Synthesis L. He et al. Paper

Iodine-Mediated Oxidative Cyclization of 2-(Pyridin-2-yl)acetate Derivatives with Alkynes: Condition-Controlled Selective Synthesis of Multisubstituted Indolizines

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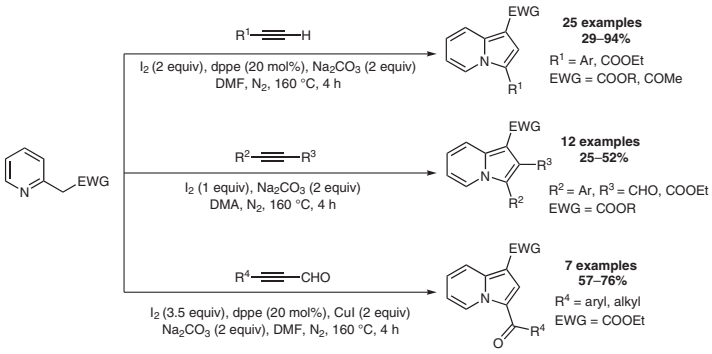

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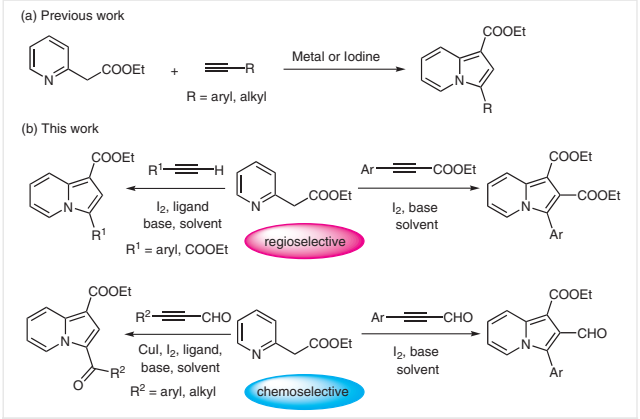
Abstract An iodine-mediated oxidative cyclization reaction between 2-(pyridin-2-yl)acetate derivatives and different alkynes has been developed, which provides regioselective and chemoselective syntheses of multiply substituted indolizines under modified reaction conditions. Plausible mechanisms have been proposed to explain the selective syntheses of indolizines. This protocol can be also applied to the stepwise synthesis of 2,2′-biindolizines.

Key words indolizines, iodine, radical process, regioselective, chemoselective

As N-fused heterocycles, indolizines are ubiquitous scaffolds found in many natural products and bioactive compounds.[1] Functionalized indolizines have found wide applications in pharmaceuticals with several biological activities, such as antitubercular,[2] anti-inflammatory,[3] antifungal,[4] anticancer,[5] antioxidant,[6] and usage as molecular probes.[7] Accordingly, the development of efficient methods for the generation of indolizines continues to receive considerable attention in organic chemistry over the years. The majority of the approaches for indolizine synthesis include 1,3-dipolar cycloaddition,[8] intramolecular cyclization of pyridine derivatives with alkynes,[9] and intermolecular cyclization of 2-alkylpyridine derivatives with alkenes.[10] It is noteworthy that the reaction of terminal alkynes with 2-(pyridin-2-yl)acetate derivatives for the synthesis of 1,3-disubstituted indolizines under metal catalysis or in the presence of iodine have been reported by Agrawal,[11] Lei,[12] and Adimurthy[13] (Scheme 1a). However, only terminal alkynes were investigated and no issue of regioselectivity or chemoselectivity was discussed in the above reports. Herein we report our results of the condition-controlled selective syntheses of multiply substituted indolizines from 2-(pyridin-2-yl)acetates and alkynes. Under iodine-promoted reaction conditions, terminal alkynes and 3-phenylpropiolate could react with 2-(pyridin-2-yl)acetates to give substituted indolizines regioselectively via radical process. Additionally, 3-phenylpropiolaldehyde could react with 2-(pyridin-2-yl)acetates to chemoselectively give C3-acylated indolizines via a condensation/intramolecular cyclization pathway, or give C2-carbaldehyde substituted indolizines via an annulation pathway (Scheme 1b).



Scheme 1 Synthesis of indolizines via cyclization of 2-(pyridin-2-yl)-acetate derivatives and alkynes

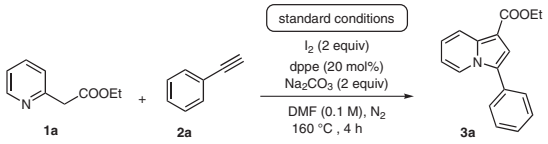
Georg Thieme Verlag KG, Rüdigerstraße 14, 70469 Stuttgart, Germany

We performed the reaction of ethyl 2-(pyridin-2-yl)acetate (**1a**) and phenylacetylene (**2a**) as model substrates for optimization. It was found that the combination of iodine and dppe in the presence of Na_2CO_3 afforded the highest 93% yield after stirring in DMF at 160 °C for 4 hours (Table 1, entry 1). By decreasing or increasing the amount of iodine, the yield of the desired product dropped. No product was detected in the absence of iodine (entries 2–4). The results revealed that iodine was necessary for initiating the reaction. Without the addition of dppe, the yield decreased to 69%, while increasing the amount of dppe to 40 mol% delivered the product in slightly decreased yield (entries 5, 6). After screening other phosphine ligands as well as nitrogen ligands, it was found that dppe was still the best choice (entries 7–14). Only trace amount of product could be detected without the addition of Na_2CO_3, while decreasing or increasing the amount of Na_2CO_3 leads to no better yields (entries 15–17). Furthermore, other bases such as Li_2CO_3, K_2CO_3, or Cs_2CO_3 led to decreased yields (entries 18–20). In spite of DMF, other solvents like NMP, DMA, and DMSO could also be used for this reaction, albeit affording the product in lower yields (entries 21–23). After the investigation of concentration of this reaction, 0.1 M concentration could generate the product **3a** with the highest yield (entries 24, 25). Subsequently, the reaction temperature, the reaction time, and the atmosphere were investigated. It was found that decreasing the temperature to 140 °C could not increase the yield (entry 26), shortening the reaction time to 1 hour or 2 hours, and prolonging the reaction time to 8 hours resulted in reduced yields (entry 27–29). The ratio of the reactants was also examined and the results indicated that the best case is the ratio of **1a** and **2a** equals to 0.5 (entries 30, 31). Finally the yield dropped to 67% when the reaction was performed under air atmosphere (entry 32).

With the optimal reaction conditions in hand, we next extended the scope of 2-(pyridin-2-yl)acetate derivatives (Scheme 2). Different 2-pyridyl esters (COOMe, COO^{i}Pr, COO^{t}Bu, and COO^{n}Bu groups) reacted well with phenylacetylene (**2a**) to afford the corresponding indolizines **3b–e** in moderate to good yields. When 1-(pyridin-2-yl)propan-2-one was used under these reaction conditions, the product **3f** was isolated in only 38% yield. Ethyl 2-(6-methylpyridin-2-yl)acetate could react with phenylacetylene to give the product **3g** in 74% yield. Ethyl 2-(5-methylpyridin-2-yl)-acetate and ethyl 2-(5-bromopyridin-2-yl)acetate are also work well under these conditions to afford the corresponding products **3h** in 60% yield and **3i** in 48% yield.

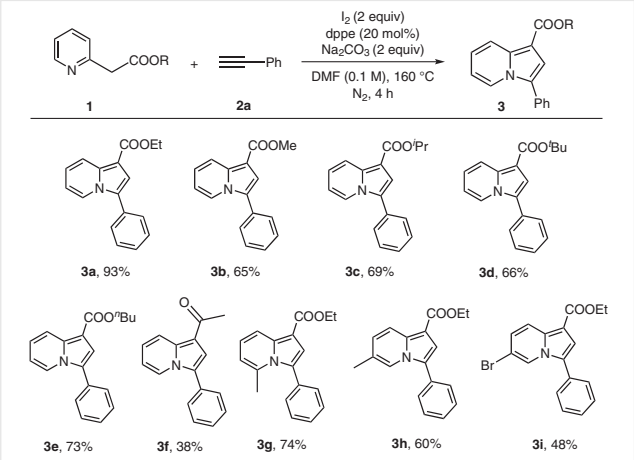
Subsequently, we investigated the scope of alkynes under the optimized conditions (Scheme 3). Most of the terminal alkyne substrates could proceed smoothly under the conditions to give the corresponding products in moderate yields. The *ortho*-fluorinated product **4a** was isolated in only 54% yield possibly due to the steric hindrance effect. Notably, electron-withdrawing groups (such as F, CF_3, Cl, Br, and NO_2) at the *para*-position in phenylacetylene gave the products **4c–g** in moderate to good yields (69–94%). Furthermore, arylalkynes with electron-donating groups (such as Me, ^{t}Bu, OMe, and Ph) at the *para*-position proceeded smoothly to deliver the desired products **4h–k** in moderate

Table 1 Optimization of Reaction Conditions[a]



Entry	Deviation from the standard conditions	Yield (%)[b] of **3a**
1	no change	93
2	without I_2	0
3	1 equiv I_2	45
4	3 equiv I_2	64
5	without dppe	69
6	40% dppe	90
7	PPh_3 instead of dppe	69
8	dppp instead of dppe	85
9	dppb instead of dppe	78
10	DPEphos instead of dppe	83
11	P(4-MeOC$_6$H$_4$)$_3$ instead of dppe	69
12	P(4-FC$_6$H$_4$)$_3$ instead of dppe	67
13	1,10-phenanthroline instead of dppe	61
14	2,2′-bipyridine instead of dppe	68
15	without Na_2CO_3	4
16	1 equiv Na_2CO_3	46
17	3 equiv Na_2CO_3	70
18	Li_2CO_3 instead of Na_2CO_3	51
19	K_2CO_3 instead of Na_2CO_3	54
20	Cs_2CO_3 instead of Na_2CO_3	47
21	DMA instead of DMF	72
22	NMP instead of DMF	64
23	DMSO instead of DMF	25
24	0.2 M instead of 0.1 M	64
25	0.07 M instead of 0.1 M	80
26	140 °C instead of 160 °C	35
27	1 h instead of 4 h	72
28	2 h instead of 4 h	75
29	8 h instead of 4 h	74
30	ratio of **1a**/**2a** = 1:1	47
31	ratio of **1a**/**2a** = 2:1	60
32	under air atmosphere	67

[a] Reaction conditions: **1a** (0.2 mmol), **2a** (0.4 mmol), I_2 (0.4 mmol), dppe (0.04 mmol), Na_2CO_3 (0.4 mmol) in DMF (2 mL) at 160 °C for 4 h.
[b] Isolated yield.

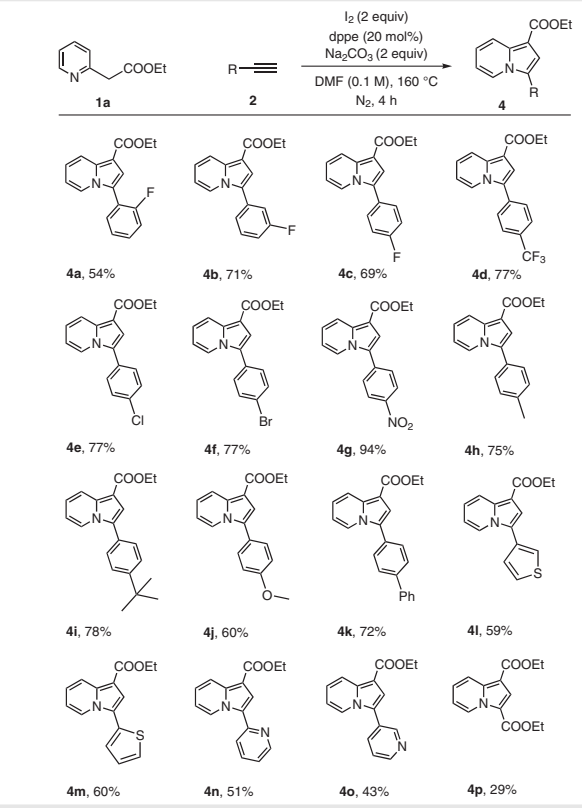


Scheme 2 Substrate scope of 2-(pyridin-2-yl)acetates **1**. *Reagents and conditions*: **1** (0.2 mmol), **2a** (0.4 mmol), I_2 (0.4 mmol), dppe (0.04 mmol), Na_2CO_3 (0.4 mmol), in DMF (2 mL) at 160 °C for 4 h. Isolated yields are shown.

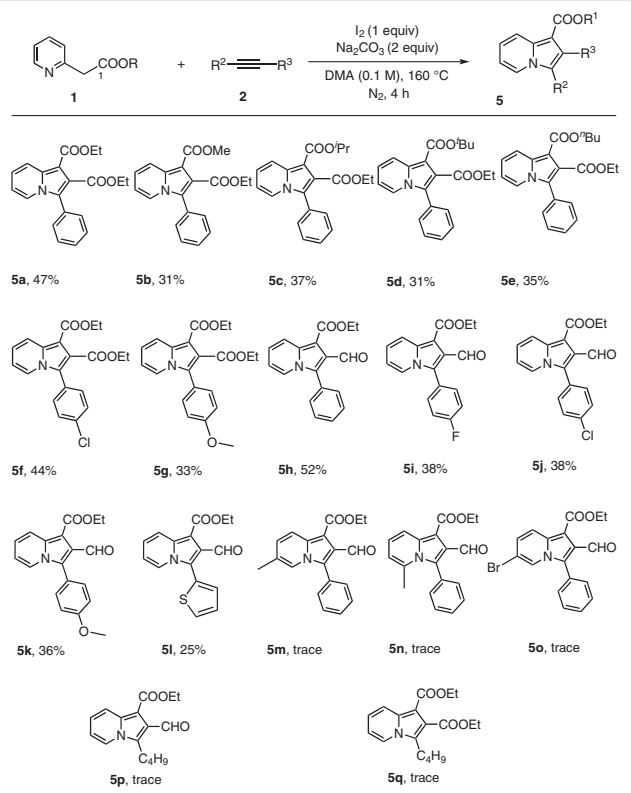
yields (60–78%). The terminal alkynes containing thiophene moiety or pyridine moiety could also afford the corresponding products **4l–o** in 43–60% yields. When ethyl propiolate was subjected to the reaction conditions, the desired product **4p** was isolated in only 29% yield, and the structure was confirmed by single-crystal X-ray diffraction (see ORTEP diagram in SI).

It is noteworthy that in this reaction system, internal alkynes such as ethyl phenylpropynoate could also work under modified reaction conditions to give the regiospecific products in moderate yields (Scheme 4). 3-Phenylpropiolaldehyde was chosen as model substrate for optimization (Table S1 in SI). The amount of iodine was investigated and one equivalent of iodine showed better yield (Table S1, entries 1–5). It is gratifying that the yield of product **5h** increased to 52% when the reaction was conducted in DMA solvent without ligand (entry 7). Other solvents such as NMP and DMSO do not help to increase the yield (entries 8, 9). After the optimization process, we began to extend the substrate scope of this reaction. Various 2-alkylpyridine derivatives bearing different ester groups (such as COOEt, COOMe, COO^{i}Pr, COO^{t}Bu, and COO^{n}Bu) were well tolerated under the optimized reaction conditions and the corresponding indolizine derivatives **5a–e** were obtained in 31–47% yields. The structure of **5a** was confirmed by single-crystal X-ray diffraction (see ORTEP diagram in SI). In addition, substrates with both electron-withdrawing group (Cl) and electron-donating group (OMe) at the *para*-position reacted under these conditions to afford the products **5f** in 44% yield and **5g** in 33% yield. 3-Phenylpropiolaldehyde also worked well in this reaction to give the annulation product **5h** with C2-carbaldehyde group in 52% yield. Substrates with electron-withdrawing groups (F and Cl) and electron-donating groups group (OMe) at the *para*-position afforded the desired products **5i–k**. 3-(Thiophen-2-yl)propiolaldehyde could also be employed in this reaction to give the corresponding product **5l**, but in only 25% yield. However, substrates with substituents on the pyridine ring are not compatible with the reaction conditions: only trace amounts of products were detected. When hept-2-ynal or ethyl hept-2-ynoate were subjected to this reaction, no product was isolated.

Based upon the above conditions for the annulation reaction involving 3-phenylpropiolaldehyde, the addition of copper iodide and dppe could switch the product to C3-acylated indolizines **6a** in 76% yield (Scheme 5; for detailed optimization, see Table S2 in SI). Thus, a condition-controlled chemoselective synthesis of C2-carbaldehyde-substituted indolizines and C3-acylated indolizines has been established. Substrates bearing both electron-withdrawing groups (F and Cl) and an electron-donating group (OMe) at the *para*-position were compatible with the reaction conditions, delivering the indolizine products **6b–d** in 54–71% yields. Moreover, 3-(thiophen-2-yl)propiolaldehyde and hept-2-ynal could also react in this reaction, affording the corresponding product **6e** in 57% yield and **6f** in 59% yield, respectively. Ethyl 2-(5-methylpyridin-2-yl)acetate deliv-



Scheme 3 Substrate scope of alkynes **2**. *Reagents and conditions*: **1a** (0.2 mmol), **2** (0.4 mmol), I_2 (0.4 mmol), dppe (0.04 mmol), Na_2CO_3 (0.4 mmol) in DMF (2 mL) at 160 °C for 4 h. Isolated yields are shown.



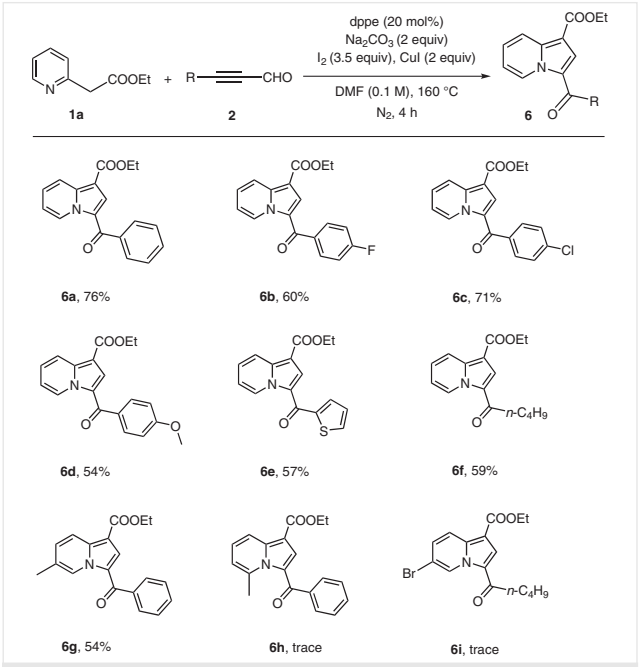
Scheme 4 Substrate scope of 2-(pyridin-2-yl)acetates **1** and internal alkynes **2**. *Reagents and conditions*: **1** (0.2 mmol), **2** (0.4 mmol), I_2 (0.2 mmol), Na_2CO_3 (0.4 mmol) in DMF (2 mL) at 160 °C for 4 h. Isolated yields are shown.

ered the expected product **6g** in 54% yield, while ethyl 2-(6-methylpyridin-2-yl)acetate and ethyl 2-(5-bromopyridin-2-yl)acetate did not react: only trace amounts of products were detected.

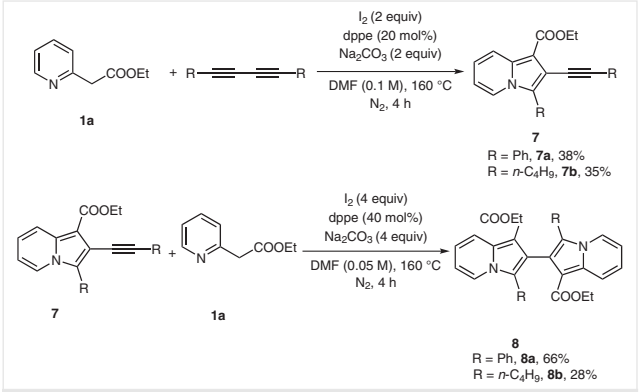
To the best of our knowledge, there is no report describing the preparation of 2,2′-biindolizines, while only one paper from You's group reported the synthesis of 3,3′-biindolizines via palladium-catalyzed homo-coupling reaction.[14] The demonstration of this protocol for the synthesis of 2,2′-biindolizines is shown in Scheme 6. The reaction of **1a** with 1,4-diphenylbuta-1,3-diyne could proceed under the standard conditions smoothly to generate **7a** in 38% yield. The reaction of **7a** with **1a** afforded 2,2′-biindolizine **8a** in 66% yield. When the reaction was performed with the aliphatic diyne, dodeca-5,7-diyne, under the same conditions, the corresponding product was isolated with **7b** in 35% yield and **8b** in 28% yield.

In order to elucidate the mechanism of the reaction, control experiments were investigated (Scheme 7). First, radical trapping experiment (Scheme 7, eq 1) was performed in the presence of 2,2,6,6-tetramethylpiperidinyloxyl (TEMPO). The addition of 2 equivalents of TEMPO led to the oxidative process being remarkably suppressed and the coupling product **9** was isolated in 49% yield. Then ^{18}O-labeled water was added to the reaction of **1a** with 3-phenylpropiolaldehyde for the synthesis of C3-acylated indolizines. Product **6a′** with ^{18}O in the carbonyl group was not detected by using $^{18}O_2$ as atmosphere in the reaction (Scheme 7, eq 2). The products **6a** and **6a′** were detected by LC–MS when the reaction was performed with the combination of DMF and $H_2{}^{18}O$ (Scheme 7, eq 3).

On the basis of the above results and previous reports,[15] a plausible mechanism of the regioselective annulation reaction is proposed as shown in Scheme 8. In Path A, oxidation of **1a** by I_2 generates the radical intermediate **A**, which

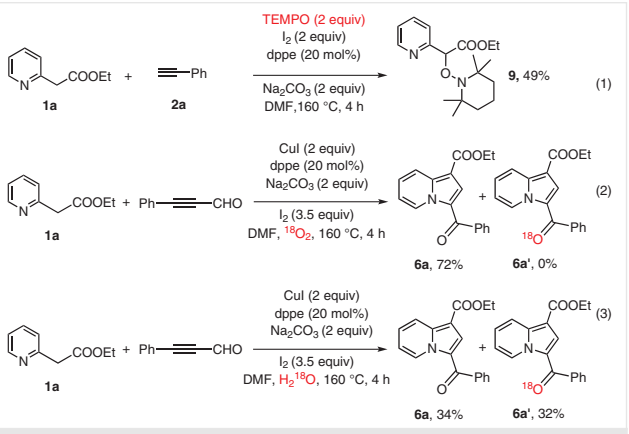


Scheme 5 Substrate scope of ynals **2**. *Reagents and conditions*: **1a** (0.2 mmol), **2** (0.4 mmol), I_2 (0.7 mmol), CuI (0.4 mmol), dppe (0.04 mmol), Na_2CO_3 (0.4 mmol), in DMF (2 mL) at 160 °C for 4 h. Isolated yields are given.

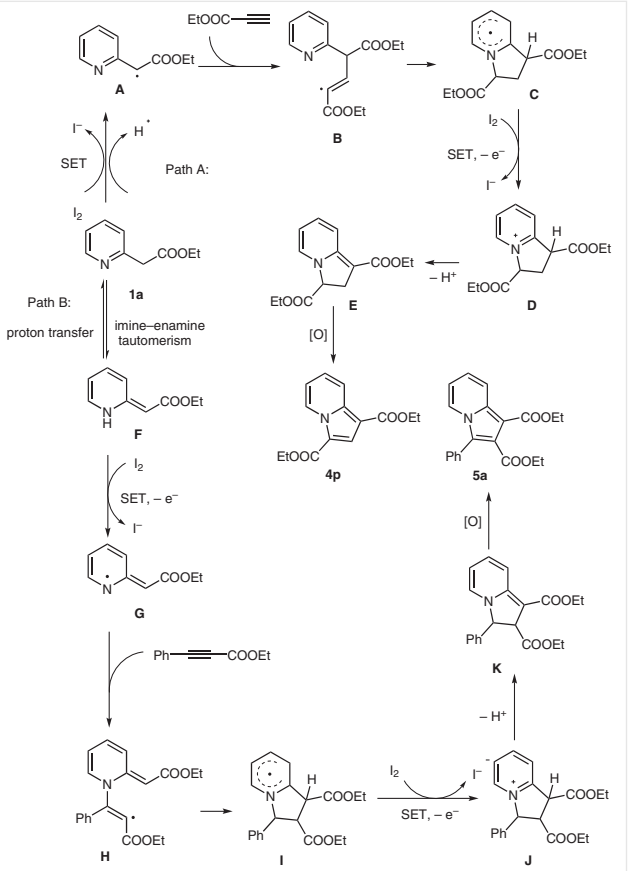


Scheme 6 Demonstration of this protocol for the stepwise synthesis of 2,2′-biindolizines **8**

reacts with ethyl propiolate to afford the radical intermediate **B**. Subsequently, intramolecular cyclization would generate the intermediate **C**, which undergoes oxidation to form the intermediate **D** in the presence of I_2. Further deprotonation and dehydrogenative aromatization would give the final product **4p**. In Path B, the imine–enamine tautomerism would generate the intermediate **F** under basic conditions. Oxidation of the intermediate **F** would produce nitrogen radical in the intermediate **G**, which reacts with ethyl 3-phenylpropiolate to give the intermediate **H** followed by intramolecular ring closure to afford the intermediate **I**. Similar transformation involving oxidation, deprotonation, and dehydrogenative aromatization would produce the final product **5a**.

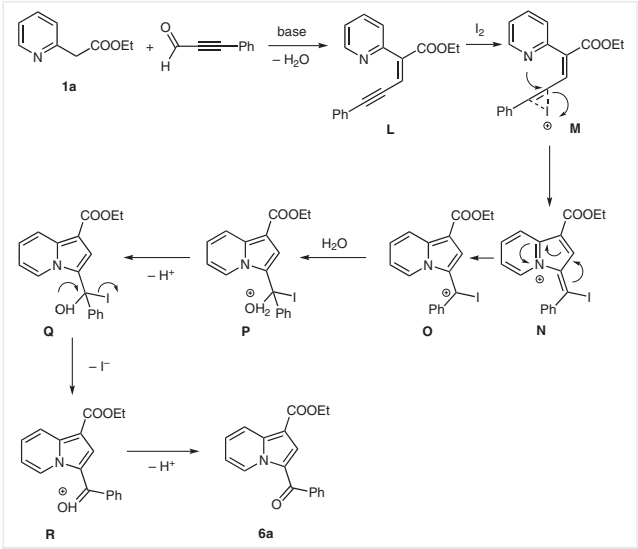


Scheme 7 Control experiments



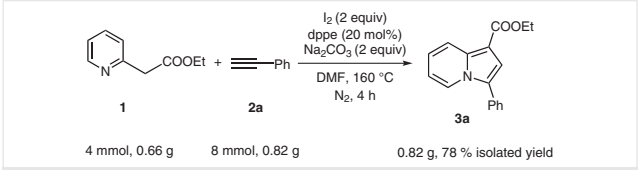
Scheme 8 Plausible mechanism for product **4** and **5**

For the C3-acylated product from 3-phenylpropiolaldehyde via condensation/intramolecular cyclization sequence, a plausible mechanism is proposed as shown in Scheme 9 based on the results from control experiments and previous reports.[16] The initial condensation of starting materials would generate the intermediate **L**, followed by the complexation with iodine to form the iodonium complex **M**. The intramolecular cyclization would produce the intermediate **N**. Isomerization of the intermediate **N** would generate the intermediate **O**, which reacts with water to form the intermediate **P**. Subsequent deprotonation, deiodination, and deprotonation would generate the final product.



Scheme 9 Plausible mechanism for product **6**

We also performed the reaction in gram scale to verify the feasibility of this protocol (Scheme 10). When 4 mmol 2-(pyridin-2-yl)acetate was subjected to this reaction, 0.82 gram of the product **3a** was isolated (78% yield).



Scheme 10 Gram-scale synthesis of product **3a**

In summary, we have developed the iodine-mediated condition-controlled oxidative cyclization for the selective synthesis of indolizines. Regioselective annulation reaction has been accomplished via carbon-radical or nitrogen-radical initiated reaction pathways. Chemoselective synthesis of C2-carbaldehyde substituted indolizines or C3-acylated indoliznes has been realized via different reaction pathways. More detailed mechanism investigation and application of the reaction system to the synthesis of other molecules are currently ongoing in our laboratory.

All reactions were performed under N_2, unless otherwise stated. The solvents were dried before use by standard procedures. Melting points were measured with a WRX-4 melting point apparatus purchased from Shanghai YICE Instrumental Company. ^{1}H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$ on a 400 MHz, 500 MHz or 600 MHz instrument. All ^{1}H NMR spectra were measured relative to the signals for residual $CHCl_3$ (7.26 ppm) and all ^{13}C NMR spectral data are reported relative to $CDCl_3$ (77.16 ppm). HRMS data were recorded on a micrOTOF instrument using ESI technique. All column chromatography were performed using silica gel (200–300 microns). Unless otherwise noted, commercially available chemicals were used as received.

Products 3a–i, 4a–p; Typical Procedure for Ethyl 3-Phenylindolizine-1-carboxylate (3a)[17]

[CAS Reg. No. 93315-81-2]

Under N_2 atmosphere, ethyl 2-(pyridin-2-yl)acetate (**1a**; 33.0 mg, 0.2 mmol), phenylacetylene (**2a**; 40.9 mg, 0.4 mmol), I_2 (101.5 mg, 0.4 mmol), dppe (15.9 mg, 0.04 mmol), and Na_2CO_3 (42.4 mg, 0.4 mmol) were mixed in DMF (2 mL). The reaction tube was heated in an oil bath at 160 °C for 4 h. After completion of the reaction, the reaction mixture was washed with sat. aq $Na_2S_2O_3$ and extracted with EtOAc (3 40 mL), dried (anhyd Na_2SO_4), and the solvent was removed under reduced pressure. The remaining crude product was then purified through column chromatography using silica gel (EtOAc/PE 1/5, v/v) to afford **3a** as a dark green solid; yield: 49.3 mg (93%); mp 68–70 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.28 (t, *J* = 7.9 Hz, 2 H), 7.54 (d, *J* = 7.7 Hz, 2 H), 7.49 (t, *J* = 7.6 Hz, 2 H), 7.39 (t, *J* = 7.3 Hz, 1 H), 7.31 (s, 1 H), 7.10–7.03 (m, 1 H), 6.69 (t, *J* = 6.9 Hz, 1 H), 4.40 (q, *J* = 7.2 Hz, 2 H), 1.43 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): 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 $C_{17}H_{15}NO_2$ [M + H]$^+$: 266.1176; found: 266.1181.

Methyl 3-Phenylindolizine-1-carboxylate (3b)[17]

[CAS Reg. No. 947381-33-1]

Eluent: EtOAc/PE (1/10, v/v); yield: 32.3 mg (65%); yellow solid; mp 111–113 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.28 (t, *J* = 8.6 Hz, 2 H), 7.54 (d, *J* = 7.7 Hz, 2 H), 7.49 (t, *J* = 7.5 Hz, 2 H), 7.41 (d, *J* = 7.3 Hz, 1 H), 7.29 (s, 1 H), 7.07 (dd, *J* = 9.0, 6.7 Hz, 1 H), 6.70 (t, *J* = 6.9 Hz, 1 H), 3.92 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 165.4, 136.4, 131.2, 129.0, 128.6, 128.0, 126.4, 123.3, 122.3, 120.1, 116.0, 112.6, 103.82, 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)[13]

[CAS Reg. No. 1795248-49-5]

Eluent: EtOAc/PE (1/20, v/v); yield: 38.2 mg (69%); yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.27 (t, *J* = 7.5 Hz, 2 H), 7.54 (d, *J* = 7.7 Hz, 2 H), 7.49 (t, *J* = 7.6 Hz, 2 H), 7.39 (t, *J* = 7.3 Hz, 1 H), 7.32 (s, 1 H), 7.06 (dd, *J* = 9.1, 6.7 Hz, 1 H), 6.69 (t, *J* = 6.9 Hz, 1 H), 5.36–5.24 (m, 1 H), 1.41 (s, 3 H), 1.40 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 164.6, 136.2, 131.2, 129.0, 128.6, 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)**[18]

[CAS Reg. No. 1428552-42-4]

Eluent: EtOAc/PE (1/10, v/v); yield: 38.6 mg (66%); yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.25 (dd, *J* = 15.8, 8.1 Hz, 2 H), 7.54 (d, *J* = 7.6 Hz, 2 H), 7.49 (t, *J* = 7.5 Hz, 2 H), 7.40 (d, *J* = 7.3 Hz, 1 H), 7.28 (s, 1 H), 7.03 (dd, *J* = 9.1, 6.7 Hz, 1 H), 6.67 (t, *J* = 6.9 Hz, 1 H), 1.65 (s, 9 H).

^{13}C NMR (100 MHz, $CDCl_3$): 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 $C_{19}H_{19}NO_2$ [M + H]$^+$: 294.1489; found: 294.1498.

Butyl 3-Phenylindolizine-1-carboxylate (3e)[18]

[CAS Reg. No. 1394827-53-2]

Eluent: EtOAc/PE (1/20, v/v); yield: 42.6 mg (73%); yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.27 (t, *J* = 7.7 Hz, 2 H), 7.54 (d, *J* = 7.7 Hz, 2 H), 7.49 (t, *J* = 7.5 Hz, 2 H), 7.39 (t, *J* = 7.3 Hz, 1 H), 7.31 (s, 1 H), 7.06 (dd, *J* = 9.1, 6.6 Hz, 1 H), 6.69 (t, *J* = 6.9 Hz, 1 H), 4.35 (t, *J* = 6.7 Hz, 2 H), 1.79 (pent, *J* = 6.9 Hz, 2 H), 1.52 (q, *J* = 7.5 Hz, 2 H), 1.00 (t, *J* = 7.4 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 165.1, 136.2, 131.2, 129.0, 128.6, 128.0, 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 $C_{19}H_{19}NO_2$ [M + H]$^+$: 294.1489; found: 294.1496.

1-(3-Phenylindolizin-1-yl)ethanone (3f)[19]

[CAS Reg. No. 1126444-46-9]

Eluent: EtOAc/PE (1/10, v/v); yield: 17.6 mg (38%); pale yellow solid; mp 132–134 °C.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.53 (dt, *J* = 9.0, 1.3 Hz, 1 H), 8.29 (dt, *J* = 6.9, 1.1 Hz, 1 H), 7.56–7.53 (m, 2 H), 7.51 (dd, *J* = 8.6, 6.8 Hz, 2 H), 7.44–7.40 (m, 1 H), 7.19 (s, 1 H), 7.16 (ddd, *J* = 9.0, 6.6, 1.1 Hz, 1 H), 6.77 (td, *J* = 6.8, 1.4 Hz, 1 H), 2.56 (s, 3 H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 193.1, 135.9, 131.1, 129.2, 128.7, 128.2, 123.89, 123.2, 121.1, 116.5, 113.6, 113.5, 28.0.

HR-ESI-MS: *m*/*z* calcd for $C_{16}H_{13}NO$ [M + H]$^+$: 236.1070; found: 236.1074.

Ethyl 5-Methyl-3-phenylindolizine-1-carboxylate (3g)

Eluent: EtOAc/PE (1/20, v/v); yield: 41 mg (74%); yellow solid; mp 115–117 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.27 (d, *J* = 9.0 Hz, 1 H), 7.39 (q, *J* = 6.4, 5.6 Hz, 5 H), 7.20 (s, 1 H), 7.00 (dd, *J* = 9.0, 6.8 Hz, 1 H), 6.45 (d, *J* = 6.7 Hz, 1 H), 4.38 (t, *J* = 7.1 Hz, 2 H), 2.12 (s, 3 H), 1.40 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): 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 $C_{18}H_{17}NO_2$ [M + H]$^+$: 280.1332; found: 280.1344.

Ethyl 6-Methyl-3-phenylindolizine-1-carboxylate (3h)

Eluent: EtOAc/PE (1/20, v/v); yield: 33.2 mg (60%); yellow solid; mp 108–110 °C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.22 (d, *J* = 8.9 Hz, 1 H), 8.12 (s, 1 H), 7.59 (d, *J* = 6.6 Hz, 2 H), 7.54 (t, *J* = 6.7 Hz, 2 H), 7.44 (s, 1 H), 7.30 (s, 1 H), 6.98 (d, *J* = 8.9 Hz, 1 H), 4.43 (q, *J* = 5.8, 4.6 Hz, 2 H), 2.30 (s, 3 H), 1.47 (t, *J* = 7.0 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): 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 $C_{18}H_{17}NO_2$ [M + H]$^+$: 280.1332; found: 280.1339.

Ethyl 6-Bromo-3-phenylindolizine-1-carboxylate (3i)

Eluent: EtOAc/PE (1/20, v/v); yield: 33.2 mg (48%); yellow solid; mp 105–107 °C.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.38 (s, 1 H), 8.16 (d, *J* = 10.1 Hz, 1 H), 7.52 (d, *J* = 4.5 Hz, 4 H), 7.44 (d, *J* = 4.1 Hz, 1 H), 7.28 (s, 1 H), 7.11 (d, *J* = 1.6 Hz, 1 H), 4.39 (q, *J* = 7.1 Hz, 2 H), 1.42 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 164.7, 134.3, 130.6, 129.3, 128.7, 128.5, 126.8, 125.2, 123.3, 120.9, 116.5, 107.8, 105.6, 59.8, 14.6.

HR-ESI-MS: *m*/*z* calcd for $C_{17}H_{14}BrNO_2$ [M + H]$^+$: 345.0208; found: 345.0210.

Ethyl 3-(2-Fluorophenyl)indolizine-1-carboxylate (4a)[13]

[CAS Reg. No. 1631741-05-3]

Eluent: EtOAc/PE (1/20, v/v); yield: 30.7 mg (54%); pale yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.29 (d, *J* = 9.1 Hz, 1 H), 7.89 (dd, *J* = 7.1, 3.4 Hz, 1 H), 7.50 (dd, *J* = 7.5, 1.6 Hz, 1 H), 7.44 (d, *J* = 7.2 Hz, 1 H), 7.37 (s, 1 H), 7.29 (d, *J* = 7.6 Hz, 1 H), 7.22 (d, *J* = 9.1 Hz, 1 H), 7.12 (dd, *J* = 9.0, 6.7 Hz, 1 H), 6.74 (t, *J* = 6.9 Hz, 1 H), 4.41 (q, *J* = 7.1 Hz, 2 H), 1.43 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): 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 $C_{17}H_{14}FNO_2$ [M + H]$^+$: 284.1081; found: 284.1092.

Ethyl 3-(3-Fluorophenyl)indolizine-1-carboxylate (4b)[13]

[CAS Reg. No. 2027550-24-7]

Eluent: EtOAc/PE (1/20, v/v); yield: 40 mg (71%); yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.28 (t, *J* = 8.0 Hz, 2 H), 7.51–7.37 (m, 1 H), 7.33 (d, *J* = 3.9 Hz, 2 H), 7.24 (dt, *J* = 9.8, 2.0 Hz, 1 H), 7.08 (dd, *J* = 9.1, 6.8 Hz, 2 H), 6.72 (t, *J* = 6.9 Hz, 1 H), 4.39 (q, *J* = 7.1 Hz, 2 H), 1.42 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 164.8, 136.5, 133.3, 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)[13]

[CAS Reg. No. 1621928-41-3]

Eluent: EtOAc/PE (1/20, v/v); yield: 34.6 mg (69%); yellow solid; mp 98–100 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.25 (d, *J* = 9.1 Hz, 1 H), 8.17 (d, *J* = 7.1 Hz, 1 H), 7.49 (d, *J* = 5.4 Hz, 1 H), 7.47 (d, *J* = 5.3 Hz, 1 H), 7.26 (s, 1 H), 7.18 (t, *J* = 8.5 Hz, 2 H), 7.06 (dd, *J* = 9.0, 6.7 Hz, 1 H), 6.69 (t, *J* = 6.9 Hz, 1 H), 4.38 (q, *J* = 7.1 Hz, 2 H), 1.41 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): 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.

Ethyl 3-[4-(Trifluoromethyl)phenyl]indolizine-1-carboxylate (4d)[20]

[CAS Reg. No. 1714114-01-8]

Eluent: EtOAc/PE (1/20, v/v); yield: 50.9 mg (77%); yellow solid; mp 91–93 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.33–8.24 (m, 2 H), 7.74 (d, *J* = 8.1 Hz, 2 H), 7.67 (d, *J* = 8.1 Hz, 2 H), 7.37 (s, 1 H), 7.10 (dd, *J* = 9.2, 6.6 Hz, 1 H), 6.75 (t, *J* = 7.0 Hz, 1 H), 4.39 (q, *J* = 7.1 Hz, 2 H), 1.42 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): 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)[17]

[CAS Reg. No. 1621928-42-4]

Eluent: EtOAc/PE (1/20, v/v); yield: 46 mg (77%); yellow solid; mp 107–109 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.26 (d, *J* = 9.1 Hz, 1 H), 8.21 (d, *J* = 7.1 Hz, 1 H), 7.45 (s, 4 H), 7.28 (s, 1 H), 7.10–7.03 (m, 1 H), 6.70 (t, *J* = 6.8 Hz, 1 H), 4.38 (q, *J* = 7.1 Hz, 2 H), 1.41 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): 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, 59.58, 14.6.

HR-ESI-MS: *m*/*z* calcd for $C_{17}H_{14}ClNO_2$ [M + H]$^+$: 300.0786; found: 300.0795.

Ethyl 3-(4-Bromophenyl)indolizine-1-carboxylate (4f)[17]

[CAS Reg. No. 1714114-00-7]

Eluent: EtOAc/PE (1/20, v/v); yield: 52.6 mg (77%); yellow solid; mp 99–101 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.25 (d, *J* = 9.1 Hz, 1 H), 8.21 (d, *J* = 7.2 Hz, 1 H), 7.60 (d, *J* = 8.2 Hz, 2 H), 7.39 (d, *J* = 8.2 Hz, 2 H), 7.28 (s, 1 H), 7.06 (dd, *J* = 9.0, 6.7 Hz, 1 H), 6.70 (t, *J* = 6.9 Hz, 1 H), 4.38 (q, *J* = 7.1 Hz, 2 H), 1.41 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): 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 $C_{17}H_{14}BrNO_2$ [M + H]$^+$: 344.0281; found: 344.0284.

Ethyl 3-(4-Nitrophenyl)indolizine-1-carboxylate (4g)[19]

[CAS Reg. No. 158670-22-5]

Eluent: EtOAc/PE (1/10, v/v); yield: 51.1 mg (94%); orange-red solid; mp 140–142 °C.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.37 (d, *J* = 7.1 Hz, 1 H), 8.30 (dd, *J* = 15.8, 8.7 Hz, 3 H), 7.71 (d, *J* = 8.3 Hz, 2 H), 7.43 (s, 1 H), 7.17–7.11 (m, 1 H), 6.81 (t, *J* = 6.9 Hz, 1 H), 4.38 (q, *J* = 7.1 Hz, 2 H), 1.41 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 164.5, 146.5, 137.8, 137.5, 130.6, 128.0, 124.6, 124.0, 123.4, 123.2, 120.5, 118.20, 113.7, 105.6, 59.9, 14.6.

HR-ESI-MS: *m*/*z* calcd for $C_{17}H_{14}N_2O_4$ $[M + H]^+$: 311.1026; found: 311.1035.

Ethyl 3-(*p*-Tolyl)indolizine-1-carboxylate (4h)[17]

[CAS Reg. No. 247075-84-9]

Eluent: EtOAc/PE (1/10, v/v); yield: 41.8 mg (75%); yellow solid; mp 96–98 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.29–8.21 (m, 2 H), 7.42 (d, *J* = 7.8 Hz, 2 H), 7.29 (d, *J* = 7.7 Hz, 3 H), 7.05 (dd, *J* = 9.1, 6.7 Hz, 1 H), 6.67 (t, *J* = 6.9 Hz, 1 H), 4.40 (q, *J* = 7.1 Hz, 2 H), 2.42 (s, 3 H), 1.43 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 165.0, 137.9, 136.2, 129.7, 128.5, 128.2, 126.5, 123.3, 122.0, 120.1, 115.8, 112.4, 104.04, 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)[21]

[CAS Reg. No. 1776070-38-2]

Eluent: EtOAc/PE (1/20, v/v); yield: 49.8 mg (78%); yellow solid; mp 95–97 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.28 (dd, *J* = 17.0, 8.1 Hz, 2 H), 7.50 (q, *J* = 8.3 Hz, 4 H), 7.29 (s, 1 H), 7.10–7.02 (m, 1 H), 6.68 (t, *J* = 6.8 Hz, 1 H), 4.40 (q, *J* = 7.1 Hz, 2 H), 1.43 (t, *J* = 7.1 Hz, 3 H), 1.39 (s, 9 H).

^{13}C NMR (100 MHz, $CDCl_3$): 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.

Ethyl 3-(4-Methoxyphenyl)indolizine-1-carboxylate (4j)[17]

[CAS Reg. No. 1621928-40-2]

Eluent: EtOAc/PE (1/10, v/v); yield: 35.2 mg (60%); yellow solid; mp 124–126 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.25 (d, *J* = 9.1 Hz, 1 H), 8.19 (d, *J* = 7.1 Hz, 1 H), 7.44 (d, *J* = 8.3 Hz, 2 H), 7.24 (s, 1 H), 7.03 (dd, *J* = 8.5, 6.2 Hz, 3 H), 6.67 (t, *J* = 6.8 Hz, 1 H), 4.39 (q, *J* = 7.1 Hz, 2 H), 3.86 (s, 3 H), 1.42 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 165.1, 159.4, 136.0, 130.1, 123.5, 123.3, 122.0, 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)[13]

[CAS Reg. No. 1776070-42-8]

Eluent: EtOAc/PE (1/20, v/v); yield: 48.9 mg (72%); yellow solid; mp 143–145 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.36 (d, *J* = 7.1 Hz, 1 H), 8.31 (d, *J* = 9.1 Hz, 1 H), 7.73 (d, *J* = 8.0 Hz, 2 H), 7.66 (d, *J* = 7.7 Hz, 2 H), 7.62 (d, *J* = 8.0 Hz, 2 H), 7.49 (t, *J* = 7.6 Hz, 2 H), 7.43–7.36 (m, 2 H), 7.12–7.05 (m, 1 H), 6.72 (t, *J* = 6.9 Hz, 1 H), 4.43 (q, *J* = 7.1 Hz, 2 H), 1.45 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): 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 $C_{23}H_{19}NO_2$ $[M + H]^+$: 342.1489; found: 342.1495.

Ethyl 3-(Thiophen-3-yl)indolizine-1-carboxylate (4l)[22]

[CAS Reg. No. 1638213-47-4]

Eluent: EtOAc/PE (1/10, v/v); yield: 31.9 mg (59%); pale yellow solid; mp 111–113 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.29–8.22 (m, 2 H), 7.46 (dd, *J* = 4.8, 3.1 Hz, 1 H), 7.43 (d, *J* = 2.8 Hz, 1 H), 7.32 (s, 1 H), 7.30 (d, *J* = 5.0 Hz, 1 H), 7.05 (dd, *J* = 9.2, 6.7 Hz, 1 H), 6.71 (t, *J* = 6.9 Hz, 1 H), 4.39 (q, *J* = 7.1 Hz, 2 H), 1.42 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): 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, 59.6, 14.6.

HR-ESI-MS: *m*/*z* calcd for $C_{15}H_{13}NO_2S$ $[M + H]^+$: 271.0740; found: 271.0748.

Ethyl 3-(Thiophen-2-yl)indolizine-1-carboxylate (4m)[19]

[CAS Reg. No. 1621928-45-7]

Eluent: EtOAc/PE (1/10, v/v); yield: 32.4 mg (60%); orange-yellow solid; mp 78–80 °C.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.37 (dd, *J* = 7.1, 1.1 Hz, 1 H), 8.26 (dt, *J* = 9.1, 1.3 Hz, 1 H), 7.41–7.37 (m, 2 H), 7.25 (dd, *J* = 3.6, 1.2 Hz, 1 H), 7.16 (dd, *J* = 5.2, 3.6 Hz, 1 H), 7.10–7.07 (m, 1 H), 6.78–6.74 (m, 1 H), 4.39 (q, *J* = 7.1 Hz, 2 H), 1.42 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (150 MHz, $CDCl_3$): 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 $C_{15}H_{13}NO_2S$ $[M + H]^+$: 272.0740; found: 272.0749.

Ethyl 3-(Pyridin-2-yl)indolizine-1-carboxylate (4n)[19]

[CAS Reg. No. 1776070-49-5]

Eluent: EtOAc/PE (1/10, v/v); yield: 26.9 mg (51%); yellow solid; mp 144–146 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.04 (d, *J* = 7.2 Hz, 1 H), 8.59 (d, *J* = 4.8 Hz, 1 H), 8.27 (d, *J* = 9.0 Hz, 1 H), 7.74 (s, 1 H), 7.67 (d, *J* = 4.2 Hz, 2 H), 7.15 (dd, *J* = 9.0, 6.8 Hz, 1 H), 7.09 (d, *J* = 4.3 Hz, 1 H), 6.82 (t, *J* = 7.0 Hz, 1 H), 4.39 (d, *J* = 7.1 Hz, 2 H), 1.43 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): 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 $C_{16}H_{14}N_2O_2$ $[M + H]^+$: 267.1128; found: 267.1136.

Ethyl 3-(Pyridin-3-yl)indolizine-1-carboxylate (4o)

Eluent: EtOAc/PE (1/3, v/v); yield: 23 mg (43%); yellow solid; mp 80–82 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.78 (d, *J* = 2.3 Hz, 1 H), 8.62–8.57 (m, 1 H), 8.24 (d, *J* = 9.0 Hz, 1 H), 8.19 (d, *J* = 7.1 Hz, 1 H), 7.82 (dt, *J* = 8.1, 2.0 Hz, 1 H), 7.39 (dd, *J* = 7.9, 4.8 Hz, 1 H), 7.32 (s, 1 H), 7.10–7.03 (m, 1 H), 6.71 (t, *J* = 6.9 Hz, 1 H), 4.36 (q, *J* = 7.1 Hz, 2 H), 1.39 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 164.7, 149.3, 148.9, 136.7, 135.6, 127.4, 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 $C_{16}H_{14}N_2O_2$ [M + H]$^+$: 267.1128; found: 267.1136.

Diethyl Indolizine-1,3-dicarboxylate (4p)[23]

[CAS Reg. No. 55814-13-6]

Eluent: EtOAc/PE (1/20, v/v); yield: 15 mg (29%); pale yellow solid; mp 112–114 °C.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 9.50 (dt, *J* = 7.1, 1.1 Hz, 1 H), 8.34–8.29 (m, 1 H), 7.97 (s, 1 H), 7.31–7.27 (m, 1 H), 6.96 (dd, *J* = 7.0, 1.4 Hz, 1 H), 4.40–4.34 (m, 4 H), 1.41 (td, *J* = 7.2, 5.2 Hz, 6 H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 164.2, 161.2, 139.1, 127.9, 125.6, 124.2, 119.6, 114.3, 105.2, 60.3, 59.9, 14.6, 14.5.

HR-ESI-MS: *m*/*z* calcd for $C_{14}H_{15}NO_4$ [M + H]$^+$: 262.1074; found: 262.1073.

Products 5a–l; Typical Procedure for Diethyl 3-Phenylindolizine-1,2-dicarboxylate (5a)[24]

[CAS Reg. No. 1268825-51-9]

Under N_2 atmosphere, ethyl 2-(pyridin-2-yl)acetate (**1a**; 33.0 mg, 0.2 mmol), ethyl phenyl propynoate (69.7 mg, 0.4 mmol), I_2 (50.8 mg, 0.2 mmol,), and Na_2CO_3 (42.4 mg, 0.4 mmol) were mixed in DMA (2 mL). The reaction tube was heated in an oil bath at 160 °C for 4 h. After completion of the reaction, the reaction mixture was washed with sat. aq $Na_2S_2O_3$ and extracted with EtOAc (3 × 40 mL), dried (anhyd Na_2SO_4), and the solvent was removed under reduced pressure. The remaining crude product was then purified through column chromatography using silica gel (EtOAc/PE 1/10) to afford **5a** as a pale yellow solid; yield: 31.6 mg (47%); mp 40–42 °C.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.24 (dd, *J* = 9.2, 1.3 Hz, 1 H), 8.04–8.01 (m, 1 H), 7.52–7.48 (m, 4 H), 7.46–7.43 (m, 1 H), 7.11 (ddd, *J* = 9.2, 6.6, 1.1 Hz, 1 H), 6.71 (td, *J* = 6.9, 1.4 Hz, 1 H), 4.37 (q, *J* = 7.1 Hz, 2 H), 4.26 (q, *J* = 7.2 Hz, 2 H), 1.38 (t, *J* = 7.1 Hz, 3 H), 1.20 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 166.3, 163.8, 149.5, 135.3, 130.0, 129.0, 129.0, 124.9, 123.9, 123.5, 123.4, 122.4, 122.1, 120.4, 113.4, 102.1, 61.3, 59.9, 14.5, 14.0.

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: EtOAc/PE (1/10, v/v); yield: 20 mg (31%); yellow solid; mp 80–82 °C.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.23 (dt, *J* = 9.1, 1.3 Hz, 1 H), 8.02 (d, *J* = 7.2 Hz, 1 H), 7.53–7.47 (m, 4 H), 7.45 (d, *J* = 6.8 Hz, 1 H), 7.11 (ddd, *J* = 9.1, 6.6, 1.1 Hz, 1 H), 6.71 (td, *J* = 6.9, 1.4 Hz, 1 H), 4.27 (q, *J* = 7.1 Hz, 2 H), 3.89 (s, 3 H), 1.20 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 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: EtOAc/PE (1/10, v/v); yield: 26 mg (37%); yellow oil.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.24 (dt, *J* = 9.0, 1.3 Hz, 1 H), 8.02 (dd, *J* = 7.1, 1.2 Hz, 1 H), 7.52–7.46 (m, 4 H), 7.46–7.41 (m, 1 H), 7.09 (ddd, *J* = 9.1, 6.6, 1.1 Hz, 1 H), 6.70 (dd, *J* = 6.9, 1.4 Hz, 1 H), 5.30–5.25 (m, 1 H), 4.26 (q, *J* = 7.2 Hz, 2 H), 1.36 (d, *J* = 6.2 Hz, 6 H), 1.21 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 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, 67.21, 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: EtOAc/PE (1/10, v/v); yield: 22.6 mg (31%); yellow oil.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.22 (dt, *J* = 9.2, 1.3 Hz, 1 H), 8.00 (dd, *J* = 7.1, 1.2 Hz, 1 H), 7.49 (d, *J* = 6.4 Hz, 4 H), 7.45–7.41 (m, 1 H), 7.06 (ddd, *J* = 9.1, 6.6, 1.1 Hz, 1 H), 6.67 (td, *J* = 6.8, 1.4 Hz, 1 H), 4.24 (q, *J* = 7.2 Hz, 2 H), 1.60 (s, 9 H), 1.17 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 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: EtOAc/PE (1/10, v/v); yield: 25.6 mg (35%); yellow solid; mp 83–85 °C.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.24 (dt, *J* = 9.1, 1.3 Hz, 1 H), 8.02 (dt, *J* = 7.2, 1.1 Hz, 1 H), 7.52–7.47 (m, 4 H), 7.46–7.41 (m, 1 H), 7.10 (ddd, *J* = 9.2, 6.6, 1.1 Hz, 1 H), 6.70 (td, *J* = 6.8, 1.4 Hz, 1 H), 4.32 (t, *J* = 6.7 Hz, 2 H), 4.25 (q, *J* = 7.1 Hz, 2 H), 1.76–1.71 (m, 2 H), 1.52–1.43 (m, 2 H), 1.19 (t, *J* = 7.1 Hz, 3 H), 0.97 (t, *J* = 7.4 Hz, 3 H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 166.4, 164.0, 135.3, 130.0, 129.0, 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: EtOAc/PE (1/20, v/v); yield: 32.6 mg (44%); brown oil.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.25 (dt, *J* = 9.2, 1.2 Hz, 1 H), 7.97 (dd, *J* = 7.1, 1.1 Hz, 1 H), 7.52–7.43 (m, 4 H), 7.12 (ddd, *J* = 9.1, 6.6, 1.1 Hz, 1 H), 6.73 (td, *J* = 6.9, 1.3 Hz, 1 H), 4.37 (q, *J* = 7.1 Hz, 2 H), 4.27 (q, *J* = 7.1 Hz, 2 H), 1.38 (t, *J* = 7.1 Hz, 3 H), 1.24 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 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: EtOAc/PE (1/5, v/v); yield: 24.2 mg (33%); brown oil.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.23 (dd, *J* = 9.2, 1.5 Hz, 1 H), 7.97 (d, *J* = 7.1 Hz, 1 H), 7.45–7.40 (m, 2 H), 7.11–7.06 (m, 1 H), 7.02 (d, *J* = 8.6 Hz, 2 H), 6.69 (td, *J* = 6.9, 1.4 Hz, 1 H), 4.36 (q, *J* = 7.1 Hz, 2 H), 4.26 (q, *J* = 7.2 Hz, 2 H), 3.86 (s, 3 H), 1.38 (t, *J* = 7.1 Hz, 3 H), 1.23 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 166.5, 163.9, 160.1, 135.11, 131.5, 124.8, 123.5, 123.3, 122.1, 121.0, 120.3, 114.5, 113.3, 101.8, 61.28, 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)

Eluent: EtOAc/PE (1/10, v/v); yield: 30.4 mg (52%); yellow solid; mp 77–79 °C.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 10.77 (s, 1 H), 8.32 (d, *J* = 9.2 Hz, 1 H), 7.86 (d, *J* = 7.2 Hz, 1 H), 7.55–7.50 (m, 3 H), 7.44 (dd, *J* = 8.1, 1.6 Hz, 2 H), 7.13 (dd, *J* = 10.2, 6.6 Hz, 1 H), 6.72 (t, *J* = 7.5 Hz, 1 H), 4.46 (q, *J* = 7.1 Hz, 2 H), 1.46 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (150 MHz, $CDCl_3$): 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)

Eluent: EtOAc/PE (1/10, v/v); yield: 23.6 mg (38%); yellow solid; mp 78–80 °C.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 10.77 (s, 1 H), 8.32 (d, *J* = 9.2 Hz, 1 H), 7.82 (d, *J* = 7.2 Hz, 1 H), 7.43 (dd, *J* = 8.7, 5.3 Hz, 2 H), 7.22 (t, *J* = 8.6 Hz, 2 H), 7.13 (dd, *J* = 8.8, 6.1 Hz, 1 H), 6.74 (t, *J* = 6.3 Hz, 1 H), 4.46 (q, *J* = 7.1 Hz, 2 H), 1.45 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (150 MHz, $CDCl_3$): 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, 114.5, 103.9, 60.3, 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-Chlorophenyl)-2-formylindolizine-1-carboxylate (5j)

Eluent: EtOAc/PE (1/10, v/v); yield: 25 mg (38%); yellow solid; mp 84–86 °C.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 10.77 (s, 1 H), 8.33 (d, *J* = 9.2 Hz, 1 H), 7.83 (d, *J* = 7.1 Hz, 1 H), 7.51 (d, *J* = 8.3 Hz, 2 H), 7.39 (d, *J* = 8.3 Hz, 2 H), 7.16–7.12 (m, 1 H), 6.74 (td, *J* = 6.9, 1.3 Hz, 1 H), 4.46 (q, *J* = 7.2 Hz, 2 H), 1.45 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 190.2, 164.5, 136.2, 135.6, 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 $C_{18}H_{14}ClNO_3$ $[M + H]^+$: 328.0735; found: 328.0734.

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

Eluent: EtOAc/PE (1/10, v/v); yield: 23 mg (36%); yellow solid; mp 83–85 °C.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 10.76 (s, 1 H), 8.30 (d, *J* = 9.2 Hz, 1 H), 7.87 (d, *J* = 7.1 Hz, 1 H), 7.38–7.36 (m, 2 H), 7.11 (ddd, *J* = 9.2, 6.5, 1.1 Hz, 1 H), 7.06–7.03 (m, 2 H), 6.71 (td, *J* = 6.9, 1.3 Hz, 1 H), 4.45 (q, *J* = 7.1 Hz, 2 H), 3.88 (s, 3 H), 1.45 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 190.3, 164.6, 160.3, 136.0, 132.3, 128.7, 124.6, 123.9, 123.9, 121.0, 120.9, 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: EtOAc/PE (1/10, v/v); yield: 15.1 mg (25%); brown solid; mp 72–74 °C.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 10.76 (s, 1 H), 8.32 (d, *J* = 8.4 Hz, 1 H), 8.02 (d, *J* = 7.1 Hz, 1 H), 7.59 (d, *J* = 6.2 Hz, 1 H), 7.27 (dd, *J* = 3.5, 1.1 Hz, 1 H), 7.22 (dd, *J* = 5.1, 3.6 Hz, 1 H), 7.16 (dd, *J* = 9.2, 6.6 Hz, 1 H), 6.79 (t, *J* = 6.9 Hz, 1 H), 4.45 (q, *J* = 7.1 Hz, 2 H), 1.45 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (150 MHz, $CDCl_3$): 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 $C_{16}H_{13}NO_3S$ $[M + H]^+$: 300.0689; found: 300.0688.

Products 6a–g: Typical Procedure for Ethyl 3-Benzoylindolizine-1-carboxylate (6a)[25]

[CAS Reg. No. 40624-43-9]

Under N_2 atmosphere, ethyl 2-(pyridin-2-yl)acetate (**1a**; 33.0 mg, 0.2 mmol), phenylpropynyl aldehyde (52.0 mg, 0.4 mmol), I_2 (177.7 mg, 0.7 mmol), dppe (15.9 mg, 0.04 mmol), CuI (77.8 mg, 0.4 mmol), and Na_2CO_3 (42.4 mg, 0.4 mmol) were mixed in DMF (2 mL). The reaction tube was heated in an oil bath at 160 °C for 4 h. After completion of the reaction, the reaction mixture was washed with sat. aq $Na_2S_2O_3$ and extracted with EtOAc (3 × 40 mL), dried (anhyd Na_2SO_4), and the solvent was removed under reduced pressure. The remaining crude product was then purified through column chromatography using silica gel (EtOAc/PE 1/10) to afford **6a** as a yellow solid; yield; 44.3 mg (76%); mp 148–150 °C.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 9.97 (d, *J* = 7.0 Hz, 1 H), 8.39 (d, *J* = 8.9 Hz, 1 H), 7.83–7.80 (m, 3 H), 7.58 (t, *J* = 7.4 Hz, 1 H), 7.51 (t, *J* = 7.5 Hz, 2 H), 7.46–7.43 (m, 1 H), 7.09 (t, *J* = 7.5 Hz, 1 H), 4.37 (q, *J* = 7.1 Hz, 2 H), 1.39 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 185.6, 164.1, 140.0, 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)[26]

[CAS Reg. No. 1003050-05-2]

Eluent: EtOAc/PE (1/10, v/v); yield: 37.3 mg (60%); pale yellow solid; mp 102–104 °C.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 9.91 (d, *J* = 7.0 Hz, 1 H), 8.38 (d, *J* = 8.9 Hz, 1 H), 7.84 (dd, *J* = 8.7, 5.4 Hz, 2 H), 7.78 (s, 1 H), 7.46–7.43 (m, 1 H), 7.19 (t, *J* = 8.6 Hz, 2 H), 7.08 (t, *J* = 6.3 Hz, 1 H), 4.37 (q, *J* = 7.1 Hz, 2 H), 1.40 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (150 MHz, $CDCl_3$): 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)[26]

[CAS Reg. No. 1003050-06-3]

Eluent: EtOAc/PE (1/10, v/v); yield: 46.4 mg (71%); yellow solid; mp 81–83 °C.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 9.92 (d, *J* = 7.0 Hz, 1 H), 8.39 (d, *J* = 8.9 Hz, 1 H), 7.77 (d, *J* = 3.0 Hz, 2 H), 7.75 (s, 1 H), 7.50–7.44 (m, 3 H), 7.09 (t, *J* = 6.9 Hz, 1 H), 4.37 (q, *J* = 7.2 Hz, 2 H), 1.40 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 184.1, 164.0, 140.0, 138.2, 137.8, 130.4, 129.2, 128.8, 128.7, 127.9, 122.2, 119.6, 115.5, 106.5, 60.2, 14.6.

HR-ESI-MS: *m*/*z* calcd for $C_{18}H_{14}ClNO_3$ [M + H]$^+$: 328.0735; found: 328.0734.

Ethyl 3-(4-Methoxybenzoyl)indolizine-1-carboxylate (6d)[25]

[CAS Reg. No. 1003050-04-1]

Eluent: EtOAc/PE (1/20, v/v); yield: 35 mg (54%); yellow solid; mp 88–90 °C.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 9.89 (d, *J* = 7.0 Hz, 1 H), 8.36 (s, 1 H), 7.84 (s, 1 H), 7.82 (d, *J* = 5.8 Hz, 2 H), 7.43–7.38 (m, 1 H), 7.05 (t, *J* = 6.5 Hz, 1 H), 7.01 (d, *J* = 8.8 Hz, 2 H), 4.37 (q, *J* = 7.1 Hz, 2 H), 3.89 (s, 3 H), 1.40 (t, J = 7.1 Hz, 3 H).

^{13}C NMR (150 MHz, $CDCl_3$): 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 $C_{19}H_{17}NO_4$ [M + H]$^+$: 324.1230; found: 324.1229.

Ethyl 3-(Thiophene-2-carbonyl)indolizine-1-carboxylate (6e)[25]

[CAS Reg. No. 1003050-07-4]

Eluent: EtOAc/PE (1/10, v/v); yield: 34 mg (57%); yellow solid; mp 81–83 °C.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 9.83 (d, *J* = 7.1 Hz, 1 H), 8.37 (d, *J* = 8.9 Hz, 1 H), 8.13 (d, *J* = 1.6 Hz, 1 H), 7.81 (d, *J* = 4.7 Hz, 1 H), 7.66 (d, *J* = 5.0 Hz, 1 H), 7.44–7.39 (m, 1 H), 7.21–7.18 (m, 1 H), 7.05 (t, *J* = 6.9 Hz, 1 H), 4.40 (q, *J* = 6.9 Hz, 2 H), 1.42 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (150 MHz, $CDCl_3$): 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 $C_{16}H_{13}NO_3S$ [M + H]$^+$: 300.0689; found: 300.0688.

Ethyl 3-Pentanoylindolizine-1-carboxylate (6f)

Eluent: EtOAc/PE (1/10, v/v); yield: 32 mg (59%); yellow solid; mp 42–44 °C.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 9.93 (d, *J* = 7.1 Hz, 1 H), 8.33 (d, *J* = 8.9 Hz, 1 H), 8.01 (s, 1 H), 7.38 (ddd, *J* = 8.8, 6.8, 1.0 Hz, 1 H), 7.01 (td, *J* = 7.0, 1.4 Hz, 1 H), 4.40 (q, *J* = 7.1 Hz, 2 H), 2.93–2.89 (m, 2 H), 1.76 (p, *J* = 7.7 Hz, 2 H), 1.43 (td, *J* = 7.4, 3.4 Hz, 5 H), 0.96 (t, *J* = 7.4 Hz, 3 H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 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: EtOAc/PE (1/10, v/v); yield: 33.1 mg (54%); brown solid; mp 123–125 °C.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 9.80 (s, 1 H), 8.27 (d, *J* = 9.0 Hz, 1 H), 7.82–7.78 (m, 2 H), 7.75 (s, 1 H), 7.59–7.54 (m, 1 H), 7.50 (t, *J* = 7.4 Hz, 2 H), 7.30 (d, *J* = 9.1 Hz, 1 H), 4.36 (q, *J* = 7.1 Hz, 2 H), 2.43 (d, *J* = 1.2 Hz, 3 H), 1.38 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 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, 59.9, 18.5, 14.5.

HR-ESI-MS: *m*/*z* calcd for $C_{19}H_{17}NO_3$ [M + H]$^+$: 308.3490; found: 308.3493.

Products 7a,b; Typical Procedure for Ethyl 3-Phenyl-2-(phenylethynyl)indolizine-1-carboxylate (7a)

Under N_2 atmosphere, ethyl 2-(pyridin-2-yl)acetate (**1a**; 132.2 mg, 0.8 mmol), 1,4-diphenylbutadiyne (40.4 mg, 0.2 mmol), I_2 (101.5 mg, 0.4 mmol), dppe (15.9 mg, 0.04 mmol), and Na_2CO_3 (42.4 mg, 0.4 mmol) were mixed in DMF (2 mL). The reaction tube was heated in an oil bath at 160 °C for 4 h. After completion of the reaction, the reaction mixture was washed with sat. aq Na_2S_2O3 and extracted with EtOAc (3 × 40 mL), dried (anhyd Na_2SO_4), and the solvent was removed under reduced pressure. The remaining crude product was then purified through column chromatography using silica gel (EtOAc/PE 1/20, v/v) to afford **7a** as a yellow solid; yield: 28 mg (38%); mp 111–113 °C.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.43 (dt, *J* = 6.8, 1.2 Hz, 1 H), 8.33 (dt, *J* = 9.1, 1.2 Hz, 1 H), 7.65 (dt, *J* = 6.4, 1.4 Hz, 2 H), 7.47–7.41 (m, 4 H), 7.41–7.37 (m, 1 H), 7.35–7.30 (m, 3 H), 7.21 (ddd, *J* = 9.0, 6.7, 1.2 Hz, 1 H), 6.91 (td, *J* = 6.8, 1.3 Hz, 1 H), 4.26 (q, *J* = 7.1 Hz, 2 H), 1.22 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (150 MHz, $CDCl_3$): 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-Butyl-2-(hex-1-yn-1-yl)indolizine-1-carboxylate (7b)

Eluent: EtOAc/PE (1/20, v/v); yield: 22.7 mg (35%); brown oil.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.21 (d, *J* = 5.9 Hz, 1 H), 8.18 (d, *J* = 8.0 Hz, 1 H), 7.08 (s, 1 H), 6.77 (d, *J* = 14.7 Hz, 1 H), 4.37 (q, *J* = 7.1 Hz, 2 H), 3.03–2.99 (m, 2 H), 2.59 (t, *J* = 7.0 Hz, 2 H), 1.69–1.62 (m, 4 H), 1.58 (s, 2 H), 1.41 (t, *J* = 7.1 Hz, 5 H), 0.98 (t, *J* = 7.3 Hz, 3 H), 0.95 (t, *J* = 7.4 Hz, 3 H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 165.1, 137.2, 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 $C_{21}H_{27}NO_2$ [M + H]$^+$: 326.4522; found: 326.4524.

Products 8a,b; Typical Procedure for Diethyl 3,3′-Diphenyl-[2,2′-biindolizine]-1,1′-dicarboxylate (8a)

Under N_2 atmosphere, ethyl 2-(pyridin-2-yl)acetate (**1a**; 66.0 mg 0.4 mmol), ethyl 3-phenyl-2-(phenylethynyl)indolizine-1-carboxylate (**7a**; 36.5 mg, 0.1 mmol), I_2 (101.5 mg, 0.4 mmol), dppe (15.9 mg, 0.04 mmol), and Na_2CO_3 (42.4 mg, 0.4 mmol) were mixed in DMF (2 mL). The reaction tube was heated in an oil bath at 160 °C for 4 h. After completion of the reaction, the reaction mixture was washed with sat. aq $Na_2S_2O_3$ and extracted with EtOAc (3 × 40 mL), dried (anhyd Na_2SO_4), and the solvent was removed under reduced pressure. The remaining crude product was then purified through column chromatography using silica gel (EtOAc/PE 1/20, v/v) to afford **8a** as a yellow solid; yield: 34.7 mg (66%); yellow solid; mp 134–136 °C.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.35–8.30 (m, 2 H), 7.42 (d, *J* = 6.9 Hz, 2 H), 7.16–7.13 (m, 4 H), 7.10 (dd, *J* = 8.2, 6.5 Hz, 4 H), 6.93 (dt, *J* = 7.0, 1.4 Hz, 4 H), 6.65 (td, *J* = 6.8, 1.3 Hz, 2 H), 4.20 (qt, *J* = 7.1, 3.7 Hz, 4 H), 1.14 (t, *J* = 7.1 Hz, 6 H).

^{13}C NMR (150 MHz, $CDCl_3$): 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 $C_{34}H_{28}N_2O_4$ [M + H]$^+$: 529.2122; found: 529.2121.

Ethyl 3,3′-Dibutyl-1′-ethyl-[2,2′-biindolizine]-1-carboxylate (8b)

Eluent: EtOAc/PE (1/20, v/v); yield: 27.2 mg (28%); yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.30 (d, *J* = 9.0 Hz, 2 H), 7.24 (s, 2 H), 7.12–7.06 (m, 2 H), 6.62–6.56 (m, 2 H), 4.40 (q, *J* = 7.1 Hz, 4 H), 2.73–2.63 (m, 4 H), 1.43 (t, *J* = 7.1 Hz, 10 H), 1.22–1.11 (m, 4 H), 0.70 (t, *J* = 7.3 Hz, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 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 $C_{30}H_{36}N_2O_4$ [M + H]$^+$: 489.2676; found: 489.2680.

Ethyl 2-(Pyridin-2-yl)-2-[(2,2,6,6-tetramethylpiperidin-1-yl)oxy]acetate (9)

Under N_2 atmosphere, ethyl 2-(pyridin-2-yl)acetate (**1a**; 33.0 mg, 0.2 mmol), phenylacetylene (**2a**; 40.9 mg, 0.4 mmol), TEMPO (63.8 mg, 0.4 mmol), I_2 (101.5 mg, 0.4 mmol), dppe (15.9 mg, 0.04 mmol), and Na_2CO_3 (42.4 mg, 0.4 mmol) were mixed in DMF (2 mL). The reaction tube was heated in an oil bath at 160 °C for 4 h. After completion of the reaction, the reaction mixture was washed with sat. aq $Na_2S_2O_3$ and extracted with EtOAc (3 × 40 mL), dried (anhyd Na_2SO_4), and the solvent was removed under reduced pressure. The remaining crude product was then purified through column chromatography using silica gel (EtOAc/PE 1/5, v/v) to afford the product **9** as a brown oil; yield: 31.4 mg (49%).

^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.56 (d, *J* = 4.4 Hz, 1 H), 7.73 (td, *J* = 7.7, 1.7 Hz, 1 H), 7.62 (d, *J* = 7.8 Hz, 1 H), 7.23–7.20 (m, 1 H), 5.42 (s, 1 H), 4.23–4.13 (m, 2 H), 1.50 (d, *J* = 6.8 Hz, 2 H), 1.42 (s, 2 H), 1.32 (d, *J* = 11.7 Hz, 1 H), 1.28–1.21 (m, 7 H), 1.19 (s, 3 H), 1.13 (s, 3 H), 0.71 (s, 3 H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 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 $C_{18}H_{28}N_2O_3K$ [M + K]$^+$: 359.1732; found: 359.1731.

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Supporting Information

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