Metal-free cascade oxidative decarbonylative alkylation of acrylamides with aliphatic aldehydes: a convenient approach to oxindoles via dual C(sp2)-H bonds functionalization

Luo Yang*, a Wen Lu, a Wang Zhou a and Feng Zhang*, b

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I. General information

Unless otherwise noted, all commercially available compounds were used as provided without further purification. Dry solvents (toluene, benzene, chlorobenzene, o-dichlorobenzene, 1,2-dichloroethane) were used as commercially available;

Thin-layer chromatography (TLC) was performed using E. Merck silica gel 60 F254 precoated plates (0.25 mm) or Sorbent Silica Gel 60 F254 plates. The developed chromatography was analyzed by UV lamp (254 nm). High-resolution mass spectra (HRMS) were obtained from a JEOL JMS-700 instrument (ESI). Melting points are uncorrected. Nuclear magnetic resonance (NMR) spectra were recorded on a Bruker Avance 400 spectrometer at ambient temperature. Chemical shifts for ¹H NMR spectra are reported in parts per million (ppm) from tetramethylsilane with the solvent resonance as the internal standard (chloroform: δ 7.26 ppm). Chemical shifts for ¹³C NMR spectra are reported in parts per million (ppm) from tetramethylsilane with the solvent as the internal standard (CDCl₃: δ 77.16 ppm). Data are reported as following: chemical shift, multiplicity (s = singlet, d = doublet, dd = doublet of doublets, t = triplet, q = quartet, m = multiplet, br = broad signal), coupling constant (Hz), and integration.

II. General experimental procedures

A general experimental procedure is described as following:

To a solution of N-methyl-N-phenylmethacrylamide (1a, 0.2 mmol, 1 equiv.) and pivalaldehyde (2a, 0.6 mmol, 3 equiv.) in chlorobenzene (1.5 mL) at ambient temperature, DTBP (0.4 mmol, 2.0 equiv.) was added with vigorous stirring. The reaction mixture was stirred at 140°C (oil bath temperature) for 12 h. Afterwards The resulting mixture was cooled to room temperature, transferred to silica gel column directly and purified by column chromatography on silica gel with a mixture of EtOAc in petroleum ether as eluent to afford the pure product 3a.
III. Condition optimization

Table S1. Optimization of the oxidants

<table>
<thead>
<tr>
<th>Entry</th>
<th>Oxidant (equiv)</th>
<th>Yield (%)$^b$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>DTBP</td>
<td>65</td>
</tr>
<tr>
<td>2</td>
<td>BPO</td>
<td>26</td>
</tr>
<tr>
<td>3</td>
<td>DCP</td>
<td>45</td>
</tr>
<tr>
<td>4</td>
<td>H$_2$O$_2$</td>
<td>34</td>
</tr>
<tr>
<td>5</td>
<td>PhI(OAc)$_2$</td>
<td>41</td>
</tr>
<tr>
<td>6</td>
<td>TBHP</td>
<td>56</td>
</tr>
</tbody>
</table>

$^a$To a solution of 1a (0.2 mmol, 1 equiv.) and 2a (0.6 mmol, 3 equiv.) in chlorobenzene (1.5 mL) at ambient temperature, oxidant (0.4 mmol, 2.0 equiv.) was added with vigorous stirring. The reaction mixture was stirring at 130°C for 12 h under air. $^b$ Isolated yields.

Table S2. Optimization of the temperature

<table>
<thead>
<tr>
<th>Entry</th>
<th>Temperature (°C)</th>
<th>Yield (%)$^b$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>140</td>
<td>76</td>
</tr>
<tr>
<td>2</td>
<td>130</td>
<td>65</td>
</tr>
<tr>
<td>3</td>
<td>150</td>
<td>57</td>
</tr>
</tbody>
</table>

$^a$To a solution of 1a (0.2 mmol, 1 equiv.) and 2a (0.6 mmol, 3 equiv.) in chlorobenzene (1.5 mL) at ambient temperature, DTBP (0.4 mmol, 2.0 equiv.) was added with vigorous stirring. The reaction mixture was stirring at given temperature for 12 h under air. $^b$ Isolated yields.
Table S3. Optimization of the reactants ratio\textsuperscript{[a]}

![Reaction Scheme]

<table>
<thead>
<tr>
<th>Entry</th>
<th>2a (X equiv)</th>
<th>DTBP (Y equiv)</th>
<th>Yield (%)\textsuperscript{[b]}</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>3</td>
<td>1.5</td>
<td>59</td>
</tr>
<tr>
<td>2</td>
<td>3</td>
<td>2.0</td>
<td>65</td>
</tr>
<tr>
<td>3</td>
<td>3</td>
<td>2.5</td>
<td>65</td>
</tr>
<tr>
<td>4</td>
<td>1.5</td>
<td>2.0</td>
<td>66</td>
</tr>
<tr>
<td>5</td>
<td>3.0</td>
<td>2.0</td>
<td>76</td>
</tr>
<tr>
<td>6</td>
<td>5.0</td>
<td>2.0</td>
<td>71</td>
</tr>
</tbody>
</table>

\textsuperscript{[a]}To a solution of 1a (0.2 mmol, 1 equiv.) and 2a (X equiv.) in chlorobenzene (1.5 mL) at ambient temperature, DTBP (Y equiv.) was added with vigorous stirring. The reaction mixture was stirring at 140°C for 12 h under air. \textsuperscript{[b]}Isolated yields.

Table S4. Optimization of the solvents\textsuperscript{[a]}

![Reaction Scheme]

<table>
<thead>
<tr>
<th>Entry</th>
<th>Solvent (mL)</th>
<th>Yield (%)\textsuperscript{[b]}</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Benzene (1.5)</td>
<td>53</td>
</tr>
<tr>
<td>2</td>
<td>o-Dichlorobenzene (1.5)</td>
<td>74</td>
</tr>
<tr>
<td>3</td>
<td>Toluene (1.5)</td>
<td>33</td>
</tr>
<tr>
<td>4</td>
<td>Fluorobenzene (1.5)</td>
<td>51</td>
</tr>
<tr>
<td>5</td>
<td>chlorobenzene (1.5)</td>
<td>76</td>
</tr>
<tr>
<td>6</td>
<td>Fluorobenzene (1.5)</td>
<td>36</td>
</tr>
<tr>
<td>9</td>
<td>1,2-Dichloroethane (1.5)</td>
<td>43</td>
</tr>
</tbody>
</table>

\textsuperscript{[a]}To a solution of 1a (0.2 mmol, 1 equiv.) and 2a (0.6 mmol, 3 equiv.) in solvent (1.5 mL) at ambient temperature, DTBP (0.4 mmol, 2.0 equiv.) was added with vigorous stirring. The reaction mixture was stirring at 140°C for 12 h under air. \textsuperscript{[b]}Isolated yields.
Table S5. Optimization of the additives\textsuperscript{[a]}

<table>
<thead>
<tr>
<th>Entry</th>
<th>Additive (mL)</th>
<th>Yield (%)\textsuperscript{[b]}</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1.5 equiv. Na\textsubscript{2}CO\textsubscript{3}</td>
<td>53</td>
</tr>
<tr>
<td>2</td>
<td>1.5 equiv. Pivalic acid</td>
<td>74</td>
</tr>
</tbody>
</table>

\textsuperscript{[a]}To a solution of 1\textsubscript{a} (0.2 mmol, 1 equiv.), 2\textsubscript{a} (0.6 mmol, 3 equiv.) and additive in chlorobenzene (1.5 mL) at ambient temperature, DTBP (0.4 mmol, 2.0 equiv.) was added with vigorous stirring. The reaction mixture was stirring at 140\textdegree C for 12 h under air. \textsuperscript{[b]}Isolated yields.
V. Spectra data of products 3a-3h, 4b-4x, 5, 6, 6'

(3a) 1,3-dimethyl-3-neopentylindolin-2-one ¹

The title compound was prepared according to the general procedure described above by the reaction between N-methyl-N-phenylmethacrylamide (1a) with pivalaldehyde (2a), and purified by flash column chromatography as light yellow solid (35.1 mg, 76%).

M.p. 104-105°C; ¹H NMR (400 MHz, CDCl₃) δ 7.26 (t, J = 7.2 Hz, 1H), 7.20 (d, J = 6.8 Hz, 1H), 7.03 (t, J = 7.2 Hz, 1H), 6.85 (d, J = 7.6 Hz, 1H), 5.22 (s, 4H), 2.16 (d, J = 14.4 Hz, 1H), 1.86 (d, J = 14.4 Hz, 1H), 1.29 (s, 3H), 0.61 (s, 9H). ¹³C NMR (100 MHz, CDCl₃) δ 181.12, 142.96, 134.30, 127.64, 123.96, 122.08, 108.12, 50.89, 47.49, 31.87, 30.92, 28.38, 26.33.

(3b) N-methyl-N-(p-tolyl)methacrylamide ²

The title compound was prepared according to the general procedure described above by the reaction between N-methyl-N-(p-tolyl)methacrylamide (1b) with pivalaldehyde (2a), and purified by flash column chromatography as white solid (42.14 mg, 86%).

M.p. 120-121°C; ¹H NMR (400 MHz, CDCl₃) δ 7.05 (d, J = 8.0 Hz, 1H), 7.01 (s, 1H), 6.73 (d, J = 8.0 Hz, 1H), 3.20 (s, 3H), 2.34 (s, 3H), 2.14 (d, J = 14.4 Hz, 1H), 1.83 (d, J = 14.4 Hz, 1H), 1.28 (s, 3H), 0.61 (s, 9H). ¹³C NMR (100 MHz, CDCl₃) δ 181.08, 140.63, 134.37, 131.48, 127.83, 124.80, 107.80, 50.88, 47.53, 31.86, 30.92, 28.41, 26.34, 21.23.

(3c) 5-methoxy-1,3-dimethyl-3-neopentylindolin-2-one ²

The title compound was prepared according to the general procedure described above by the reaction between N-(4-methoxyphenyl)-N-methylmethacrylamide (1c) with pivalaldehyde (2a), and purified by flash column chromatography as light yellow oil (39.67 mg, 76%).

¹H NMR (400 MHz, CDCl₃) δ 6.85 – 6.63 (m, 3H), 3.79 (s, 3H), 3.19 (s, 3H), 2.15 (d, J = 14.4 Hz, 1H), 1.82 (d, J = 14.4 Hz, 3H), 1.28 (s, 1H), 0.63 (s, 9H). ¹³C NMR (100 MHz, CDCl₃) δ 180.80, 155.83, 136.69, 135.82, 111.88, 111.68, 108.32, 55.98, 50.92, 47.95, 31.90, 30.96, 28.47, 26.42.

(3d) N-([1,1'-biphenyl]-4-yl)-N-methylmethacrylamide

The title compound was prepared according to the general procedure described above by the

reaction between N-[(1,1'-biphenyl)-4-yl]-N-methylmethacrylamide (1d) with pivalaldehyde (2a), and purified by flash column chromatography as white solid (46.66 mg, 76%). M.p. 125-126 °C;\(^{1}\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.55 (d, \(J = 7.2\) Hz, 2H), 7.49 (dd, \(J = 8.0, 1.6\) Hz, 1H), 7.44 (t, \(J = 8.0\) Hz, 3H), 7.33 (t, \(J = 7.2\) Hz, 1H), 6.92 (d, \(J = 8.0\) Hz, 1H), 3.26 (s, 3H), 2.20 (d, \(J = 14.8\) Hz, 1H), 1.92 (d, \(J = 14.4\) Hz, 1H), 1.34 (s, 3H), 0.65 (s, 9H). \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 181.20, 142.38, 141.28, 135.52, 134.83, 128.90, 127.00, 126.93, 126.59, 122.95, 108.35, 50.92, 47.66, 31.93, 30.99, 28.44, 26.47. IR(cm\(^{-1}\)): 2969, 2355, 1706, 1617, 1489, 1473, 1349, 758, 688; HRMS: calcd. for [M+H]\(^{+}\) \(C_{21}H_{26}NO\): 308.20146, found: 308.20089.

(3e) 5-fluoro-1,3-dimethyl-3-neopentylindolin-2-one \(^2\)

The title compound was prepared according to the general procedure described above by the reaction between N-(4-fluorophenyl)-N-methylmethacrylamide (1e) with pivalaldehyde (2a), and purified by flash column chromatography as white solid (38.34 mg, 77%). M.p. 121-123 °C;\(^{1}\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 6.98-6.93 (m, 2H), 6.76 (dd, \(J = 8.0, 4.0\) Hz, 1H), 3.21 (s, 3H), 2.16 (d, \(J = 14.4\) Hz, 1H), 1.82 (d, \(J = 14.4\) Hz, 1H), 1.29 (s, 3H), 0.63 (s, 9H). \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 180.69, 160.41, 158.03, 138.93, 136.22, 136.14, 113.95, 113.72, 112.10, 111.85, 108.54, 108.46, 50.91, 47.99, 47.97, 31.87, 30.92, 28.30, 26.45.

(3f) 5-chloro-1,3-dimethyl-3-neopentylindolin-2-one \(^2\)

The title compound was prepared according to the general procedure described above by the reaction between N-(4-chlorophenyl)-N-methylmethacrylamide (1f) with pivalaldehyde (2a), and purified by flash column chromatography as white solid (33.86 mg, 81%). M.p. 132-134 °C;\(^{1}\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.25-7.21 (m, 1H), 7.17 (s, 1H), 6.77 (d, \(J = 8.0\) Hz, 1H), 3.21 (s, 3H), 2.16 (d, \(J = 14.4\) Hz, 1H), 1.83 (d, \(J = 14.4\) Hz, 1H), 1.29 (s, 3H), 0.63 (s, 9H). \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 180.56, 141.55, 136.25, 127.60, 124.41, 109.05, 50.93, 47.90, 31.93, 30.97, 28.36, 26.49.

(3g) 5-bromo-1,3-dimethyl-3-neopentylindolin-2-one \(^2\)

The title compound was prepared according to the general procedure described above by the reaction between N-(4-bromophenyl)-N-methylmethacrylamide (1g) with pivalaldehyde (2a), and purified by flash column chromatography as white solid (36.46 mg, 59%). M.p. 147-149 °C;\(^{1}\)H NMR (400 MHz, DMSO) \(\delta\) 7.39 (d, \(J = 8.0\) Hz, 1H), 7.31 (s, 1H), 6.73 (d, \(J = 8.0\) Hz, 1H), 3.20 (s, 3H), 2.15 (d, \(J = 14.4\) Hz, 1H), 1.83 (d, \(J = 14.4\) Hz, 1H), 1.29 (s, 3H), 0.62 (s, 9H). \(^{13}\)C NMR (100 MHz, DMSO) \(\delta\) 180.56, 141.55, 136.25, 127.60, 124.41, 109.05, 50.93, 47.90, 31.93, 30.97, 28.36, 26.49.
MHz, CDCl$_3$) $\delta$ 180.47, 142.08, 136.64, 130.53, 127.19, 114.94, 109.60, 50.97, 47.80, 31.94, 31.00, 28.34, 26.47.

(3h) 5-ido-1,3-dimethyl-3-neopentylindolin-2-one $^2$

The title compound was prepared according to the general procedure described above by the reaction between N-(4-iodophenyl)-N-methylmethacrylamide (1h) with pivalaldehyde (2a), and purified by flash column chromatography as white solid (59.26 mg, 83%).

M.p. 110-111°C; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.58 (d, $J$ = 8.0 Hz, 1H), 7.48 (s, 1H), 6.63 (d, $J$ = 8.4 Hz, 1H), 3.19 (s, 3H), 2.13 (d, $J$ = 14.4 Hz, 1H), 1.82 (d, $J$ = 14.4 Hz, 1H), 1.28 (s, 3H), 0.62 (s, 9H).

$^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 180.31, 142.70, 136.94, 136.48, 132.76, 110.24, 84.71, 50.90, 47.60, 31.94, 30.99, 28.29, 26.42.

(3i) N-methyl-N-(4-(trifluoromethyl)phenyl)methacrylamide $^2$

The title compound was prepared according to the general procedure described above by the reaction between N-methyl-N-(4-(trifluoromethyl)phenyl)methacrylamide (1i) with pivalaldehyde (2a), and purified by flash column chromatography as light yellow oil (47.24 mg, 79%).

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.55 (d, $J$ = 8.0 Hz, 1H), 7.42 (s, 1H), 6.91 (d, $J$ = 8.0 Hz, 1H), 3.25 (s, 3H), 2.19 (d, $J$ = 14.4 Hz, 1H), 1.89 (d, $J$ = 14.4 Hz, 1H), 1.32 (s, 3H), 0.60 (s, 9H).

$^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 181.04, 181.04, 145.97, 135.02, 131.36 – 131.16 (m), 126.01, 125.49 (q, $J$ = 3.9 Hz), 124.67, 124.35, 123.31, 121.02 (q, $J$ = 3.6 Hz), 107.87, 50.98, 47.53, 31.92, 30.93, 28.26, 26.58.

(3j) 1,3-dimethyl-3-neopentyl-2-oxoindoline-5-carbonitrile

The title compound was prepared according to the general procedure described above by the reaction between N-(4-cyanophenyl)-N-methylmethacrylamide (1j) with pivalaldehyde (2a), and purified by flash column chromatography as light white solid (38.40 mg, 75%).

M.p. 174-175°C; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.61 (s, 1H), 7.44 (s, 1H), 6.92 (s, 1H), 3.25 (s, 3H), 2.18 (d, $J$ = 14.4 Hz, 1H), 1.87 (d, $J$ = 14.4 Hz, 1H), 1.31 (s, 3H), 0.61 (s, 9H).

$^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 180.63, 146.80, 135.42, 133.09, 127.14, 119.47, 108.59, 105.21, 50.85, 47.29, 31.87, 30.93, 28.17, 26.56. IR(cm$^{-1}$): 2941, 2216, 1717, 1607, 1499, 1346, 813. MS (EI) m/z (%): 256(68)[M]$^+$, 201(31), 186(100), 155(13).

(3k) 1,3,7-trimethyl-3-neopentylindolin-2-one $^2$

S7
The title compound was prepared according to the general procedure described above by the reaction between N-methyl-N-(o-tolyl)methacrylamide (1j) with pivalaldehyde (2a), and purified by flash column chromatography as light yellow oil (23.03 mg, 47%).

$^{1}$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.03 (d, $J = 7.2$ Hz, 1H), 6.98 (d, $J = 7.2$ Hz, 1H), 6.91 (t, $J = 7.4$ Hz, 1H), 3.50 (s, 3H), 2.59 (s, 3H), 2.13 (d, $J = 14.4$ Hz, 1H), 1.82 (d, $J = 14.4$ Hz, 1H), 1.27 (s, 3H), 0.61 (s, 9H).

$^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 181.91, 140.75, 134.91, 131.31, 121.97, 121.95, 119.70, 51.11, 46.82, 31.89, 30.95, 29.70, 28.78, 19.22.

(3l) 1,3,6-trimethyl-3-neopentylindolin-2-one and 1,3,4-trimethyl-3-neopentylindolin-2-one

[A mixture of regio-isomers (1,3,5-trimethyl-3-neopentylindolin-2-one and 1,3,4-trimethyl-3-neopentylindolin-2-one) in a ratio of 66:34]

The title compound was prepared according to the general procedure described above by the reaction between N-methyl-N-(m-tolyl)methacrylamide (1k) with pivalaldehyde (2a), and purified by flash column chromatography as light yellow oil (38.22 mg, 78%).

$^{1}$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.17 (t, $J = 7.7$ Hz, 0.38×1H), 7.07 (d, $J = 7.4$ Hz, 0.69×1H), 6.84 (d, $J = 7.3$ Hz, 0.67×1H), 6.80 (d, $J = 7.7$ Hz, 0.36×1H), 6.69 (d, $J = 13.1$ Hz, 1H), 3.20 (s, 3H), 2.39 (s, 3H), 2.15-2.09 (m, 0.76×2H), 1.83 (d, $J = 14.4$ Hz, 0.36×2H), 1.36 (s, 0.34×3H), 1.27 (s, 0.70×3H), 0.62 (d, $J = 7.4$ Hz, 9H).

$^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 181.47, 181.14, 143.18, 142.97, 137.63, 134.97, 131.26, 127.55, 125.00, 123.69, 122.60, 109.06, 105.86, 105.83, 49.18, 48.27, 47.27, 31.82, 30.91, 30.09, 28.46, 26.37, 26.27, 25.34, 21.87, 18.83. HRMS: calcd. for [M+H]$^+$ C$_{16}$H$_{22}$NO: 246.18538; found: 246.18524.

(3m) 7-chloro-1,3-dimethyl-3-neopentylindolin-2-one

The title compound was prepared according to the general procedure described above by the reaction between N-(2-chlorophenyl)-N-methylmethacrylamide (1l) with pivalaldehyde (2a), and purified by flash column chromatography as light yellow oil (31.27 mg, 59%).

$^{1}$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.18 (d, $J = 7.6$ Hz, 1H), 7.07 (d, $J = 6.8$ Hz, 1H), 6.93 (t, $J = 7.6$ Hz, 1H), 3.59 (s, 3H), 2.15 (d, $J = 14.4$ Hz, 1H), 1.83 (d, $J = 14.3$ Hz, 1H), 1.28 (s, 3H), 0.62 (s, 9H).

$^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 181.31, 138.88, 137.17, 129.97, 122.87, 122.48, 115.58, 51.17, 47.31, 31.93, 30.98, 29.71, 28.70. IR(cm$^{-1}$): 2957, 1718, 1605, 1583, 1470, 1364, 739. HRMS: calcd. for [M+H]$^+$ C$_{16}$H$_{22}$NOCl: 266.13112; found:266.13062.

(3n) 6,7-dichloro-1,3-dimethyl-3-neopentylindolin-2-one
The title compound was prepared according to the general procedure described above by the reaction between N-(2,3-dichlorophenyl)-N-methylmethacrylamide (1m) with pivalaldehyde (2a), and purified by flash column chromatography as light yellow oil (38.27 mg, 64%). M.p. 75-76 °C; \( ^1H \) NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.14 (d, \( J = 8.0 \) Hz, 1H), 7.01 (d, \( J = 7.6 \) Hz, 1H), 3.62 (s, 3H), 2.16 (d, \( J = 14.4 \) Hz, 1H), 1.82 (d, \( J = 14.4 \) Hz, 1H), 1.27 (s, 3H), 0.63 (s, 9H). \( ^{13}C \) NMR (100 MHz, CDCl\(_3\)) \( \delta \) 181.31, 140.68, 135.22, 132.96, 123.63, 122.66, 114.7 7,51.10, 47.14, 31.95, 31.02, 30.01, 28.67. IR(cm\(^{-1}\)): 2960, 2363, 1714, 1602, 1493, 1462, 1362, 807. HRMS: calcd. for [M+H]\(^+\) C\(_{15}\)H\(_{20}\)NOCl\(_2\): 300.09222; found: 266.09165.

(3o) 3-(methoxymethyl)-1-methyl-3-neopentylindolin-2-one

The title compound was prepared according to the general procedure described above by the reaction between N-ethyl-2-(methoxymethyl)-N-phenylacrylamide (1n) with pivalaldehyde (2a), and purified by flash column chromatography as light yellow solid (45.41 mg, 87%). M.p. 73-74 °C; \( ^1H \) NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.30 – 7.27 (m, 2H), 7.03 (t, \( J = 7.6 \) Hz, 1H), 6.84 (d, \( J = 8.0 \) Hz, 1H), 3.54 (d, \( J = 8.4 \) Hz, 1H), 3.44 (d, \( J = 8.8 \) Hz, 1H), 3.20 (d, \( J = 16.4 \) Hz, 6H), 2.02 (d, \( J = 14.0 \) Hz, 1H), 1.92 (d, \( J = 14.4 \) Hz, 1H), 0.62 (s, 9H). \( ^{13}C \) NMR (100 MHz, CDCl\(_3\)) \( \delta \) 178.83, 144.02, 131.24, 128.03, 124.89, 121.98, 108.04, 79.48, 59.69, 53.02, 45.66, 31.76, 31.12, 26.40. IR(cm\(^{-1}\)): 2953, 2655, 1702, 1612, 1468, 1380, 1344, 748. HRMS: calcd. for [M+Na]\(^+\) C\(_{16}\)H\(_{23}\)NO\(_2\)Na: 284.16220; found: 284.16210.

(3p) (1-methyl-3-neopentyl-2-oxoindolin-3-yl)methyl acetate

The title compound was prepared according to the general procedure described above by the reaction between 2-(ethyl(phenyl)carbamoyl)allyl acetate (1o) with pivalaldehyde (2a), and purified by flash column chromatography as light yellow oil (52.60 mg, 91%). \( ^1H \) NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.29 (t, \( J = 7.6 \) Hz, 1H), 7.23 (d, \( J = 7.2 \) Hz, 1H), 7.03 (t, \( J = 7.6 \) Hz, 1H), 6.85 (d, \( J = 7.6 \) Hz, 1H), 4.41 (d, \( J = 10.4 \) Hz, 1H), 4.01 (d, \( J = 10.4 \) Hz, 1H), 3.23 (s, 3H), 2.07 (d, \( J = 14.4 \) Hz, 1H), 1.89 (d, \( J = 14.0 \) Hz, 1H), 1.81 (s, 3H), 0.64 (s, 9H). \( ^{13}C \) NMR (100 MHz, CDCl\(_3\)) \( \delta \) 178.05, 170.43, 144.03, 129.66, 128.47, 125.00, 122.18, 108.14, 69.55, 51.66, 45.46, 31.78, 31.07, 26.44, 20.63. IR(cm\(^{-1}\)): 3060, 2949, 2364, 1719, 1618, 1498, 1467, 1372, 1215, 750. HRMS: calcd. for [M+Na]\(^+\) C\(_{17}\)H\(_{23}\)NO\(_3\)Na: 312.15710; found: 312.15701.

(3q) 1-ethyl-3-methyl-3-neopentylindolin-2-one
The title compound was prepared according to the general procedure described above by the reaction between N-ethyl-N-phenylmethacrylamide (1p) with pivalaldehyde (2a), and purified by flash column chromatography as light yellow solid (31.85 mg, 65%).

**M.p. 60-61 °C;**

H NMR (400 MHz, CDCl$_3$) $\delta$ 7.22 (dd, $J = 13.6, 8.0$ Hz, 2H), 7.02 (t, $J = 7.6$ Hz, 1H), 6.87 (d, $J = 7.6$ Hz, 1H), 3.915-3.826 (m, 1H), 3.730-3.641 (m, 1H), 2.16 (d, $J = 14.4$ Hz, 1H), 1.86 (d, $J = 14.4$ Hz, 1H), 1.36 – 1.20 (m, 3H), 0.63 (s, 9H).

C NMR (100 MHz, CDCl$_3$) $\delta$ 180.70, 142.08, 134.59, 127.55, 124.22, 121.83, 108.29, 50.70, 47.53, 34.64, 31.98, 31.02, 28.76, 12.37.

IR (cm$^{-1}$): 2955, 2363, 1703, 1610, 1487, 1466, 1374, 753. HRMS: calcd. for [M+H]$^+$ C$_{16}$H$_{24}$NO: 246.18547; found: 246.18524.

(3r) 3-methyl-3-neopentyl-1-phenylindolin-2-one

The title compound was prepared according to the general procedure described above by the reaction between N,N-diphenylmethacrylamide (1q) with pivalaldehyde (2a), and purified by flash column chromatography as white solid (42.19 mg, 72%).

**M.p. 103-104 °C;**

H NMR (400 MHz, CDCl$_3$) $\delta$ 7.52 (t, $J = 7.6$ Hz, 2H), 7.40 (dd, $J = 13.6, 7.6$ Hz, 3H), 7.27 (d, $J = 7.6$ Hz, 1H), 7.18 (t, $J = 7.6$ Hz, 1H), 7.07 (t, $J = 7.6$ Hz, 1H), 6.86 (d, $J = 8.0$ Hz, 1H), 2.25 (d, $J = 14.4$ Hz, 1H), 1.95 (d, $J = 14.4$ Hz, 1H), 1.42 (s, 3H), 0.73 (s, 9H).

C NMR (100 MHz, CDCl$_3$) $\delta$ 180.43, 142.83, 135.00, 134.12, 129.67, 127.91, 127.55, 126.42, 124.39, 122.56, 109.57, 51.13, 47.73, 32.10, 31.15, 29.03. IR (cm$^{-1}$): 2949, 2363, 1713, 1608, 1496, 1470, 1375, 754, 692.

(3s) 1-benzyl-3-methyl-3-neopentylindolin-2-one

The title compound was prepared according to the general procedure described above by the reaction between N-benzyl-N-phenylmethacrylamide (1r) with pivalaldehyde (2a), and purified by flash column chromatography as light yellow solid (38.07 mg, 62%).

**M.p. 107-108 °C;**

H NMR (400 MHz, CDCl$_3$) $\delta$ 7.34 – 7.27 (m, 5H), 7.20 (d, $J = 7.2$ Hz, 1H), 7.14 (d, $J = 7.6$ Hz, 1H), 7.01 (d, $J = 7.2$ Hz, 1H), 6.77 (d, $J = 7.6$ Hz, 1H), 5.06 (d, $J = 15.6$ Hz, 1H), 4.78 (d, $J = 15.6$ Hz, 1H), 2.21 (d, $J = 14.4$ Hz, 1H), 1.90 (d, $J = 14.4$ Hz, 1H), 1.35 (s, 4H), 0.64 (s, 9H).

C NMR (100 MHz, CDCl$_3$) $\delta$ 181.22, 142.20, 136.27, 134.39, 128.82, 127.77, 127.57, 127.54, 124.12, 122.10, 109.26, 50.67, 47.64, 44.08, 32.00, 31.08, 29.19. IR (cm$^{-1}$): 2949, 2363, 1713, 1608, 1496, 1470, 1375, 754, 693. HRMS: calcd. for [M+H]$^+$ C$_{21}$H$_{26}$NO: 308.20102, found: 308.20089.
(4b) 3-isobutyl-1,3-dimethylindolin-2-one

The title compound was prepared according to the general procedure described above by the reaction between N-methyl-N-phenylmethacrylamide (1a) with isobutyaldehyde (2b), and purified by flash column chromatography as light yellow oil (27.78 mg, 64%).

\[
^1H\text{ NMR (400 MHz, CDCl}_3\delta^{7.26 (t, J = 7.6 Hz, 1H), 7.16 (d, J = 7.2 Hz, 1H), 7.06 (t, J = 7.6 Hz, 1H), 6.84 (d, J = 7.6 Hz, 1H), 3.22 (s, 3H), 1.94 (dd, J = 14.0, 7.6 Hz, 1H), 1.76 (dd, J = 14, 5.6 Hz, 1H), 1.32 (s, 3H), 1.24 (m, 1H), 0.65 (d, J = 6.8 Hz, 3H), 0.61 (d, J = 6.4 Hz, 3H).}
\]

\[
^{13}C\text{ NMR (100 MHz, CDCl}_3\delta^{181.19, 143.29, 134.31, 127.66, 122.91, 122.43, 108.05, 48.18, 46.84, 26.28, 26.24, 25.63, 24.22, 22.93.}
\]

(4c) 1,3-dimethyl-3-(2-methylbutyl)indolin-2-one

The title compound was prepared according to the general procedure described above by the reaction between N-methyl-N-phenylmethacrylamide (1a) with 2-methylbutyaldehyde (2c), and purified by flash column chromatography as light yellow oil (34.19 mg, 74%).

\[
^1H\text{ NMR (400 MHz, CDCl}_3\delta^{7.30-7.24 (m, 1H), 7.18-7.14 (m, 1H), 7.08-7.03 (m, 1H), 3.21 (s, 3H), 2.05-2.00 (m, 0.57×1H), 1.86 (d, J = 5.7 Hz, 1H), 1.68-1.64 (m, 0.60×1H), 1.33 (s, 3H), 1.16-0.92 (m, 3H), 0.74-0.69 (m, 3H), 0.60 (d, J = 6.2 Hz, 0.59×3H), 0.49 (d, J = 6.4 Hz, 0.52×3H).}
\]

\[
^{13}C\text{ NMR (100 MHz, CDCl}_3\delta^{181.40, 143.30, 134.65, 134.13, 127.64, 122.95, 122.88, 122.42, 122.37, 110.09, 108.02, 108.00, 48.26, 48.00, 45.12, 44.51, 31.74, 31.67, 30.82, 30.15, 26.29, 26.23, 25.88, 20.41, 19.37, 11.16, 11.03. IR(cm}^{-1})\text{: 3059, 2933, 1705, 1607, 1496, 1467, 1374, 756. HRMS: calcd. for [M+H]^+\text{ C}_{15}H_{22}NO: 232.16995, found: 232.16959.}
\]

(4d) 1,3-dimethyl-3-(2-methylpentyl)indolin-2-one

The title compound was prepared according to the general procedure described above by the reaction between N-methyl-N-phenylmethacrylamide (1a) with methyl valeraldehyde (2d), and purified by flash column chromatography as light yellow oil (36.75 mg, 75%).

\[
^1H\text{ NMR (400 MHz, CDCl}_3\delta^{7.28-7.24 (m, 1H), 7.18-7.14 (m, 1H), 7.08-7.03 (m, 1H), 3.21 (s, 3H), 2.04-1.99 (m, 0.51×1H), 1.86 (d, J = 6.0 Hz, 1H), 1.68-1.63 (m, 0.53×1H), 1.33 (s, 3H), 1.26-0.89 (m, 5H), 0.77-0.69 (m, 3H), 0.60 (d, J = 6.4 Hz, 0.53×3H), 0.50 (d, J = 6.5 Hz, 0.63×3H).}
\]

\[
^{13}C\text{ NMR (100 MHz, CDCl}_3\delta^{165.97, 142.06, 134.45, 129.64, 127.63, 127.01, 126.92, 124.88, 118.93, 37.85, 29.72, 20.27, 12.49.}
\]

(4e) 3-(cyclohexylmethyl)-1,3-dimethylindolin-2-one

The title compound was prepared according to the general procedure described above by the reaction between N-methyl-N-phenylmethacrylamide (1a) with methyl valeraldehyde (2d), and purified by flash column chromatography as light yellow oil (36.75 mg, 75%).

\[
^1H\text{ NMR (400 MHz, CDCl}_3\delta^{7.28-7.24 (m, 1H), 7.18-7.14 (m, 1H), 7.08-7.03 (m, 1H), 3.21 (s, 3H), 2.04-1.99 (m, 0.51×1H), 1.86 (d, J = 6.0 Hz, 1H), 1.68-1.63 (m, 0.53×1H), 1.33 (s, 3H), 1.26-0.89 (m, 5H), 0.77-0.69 (m, 3H), 0.60 (d, J = 6.4 Hz, 0.53×3H), 0.50 (d, J = 6.5 Hz, 0.63×3H).}
\]

\[
^{13}C\text{ NMR (100 MHz, CDCl}_3\delta^{165.97, 142.06, 134.45, 129.64, 127.63, 127.01, 126.92, 124.88, 118.93, 37.85, 29.72, 20.27, 12.49.}
\]

\[^3\text{Z.-J Li, Y. Zhang, L.-Z Zhang, and Z.-Q Liu, Org. Lett. 2014, 16, 382.}
\]
The title compound was prepared according to the general procedure described above by the reaction between N-methyl-N-phenylmethacrylamide (1a) with cyclohexanecarbaldehyde (2e), and purified by flash column chromatography as light yellow oil (38.55 mg, 75%).

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.26 (s, 1H), 7.15 (d, $J = 6.4$ Hz, 1H), 7.06 (d, $J = 6.4$ Hz, 1H), 6.84 (d, $J = 6.8$ Hz, 1H), 3.22 (s, 3H), 1.92 (dd, $J = 13.6$, 6.0 Hz, 1H), 1.72 (d, $J = 13.6$ Hz, 1H), 1.46 (d, $J = 9.2$ Hz, 3H), 1.31 (s, 3H), 1.20 (d, $J = 12.4$ Hz, 1H), 1.09 – 0.65 (m, 7H).

$^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 181.27, 143.15, 134.45, 127.61, 122.80, 122.44, 108.06, 47.95, 45.48, 34.82, 34.53, 33.58, 26.31, 26.17, 26.11.

(4f) 3-isopentyl-1,3-dimethylindolin-2-one

The title compound was prepared according to the general procedure described above by the reaction between N-methyl-N-phenylmethacrylamide (1a) with 3-methylbutanal (2f), and purified by flash column chromatography as light yellow oil (15.25 mg, 33%).

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.26 (d, $J = 14.4$ Hz, 1H), 7.16 (d, $J = 7.2$ Hz, 1H), 7.06 (t, $J = 7.6$ Hz, 1H), 6.84 (d, $J = 7.6$ Hz, 1H), 3.21 (s, 3H), 1.92-1.84 (m, 1H), 1.76-1.69 (m, 1H), 1.35 (s, 3H), 0.96 – 0.82 (m, 1H), 0.77 (t, $J = 6.8$Hz, 6H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 181.03, 143.46, 134.44, 127.68, 122.56, 107.99, 48.49, 36.48, 33.30, 28.28, 26.24, 24.00, 22.61, 22.40.

IR(cm$^{-1}$): 3057, 2962, 1703, 1610, 1495, 1472, 1387, 753. HRMS: calcd. for [M+H]$^+$ C$_{15}$H$_{22}$N O:232.16998found: 232.16959.

(4g) 3-hexyl-1,3-dimethylindolin-2-one

The title compound was prepared according to the general procedure described above by the reaction between N-methyl-N-phenylmethacrylamide (1a) with hexanal (2g), and purified by flash column chromatography as light yellow oil (21.07 mg, 43%).

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.26 (t, $J = 8.0$ Hz, 1H), 7.17 (d, $J = 6.4$ Hz, 1H), 7.07 (t, $J = 7.2$ Hz, 1H), 6.84 (d, $J = 7.6$ Hz, 1H), 3.21 (s, 3H), 1.88 (td, $J = 12.8$, 4.4 Hz, 1H), 1.72 (td, $J = 12.8$, 4.4 Hz, 1H), 1.35 (s, 3H), 1.27 – 0.89 (m, 8H), 0.80 (t, $J = 6.8$ Hz, 3H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 181.03, 143.44, 134.45, 127.68, 122.58, 122.53, 107.97, 48.59, 38.66, 31.64, 29.52, 26.23, 24.52, 23.92, 22.67, 14.14.

(4h) 1,3-dimethyl-3-phenethylindolin-2-one

The title compound was prepared according to the general procedure described above by the reaction between N-methyl-N-phenylmethacrylamide (1a) with 2-phenylacetaldehyde (2h), and purified by flash column chromatography as light yellow oil (30.74 mg, 58%).

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.29 (dd, $J = 15.8, 7.6$ Hz, 1H), 7.21 (dd, $J = 13.6, 6.8$ Hz, 3H), 7.12 (dd, $J = 14.8, 7.2$ Hz, 2H), 7.02 (d, $J = 7.2$ Hz, 2H), 6.87 (d, $J = 7.6$ Hz, 1H), 3.21 (s, 3H), 2.43 – 2.20 (m, 2H), 2.19 – 2.08 (m, 1H), 2.07 – 1.91 (m, 1H), 1.40 (s, 3H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 180.46, 143.53, 141.50, 133.86, 128.39, 128.34, 127.95, 125.95, 122.71, 122.59, 108.13, 48.49, 40.35, 31.08, 26.24, 24.07.

(4i) 1,3-dimethyl-3-(3-phenylpropyl)indolin-2-one

The title compound was prepared according to the general procedure described above by the reaction between N-methyl-N-phenylmethacrylamide (1a) with 3-phenylpropanal (2i), and purified by flash column chromatography as light yellow oil (25.11 mg, 45%).

$^1$H NMR (400 MHz, D$_2$O) $\delta$ 7.22 (dd, $J = 13.6, 7.2$ Hz, 3H), 7.13 (t, $J = 7.2$ Hz, 2H), 7.05 (t, $J = 7.2$ Hz, 3H), 6.82 (d, $J = 7.6$ Hz, 1H), 3.20 (s, 3H), 2.80 – 2.28 (m, 2H), 1.96 (td, $J = 13.2, 4.4$ Hz, 1H), 1.78 (td, $J = 12.8, 4.0$ Hz, 1H), 1.34 (s, 5H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 180.85, 143.42, 142.04, 134.16, 128.48, 128.37, 127.80, 125.87, 122.60, 108.07, 48.49, 38.27, 36.09, 26.51, 26.27, 24.01.
VI. Copies of 1H and 13C NMR spectra of products
$\text{H}_2\text{CO}$

S18
3l and

66% 34%
3m

![Chemical Structure](image)

**S39**