SUPPORTING INFORMATION

Concise route to indoloazocines via a sequential Ugi / gold-catalyzed intramolecular hydroarylation

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Table of Contents

This page .............................................................................................................................1

General experimental procedures and data.................................................................2

Crystallographic data for compound 6s.................................................................20

References..................................................................................................................21

Copies of $^1$H and $^{13}$C NMR spectra.................................................................22
General Experimental Methods

NMR spectra were recorded on a 300 MHz instrument using CDCl$_3$ and DMSO d$_6$ as solvent unless and otherwise stated. The $^1$H and $^{13}$C chemical shifts are reported in parts per million relative to tetramethylsilane as an internal standard. For the Mass spectrometry, ion source temperature was 150-250 °C, as required. High-resolution EI-mass spectra were performed with a resolution of 10,000. For chromatography, analytical TLC plates and 70-230 mesh silica gel were used. All the solvents and chemicals were purchased and used as available. Optical rotations were measured using a PROPOL ® Automatic Process Polarimeter.

Table 1. Starting materials

<table>
<thead>
<tr>
<th>Amine</th>
<th>Aldehyde</th>
<th>Isonitrile</th>
<th>2-alkynoic acid</th>
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<tr>
<td><img src="image1a.png" alt="Image 1a" /></td>
<td><img src="image2a.png" alt="Image 2a" /></td>
<td><img src="image3a.png" alt="Image 3a" /></td>
<td><img src="image4a.png" alt="Image 4a" /></td>
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<td><img src="image1b.png" alt="Image 1b" /></td>
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<td><img src="image3b.png" alt="Image 3b" /></td>
<td><img src="image4b.png" alt="Image 4b" /></td>
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<td><img src="image1c.png" alt="Image 1c" /></td>
<td><img src="image2c.png" alt="Image 2c" /></td>
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<td><img src="image2d.png" alt="Image 2d" /></td>
<td><img src="image2e.png" alt="Image 2e" /></td>
<td><img src="image3d.png" alt="Image 3d" /></td>
<td><img src="image4d.png" alt="Image 4d" /></td>
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<td><img src="image2g.png" alt="Image 2g" /></td>
<td><img src="image3e.png" alt="Image 3e" /></td>
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<td><img src="image2h.png" alt="Image 2h" /></td>
<td><img src="image2i.png" alt="Image 2i" /></td>
<td><img src="image3f.png" alt="Image 3f" /></td>
<td><img src="image4f.png" alt="Image 4f" /></td>
</tr>
</tbody>
</table>

General procedure for synthesis of Ugi products 5a-p

To a solution of tryptamine 1a-b (100mg, 1 equiv) in methanol (3 mL) were added successively Na$_2$SO$_4$ (0.3g), aldehyde 2a-g (1 equiv), isonitrile 3a-c (1 equiv) and 2-alkynoic acid 4a-e (1 equiv) in a screw capped vial equipped with a magnetic stir bar.
The reaction mixture was stirred at room temperature for 20-24h in closed vial. After completion of the reaction, the mixture was diluted with EtOAc (100 mL) and was extracted with water (50 mL). Organic layer was washed with brine (50 mL), dried over magnesium sulfate and evaporated under reduced pressure to obtained residue which was subjected to silica gel column chromatography (80 % EtOAc in Heptane) to afford the desired product 5a-p as white solid.

Ugi products appear as mixture of two rotamers, so $^1$H and $^{13}$C NMR spectra are not very characteristic. Only representative data for one compound are given.

\[
\begin{align*}
N-(2-(1H-indol-3-yl)ethyl)-N-(2-(\text{tert-butylamino})-1-(4-methoxyphenyl)-2-oxoethyl)\text{but-2-ynamide (5a)}
\end{align*}
\]

White solid, Yield 82% (mixture of rotamers ~ 3/2).

$^1$H NMR (400 MHz, DMSO-d$_6$) $\delta$ 10.7 (bs, 0.6H), 10.6 (bs, 0.4H), 7.90 (s, 0.4H), 7.77 (s, 0.6H), 7.37-7.23 (m, 3H), 7.13-6.95 (m, 4H), 6.94-6.79 (m, 2H), 6.02 (s, 0.4H), 5.93 (s, 0.6H), 3.79 (s, 3H), 3.66-3.44 (m, 2H), 2.85-2.71 (m, 1H), 2.24-2.14 (m, 1H), 2.06 (s, 1.2H), 2.01 (s, 1.8H), 1.28 (s, 3.1H), 1.24 (s, 5.9H).

$^{13}$C NMR (100 MHz, DMSO-d$_6$) $\delta$ 169.1, 159.7, 154.7, 136.5, 131.2, 130.9, 128.4, 127.3, 123.0, 121.3, 121.2, 118.6, 118.4, 118.3, 114.5, 111.9, 111.8, 111.7, 111.4, 88.8, 74.5, 60.1, 55.7, 50.8 (x 2), 28.8, 26.5, 4.1, 3.7.

HRMS calculated for C$_{27}$H$_{31}$N$_3$O$_3$ 445.2365, found 445.2347.
<table>
<thead>
<tr>
<th>Structure</th>
<th>Data</th>
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</thead>
<tbody>
<tr>
<td><img src="image" alt="Structure 5b" /></td>
<td><strong>N-(2-(1H-indol-3-yl)ethyl)-N-(2(tert-butylamino)-1-cyclohexyl-2-oxoethyl)but-2-ynamide (5b)</strong>&lt;br&gt;White solid, Yield 95%&lt;br&gt;HRMS calculated for C_{27}H_{31}N_{3}O_{3} 445.2365&lt;br&gt;found 445.2347</td>
</tr>
<tr>
<td><img src="image" alt="Structure 5c" /></td>
<td><strong>N-(2-(1H-indol-3-yl)ethyl)-N-(1(tert-butylamino)-3,3-dimethyl-1-oxobutan-2-yl)but-2-ynamide (5c)</strong>&lt;br&gt;White solid, Yield 89%,&lt;br&gt;HRMS calculated for C_{26}H_{35}N_{3}O_{2} 421.2729&lt;br&gt;found 421.2754</td>
</tr>
<tr>
<td><img src="image" alt="Structure 5d" /></td>
<td><strong>N-(2-(1H-indol-3-yl)ethyl)-N-(2(tert-butylamino)-1-(2,6-dichlorophenyl)-2-oxoethyl)but-2-ynamide (5d)</strong>&lt;br&gt;White solid, Yield 76%,&lt;br&gt;HRMS calculated for C_{26}H_{27}Cl_{2}N_{3}O_{2} 483.1480&lt;br&gt;found 483.1479</td>
</tr>
<tr>
<td><img src="image" alt="Structure 5e" /></td>
<td><strong>N-(2-(1H-indol-3-yl)ethyl)-N-(1(tert-butylamino)-1-oxo-4-phenylbutan-2-yl)but-2-ynamide (5e)</strong>&lt;br&gt;White solid, Yield 75%,&lt;br&gt;HRMS calculated for C_{28}H_{33}N_{3}O_{2} 443.2573&lt;br&gt;found 443.2551</td>
</tr>
<tr>
<td><img src="image" alt="Structure 5f" /></td>
<td><strong>N-(2-(1H-indol-3-yl)ethyl)-N-(2(tert-butylamino)-1-(furan-2-yl)-2-oxoethyl)but-2-ynamide (5f)</strong>&lt;br&gt;White solid, Yield 43%,&lt;br&gt;HRMS calculated for C_{24}H_{27}N_{3}O_{3} 405.2052&lt;br&gt;found 405.2031</td>
</tr>
<tr>
<td>Compound Description</td>
<td>Yields (%)</td>
</tr>
<tr>
<td>-------------------------------------------------------------------------------------</td>
<td>------------</td>
</tr>
<tr>
<td>$N$-(2-(1H-indol-3-yl)ethyl)-$N$-(1-cyclohexyl-2-(cyclohexylamino)-2-oxoethyl)but-2-ynamide (5g)</td>
<td>84%</td>
</tr>
<tr>
<td>$N$-(2-(1H-indol-3-yl)ethyl)-$N$-(2-(cyclohexylamino)-1-(2,6-dichlorophenyl)-2-oxoethyl)but-2-ynamide (5h)</td>
<td>84%</td>
</tr>
<tr>
<td>$N$-(2-(1H-indol-3-yl)ethyl)-$N$-(2-(butylamino)-1-cyclohexyl-2-oxoethyl)but-2-ynamide (5i)</td>
<td>88%</td>
</tr>
<tr>
<td>$N$-(2-(1H-indol-3-yl)ethyl)-$N$-(2-(butylamino)-1-(2,6-dichlorophenyl)-2-oxoethyl)but-2-ynamide (5j)</td>
<td>91%</td>
</tr>
<tr>
<td>$N$-tert-butyl-2-($N$-(2-(5-methoxy-1H-indol-3-yl)ethyl)but-2-ynamido)heptanamide (5k)</td>
<td>34%</td>
</tr>
<tr>
<td>Compound Description</td>
<td>Yield</td>
</tr>
<tr>
<td>-------------------------------------------------------------------------------------</td>
<td>-------</td>
</tr>
<tr>
<td>N-(2-(tert-buty lamino)-1-cyclohexyl-2-oxoethyl)-N-(2-(5-methoxy-1H-indol-3-yl)ethyl)but-2-ynamide (5l)</td>
<td>48%</td>
</tr>
<tr>
<td>N-(2-(1H-indol-3-yl)ethyl)-N-(1-(tert-buty lamino)-3,3-dimethyl-1-oxobutan-2-yl)pent-2-ynamide (5m)</td>
<td>82%</td>
</tr>
<tr>
<td>2-(N-(2-(1H-indol-3-yl)ethyl)-3-phenylpropionlamido)-N-tert-buty l-3,3-dimethylbutanamide (5n)</td>
<td>75%</td>
</tr>
<tr>
<td>N-(2-(1H-indol-3-yl)ethyl)-N-(2-(tert-buty lamino)-1-cyclohexyl-2-oxoethyl)-4-methylpent-2-ynamide (5o)</td>
<td>86%</td>
</tr>
<tr>
<td>N-(2-(1H-indol-3-yl)ethyl)-N-(2-(tert-buty lamino)-1-cyclohexyl-2-oxoethyl)-4,4-dimethylpent-2-ynamide (5p)</td>
<td>84%</td>
</tr>
</tbody>
</table>
General procedure for synthesis of 5q

To a solution of tryptamine 1a (200mg, 1 equiv) in methanol (3 mL) were added successively Na₂SO₄ (0.5g), cyclohexylcarboxaldehyde 2b (1 equiv), tert-butylisonitrile 3a (1 equiv) and 3-(triisopropylsilyl)propiolic acid 4f (1 equiv) in a screw capped vial equipped with a magnetic stir bar. The reaction mixture was stirred at room temperature for 24h in closed vial. After completion of the reaction, the mixture was diluted with EtOAc (100 mL) and was extracted with water (50 mL). Organic layer was washed with brine (50 mL), dried over magnesium sulfate and evaporated under reduced pressure to obtained residue which was used directly for the deprotection step without purification. Residue was dissolved in THF (3 mL) and solution of tetrabutylammonium fluoride, 1M in THF (560 µL, 1 equiv) was added at 0 °C. Reaction was completed in 30 min. Reaction mixture was partitioned between diethyl (100 mL) ether and water (50 mL). Organic layer was separated, washed with brine, dried over magnesium sulfate and evaporated under reduced pressure to obtain residue. This residue was subjected to silica gel column chromatography (50 % EtOAc in Heptane) to afford the desired product 5q as white solid in 92% yield.

Table 3. Ugi product 5q

<table>
<thead>
<tr>
<th>Structure</th>
<th>Data</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image" alt="Structure" /></td>
<td>(N)-(2-(1H-indol-3-yl)ethyl)-N-(2-(tert-butylamino)-1-cyclohexyl-2-oxoethyl)propiolamide (5q)</td>
</tr>
<tr>
<td></td>
<td>White solid, Yield 92%, HRMS calculated for C_{25}H_{33}N_{3}O_{2} 407.2573 found 407.2569</td>
</tr>
</tbody>
</table>
General procedure for synthesis of Ugi adducts 5r & 5s.

To a solution of L-tryptophan methylester 1c (100mg, 1 equiv) in methanol (3 mL) were added successively Na₂SO₄ (0.3g), 2,6-dichlorobenzaldehyde 2d (1 equiv), tert-butylisonitrile 3a (1 equiv) and 2-butynoic acid 4a (1 equiv) in a screw capped vial equipped with a magnetic stir bar. The reaction mixture was stirred at room temperature for 24h in closed vial. After completion of the reaction, the mixture was diluted with EtOAc (100 mL) and was extracted with water (50 mL). Organic layer was washed with brine (50 mL), dried over magnesium sulfate and evaporated under reduced pressure to obtained residue. The diastereoisomers formed during the reaction were separated by silica gel column chromatography (40-80 % EtOAc in Heptane) to afford pure diastereoisomers 5r and 5s. Isolated yield was 14% (5r) and 29% (5s) and also there were fractions were both of these were together so combined yield was 92%.

White solid, Yield 14%, [α]D = +7.23° (c = 0.79, CHCl₃)

¹H NMR (300 MHz, CDCl₃) δ 8.63 (bs, 1H), 7.78 (bs, 1H), 7.12 (d, J = 8.03 Hz 1H), 7.12-7.02 (m, 2H), 6.93-6.84 (m, 3H), 6.73 (t, J = 8.20 Hz, 1H), 6.59 (s, 1H), 6.53 (s, 1H), 4.30 (t, J = 6.55 Hz, 1H), 3.84 (s, 3H), 3.62 (dd, J = 5.96, 15.4 Hz, 1H), 3.03 (dd, J = 6.83, 15.5 Hz, 1H), 2.04 (s, 3H), 1.41 (s, 9H).

¹³C NMR (75 MHz, CDCl₃) δ 172.4, 167.8, 155.8, 136.1, 130.6, 129.6, 129.2, 128.4, 126.8, 122.8, 121.5, 119.1, 118.0, 111.5, 110.8, 91.3, 72.8, 64.5, 59.7, 53.1, 51.6, 28.2, 25.2, 4.1.

HRMS calculated for C₂₈H₂₀Cl₂N₃O₄ 541.1535, found 541.1540.
White solid, Yield 29%, $[\alpha]_D = -40.7^\circ$ (c = 0.33, CHCl$_3$)

$^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 8.07 (bs, 1H), 7.78 (d, $J = 7.92$ Hz 1H), 7.37-7.27 (m, 3H), 7.25-7.08 (m, 4H), 6.66 (s, 1H), 5.65 (bs, 1H), 4.19 (t, $J = 7.01$ Hz, 1H), 3.86 (dd, $J = 7.92$, 14.6 Hz, 1H), 3.68 (dd, $J = 6.02$, 14.8 Hz, 1H), 3.39 (s, 3H), 2.03 (s, 3H), 1.17 (s, 9H).

$^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 170.1, 166.9, 156.7, 136.0, 130.6, 129.1, 127.6, 124.4, 124.2, 122.0, 119.3, 112.1, 111.2, 90.6, 73.2, 64.7, 59.4, 51.7, 51.5, 28.1, 26.6, 4.1.

HRMS calculated for C$_{28}$H$_{29}$Cl$_2$N$_3$O$_4$ 541.1535, found 541.1505.
General procedure for Au(PPh$_3$)OTf catalyzed cyclization

To a glass vial Au(PPh$_3$)Cl (5 mol %) and AgOTf (5 mol %) were loaded along with chloroform (2 mL). Ugi product 5a-s was added and reaction mixture was stirred at rt for 8-10h in screw capped vial. After completion, reaction mixture was partitioned between EtOAc (100 mL) and water (50 mL). Organic layer was washed with brine (50 mL), dried over magnesium sulfate and evaporated under reduced pressure. The residue obtained was purified by silica gel column chromatography (20% diethyl ether in dichloromethane) to afford compound 6a-s as white solid.

In $^1$H NMR spectra of indoloazocines 6a-s, recorded at 298 K, signals of the 8-membered ring protons are often broadened due to the ring flipping.

\[
\text{(Z)-N-tert-butyl-2-(4-methoxyphenyl)-2-(6-methyl-4-oxo-1H-azocino[5,4-b]indol-3(2H,4H,7H)-yl)acetamide (6a)}
\]

White solid, Yield 85%.

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.30 (s, 1H), 7.29-7.23 (m, 4H), 7.17 (t, $J = 7.00$ Hz, 1H), 7.12-7.10 (m, 1H), 7.04 (t, $J = 7.20$ Hz, 1H), 6.83 (d, $J = 8.60$ Hz, 2H), 6.00 (d, $J = 1.3$ Hz, 1H), 5.84, (s, 1H), 5.64 (bs, 1H), 4.23-4.05 (m, 1H), 4.02-3.92 (m, 1H), 3.84 (s, 3H), 2.70-2.60 (m, 1H), 2.20-2.16 (m, 4H), 1.18 (s, 9H).

$^{13}$C NMR (100 MHz, DMSO-d$_6$) $\delta$ 169.4, 169.0, 159.4, 136.2, 134.1, 132.5, 130.9, 128.7, 128.6, 123.0, 122.5, 118.9, 118.5, 114.3, 111.3, 109.2, 60.11, 55.6, 50.6, 44.5, 28.7, 25.5, 24.1.

HRMS calculated for C$_{27}$H$_{31}$N$_3$O$_3$ 445.2365, found 445.2371.
White solid, Yield 84%.

\[ ^1H \text{ NMR } (300 \text{ MHz, } CDCl}_3 \delta 8.06 (s, 1H), 7.46 (d, J = 7.90 \text{ Hz, } 1H), 7.28-7.26 (m, 1H), 7.17 (t, J = 7.10 \text{ Hz, } 1H), 7.07 (t, J = 7.21 \text{ Hz, } 1H), 5.94 (s, 1H), 4.54-4.04 (m, 2H), 4.03-3.80 (m, 1H), 3.30-3.20 (m, 1H), 3.16-2.98 (m, 1H), 2.25-2.17 (m, 4H), 1.83-1.69 (m, 3H), 1.53-1.08 (m, 5H), 1.05 (s, 9H), 0.94-0.70 (m, 3H). \]

\[ ^13C \text{ NMR } (75 \text{ MHz, DMSO-}d_6) \delta 171.0, 168.5, 136.0, 132.9, 131.6, 129.0, 122.9, 121.6, 119.4, 118.9, 110.7, 109.4, 51.0, 35.7, 30.2, 29.7, 29.2, 28.3, 26.3, 25.7, 25.6, 23.9. \]

HRMS calculated for C_{26}H_{35}N_{3}O_{2} 421.2729, found 421.2736.

White solid, Yield 90%.

\[ ^1H \text{ NMR } (300 \text{ MHz, } CDCl}_3 \delta 8.06 (s, 1H), 7.43 (d, J = 7.81 \text{ Hz, } 1H), 7.29-7.26 (m, 1H), 7.17 (t, J = 7.56 \text{ Hz, } 1H), 7.06 (t, J = 7.56 \text{ Hz, } 1H), 5.94 (s, 1H), 5.79-5.5.50 (m, 1H), 4.92-4.60 (m, 1H), 4.55-4.16 (m, 2H), 3.43-3.12 (m, 1H), 3.16-2.88 (m, 1H), 2.21 (s, 3H), 1.28-1.00 (m, 18H). \]

\[ ^13C \text{ NMR } (75 \text{ MHz, } CDCl}_3 \delta 171.0, 168.5, 136.0, 132.9, 131.6, 129.0, 122.9, 121.6, 119.4, 118.9, 110.7, 109.4, 51.2, 36.8, 29.7, 28.8, 28.4, 28.2, 27.9, 23.3. \]

HRMS calculated for C_{24}H_{33}N_{3}O_{2} 395.2573, found 395.2549.
White solid, Yield 91%

$^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 8.36 (s, 1H), 7.37-7.19 (m, 6H), 7.14-7.06 (m, 1H), 6.79 (s, 1H), 6.08 (s, 1H), 5.60 (bs, 1H), 4.40-4.22 (m, 1H), 3.97-3.03 (m, 2H), 2.93-2.48 (m, 1H), 2.25 (s, 3H), 0.87 (bs, 9H).

$^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 170.4, 166.7, 138.1, 136.2, 135.7, 132.0, 131.5, 130.2, 129.4, 128.5, 123.3, 121.3, 119.6, 118.4, 111.1, 108.3, 65.8, 51.2, 43.9, 27.6, 24.3, 15.2.

HRMS calculated for C$_{26}$H$_{27}$Cl$_2$N$_3$O$_2$ 483.1480, found 483.1480.

White solid, Yield 85%

$^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 8.05 (s, 1H), 7.44 (d, $J = 7.96$ Hz, 1H), 7.30-7.17 (m, 5H), 7.12-7.05 (m, 3H), 6.27 (s, 1H), 5.97 (s, 1H), 467-4.58 (m, 1H), 4.14-3.91 (m, 2H), 3.31-3.03 (m, 2H), 2.65-2.40 (m, 3H), 2.24 (s, 3H), 2.16-2.02 (m, 1H), 0.96 (s, 9H).

$^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 170.5, 169.5, 140.9, 135.8, 134.7, 131.3, 128.7, 128.4, 128.3, 126.0, 123.3, 121.8, 119.7, 119.0, 110.5, 109.8, 50.8, 32.4, 29.6, 28.1, 25.8, 24.1.

HRMS calculated for C$_{28}$H$_{33}$N$_3$O$_2$ 443.2573, found 443.2548.
(Z)-N-tert-butyl-2-(furan-2-yl)-2-(6-methyl-4-oxo-1H-azocino[5,4-b]indol-3(2H,4H,7H)-yl)acetamide (6f).

White solid, Yield 72%

\(^1\text{H NMR}\ (300\ \text{MHz, DMSO-d}_6) \delta 10.83\ (s, 1\text{H}), 7.69\ (s, 1\text{H}), 7.59\ (s, 1\text{H}), 7.29\ (d, J = 8.30\ \text{Hz, 1H}), 7.12-7.07\ (m, 2\text{H}), 6.96\ (t, J = 7.41\ \text{Hz, 1H}), 6.56\ (s, 1\text{H}), 5.94-5.93\ (m, 2\text{H}), 4.20-4.03\ (m, 1\text{H}), 3.93-3.82\ (m, 1\text{H}), 2.60-2.42\ (m, 1\text{H}), 2.23\ (s, 3\text{H}), 1.98-1.92\ (m, 1\text{H}), 1.19\ (s, 9\text{H}).

\(^{13}\text{C NMR}\ (75\ \text{MHz, CDCl}_3) \delta 170.2, 166.4, 148.0, 143.0, 136.0, 135.7, 131.5, 128.7, 123.0, 121.2, 119.3, 118.7, 112.2, 110.9\ (x 2), 109.7, 55.7, 51.4, 44.6, 28.2, 25.0, 24.2.

HRMS calculated for C\(_{24}\)H\(_{27}\)Cl\(_2\)N\(_3\)O\(_3\) 405.2052, found 405.2050.

(Z)-N,2-dicyclohexyl-2-(6-methyl-4-oxo-1H-azocino[5,4-b]indol-3(2H,4H,7H)-yl)acetamide (6g)

White solid, Yield 88%

\(^1\text{H NMR}\ (300\ \text{MHz, CDCl}_3) \delta 7.99\ (s, 1\text{H}), 7.47\ (d, J = 7.82\ \text{Hz, 1H}), 7.27-7.26\ (m, 1\text{H}), 7.17\ (t, J = 7.10\ \text{Hz, 1H}), 7.08\ (t, J = 7.40\ \text{Hz, 1H}), 5.95\ (s, 1\text{H}), 4.40-4.08\ (m, 1\text{H}), 3.99-3.76\ (m, 1\text{H}), 3.42-3.24\ (m, 2\text{H}), 3.09-2.94\ (m, 1\text{H}), 2.31-2.20\ (m, 4\text{H}), 1.87-1.58\ (m, 4\text{H}), 1.52-0.49\ (m, 17\text{H}).

\(^{13}\text{C NMR}\ (75\ \text{MHz, CDCl}_3) \delta 170.9, 169.4, 135.8, 134.6, 131.4, 128.8, 123.1, 122.0, 119.6, 118.8, 110.4, 109.8, 47.9, 35.1, 32.6, 31.9, 30.3, 29.7, 29.1, 26.3, 25.7, 25.6, 25.4, 25.3, 24.4, 24.3, 23.8.

HRMS calculated for C\(_{28}\)H\(_{37}\)N\(_3\)O\(_2\) 447.2886, found 447.2868.
White solid, Yield 89%

**1H NMR (300 MHz, CDCl₃)** δ 8.20 (s, 1H), 7.40-7.30 (m, 4H), 7.29-7.20 (m, 2H), 7.17-7.09 (m, 1H), 6.81 (s, 1H), 6.10 (s, 1H), 5.72-5.62 (m, 1H), 4.41-4.28 (m, 1H), 3.75-3.57 (m, 1H), 3.56-3.36 (m, 2H), 2.87-2.68 (m, 1H), 2.27 (s, 3H), 1.76-1.66 (m, 1H), 1.44-1.20 (m, 6H), 1.13-0.85 (m, 3H).

**13C NMR (75 MHz, DMSO-d₆)** δ 168.7, 166.1, 136.9, 135.8, 134.5, 132.1, 131.7, 130.6, 129.4, 128.0, 122.1, 121.9, 118.4, 118.1, 110.7, 107.8, 54.8, 48.0, 44.0, 31.7, 31.5, 24.9, 24.6, 23.7.

**HRMS** calculated for C₂₉H₂₉Cl₂N₅O₂ 509.1637, found 509.1634.

White solid, Yield 89%

**1H NMR (300 MHz, DMSO-d₆)** δ 10.79 (s, 1H), 7.83 (bs, 1H), 7.36 (d, J = 7.72 Hz, 1H), 7.27 (d, J = 8.10 Hz, 1H), 7.09 (t, J = 7.26 Hz, 1H), 6.95 (t, J = 7.57 Hz, 1H), 5.91 (s, 1H), 4.57 (d, J = 11.0 Hz, 1H), 4.25-4.12 (m, 1H), 3.99-3.79 (m, 1H), 3.13-2.78 (m, 4H), 2.21 (s, 3H), 2.05-1.90 (m, 1H), 1.69-1.48 (m, 3H), 1.40-0.98 (m, 9H), 0.93-0.60 (m, 5H).

**13C NMR (75 MHz, DMSO-d₆)** δ 169.1, 169.0, 135.8, 133.1, 132.1, 128.3, 122.5, 122.0, 118.5, 118.1, 110.7, 108.4, 38.1, 36.2, 30.6, 29.7, 28.6, 25.9, 25.5, 25.3 (2), 23.4, 19.4, 13.5.

**HRMS** calculated for C₂₆H₃₅N₃O₂ 421.2729, found 421.2726.
(Z)-N-butyl-2-(2,6-dichlorophenyl)-2-(6-methyl-4-oxo-1H-azocino[5,4-b]indol-3(2H,4H,7H)-yl)acetamide (6j)

White solid, Yield 80%

\[^{1}H\text{ NMR (300 MHz, DMSO-}\delta\text{) d} 10.8 \text{ (s, 1H), 7.96-7.67 (m, 1H), 7.49-7.30 (m, 3H), 7.25 (d, } J = 8.22 \text{ Hz, 1H), 7.07 (t, } J = 7.22 \text{ Hz, 1H), 6.88 (t, } J = 7.45 \text{ Hz, 1H), 6.81-6.67 (m, 1H), 6.37 \text{ (s, 1H), 5.97 (s, 1H), 4.37-4.05 (m, 1H), 3.97-3.81 (m, 1H), 3.09-2.92 (m, 2H), 2.76-2.54 (m, 1H), 2.28 (s, 3H), 2.04-1.88 (m, 1H), 1.40-1.10 (m, 4H), 0.88-0.78 (m, 3H).

\[^{13}C\text{ NMR (75 MHz, DMSO-}\delta\text{) d} 168.7, 167.1, 135.7, 134.2, 132.0, 131.8, 130.6, 130.8, 129.4, 128.0, 122.0, 121.9, 118.8, 117.8, 110.6, 107.7, 57.3, 44.2, 30.5, 24.8, 23.6, 19.5, 13.6.

HRMS calculated for C\text{_{26}H\text{_{27}Cl}_{2}N\text{_{5}O}_{2}} 483.1480, found 483.1468.

(Z)-N-tert-butyl-2-(10-methoxy-6-methyl-4-oxo-1H-azocino[5,4-b]indol-3(2H,4H,7H)-yl)heptanamide (6k)

White solid, Yield 85%

\[^{1}H\text{ NMR (300 MHz, DMSO-}\delta\text{) d} 10.68 \text{ (s, 1H), 7.17 (d, } J = 8.65 \text{ Hz, 1H), 7.14-7.06 (m, 1H), 6.83 \text{ (s, 1H), 6.74 (d, } J = 8.75 \text{ Hz, 1H), 5.89 \text{ (s, 1H), 4.60-4.51 (m, 1H), 4.17-3.83 (m, 2H), 3.73 \text{ (s, 3H), 3.09-2.89 (m, 2H), 2.20 (s, 3H), 1.86-1.83 (m, 1H), 1.66-1.53 (m, 1H), 1.22-0.98 (m, 15H), 0.75 \text{ (t, } J = 7.19 \text{ Hz, 3H).

\[^{13}C\text{ NMR (75 MHz, CDCl}_{3}\text{) d} 170.6, 169.9, 154.1, 134.8, 132.1, 131.0, 129.1, 121.6, 113.8, 111.5, 109.6, 100.2, 55.8, 50.8, 31.6, 28.2, 27.8, 26.0, 25.9, 24.1, 22.4, 13.9.

HRMS calculated for C\text{_{26}H\text{_{37}N}_{3}O}_{3} 439.2835, found 439.2842.
(Z)-N-tert-butyl-2-cyclohexyl-2-(10-methoxy-6-methyl-4-oxo-1H-azocino[5,4-b]indol-3(2H,4H,7H)-yl)acetamide (6l)

White solid, Yield 65%

$^1$H NMR (300 MHz, DMSO-d$_6$) $\delta$ 10.64 (s, 1H), 7.53 (bs, 1H), 7.16 (d, $J = 8.69$ Hz, 1H), 6.79 (s, 1H), 6.72 (dd, $J = 1.70, 8.75$ Hz, 1H), 5.88 (s, 1H), 4.61-4.48 (m, 1H), 4.22-4.09 (m, 1H), 3.98-3.84 (m, 1H), 3.71 (s, 3H), 3.14-2.80 (m, 2H), 2.20 (s, 3H), 2.02-1.88 (m, 1H), 1.72-1.50 (m, 3H), 1.49-1.17 (m, 3H), 1.12 (s, 9H), 1.09-0.79 (m, 3H).

$^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 170.8, 169.4, 154.0, 134.5, 132.1, 131.0, 129.2, 121.4, 113.7, 111.4, 109.8, 100.2, 55.8, 51.0, 35.6, 30.2, 29.1, 28.3, 26.3, 25.7 (x 2), 23.9.

HRMS calculated for C$_{27}$H$_{37}$N$_3$O$_3$ 451.2835, found 451.2847.

(Z)-N-tert-butyl-2-(6-ethyl-4-oxo-1H-azocino[5,4-b]indol-3(2H,4H,7H)-yl)-3,3-dimethylbutanamide (6m)

White solid, Yield 85%

$^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 8.04-7.84 (m, 1H), 7.44 (d, $J = 8.04$ Hz, 1H), 7.29-7.24 (m, 1H), 7.17 (t, $J = 7.08$ Hz, 1H), 7.06 (t, $J = 7.47$ Hz, 1H), 5.94 (s, 1H), 5.79-5.47 (m, 1H), 4.93-4.59 (m, 1H), 4.53-4.16 (m, 2H), 3.42-3.20 (m, 1H), 3.15-2.86 (m, 1H), 2.53 (q, $J = 7.17$ Hz, 2H), 1.42-0.77 (m, 21H).

$^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 171.4, 168.5, 138.9, 136.0, 131.0, 129.0, 122.8, 120.2, 119.3, 118.8, 110.6, 109.9, 65.8, 51.2, 29.9, 28.3, 27.8, 15.2, 14.0, 12.8.

HRMS calculated for C$_{25}$H$_{35}$N$_3$O$_2$ 409.2729, found 409.2723.
(Z)-N-tert-butyl-2-cyclohexyl-2-(6-isopropyl-4-oxo-1H-azocino[5,4-b]indol-3(2H,4H,7H)-yl)acetamide (6o)

White solid, Yield 81%

\(^1\)H NMR (300 MHz, DMSO-\(d_6\)) \(\delta\) 10.75 (s, 1H), 7.52 (bs, 1H), 7.33 (bs, 1H), 7.25 (d, \(J = 8.20\) Hz, 1H), 7.06 (t, \(J = 7.33\) Hz, 1H), 6.94 (t, \(J = 7.48\) Hz, 1H), 5.80 (s, 1H), 4.66-4.38 (m, 1H), 4.21-4.07 (m, 1H), 3.98-3.59 (m, 1H), 3.07-2.69 (m, 2H), 2.00-1.83 (m, 1H), 1.70-1.47 (m, 3H), 1.37-0.47 (m, 23H).

\(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 171.6, 169.2, 145.0, 135.9, 131.2, 128.8, 122.7, 119.3, 118.8, 110.4, 50.9, 34.1, 30.1, 28.3, 26.3, 25.7 (x 2), 25.3.

HRMS calculated for C\(_{28}\)H\(_{39}\)N\(_2\)O\(_2\) 449.3042, found 449.3054.

\(\text{N-tert-butyl-2-cyclohexyl-2-(5-methylene-4-oxo-1,2,4,5-tetrahydroazepino[4,5-b]indol-3(6H)-yl)acetamide (6q)}\)

White solid, Yield 56%

\(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta\) 8.12 (s, 1H), 7.47 (d, \(J = 8.10\) Hz, 1H), 7.35 (d, \(J = 7.89\) Hz, 1H), 7.26-7.20 (m, 1H), 7.11 (t, \(J = 7.68\) Hz, 1H), 6.07-5.88 (m, 2H), 5.73 (s, 1H), 4.61-4.47 (m, 1H), 3.91-.82 (m, 2H), 2.99-2.91 (m, 2H), 2.18-2.02 (m, 1H), 1.86-1.53 (m, 4H), 1.40-1.11 (m, 13H), 1.06-0.91 (m, 2H).

\(^{13}\)C NMR (75 MHz, CDCl\(_3\)) \(\delta\) 171.2, 169.3, 138.6, 136.2, 128.5, 128.4, 123.3, 120.2, 119.8, 118.9, 113.8, 111.0, 51.3, 35.8, 29.9, 29.0, 28.5, 26.3, 25.7, 25.6, 25.0.

HRMS calculated for C\(_{25}\)H\(_{33}\)N\(_2\)O\(_2\) 407.2573, found 407.2573.
White solid, Yield 62%, $[\alpha]_D = +145.6^\circ$ (c = 0.15, CHCl$_3$)

$^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 8.19 (s, 1H), 7.58 (s, 1H), 7.42-7.31 (m, 1H), 7.28-7.26 (m, 1H), 7.25-7.20 (m, 1H), 7.14 (t, $J = 7.33$ Hz, 1H), 6.93 (t, $J = 7.71$ Hz, 1H), 6.89-6.80 (m, 1H), 6.73 (s, 1H), 6.63 (d, $J = 7.85$ Hz, 1H), 5.81 (s, 1H), 5.29 (s, 1H), 4.97 (d, $J = 8.35$ Hz, 1H), 3.87 (s, 3H), 3.32 (d, $J = 17.3$ Hz, 1H), 2.13 (s, 3H), 1.44 (s, 9H).

$^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 172.0, 169.4, 166.7, 136.1, 135.6, 131.5, 131.2, 130.0, 129.5, 127.7, 122.7, 121.5, 118.9, 118.0, 111.2, 106.2, 59.4, 58.0, 53.3, 51.6, 28.4, 24.9, 23.5.

HRMS calculated for C$_{28}$H$_{29}$Cl$_2$N$_3$O$_4$ 541.1535, found 541.1535.
(S,Z)-methyl 3-((R)-2-(tert-butylamino)-1-(2,6-dichlorophenyl)-2-oxoethyl)-6-methyl-4-oxo-2,3,4,7-tetrahydro-1H-azocino[5,4-b]indole-2-carboxylate (6s)

White solid, Yield 49%, \([\alpha]_D = +161.7^\circ \) (c = 0.59, CHCl₃)

\(^1\)H NMR (400 MHz, CDCl₃) \(\delta\) 8.40 (s, 1H), 7.56 (d, \(J = 7.72\) Hz, 1H), 7.45-7.40 (m, 2H), 7.36-7.15 (m, 4H), 7.00 (s, 1H), 5.86 (s, 1H), 5.59 (s, 1H), 4.20 (d, \(J = 6.22\) Hz, 1H), 3.91 (dd, \(J = 7.72, 17.1\) Hz, 1H), 3.72-3.65 (m, 1H), 3.61 (s, 3H), 2.14 (s, 3H), 0.68 (s, 9H).

\(^{13}\)C NMR (100 MHz, CDCl₃) \(\delta\) 170.1, 169.7, 166.5, 136.4, 134.3, 132.2, 131.4, 130.6, 129.2, 128.4, 123.6, 122.3, 120.2, 118.4, 111.4, 106.4, 61.3, 56.5, 52.5, 51.1, 27.3, 26.8, 23.4.

HRMS calculated for C₂₈H₂₉Cl₂N₃O₄ 541.1535, found 541.1542.

Electronic Supplementary Material (ESI) for Chemical Communications
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Crystallographic data for compound 6s

Crystals of 6s, suitable for X-ray diffraction were obtained by slow evaporation from Methanol at rt. A cubic shaped crystal with approximate dimensions 0.4 x 0.2 x 0.1 mm$^2$, was selected and mounted in a nylon loop for data collection. X-ray intensity data were collected on an Agilent Supernova diffractometer equipped with a CCD detector using Mo Ka radiation ($\lambda = 0.7107\text{Å}$). The images were interpreted and integrated with the CrysAlisPro software from Agilent. Using Olex2, the structure was solved with the ShelXS$^2$ structure solution program using Direct Methods and refined with the ShelXL$^2$ refinement package using full-matrix least squares minimization on $F^2$. Non hydrogen atoms were anisotropically refined and the hydrogen atoms in the riding mode with isotropic temperature factors were fixed at 1.2 times U$_{eq}$ of the parent atoms (1.5 for methyl groups). CCDC 873949 contains the supplementary crystallographic data for this paper and can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; fax: +44-1223-336033; or deposit@ccdc.cam.ac.uk).

Summarized crystallographic data for 6s

C$_{28}$H$_{29}$N$_3$O$_4$Cl$_2$, $M=542.44$ g mol$^{-1}$, orthorhombic, P2$_1$2$_1$2$_1$ (no. 19), $a = 11.4032(7)$ Å, $b = 14.2768(8)$ Å, $c = 16.2935(7)$ Å, $V = 2652.6(2)$ Å$^3$, $T = 293(2)$ K, $Z = 4$, $\rho_{\text{calc}} = 1.358$ g cm$^{-3}$, $\mu$(Mo Ka) = 0.284 mm$^{-1}$, $F(000) = 1136$, crystal size 0.4 x 0.2 x 0.1 mm$^3$, 12398 reflections measured, 6146 unique ($R_{\text{int}} = 0.0337$) which were used in all calculations. The final $wR_2$ was 0.1038 (all data) and $R_1$ was 0.0448 (>2sigma(I))

![Figure 1. Single crystal X-ray molecular structure of 6s, with atom-labelling scheme. Displacement ellipsoids are drawn at the 50% probability level. CCDC 873949](image)
Figure 2. Depiction of intermolecular hydrogen bonds in the crystal packing of 6s.

Intermolecular hydrogen bonding between indole nitrogen N3 and oxygen O1 from amide makes a chain like network in the crystal packing (Fig 2.). Amide oxygen O2 from the 8-membered ring and oxygen O3/O4 from ester group does not take part in any critical intermolecular hydrogen bonding.

References

$^1$H and $^{13}$C NMR spectra of compound 5a (400 MHz, DMSO-d$_6$)
$^1$H and $^{13}$C NMR spectra of compound 5r (300 MHz, CDCl$_3$)
$^1$H and $^{13}$C NMR spectra of compound 5s (300 MHz, CDCl$_3$)
$^1$H NMR (400 MHz, CDCl$_3$) and $^{13}$C NMR (100 MHz, DMSO-d$_6$) of compound 6a
$^1$H NMR (300 MHz, CDCl$_3$) and $^{13}$C NMR (75 MHz, DMSO-d$_6$) of compound 6b
$^1$H and $^{13}$C NMR of compound 6c (300 MHz, CDCl$_3$)
$^1$H and $^{13}$C NMR of compound 6d (300 MHz, CDCl$_3$)

[Diagram of the compound with NMR spectral data]

Integral

1.06 0.81 1.13 1.04 1.00 0.92 0.98

(ppm)

0.0 0.5 1.0 1.5 2.0 2.5 3.0 3.5 4.0 4.5

N

H

N

H

N

O

O

Cl

Cl

[Diagram of the compound with C NMR spectral data]

170.4 166.7 138.2 136.3 135.8 132.0 131.6 130.3 129.4 128.6 123.3 121.4 119.6 118.4 111.2 108.4 77.0 65.9 51.2 43.9 27.7 24.4 15.3

(ppm)

0 10 20 30 40 50 60 70 80 90 100
$^1$H and $^{13}$C NMR of compound 6e (300 MHz, CDCl$_3$)
$^1$H NMR (300 MHz, DMSO-$d_6$) and $^{13}$C NMR (75 MHz, CDCl$_3$) of compound 6f
\(^1\)H and \(^{13}\)C NMR of compound 6g (300 MHz, CDCl\(_3\))

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$^1$H NMR (300 MHz, CDCl$_3$) and $^{13}$C NMR (75 MHz, DMSO-d$_6$) of compound 6h
$^1$H and $^{13}$C NMR of compound 6i (300 MHz, DMSO-d$_6$)
$^1$H NMR (300 MHz, DMSO-d$_6$) and $^{13}$C NMR (75 MHz, DMSO-d$_6$) of compound 6j
$^1$H NMR (300 MHz, DMSO-$d_6$) and $^{13}$C NMR (75 MHz, CDCl$_3$) of compound 6k

![NMR Spectra of Compound 6k](image)

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$^1$H NMR (300 MHz, DMSO-$d_6$) and $^{13}$C NMR (75 MHz, CDCl$_3$) of compound 61

![NMR Spectra]
$^1$H NMR and $^{13}$C NMR of compound 6m (300 MHz, CDCl$_3$)
$^1$H NMR (300 MHz, DMSO-d$_6$) and $^{13}$C NMR (100 MHz, CDCl$_3$) of compound 60
$^1$H and $^{13}$C NMR spectra of compound 6q (300 MHz, CDCl$_3$)
$^1$H and $^{13}$C NMR spectra of compound 6r (300 MHz, CDCl$_3$)
$^1$H and $^{13}$C NMR spectra of compound 6s (400 MHz, CDCl$_3$)