Iodine-promoted synthesis of 3-arylindolizine-1-carboxylates from 2-(2-nitro-1-arylethyl)malonates and pyridine

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An efficient and straightforward one-pot synthetic protocol has been developed for the synthesis of 3-arylindolizine-1-carboxylates via 1,3-dipolar annulation of 2-(2-nitro-1-arylethyl)malonates with pyridine and subsequent aromatisation in the presence of molecular iodine. The structure of methyl 3-(4-methoxyphenyl)indolizine-1-carboxylate (**2a**) and methyl 3-iodo-2-(4-nitrophenyl)indolizine-1-carboxylate (**2f**) was further confirmed by X-ray single crystal analysis.

Keywords: indolizine; 3-arylindolizine-1-carboxylate; molecular iodine; 1,3-dipolar annulation; aromatisation

The indolizine ring is a key structural unit for many natural products, synthetic pharmaceuticals, and a wide variety of biologically active compounds.[1–3] Indolizine derivatives with the π-conjugated heteroaryl–(hetero)aryl motifs as the fluorescent core objects have been frequently used in molecular materials.[4–7] The novel polysubstituted indolizine derivatives have been a rich source of candidates with potential pharmaceutical and fluorescent applications that have encouraged the design and synthesis of new analogues with increased pharmacological activity and photonic luminescence. Thus, to meet the need of modern drug discovery and molecular materials, the synthetic methodology of polysubstituted indolizines is developed continually to address the many challenges associated with the design of new pharmaceutical agents and photoelectric material. Although, there are several methods for the preparation of the polysubstituted indolizine derivatives, most current procedures involve multistep.[8–14] The development of efficient methods for the synthesis of polysubstituted indolizine derivatives requires attention.

In one of our electroluminescent materials and medicinal chemistry programmes, we needed 3-arylindolizine-1-carboxylates to prepare more complex analogues containing indolizine core. During the past decade, the development of synthetic routes to 3-arylindolizine-1-carboxylates has been the focus of intense research. As a key intermediate, 3-arylindolizine-1-carboxylates were frequently synthesised by multistep and metal-catalysed direct functionalisation of indolizines using an indolizine as a starting material. For example, Xia and co-worker reported that 3-haloindolizines were synthesised firstly via Cu(II) halide mediated halogenation of indolizines, following the Suzuki–Miyaura reaction of 3-haloindolizines and phenylboronic acid provided 3-arylindolizines.[15,16] Afterwards Liu and co-workers developed the direct Suzuki–Miyaura-type coupling of indolizines without 3-halo substitutent with arylboronic acids to synthesis of 3-arylated indolizines.[17] Subsequently, You and co-workers described a palladium–copper bimetallic catalytic system with the assistance of Cu_2Cl_2 and BQ to yield the arylation of indolizine with arylboronic acids in one step.[18] Gevorgyan and co-workers also reported the palladium-catalysed direct arylation of indolizines with aryl bromides. In this reaction, the C–H bond of indolizines directly coupled with aryl bromides to selectively give the C-3 arylated indolizines.[19] Recently, Zhao[20] investigated the C-3 arylation of indolizines with aryltrifluoroborate salts in the presence of a $Pd(OAc)_2$/AgOAc/ KOAc catalytic system to yield 3-arylated indolizines derivatives. Our continued interest in expanding the scope and potential application of the 3-arylated indolizines derivatives prompted us to explore the feasibility of construction of a 3-arylindolizine-1-carboxylate skeleton by using 2-(2-nitro-1-arylethyl)malonates as a 1,3-dipolar addition species under appropriate conditions. Thus, we designed and synthesised some 3-arylindolizine-1-carboxylates. As a result of this study, we achieved a facile, efficient and concise synthesis of 3-arylindolizine-1-carboxylates via 1,3-dipolar annulation of 2-(2-nitro-1-arylethyl)malonates with pyridine and subsequent aromatisation in the presence of molecular iodine. Here we report our preliminary results and a proposed mechanism for the process.

Results and discussion

The substrates, 2-(2-nitro-1-arylethyl)malonates, were prepared in excellent yields by the Knoevenagel condensation of dimethyl malonate with various substituted benzaldehydes, following the Michael addition with nitromethane under basic conditions according to the reported procedure.[21,22] Then, methyl 3-(4-methoxyphenyl)indolizine-1-carboxylate (**2a**) was chosen as the model product to test the direct 1,3-dipolar annulation process of 2-(2-nitro-4-methoxyphenylethyl) malonate with pyridine in the presence of molecular iodine at room temperature, however, no reaction occurred as indicated by TLC result (Scheme 1). A complex mixture was formed when the reaction temperature was increased to 80 °C, the isolated yield in 38% (entry 2, Table 1) was achieved after work-up and purification by column chromatography. The product was characterised as methyl 3-(4-methoxyphenyl)indolizine-1-carboxylate (**2a**) on the basis of its spectral and analytical data. The stereochemistry of **2a** was obtained from a single crystal X-ray analysis. ORTEP diagrams of **2a** is shown in Fig. 1. To our delight, reaction of 2-(2-nitro-4-methoxyphenylethyl) malonate **1a** with 2.0 equiv. of iodine in pyridine at 120 °C gave methyl 3-(4-methoxyphenyl) indolizine-1-carboxylate (**2a**) in 65% yield (entry 3, Table 1). Higher reaction temperature, for example 140 °C, could make the reaction time shorter, but meanwhile results in a slightly lower yield (entry 4, Table 1). Encouraged by these results, the reaction conditions were then screened with the aim of optimising the yield of **2a**. Increasing the amount of iodine to 2.4 equiv., the yield in 65% of **2a** was obtained (entry 5, Table 1). In view of this, further increase of the amount of iodine had no significant effect on the reaction. But decreasing the amount of iodine to 1.5 equiv., the reaction rate was decelerated along with low yield (entry 6, Table 1). Moreover, expanding reaction time had also no significant effect on the reaction (entry 7, Table 1). The reaction of **2a** and pyridine could proceed in other reaction media, such as DMSO and DMF (entries 8–9, Table 1). Among these tested solvents (entries 3, 8 and 9, Table 1), pyridine was demonstrated to be the best. A series of experiments revealed that the optimal results were obtained when the reaction of **1a** with pyridine was performed in the presence of iodine (2.0 equiv.) at 120 °C for 48 h, whereby the yield of **2a** reached 65% (entry 3, Table 1).Thus, having established the optimal

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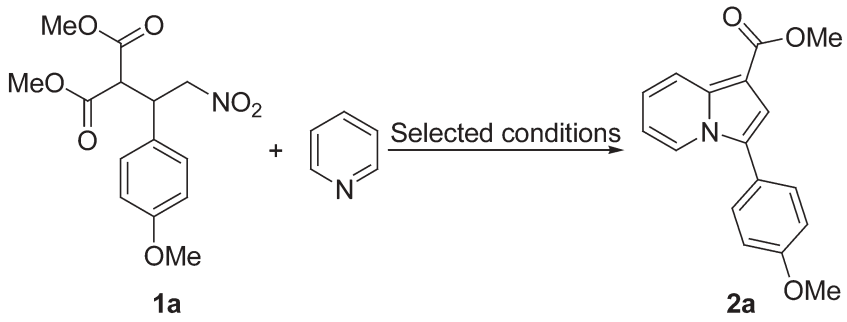


Scheme 1 I_2-promoted synthesis of indolizine-1-carboxylate **2a**.

Table 1 Optimisation of temperature, time and solvents in the synthesis of **2a**

Entry	**1a**(mol)/I_2(mol)/Pyridine/T(°C)/t(h)/Solvent[a]	Yield/%[b]
1	1/2/Pyridine/rt/48/ Pyridine	0
2	1/2/Pyridine/80/48/ Pyridine	38
3	1/2/Pyridine/120/48/ Pyridine	65
4	1/2/Pyridine/140/36/ Pyridine	48
5	1/2.4/Pyridine/120/48/ Pyridine	65
6	1/1.5/Pyridine/120/48/ Pyridine	42
7	1/2/Pyridine/120/56/ Pyridine	64
8	1/2/Pyridine(1mL)/120/48/ DMSO	42
9	1/2/Pyridine(1mL)/120/48/ DMF	18

[a] **1a**/I_2 (mol/mol). [b] Isolated yield.

conditions for the **2a** synthesis, a series of reactions of substrates **1b**–**f** with pyridine were carried out under the identical conditions as for **2a** in Table 1, entry 3. It was found that the 2-(2-nitro-1-arylethyl)malonates **1** bearing a methoxy, methyl, chloro or bromo at the 4-position of aryl substituents were tolerated under the above conditions to afford the corresponding 3-arylindolizine-1-carboxylates (**2a**-**2e**) in moderate yields (Scheme 2). However, under identical conditions as that for **2a**, the reaction of 2-[2-nitro-1-(4-nitrophenyl)ethyl]malonate (**1f**) with pyridine in the presence of iodine (2.0 equiv.) at 120 °C for 48 h gave the different indolizine-1-carboxylate (**2f**) in 62% (entry 6, Table 2). The structure of **2f** was further confirmed by X-ray single crystal analysis and its spectral and analytical data (Fig. 2). Crystallographic data of **2a** and **2f** were listed in Table 3. Crystallographic data for **2a** and **2f** have been deposited with the Cambridge Crystallographic Data Centre with the deposition number CCDC 809149 and 921514.

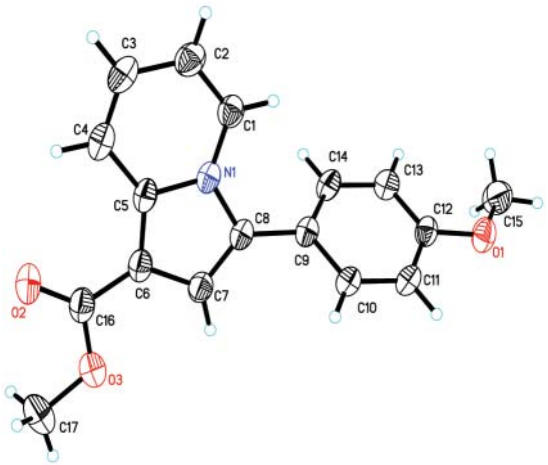


Fig. 1 Molecular structure of indolizine-1-carboxylate **2a**, non-hydrogen atoms are shown at the 30% probability level.

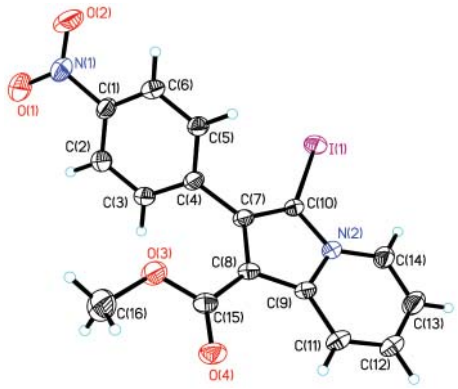


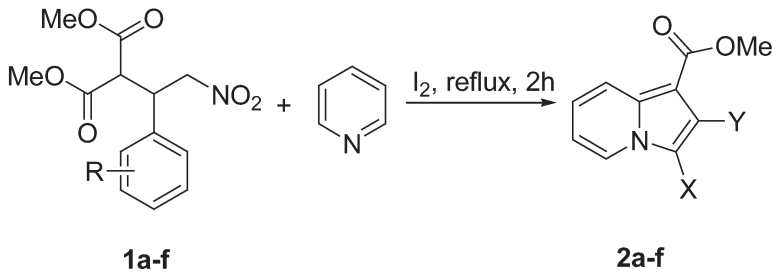
Fig. 2 Molecular structure of 3-iodoindolizine-1-carboxylate **2f**, non-hydrogen atoms are shown at the 30% probability level.

These data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax (+44) 1223 336033, E-mail: deposit@ccdc.cam.ac.uk].[23]

On the basis of the above experimental results together with X-ray single crystal analysis, a plausible mechanism for the synthesis of indolizine-1-carboxylate (**2a**–**f**) is proposed as depicted in Scheme 3–5. The transformation starts from an intermolecular annulation reaction of 2-(2-nitro-1-arylethyl) malonates **1** in pyridine in the presence of iodine generating a key intermediate **A**. Intermediate methyl 2-(4-methoxyphenyl)-3-nitrocyclopropanecarboxylate was isolated once before the reaction was completed, its structure was further confirmed by its spectral and analytical data (Scheme 3).

Subsequently, when the substituent of aromatic ring is methoxy, methyl, chloro or bromo, selectively nucleophilic addition of pyridine to intermediate **A** gives rise to pyridinium compound, which then undergoes intramolecular nucleophilic annulation reaction to furnish a tetrahydroindolizine. Finally, the denitration and aromatisation of tetrahydroindolizine yield the product **2a**–**e** (Scheme 4).

Additionally, a possible mechanism for the formation of the indolizine-1-carboxylate **2f** is depicted in Scheme 5. Because of the electron-withdrawing of nitro aromatic ring, selectively nucleophilic addition of pyridine to α-carbon of nitrocyclopropane intermediate **A** gives rise to a pyridinium compound, following intramolecular annulation reaction to gives a 3-nitrotetrahydroindolizine. Under the base conditions, 3-nitrotetrahydroindolizine undergoes keto–enol tautomerism between nitro and α-carbon-hydrogen to form the intermediate enol. Then the enol intermediate reacts with iodine to furnish a electrophilic product 3-iodo-3-nitrotetrahydroindolizine. The final aromatisation achieves via the denitration reaction by the utilization of nitro as the leaving group to keep 3-postion iodo substitutent in indolizine-1-carboxylate **2f** (Scheme 5).



1a-f **2a-f**

Scheme 2 Iodine-promoted synthesis of indolizine-1-carboxylates.

Table 2 I_2-promoted synthesis of indolizine-1-carboxylates

Entry	R	X	Y	Yield/%
1	4-CH_3O	4-$CH_3OC_6H_4$	H	**2a** 65
2	H	C_6H_5	H	**2b** 51
3	4-CH_3	4-$CH_3C_6H_4$	H	**2c** 58
4	4-Br	4-BrC_6H_4	H	**2d** 60
5	4-Cl	4-ClC_6H_4	H	**2e** 55
6	4-NO_2	I	4-$O_2NC_6H_4$	**2f** 62

In summary, a facile and efficient synthesis of 3-arylindolizine-1-carboxylates has been developed via 1,3-dipolar annulation of 2-(2-nitro-1-arylethyl)malonates with pyridine and subsequent aromatisation in the presence of molecular iodine for the generation of a wide range of structurally interesting, pharmacologically and photoelectrically significant compounds. This protocol, combining construction and modification of the 3-arylindolizine-1-carboxylate and 2-arylindolizine-1-carboxylate skeleton, increases the structural diversity of final products from readily available starting materials. Further work on the utilisation and extension of the scope of the methodology is currently under investigation in our laboratory.

Experimental

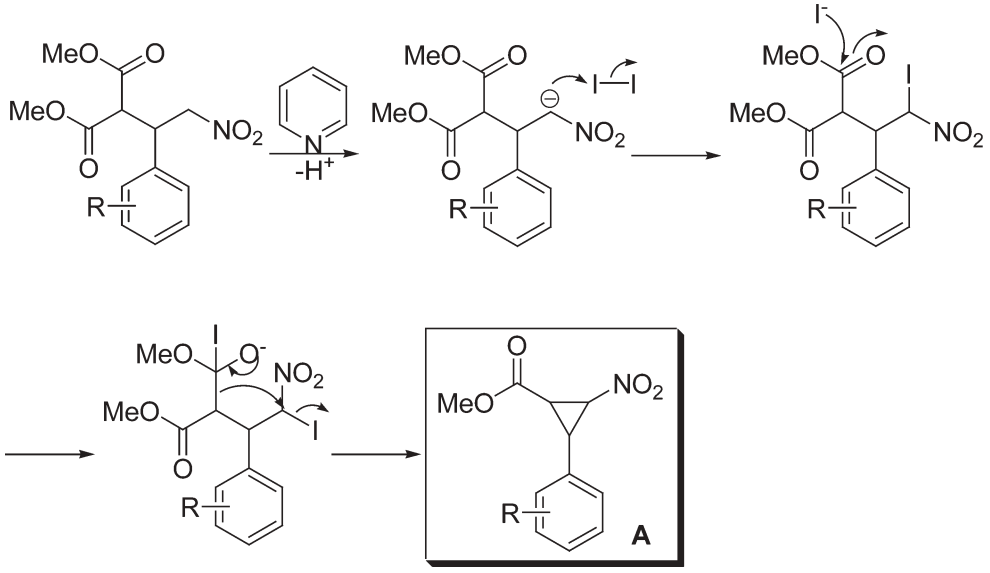
All melting points were determined in a Yanaco melting point apparatus and are uncorrected. IR spectra were recorded in a Nicolet FT-IR 5DX spectrometer. The ^{1}H NMR (600 MHz) and ^{13}C NMR (150 MHz) spectra were recorded in a Bruker AV-600 spectrometer with TMS as internal reference in $CDCl_3$ solutions. *J* values are given in Hz. Only discrete or characteristic signals for the ^{1}H NMR are reported. The MS spectra were obtained on a ZAB-HS mass spectrometer with 70 eV. X-ray crystallographic analysis was performed with a Smart-1000 CCD diffractometer using monochromatic Mo KR radiation (λ) 0.71073 Å) and integrated with the SAINT-Plus program. All calculations were performed with programs from the SHELXTL crystallographic software package. The elemental analyses were performed in a Perkin-Elmer 240C instrument. Flash chromatography was performed on silica gel (230–400 mesh) eluting with ethyl acetate–hexanes mixture. All reactions were monitored by TLC. All reagents and solvents were purchased from commercial sources and purified commonly before used.

The syntheses of 2-(2-nitro-1-arylethyl)malonates **1** were achieved starting from commercially available substituted benzaldehydes, nitromethane and dimethyl malonate using the standard procedure

*Synthesis of indolizine-1-carboxylates (***2a–f***); general procedure*

The appropriate 2-(2-nitro-1-arylethyl)malonates (2 mmol) and iodine (1.02 mg, 4 mmol) were dissolved in 5 mL of pyridine at room temperature, and the resultant mixture was stirred under 120 °C for 48 h, the completion of reaction was confirmed by TLC (EtOAc/hexanes, 1:10). Subsequently, the mixture was cooled to room temperature, excessive pyridine was removed by decreased pressure. The residues were added with water (10 mL), then the resultant was extracted with dichloromethane (2 x 10 mL), the organic phase was washed with 10% sodium thiosulfate, water and brine, dried over anhydrous sodium sulfate. After removal of dichloromethane, the residues were purified by flash chromatography (silica gel, EtOAc/hexanes, 1/20) to give product **2a–f**.

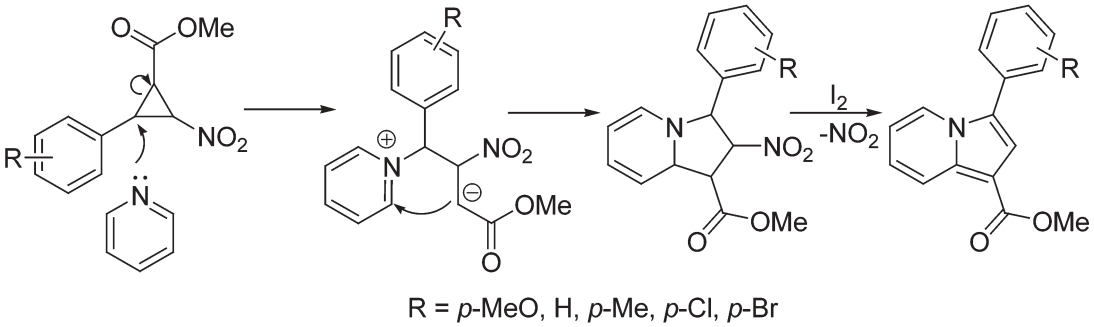
Methyl 3-(4-methoxyphenyl)indolizine-1-carboxylate (**2a**): Yellow solid, m.p. 130–132 °C (CH_2Cl_2/PE); ^{1}H NMR ($CDCl_3$, 600 MH) δ (ppm) 8.15 (dd, *J* = 9.3, 7.2 Hz, 2H), 7.39 (d, *J* = 7.8 Hz, 2H), 7.29 (s, 1H), 7.15 (d, *J* = 9.3 Hz, 1H), 6.98 (d, *J* = 7.8 Hz, 2H), 6.78–6.61 (m, 1H), 3.81 (s, 3H), 3.64 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 163.6, 162.9, 138.1, 132.2, 131.1(2C), 130.6, 128.2, 127.5, 121.3, 120.0, 115.6, 113.4(2C), 103.5, 55.5, 52.3; IR (KBr, cm^{-1}): 2993, 2838, 1689, 1636, 1609, 1510, 1492, 1223, 1174, 1106, 950, 838;



Scheme 3 Plausible mechanism for the formation of intermediate **A**.

Table 3 Crystallographic data for compounds **2a** and **2f**

Entry	Compound **2a**	Compound **2f**
Empirical formula	$C_{17}H_{15}NO_3$	$C_{16}H_{11}IN_2O_4$
Formula weight	281.30	422.17
Wavelength/Å	0.71073	0.71073
Temperature/K	296(2)	296(2)
Crystal system	Triclinic,	Triclinic,
Space group	P-1	P-1
Unit cell dimensions	a = 8.3888(14) Å b = 8.9604(15) Å c = 10.6074(18) Å α = 75.211(2) ° β = 71.373(2) ° γ = 84.738(2) °	*a* = 8.2774(12) Å *b* = 9.9061(14) Å *c* = 10.0956(14) Å α = 83.048(2) ° β = 79.836(2) ° γ = 81.262(2) °
Volume/Å^3	730.5(2)	801.6(2)
Z	2	2
Calculated density/g cm^{-3}	1.279	1.749
Absorption correction	None	None
F(000)	296	412
Crystal size/mm	0.28 × 0.26× 0.24	0.28 ×0.26 ×0.24
θ range for data collection	2.09 to 27.40 °	2.06 to 27.44 °
h,k,l ranges	$-10\leq h\leq 10$, $-11\leq k\leq 11$, $-13\leq l\leq 12$	$-10\leq h\leq 10$, $-12\leq k\leq 12$, $-12\leq l\leq 13$
Reflections collected/unique	6392/3253 [R(int) = 0.0228]	7005/3575 [R(int) = 0.0294]
Completeness	97.9%	97.7%
Data/restraints/parameters	3253/0/192	3575/0/209
Goodness-of-fit on F^2	1.072	1.072
Final R indices [I>2sigma(I)]	R^1 = 0.0545, wR^2 = 0.1695	R^1 = 0.0345, wR^2 = 0.0911
R indices (all data)	R^1 = 0.0726, wR^2 = 0.1898	R^1 = 0.0413, wR^2 = 0.1070
Largest diff. peak and hole/e Å^{-3}	0.616 and -0.205	1.105 and –0.685



Scheme 4 Plausible mechanism for the formation of **2a**–**e**.

MS(EI)(*m/z*): 282.09 [(M+H)$^+$] (78%); HRESIMS calcd for $C_{17}H_{15}NO_3$ (M+H)$^+$ 282.1130; found 282.1043; Anal. Calcd for $C_{17}H_{16}NO_3$: C, 72.58; H, 5.37; N, 4.98. Found: C, 72.77; H, 5.28; N, 5.08%.

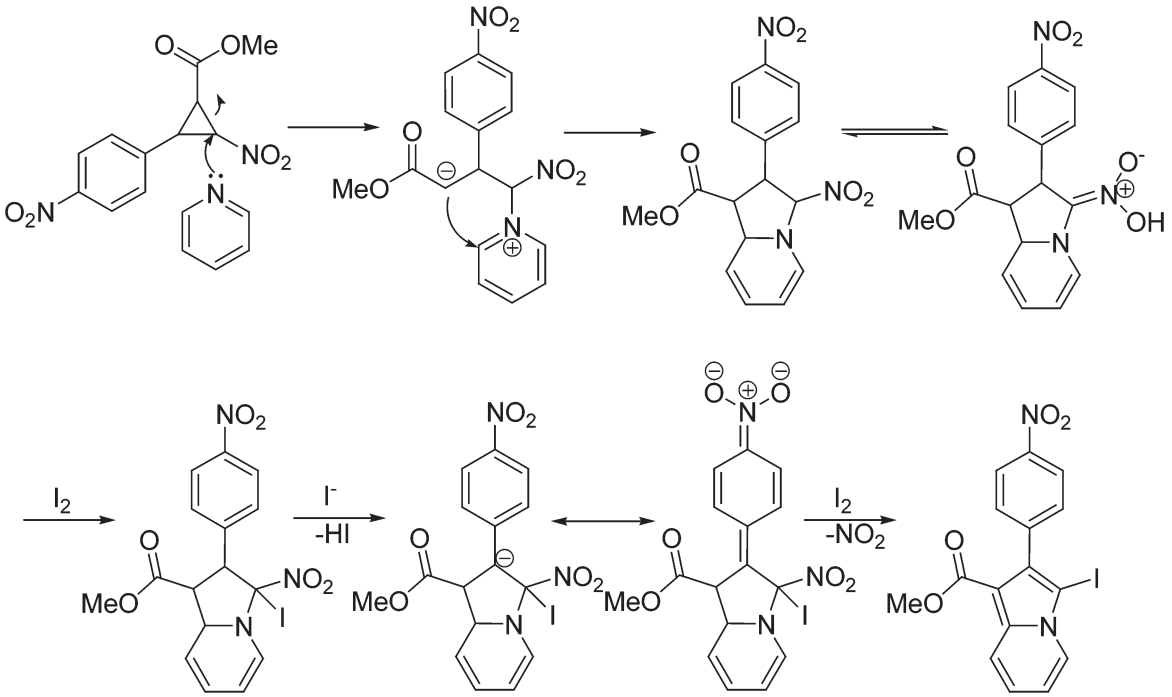
Methyl 3-phenylindolizine-1-carboxylate (**2b**):[15] Yellow solid, m.p. 114–116 °C (CH_2Cl_2/PE); ^{1}H NMR ($CDCl_3$, 600 MH) δ (ppm) 8.23 (d, *J* = 9.3 Hz, 1H), 8.20 (d, *J* = 7.2 Hz, 1H), 7.54–7.42 (m, 4H), 7.39–7.35 (m, 1H), 7.29 (s, 1H), 7.09–7.06 (m, 1H), 6.70–6.66 (m, 1H), 3.87 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 163.6, 139.8, 138.5, 132.0, 131.9, 128.9(2C), 128.8, 128.7, 128.3(2C), 128.2, 121.0, 120.2, 116.1, 52.4; IR (KBr, cm^{-1}): 2954, 1690, 1607, 1519, 1498, 1081, 855, 758; MS(EI)(*m/z*): 251.02 [M$^+$] (51%); HRESIMS calcd for $C_{16}H_{14}NO_2$ (M+H)$^+$ 252.1025; found 252.0954; Anal. Calcd for $C_{16}H_{13}NO_2$: C, 76.48; H, 5.21; N, 5.57. Found: C, 76.52; H, 5.20; N, 5.68%.

Methyl 3-(4-methylphenyl)indolizine-1-carboxylate (**2c**):[23] Yellow solid, m.p. 140–142 °C (CH_2Cl_2/PE); ^{1}H NMR (DMSO-d_6, 600 MH) δ (ppm) 8.26–8.24 (m, 2H), 7.42 (d, *J* = 7.8 Hz, 2H), 7.30 (d, *J* = 7.8 Hz, 2H), 7.22 (s, 1H), 7.07 (t, *J* = 6.0 Hz, 1H), 6.69 (t, *J* = 7.2 Hz, 1H), 3.91 (s, 3H), 2.42 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 163.5, 142.6, 138.1, 136.9, 131.1, 128.9(2C), 128.8(2C), 128.4, 127.7, 121.1, 119.9, 115.7, 103.7, 52.2, 21.6; IR (KBr, cm^{-1}): 2945, 2855, 1691, 1547, 1510, 1446, 1365, 1218, 1046, 820, 772, 742, 564; MS(EI) (*m/z*): 266.32 [(M+1)$^+$] (70%); HRESIMS calcd for $C_{17}H_{15}NO_2$ (M+H)$^+$ 266.1181; found 266.1099; Anal. Calcd for $C_{17}H_{16}NO_2$: C, 76.96; H, 5.70; N, 5.28. Found: C, 76.88; H, 5.89; N, 5.32%.

Methyl 3-(4-bromophenyl)indolizine-1-carboxylate (**2d**): Yellow solid, m.p. 152–154 °C (CH_2Cl_2/PE); ^{1}H NMR ($CDCl_3$, 600 MH) δ (ppm) 9.26 (d, *J* = 7.2 Hz, 1H), 8.22 (d, *J* = 6.6 Hz, 1H), 7.51–7.45 (m, 4H), 7.29 (s, 1H), 7.12–7.05 (m, 1H), 6.77 (d, *J* = 7.2 Hz, 1H), 3.86 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 163.3, 138.4, 138.3, 131.8, 131.3(2C), 130.2(2C), 128.5, 128.2, 126.6, 120.4, 120.0, 116.1, 104.2, 52.3; IR (KBr, cm^{-1}): 2946, 1672, 1554, 1512, 825; MS(EI) (*m/z*): 330.20 [(M+1)$^+$] (47%); HRESIMS calcd for $C_{16}H_{12}BrNO_2$ (M+H)$^+$ 330.0130; found 330.0067; Anal. Calcd for $C_{16}H_{13}BrNO_2$: C, 58.20; H, 3.66; N, 4.24. Found: C, 58.32; H, 3.56; N, 4.44%.

Methyl 3-(4-chlorophenyl)indolizine-1-carboxylate (**2e**): Yellow solid, m.p. 139–141 °C (CH_2Cl_2/PE); ^{1}H NMR ($CDCl_3$, 600 MH) δ (ppm) 8.27 (d, *J* = 12 Hz, 1H), 8.23 (d, *J* = 6.6 Hz, 1H), 7.52–7.47 (m, 4H), 7.27 (s, 1H), 7.10–7.07 (m, 1H), 6.74 (d, *J* = 7.2 Hz, 1H), 3.91 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 163.0, 149.3, 138.4, 132.6, 131.8, 129.5(2C), 129.3, 129.2, 123.2(2C), 120.4, 119.0, 116.1, 104.2, 52.5; IR (KBr, cm^{-1}): 2946, 2858, 1730, 1652, 1550, 1510, 820; MS(EI)(*m/z*): 286.20 [(M+1)$^+$] (38%); HRESIMS calcd for $C_{16}H_{12}ClNO_2$ (M+H)$^+$ 286.0635; found 286.0544; Anal. Calcd for $C_{16}H_{13}ClNO_2$: C, 67.26; H, 4.23; N, 4.90. Found: C, 67.37; H, 4.09; N, 4.96%.

Methyl 3-iodo-2-(4-nitrophenyl)indolizine-1-carboxylate (**2f**): Yellow solid, m.p. 142–143 °C (CH_2Cl_2/PE); ^{1}H NMR ($CDCl_3$, 600 MH) δ (ppm) 8.24 (d, *J* = 8.4 Hz, 2H), 8.19–8.17 (m, 2H), 7.48



Scheme 5 Plausible mechanism for the formation of **2f**.

(d, J = 8.4 Hz, 2H), 7.14–7.11 (m, 1H), 6.89–6.86 (m, 1H), 3.64 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 163.0, 150.4, 146.3, 141.4, 130.6(2C), 130.3, 130.2, 129.7, 124.6(2C), 122.9, 120.0, 117.6, 107.8, 50.4; IR (KBr, cm^{-1}): 3088, 2982, 2938, 1720, 1679, 1595, 1508, 1099, 1042, 858; MS(EI)(*m/z*): 423.08 [(M+1)$^+$] (49%); HRESIMS calcd for $C_{16}H_{11}IN_2O_4$ (M+H)$^+$ 422.9840; found 422.9750; Anal. Calcd for $C_{16}H_{12}IN_2O_4$: C, 45.52; H, 2.63; N, 6.64. Found: C, 45.38; H, 2.72; N, 6.88%.

Methyl 2-(4-methoxyphenyl)-3-nitrocyclopropanecarboxylate: White solid, m.p. 87–89 °C (AcOEt/PE); ^{1}H NMR ($CDCl_3$, 600 MH) δ (ppm) 7.16 (d, J = 7.2 Hz, 2H), 6.88 (d, J = 7.2 Hz, 2H), 4.73 (dd, J_1 = 6.6 Hz, J_2= 8.4Hz, 1H), 4.63 (dd, J_1 = 9.0 Hz, J_2 = 10.2Hz, 1H), 3.96 (dd, J_1 = 7.2 Hz, J_2 = 5.4Hz, 1H), 3.80 (s, 3H), 3.65 (s, 3H); ^{13}C NMR ($CDCl_3$, 150 MHz) δ (ppm) 170.1, 158.2, 129.1(2C), 127.3(2C), 113.4, 78.6, 54.2, 50.9, 38.4, 36.7; IR (KBr, cm^{-1}): 2954, 2837, 1731, 1613, 1552, 1516, 1440, 1384, 1327, 1300, 1257, 1117, 1027, 987, 836, 622.

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References

1 J.P. Michael, *Nat. Prod. Rep*., 2002, **19**, 742.
2 J.P. Michael, *Alkaloids*, 2001, **55**, 91.
3 R. Millet, J. Domarkas, B. Rigo, L. Goossens, J.-F. Goossens, R. Houssin and J.-P. Henichart, *Bioorg. Med. Chem.*, 2002, **10**, 2905.
4 E.M. Beck, R. Hatley and M.J. Gaunt, *Angew. Chem. Int. Ed.*, 2008, **47**, 3004.
5 M. Becuwe, D. Landy, F. Delattre, F. Cazier and S. Fourmentin, *Sensors*, 2008, **8**, 3689.
6 E. Kim, M. Koh, J. Ryu and S.B. Park, *J. Am. Chem. Soc.*, 2008, **130**, 12206.
7 E. Kim, M. Koh, B.J. Lim and S.B. Park, *J. Am. Chem. Soc.*, 2011, **133**, 6642.
8 I.V. Seregin, V. Ryabova and V. Gevorgyan, *J. Am. Chem. Soc.*, 2007, **129**, 7742.
9 T. Schwier, A.W. Sromek, D.M.L. Yap, D. Chernyak and V. Gevorgyan, *J. Am. Chem. Soc.*, 2007, **129**, 9868.
10 I.V. Seregin, A.W. Schammel and V. Gevorgyan, *Org. Lett.*, 2007, **9**, 3433.
11 B. Yan and Y. Liu, *Org. Lett.*, 2007, **9**, 4323.
12 B. Yan, Y. Zhou, H. Zhang, J. Chen and Y. Liu, *J. Org. Chem.*, 2007, **72**, 7783.
13 G.G. Surpateanu, D. Landy, N.C. Lungu, S. Fourmentin and G. Surpateanu, *J. Heterocyclic Chem.*, 2007, **44**, 783.
14 Y.M. Shen, G. Grampp, N. Leesakul, H.W. Hu and J.H. Xu, *Eur. J. Org. Chem.*, 2007, 3718.
15 J.B. Xia, X.Q. Wang and S.L. You, *J. Org. Chem.*, 2009, **74**, 456.
16 J.B. Xia, S.L. You, *Org. Lett.* 2009, **11**, 1187.
17 B. Liu, X. Qin, K. Li, X. Li, Q. Guo, J. Lan and J. You, *Chem. Eur. J.*, 2010, **16**, 11836.
18 P. Xi, F. Yang, S. Qin, D. Zhao, J. Lan, G. Gao, C. Hu and J. You, *J. Am. Chem. Soc.*, 2010, **132**, 1822.
19 C.-H. Park, V. Ryabova, I.V. Seregin, A.W. Sromek and V. Gevorgyan, *Org. Lett*., 2004, **6**, 1159.
20 B. Zhao, *Org. Biomol. Chem.*, 2012, **10**, 7108.
21 E.F. Douglas and N.J. Eric, *J. Am. Chem. Soc.*, 2005, **127**, 8964.
22 T. Okino, Y. Hoashi, T. Furukawa, X. Xu and Y. Takemoto, *J. Am. Chem. Soc.*, 2005, **127**, 119.
23 B. Liu, Z. Wang, N. Wu, M. Li, J. You and J. Lan, *Chem. Eur. J.* 2012, **18**, 1599.