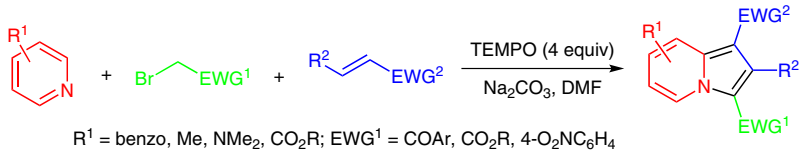
Synthesis F. Shi et al. Paper

# Transition-Metal-Free Synthesis of Indolizines from Electron-Deficient Alkenes via One-Pot Reaction Using TEMPO as an Oxidant

**Fei Shi**[a,b]
**Yu Zhang**[*a,b]
**Zhaole Lu**[b]
**Xiaolei Zhu**[b]
**Weiqiu Kan**[b]
**Xiang Wang**[b]
**Huayou Hu**[*a,b]

[a] School of Chemistry and Chemical Engineering, Ningxia University, Yinchuan 750021, P. R. of China
[b] Jiangsu Key Laboratory for Chemistry of Low-Dimensional Materials, School of Chemistry and Chemical Engineering, Huaiyin Normal University, Huaian 223300, P. R. of China
huayouhu@hytc.edu.cn




$R^1$ = benzo, Me, $NMe_2$, $CO_2R$; $EWG^1$ = COAr, $CO_2R$, 4-$O_2NC_6H_4$
$R^2$ = alkyl, aryl, $CO_2R$; $EWG^2$ = $SO_2Ph$, CN, $CO_2R$, $CONMe_2$, CHO, COR
25 examples, 37–96%
one-pot and transtion-metal-free!

Received: 10.09.2015
Accepted after revision: 30.10.2015
Published online: 19.11.2015
DOI: 10.1055/s-0035-1560973; Art ID: ss-2015-h0528-op

**Abstract** A one-pot method for the synthesis of multisubstituted indolizines from α-halo carbonyl compounds, pyridines, and electron-deficient alkenes is reported. The oxidative dehydrogenation reaction takes place under transition-metal-free conditions using TEMPO as an oxidant. This protocol uses ready available starting materials in a convenient procedure under mild reaction conditions.

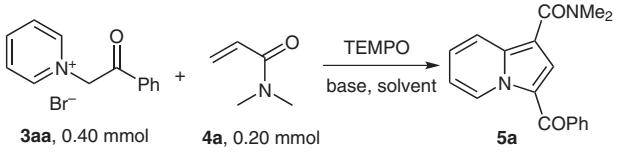
**Key words** N-ylide, alkenes, 1,3-dipolar cycloaddition, tandem reaction, dehydrogenation

Transition-metal-based reagents are used in numerous organic reactions as oxidants or catalysts. However, many of these reagents are highly toxic, expensive, or not ready available. Furthermore, the energy consumption for the removal of traces of transition metals to the ppm or even ppb level, which is often required for pharmaceutical intermediates or final products, is high. Therefore, the replacement of transition-metal-based oxidants by organic reagents is a valuable alternative.[1]

The indolizine skeleton is abundant in many natural products, such as erythrinan alkaloids, swainsonine, slaframine, gephyrotoxine, cryptowoline, and myrmicarin.[2] Indolizines are also important heterocyclic compounds that exhibit a broad array of bioactivity, such as antibacterial, phosphatase and aromatase inhibiting, antioxidant, antidepressant, and antitumor activity.[3] Moreover, indolizines are extensively applied as fluorescence dyes and organic semiconductors in materials science.[4]

Therefore, the development of new methods for the synthesis of indolizines is currently a 'hot topic' in organic chemistry.[5] One of the most efficient ways to synthesize in-

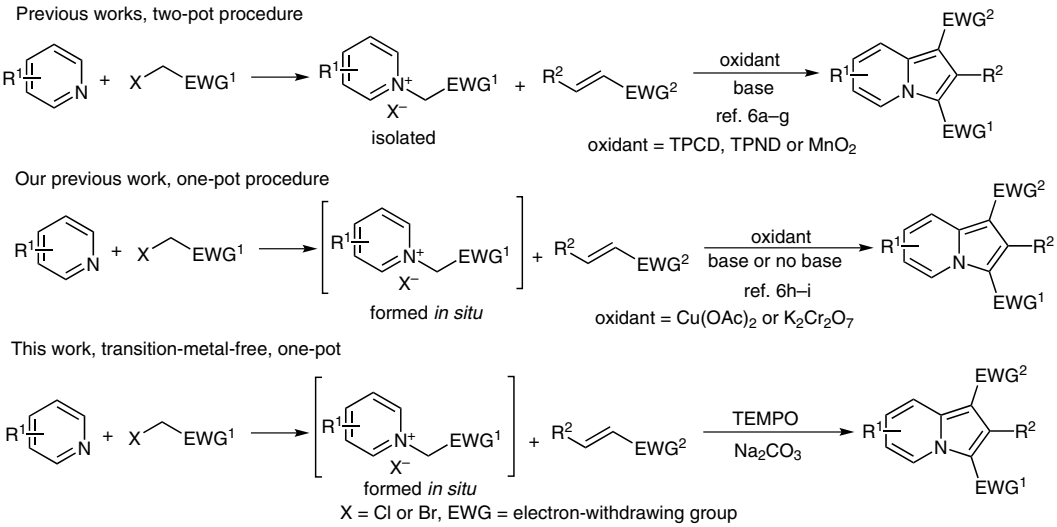
**Table 1** Screened Reaction Conditions for the Synthesis of Indolizine **4a**




**3aa**, 0.40 mmol **4a**, 0.20 mmol **5a**

| Entry | TEMPO (mmol) | Base (mmol) | Solvent (mL) | Temp (°C), time (h) | Yield[a] (%) |
|---|---|---|---|---|---|
| 1 | 0.60 | $Na_2CO_3$ (0.60) | DMF (2.0) | 90, 14 | 87 |
| 2 | 0.60 | –[b] | DMF (2.0) | 90, 14 | 28 |
| 3 | 0.60 | KHCO (0.60) | DMF (2.0) | 90, 14 | 71 |
| 4 | 0.60 | $K_3PO_4$ (0.60) | DMF (2.0) | 90, 14 | 74 |
| 5 | 0.60 | NaOAc (0.60) | DMF (2.0) | 90, 14 | 62 |
| 6 | 0.60 | $Et_3N$ (0.60) | DMF (2.0) | 90, 14 | 80 |
| 7 | 0.60 | $Cs_2CO_3$ (0.60) | DMF (2.0) | 90, 14 | 77 |
| 8 | 0.50 | $Na_2CO_3$ (0.60) | DMF (2.0) | 90, 14 | 79 |
| 9 | 0.30 | $Na_2CO_3$ (0.60) | DMF (2.0) | 90, 14 | 49 |
| 10 | 0.60 | $Na_2CO_3$ (0.60) | DMF (1.0) | 90, 14 | 70 |
| 11 | 0.60 | $Na_2CO_3$ (0.60) | DMF (4.0) | 90, 14 | 87 |
| 12 | 0.60 | $Na_2CO_3$ (0.40) | DMF (2.0) | 90, 14 | 77 |
| 13 | 0.60 | $Na_2CO_3$ (0.60) | $H_2O$ (2.0) | 90, 14 | trace |
| 14 | 0.60 | $Na_2CO_3$ (0.60) | $H_2O$–DMF (1:2, 2 mL) | 90, 14 | 27 |
| 15 | 0.80 | $Na_2CO_3$ (0.60) | DMF (2.0) | 120, 4 | 98 |
| **16**[c] | **0.80** | **$Na_2CO_3$ (0.60)** | **DMF (2.0)** | **120, 4** | **90** |

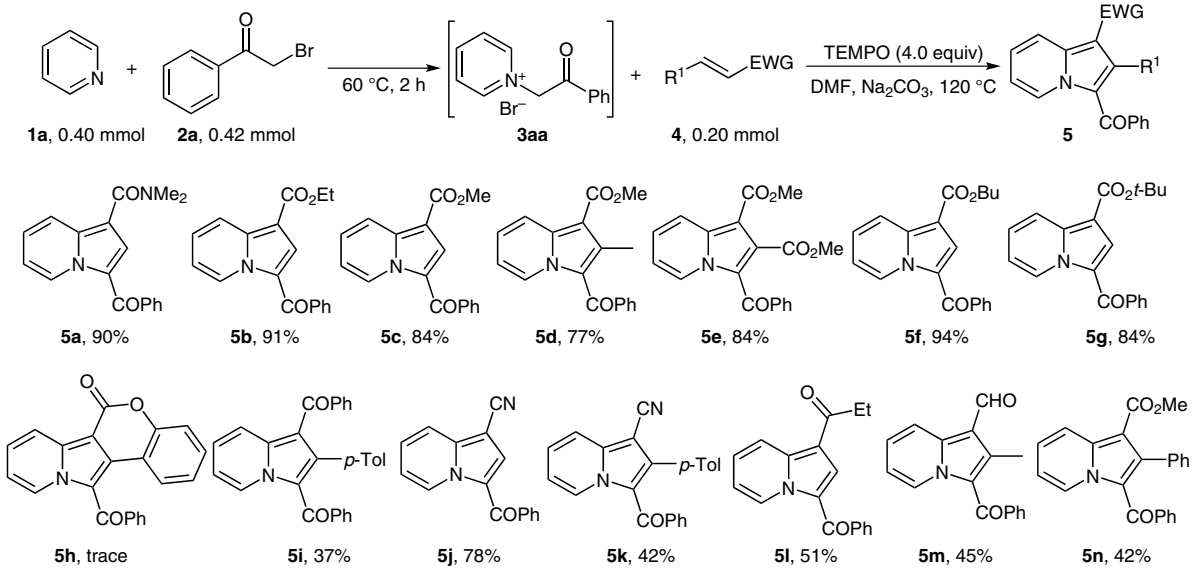
[a] Isolated yield.
[b] No base added.
[c] One-pot procedure: pyridine (**1a**, 0.40 mmol) and α-bromoacetophenone (**2a**, 0.42 mmol) was mixed and then heated at 60 °C for 2 h in a test tube, the thus-formed **3aa** was used immediately without isolation.



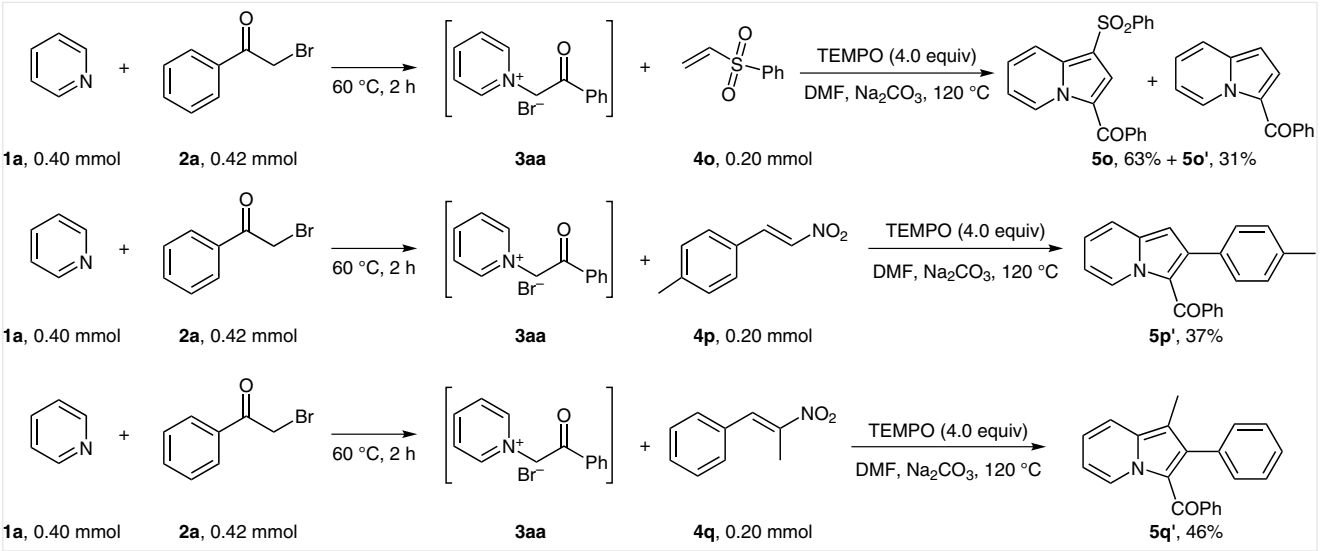

**Scheme 1** Schematic comparison of this work with previous work

dolizines is by a 1,3-dipolar cycloaddition reaction between an electron-deficient alkene and a pyridinium ylide, which produces the indolizine through oxidative dehydrogenation in the presence of an oxidant. The oxidants include freshly prepared manganese dioxide, tetrakis(pyridine)cobalt(II) dichromate (TPCD), tetrakis(pyridine)nickel(II) dichromate (TPND), copper acetate monohydrate, chromium trioxide, and potassium dichromate, which are all transition-metal-based reagents.[6] Therefore, there is great demand for a ready available and easily removed non-transition-metal oxidant that is used in a one-pot reaction for the synthesis of indolizine.

2,2,6,6-Tetramethylpiperidin-1-oxyl (TEMPO) is a commercially available organic compound that is generally used as radical trapping reagent. Recently, TEMPO has also been reported to be used as an oxidant or organocatalyst in oxidation reactions.[7] As a consequence of our interest in indolizines,[6h,i,8] we wished to explore the use of TEMPO as an oxidant in the synthesis of indolizines from electron-deficient alkenes. Herein, we report a transition-metal-free, one-pot protocol for the synthesis of indolizines from electron-deficient alkenes using TEMPO as the oxidant (Scheme 1).

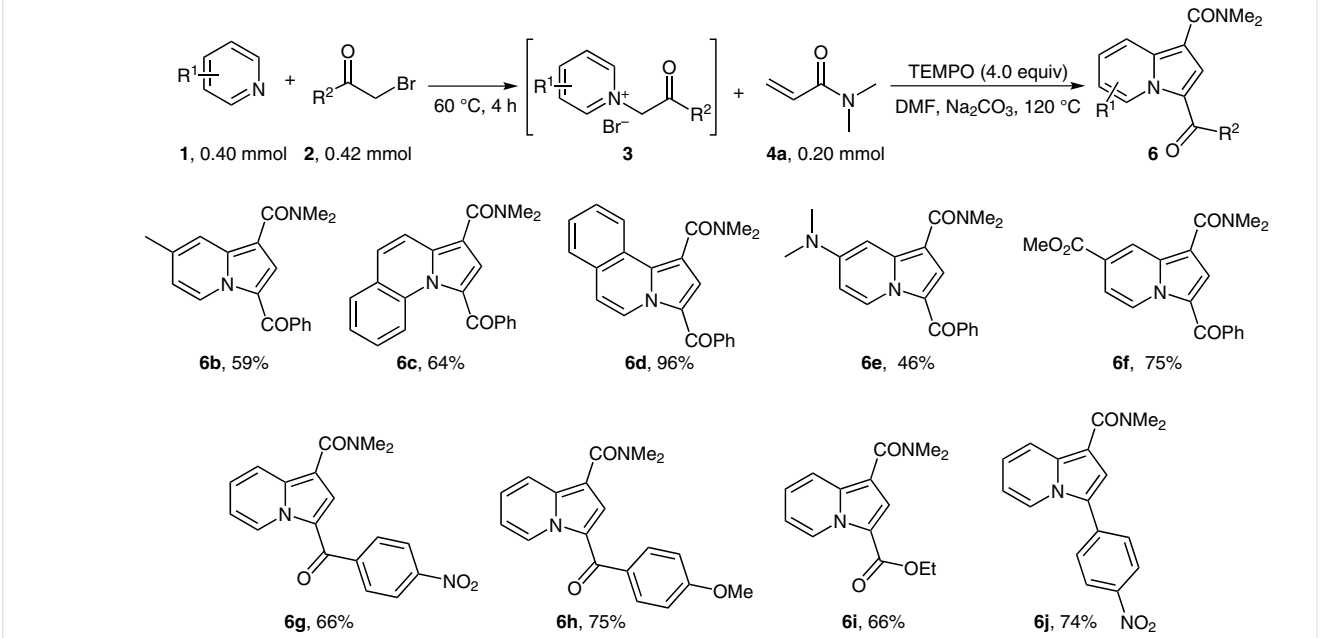



**Scheme 2** The scope of the electron-deficient alkene




**Scheme 3** Reactions of alkenes containing a leaving group

In the preliminary study, in order to optimize the reaction conditions, we chose 1-(2-oxo-2-phenylethyl)pyridinium bromide (**3aa**, 0.40 mmol, 2.0 equiv) and *N*,*N*-dimethylacrylamide (**4a**, 0.20 mmol, 1.0 equiv) as our model substrates. Fortunately, the desired product **5a** was isolated in 87% yield with sodium carbonate (0.60 mmol, 3.0 equiv) as the base and TEMPO (0.60 mmol, 3.0 equiv) as the oxidant in *N*,*N*-dimethylformamide (2.0 mL) at 90 °C for 14 hours (Table 1, entry 1). In the absence of a base, **5a** was obtained in only 28% yield (entry 2). Bases that were stronger or weaker than sodium carbonate were less efficient (entries 3–7). The addition of a lower amount of sodium carbonate or TEMPO also decreased the yield of **5a** (entries 8, 9, and 12). Attempts to use water or aqueous *N*,*N*-dimethylformamide as the solvent also failed (entries 13 and 14). In an attempt to shorten the reaction time, TEMPO (0.80 mmol, 4.0 equiv) was used at a higher temperature (120 °C) and the reaction was complete within four hours giving **5a** in nearly quantitative yield (98%, entry 15). Next, a one-pot procedure was applied in this transformation: **3aa** was



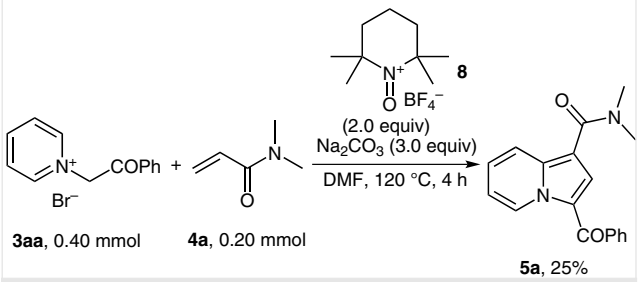

**Scheme 4** The scope of pyridine and α-halo carbonyl compounds

formed in situ from pyridine (**1a**, 0.40 mmol) and α-bromoacetophenone (**2a**, 0.42 mmol) at 60 °C for two hours and then used directly. Using **3aa** formed by this route gave **5a** in 90% yield, which is comparable to the yield of the two-step procedure (entry 16).

The scope of the alkene was examined. A series of different electron-deficient alkenes **4** that reacted with **3aa**, formed from **1a** and **2a**, in a one-pot reaction were studied under the standard conditions (Scheme 2). Most electron-deficient alkenes reacted with in situ formed **3aa** and gave the corresponding product **5** smoothly. However, coumarin (**4h**) only gave the corresponding product **5h** in trace amounts. Alkenes bearing a phenyl group ($R^1$ = Ph, *p*-Tol) gave the corresponding products **5i**,**k**,**n** in moderate yields, possibly due to steric hindrance. Notably, nitroalkenes **4p**,**q** gave the product **5p′** and **5q′** that do not contain a nitro group (Scheme 3), but phenyl vinyl sulfone (**4o**) gave two products **5o** and **5o′** in 63% and 31% yields, respectively. This is because that the nitro group is a better leaving group compared to the phenylsulfonyl group.

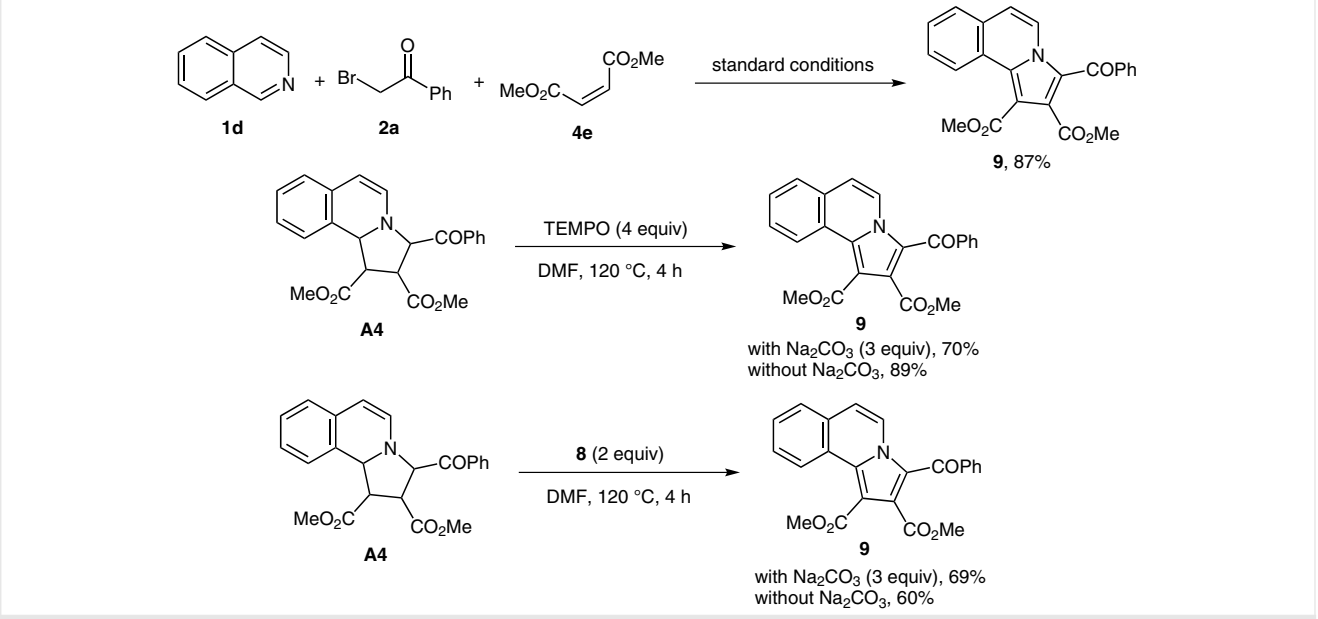
To study the substrate scope of the pyridine and α-halo carbonyl compound, various pyridines and α-halo carbonyl compounds were reacted with *N*,*N*-dimethylacrylamide (**4a**) under the standard conditions (Scheme 4). Various pyridines smoothly produced the corresponding products **6a**–**f**. Several types of α-halo carbonyl compound were applied in this transformation, including derivatives of α-bromoacetophenone and an α-bromoacetate, and these gave **6g**–**i** in good yields. Of note is the synthesis of **6j** in 74% yield starting from 1-(bromomethyl)-4-nitrobenzene.

To understand the reaction mechanism, the reaction mixture was analyzed by GC-MS before workup and it contained 2,2,6,6-tetramethylpiperidin-1-ol in addition to unreacted TEMPO. A control experiment using oxoammonium salt **8** (TEMPO$^+$ $BF_4^-$, 2.0 equiv were used due to higher oxidation state)[9] as the oxidant was also conducted and, as shown in Scheme 5, the expected product **5a** was isolated but in only 25% yield.




**Scheme 5** The control experiments

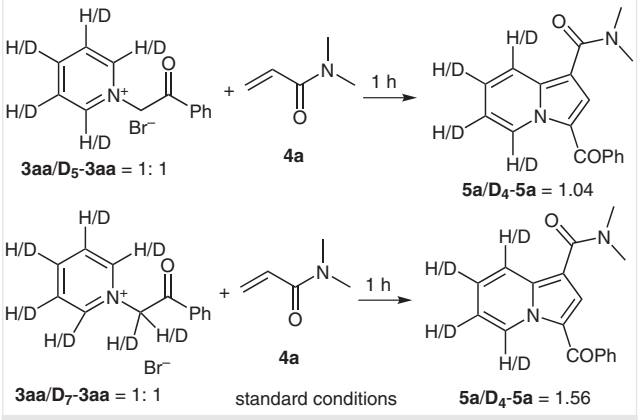
We have successful isolated a tetrahydroindolizine intermediate **A4**, although we failed to isolate sufficient amounts of the other three intermediates (**A1**, **A2** and **A3**, see details in the Supporting Information) according to reference.[10] Then intermediate **A4** reacts with TEMPO or **8** under different conditions. As shown in Scheme 6, both TEMPO and **8** can serve as an oxidant in the presence or absence of sodium carbonate. The highest yield of **9** (89%) are achieved using TEMPO as the oxidant in the absence of sodium carbonate. Using **8** as the oxidant, the yields of **9** in the presence or absence of sodium carbonate are less than




**Scheme 6** The control experiments

70%. However, one-pot reaction of **1d**, **2a**, and **4e** gives **9** in 87% yield, which is much higher than 70%. These results also indicate that sodium carbonate only plays an important role in the formation of intermediate **A**, while TEMPO is the real oxidant.

Isotope experiments were also conducted to understand the reaction mechanism. $D_5$-**3aa** was prepared from pyridine-$d_5$ in ethyl acetate; $D_7$-**3aa** was generated by deuterium exchange from $D_5$-**3aa** and ethanol-$d_6$. The in situ competitive reactions were conducted under the standard reaction conditions for one hour (Scheme 7). The ratios of **5a**/$D_4$-**5a** were 1.04 (**3aa** with $D_5$-**3aa**) and 1.56 (**3aa** with $D_7$-**3aa**), respectively. These results indicated that the cleavage of the C–H bond at 3-position to form intermediate **B** is the rate-determining step.

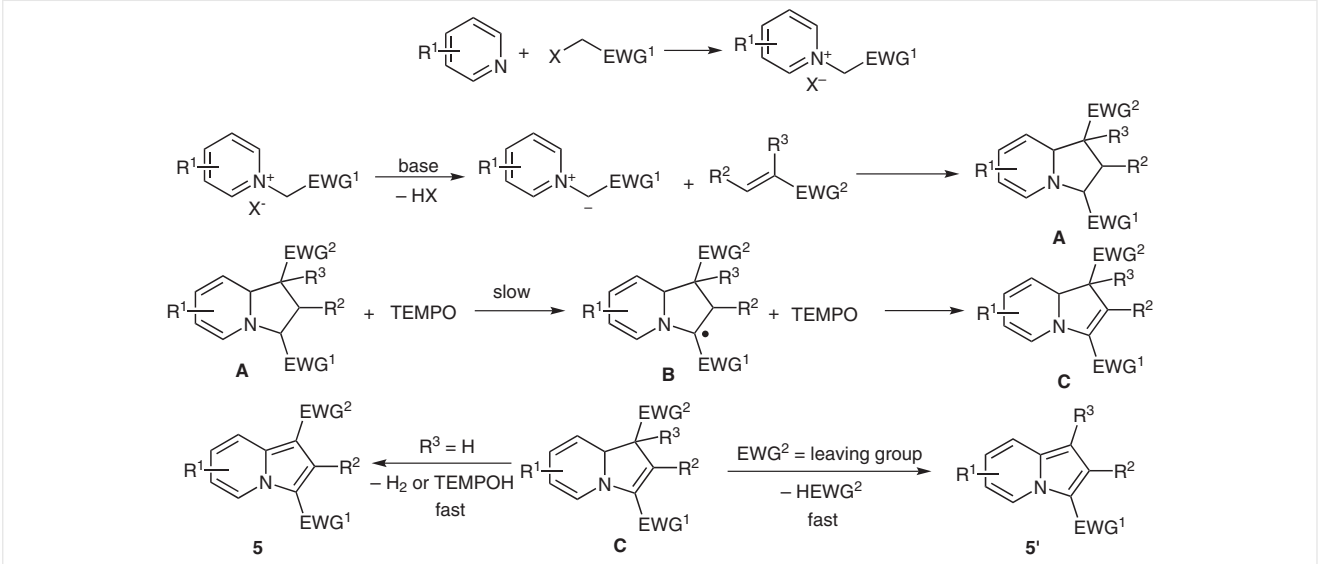



**Scheme 7** The isotope experiments

Based on these results and previous works,[6] a possible reaction mechanism is presented in Scheme 8. Intermediate **A** was formed in situ through 1,3-dipolar cycloaddition and oxidized to radical **B** and then to intermediate **C** by TEMPO through radical hydrogen abstraction. When the electron-withdrawing group at the 1-position of **C** is a leaving group, an elimination reaction occurs to form **5′**. Otherwise, product **5** is obtained by elimination of molecular hydrogen or oxidization by TEMPO.

In conclusion, a one-pot method for the synthesis indolizine from pyridines, α-halo carbonyl compounds, and electron-deficient alkenes under transitional-metal-free conditions is reported. Commercially available TEMPO is used as the oxidant in this transformation. These economic, efficient, easily handled, and transition-metal-free conditions should attract the interest of scientists in the fields of synthetic, medicinal, and materials chemistry.

All organic solutions were concentrated by rotary evaporation under reduced pressure. Flash column chromatography was performed employing 300–400 mesh silica gels. Petroleum ether = PE. TLC was performed using plates pre-coated to a depth of 0.25 mm with 300–400 mesh silica gel impregnated with a fluorescent indicator. All chemicals and solvents were obtained from commercial vendors and used without further purification. Melting points are uncorrected. IR spectra were obtained using a Thermo-Fisher Nicolet iS50. HRMS were recorded on a TOF-Q spectrometer. $^1$H and $^{13}$C NMR spectra were recorded on a Bruker 400 NMR spectrometer referenced to residual proton in the NMR solvent ($CHCl_3$: δ = 7.26). Compounds **5a**–**q** and **6a** are known.[6,8] Compounds **5a**–**j**,**m**,**q′**[6h] **5k**,**l**,**n**,**o**[6i] **5o′**,[6j] and **9**[10] have previously been reported in the literature.




**Scheme 8** The proposed mechanism

**Indolizines 5, 6 and 9; General Procedure**

Pyridine derivative **1** (0.40 mmol, 2.0 equiv) and α-halo carbonyl compound **2** (0.42 mmol, 2.1 equiv) in DMF (0.20 mL) were heated at 60 °C in a test tube with a stopper for 4 h to form **3** in situ. Then alkene **4** (0.20 mmol, 1.0 equiv), $Na_2CO_3$ (0.60 mmol, 3.0 equiv), TEMPO (0.80 mmol, 4.0 equiv), and further DMF (1.80 mL) were added to the tube; the mixture was heated at 120 °C for an additional 4 h (TLC monitoring). The mixture was cooled to r.t., poured into water, and extracted with $CHCl_3$ (3 × 10 mL). The combined extracts were washed with sat. brine, dried ($Na_2SO_4$), and filtered; solvent was removed under reduce pressure. The residue was purified by flash chromatography (silica gel, PE–EtOAc) to give the corresponding indolizine.

**3-Benzoyl-*N*,*N*,7-trimethylindolizine-1-carboxamide (6b)**

Chromatography (PE–EtOAc, 2:1); yellow solid; yield: 36.2 mg (59%); mp 100–102 °C.

IR (KBr): 1617, 1567, 1541, 1535, 1457 $cm^{-1}$.

$^1H$ NMR (400 MHz, $CDCl_3$): δ = 9.82 (d, *J* = 7.1 Hz, 1 H), 7.86 (s, 1 H), 7.77 (d, *J* = 7.4 Hz, 2 H), 7.54 (t, *J* = 7.4 Hz, 1 H), 7.47 (t, *J* = 7.4 Hz, 2 H), 7.38 (s, 1 H), 6.88 (d, *J* = 7.2 Hz, 1 H), 3.13 (s, 6 H), 2.44 (s, 3 H).

$^{13}C$ NMR (100 MHz, $CDCl_3$): δ = 184.7, 166.6, 140.3, 140.1, 138.0, 131.2, 128.9, 128.3, 128.1, 126.8, 121.1, 118.1, 117.6, 108.5, 21.5.

HRMS (APCI): *m*/*z* [M + H]$^+$ calcd for $C_{19}H_{19}N_2O_2$: 307.1141; found: 307.1147.

**1-Benzoyl-*N*,*N*-dimethylpyrrolo[1,2-*a*]quinoline-3-carboxamide (6c)**

Chromatography (PE–EtOAc, 2:1); red solid; yield: 44.0 mg (64%); mp 50–52 °C.

IR (KBr): 1632, 1541, 1456, 1411, 1384 $cm^{-1}$.

$^1H$ NMR (400 MHz, $CDCl_3$): δ = 8.11–8.02 (m, 3 H), 7.83 (d, *J* = 9.3 Hz, 1 H), 7.76 (d, *J* = 7.9 Hz, 1 H), 7.63 (t, *J* = 7.4 Hz, 1 H), 7.56 (d, *J* = 9.4 Hz, 2 H), 7.52 (d, *J* = 7.8 Hz, 2 H), 7.44 (t, *J* = 7.5 Hz, 1 H), 7.28 (s, 1 H), 3.12 (s, 6 H).

$^{13}C$ NMR (100 MHz, $CDCl_3$): δ = 184.8, 166.5, 138.9, 138.7, 133.2, 132.8, 130.1, 128.8, 128.5, 128.4, 127.54, 127.50, 127.3, 125.3, 125.1, 120.1, 117.6, 111.4.

HRMS (APCI): *m*/*z* [M + H]$^+$ calcd for $C_{22}H_{19}N_2O_2$: 343.1441; found: 343.1445.

**3-Benzoyl-*N*,*N*-dimethylpyrrolo[2,1-*a*]isoquinoline-1-carboxamide (6d)**

Chromatography (PE–EtOAc, 2:1); yellow solid; yield: 66.3 mg (96%); mp 57–60 °C.

IR (KBr): 1631, 1575, 1561, 1541, 1457, 1418 $cm^{-1}$.

$^1H$ NMR (400 MHz, $CDCl_3$): δ = 9.59 (d, *J* = 7.6 Hz, 1 H), 8.24–8.13 (m, 1 H), 7.84 (d, *J* = 7.6 Hz, 2 H), 7.77–7.70 (m, 1 H), 7.64–7.53 (m, 3 H), 7.49 (t, *J* = 7.6 Hz, 2 H), 7.28 (s, 1 H), 7.18 (d, *J* = 7.5 Hz, 1 H), 3.24 (s, 3 H), 2.94 (s, 3 H).

$^{13}C$ NMR (100 MHz, $CDCl_3$): δ = 185.7, 168.3, 134.0, 132.5, 131.6, 129.6, 129.2, 128.5, 128.3, 128.3, 127.1, 125.4, 124.7, 124.2, 124.2, 123.6, 114.4, 113.3, 39.0, 35.2.

HRMS (APCI): *m*/*z* [M + H]$^+$ calcd for $C_{22}H_{19}N_2O_2$: 343.1441; found: 343.1446.

**3-Benzoyl-7-(dimethylamino)-*N*,*N*-dimethylindolizine-1-carboxamide (6e)**

Chromatography (PE–EtOAc, 1:2); yellow solid; yield: 30.6 mg (46%); mp 179–180 °C.

IR (KBr): 2971, 2936, 1643, 1617, 1560, 1464, 1430, 1384 $cm^{-1}$.

$^1H$ NMR (400 MHz, $CDCl_3$): δ = 9.78 (d, *J* = 7.8 Hz, 1 H), 7.77–7.71 (m, 2 H), 7.53–7.40 (m, 3 H), 7.30 (s, 1 H), 7.12 (d, *J* = 2.8 Hz, 1 H), 6.63 (dd, *J* = 7.8, 2.8 Hz, 1 H), 3.12 (s, 6 H), 3.10 (s, 6 H).

$^{13}C$ NMR (100 MHz, $CDCl_3$): δ = 182.8, 167.3, 148.8, 143.2, 140.9, 130.5, 129.8, 128.73, 128.66, 128.1, 119.6, 106.0, 104.5, 95.8, 40.0.

HRMS (APCI): *m*/*z* [M + H]$^+$ calcd for $C_{20}H_{22}N_3O_2$: 336.1707; found: 336.1710.

**Methyl 3-Benzoyl-1-(dimethylcarbamoyl)indolizine-7-carboxylate (6f)**

Chromatography (PE–EtOAc, 2:1); yellow solid; yield: 52.3 mg (75%); mp 172–173 °C.

IR (KBr): 2971, 1732, 1632, 1611, 1560, 1461, 1384 $cm^{-1}$.

$^1H$ NMR (400 MHz, $CDCl_3$): δ = 9.85 (d, *J* = 7.0 Hz, 1 H), 8.69 (s, 1 H), 7.78 (d, *J* = 7.4 Hz, 2 H), 7.59–7.52 (m, 2 H), 7.52–7.42 (m, 3 H), 3.93 (s, 3 H), 3.12 (s, 6 H).

$^{13}C$ NMR (100 MHz, $CDCl_3$): δ = 185.6, 165.7, 165.3, 139.6, 137.5, 131.8, 129.0, 128.5, 127.9, 126.7, 126.3, 122.7, 121.8, 113.8, 112.9, 52.6.

HRMS (APCI): *m*/*z* [M + H]$^+$ calcd for $C_{20}H_{19}N_2O_4$: 351.1345; found: 351.1343.

***N*,*N*-Dimethyl-3-(4-nitrobenzoyl)indolizine-1-carboxamide (6g)**

Chromatography (PE–EtOAc, 1:2); red solid; yield: 44.3 mg (66%); mp 199–200 °C.

IR (KBr): 2972, 2936, 1685, 1654, 1617, 1560, 1462, 1427, 1384 $cm^{-1}$.

$^1H$ NMR (400 MHz, $CDCl_3$): δ = 9.94 (d, *J* = 7.0 Hz, 1 H), 8.33 (d, *J* = 8.7 Hz, 2 H), 8.06 (d, *J* = 9.0 Hz, 1 H), 7.92 (d, *J* = 8.7 Hz, 2 H), 7.42 (td, *J* = 7.9, 1.2 Hz, 1 H), 7.35 (s, 1 H), 7.11 (td, *J* = 6.9, 1.4 Hz, 1 H), 3.13 (s, 6 H).

$^{13}C$ NMR (100 MHz, $CDCl_3$): δ = 182.3, 165.9, 149.2, 145.7, 139.9, 129.7, 128.8, 127.3, 126.4, 123.6, 121.95, 119.56, 115.7, 110.8.

HRMS (APCI): *m*/*z* [M + H]$^+$ calcd for $C_{18}H_{16}N_3O_4$: 338.1135; found: 338.1141.

**3-(4-Methoxybenzoyl)-*N*,*N*-dimethylindolizine-1-carboxamide (6h)**

Chromatography (PE–EtOAc, 1:2); yellow solid; yield: 48.2 mg (75%); mp 145–146 °C.

IR (KBr): 2972, 2935, 1622, 1603, 1560, 1526, 1473, 1417, 1352 $cm^{-1}$.

$^1H$ NMR (400 MHz, $CDCl_3$): δ = 9.85 (d, *J* = 7.0 Hz, 1 H), 8.02 (d, *J* = 9.0 Hz, 1 H), 7.80 (d, *J* = 8.7 Hz, 2 H), 7.43 (s, 1 H), 7.30 (td, *J* = 7.9, 1.2 Hz, 1 H), 7.03–6.94 (m, 3 H), 3.87 (s, 3 H), 3.13 (s, 6 H).

$^{13}C$ NMR (100 MHz, $CDCl_3$): δ = 184.2, 166.6, 162.4, 139.1, 132.7, 131.1, 128.5, 126.0, 125.8, 121.6, 119.3, 114.7, 113.6, 109.3, 55.5.

HRMS (APCI): *m*/*z* [M + H]$^+$ calcd for $C_{19}H_{19}N_2O_3$: 323.1390; found: 323.1396.

**Ethyl 1-(Dimethylcarbamoyl)indolizine-3-carboxylate (6i)**

Chromatography (PE–EtOAc, 3:2); yellow solid; yield: 34.3 mg (66%); mp 83–85 °C.

IR (KBr): 2971, 2933, 1685, 1654, 1617, 1560, 1529, 1419, 1376 $cm^{-1}$.

$^1H$ NMR (400 MHz, $CDCl_3$): δ = 9.44 (d, *J* = 7.1 Hz, 1 H), 8.03 (dd, *J* = 9.0, 1.5 Hz, 1 H), 7.63 (s, 1 H), 7.21–7.14 (m, 1 H), 6.90 (td, *J* = 6.9, 1.4 Hz, 1 H), 4.37 (q, *J* = 7.1 Hz, 2 H), 3.18 (s, 6 H), 1.39 (t, *J* = 7.1 Hz, 3 H).

$^{13}C$ NMR (100 MHz, $CDCl_3$): δ = 166.6, 161.2, 138.6, 127.3, 124.0, 121.8, 119.7, 114.0, 113.4, 108.3, 60.1, 14.5.

HRMS (APCI): *m*/*z* [M + H]$^+$ calcd for $C_{14}H_{17}N_2O_3$: 261.1234; found: 261.1235.

***N*,*N*-Dimethyl-3-(4-nitrophenyl)indolizine-1-carboxamide (6j)**

Chromatography (PE–EtOAc, 1:1); red solid; yield: 45.9 mg (74%); mp 143–144 °C.

IR (KBr): 2971, 2939, 1636, 1617, 1560, 1466, 1413, 1384 $cm^{-1}$.

$^1H$ NMR (400 MHz, $CDCl_3$): δ = 8.35–8.27 (m, 3 H), 7.95 (d, *J* = 9.1 Hz, 1 H), 7.70 (d, *J* = 8.6 Hz, 2 H), 7.10 (s, 1 H), 6.99 (dd, *J* = 9.2, 6.7 Hz, 1 H), 6.72 (t, *J* = 6.7 Hz, 1 H), 3.19 (s, 6 H).

$^{13}C$ NMR (100 MHz, $CDCl_3$): δ = 167.0, 146.2, 138.1, 136.4, 127.7, 124.6, 122.8, 122.5, 121.5, 120.5, 116.4, 113.2, 109.0.

HRMS (APCI): *m*/*z* [M + H]$^+$ calcd for $C_{17}H_{16}N_3O_3$: 309.1186; found: 310.1186.

**Synthesis of 5a with Oxoammonium Salt as the Oxidant**

Isolated pyridinium salt **3aa** (0.40 mmol, 2.0 equiv), alkene **4a** (0.20 mmol, 1.0 equiv), $Na_2CO_3$ (0.60 mmol, 3.0 equiv), oxoammonium salt **8** (0.40 mmol, 2.0 equiv due to higher oxidant state) and 2.0 mL of DMF were added to a test tube. Then the mixture was heated at 120 °C for 4 h (TLC monitoring). The mixture was cooled to r.t., poured into water, and extracted with $CHCl_3$ (3 × 10 mL). The combined extracts were washed with sat. brine, dried ($Na_2SO_4$), and filtered; solvent was removed under reduced pressure. The residue was purified by flash chromatography (silica gel, PE–EtOAc) to give the corresponding indolizine.

**Synthesis of 9 from A4**

Isolated **A4** (0.20 mmol, 1.0 equiv), without or with $Na_2CO_3$ (0.60 mmol, 3.0 equiv), oxoammonium salt **8** (0.40 mmol, 2.0 equiv due to higher oxidant state) or TEMPO (0.80 mmol, 4.0 equiv) and 2.0 mL of DMF were added to a test tube. The mixture was heated at 120 °C for 4 h (TLC monitoring). The mixture was cooled to r.t., poured into water, and extracted with $CHCl_3$ (3 × 10 mL). The combined extracts were washed with sat. brine, dried ($Na_2SO_4$), and filtered; solvent was removed under reduced pressure. The residue was purified by flash chromatography (silica gel, PE–EtOAc) to give the corresponding indolizine.

## Acknowledgment

We are grateful to funding of NSFC (No.: 21202058, 21401063), Education Department of Jiangsu Province (No. 13KJA150001) and CPSF (No.: 2012M511645, 2013T60483) for their financial support.

## Supporting Information

Supporting information for this article is available online at http://dx.doi.org/10.1055/s-0035-1560973.

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