Supporting Information

Iodine-Mediated Oxidative Cyclization from 2-(Pyridin-2-yl)acetates Derivatives and Alkynes: Condition-Controlled Selective Synthesis of Multi-substituted Indolizines

Lisheng He\textsuperscript{a,b,c}, Yuzhu Yang \textsuperscript{*a,b,c}, Xiaolan Liu,\textsuperscript{a,b,c} Guangyan Liang,\textsuperscript{a,b,c} Chunyan Li,\textsuperscript{a,b,c} Daoping Wang\textsuperscript{a,b,c} and Weidong Pan\textsuperscript{*a,b,c}

\textsuperscript{a}College of Pharmacy, Guizhou Medical University, 9 Beijing Road, Guiyang, Guizhou 550004, P. R. China.

\textsuperscript{b}State Key Laboratory of Functions and Applications of Medicinal Plants, Guizhou Medical University, 3491 Baijin Road, Guiyang 550014, P. R. China

\textsuperscript{c}The Key Laboratory of Chemistry for Natural Products of Guizhou Province and Chinese Academy of Sciences, 3491 Baijin Road, Guiyang 550014, P. R. China

E-mail: yangyuzhu15@126.com, wdpan@163.com

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**General Information:** All reactions were performed under N₂ unless otherwise stated. The solvents were dried before use by standard procedures. $^1$H NMR and $^{13}$C NMR spectra were recorded in CDCl₃ on a 400 MHz or 600 MHz instrument. All $^1$H NMR spectra are measured relative to the signals for residual CHCl₃ (7.26 ppm) and all $^{13}$C NMR spectral data are reported relative to CDCl₃ (77.16 ppm). Melting point Melting points are measured in WRX-4 melting point apparatus purchased from Shanghai YICE Instrumental Company. HRMS data were recorded on a micrOTOF instrument using ESI technique. All column chromatography was performed using silica gel (200-300 microns). Unless otherwise noted, commercially available chemicals were used as received.
Table S1. Optimization of reaction conditions of 5h

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<th>ratio of 1a:2a</th>
<th>I₂(equiv)</th>
<th>L(%)</th>
<th>Base(equiv)</th>
<th>Solvent(mL)</th>
<th>Temp(°C)</th>
<th>Time(h)</th>
<th>yield(%)&lt;sup&gt;b&lt;/sup&gt;</th>
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<sup>a</sup>Reaction conditions: 1a (0.2 mmol), 2a (0.4 mmol), I₂ (0.2 mmol), Na₂CO₃(0.4 mmol), DMA(2 mL). <sup>b</sup>Isolated yield.
Table S2. Optimization of reaction conditions of 6a

![Chemical structure of 6a]

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<th>Temp (°C)</th>
<th>Metal (equiv)</th>
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<td>CuI(2)</td>
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aReaction conditions: 1a (0.2 mmol), 2a (0.4 mmol), I₂ (0.7 mmol), dppe (0.04mmol), Na₂CO₃ (0.4 mmol), CuI (0.4 mmol), DMF (2 mL). b1mL H₂O was added. cIsolated yield.
General procedure for synthesis of 3-substituted indolizines derivatives: 3a-3i, 4a-4p

Under N₂ atmosphere, 2-pyridylacetates (1a, 0.2 mmol, 33.0 mg), phenylacetylene (2a, 0.4 mmol, 40.9 mg), I₂ (0.4 mmol, 101.5 mg), dppe (0.04 mmol, 15.9 mg), Na₂CO₃ (0.4 mmol, 42.4 mg), were mixed in 2 mL DMF. The reaction tube was heated in an oil bath at 160 °C for 4 hours. After completion of the reaction, the reaction mixture was washed with saturated sodium thiosulfate solution and extracted with EtOAc (40 mL × 3), dried over anhydrous Na₂SO₄ and the solvent was removed under reduced pressure. The remaining crude product was then purified through column chromatography using silica gel (EtOAc/petroleum ether = 1/5) to afford 3a as a green dark solid in 93% yield.

**Ethyl 3-phenylindolizine-1-carboxylate (3a, CAS: 93315-81-2)¹**

![Chemical Structure of Ethyl 3-phenylindolizine-1-carboxylate](image)

(Eluent: ethyl acetate/petroleum ether = 1/5, v/v); 93% yield (dark green solid, mp 68–70 °C, 49.3 mg); ¹H NMR (400 MHz, Chloroform-d) δ 8.28 (t, J = 7.9 Hz, 2H), 7.54 (d, J = 7.7 Hz, 2H), 7.49 (t, J = 7.6 Hz, 2H), 7.39 (t, J = 7.3 Hz, 1H), 7.31 (s, 1H), 7.10 – 7.03 (m, 1H), 6.69 (t, J = 6.9 Hz, 1H), 4.40 (q, J = 7.2 Hz, 2H), 1.43 (t, J = 7.1 Hz, 3H). ¹³C NMR (100 MHz, Chloroform-d) δ 165.0, 136.3, 131.2, 129.0, 128.6, 127.9, 123.3, 122.2, 120.1, 116.1, 116.0, 112.5, 104.2, 59.5, 14.6. HR-ESI-MS (m/z): calcd. for C₁₇H₁₅NO₂ [M+H]⁺ 266.1176, found 266.1181.

**Methyl 3-phenylindolizine-1-carboxylate (3b, CAS: 947381-33-1)¹**

![Chemical Structure of Methyl 3-phenylindolizine-1-carboxylate](image)

(Eluent: ethyl acetate/petroleum ether = 1/10, v/v); 65% yield (yellow solid, mp 68–70 °C, 49.3 mg); ¹H NMR (400 MHz, Chloroform-d) δ 8.28 (t, J = 7.9 Hz, 2H), 7.54 (d, J = 7.7 Hz, 2H), 7.49 (t, J = 7.6 Hz, 2H), 7.39 (t, J = 7.3 Hz, 1H), 7.31 (s, 1H), 7.10 – 7.03 (m, 1H), 6.69 (t, J = 6.9 Hz, 1H), 4.40 (q, J = 7.2 Hz, 2H), 1.43 (t, J = 7.1 Hz, 3H). ¹³C NMR (100 MHz, Chloroform-d) δ 165.0, 136.3, 131.2, 129.0, 128.6, 127.9, 123.3, 122.2, 120.1, 116.1, 116.0, 112.5, 104.2, 59.5, 14.6. HR-ESI-MS (m/z): calcd. for C₁₇H₁₅NO₂ [M+H]⁺ 266.1176, found 266.1181.
111–113 °C, 32.3 mg); $^1$H NMR (400 MHz, Chloroform-d) δ 8.28 (t, J = 8.6 Hz, 2H), 7.54 (d, J = 7.7 Hz, 2H), 7.49 (t, J = 7.5 Hz, 2H), 7.41 (d, J = 7.3 Hz, 1H), 7.29 (s, 1H), 7.07 (dd, J = 9.0, 6.7 Hz, 1H), 6.70 (t, J = 6.9 Hz, 1H), 3.92 (s, 3H). $^{13}$C NMR (100 MHz, Chloroform-d) δ 165.4, 136.4, 131.2, 129.0, 128.6, 127.9, 126.4, 123.3, 122.30, 120.1, 115.9, 112.6, 103.8, 50.9. HR-ESI-MS (m/z): calcd. for C$_{16}$H$_{13}$NO$_2$ [M+H]$^+$ 252.1019, found 252.1028.

**Isopropyl 3-phenylindolizine-1-carboxylate (3c, CAS: 1795248-49-5)$^2$**

(Eluent: ethyl acetate/petroleum ether = 1/20, v/v); 69% yield (yellow oil, 38.2 mg); $^1$H NMR (400 MHz, Chloroform-d) δ 8.27 (t, J = 7.5 Hz, 2H), 7.54 (d, J = 7.7 Hz, 2H), 7.49 (t, J = 7.6 Hz, 2H), 7.39 (t, J = 7.3 Hz, 1H), 7.32 (s, 1H), 7.06 (dd, J = 9.1, 6.7 Hz, 1H), 6.69 (t, J = 6.9 Hz, 1H), 5.36 – 5.24 (m, 1H), 1.41 (s, 3H), 1.40 (s, 3H). $^{13}$C NMR (100 MHz, Chloroform-d) δ 164.6, 136.2, 131.2, 129.0, 128.5, 127.9, 126.3, 123.3, 122.1, 120.2, 116.1 (d, J = 1.6 Hz), 112.5, 104.7, 66.6, 22.3. HR-ESI-MS (m/z): calcd. for C$_{18}$H$_{17}$NO$_2$ [M+H]$^+$ 280.1332, found 280.1342.

**Tert-butyl 3-phenylindolizine-1-carboxylate (3d, CAS: 1428552-42-4)$^3$**

(Eluent: ethyl acetate/petroleum ether = 1/10, v/v); 66% yield (yellow oil, 38.6 mg); $^1$H NMR (400 MHz, Chloroform-d) δ 8.25 (dd, J = 15.8, 8.1 Hz, 2H), 7.54 (d, J = 7.6 Hz, 2H), 7.49 (t, J = 7.5 Hz, 2H), 7.40 (d, J = 7.3 Hz, 1H), 7.28 (s, 1H), 7.03 (dd, J = 9.1, 6.7 Hz, 1H), 6.67 (t, J = 6.9 Hz, 1H), 1.65 (s, 9H). $^{13}$C NMR (101 MHz, Chloroform-d) δ 164.6, 135.9, 131.3, 129.0, 128.6, 127.9, 126.1, 123.2, 121.8, 120.1, 116.3, 116.3, 112.3, 105.9, 79.6, 28.6. HR-ESI-MS (m/z): calcd. for C$_{19}$H$_{19}$NO$_2$
Butyl 3-phenylindolizine-1-carboxylate (3e, CAS: 1394827-53-2)\(^3\)

\[
\text{COO}^\text{Bu}
\]

(Eluent: ethyl acetate/petroleum ether = 1/20, v/v); 73% yield (yellow oil, 42.6 mg);

\(^1\)H NMR (400 MHz, Chloroform-d) \(\delta\) 8.27 (t, \(J = 7.7\) Hz, 2H), 7.54 (d, \(J = 7.7\) Hz, 2H), 7.49 (t, \(J = 7.5\) Hz, 2H), 7.39 (t, \(J = 7.3\) Hz, 1H), 7.31 (s, 1H), 7.06 (dd, \(J = 9.1, 6.6\) Hz, 1H), 6.69 (t, \(J = 6.9\) Hz, 1H), 4.35 (t, \(J = 6.7\) Hz, 2H), 1.79 (p, \(J = 6.9\) Hz, 2H), 1.52 (q, \(J = 7.5\) Hz, 2H), 1.00 (t, \(J = 7.4\) Hz, 3H). \(^{13}\)C NMR (100 MHz, Chloroform-d) \(\delta\) 165.1, 136.26, 131.2, 129.0, 128.6, 127.9, 123.3, 122.2, 120.1, 116.1, 116.1, 112.5, 104.2, 63.4, 31.1, 19.4, 13.8. HR-ESI-MS (m/z): calcd. for C\(_{19}\)H\(_{19}\)NO\(_2\) \([\text{M+H}]^+\) 294.1489, found 294.1496.

1-(3-phenylindolizin-1-yl)ethanone (3f, CAS: 1126444-46-9)\(^4\)

\[
\begin{array}{c}
\text{CH}_2
\end{array}
\]

(Eluent: ethyl acetate/petroleum ether = 1/10, v/v); 38% yield (pale yellow solid, mp 132–134 °C, 17.6 mg); \(^1\)H NMR (600 MHz, Chloroform-d) \(\delta\) 8.53 (d, \(J = 9.0\) Hz, 1H), 8.29 (d, \(J = 7.0\) Hz, 1H), 7.55 (d, \(J = 7.7\) Hz, 2H), 7.51 (t, \(J = 7.7\) Hz, 2H), 7.42 (t, \(J = 8.0\) Hz, 1H), 7.19 (s, 1H), 7.17 – 7.14 (m, 1H), 6.79 – 6.75 (m, 1H), 2.56 (s, 3H). \(^{13}\)C NMR (150 MHz, Chloroform-d) \(\delta\) 193.1, 135.9, 131.1, 129.2, 128.7, 128.2, 123.9, 123.2, 121.1, 116.5, 113.6, 113.5, 28.0. HR-ESI-MS (m/z): calcd. for C\(_{16}\)H\(_{13}\)NO \([\text{M+H}]^+\) 236.1070, found 236.1074.

Ethyl 5-methyl-3-phenylindolizine-1-carboxylate (3g)
(Eluent: ethyl acetate/petroleum ether = 1/20, v/v); 74% yield (yellow solid, mp 115–117 °C, 41 mg); ^1^H NMR (400 MHz, Chloroform-d) δ 8.27 (d, J = 9.0 Hz, 1H), 7.39 (q, J = 6.4, 5.6 Hz, 5H), 7.20 (s, 1H), 7.00 (dd, J = 9.0, 6.8 Hz, 1H), 6.45 (d, J = 6.7 Hz, 1H), 4.38 (t, J = 7.1 Hz, 2H), 2.12 (s, 3H), 1.40 (t, J = 7.1 Hz, 3H). ^1^C NMR (100 MHz, Chloroform-d) δ 165.0, 137.9, 136.1, 134.8, 131.1, 128.0, 127.2, 122.3, 118.8 (d, J = 2.0 Hz), 118.0, 114.2, 103.2, 59.4, 29.7, 22.9, 14.6. HR-ESI-MS (m/z): calcd. for C\textsubscript{18}H\textsubscript{17}NO\textsubscript{2} [M+H]^+ 280.1332, found 280.1344.

**Ethyl 6-methyl-3-phenylindolizine-1-carboxylate (3h)**

(Eluent: ethyl acetate/petroleum ether = 1/20, v/v); 60% yield (yellow solid, mp 108–110 °C, 33.2 mg); ^1^H NMR (500 MHz, Chloroform-d) δ 8.22 (d, J = 8.9 Hz, 1H), 8.12 (s, 1H), 7.59 (d, J = 6.6 Hz, 2H), 7.54 (t, J = 6.7 Hz, 2H), 7.44 (s, 1H), 7.30 (s, 1H), 6.98 (d, J = 8.9 Hz, 1H), 4.43 (q, J = 5.8, 4.6 Hz, 2H), 2.30 (s, 3H), 1.47 (t, J = 7.0 Hz, 3H). ^1^C NMR (125 MHz, Chloroform-d) δ 165.1, 135.3, 131.5, 129.1, 128.7, 127.9, 126.1, 125.5, 122.2, 121.1, 120.9, 119.6, 119.5, 115.9, 103.9, 59.5, 18.5, 14.7. HR-ESI-MS (m/z): calcd. for C\textsubscript{18}H\textsubscript{17}NO\textsubscript{2} [M+H]^+ 280.1332, found 280.1339.

**Ethyl 6-bromo-3-phenylindolizine-1-carboxylate (3i)**

(Eluent: ethyl acetate/petroleum ether = 1/20, v/v); 48% yield (yellow solid, mp
105–107 °C, 33.2 mg); ¹H NMR (600 MHz, Chloroform-d) δ 8.38 (s, 1H), 8.16 (d, J = 10.1 Hz, 1H), 7.52 (d, J = 4.5 Hz, 4H), 7.44 (d, J = 4.1 Hz, 1H), 7.28 (s, 1H), 7.11 (d, J = 1.6 Hz, 1H), 4.39 (q, J = 7.1 Hz, 2H), 1.42 (t, J = 7.1 Hz, 3H). ¹³C NMR (150 MHz, Chloroform-d) δ 164.7, 134.3, 130.6, 129.3, 128.7, 128.5, 126.8, 125.2, 123.26, 120.9, 116.5, 107.8, 105.6, 59.8, 14.6. HR-ESI-MS (m/z): calcd. for C₁₇H₁₄BrNO₂ [M+H]⁺ 345.0208, found 345.0210.

**Ethyl 3-(2-fluorophenyl)indolizine-1-carboxylate (4a,CAS:1631741-05-3)²**

(Eluent: ethyl acetate/petroleum ether = 1/20, v/v); 68% yield (pale yellow oil, 38.5 mg); ¹H NMR (400 MHz, Chloroform-d) δ 8.29 (d, J = 9.1 Hz, 1H), 7.89 (dd, J = 7.1, 3.4 Hz, 1H), 7.50 (dd, J = 7.5, 1.6 Hz, 1H), 7.44 (d, J = 7.2 Hz, 1H), 7.37 (s, 1H), 7.29 (d, J = 7.6 Hz, 1H), 7.22 (d, J = 9.1 Hz, 1H), 7.12 (dd, J = 9.0, 6.7 Hz, 1H), 6.74 (t, J = 6.9 Hz, 1H), 4.41 (q, J = 7.1 Hz, 2H), 1.43 (t, J = 7.1 Hz, 3H). ¹³C NMR (100 MHz, Chloroform-d) δ 164.8, 136.4, 133.7, 129.7, 129.6, 129.3, 125.0, 123.1, 122.4, 120.2, 116.3, 116.3, 112.8, 104.4, 59.6, 14.6. HR-ESI-MS (m/z): calcd. for C₁₇H₁₄FNO₂ [M+H]⁺ 284.1081, found 284.1092.

**Ethyl 3-(3-fluorophenyl)indolizine-1-carboxylate (4b,CAS:2027550-24-7)²**

(Eluent: ethyl acetate/petroleum ether = 1/20, v/v); 71% yield (yellow oil, 40 mg); ¹H NMR (400 MHz, Chloroform-d) δ 8.28 (t, J = 8.0 Hz, 2H), 7.51 – 7.37 (m, 1H), 7.33 (d, J = 3.9 Hz, 2H), 7.24 (dt, J = 9.8, 2.0 Hz, 1H), 7.08 (dd, J = 9.1, 6.8 Hz, 2H), 6.72 (t, J = 6.9 Hz, 1H), 4.39 (q, J = 7.1 Hz, 2H), 1.42 (t, J = 7.1 Hz, 3H). ¹³C NMR (100 MHz, Chloroform-d) δ 164.8, 136.5, 133.5, 133.2, 130.7, 130.6, 124.0, 123.9,
123.2, 122.5, 120.2, 116.6, 116.5, 112.8, 104.5, 59.6, 14.6. HR-ESI-MS (m/z): calcd. for C_{17}H_{14}FNO_2 [M + H]^+ 284.1081, found 284.1093.

**Ethyl 3-(4-fluorophenyl)indolizine-1-carboxylate (4c,CAS:1621928-41-3)**

![Chemical Structure](image1)

(Eluent: ethyl acetate/petroleum ether = 1/20, v/v); 69% yield (yellow solid, mp 98–100 °C, 34.6 mg); \(^1\)H NMR (400 MHz, Chloroform-d) δ 8.25 (d, J = 9.1 Hz, 1H), 8.17 (d, J = 7.1 Hz, 1H), 7.49 (d, J = 5.4 Hz, 1H), 7.47 (d, J = 5.3 Hz, 1H), 7.26 (s, 1H), 7.18 (t, J = 8.5 Hz, 2H), 7.06 (dd, J = 9.0, 6.7 Hz, 1H), 6.69 (t, J = 6.9 Hz, 1H), 4.38 (q, J = 7.1 Hz, 2H), 1.41 (t, J = 7.1 Hz, 3H). \(^{13}\)C NMR (100 MHz, Chloroform-d) δ 164.9, 163.6, 136.2, 130.5, 130.4, 123.0, 122.2, 120.1, 116.2, 116.0, 112.7, 104.2, 59.5, 14.6. HR-ESI-MS (m/z): calcd. for C_{17}H_{14}FNO_2 [M+H]^+ 284.1081, found 284.1088.

**Ethyl3-(4-(trifluoromethyl)phenyl)indolizine-1-carboxylate**

(4d,CAS:1714114-01-8)

![Chemical Structure](image2)

(Eluent: ethyl acetate/petroleum ether = 1/20, v/v); 77% yield (yellow solid, mp 91–93 °C, 50.9 mg); \(^1\)H NMR (400 MHz, Chloroform-d) δ 8.33 – 8.24 (m, 2H), 7.74 (d, J = 8.1 Hz, 2H), 7.67 (d, J = 8.1 Hz, 2H), 7.37 (s, 1H), 7.10 (dd, J = 9.2, 6.6 Hz, 1H), 6.75 (t, J = 7.0 Hz, 1H), 4.39 (q, J = 7.1 Hz, 2H), 1.42 (t, J = 7.1 Hz, 3H). \(^{13}\)C NMR (100 MHz, Chloroform-d) δ 164.7, 136.8, 134.8, 128.3, 126.1, 126.0, 124.7, 123.0, 122.7, 120.3, 117.0, 113.1, 104.8, 59.7, 29.7, 14.6. HR-ESI-MS (m/z): calcd. for C_{18}H_{14}F_3NO_2 [M + H]^+ 334.1049, found 334.1056.
Ethyl 3-(4-chlorophenyl)indolizine-1-carboxylate (4e,CAS:1621928-42-4)$^1$

(Eluent: ethyl acetate/petroleum ether = 1/20, v/v); 77% yield (yellow solid, mp 107–109 °C, 46 mg); $^1$H NMR (400 MHz, Chloroform-d) δ 8.26 (d, J = 9.1 Hz, 1H), 8.21 (d, J = 7.1 Hz, 1H), 7.45 (s, 4H), 7.28 (s, 1H), 7.10 – 7.03 (m, 1H), 6.70 (t, J = 6.8 Hz, 1H), 4.38 (q, J = 7.1 Hz, 2H), 1.41 (t, J = 7.1 Hz, 3H). $^{13}$C NMR (100 MHz, Chloroform-d) δ 164.8, 136.4, 133.7, 129.7, 129.6, 129.3, 125.0, 123.1, 122.4, 120.2, 116.3, 116.3, 112.8, 104.4, 59.6, 14.6. HR-ESI-MS (m/z): calcd. for C$_{17}$H$_{16}$ClNO$_2$ [M+H]$^+$ 300.0786, found 300.0795 .

Ethyl 3-(4-bromophenyl)indolizine-1-carboxylate (4f,CAS:1714114-00-7)$^1$

(Eluent: ethyl acetate/petroleum ether = 1/20, v/v); 77% yield (yellow solid, mp 99–101 °C, 52.6 mg); $^1$H NMR (400 MHz, Chloroform-d) δ 8.25 (d, J = 9.1 Hz, 1H), 8.21 (d, J = 7.2 Hz, 1H), 7.60 (d, J = 8.2 Hz, 2H), 7.39 (d, J = 8.2 Hz, 2H), 7.28 (s, 1H), 7.06 (dd, J = 9.0, 6.7 Hz, 1H), 6.70 (t, J = 6.9 Hz, 1H), 4.38 (q, J = 7.1 Hz, 2H), 1.41 (t, J = 7.1 Hz, 3H). $^{13}$C NMR (100 MHz, Chloroform-d) δ 164.8, 136.4, 132.2, 130.1, 129.9, 125.0, 123.0, 122.4, 121.8, 120.2, 116.3, 112.8, 104.5, 59.6, 14.6. HR-ESI-MS (m/z): calcd. for C$_{17}$H$_{16}$BrNO$_2$ [M+H]$^+$ 344.0281, found 344.0284 .

Ethyl 3-(4-nitrophenyl)indolizine-1-carboxylate (4g,CAS:158670-22-5)$^4$
(Eluent: ethyl acetate/petroleum ether = 1/10, v/v); 94% yield (orange-red solid, mp 140–142 °C, 51.1 mg); \(^1\)H NMR (600 MHz, Chloroform-d) \(\delta\) 8.37 (d, \(J = 7.1\) Hz, 1H), 8.30 (dd, \(J = 15.8, 8.7\) Hz, 3H), 7.71 (d, \(J = 8.3\) Hz, 2H), 7.43 (s, 1H), 7.17 – 7.11 (m, 1H), 6.81 (t, \(J = 6.9\) Hz, 1H), 4.38 (q, \(J = 7.1\) Hz, 2H), 1.41 (t, \(J = 7.2\) Hz, 3H). \(^{13}\)C NMR (150 MHz, Chloroform-d) \(\delta\) 164.5, 146.5, 137.8, 137.5, 130.6, 128.0, 124.6, 124.0, 123.4, 123.2, 120.5, 118.2, 113.7, 105.6, 59.9, 14.6. HR-ESI-MS (m/z): calcd. for C\(_{17}\)H\(_{14}\)N\(_2\)O\(_4\) [M+H]\(^+\) 311.1026, found 311.1035.

**Ethyl 3-(p-tolyl)indolizine-1-carboxylate (4h,CAS:247075-84-9)\(^1\)**

(Eluent: ethyl acetate/petroleum ether = 1/10, v/v); 75% yield (yellow solid, mp 96 –98 °C, 41.8 mg); \(^1\)H NMR (400 MHz, Chloroform-d) \(\delta\) 8.29 – 8.21 (m, 2H), 7.42 (d, \(J = 7.8\) Hz, 2H), 7.29 (d, \(J = 7.7\) Hz, 3H), 7.05 (dd, \(J = 9.1, 6.7\) Hz, 1H), 6.67 (t, \(J = 6.9\) Hz, 1H), 4.40 (q, \(J = 7.1\) Hz, 2H), 2.42 (s, 3H), 1.43 (t, \(J = 7.1\) Hz, 3H). \(^{13}\)C NMR (100 MHz, Chloroform-d) \(\delta\) 165.0, 137.9, 136.2, 129.7, 128.5, 128.2, 126.5, 123.3, 122.0, 120.1, 115.8, 112.4, 104.0, 59.5, 21.3, 14.7. HR-ESI-MS (m/z): calcd. for C\(_{18}\)H\(_{17}\)NO\(_2\) [M + H]\(^+\) 280.1332, found 280.1344.

**Ethyl 3-(4-(tert-butyl)phenyl)indolizine-1-carboxylate (4i,CAS:1776070-38-2)\(^6\)**
Ethyl 3-(4-methoxyphenyl)indolizine-1-carboxylate (4j, CAS: 1621928-40-2)$^1$

(Eluent: ethyl acetate/petroleum ether = 1/10, v/v); 60% yield (yellow solid, mp 124–126 °C, 35.2 mg); $^1$H NMR (400 MHz, Chloroform-d) δ 8.25 (d, J = 9.1 Hz, 1H), 8.19 (d, J = 7.1 Hz, 1H), 7.44 (d, J = 8.3 Hz, 2H), 7.24 (s, 1H), 7.03 (dd, J = 8.5, 6.2 Hz, 3H), 6.67 (t, J = 6.8 Hz, 1H), 4.39 (q, J = 7.1 Hz, 2H), 3.86 (s, 3H), 1.42 (t, J = 7.1 Hz, 3H). $^{13}$C NMR (100 MHz, Chloroform-d) δ 165.1, 159.4, 136.0, 130.1, 123.5, 123.3, 121.9, 120.0, 115.6, 115.5, 114.5, 112.4, 103.9, 59.5, 55.3, 55.3, 14.6. HR-ESI-MS (m/z): calcd. for C$_{18}$H$_{17}$NO$_2$ [M+H]$^+$ 296.1281, found 296.1294.

Ethyl 3-([1,1'-biphenyl]-4-yl)indolizine-1-carboxylate (4k, CAS: 1776070-42-8)$^2$

(Eluent: ethyl acetate/petroleum ether = 1/20, v/v); 78% yield (yellow solid, mp 95–97 °C, 49.8 mg); $^1$H NMR (400 MHz, Chloroform-d) δ 8.28 (dd, J = 17.0, 8.1 Hz, 2H), 7.50 (q, J = 8.3 Hz, 4H), 7.29 (s, 1H), 7.10 – 7.02 (m, 1H), 6.68 (t, J = 6.8 Hz, 1H), 4.40 (q, J = 7.1 Hz, 2H), 1.43 (t, J = 7.1 Hz, 3H), 1.39 (s, 9H). $^{13}$C NMR (100 MHz, Chloroform-d) δ 165.1, 151.0, 136.2, 128.3, 128.3, 126.4, 126.0, 123.5, 122.0, 120.1, 115.8, 115.8, 112.4, 104.1, 59.5, 34.7, 31.3, 14.6. HR-ESI-MS (m/z): calcd. for C$_{21}$H$_{23}$NO$_2$ [M+H]$^+$ 322.1802, found 322.1814.
(Eluent: ethyl acetate/petroleum ether = 1/20, v/v); 72% yield (yellow solid, mp 143–145 °C, 48.9 mg); ¹H NMR (400 MHz, Chloroform-d) δ 8.36 (d, J = 7.1 Hz, 1H), 8.31 (d, J = 9.1 Hz, 1H), 7.73 (d, J = 8.0 Hz, 2H), 7.66 (d, J = 7.7 Hz, 2H), 7.62 (d, J = 8.0 Hz, 2H), 7.49 (t, J = 7.6 Hz, 2H), 7.43 – 7.36 (m, 2H), 7.12 – 7.05 (m, 1H), 6.72 (t, J = 6.9 Hz, 1H), 4.43 (q, J = 7.1 Hz, 2H), 1.45 (t, J = 7.1 Hz, 3H). ¹³C NMR (101 MHz, Chloroform-d) δ 165.0, 140.7, 140.3, 136.4, 130.1, 128.9, 128.8, 127.7, 127.6, 127.0, 126.0, 123.4, 122.3, 120.2, 116.2, 112.7, 104.4, 59.6, 14.7. HR-ESI-MS (m/z): calcd. for C₂₃H₁₉NO₂ [M+H]⁺ 342.1489, found 342.1495.

**Ethyl 3-(thiophen-3-yl)indolizine-1-carboxylate (4l,CAS:1638213-47-4)**

(Eluent: ethyl acetate/petroleum ether = 1/10, v/v); 59% yield (pale yellow solid, mp 111–113 °C, 31.9 mg); ¹H NMR (400 MHz, Chloroform-d) δ 8.29 – 8.22 (m, 2H), 7.46 (dd, J = 4.8, 3.1 Hz, 1H), 7.43 (d, J = 2.8 Hz, 1H), 7.32 (s, 1H), 7.30 (d, J = 5.0 Hz, 1H), 7.05 (dd, J = 9.2, 6.7 Hz, 1H), 6.71 (t, J = 6.9 Hz, 1H), 4.39 (q, J = 7.1 Hz, 2H), 1.42 (t, J = 7.1 Hz, 3H). ¹³C NMR (100 MHz, Chloroform-d) δ 164.9, 136.1, 131.5, 127.5, 126.5, 123.6, 122.6, 122.1, 121.7, 120.0, 116.0, 112.7, 104.0, 59.5, 14.6. HR-ESI-MS (m/z): calcd. for C₁₅H₁₃NO₂S [M+H]⁺ 271.0740, found 271.0748.

**Ethyl 3-(thiophen-2-yl)indolizine-1-carboxylate (4m,CAS:1621928-45-7)**

Ethyl 3-(thiophen-2-yl)indolizine-1-carboxylate (4m,CAS:1621928-45-7)
(Eluent: ethyl acetate/petroleum ether = 1/10, v/v); 60% yield (orange-yellow solid, mp 78–80 °C, 32.4 mg); ^1^H NMR (600 MHz, Chloroform-d) δ 8.37 (dd, J = 7.1, 1.1 Hz, 1H), 8.26 (dt, J = 9.1, 1.3 Hz, 1H), 7.41 – 7.37 (m, 2H), 7.25 (dd, J = 3.6, 1.2 Hz, 1H), 7.16 (dd, J = 5.2, 3.6 Hz, 1H), 7.10 – 7.07 (m, 1H), 6.78 – 6.74 (m, 1H), 4.39 (q, J = 7.1 Hz, 2H), 1.42 (t, J = 7.1 Hz, 3H). \(^{13}\)C NMR (150 MHz, Chloroform-d) δ 164.8, 136.6, 132.3, 127.7, 126.2, 125.8, 123.8, 122.5, 120.1, 119.2, 117.5, 113.0, 104.4, 59.7, 14.7. HR-ESI-MS (m/z): calcd. for C\(_{15}\)H\(_{13}\)NO\(_2\)S [M+H]^+ 272.0740, found 272.0749.

**Ethyl 3-(pyridin-2-yl)indolizine-1-carboxylate (4n,CAS:1776070-49-5)**

![Chemical Structure](image)

(Eluent: ethyl acetate/petroleum ether = 1/10, v/v); 51% yield (yellow solid, mp 144–146 °C, 26.9 mg); ^1^H NMR (400 MHz, Chloroform-d) δ 10.04 (d, J = 7.2 Hz, 1H), 8.59 (d, J = 4.8 Hz, 1H), 8.27 (d, J = 9.0 Hz, 1H), 7.74 (s, 1H), 7.67 (d, J = 4.2 Hz, 2H), 7.15 (dd, J = 9.0, 6.8 Hz, 1H), 7.09 (d, J = 4.3 Hz, 1H), 6.82 (t, J = 7.0 Hz, 1H), 4.39 (d, J = 7.1 Hz, 2H), 1.43 (t, J = 7.1 Hz, 3H). \(^{13}\)C NMR (100 MHz, Chloroform-d) δ 164.7, 151.7, 148.2, 137.8, 136.4, 127.8 (d, J = 1.5 Hz), 123.5 (d, J = 6.5 Hz), 121.0, 120.5, 119.3, 117.8 (d, J = 1.7 Hz), 113.0, 104.5, 59.6, 14.6. HR-ESI-MS (m/z): calcd. for C\(_{16}\)H\(_{14}\)N\(_2\)O\(_2\) [M+H]^+ 267.1128, found 267.1136.

**Ethyl 3-(pyridin-3-yl)indolizine-1-carboxylate (4o)**

![Chemical Structure](image)

(Eluent: ethyl acetate/petroleum ether = 1/3, v/v); 43% yield (yellow solid, mp 80–82 °C, 23 mg); ^1^H NMR (400 MHz, Chloroform-d) δ 8.78 (d, J = 2.3 Hz, 1H), 8.62 – 8.57 (m, 1H), 8.24 (d, J = 9.0 Hz, 1H), 8.19 (d, J = 7.1 Hz, 1H), 7.82 (dt, J =
8.1, 2.0 Hz, 1H), 7.39 (dd, J = 7.9, 4.8 Hz, 1H), 7.32 (s, 1H), 7.10 – 7.03 (m, 1H), 6.71 (t, J = 6.9 Hz, 1H), 4.36 (q, J = 7.1 Hz, 2H), 1.39 (t, J = 7.1 Hz, 3H). 13C NMR (100 MHz, Chloroform-d) δ 164.7, 149.3, 148.9, 136.7, 135.6, 127.41, 123.7, 122.8, 122.7, 122.6, 120.3, 116.9, 113.1, 104.7, 59.6, 14.6. HR-ESI-MS (m/z): calcd. for C16H14N2O2 [M + H]+ 267.1128, found 267.1136.

**Diethyl indolizine-1,3-dicarboxylate (4p, CAS: 55814-13-6)**

![Diagram](image)

(Eluent: ethyl acetate/petroleum ether = 1/20, v/v); 29% yield (pale yellow solid, mp 112–114 °C, 15 mg); 1H NMR (600 MHz, Chloroform-d) δ 9.50 (dt, J = 7.1, 1.1 Hz, 1H), 8.34 – 8.29 (m, 1H), 7.97 (s, 1H), 7.31 – 7.27 (m, 1H), 6.96 (dd, J = 7.0, 1.4 Hz, 1H), 4.40 – 4.34 (m, 4H), 1.41 (td, J = 7.2, 5.2 Hz, 6H). 13C NMR (150 MHz, Chloroform-d) δ 164.2, 161.2, 139.1, 127.9, 125.6, 124.2, 119.6, 114.7, 114.3, 105.2, 60.3, 59.9, 14.6, 14.5. HR-ESI-MS (m/z): calcd. for C14H15NO4 [M+H]+ 262.1074, found 262.1073.

**General procedure for synthesis of multi-substituted indolizines derivatives:**

**5a-5l**

Under N2 atmosphere, 2-pyridylacetates (1a, 0.2 mmol, 33.0 mg), ethyl phenyl propynoate (2a, 0.4 mmol, 69.7 mg), I2 (0.2 mmol, 50.8 mg), Na2CO3 (0.4 mmol, 42.4 mg), were mixed in 2 mL DMA. The reaction tube was heated in an oil bath at 160 °C for 4 hours. After completion of the reaction, the reaction mixture was washed with saturated sodium thiosulfate solution and extracted with EtOAc (40 mL × 3), dried over anhydrous Na2SO4 and the solvent was removed under reduced pressure. The remaining crude product was then purified through column chromatography using silica gel (EtOAc/petroleum ether = 1/10) to afford 5a as a pale yellow solid in 47% yield.
Diethyl 3-phenylindolizine-1,2-dicarboxylate (5a,CAS:1268825-51-9)$^9$

(Eluent: ethyl acetate/petroleum ether = 1/10, v/v); 47% yield (pale yellow solid, mp 40–42 °C, 31.6 mg); $^1$H NMR (600 MHz, Chloroform-d) $\delta$ 8.24 (dd, $J = 9.2$, 1.3 Hz, 1H), 8.04 – 8.01 (m, 1H), 7.52 – 7.48 (m, 4H), 7.46 – 7.43 (m, 1H), 7.11 (ddd, $J = 9.2$, 6.6, 1.1 Hz, 1H), 6.71 (td, $J = 6.9$, 1.4 Hz, 1H), 4.37 (q, $J = 7.1$ Hz, 2H), 4.26 (q, $J = 7.2$ Hz, 2H), 1.38 (t, $J = 7.1$ Hz, 3H), 1.20 (t, $J = 7.1$ Hz, 3H). $^{13}$C NMR (150 MHz, Chloroform-d) $\delta$ 166.3, 164.3, 135.3, 130.1, 129.1, 129.0, 125.1, 123.6, 122.3, 120.4, 113.5, 101.8, 61.4, 51.2, 14.1. HR-ESI-MS (m/z): calcd. for C$_{20}$H$_{19}$NO$_4$ [M+H]$^+$ 338.1387, found 338.1390.

1-ethyl 1-methyl 3-phenylindolizine-1,2-dicarboxylate (5b)

(Eluent: ethyl acetate/petroleum ether = 1/10, v/v); 31% yield (yellow solid, mp 80–82 °C, 20 mg); $^1$H NMR (600 MHz, Chloroform-d) $\delta$ 8.23 (dt, $J = 9.1$, 1.3 Hz, 1H), 8.02 (d, $J = 7.2$ Hz, 1H), 7.53 – 7.47 (m, 4H), 7.45 (d, $J = 6.8$ Hz, 1H), 7.11 (ddd, $J = 9.1$, 6.6, 1.1 Hz, 1H), 6.71 (td, $J = 6.9$, 1.4 Hz, 1H), 4.27 (q, $J = 7.1$ Hz, 2H), 3.89 (s, 3H), 1.20 (t, $J = 7.1$ Hz, 3H). $^{13}$C NMR (150 MHz, Chloroform-d) $\delta$ 166.3, 164.3, 135.3, 130.1, 129.1, 129.0, 125.1, 123.6, 122.3, 120.4, 113.5, 101.8, 61.4, 51.2, 14.1. HR-ESI-MS (m/z): calcd. for C$_{19}$H$_{17}$NO$_4$ [M+H]$^+$ 324.1230, found 324.1233.

1-ethyl 1-isopropyl 3-phenylindolizine-1,2-dicarboxylate (5c)
(Eluent: ethyl acetate/petroleum ether = 1/10, v/v); 37% yield (yellow oil, 26 mg); $^1$H NMR (600 MHz, Chloroform-d) $\delta$ 8.24 (dt, $J = 9.0$, 1.3 Hz, 1H), 8.02 (dd, $J = 7.1$, 1.2 Hz, 1H), 7.52 – 7.46 (m, 4H), 7.46 – 7.41 (m, 1H), 7.09 (ddd, $J = 9.1$, 6.6, 1.1 Hz, 1H), 6.70 (dd, $J = 6.9$, 1.4 Hz, 1H), 5.30 – 5.25 (m, 1H), 4.26 (q, $J = 7.2$ Hz, 2H), 1.36 (d, $J = 6.2$ Hz, 6H), 1.21 (t, $J = 7.1$ Hz, 3H). $^{13}$C NMR (150 MHz, Chloroform-d) $\delta$ 166.4, 163.4, 135.2, 130.0, 129.1, 129.0, 124.7, 123.5, 123.3, 122.4, 120.4, 113.4, 102.4, 67.2, 61.3, 22.2, 14.0. HR-ESI-MS (m/z): calcd. for C$_{21}$H$_{21}$NO$_4$ [M+H]$^+$ 352.1543, found 352.1549.

1-tert-butyl 2-ethyl 3-phenylindolizine-1,2-dicarboxylate (5d)

(Eluent: ethyl acetate/petroleum ether = 1/10, v/v); 31% yield (yellow oil, 22.6 mg); $^1$H NMR (600 MHz, Chloroform-d) $\delta$ 8.22 (dt, $J = 9.2$, 1.3 Hz, 1H), 8.00 (dd, $J = 7.1$, 1.2 Hz, 1H), 7.49 (d, $J = 6.4$ Hz, 4H), 7.45 – 7.41 (m, 1H), 7.06 (ddd, $J = 9.1$, 6.6, 1.1 Hz, 1H), 6.67 (td, $J = 6.8$, 1.4 Hz, 1H), 4.24 (q, $J = 7.2$ Hz, 2H), 1.60 (s, 9H), 1.17 (t, $J = 7.2$ Hz, 3H). $^{13}$C NMR (150 MHz, Chloroform-d) $\delta$ 166.4, 163.2, 135.1, 130.0, 129.2, 129.0, 128.9, 124.5, 123.4, 123.0, 122.3, 120.4, 113.3, 103.5, 80.3, 61.2, 28.5, 14.0. HR-ESI-MS (m/z): calcd. for C$_{22}$H$_{23}$NO$_4$ [M+H]$^+$ 366.1700, found 366.1704.

1-butyl 2-ethyl 3-phenylindolizine-1,2-dicarboxylate (5e)

(Eluent: ethyl acetate/petroleum ether = 1/10, v/v); 35% yield (yellow solid, mp
83–85 °C, 25.6 mg); \(^1\)H NMR (600 MHz, Chloroform-d) \(\delta\) 8.24 (dt, \(J = 9.1, 1.3\) Hz, 1H), 8.02 (dt, \(J = 7.2, 1.1\) Hz, 1H), 7.52 – 7.47 (m, 4H), 7.46 – 7.41 (m, 1H), 7.10 (ddd, \(J = 9.2, 6.6, 1.1\) Hz, 1H), 6.70 (td, \(J = 6.8, 1.4\) Hz, 1H), 4.32 (t, \(J = 6.7\) Hz, 2H), 4.25 (q, \(J = 7.1\) Hz, 2H), 1.76 – 1.71 (m, 2H), 1.52 – 1.43 (m, 2H), 1.19 (t, \(J = 7.1\) Hz, 3H), 0.97 (t, \(J = 7.4\) Hz, 3H). \(^{13}\)C NMR (150 MHz, Chloroform-d) \(\delta\) 166.4, 164.0, 135.3, 130.0, 129.0, 124.8, 123.5, 123.5, 122.4, 120.4, 113.4, 102.1, 63.9, 61.3, 31.0, 19.3, 14.0, 13.8. HR-ESI-MS (m/z): calcd. for C\(_{22}\)H\(_{23}\)NO\(_4\) [M+H]\(^+\) 366.1700, found 366.1705.

**Diethyl 3-(4-chlorophenyl)indolizine-1,2-dicarboxylate (5f)**

(Eluent: ethyl acetate/petroleum ether = 1/20, v/v); 44% yield (brown oil, 32.6 mg); \(^1\)H NMR (600 MHz, Chloroform-d) \(\delta\) 8.25 (dt, \(J = 9.2, 1.2\) Hz, 1H), 7.97 (dd, \(J = 7.1, 1.1\) Hz, 1H), 7.52 – 7.43 (m, 4H), 7.12 (ddd, \(J = 9.1, 6.6, 1.1\) Hz, 1H), 6.73 (td, \(J = 6.9, 1.3\) Hz, 1H), 4.37 (q, \(J = 7.1\) Hz, 2H), 4.27 (q, \(J = 7.1\) Hz, 2H), 1.38 (t, \(J = 7.1\) Hz, 3H), 1.24 (t, \(J = 7.2\) Hz, 3H). \(^{13}\)C NMR (150 MHz, Chloroform-d) \(\delta\) 166.1, 163.7, 135.4, 135.1, 131.4, 129.4, 127.5, 123.6, 123.2, 120.5, 113.7, 61.5, 60.0, 14.5, 14.1. HR-ESI-MS (m/z): calcd. for C\(_{20}\)H\(_{18}\)ClNO\(_4\) [M+H]\(^+\) 372.0997, found 372.1000.

**Diethyl 3-(4-methoxyphenyl)indolizine-1,2-dicarboxylate (5g)**

(Eluent: ethyl acetate/petroleum ether = 1/5, v/v); 33% yield (brown oil, 24.2 mg); \(^1\)H NMR (600 MHz, Chloroform-d) \(\delta\) 8.23 (dd, \(J = 9.2, 1.5\) Hz, 1H), 7.97 (d, \(J = 7.1\) Hz, 1H), 7.45 – 7.40 (m, 2H), 7.11 – 7.06 (m, 1H), 7.02 (d, \(J = 8.6\) Hz, 2H), 6.69 (td, \(J = 119\) Hz, 3H). \(^{13}\)C NMR (150 MHz, Chloroform-d) \(\delta\) 166.1, 163.7, 135.4, 135.1, 131.4, 129.4, 127.5, 123.6, 123.2, 120.5, 113.7, 61.5, 60.0, 14.5, 14.1. HR-ESI-MS (m/z): calcd. for C\(_{20}\)H\(_{18}\)ClNO\(_4\) [M+H]\(^+\) 372.0997, found 372.1000.
6.9, 1.4 Hz, 1H), 4.36 (q, J = 7.1 Hz, 2H), 4.26 (q, J = 7.2 Hz, 2H), 3.86 (s, 3H), 1.38 (t, J = 7.1 Hz, 3H), 1.23 (t, J = 7.1 Hz, 3H). $^{13}$C NMR (150 MHz, Chloroform-d) δ 166.5, 163.9, 160.1, 135.1, 131.5, 124.8, 123.5, 123.3, 122.1, 121.0, 120.3, 114.5, 113.3, 101.8, 61.3, 59.9, 55.4, 14.5, 14.1. HR-ESI-MS (m/z): calcd. for C$_{21}$H$_{21}$NO$_5$ [M+H]$^+$ 368.1492, found 368.1498.

**Ethyl 2-formyl-3-phenylindolizine-1-carboxylate (5h)**

![Ethyl 2-formyl-3-phenylindolizine-1-carboxylate (5h)](image)

(Eluent: ethyl acetate/petroleum ether = 1/10, v/v); 52% yield (yellow solid, mp 77–79 °C, 30.4 mg); $^1$H NMR (600 MHz, Chloroform-d) δ 10.77 (s, 1H), 8.32 (d, J = 9.2 Hz, 1H), 7.86 (d, J = 7.2 Hz, 1H), 7.55 – 7.50 (m, 3H), 7.44 (dd, J = 8.1, 1.6 Hz, 2H), 7.13 (dd, J = 10.2, 6.6 Hz, 1H), 6.72 (t, J = 7.5 Hz, 1H), 4.46 (q, J = 7.1 Hz, 2H), 1.46 (t, J = 7.2 Hz, 3H). $^{13}$C NMR (150 MHz, Chloroform-d) δ 190.1, 164.6, 136.1, 130.9, 129.4, 129.1, 129.0, 128.7, 124.8, 123.9, 123.9, 121.1, 114.3, 103.8, 60.3, 14.6. HR-ESI-MS (m/z): calcd. for C$_{18}$H$_{15}$NO$_3$ [M+H]$^+$ 294.1125, found 294.1124.

**Ethyl 3-(4-fluorophenyl)-2-formylindolizine-1-carboxylate (5i)**

![Ethyl 3-(4-fluorophenyl)-2-formylindolizine-1-carboxylate (5i)](image)

(Eluent: ethyl acetate/petroleum ether = 1/10, v/v); 38% yield (yellow solid, mp 78–80 °C, 23.6 mg); $^1$H NMR (600 MHz, Chloroform-d) δ 10.77 (s, 1H), 8.32 (d, J = 9.2 Hz, 1H), 7.82 (d, J = 7.2 Hz, 1H), 7.43 (dd, J = 8.7, 5.3 Hz, 2H), 7.22 (t, J = 8.6 Hz, 2H), 7.13 (dd, J = 8.8, 6.1 Hz, 1H), 6.74 (t, J = 6.3 Hz, 1H), 4.46 (q, J = 7.1 Hz, 2H), 1.45 (t, J = 7.1 Hz, 3H). $^{13}$C NMR (150 MHz, Chloroform-d) δ 190.2, 164.5, 162.4, 136.1, 133.0, 132.9, 127.3, 125.1, 124.9, 124.0, 123.6, 121.2, 116.3, 116.1,
Ethyl 3-(4-chlorophenyl)-2-formylindolizine-1-carboxylate (5j)

(Eluent: ethyl acetate/petroleum ether = 1/10, v/v); 38% yield (yellow solid, mp 84–86 °C, 25 mg); \( ^1H \) NMR (600 MHz, Chloroform-d) \( \delta \) 10.77 (s, 1H), 8.33 (d, \( J = 9.2 \) Hz, 1H), 7.83 (d, \( J = 7.1 \) Hz, 1H), 7.51 (d, \( J = 8.3 \) Hz, 2H), 7.39 (d, \( J = 8.3 \) Hz, 2H), 7.16 – 7.12 (m, 1H), 6.74 (td, \( J = 6.9, 1.3 \) Hz, 1H), 4.46 (q, \( J = 7.2 \) Hz, 2H), 1.45 (t, \( J = 7.1 \) Hz, 3H). \( ^{13}C \) NMR (150 MHz, Chloroform-d) \( \delta \) 190.2, 164.5, 136.2, 135.55, 132.3, 129.3, 127.6, 127.0, 124.9, 124.0, 123.6, 121.2, 114.6, 104.1, 60.4, 14.6. HR-ESI-MS (m/z): calcd. for \( C_{18}H_{14}FNO_3 \) [M+H]\(^+\) 312.0735, found 312.0734.

Ethyl 2-formyl-3-(4-methoxyphenyl)indolizine-1-carboxylate (5k)

(Eluent: ethyl acetate/petroleum ether = 1/10, v/v); 36% yield (yellow solid, mp 83–85 °C, 23 mg); \( ^1H \) NMR (600 MHz, Chloroform-d) \( \delta \) 10.76 (s, 1H), 8.30 (d, \( J = 9.2 \) Hz, 1H), 7.87 (d, \( J = 7.1 \) Hz, 1H), 7.38 – 7.36 (m, 2H), 7.11 (ddd, \( J = 9.2, 6.5, 1.1 \) Hz, 1H), 7.06 – 7.03 (m, 2H), 6.71 (td, \( J = 6.9, 1.3 \) Hz, 1H), 4.45 (q, \( J = 7.1 \) Hz, 2H), 3.88 (s, 3H), 1.45 (t, \( J = 7.1 \) Hz, 3H). \( ^{13}C \) NMR (150 MHz, Chloroform-d) \( \delta \) 190.3, 164.6, 160.3, 136.0, 132.3, 128.7, 124.6, 123.9, 123.9, 121.0, 121.0, 114.4, 114.2, 103.6, 60.3, 55.4, 14.6. HR-ESI-MS (m/z): calcd. for \( C_{19}H_{17}NO_4 \) [M+H]\(^+\) 324.1230, found 324.1229.
Ethyl 2-formyl-3-(thiophen-2-yl)indolizine-1-carboxylate (5l)

(Eluent: ethyl acetate/petroleum ether = 1/10, v/v); 25% yield (brown solid, mp 72–74 °C, 15.1 mg); ¹H NMR (600 MHz, Chloroform-d) δ 10.76 (s, 1H), 8.32 (d, J = 8.4 Hz, 1H), 8.02 (d, J = 7.1 Hz, 1H), 7.59 (d, J = 6.2 Hz, 1H), 7.27 (dd, J = 3.5, 1.1 Hz, 1H), 7.22 (dd, J = 5.1, 3.6 Hz, 1H), 7.16 (dd, J = 9.2, 6.6 Hz, 1H), 6.79 (t, J = 6.9 Hz, 1H), 4.45 (q, J = 7.1 Hz, 2H), 1.45 (t, J = 7.2 Hz, 3H). ¹³C NMR (150 MHz, Chloroform-d) δ 189.9, 164.4, 136.5, 131.0, 128.9, 128.8, 127.6, 126.6, 124.4, 124.3, 120.9, 114.6, 104.1, 60.4, 14.6. HR-ESI-MS (m/z): calcd. for C₁₆H₁₃NO₃S [M+H]+ 300.0689, found 300.0688.

General procedure for synthesis of 3-acylated indolizines derivatives : 6a-6g

Under N₂ atmosphere, 2-pyridylacetates (1a, 0.2 mmol, 33.0 mg), phenylpropynyl aldehyde (4, 0.4 mmol, 52.0 mg), I₂ (0.7 mmol, 177.7 mg), dppe (0.04 mmol, 15.9 mg), CuI (0.4 mmol, 77.8 mg), Na₂CO₃ (0.4 mmol, 42.4 mg), were mixed in 2 mL DMF. The reaction tube was heated in an oil bath at 160 °C for 4 hours. After completion of the reaction, the reaction mixture was washed with saturated sodium thiosulfate solution and extracted with EtOAc (40 mL × 3), dried over anhydrous Na₂SO₄ and the solvent was removed under reduced pressure. The remaining crude product was then purified through column chromatography using silica gel (EtOAc/petroleum ether = 1/10) to afford 6a as a yellow solid in 76% yield.

Ethyl 3-benzoylindolizine-1-carboxylate (6a,CAS:40624-43-9)¹⁰

(Eluent: ethyl acetate/petroleum ether = 1/10, v/v); 76% yield (yellow solid, mp 72–74 °C, 15.1 mg); ¹H NMR (600 MHz, Chloroform-d) δ 10.76 (s, 1H), 8.32 (d, J = 8.4 Hz, 1H), 8.02 (d, J = 7.1 Hz, 1H), 7.59 (d, J = 6.2 Hz, 1H), 7.27 (dd, J = 3.5, 1.1 Hz, 1H), 7.22 (dd, J = 5.1, 3.6 Hz, 1H), 7.16 (dd, J = 9.2, 6.6 Hz, 1H), 6.79 (t, J = 6.9 Hz, 1H), 4.45 (q, J = 7.1 Hz, 2H), 1.45 (t, J = 7.2 Hz, 3H). ¹³C NMR (150 MHz, Chloroform-d) δ 189.9, 164.4, 136.5, 131.0, 128.9, 128.8, 127.6, 126.6, 124.4, 124.3, 120.9, 114.6, 104.1, 60.4, 14.6. HR-ESI-MS (m/z): calcd. for C₁₆H₁₃NO₃S [M+H]+ 300.0689, found 300.0688.
148–150 °C, 44.3 mg); $^1$H NMR (600 MHz, Chloroform-d) δ 9.97 (d, J = 7.0 Hz, 1H), 8.39 (d, J = 8.9 Hz, 1H), 7.83–7.80 (m, 3H), 7.58 (t, J = 7.4 Hz, 1H), 7.51 (t, J = 7.5 Hz, 2H), 7.46–7.43 (m, 1H), 7.09 (t, J = 7.5 Hz, 1H), 4.37 (q, J = 7.1 Hz, 2H), 1.39 (t, J = 7.1 Hz, 3H). $^{13}$C NMR (150 MHz, Chloroform-d) δ 185.6, 164.1, 139.9, 131.5, 129.2, 129.1, 129.0, 128.4, 127.7, 122.5, 119.5, 115.3, 106.3, 60.1, 14.6. HR-ESI-MS (m/z): calcd. for C$_{18}$H$_{16}$NO$_3$ [M+H]$^+$ 294.1125, found 294.1131.

**Ethyl 3-(4-fluorobenzoyl)indolizine-1-carboxylate (6b,CAS:1003050-05-2)$^{11}$**

![Chemical structure of ethyl 3-(4-fluorobenzoyl)indolizine-1-carboxylate](image)

(Eluent: ethyl acetate/petroleum ether = 1/10, v/v); 60% yield (pale yellow solid, mp 102–104 °C, 37.3 mg); $^1$H NMR (600 MHz, Chloroform-d) δ 9.91 (d, J = 7.0 Hz, 1H), 8.38 (d, J = 8.9 Hz, 1H), 7.84 (dd, J = 8.7, 5.4 Hz, 2H), 7.78 (s, 1H), 7.46–7.43 (m, 1H), 7.19 (t, J = 8.6 Hz, 2H), 7.08 (t, J = 6.3 Hz, 1H), 4.37 (q, J = 7.1 Hz, 2H), 1.40 (t, J = 7.1 Hz, 3H). $^{13}$C NMR (150 MHz, Chloroform-d) δ 184.1, 165.6, 164.0, 139.9, 136.1, 131.4, 131.3, 129.2, 128.8, 127.8, 122.3, 119.6, 115.6, 115.5, 115.4, 106.4, 60.2, 14.6. HR-ESI-MS (m/z): calcd. for C$_{18}$H$_{14}$FNO$_3$ [M+H]$^+$ 312.1030, found 312.1029.

**Ethyl 3-(4-chlorobenzoyl)indolizine-1-carboxylate (6c,CAS:1003050-06-3)$^{11}$**

![Chemical structure of ethyl 3-(4-chlorobenzoyl)indolizine-1-carboxylate](image)

(Eluent: ethyl acetate/petroleum ether = 1/10, v/v); 71% yield (yellow solid, mp 81–83 °C, 46.4 mg); $^1$H NMR (600 MHz, Chloroform-d) δ 9.92 (d, J = 7.0 Hz, 1H), 8.39 (d, J = 8.9 Hz, 1H), 7.77 (d, J = 3.0 Hz, 2H), 7.75 (s, 1H), 7.50–7.44 (m, 3H), 7.09 (t, J = 6.9 Hz, 1H), 4.37 (q, J = 7.2 Hz, 2H), 1.40 (t, J = 7.1 Hz, 3H). $^{13}$C NMR (150 MHz, Chloroform-d) δ 184.1, 164.0, 140.0, 138.2, 137.8, 130.4, 129.2, 128.8,
Ethyl 3-((4-methoxybenzoyl)indolizine-1-carboxylate (6d, CAS: 1003050-04-1)\textsuperscript{11}

![Chemical Structure]

(Eluent: ethyl acetate/petroleum ether = 1/20, v/v); 60% yield (yellow solid, mp 88–90 °C, 35 mg); \textsuperscript{1}H NMR (600 MHz, Chloroform-d) \textsuperscript{\textdagger} δ 9.89 (d, J = 7.0 Hz, 1H), 8.36 (s, 1H), 7.84 (s, 1H), 7.82 (d, J = 5.8 Hz, 2H), 7.43 – 7.38 (m, 1H), 7.05 (t, J = 6.5 Hz, 1H), 7.01 (d, J = 8.8 Hz, 2H), 4.37 (q, J = 7.1 Hz, 2H), 3.89 (s, 3H), 1.40 (t, J = 7.1 Hz, 3H). \textsuperscript{13}C NMR (150 MHz, Chloroform-d) \textsuperscript{\textdagger} δ 184.6, 164.2, 162.5, 139.7, 132.4, 131.2, 129.1, 128.4, 127.4, 122.6, 119.5, 115.1, 113.7, 105.9, 60.1, 55.5, 14.6. HR-ESI-MS (m/z): calcd. for C\textsubscript{19}H\textsubscript{17}NO\textsubscript{4} [M+H]\textsuperscript{+} 324.1230, found 324.1229.

Ethyl 3-((thiophene-2-carbonyl)indolizine-1-carboxylate (6e, CAS: 1003050-07-4)\textsuperscript{10}

![Chemical Structure]

(Eluent: ethyl acetate/petroleum ether = 1/10, v/v); 57% yield (yellow solid, mp 81–83 °C, 34 mg); \textsuperscript{1}H NMR (600 MHz, Chloroform-d) \textsuperscript{\textdagger} δ 9.83 (d, J = 7.1 Hz, 1H), 8.37 (d, J = 8.9 Hz, 1H), 8.13 (d, J = 1.6 Hz, 1H), 7.81 (d, J = 4.7 Hz, 1H), 7.66 (d, J = 5.0 Hz, 1H), 7.44 – 7.39 (m, 1H), 7.21 – 7.18 (m, 1H), 7.05 (t, J = 6.9 Hz, 1H), 4.40 (q, J = 6.9 Hz, 2H), 1.42 (t, J = 7.1 Hz, 3H). \textsuperscript{13}C NMR (150 MHz, Chloroform-d) \textsuperscript{\textdagger} δ 176.4, 164.1, 144.3, 139.9, 132.1, 132.1, 129.1, 127.8, 127.6, 127.3, 122.2, 119.6, 115.2, 106.4, 60.2, 14.6. HR-ESI-MS (m/z): calcd. for C\textsubscript{16}H\textsubscript{13}NO\textsubscript{3}S [M+H]\textsuperscript{+} 300.0689, found 300.0688.

Ethyl 3-pentanoylindolizine-1-carboxylate (6f)
(Eluent: ethyl acetate/petroleum ether = 1/10, v/v); 59% yield (yellow solid, mp 42–44 °C, 32 mg); \(^1\)H NMR (600 MHz, Chloroform-d) \(\delta\) 9.93 (d, J = 7.1 Hz, 1H), 8.33 (d, J = 8.9 Hz, 1H), 8.01 (s, 1H), 7.38 (ddd, J = 8.8, 6.8, 1.0 Hz, 1H), 7.01 (td, J = 7.0, 1.4 Hz, 1H), 4.40 (q, J = 7.1 Hz, 2H), 2.93 – 2.89 (m, 2H), 1.76 (p, J = 7.7 Hz, 2H), 1.43 (td, J = 7.4, 3.4 Hz, 5H), 0.96 (t, J = 7.4 Hz, 3H). \(^{13}\)C NMR (150 MHz, Chloroform-d) \(\delta\) 191.1, 164.2, 139.3, 129.2, 127.1, 125.6, 122.7, 119.4, 115.1, 105.6, 60.1, 39.2, 27.7, 22.6, 14.6, 14.0. HR-ESI-MS (m/z): calcd. for C\(_{16}\)H\(_{19}\)NO\(_3\) [M+H]\(^+\) 274.1438, found 274.1437.

**Ethyl 3-benzoyl-6-methylindolizine-1-carboxylate (6g)**

(Eluent: ethyl acetate/petroleum ether = 1/10, v/v); 54% yield (brown solid, mp 123–125 °C, 33.1 mg); \(^1\)H NMR (600 MHz, Chloroform-d) \(\delta\) 9.80 (s, 1H), 8.27 (d, J = 9.0 Hz, 1H), 7.82 – 7.78 (m, 2H), 7.75 (s, 1H), 7.59 – 7.54 (m, 1H), 7.50 (t, J = 7.4 Hz, 2H), 7.30 (d, J = 9.1 Hz, 1H), 4.36 (q, J = 7.1 Hz, 2H), 2.43 (d, J = 1.2 Hz, 3H), 1.38 (t, J = 7.1 Hz, 3H). \(^{13}\)C NMR (150 MHz, Chloroform-d) \(\delta\) 185.4, 164.1, 140.0, 138.6, 131.3, 130.6, 128.9, 128.8, 128.3, 127.3, 125.3, 122.2, 118.7, 106.0, 60.0, 18.5, 14.5. HR-ESI-MS (m/z): calcd. for C\(_{19}\)H\(_{17}\)NO\(_3\) [M+H]\(^+\) 308.3490, found 308.3493.

**General procedure for synthesis of product 7a-7b :**

Under N\(_2\) atmosphere, 2-pyridylacetates (1a, 0.8 mmol, 132.2 mg), 1,4-diphenyl butadiyne (6, 0.2 mmol, 40.4 mg), I\(_2\) (0.4 mmol, 101.5 mg), dppe (0.04 mmol, 15.9 mg), Na\(_2\)CO\(_3\) (0.4 mmol, 42.4 mg), were mixed in 2 mL DMF. The reaction tube was heated in an oil bath at 160 °C for 4 hours. After completion of the reaction, the
reaction mixture was washed with saturated sodium thiosulfate solution and extracted with EtOAc (40 mL × 3), dried over anhydrous Na$_2$SO$_4$ and the solvent was removed under reduced pressure. The remaining crude product was then purified through column chromatography using silica gel (EtOAc/petroleum ether = 1/20) to afford 7a as a yellow solid in 38% yield.

**Ethyl 3-phenyl-2-(phenylethynyl)indolizine-1-carboxylate (7a)**

![Chemical Structure]

(Eluent: ethyl acetate/petroleum ether = 1/20, v/v); 38% yield (yellow solid, mp 111–113 °C, 28 mg); $^1$H NMR (600 MHz, Chloroform-d) δ 8.43 (dt, J = 6.8, 1.2 Hz, 1H), 8.33 (dt, J = 9.1, 1.2 Hz, 1H), 7.65 (dt, J = 6.4, 1.4 Hz, 2H), 7.47 – 7.41 (m, 4H), 7.41 – 7.37 (m, 1H), 7.35 – 7.30 (m, 3H), 7.21 (ddd, J = 9.0, 6.7, 1.2 Hz, 1H), 6.91 (td, J = 6.8, 1.3 Hz, 1H), 4.26 (q, J = 7.1 Hz, 2H), 1.22 (t, J = 7.1 Hz, 3H). $^{13}$C NMR (150 MHz, Chloroform-d) δ 164.5, 137.0, 136.3, 133.9, 131.0, 130.7, 128.4, 128.3, 127.5, 127.4, 125.2, 124.2, 122.9, 120.2, 113.4, 108.3, 102.4, 98.5, 79.3, 59.6, 14.2. HR-ESI-MS (m/z): calcd. for C$_{25}$H$_{19}$NO$_2$ [M+H]$^+$ 366.1489, found 366.1497.

**Ethyl 3-buty1-2-(hex-1-yn-1-yl)indolizine-1-carboxylate (7b)**

![Chemical Structure]

(Eluent: ethyl acetate/petroleum ether = 1/20, v/v); 35% yield (brown oil, 22.7 mg); $^1$H NMR (600 MHz, Chloroform-d) δ 8.21 (d, J = 5.9 Hz, 1H), 8.18 (d, J = 8.0 Hz, 1H), 7.08 (s, 1H), 6.77 (d, J = 14.7 Hz, 1H), 4.37 (q, J = 7.1 Hz, 2H), 3.03 – 2.99 (m, 2H), 2.59 (t, J = 7.0 Hz, 2H), 1.69 – 1.62 (m, 4H), 1.58 (s, 2H), 1.41 (t, J = 7.1 Hz, 5H), 0.98 (t, J = 7.3 Hz, 3H), 0.95 (t, J = 7.4 Hz, 3H). $^{13}$C NMR (150 MHz, Chloroform-d) δ 165.1, 137.3, 136.3, 124.7, 123.0, 119.6, 112.5, 108.8, 101.6, 69.9, 59.3, 33.0, 31.0, 26.4, 22.8, 19.6, 14.6, 14.0, 13.6. HR-ESI-MS (m/z): calcd. for
General procedure for synthesis of product 8a-8b:
Under N₂ atmosphere, 2-pyridylacetates (1a, 0.4 mmol, 66.0 mg), ethyl 3-phenyl-2-(phenylethynyl)indolizine-1-carboxylate (7a, 0.1 mmol, 36.5 mg), I₂ (0.4 mmol, 101.5 mg), dppe (0.04 mmol, 15.9 mg), Na₂CO₃ (0.4 mmol, 42.4 mg), were mixed in 2 mL DMF. The reaction tube was heated in an oil bath at 160 °C for 4 hours. After completion of the reaction, the reaction mixture was washed with saturated sodium thiosulfate solution and extracted with EtOAc (40 mL × 3), dried over anhydrous Na₂SO₄ and the solvent was removed under reduced pressure. The remaining crude product was then purified through column chromatography using silica gel (EtOAc/petroleum ether = 1/20) to afford 8a as a yellow solid in 66% yield.

Diethyl 3,3'-diphenyl-[2,2'-biindolizine]-1,1'-dicarboxylate (8a)

(Eluent: ethyl acetate/petroleum ether = 1/20, v/v); 66% yield (yellow solid, mp 134–136 °C, 34.7 mg); ¹H NMR (600 MHz, Chloroform-d) δ 8.35 – 8.30 (m, 2H), 7.42 (d, J = 6.9 Hz, 2H), 7.16 – 7.13 (m, 4H), 7.10 (dd, J = 8.2, 6.5 Hz, 4H), 6.93 (dt, J = 7.0, 1.4 Hz, 4H), 6.65 (td, J = 6.8, 1.3 Hz, 2H), 4.20 (qt, J = 7.1, 3.7 Hz, 4H), 1.14 (t, J = 7.1 Hz, 6H). ¹³C NMR (150 MHz, Chloroform-d) δ 164.9, 137.2, 135.2, 134.0, 129.6, 127.2, 127.0, 123.5, 123.4, 120.3, 113.2, 112.9, 102.6, 59.5, 14.1. HR-ESI-MS (m/z): calcd. for C₃₄H₃₈N₂O₄ [M+H]⁺ 529.2122, found 529.2121.

Ethyl 3,3'-dibutyl-1'-ethyl-[2,2'-biindolizine]-1-carboxylate (8b)
(Eluent: ethyl acetate/petroleum ether = 1/20, v/v); 28% yield (yellow oil, 27.2 mg); 

$^1$H NMR (400 MHz, Chloroform-d) $\delta$ 8.30 (d, $J = 9.0$ Hz, 2H), 7.24 (s, 2H), 7.12 – 7.06 (m, 2H), 6.62 – 6.56 (m, 2H), 4.40 (q, $J = 7.1$ Hz, 4H), 2.73 – 2.63 (m, 4H), 1.43 (t, $J = 7.1$ Hz, 10H), 1.22 – 1.11 (m, 4H), 0.70 (t, $J = 7.3$ Hz, 6H). $^{13}$C NMR (100 MHz, Chloroform-d) $\delta$ 165.3, 137.6, 136.4, 123.3, 123.1, 119.9, 112.6, 112.3, 102.3, 59.4, 33.2, 26.3, 22.9, 14.6, 13.8. HR-ESI-MS (m/z): calcd. for C$_{30}$H$_{36}$N$_{2}$O$_{4}$ [M+H]$^+$ 489.2676, found 489.2680.

**General procedure for synthesis of product 9:**

Under N$_2$ atmosphere, 2-pyridylacetates (1a, 0.2 mmol, 33.0 mg), phenylacetylene (2a, 0.4 mmol, 40.9 mg), 2,2,6,6-ter-amethylpiperidine N-oxide (TEMPO) (0.4 mmol, 63.8 mg), I$_2$ (0.4 mmol, 101.5 mg), dppe (0.04 mmol, 15.9 mg), Na$_2$CO$_3$ (0.4 mmol, 42.4 mg), were mixed in 2 mL DMF. The reaction tube was heated in an oil bath at 160 °C for 4 hours. After completion of the reaction, the reaction mixture was washed with saturated sodium thiosulfate solution and extracted with EtOAc (40 mL × 3), dried over anhydrous Na$_2$SO$_4$ and the solvent was removed under reduced pressure. The remaining crude product was then purified through column chromatography using silica gel (EtOAc/petroleum ether = 1/5) to afford product 9 as a brown oil in 49% yield.

**Ethyl 2-(pyridin-2-yl)-2-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)acetate (9).**
(Eluent: ethyl acetate/petroleum ether = 1/5, v/v); 49% yield (brown oil, 31.4 mg); $^1$H NMR (600 MHz, Chloroform-d) $\delta$ 8.56 (d, J = 4.4 Hz, 1H), 7.73 (td, J = 7.7, 1.7 Hz, 1H), 7.62 (d, J = 7.8 Hz, 1H), 7.23 – 7.20 (m, 1H), 5.42 (s, 1H), 4.23 – 4.13 (m, 2H), 1.50 (d, J = 6.8 Hz, 2H), 1.42 (s, 2H), 1.32 (d, J = 11.7 Hz, 1H), 1.28 – 1.21 (m, 7H), 1.19 (s, 3H), 1.13 (s, 3H), 0.71 (s, 3H). $^{13}$C NMR (150 MHz, Chloroform-d) $\delta$ 171.2, 158.1, 149.1, 136.8, 122.9, 121.8, 89.7, 61.0, 60.1, 40.2, 33.3, 32.9, 20.3, 17.1, 14.2. HR-ESI-MS (m/z): calcd. For C$_{18}$H$_{28}$N$_2$O$_3$K [M+K]$^+$ 359.1732, found 359.1731.
5c

![Diagram of a chemical structure with labels COO\text{Pr} and COOEt]
S106
COOEt, C₄H₉, C₄H₉COOEt

8b
\begin{align*}
\text{COOEt} & \quad C_4H_9 \\
C_4H_9C\text{OOC}=\text{Et} & \quad C_4H_9
\end{align*}

8b
ORTEP diagram of product 4p:
ORTEP diagram of product 5a:
References: