, 9, 10 and 14.

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<td>c = 8.4454(4) Å</td>
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<td>-8 to 8</td>
<td>-12 to 12</td>
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<td>l range</td>
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<td>4192 / 847</td>
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<td>R₁ = 0.0277, wR₂ = 0.0719</td>
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