Supporting Information

Synthesis of Isoquinoline-1,3(2H,4H)-dione Derivatives via Cascade Reactions of $N$-Alkyl-$N$-methacryloyl Benzamide with Aryl Aldehydes

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Experimental section
**General:** All reactions were carried out under an atmosphere of nitrogen; stirring was achieved with an oven-dried magnetic stirring bar. Solvents were purified by standard methods unless otherwise noted. Commercially available reagents were purchased from Aladdin Company in China and used throughout without further purification other than those detailed below. Flash column chromatography was performed on silica gel (200-300 mesh). All reactions were monitored by TLC analysis. Deuterated solvents were purchased from Cambridge Isotope laboratories. $^1$H and $^{13}$C NMR spectra were recorded on a Bruker DRX-400 spectrometer operating at 400 MHz and 100 MHz respectively. Mass spectrometry (LC-MS) was recorded on a LXQ Spectrometer (Thermo Scientific) operating on ESI (MeOH as a solvent)

**General procedure for the synthesis of compounds 3a-h**

$N$-Methyl-$N$-phenylacrylamide (2.0 mmol, 1.0 equiv) was added to a dried flask, followed by the addition of benzaldehyde (10 mmol, 5.0 equiv). Then aqueous TBHP (3.0 equiv., 70 wt% in water) was injected into the flask under $N_2$. The reaction mixture was stirred at 90 °C for 24 h. After the reaction was completed, the reaction mixture was concentrated under reduced pressure and purified by flash chromatography (Petroleum ether: EtOAc =20:1) to provide the title compound 3a as a sticky solid in a 75% yield. The same procedure was applied for producing other compounds 3b-h.

**4-(2-(4-methoxyphenyl)-2-oxoethyl)-2,4-dimethylisoquinoline-1,3(2$H,4$H)-dione (3a)**

![Chemical Structure](image)

**IR:** 2925, 2854, 2360, 1712, 1665, 1605, 764, 702 cm$^{-1}$; $^1$H-NMR (CDCl$_3$, 400MHz): δ (ppm) 8.30-6.85 (aromatic H, 8H), 4.16 (d, $J=16.2$ Hz, 1H), 3.96 (d, $J=16.2$ Hz, 1H), 3.80 (s, 3H), 3.44 (s, 3H), 1.60 (s, 3H); $^{13}$C-NMR (CDCl$_3$,100 Hz): 1964.7, 176.9, 164.7, 163.8, 143.9, 133.7,
130.3, 129.2, 129.0, 127.0, 125.0, 123.7, 113.8, 55.4, 48.9, 44.6, 29.7, 27.3; MS (ESI) m/z calculated for C_{18}H_{17}NNaO_{2} 360.13 (M+Na)^+, found 360.21.

4-(2-(4-bromophenyl)-2-oxoethyl)-2,4-dimethylisoquinoline-1,3(2H,4H)-dione (3b)

![Chemical Structure of 4-(2-(4-bromophenyl)-2-oxoethyl)-2,4-dimethylisoquinoline-1,3(2H,4H)-dione (3b)]

IR: 2968, 2924, 2360, 1705, 1672, 1602, 758, 704 cm^{-1}; \textbf{1H-NMR} (CDCl$_3$, 400MHz): \delta (ppm) 8.33-7.28 (aromatic H, 8H), 4.22 (d, J=16.2 Hz, 1H), 4.17 (d, J=16.2 Hz, 1H), 3.46 (s, 3H), 1.63 (s, 3H); \textbf{13C-NMR} (CDCl$_3$,100Hz): 195.3, 176.6, 143.5, 134.6, 133.8, 132.0, 129.5, 129.4, 128.8, 127.3, 125.0, 123.5, 49.1, 44.5, 29.4, 27.3; MS (ESI) m/z calculated for C_{19}H_{19}NNaO_{3} 408.03 (M+Na)^+, found 408.32.

2-ethyl-4-methyl-4-(2-oxo-2-(p-tolyl)ethyl)isoquinoline-1,3(2H,4H)-dione (3c)

![Chemical Structure of 2-ethyl-4-methyl-4-(2-oxo-2-(p-tolyl)ethyl)isoquinoline-1,3(2H,4H)-dione (3c)]

IR: 2978, 2933, 2361, 1709, 1663, 1606, 760, 704 cm^{-1}; \textbf{1H-NMR} (CDCl$_3$, 400MHz): \delta (ppm) 8.31-7.19 (aromatic H, 8H), 4.19 (d, J=17.6 Hz, 1H), 4.13 (m, 2H), 3.99 (d, J=17.6 Hz, 1H), 3.37 (s, 3H), 1.60 (s, 3H), 1.28 (t, J=8.0 Hz, 3H); \textbf{13C-NMR} (CDCl$_3$,100 Hz): 195.8, 176.3, 164.2, 144.3, 143.9, 133.7, 133.6, 129.3, 129.3, 128.1, 127.1, 125.2, 123.6, 49.0, 44.5, 30.8, 21.6, 12.9; MS (ESI) m/z calculated for C_{19}H_{19}NNaO_{3} 358.15 (M+Na)^+, found 358.27.

2-isopropyl-4-methyl-4-(2-oxo-2-phenylethyl)isoquinoline-1,3(2H,4H)-dione (3d)
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\begin{align*}
\text{IR: } & 2964, 2928, 2869, 1715, 1614, 734, 700 \text{ cm}^{-1}; \textbf{H-NMR} (\text{CDCl}_3, 400\text{MHz}): \delta (\text{ppm}) 8.30-7.24 \\
& (\text{aromatic H, 9H}), 5.27 (\text{m, 1H}), 4.20 (\text{d, } J=17.6 \text{ Hz, 1H}), 3.96 (\text{d, } J=17.6 \text{ Hz, 1H}), 1.61 (\text{s, 3H}), \\
& 1.55 (\text{d, } J=6.8 \text{ Hz, 3H}), 1.53 (\text{d, } J=6.8 \text{ Hz, 3H}); \textbf{C-NMR} (\text{CDCl}_3, 100\text{Hz}): 196.1, 176.7, 164.7, \\
& 143.7, 136.1, 133.5, 133.4, 129.3, 128.6, 128.0, 127.0, 125.7, 123.5, 49.0, 45.4, 44.8, 30.8, 19.8; \textbf{MS} (\text{ESI}) m/z \text{calculated for } C_{22}H_{25}NNaO_2 \text{ 358.15 (M+Na)^+}, \text{found 358.28.}
\end{align*}

2-isopropyl-4-methyl-4-(2-oxo-2-(p-tolyl)ethyl)isoquinoline-1,3(2\textit{H},4\textit{H})-dione (3e)

\begin{align*}
\text{IR: } & 2971, 2928, 2360, 1709, 1661, 1602, 760, 704 \text{ cm}^{-1}; \textbf{H-NMR} (\text{CDCl}_3, 400\text{MHz}): \delta (\text{ppm}) 8.30-7.20 \\
& (\text{aromatic H, 8H}), 5.27 (\text{m, 1H}), 4.17 (\text{d, } J=17.6 \text{ Hz, 1H}), 3.93 (\text{d, } J=17.6 \text{ Hz, 1H}), 2.38 \\
& (\text{s, 3H}), 1.60 (\text{s, 3H}), 1.55 (\text{d, } J=6.8 \text{ Hz, 3H}), 1.54 (\text{d, } J=6.8 \text{ Hz, 3H}); \textbf{C-NMR} (\text{CDCl}_3, 100\text{Hz}): \\
& 195.7, 176.7, 164.7, 144.2, 143.8, 133.7, 133.4, 129.3, 129.2, 128.1, 127.0, 125.7, 123.4, 48.8, \\
& 45.4, 44.8, 30.8, 21.6, 19.8; \textbf{MS} (\text{ESI}) m/z \text{calculated for } C_{19}H_{16}NNaO_2 \text{ 372.17 (M+Na)^+}, \text{found 372.23.}
\end{align*}

2-isopropyl-4-(2-(4-methoxyphenyl)-2-oxoethyl)-4-methylisoquinoline-1,3(2\textit{H},4\textit{H})-dione (3f)
IR: 2968, 2931, 2361, 1709, 1661, 1600, 759, 705 cm⁻¹; \(^1\)H-NMR (CDCl₃, 400MHz): δ (ppm) 8.28-6.85 (aromatic H, 8H), 5.26 (m, 1H), 4.14 (d, J=17.6 Hz, 1H), 3.90 (d, J=17.6 Hz, 1H), 3.82 (s, 3H) 1.59 (s, 3H), 1.54 (d, J=6.8 Hz, 3H), 1.53 (d, J=6.8 Hz, 3H); \(^{13}\)C-NMR (CDCl₃, 100Hz): 194.6, 176.7, 164.7, 143.8, 133.4, 130.2, 129.2, 127.0, 125.7, 123.4, 113.7, 55.5, 48.6, 45.3, 44.8, 30.7, 19.5; MS (ESI) m/z calculated for C\(_{20}\)H\(_{21}\)NNaO\(_2\) 388.16 (M+Na)\(^+\), found 388.37.

4-(2-(4-(tert-butyl)phenyl)-2-oxoethyl)-2-isopropyl-4-methylisoquinoline-1,3(2\(H\),4\(H\))-dione (3g)

IR: 2966, 2871, 2359, 1709, 1663, 1604, 765, 704 cm⁻¹; \(^1\)H-NMR (CDCl₃, 400MHz): δ (ppm) 8.30-7.23 (aromatic H, 8H), 5.27 (m, 1H), 4.19 (d, J=17.6 Hz, 1H), 3.95 (d, J=17.6 Hz, 1H), 1.61 (s, 3H), 1.55 (d, J=6.8 Hz, 3H), 1.53 (d, J=6.8 Hz, 3H), 1.33 (s, 9H); \(^{13}\)C-NMR (CDCl₃, 100 Hz): 194.6, 176.7, 164.7, 143.8, 133.4, 130.2, 129.2, 127.0, 125.7, 123.4, 113.7, 55.5, 48.6, 45.3, 44.8, 30.7, 19.5; MS (ESI) m/z calculated for C\(_{20}\)H\(_{21}\)NNaO\(_3\) 414.21 (M+Na)\(^+\), found 414.42.
4-(2-(4-bromophenyl)-2-oxoethyl)-2-isopropyl-4-methylisoquinoline-1,3(2H,4H)-dione (3h)

IR: 2972, 2928, 2361, 1709, 1686, 1604, 765, 706 cm\(^{-1}\); \(^1\)H-NMR (CDCl\(_3\), 400MHz): \(\delta\) (ppm) 8.30-7.22 (aromatic H, 8H), 5.25 (m, 1H) 4.17 (d, \(J=17.6\) Hz, 1H), 3.88 (d, \(J=17.6\) Hz, 1H), 1.59 (s, 3H), 1.54 (d, \(J=6.8\) Hz, 3H), 1.53 (d, \(J=6.8\) Hz, 3H); \(^1\)C-NMR (CDCl\(_3\),100 Hz): 195.2, 176.5, 164.6, 143.4, 134.8, 133.5, 131.9, 129.5, 129.4, 128.6, 127.2, 125.7, 123.3, 48.8, 45.5, 44.8, 30.8, 19.5; MS (ESI) m/z calculated for C\(_{23}\)H\(_{27}\)NNaO\(_2\), 436.06 (M+Na)\(^+\), found 436.42.