First report on the synthesis of isatins via pyridinium chlorochromate catalyzed intramolecular cyclization reactions

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1. General details

All the reactions were monitored by thin-layer chromatography (TLC) and were visualized using UV light. The product purification was done using silica gel column chromatography. Thin layer chromatography (TLC) characterization was performed with precoated silica gel GF254 (0.2mm), while column chromatography characterization was performed with silica gel (100-200mesh). \(^1\)H and \(^{13}\)C NMR spectra were recorded with tetramethylsilane as the internal standard. \(^1\)H NMR spectra were recorded at 400 or 600 MHz (Varian) and \(^{13}\)C NMR spectra were recorded 150 MHz (Varian). Chemical shifts are reported in ppm downfield from CDCl\(_3\) (δ = 7.26 ppm) for \(^1\)H NMR and relative to the central CDCl\(_3\) resonance (δ = 77.0 ppm) for \(^{13}\)C NMR spectroscopy. Coupling constants are given in Hz. Melting points were measured with YRT-3 melting point apparatus (Shantou Keyi Instrument & Equipment Co., Ltd., Shantou, China). High resolution mass spectroscopy data of the products were collected on a Waters Micromass GCT or a Bruker Apex IV FTMS instrument. All the N-methyl-2-oxo-N-phenylacetamide 1 were prepared according to the reported procedures.\(^1\)

2. General procedure for the synthesis of 2 (2a as an example)

![Diagram](image)

A mixture of N-methyl-2-oxo-N-phenylacetamide 1a (0.5 mmol) and PCC (0.5 mmol) were added in 2 mL DMSO with a condenser and then stirred under air at 100 °C for 3h. After the completion of the reaction (monitored by TLC), the reaction mixture was cooled to room temperature, diluted with water and extracted with ethyl acetate. The organic layer was washed with saturated brine, dried over anhydrous sodium sulfate and the solvent was evaporated to dryness. The crude residue was purified by flash chromatography on silica (PE/EA=10/1) to afford pure 1-methylindoline-2,3-dione 2a as a red solid (66 mg, 82% yield).
3. Spectroscopic characterization data of products

1-methylindoline-2,3-dione (2a)

\[
\begin{align*}
\text{ Yield } & 82\%; \text{ red solid; mp. } 130-133 \degree C; ^1H \text{ NMR (400 MHz, CDCl}_3\): } \delta 7.64-7.58 \text{ (m, 2H), } \\
& 7.14 \text{ (t, } J = 7.6 \text{ Hz, 1H), } 6.92 \text{ (d, } J = 8.0 \text{ Hz, 1H), } 3.26 \text{ (s, 3H)}; ^{13}C \text{ NMR (CDCl}_3\), 150 MHz): } \delta 183.3, 158.1, 151.4, 138.4, 125.1, 123.8, 117.3, 109.9, 26.2; \text{ HRMS (ESI): } m/z [M + Na]^{+} \text{ calcd for C}_9\text{H}_7\text{NO}_2\text{Na}^{+} 184.0369, \text{ found } 184.0372.
\end{align*}
\]

1-ethylindoline-2,3-dione (2b)

\[
\begin{align*}
\text{ Yield } & 83\%; \text{ red solid; mp. } 92-94 \degree C; ^1H \text{ NMR (400 MHz, CDCl}_3\): } \delta 7.62-7.58 \text{ (m, 2H), } \\
& 7.12 \text{ (t, } J = 7.6 \text{ Hz, 1H), } 6.93 \text{ (d, } J = 8.0 \text{ Hz, 1H), } 3.80 \text{ (q, } J = 7.6 \text{ Hz, 2H), } 1.32 \text{ (t, } J = 7.6 \text{ Hz, 3H)}; ^{13}C \text{ NMR (CDCl}_3\), 150 MHz): } \delta 182.3, 158.3, 151.4, 138.2, 125.2, 123.9, 117.0, 109.6, 36.0, 14.4; \text{ HRMS (ESI): } m/z [M + Na]^{+} \text{ calcd for C}_{10}\text{H}_9\text{NO}_2\text{Na}^{+} 198.0525, \text{ found } 198.0521.
\end{align*}
\]

1-butylindoline-2,3-dione (2c)

\[
\begin{align*}
\text{ Yield } & 81\%; \text{ red solid; mp. } 35-36 \degree C; ^1H \text{ NMR (400 MHz, CDCl}_3\): } \delta 7.61-7.57 \text{ (m, 2H), } \\
& 7.11 \text{ (t, } J = 7.2 \text{ Hz, 1H), } 6.90 \text{ (m, 1H), } 3.76-3.71 \text{ (m, 2H), } 1.73-1.64 \text{ (m, 2H), } 1.58 \text{ (q, } J = 7.6 \text{ Hz, 1H), } \\
& 1.42 \text{ (q, } J = 7.6 \text{ Hz, 1H), } 0.99 \text{ (t, } J = 7.6 \text{ Hz, 3H)}; ^{13}C \text{ NMR (CDCl}_3\), 150 MHz): } \delta 183.4, 158.5, 151.3, 138.5, 125.1, 123.5, 116.9, 109.8, 43.1, 31.0, 20.7, 13.8; \text{ HRMS (ESI): } m/z [M + Na]^{+} \text{ calcd for C}_{12}\text{H}_{13}\text{NO}_2\text{Na}^{+} 226.0838, \text{ found } 226.0843.
\end{align*}
\]

1-allylindoline-2,3-dione (2d)
Yield 78%; red solid; mp. 89-90 °C; $^1$H NMR (600 MHz, CDCl$_3$): δ 7.62 (d, $J = 7.2$ Hz, 1H), 7.57 (t, $J = 7.2$ Hz, 1H), 7.13 (t, $J = 7.2$ Hz, 1H), 6.90 (d, $J = 7.2$ Hz, 1H), 5.85 (m, 1H), 5.30 (m, 2H), 4.37 (d, $J = 5.4$ Hz, 2H); $^{13}$C NMR (CDCl$_3$, 150 MHz): δ 183.2, 157.8, 150.8, 138.3, 130.3, 125.4, 123.8, 118.6, 117.5, 110.8, 42.5; HRMS (ESI): m/z [M + Na$^+$] calcd for C$_{11}$H$_9$NO$_2$Na$^+$ 210.0525, found 210.0521.

1-(4-methoxybenzyl)indoline-2,3-dione (2e)

Yield 80%; red solid; mp. 169-171 °C; $^1$H NMR (400 MHz, CDCl$_3$): δ 7.59 (d, $J = 7.2$ Hz, 1H), 7.51-7.46 (m, 1H), 7.27 (d, $J = 8.8$ Hz, 2H), 7.08 (t, $J = 7.6$ Hz, 1H), 6.87 (d, $J = 8.8$ Hz, 2H), 6.81 (d, $J = 8.0$ Hz, 1H), 4.86 (s, 2H), 3.78 (s, 3H); $^{13}$C NMR (CDCl$_3$, 150 MHz): δ 183.3, 159.4, 158.2, 150.7, 138.2, 128.9, 126.4, 125.3, 123.7, 117.6, 114.3, 111.0, 55.2, 43.5; HRMS (ESI): m/z [M + Na$^+$] calcd for C$_{16}$H$_{13}$NO$_3$Na$^+$ 290.0788, found 290.0790.

1,5-dimethylindoline-2,3-dione (2f)

Yield 83%; red solid; mp. 149-150 °C; $^1$H NMR (400 MHz, CDCl$_3$): δ 7.42-7.28 (m, 2H), 6.79 (d, $J = 8.0$ Hz, 1H), 3.23 (s, 3H), 2.34 (s, 3H); $^{13}$C NMR (CDCl$_3$, 150 MHz): δ 182.2, 158.7, 151.5, 150.7, 125.3, 124.4, 115.2, 110.8, 26.2, 22.9; HRMS (ESI): m/z [M + Na$^+$] calcd for C$_{10}$H$_9$NO$_2$Na$^+$ 198.0525, found 198.0528.

5-methoxy-1-methylindoline-2,3-dione (2g)
Yield 84%; red solid; mp. 175-176 °C; \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 7.17-7.15 (m, 2H), 6.82 (d, \(J = 8.0\) Hz, 1H), 3.81 (s, 3H), 3.23 (s, 3H); \(^{13}\)C NMR (CDCl\(_3\), 150 MHz): \(\delta\) 183.8, 158.2, 156.6, 145.7, 124.0, 117.8, 110.9, 109.8, 55.5, 26.1; HRMS (ESI): m/z [M + Na\(^+\)] calcd for C\(_{10}\)H\(_9\)NO\(_3\)+Na\(^+\) 214.0475, found 214.0475.

5-chloro-1-methylindoline-2,3-dione (2h)

Yield 70%; red solid; mp. 171-173 °C; \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 7.59-7.56 (m, 2H), 6.86 (d, \(J = 9.2\) Hz, 1H), 3.26 (s, 3H); \(^{13}\)C NMR (CDCl\(_3\), 150 MHz): \(\delta\) 181.5, 158.2, 152.2, 144.3, 126.4, 124.0, 115.2, 110.5, 26.5; HRMS (ESI): m/z [M + Na\(^+\)] calcd for C\(_9\)H\(_6\)ClNO\(_2\)+Na\(^+\) 217.9979, found 217.9983.

5-bromo-1-methylindoline-2,3-dione (2i)

Yield 69%; red solid; mp. 163-164 °C; \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 7.74-7.70 (m, 2H), 6.82 (d, \(J = 8.0\) Hz, 1H), 3.26 (s, 3H); \(^{13}\)C NMR (CDCl\(_3\), 150 MHz): \(\delta\) 182.1, 157.4, 150.1, 140.6, 128.0, 118.5, 116.6, 111.6, 26.3; HRMS (ESI): m/z [M + Na\(^+\)] calcd for C\(_9\)H\(_6\)BrNO\(_2\)+Na\(^+\) 261.9474, found 261.9471.

1-methyl-5-nitroindoline-2,3-dione (2j)

Yield 65%; red solid; mp. 201-202 °C; \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 7.74-7.71 (m, 2H), 6.82 (d, \(J = 8.0\) Hz, 1H), 3.26 (s, 3H); \(^{13}\)C NMR (CDCl\(_3\), 150 MHz): \(\delta\) 182.1, 157.5, 150.1,
140.6, 128.0, 118.5, 116.6, 111.6, 29.6; HRMS (ESI): m/z [M + Na⁺] calcd for C₁₀H₉N₂O₄Na⁺ 229.0225, found 229.0222.

1,7-dimethylindoline-2,3-dione (2k)

Yield 78%; red solid; mp. 162-164 °C; ¹H NMR (400 MHz, CDCl₃): δ 7.46 (d, J = 7.6 Hz, 1H), 7.33 (d, J = 7.6 Hz, 1H), 7.01 (t, J = 7.6 Hz, 1H), 3.53 (s, 3H), 2.57 (s, 3H); ¹³C NMR (CDCl₃, 150 MHz): δ 182.7, 158.0, 151.8, 150.5, 125.5, 124.5, 115.5, 110.9, 26.1, 22.9; HRMS (ESI): m/z [M + Na⁺] calcd for C₁₀H₉NO₂Na⁺ 198.0525, found 198.0527.

1-ethyl-5-methylindoline-2,3-dione (2l)

Yield 80%; red solid; mp. 74-76 °C; ¹H NMR (400 MHz, CDCl₃): δ 7.42-7.38 (m, 2H), 6.80 (d, J = 8.0 Hz, 1H), 3.81 (q, J = 7.2 Hz, 2H), 2.39 (s, 3H), 1.30 (t, J = 7.2 Hz, 3H); ¹³C NMR (CDCl₃, 150 MHz): δ 184.0, 159.2, 148.3, 142.5, 123.2, 123.1, 121.7, 118.2, 36.9, 18.7, 14.5; HRMS (ESI): m/z [M + Na⁺] calcd for C₁₁H₁₁NO₂Na⁺ 212.0682, found 212.0685.

1,6-dimethylindoline-2,3-dione (2m)

Yield 78%; red solid; mp. 150-151 °C; ¹H NMR (400 MHz, CDCl₃): δ 7.49 (d, J = 7.6 Hz, 1H), 6.93 (d, J = 7.6 Hz, 1H), 6.70 (s, 1H), 3.32 (s, 3H), 2.40 (s, 3H); ¹³C NMR (CDCl₃, 150 MHz): δ 182.6, 158.9, 151.8, 150.7, 125.3, 124.4, 115.3, 110.7, 26.1, 22.9; HRMS (ESI): m/z [M + Na⁺] calcd for C₁₀H₉NO₂Na⁺ 198.0525, found 198.0528.

6-chloro-1-methylindoline-2,3-dione (2n)
Yield 68%; red solid; mp. 177-178 °C; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.55 (d, $J = 8.0$ Hz, 1H), 7.12 (dd, $J_1 = 1.6$ Hz, $J_2 = 8.0$ Hz, 1H), 6.91 (d, $J = 1.6$ Hz, 1H), 3.27 (s, 3H); $^{13}$C NMR (CDCl$_3$, 150 MHz): $\delta$ 181.7, 158.1, 152.4, 144.8, 126.3, 124.0, 115.7, 110.8, 26.4; HRMS (ESI): m/z [M + Na$^+$] calcd for C$_9$H$_6$ClNO$_2$Na$^+$ 217.9979, found 217.9983.

6-bromo-1-methylindoline-2,3-dione (2o)

Yield 65%; red solid; mp. 118-119 °C; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.47 (d, $J = 7.6$ Hz, 1H), 7.30 (dd, $J_1 = 1.2$ Hz, $J_2 = 7.6$ Hz, 1H), 7.09 (d, $J = 1.2$ Hz, 1H), 3.25 (s, 3H); $^{13}$C NMR (CDCl$_3$, 150 MHz): $\delta$ 182.3, 157.4, 150.2, 140.6, 128.1, 118.6, 116.5, 111.7, 26.3; HRMS (ESI): m/z [M + Na$^+$] calcd for C$_9$H$_6$BrNO$_2$Na$^+$ 261.9474, found 261.9471.

1-methyl-5-phenylindoline-2,3-dione (2p)

Yield 70%; red solid; mp. 182-184 °C; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.85-7.82 (m, 2H), 7.54-7.51 (m, 2H), 7.47-7.44 (m, 2H), 7.40-7.37 (m, 1H), 6.98 (d, $J = 8.0$ Hz, 1H), 3.29 (s, 3H); $^{13}$C NMR (CDCl$_3$, 150 MHz): $\delta$ 183.3, 160.1, 150.5, 139.3, 137.2, 136.5, 129.2, 127.9, 126.6, 123.5, 117.8, 110.5, 26.4; HRMS (ESI): m/z [M + Na$^+$] calcd for C$_{15}$H$_{11}$NO$_2$Na$^+$ 260.0682, found 260.0678.

5-(4-fluorophenyl)-1-methylindoline-2,3-dione (2q)

Yield 68%; red solid; mp. 136-139 °C; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.79-7.75 (m, 2H),
7.50-7.46 (m, 2H), 7.14 (t, \( J = 8.8 \) Hz, 2H), 6.98 (d, \( J = 8.0 \) Hz, 1H), 3.29 (s, 3H); \(^{13}\)C NMR (CDCl\(_3\), 150 MHz): \( \delta \) 183.3, 162.1(d, \( J_{C-F} = 246.8 \)Hz), 158.2, 150.4, 136.6, 136.3, 135.1, 128.2(d, \( J_{C-F} = 7.6 \)Hz), 123.5, 117.8, 115.9(d, \( J_{C-F} = 21.4 \)Hz), 110.3, 26.3; HRMS (ESI): m/z [M + Na\(^+\)] calcd for C\(_{15}\)H\(_{10}\)FNO\(_2\)+Na\(^+\) 278.0588, found 278.0585.

3-(1-methyl-2,3-dioxoindolin-5-yl)benzonitrile (2r)

![Diagram](image)

Yield 65%; red solid; mp. 236-237 °C; \(^1\)H NMR (400 MHz, DMSO-\( d_6 \)): \( \delta \) 8.22 (s, 1H), 8.10-8.04 (m, 2H), 7.94 (d, \( J = 1.6 \) Hz, 1H), 7.81 (d, \( J = 8.0 \) Hz, 1H), 7.65 (t, \( J = 8.0 \) Hz, 1H), 7.27 (d, \( J = 8.0 \) Hz, 1H), 3.20 (s, 3H); \(^{13}\)C NMR (DMSO-\( d_6 \), 150 MHz): \( \delta \) 183.4, 158.5, 151.4, 139.8, 136.6, 133.2, 131.2, 130.3, 130.1, 122.7, 118.9, 118.3, 112.3, 111.3, 26.4; HRMS (ESI): m/z [M + Na\(^+\)] calcd for C\(_{16}\)H\(_{10}\)N\(_2\)O\(_2\)+Na\(^+\) 285.0634, found 285.0638.

1-methyl-5-(thiophen-2-yl)indoline-2,3-dione (2s)

![Diagram](image)

Yield 70%; red solid; mp. 206-208 °C; \(^1\)H NMR (400 MHz, CDCl\(_3\)): \( \delta \) 7.84 (d, \( J = 1.6 \) Hz, 1H), 7.82 (s, 1H), 7.30 (dd, \( J_1 = 0.8 \) Hz, \( J_2 = 4.0 \) Hz, 1H), 7.27 (d, \( J = 2.4 \) Hz, 1H), 7.10-7.08 (m, 1H), 6.92 (d, \( J = 8.8 \) Hz, 1H), 3.28 (s, 3H); \(^{13}\)C NMR (CDCl\(_3\), 150 MHz): \( \delta \) 183.1, 158.1, 150.3, 142.3, 135.2, 130.9, 128.2, 125.3, 123.1, 122.4, 117.8, 103.1, 26.4; HRMS (ESI): m/z [M + Na\(^+\)] calcd for C\(_{13}\)H\(_9\)NO\(_2\)+Na\(^+\) 266.0246, found 266.0251.
4. References

5. $^1$H and $^{13}$C NMR spectra of compounds