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A novel and efficient approach to highly substituted indolizines via 5-*endo-trig* iodocyclization

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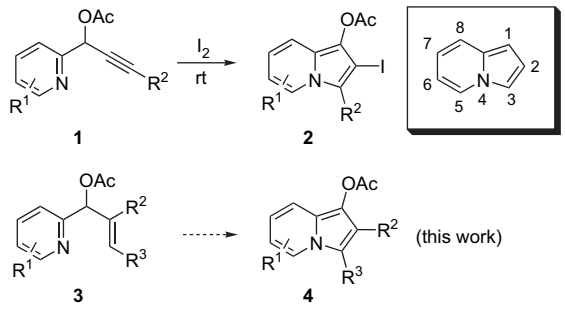
Abstract—A new approach to indolizines has been developed using a 5-*endo-trig* iodocyclization of allylic esters followed by isomerization and dehydroiodination facilitated by triethylamine at rt. This mild procedure enabled us to synthesize a number of highly substituted indolizines in good yields.

1. Introduction

Pyrrolo[1,2-*a*]pyridine, known as indolizine, is an important structural motif frequently found in nature and has been utilized as a key scaffold in the pharmaceutical industry due to the broad spectrum of biological activities associated with this privileged structure.[1] Thus, indolizine-based scaffolds have been actively investigated as antiviral, anti-inflammatory, anticancer, and cardiovascular agents.[2] Besides, indolizine-bearing polycyclic compounds have drawn much attention owing to their possible usage as dyes and chemosensors.[3] Not surprisingly, many synthetic approaches to this skeleton have been disclosed in the literature.[4] In the context of our research program on the facile synthesis of heterocycles using mild and environment-friendly conditions,[5] we recently communicated on the convenient synthesis of highly substituted indolizines based upon a facile 5-*endo-dig* iodocyclization.[5a,6] As an extension of this program, we decided to investigate 5-*endo-trig* iodocyclization[7] of allylic esters to construct the same carbon framework (Scheme 1). Here we wish to report a convenient approach to indolizine structure featuring a 5-*endo-trig* iodocyclization followed by isomerization and dehydroiodination promoted by base.

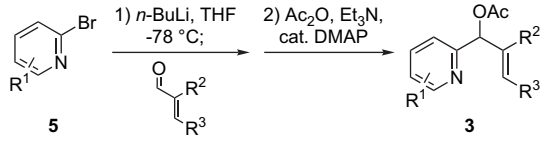


Scheme 1. Two novel approaches to indolizines.

2. Results and discussion

At the outset, we envisioned that indolizine **4** having two different groups (R^2 and R^3) at C2 and C3 centers could be obtained if the cyclization precursor, allylic ester **3**, contains two functional groups at C2 and C3 sites. In a related 5-*endo-dig* iodocyclization of propargylic acetate **1**, further functional group at C2 position of indolizine has to be installed by manipulation of an iodo group of **2**.

Our approach commenced with the preparation of allylic acetate **3**. Thus, reaction of 2-pyridinyl lithium with α,β-unsaturated aldehyde afforded allylic alcohol, which was converted to the corresponding allylic acetate **3** in good yield (Scheme 2).



Scheme 2. Preparation of the cyclization substrates **3**.

When **3a** was initially exposed to iodine (2 equiv) in CH_2Cl_2 at rt, **6** was formed as a mixture of diastereomers (in about 2.8:1 ratio)[8] almost quantitatively. This result is different from that of 5-*endo-dig* iodocyclization of propargylic

Keywords: Indolizine; Iodine; 5-*endo-trig* Iodocyclization; Environmentally benign.
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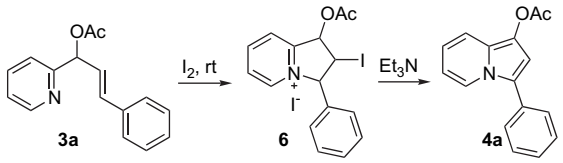
acetate **1** where indolizine structure was directly constructed. To induce both isomerization and elimination of HI, **6** was then treated with base. Pleasingly, this provided indolizine **4a** in 77% yield (Scheme 3).

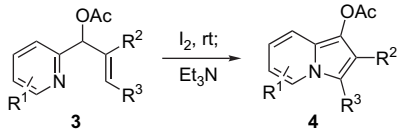


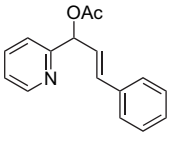
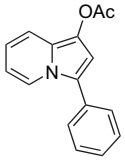
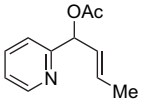
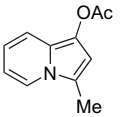
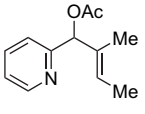
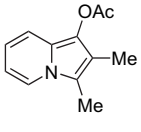
Scheme 3. One-pot procedure from allylic acetate to indolizine.

Notably, exposure of **3a** to iodine and triethylamine or $NaHCO_3$ at the same time gave rather low conversion. This result is surprising because base such as Et_3N or $NaHCO_3$ is commonly employed with iodine in most iodocyclizations. Two equivalents of iodine are needed to complete the reaction. Among the solvents screened, CH_3CN gave the best result. Thus, the following reaction condition was used. Allylic ester **3** was treated with iodine (2 equiv) in CH_3CN at rt for 3 h. After the disappearance of the starting material was checked by TLC, triethylamine (2 equiv) was added at rt. After being stirred at rt for another 3 h, the reaction mixture was concentrated in vacuo. The resulting residue was diluted with ethyl acetate and washed with $NaHSO_3$ and $NaHCO_3$, successively. The water layer was extracted with ethyl acetate one more time. The organic layer was dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography (hexanes/ethyl acetate/dichloromethane=10:1:2) to give **4**.

As shown in Table 1, other allylic esters **3** were subjected to the optimized conditions mentioned above to evaluate the reaction scope. Indeed, various indolizine derivatives were successfully synthesized in good yields. It should be mentioned that allylic acetate **3d** was exposed to the optimized

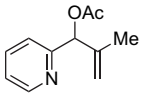
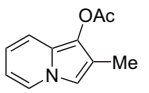
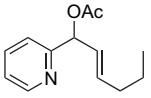
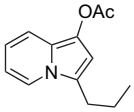
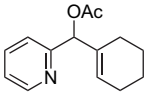
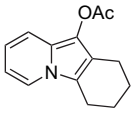
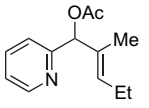
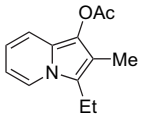
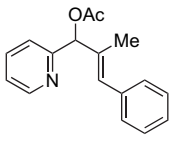
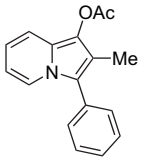
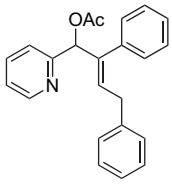
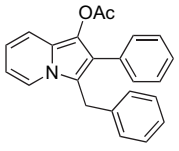
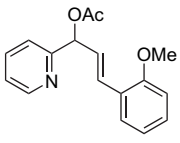
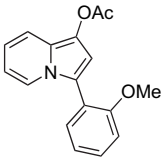
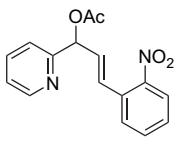
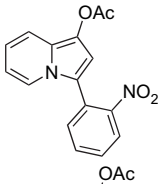
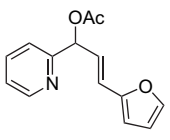
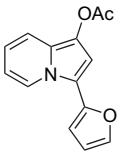
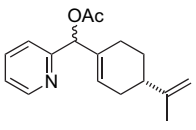
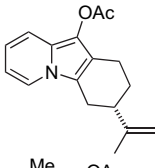
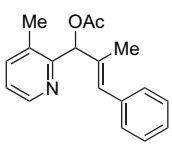
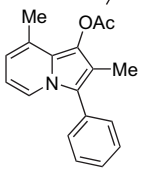
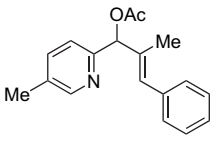
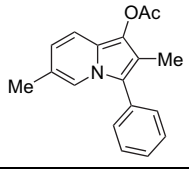
Table 1. Synthesis of various indolizine derivatives



Entry	Substrate **3**		Product **4**		Isolated yield (%)
1		**3a**		**4a**	77
2		**3b**		**4b**	65
3		**3c**		**4c**	60

(*continued*)

Table 1. (*continued*)

Entry	Substrate **3**		Product **4**		Isolated yield (%)
4		**3d**		**4d**	—
5		**3e**		**4e**	84
6		**3f**		**4f**	74
7		**3g**		**4g**	60
8		**3h**		**4h**	89
9		**3i**		**4i**	55
10		**3j**		**4j**	56
11		**3k**		**4k**	45
12		**3l**		**4l**	83
13		**3m**		**4m**	74
14		**3n**		**4n**	84
15		**3o**		**4o**	73

conditions (entry 4), but cyclization did not occur. Only the starting material was recovered.[9] In contrast, substitution at C2 position of allylic acetate **3** does not affect the yield (entries 2 and 3). Substitution at C3 of allylic acetate except hydrogen seemed crucial for the successful cyclization under our conditions. When R^2 and R^3 of allylic ester are phenyl and benzyl, respectively, a modest yield of **4i** was obtained (entry 9). Allylic acetates possessing electron-donating (2-methoxyphenyl) and electron-withdrawing (2-nitrophenyl) groups were also submitted to examine the role of these in iodocyclizations. Contrary to our expectation, yields in both cases were lower than that of **4a** although **3j** gave a better yield of product than **3k** (entries 10 and 11). Furan-containing indolizine **4l** was obtained in excellent yield (entry 12). When (*S*)-(−)-perillaldehyde was used as an α,β-unsaturated aldehyde partner, chiral indolizine derivative **4m** was prepared in good yield (entry 13). When 3-methyl- and 5-methylpyridinyllithium were coupled with α-methyl-*trans*-cinnamaldehyde, respectively, the corresponding indolizines **4n** and **4o** were synthesized in high yields (entries 14 and 15). Overall, this simple process enabled us to construct indolizine nucleus in good to excellent yields while demonstrating a wide functional group tolerance.

3. Conclusions

In conclusion, we have demonstrated a new approach to highly substituted indolizines **4** under very mild conditions where a facile and efficient 5-*endo-trig* iodocyclization of allylic acetate **3**, and subsequent isomerization and aromatization (by the loss of HI) were accomplished. In this one-pot reaction sequence, a pyridinyl nitrogen was again involved as an internal nucleophile of iodocyclization.[10] While similar 5-*endo-dig* iodocyclization provides an iodo group at C2 of indolizine ring structure, which is a functional handle for subsequent elaboration, this 5-*endo-trig* process allows direct introduction of functional groups at C2 position possible, depending on the substitution pattern of the cyclization precursor. Given the simplicity and environment-friendliness of this operation, it should be useful for the synthesis of other fused azacycles as well.

4. Experimental

4.1. General

The solvents used in the reactions were dried prior to use: tetrahydrofuran was distilled from sodium benzophenone ketyl; dichloromethane was distilled from calcium hydride. All other reagents were used as received without purification. All moisture-sensitive reactions were performed in flame-dried and/or oven-dried glassware under a positive pressure of nitrogen unless otherwise noted. 'Concentrated' refers to the removal of volatile solvents via distillation using a Buchi rotary evaporator. 'Dried' refers to pouring onto, or passing through anhydrous sodium sulfate or magnesium sulfate followed by filtration. Thin layer chromatography was carried out with E. Merck (Darmstadt) TLC plates precoated with silica gel 60 F_{254}. Visualization was accomplished using a UV lamp, iodine vapors, and/or a *p*-anisaldehyde (PAA) stain. Flash column chromatography was accomplished with Silicycle silica gel 60 (230–400 mesh). Proton nuclear magnetic resonance spectra were recorded in deuterated solvents on a Varian systems-300 (300 MHz) instrument. Chemical shifts are reported in parts per million (ppm, δ) relative to tetramethylsilane (TMS, δ 0.00). Carbon nuclear magnetic resonance spectra were recorded in deuterated solvents on a Varian systems-300 (75 MHz) instrument. Infrared spectra were measured on a Mattson Polaris FT-IR spectrometer, and signals are recorded in wavenumbers. High resolution mass spectra (HRMS) using electron ionization (EI) were measured on a Micromass mass spectrometer.

4.2. General procedure for allylic acetate 3

To a stirred solution of 2-bromopyridine (1.5 equiv) in THF was slowly added *n*-BuLi (1.6 M solution in hexanes, 1.4 equiv) at −78 °C. After 20 min, a solution of α,β-unsaturated aldehyde (8 mmol) in THF was slowly added to this mixture at −78 °C. After being stirred for 30 min, the reaction mixture was quenched with satd NH_4Cl at −78 °C. The reaction mixture was diluted with ethyl acetate, washed with H_2O and brine, successively. The water layer was extracted with ethyl acetate one more time. The combined organic layers were dried over $MgSO_4$, filtered, and concentrated in vacuo. The residue was purified by flash column chromatography (hexanes/ethyl acetate/dichloromethane=10:1:2 to 5:1:2 to 1:1:1) to afford allylic alcohol, which was dissolved in CH_2Cl_2. To this solution were added triethylamine (1.5 equiv), DMAP (0.01 equiv), and acetic anhydride (1.1 equiv) at 0 °C. After being stirred at rt for 2 h, the mixture was washed with aqueous citric acid and $NaHCO_3$, successively. The water layer was extracted with CH_2Cl_2 one more time. The organic layer was dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography (hexanes/ethyl acetate/dichloromethane=10:1:2) to give allylic acetate **3**.

4.2.1. (*E*)-3-Phenyl-1-(pyridin-2-yl)allyl acetate (3a). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.61 (ddd, *J*=4.8, 1.7, 0.9 Hz, 1H), 7.67 (dt, *J*=7.7, 1.8 Hz, 1H), 7.42–7.37 (m, 3H), 7.31–7.17 (m, 4H), 6.78–6.71 (m, 1H), 6.51–6.45 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.2, 158.6, 149.8, 137.2, 136.3, 133.7, 128.8, 128.4, 127.0, 126.5, 123.2, 121.6, 77.43, 21.5; IR (thin film) 3053, 3025, 2932, 1736, 1585, 1226 cm^{-1}; HRMS (EI) calcd for $[C_{16}H_{15}NO_2]^+$: *m/z* 253.1103, found: 253.1105.

4.2.2. (*E*)-1-(Pyridin-2-yl)but-2-enyl acetate (3b). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.60 (ddd, *J*=4.8, 1.6, 0.8 Hz, 1H), 7.69 (dt, *J*=7.7, 1.8 Hz, 1H), 7.18 (d, *J*=7.9 Hz, 1H), 7.20 (dd, *J*=7.5, 4.9 Hz, 1H), 6.24 (d, *J*=7.1 Hz, 1H), 5.86–5.76 (m, 2H), 2.14 (s, 3H), 1.73 (d, *J*=5.6 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.0, 158.9, 149.5, 137.0, 130.9, 128.6, 122.9, 121.3, 77.2, 21.3, 18.0; IR (thin film) 3011, 2932, 1737, 1588, 1371, 1232 cm^{-1}; HRMS (EI) calcd for $[C_{11}H_{13}NO_2]^+$: *m/z* 191.0946, found: 191.0943.

4.2.3. (*E*)-2-Methyl-1-(pyridin-2-yl)but-2-enyl acetate (3c). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.52 (ddd, *J*=4.9, 1.7, 0.9 Hz, 1H), 7.60 (dt, *J*=7.7, 1.8 Hz, 1H), 7.26 (d, *J*=7.9 Hz, 1H), 7.11 (dd, *J*=7.5, 4.9 Hz, 1H), 6.16 (s, 1H),

5.64 (q, J=6.8 Hz, 1H), 2.08 (s, 3H), 1.57 (d, J=6.8 Hz, 3H), 1.48 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.5, 158.4, 148.9, 136.6, 133.0, 122.5, 122.4, 120.8, 80.9, 20.9, 12.1; IR (thin film) 2982, 2923, 1739, 1587, 1234 cm^{-1}; HRMS (EI) calcd for $[C_{12}H_{15}NO_2]^+$: m/z 205.1103, found: 205.1104.

4.2.4. 2-Methyl-1-(pyridin-2-yl)allyl acetate (3d). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.27 (ddd, J=4.1, 1.5, 0.8 Hz, 1H), 7.53 (dt, J=7.7, 1.7 Hz, 1H), 7.22 (d, J=7.9 Hz, 1H), 7.05 (dd, J=7.5, 4.9 Hz, 1H), 6.10 (s, 1H), 5.00 (s, 1H), 4.87 (s, 1H), 2.00 (s, 3H), 1.54 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.2, 149.6, 142.4, 136.9, 123.0, 121.5, 114.3, 79.6, 21.4, 18.9; IR (thin film) 2960, 2900, 1741, 1580, 1220 cm^{-1}; HRMS (EI) calcd for $[C_{11}H_{13}NO_2]^+$: m/z 191.0946, found: 191.0942.

4.2.5. (*E*)-1-(Pyridin-2-yl)hex-2-enyl acetate (3e). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.59 (ddd, J=4.9, 1.8, 0.9 Hz, 1H), 7.67 (dt, J=7.7, 1.8 Hz, 1H), 7.35 (d, J=7.9 Hz, 1H), 7.19 (dd, J=7.5, 4.9 Hz, 1H), 6.25 (d, J=6.9 Hz, 2H), 5.87–5.74 (m, 2H), 2.13 (s, 3H), 2.12–2.01 (m, 2H), 1.44–1.37 (m, 2H), 0.87 (t, J=7.35 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.2, 159.1, 149.7, 136.9, 135.9, 127.3, 122.9, 121.4, 77.5, 34.5, 22.1, 21.5, 13.8; IR (thin film) 2959, 2930, 1738, 1370, 1231 cm^{-1}; HRMS (EI) calcd for $[C_{13}H_{17}NO_2]^+$: m/z 219.1259, found: 219.1261.

4.2.6. Cyclohexenyl(pyridin-2-yl)methyl acetate (3f). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.50 (ddd, J=4.8, 1.6, 0.8 Hz, 1H), 7.58 (dt, J=7.7, 1.7 Hz, 1H), 7.25 (d, J=7.9 Hz, 1H), 7.19 (dd, J=7.5, 4.9 Hz, 1H), 6.12 (s, 1H), 5.73 (s, 1H), 2.07 (s, 3H), 1.98 (s, 2H), 1.96 (d, J=3.8 Hz, 2H), 1.52–1.41 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.5, 158.4, 148.9, 136.6, 133.0, 122.5, 122.4, 120.8, 80.9, 20.9, 12.1; IR (thin film) 3055, 2924, 1737, 1583, 1434, 1299 cm^{-1}; HRMS (EI) calcd for $[C_{14}H_{17}NO_2]^+$: m/z 231.1259, found: 231.1262.

4.2.7. (*E*)-2-Methyl-1-(pyridin-2-yl)pent-2-enyl acetate (3g). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.44 (ddd, J=4.9, 1.7, 0.8 Hz, 1H), 7.35 (dt, J=7.7, 1.7 Hz, 1H), 7.05 (d, J=7.9 Hz, 1H), 6.85 (dd, J=7.4, 5.0 Hz, 1H), 5.95 (s, 1H), 5.34 (t, J=7.0 Hz, 1H), 1.83 (s, 3H), 1.80–1.73 (m, 2H), 1.27 (s, 3H), 0.66 (t, J=7.6 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.5, 158.4, 148.9, 136.6, 131.9, 122.5, 122.4, 80.9, 20.9, 20.8, 13.7, 12.3; IR (thin film) 2964, 2932, 1741, 1586, 1370, 1233 cm^{-1}; HRMS (EI) calcd for $[C_{13}H_{17}NO_2]^+$: m/z 219.1259, found: 219.1255.

4.2.8. (*E*)-2-Methyl-3-phenyl-1-(pyridin-2-yl)allyl acetate (3h). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.60 (ddd, J=4.1, 1.4, 0.8 Hz, 1H), 7.69 (dt, J=7.7, 1.7 Hz, 1H), 7.42 (d, J=7.9 Hz, 1H), 7.31–7.20 (m, 4H), 7.20–7.18 (m, 2H), 6.73 (s, 1H), 6.40 (s, 3H), 2.05 (s, 3H), 1.83 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.1, 158.3, 149.6, 137.2, 136.9, 135.2, 129.4, 128.3, 127.1, 122.9, 121.5, 81.3, 21.5, 14.6; IR (thin film) 3056, 2928, 1739, 1586, 1367, 1229 cm^{-1}; HRMS (EI) calcd for $[C_{17}H_{17}NO_2]^+$: m/z 267.1259, found: 267.1261.

4.2.9. (*E*)-2,4-Diphenyl-1-(pyridin-2-yl)but-2-enyl acetate (3i). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.60 (d, J=4.5 Hz, 1H), 7.56 (t, J=7.8 Hz, 1H), 7.28–7.12 (m, 12H), 6.58 (s, 1H), 6.11 (t, J=7.5 Hz, 1H), 3.27 (d, J=7.5 Hz, 2H), 2.11 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.1, 157.9, 149.5, 139.8, 137.3, 136.6, 130.5, 129.6, 128.7, 128.3, 127.5, 126.2, 122.9, 121.9, 80.2, 35.0, 21.5; IR (thin film) 3024, 2923, 1741, 1464, 1229 cm^{-1}; HRMS (EI) calcd for $[C_{23}H_{21}NO_2]^+$: m/z 343.1572, found: 343.1568.

4.2.10. (*E*)-3-(2-Methoxyphenyl)-1-(pyridin-2-yl)allyl acetate (3j). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.63 (dd, J=4.8, 0.9 Hz, 1H), 7.70 (dt, J=9.0, 1.8 Hz, 1H), 7.43 (dt, J=7.2, 1.5 Hz, 2H), 7.27–7.20 (m, 2H), 7.09 (d, J=15.3 Hz, 1H), 6.88 (q, J=8.7 Hz, 2H), 6.56–6.44 (m, 2H), 3.86 (s, 3H), 2.18 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.3, 158.8, 157.3, 149.8, 137.1, 129.5, 128.9, 127.5, 126.8, 125.2, 123.1, 121.7, 120.8, 111.1, 78.0, 55.6, 21.6; IR (thin film) 2936, 1738, 1591, 1490, 1243 cm^{-1}; HRMS (EI) calcd for $[C_{17}H_{17}NO_3]^+$: m/z 283.1208, found: 283.1205.

4.2.11. (*E*)-3-(2-Nitrophenyl)-1-(pyridin-2-yl)allyl acetate (3k). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.63 (dd, J=8.1, 1.2 Hz, 1H), 7.93 (dd, J=8.4, 1.1 Hz, 1H), 7.74 (dt, J=7.7, 1.8 Hz, 1H), 7.63–7.52 (m, 2H), 7.46–7.37 (m, 2H), 7.27–7.15 (m, 2H), 6.55–6.47 (m, 2H), 2.21 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.1, 157.9, 149.8, 137.3, 133.4, 132.2, 131.8, 129.0, 128.8, 128.1, 124.8, 123.4, 121.8, 76.4, 21.4; IR (thin film) 2922, 2851, 1740, 1525, 1229 cm^{-1}; HRMS (EI) calcd for $[C_{16}H_{14}N_2O_4]^+$: m/z 298.0954, found: 298.0951.

4.2.12. (*E*)-3-(Furan-2-yl)-1-(pyridin-2-yl)allyl acetate (3l). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.62 (ddd, J=4.7, 1.5, 0.9 Hz, 1H), 7.70 (dt, J=7.7, 1.7 Hz, 1H), 7.38 (d, J=7.8 Hz, 1H), 7.33 (s, 1H), 7.22 (dd, J=7.5, 4.9 Hz, 1H), 6.57–6.28 (m, 5H), 2.17 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.2, 158.4, 151.9, 149.9, 142.6, 137.1, 124.8, 123.2, 121.8, 121.5, 111.6, 109.6, 77.2, 21.5; IR (thin film) 3020, 2920, 1738, 1643, 1100 cm^{-1}; HRMS (EI) calcd for $[C_{14}H_{13}NO_3]^+$: m/z 243.0895, found: 243.0894.

4.2.13. (4-(Prop-1-en-2-yl)cyclohex-1-enyl)(pyridin-2-yl)methyl acetate (3m). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.59 (ddd, J=4.9, 1.7, 0.9 Hz, 1H), 7.68 (dt, J=7.1, 1.8 Hz, 1H), 7.34 (d, J=7.9 Hz, 1H), 7.20 (dd, J=7.4, 4.9 Hz, 1H), 6.20 (d, J=3.9 Hz, 1H), 5.85 (dd, J=10.1, 8.9 Hz, 1H), 4.68 (s, 1H), 4.67 (s, 1H), 2.16 (s, 3H), 2.09–2.08 (m, 5H), 2.04 (s, 3H), 2.00–1.69 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.3, 170.2, 158.5, 149.8, 149.8, 149.5, 149.4, 136.8, 135.2, 135.1, 126.9, 126.3, 122.8, 122.8, 121.4, 121.2, 108.9, 108.9, 79.9, 40.9, 40.9, 30.8, 30.7, 27.5, 25.3, 25.2, 21.4, 21.4, 20.9; IR (thin film) 2924, 2853, 1741, 1586, 1370, 1232 cm^{-1}; HRMS (EI) calcd for $[C_{17}H_{21}NO_2]^+$: m/z 271.1572, found: 271.1569.

4.2.14. (*E*)-2-Methyl-1-(3-methylpyridin-2-yl)-3-phenylallyl acetate (3n). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.51 (d, J=3.9 Hz, 1H), 8.47 (dd, J=7.8, 0.9 Hz, 1H), 7.34–7.21 (m, 5H), 7.16–7.12 (m, 1H), 6.54 (s, 1H), 6.48 (s, 1H), 2.45 (s, 3H), 2.20 (s, 3H), 1.89 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.7, 147.1, 138.8, 137.2, 134.5, 131.8, 129.3, 129.2, 129.1, 128.3, 127.0, 123.0, 78.0, 21.4.

18.8, 15.0; IR (thin film) 3050, 2930, 1734, 1233, 1016, 791 cm^{-1}; HRMS (EI) calcd for $[C_{18}H_{19}NO_2]^+$: *m/z* 281.1416, found: 281.1420.

4.2.15. (*E*)-2-Methyl-1-(5-methylpyridin-2-yl)-3-phenylallyl acetate (3o). ^1H NMR (300 MHz, $CDCl_3$) δ 8.44 (s, 1H), 7.50 (dd, *J*=8.1, 1.7 Hz, 1H), 7.34–7.27 (m, 5H), 7.24–7.18 (m, 1H), 6.69 (s, 1H), 6.35 (s, 1H), 2.33 (s, 3H), 2.20 (s, 3H), 1.83 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.8, 155.4, 150.0, 137.4, 137.3, 135.4, 132.5, 129.3, 128.8, 128.3, 127.0, 121.1, 81.2, 21.5, 77.7, 18.4, 14.7; IR (thin film) 2919, 2851, 1738, 1367, 1228, 1023 cm^{-1}; HRMS (EI) calcd for $[C_{18}H_{19}NO_2]^+$: *m/z* 281.1416, found: 281.1413.

4.3. General procedure for iodocyclization

To a stirred solution of allylic acetate **3** (0.5 mmol) in CH_3CN (3 mL) was added iodine (2 equiv) at rt. The reaction mixture was stirred at rt for 3 h. After the disappearance of the starting material was checked by TLC, triethylamine (2 equiv) was added at rt. After being stirred at rt for another 3 h, the reaction mixture was concentrated in vacuo. The resulting residue was diluted with ethyl acetate and washed with $NaHSO_3$ and $NaHCO_3$, successively. The water layer was extracted with ethyl acetate one more time. The organic layer was dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography (hexanes/ethyl acetate/dichloromethane=10:1:2) to give indolizine **4**.

4.3.1. 3-Phenylindolizin-1-yl acetate (4a). ^1H NMR (300 MHz, $CDCl_3$) δ 8.16 (d, *J*=7.3 Hz, 1H), 7.55 (d, *J*=7.0 Hz, 2H), 7.46 (t, *J*=7.4 Hz, 2H), 7.28–7.02 (m, 2H), 6.82 (s, 1H), 6.64 (t, *J*=6.4 Hz, 1H), 6.43 (t, *J*=7.4 Hz, 1H), 2.37 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.6, 132.1, 129.2, 129.1, 128.4, 127.5, 123.3, 122.3, 121.9, 116.7, 116.5, 111.1, 106.8, 21.2; IR (thin film) 3683, 1764, 1514, 1211, 736 cm^{-1}; HRMS (EI) calcd for $[C_{16}H_{13}NO_2]^+$: *m/z* 251.0946, found: 251.0945.

4.3.2. 3-Methylindolizin-1-yl acetate (4b). ^1H NMR (300 MHz, $CDCl_3$) δ 7.55 (d, *J*=7.1 Hz, 1H), 7.22 (d, *J*=7.8 Hz, 1H), 6.57 (t, *J*=6.4 Hz, 1H), 6.51 (s, 1H), 6.46 (t, *J*=6.9 Hz, 1H), 2.42 (s, 3H), 2.33 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.9, 125.9, 121.6, 121.2, 116.8, 116.1, 115.0, 110.4, 105.9, 21.1, 11.7; IR (thin film) 2910, 1748, 1556, 1350, 1214 cm^{-1}; HRMS (EI) calcd for $[C_{11}H_{11}NO_2]^+$: *m/z* 189.0790, found: 189.0787.

4.3.3. 2,3-Dimethylindolizin-1-yl acetate (4c). ^1H NMR (300 MHz, $CDCl_3$) δ 7.52 (d, *J*=7.1 Hz, 1H), 7.12 (d, *J*=9.0 Hz, 1H), 6.54 (t, *J*=7.1 Hz, 1H), 6.42 (t, *J*=7.1 Hz, 1H), 2.35 (s, 3H), 2.34 (s, 3H), 2.11 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.3, 125.1, 121.3, 121.0, 115.2, 116.1, 115.0, 114.6, 113.9, 109.8, 20.8, 9.5, 8.6; IR (thin film) 2909, 1761, 1454, 1368, 1211 cm^{-1}; HRMS (EI) calcd for $[C_{12}H_{13}NO_2]^+$: *m/z* 203.0946, found: 203.0943.

4.3.4. 3-Propylindolizin-1-yl acetate (4e). ^1H NMR (300 MHz, $CDCl_3$) δ 7.58 (d, *J*=7.1 Hz, 1H), 7.20 (d, *J*=9.0 Hz, 1H), 6.54 (t, *J*=6.4 Hz, 1H), 6.53 (s, 1H), 6.42 (t, *J*=7.0 Hz, 1H), 2.72 (t, *J*=7.5 Hz, 2H), 2.31 (s, 3H), 1.79–1.71 (m, 2H), 1.02 (t, *J*=7.7 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.9, 126.1, 121.7, 121.5, 121.2, 116.3, 115.1, 110.3, 104.8, 28.2, 21.1, 20.7, 14.3; IR (thin film) 2961, 1748, 1413, 1214, 1080 cm^{-1}; HRMS (EI) calcd for $[C_{13}H_{15}NO_2]^+$: *m/z* 217.1103, found: 217.1105.

4.3.5. 1,2,3,4-Tetrahydropyrido[1,2-*a*]indol-10-yl acetate (4f). ^1H NMR (300 MHz, $CDCl_3$) δ 7.49 (d, *J*=7.1 Hz, 1H), 7.13 (d, *J*=9.1 Hz, 1H), 6.54 (dt, *J*=6.4, 0.9 Hz, 1H), 6.39 (dt, *J*=7.0, 1.3 Hz, 1H), 2.69 (t, *J*=6.1 Hz, 2H), 2.59 (t, *J*=6.1 Hz, 2H), 2.34 (s, 3H), 1.97–1.92 (m, 2H), 1.91–1.79 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.1, 123.7, 121.4, 120.7, 117.4, 116.3, 115.3, 115.2, 109.5, 23.3, 22.9, 21.3, 21.2, 20.8; IR (thin film) 2930, 2848, 1762, 1367, 1210 cm^{-1}; HRMS (EI) calcd for $[C_{14}H_{15}NO_2]^+$: *m/z* 229.1103, found: 229.1100.

4.3.6. 3-Ethyl-2-methylindolizin-1-yl acetate (4g). ^1H NMR (300 MHz, $CDCl_3$) δ 7.62 (d, *J*=7.1 Hz, 1H), 7.11 (d, *J*=9.0 Hz, 1H), 6.53 (t, *J*=6.5 Hz, 1H), 6.41 (dt, *J*=7.1, 1.1 Hz, 1H), 2.88–2.80 (m, 2H), 2.35 (s, 3H), 2.11 (s, 3H), 1.18 (t, *J*=7.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.2, 121.3, 121.0, 120.5, 115.4, 114.9, 113.2, 109.7, 20.8, 17.4, 12.4, 8.4; IR (thin film) 2920, 1768, 1368, 1210, 1146 cm^{-1}; HRMS (EI) calcd for $[C_{13}H_{15}NO_2]^+$: *m/z* 217.1103, found: 217.1107.

4.3.7. 2-Methyl-3-phenylindolizin-1-yl acetate (4h). ^1H NMR (300 MHz, $CDCl_3$) δ 7.96 (d, *J*=7.1 Hz, 1H), 7.54–7.40 (m, 4H), 7.39–7.36 (m, 1H), 7.20 (d, *J*=8.4 Hz, 1H), 6.63 (t, *J*=6.8 Hz, 1H), 6.34 (t, *J*=6.5 Hz, 1H), 2.42 (s, 3H), 2.20 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.0, 131.3, 130.2, 129.2, 127.8, 126.2, 122.5, 121.8, 120.1, 116.9, 115.5, 115.3, 110.2, 20.9, 9.2; IR (thin film) 3058, 2950, 1769, 1349, 1205, 1150 cm^{-1}; HRMS (EI) calcd for $[C_{17}H_{15}NO_2]^+$: *m/z* 265.1103, found: 265.1104.

4.3.8. 3-Benzyl-2-phenylindolizin-1-yl acetate (4i). ^1H NMR (300 MHz, $CDCl_3$) δ 7.43 (d, *J*=7.1 Hz, 2H), 7.38 (d, *J*=4.1 Hz, 2H), 7.32–7.09 (m, 6H), 7.06 (d, *J*=7.4 Hz, 2H), 6.64 (t, *J*=6.5 Hz, 1H), 6.37 (t, *J*=6.8 Hz, 1H), 4.30 (s, 2H), 2.27 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.4, 161.0, 138.1, 133.2, 129.8, 129.1, 128.8, 128.0, 127.2, 126.8, 122.8, 122.1, 121.6, 116.7, 116.2, 116.1, 110.8, 30.6, 20.9; IR (thin film) 3123, 2926, 1740, 1266, 1097 cm^{-1}; HRMS (EI) calcd for $[C_{23}H_{19}NO_2]^+$: *m/z* 341.1416, found: 341.1418.

4.3.9. 3-(2-Methoxyphenyl)indolizin-1-yl acetate (4j). ^1H NMR (300 MHz, $CDCl_3$) δ 7.53 (d, *J*=7.2 Hz, 1H), 7.42–7.29 (m, 2H), 7.27 (t, *J*=9.0 Hz, 1H), 7.00 (q, *J*=8.0 Hz, 2H), 6.81 (s, 1H), 6.63 (dt, *J*=6.5, 0.6 Hz, 1H), 6.39 (dt, *J*=7.4, 2.9 Hz, 1H), 3.78 (s, 3H), 2.34 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.6, 157.5, 132.4, 129.7, 127.1, 123.8, 122.9, 121.1, 120.8, 119.1, 116.4, 116.0, 111.3, 110.1, 107.4; IR (thin film) 3100, 2915, 1762, 1475, 1244 cm^{-1}; HRMS (EI) calcd for $[C_{17}H_{15}NO_3]^+$: *m/z* 281.1052, found: 281.1050.

4.3.10. 3-(2-Nitrophenyl)indolizin-1-yl acetate (4k). ^1H NMR (300 MHz, $CDCl_3$) δ 8.09 (dd, *J*=8.1, 1.2 Hz, 1H), 7.69 (dt, *J*=7.8, 0.6 Hz, 1H), 7.63–7.53 (m, 2H), 7.46 (d,

J=7.2 Hz, 1H), 7.34 (d, J=9.1 Hz, 1H), 6.86 (s, 1H), 6.71 (dt, J=7.8, 2.2 Hz, 1H), 6.46 (dt, J=6.8, 1.1 Hz, 1H), 2.36 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.3, 149.1, 133.8, 133.3, 129.2, 127.5, 126.3, 125.1, 123.9, 121.8, 117.5, 116.6, 116.2, 111.7, 107.9, 21.2; IR (thin film) 3116, 2930, 1743, 1635, 1547, 1117 cm^{-1}; HRMS (EI) calcd for $[C_{16}H_{12}N_2O_4]^+$: m/z 296.0797, found: 296.0795.

4.3.11. 3-(Furan-2-yl)indolizin-1-yl acetate (4l). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.39 (d, J=7.2 Hz, 1H), 7.49 (t, J=0.9 Hz, 1H), 7.29 (d, J=9.0 Hz, 1H), 7.00 (s, 1H), 6.69 (dd, J=9.0, 6.5 Hz, 1H), 6.67–6.49 (m, 3H), 2.36 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.4, 147.3, 141.3, 127.5, 123.6, 117.1, 116.3, 113.4, 111.8, 111.6, 106.1, 105.7, 105.6, 21.1; IR (thin film) 3005, 2950, 1748, 1385, 1213 cm^{-1}; HRMS (EI) calcd for $[C_{14}H_{11}NO_3]^+$: m/z 241.0739, found: 241.0736.

4.3.12. (*S*)-3-(Prop-1-en-2-yl)-1,2,3,4-tetrahydropyrido[1,2-*a*]indol-10-yl acetate (4m). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.51 (d, J=7.1 Hz, 1H), 7.15 (d, J=9.1 Hz, 1H), 6.56 (t, J=6.5 Hz, 1H), 6.41 (dt, J=7.1, 1.1 Hz, 1H), 4.84 (s, 2H), 2.85 (d, J=10.3 Hz, 1H), 2.75–2.57 (m, 3H), 2.35 (s, 3H), 2.01 (d, J=11.0 Hz, 1H), 1.84 (s, 3H), 1.79–1.70 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.0, 149.3, 123.6, 121.8, 120.7, 117.1, 115.9, 115.4, 115.3, 109.9, 109.6, 42.1, 28.5, 26.8, 21.3, 21.0, 20.8; IR (thin film) 2918, 2846, 1768, 1368, 1210 cm^{-1}; HRMS (EI) calcd for $[C_{17}H_{19}NO_2]^+$: m/z 269.1416, found: 269.1418; $[\alpha]_D^{28}$ −44.97 (c 0.12, $CHCl_3$).

4.3.13. 2,8-Dimethyl-3-phenylindolizin-1-yl acetate (4n). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.78 (d, J=6.9, 1H), 7.51–7.44 (m, 4H), 7.39–7.33 (m, 1H), 6.28 (dt, J=6.6, 0.9 Hz, 1H), 6.23 (t, J=6.9 Hz, 1H), 2.43 (s, 3H), 2.37 (s, 3H), 2.09 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.8, 131.4, 130.3, 129.1, 127.7, 127.1, 126.6, 122.4, 120.2, 120.0, 117.1, 115.3, 110.0, 20.9, 18.3, 8.9; IR (thin film) 2921, 2850, 1758, 1518, 1374, 1208 cm^{-1}; HRMS (EI) calcd for $[C_{18}H_{17}NO_2]^+$: m/z 279.1259, found: 279.1262.

4.3.14. 2,6-Dimethyl-3-phenylindolizin-1-yl acetate (4o). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.71 (s, 1H), 7.51–7.43 (m, 4H), 7.38–7.34 (m, 1H), 7.07 (d, J=9.0 Hz, 1H), 6.47 (d, J=9.0 Hz, 1H), 2.38 (s, 3H), 2.11 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.1, 131.5, 130.2, 129.1, 127.6, 126.1, 121.5, 120.2, 119.6, 119.4, 119.1, 115.0, 114.6, 20.9, 18.7, 9.1; IR (thin film) 3015, 2950, 1755, 1522, 1436, 1393 cm^{-1}; HRMS (EI) calcd for $[C_{18}H_{17}NO_2]^+$: m/z 279.1259, found: 279.1260.

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Supplementary data

^{1}H and ^{13}C NMR spectra for compounds **3** and **4** are included as supplementary material. Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2007.10.037.

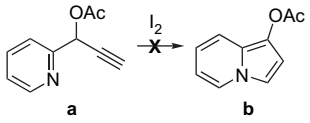
References and notes

1. For general reviews, see: (a) Shipman, M. *Sci. Synth.* **2001**, *10*, 745; (b) Michael, J. P. *Nat. Prod. Rep.* **2000**, *17*, 579; (c) Grundon, M. F. *Nat. Prod. Rep.* **1989**, *6*, 523; (d) Flitsch, W. *Comprehensive Heterocyclic Chemistry*; Katritzky, A. R., Rees, C. W., Eds.; Pergamon: Oxford, 1984; Vol. 4, p 443; (e) Uchida, T.; Matsumoto, K. *Synthesis* **1976**, *4*, 209.
2. (a) Gundersen, L.-L.; Charnock, C.; Negussie, A. H.; Rise, F.; Teklu, S. *Eur. J. Pharm. Sci.* **2007**, *30*, 26; (b) Hynd, G.; Ray, N. C.; Finch, H.; Montana, J. G.; Cramp, M. C.; Harrison, T. K.; Arienzo, R.; Blaney, P.; Griffon, Y.; Middlemiss, D. WO 2007031747 A1, 2007; (c) Millet, R.; Domarkas, J.; Rigo, B.; Goossens, L.; Goossens, J.-F.; Houssin, R.; Henichart, J.-P. *Bioorg. Med. Chem.* **2002**, *10*, 2905; (d) Sonnet, P.; Dallemagne, P.; Guillon, J.; Enguehard, C.; Stiebing, S.; Tanguy, J.; Bureau, R.; Rault, S.; Auvray, P.; Moslemi, S.; Sourdaine, P.; Seralini, G.-E. *Bioorg. Med. Chem.* **2000**, *8*, 945; (e) Hagishita, S.; Yamada, M.; Shirahase, K.; Okada, T.; Murakami, Y.; Ito, Y.; Matsuura, T.; Wada, M.; Kato, T.; Ueno, M.; Chikazawa, Y.; Yamada, K.; Ono, T.; Teshirogi, I.; Ohtani, M. *J. Med. Chem.* **1996**, *39*, 3636; (f) Gubin, J.; de Vogelaer, H.; Inion, H.; Houben, C.; Lucchetti, J.; Mahaux, J.; Rosseels, G.; Peiren, M.; Clinet, M.; Polster, P.; Chatelain, P. *J. Med. Chem.* **1993**, *36*, 1425; (g) Jaffrezou, J. P.; Levade, T.; Thurneyssen, O.; Chiron, M.; Bordier, C.; Attal, M.; Chatelain, P.; Laurent, G. *Cancer Res.* **1992**, *52*, 1352; (h) Cingolani, G. M.; Claudi, F.; Massi, M.; Venturi, F. *Eur. J. Med. Chem.* **1990**, *25*, 709.
3. (a) Surpateanu, G. G.; Becuwe, M.; Lungu, N. C.; Dron, P. I.; Fourmentin, S.; Landy, D.; Surpateanu, G. *J. Photochem. Photobiol., A* **2007**, *185*, 312; (b) Delattre, F.; Woisel, P.; Surpateanu, G.; Cazier, F.; Blach, P. *Tetrahedron* **2005**, *61*, 3939; (c) Retaru, A. V.; Druta, L. D.; Deser, T.; Mueller, T. J. *Helv. Chim. Acta* **2005**, *88*, 1798; (d) Sonnenschein, H.; Henrich, G.; Resch-Genger, V.; Schulz, B. *Dyes Pigments* **2000**, *46*, 23; (e) Saeva, F. D.; Luss, H. R. *J. Org. Chem.* **1988**, *53*, 1804.
4. For recent examples, see: (a) Schwier, T.; Sromek, A. W.; Yap, D. M. L.; Chernyak, D.; Gevorgyan, V. *J. Am. Chem. Soc.* **2007**, *129*, 9868; (b) Seregin, I. V.; Schammel, A. W.; Gevorgyan, V. *Org. Lett.* **2007**, *9*, 3433; (c) Chuprakov, S.; Hwang, F. W.; Gevorgyan, V. *Angew. Chem., Int. Ed.* **2007**, *46*, 4757; (d) El Kaim, L.; Gizolme, M.; Grimaud, L. *Synlett* **2007**, 227; (e) Smith, C. R.; Bunnelle, E. M.; Rhodes, A. J.; Sarpong, R. *Org. Lett.* **2007**, *9*, 1169; (f) Liu, Y.; Hu, H.-Y.; Liu, Q.-J.; Hu, H.-W.; Xu, J.-H. *Tetrahedron* **2007**, *63*, 2024; (g) Marchalín, S.; Žúžiová, J.; Kadlečíková, K.; Šafář, P.; Baran, P.; Dalla, V.; Daïch, A. *Tetrahedron Lett.* **2007**, *48*, 697; (h) Seregin, I. V.; Gevorgyan, V. *J. Am. Chem. Soc.* **2006**, *128*, 12050; (i) Kaloko, J., Jr.; Hayford, A. *Org. Lett.* **2005**, *7*, 4305; (j) Kel'in, A. V.; Sromek, A. W.; Gevorgyan, V. *J. Am. Chem. Soc.* **2001**, *123*, 2074; (k) Padwa, A.; Austin, D. J.; Precedo, L.; Zhi, L. *J. Org. Chem.* **1993**, *58*, 1144.
5. (a) Kim, I.; Choi, J.; Won, H. K.; Lee, G. H. *Tetrahedron Lett.* **2007**, *48*, 6863; (b) Kim, I.; Lee, G. H.; No, Z. S. *Bull. Korean Chem. Soc.* **2007**, *28*, 685.
6. For recent reviews on iodocyclizations, see: (a) Togo, H.; Iida, S. *Synlett* **2006**, 2159; (b) Martins da Silva, F.; Jones, J., Jr.; de Mattos, M. C. S. *Curr. Org. Synth.* **2005**, *2*, 393.

7. For selected examples on 5-endo-trig iodocyclizations, see: (a) Amjad, M.; Knight, D. W. *Tetrahedron Lett.* **2006**, *47*, 2825; (b) Donohue, T. J.; Sintim, H. O.; Hollinshead, J. *J. Org. Chem.* **2005**, *70*, 7297; (c) Knight, D. W.; Shaw, D. E.; Staples, E. R. *Eur. J. Org. Chem.* **2004**, 1973; (d) Knight, D. W.; Staples, E. R. *Tetrahedron Lett.* **2002**, *43*, 6771; (e) Bedford, S. B.; Bell, K. E.; Bennett, F.; Hayes, C. J.; Knight, D. W.; Shaw, D. E. *J. Chem. Soc., Perkin Trans 1* **1999**, 2143; (f) Barks, J. M.; Knight, D. W.; Seaman, C. J.; Weingarten, G. G. *Tetrahedron Lett.* **1994**, *35*, 7259; (g) Kang, S. H.; Lee, S. B. *Tetrahedron Lett.* **1993**, *34*, 7579; (h) Kang, S. H.; Lee, S. B. *Tetrahedron Lett.* **1993**, *34*, 1955.

8. The relative stereochemistry of these diastereomers was not determined.

9. Similarly, exposure of propargylic acetate **a** to iodine failed to deliver the indolizine **b**, only yielding a complex mixture. Unpublished results.



a **b**

10. A pyridine group was first used as an internal nucleophilic partner in iodocyclizations by us. See Ref. 5a.