Novel synthetic routes to nitrogen-bridged tricyclic derivatives of pyrrolo[2,1,5-*cd*]indolizine and pyrrolo[2,1,5-*de*]quinolizine derived from 2-acyl-*N*-(acylmethyl)pyridinium halides

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Novel synthetic routes to nitrogen-bridged derivatives of pyrrolo[2,1,5-*cd*]indolizine and pyrrolo[2,1,5-*de*]-quinolizine were developed starting from 2-acyl-*N*-(acylmethyl)pyridinium halides. Thus, 2-benzoyl-*N*-phenacylpyridinium bromide (**1**) afforded 3,4-diphenylpyrrolo[2,1,5-*cd*]indolizines (**4**) *via* 1,3-dipolar cycloaddition, to yield 3,5-dibenzoylindolizines (**3**), followed by intramolecular McMurry coupling. Similarly, 2-(1,3-dioxolan-2-yl)-*N*-phenacylpyridinium bromide (**5**) gave 3-phenylpyrrolo[2,1,5-*cd*]indolizine (**7**) together with the unexpected product 3-phenyl-4-hydroxypyrrolo[2,1,5-*cd*]indolizines (**8**). However, 2-acetyl-*N*-phenacylpyridinium bromide (**13**) or 2-benzoyl-*N*-acetonylpyridinium bromide (**16**) underwent a tandem reaction of aldol condensation and 1,3-dipolar cycloaddition to form 3-phenyl-5*H*-pyrrolo[2,1,5-*de*]quinolizin-5-ones (**15**) or 5-phenyl-3*H*-pyrrolo-[2,1,5-*de*]quinolizin-3-ones (**17**) in a single step. These novel procedures are general and can be carried out under convenient conditions.

Introduction

Pyrrolo[2,1,5-*cd*]indolizine and pyrrolo[2,1,5-*de*]quinolizine are members of the cyclazine family (Chart 1). They have received

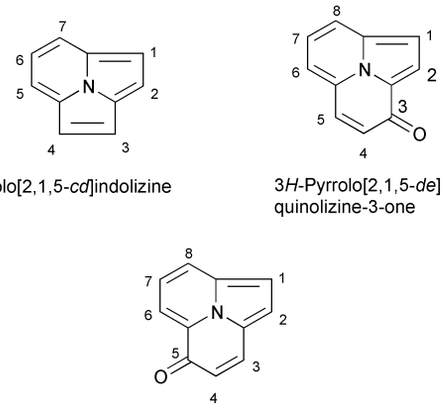

Chart 1

considerable attention in the field of synthetic organic chemistry because of their special structural properties,[1,2] increasing biological interest[1,3] and their partially saturated frameworks that are found in natural products.[4]

Among the methods for the preparation of pyrrolo[2,1,5-*cd*]indolizine derivatives,[5] [8+2]-cycloaddition of indolizines with electron-deficient acetylenes was mainly employed in the past decade.[6] Since most electron-deficient acetylenes are not commercially available and a 3-cyano- or 3-unsubstituted indolizine without electron-withdrawing substituents on C1 and C2 is required for this reaction mechanism, such methods very often suffer from the problems of inaccessible precursors and of limitations on the range of substituents possible on C1–C4 of the pyrrolo[2,1,5-*cd*]indolizine. Unfortunately, these drawbacks also arose in the very few published procedures for the preparation of pyrrolo[2,1,5-*de*]quinolizine derivatives.[7]

As part of our research project, a series of nitrogen-bridged bicyclic and tricyclic heterocyclic compounds have been designed and synthesized recently.[8] In continuation of our efforts, we describe herein an efficient and practical synthetic sequence for pyrrolo[2,1,5-*cd*]indolizines and an unexpected tandem reaction for the preparation of pyrrolo[2,1,5-*de*]quinolizinones derived from 2-acyl-*N*-(acylmethyl)pyridinium halides. These methods overcome some of the limitations of the published procedures and afford a broad range of functionalized derivatives.

Results and discussion

Intramolecular reductive coupling of dicarbonyls induced by McMurry reaction has been widely used in the synthesis of heterocyclic compounds.[9] In view of the fact that 3,5-diacylindolizines can be obtained readily by oxidant-promoted 1,3-dipolar cycloadditions of 2-acyl-*N*-(acylmethyl)pyridinium halides (precursors to the corresponding ylides) to electron-deficient alkenes,[8] McMurry coupling makes possible an efficient route to prepare pyrrolo[2,1,5-*cd*]indolizines by intramolecular reductive coupling of 3,5-diacylindolizines. Our strategy is shown in Scheme 1.

McMurry coupling of 3,5-dibenzoylindolizines

As aryl carbonyls usually give better coupling results in the McMurry reaction, 3,5-dibenzoylindolizines (**3**) were initially chosen for test studies. Following the known procedure,[8d] a mixture of 2-benzoyl-*N*-phenacylpyridinium bromide (**1**), acrylonitrile (**2a**), CrO_3 and Et_3N in DMF was warmed to 90 °C for 4 h. After normal work-up, 3,5-dibenzoylindolizine-1-carbonitrile (**3a**) was obtained as yellow crystals in 72% yield. Using

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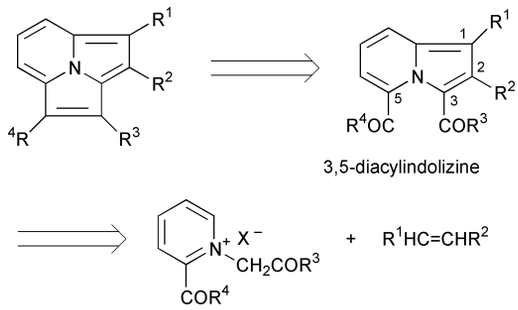
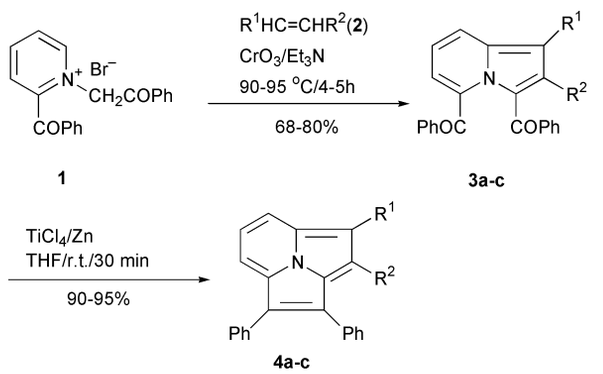


Scheme 1

2b and **2c** as dipolarophiles, the corresponding compounds **3b** and **3c** were obtained in 80 and 68% respectively.

As expected, when compounds **3a**–**c** were treated with low-valent titanium (produced from the $TiCl_4$–Zn system) at room temperature for 30 min, the desired 3,4-diphenylpyrrolo[2,1,5-*cd*]indolizines **4a**–**c** were obtained as yellow crystals in excellent yields (90–95%, Scheme 2).



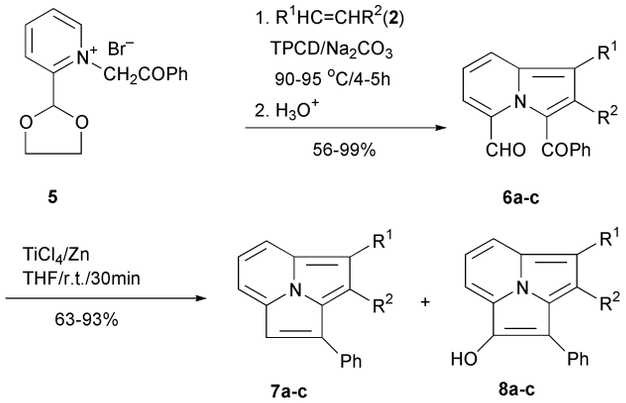
2,3, 4	R^1	R^2	Yield (%)	
			3	**4**
a	CN	H	72	95
b	CO_2Me	H	80	90
c	CO_2Et	CO_2Et	68	90

Scheme 2

McMurry coupling of 3-benzoylindolizine-5-carbaldehydes

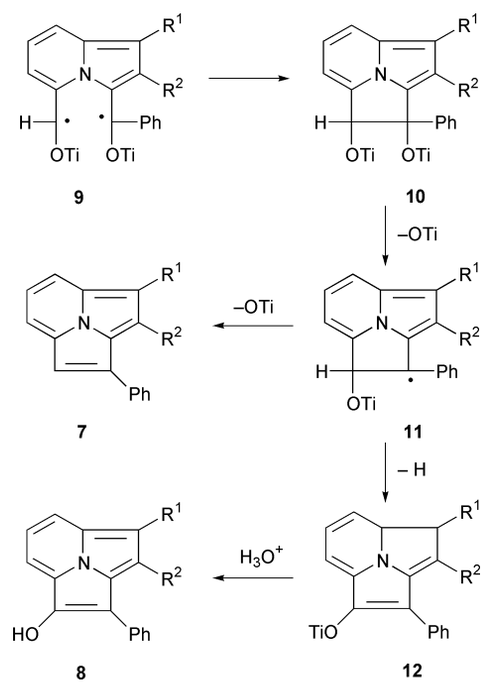
Our next attempt was to test the McMurry reaction of 3-benzoylindolizine-5-carbaldehydes **6a**–**c**, which were obtained from 2-(1,3-dioxolan-2-yl)-*N*-phenacylpyridinium bromide (**5**) by the published procedure.[10] When **6a** was treated with low-valent titanium, two products were separated. The less polar product was identical with an authentic sample of 3-phenylpyrrolo[2,1,5-*cd*]indolizine-1-carbonitrile (**7a**, 30%).[8f] In contrast, the more polar one was assigned as an "unexpected" product of the McMurry reaction, 3-phenyl-4-hydroxypyrrolo[2,1,5-*cd*]indolizine-1-carbonitrile (**8a**, 29%), from its IR, ^{1}H NMR and MS spectra. A change in the reaction conditions altered the ratio of **7a** to **8a**, but did not cause any increase in the total yield. For example, in the presence of two equivalents of pyridine, **7a** and **8a** were obtained in 39 and 16% yields respectively. However, when the reaction was carried out in boiling THF, 17% of **7a** and 35% of **8a** were obtained. Under similar conditions, **6b** and **6c** yielded the pairs **7b**–**8b** and **7c**–**8c** (Scheme 3).

To our knowledge, this is the first example of a diacyl compound that affords a phenol product in the McMurry reaction. This might result from the aromatic stability of pyrrolo[2,1,5-*cd*]indolizine. As shown in Scheme 4, two electrons are transferred initially from titanium to the carbonyls of compound **6** generating a diradical **9**. Intramolecular coupling of **9** yields **10**, which is followed by loss of TiO to give the intermediate **11**. Another TiO is then lost to afford the usual product **7**. However, if a proton is lost from **11**, a stable titanium phenoxide **12** is formed, which is subsequently converted into the unexpected product **8**.



2,6,7,8	R^1	R^2	Yield (%)	
			7	**8**
a	CN	H	30	29
b	CO_2Me	H	38	41
c	CO_2Et	CO_2Et	20	55

Scheme 3

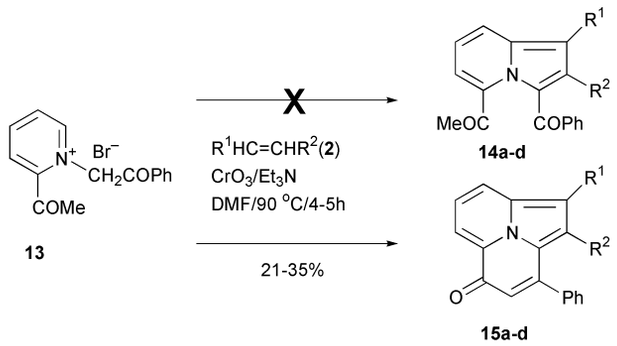


Scheme 4

Tandem reaction for the formation of pyrrolo[2,1,5-*de*]quinolizinones

Given the successful application of the McMurry reaction in the above two protocols, the coupling of 3-benzoyl-5-acetylindolizine (**14**) was investigated as an extended example. To our surprise, yellow crystals were obtained when 2-acetyl-*N*-phenacylpyridinium bromide (**13**) was treated with acrylonitrile (**2a**) under the conditions reported for the preparation of **3a**. Its IR and ^{1}H NMR do not show any features of the acetyl group and its MS and the results of elemental analyses are fully consistent with the formulation 1-cyano-3-phenyl-5*H*-pyrrolo-[2,1,5-*de*]quinolizin-5-one (**15a**, 30%)—the product of loss of H_2O from 3-benzoyl-5-acetylindolizine-1-carbonitrile (**14a**). This result indicated that the nitrogen-bridged tricyclic structure of pyrrolo[2,1,5-*de*]quinolizine could be constructed by a tandem reaction from **13** in a single step. Thus, the correspond-

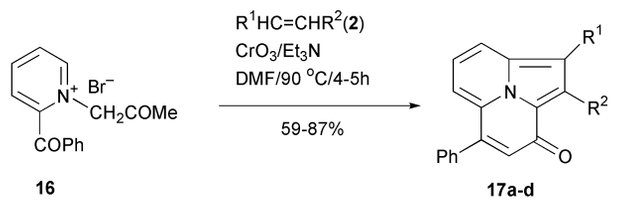
ing compounds **15b–d** were also prepared successfully in 21–35% by using **2b**, **2d** and **2e** as dipolarophiles (Scheme 5).



2,	14,15	R^1	R^2	Yield of **15** (%)
a	**a**	CN	H	30
b	**b**	CO_2Me	H	35
d	**c**	CO_2Me	CO_2Me	28
e	**d**	COPh	H	21

Scheme 5

Similarly, 2-benzoyl-*N*-acetonylpyridinium bromide (**16**) afforded 5-phenyl-3*H*-pyrrolo[2,1,5-*de*]quinolizin-3-ones **17a–d** in 59–87% yields respectively (Scheme 6). However, the fact that



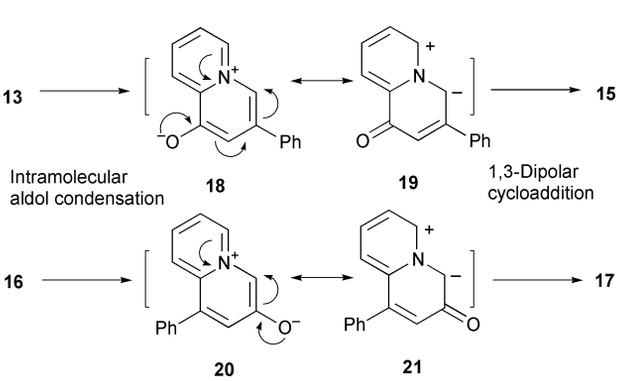
2,17	R^1	R^2	Yield of **17** (%)
a, a	CN	H	72
b, b	CO_2Me	H	80
d, c	CO_2Me	CO_2Me	87
e, d	COPh	H	59

Scheme 6

the yields of **17a–d** are more than twice those of their counterparts, **15a–d**, caught our interest because this meant that the tandem reaction route could not be explained simply by a sequence of 1,3-dipolar cycloaddition, to yield the 3,5-diacylindolizine, followed by an aldol condensation.

Exploration of the mechanism of the tandem reaction

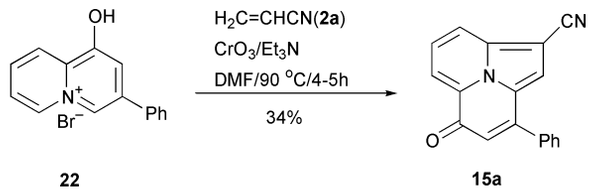
It is well known that salts **13** and **16** can provide betaines **18** and **20** by intramolecular aldol condensation under basic conditions.[11] As illustrated in Scheme 7, a contrary route *via* the sequence of aldol condensation to yield a betaine followed by 1,3-dipolar cycloaddition has been proposed. In the initial



Scheme 7

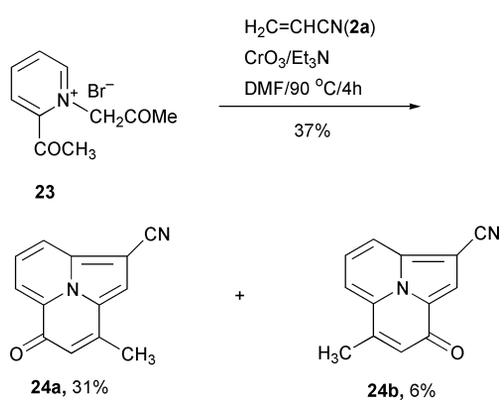
step, salts **13** or **16** yield betaines **18** or **20** by base-catalyzed intramolecular aldol condensation. They are then converted into **19** or **21** followed by 1,3-dipolar cycloaddition to an alkene to yield pyrrolo[2,1,5-*de*]quinolizinone **15** or **17**, promoted by the oxidant Cr_3O–Et_3N.

In order to confirm that the betaines are reasonable possible intermediates, 1-hydroxy-3-phenylquinolizinium bromide (**22**), obtained from salt **13**, in the presence of Et_3N, was allowed to undergo 1,3-dipolar cycloaddition to the dipolarophile **2a** in the presence of Cr_3O–Et_3N. As expected, **15a** was obtained in 34% yield (Scheme 8).



Scheme 8

Since the aldol condensation was hypothesized as the initial step, the reactivities of the methyl groups in salts **13** and **16** might be the yield-controlling factor. Unfortunately, the experiment with 2-acetyl-*N*-acetonylpyridinium bromide (**23**) produced the opposite conclusion. As shown in Scheme 9, the



Scheme 9

methyl group on the 2-acetyl group showed a much higher reactivity than that on the *N*-acetonyl group, yielding 3-methyl-5*H*-pyrrolo[2,1,5-*de*]quinolizin-5-one (**24a**) in 31% yield as the major product.

Thus, we believe that the difference in yield between **15** and **17** may depend upon the reactivities of the 1,3-dipoles **19** and **21**. As shown in Scheme 7, as the betaine **18** is converted into 1,3-dipole **19**, the negative charge not only passes through three carbons, but also is distributed partially on its α-phenyl group. In contrast, betaine **20** could be converted directly into 1,3-dipole **21**.

In summary, methods for the preparation of nitrogen-bridged tricyclic heterocyclic derivatives of pyrrolo[2,1,5-*cd*]-indolizine and pyrrolo[2,1,5-*de*]quinolizine were developed starting from 2-acyl-*N*-(acylmethyl)pyridinium halides. 2-Benzoyl-*N*-phenacylpyridinium bromide (**1**) yielded 3,4-diphenylpyrrolo[2,1,5-*cd*]indolizines (**4**) *via* the sequence of 1,3-dipolar cycloaddition to yield 3,5-dibenzoylindolizines (**3**) followed by McMurry coupling. Similarly, 2-(1,3-dioxolan-2-yl)-*N*-phenacylpyridinium bromide (**5**) gave the expected product 3-phenylpyrrolo[2,1,5-*cd*]indolizines (**7**) together with the unexpected product 3-phenyl-4-hydroxypyrrolo[2,1,5-*cd*]-indolizines (**8**). However, 2-acetyl-*N*-phenacylpyridinium bromide (**13**) and 2-benzoyl-*N*-acetonylpyridinium bromide (**16**) gave 3-phenyl-5*H*-pyrrolo[2,1,5-*de*]quinolizin-5-ones (**15**) and 5-phenyl-3*H*-pyrrolo[2,1,5-*de*]quinolizin-3-ones (**17**), respectively, by a tandem reaction in one single step. These

novel procedures are general and can be carried out under convenient conditions.

Experimental

All melting points were determined on a Yanaco melting point apparatus and are uncorrected. IR spectra were recorded on a Nicolet FT-IR 5DX spectrometer as KBr pellets. ^{1}H NMR spectra were recorded on a Bruker ACF-300 spectrometer in $CDCl_3$ with TMS as internal reference unless specified otherwise. The *J* values are given in Hz. MS spectra were obtained on a VG-ZAB-HS mass spectrometer operating at 70 eV. The elemental analyses were performed on a Perkin-Elmer 240C instrument. PE is petroleum ether (60–90 °C). 3-Benzoylindolizine-5-carbaldehydes (**5a**–**c**) were obtained by the known procedure.[10]

Preparation of 3,5-dibenzoylindolizines 3a–c

A mixture of 2-benzoylpyridine (183 mg, 10 mmol) and phenacyl bromide (199 mg, 10 mmol) was heated at 90 °C for 4–5 h without solvent. It was then cooled to room temperature and EtOAc (20 cm^3) was added. Crude 2-benzoyl-*N*-phenacylpyridinium bromide (**1**) was obtained as an off-white solid in 95% yield (mp 137–138 °C) by filtration, and was used for the next step without further purification or characterization.

CrO_3 (650 mg, 6.5 mmol), alkene **2** (1.3 g, 25 mmol) and salt **1** (1.9 g, 5 mmol) were added in sequence to a stirred solution of Et_3N (3.0 g, 30 mmol) in DMF (20 cm^3). After the resultant mixture had been stirred for 4–5 h at 90 °C, it was poured into a solution of 5% HCl in brine. The crude product was filtered and purified by chromatography (silica gel, acetone–PE) to give compound **3**.

3,5-Dibenzoylindolizine-1-carbonitrile (3a). Yellow needles, mp 234–235 °C (EtOAc–PE) (Found: C, 78.94; H, 3.95; N, 7.94. $C_{23}H_{14}N_2O_2$ requires: C, 78.84; H, 4.03; N, 7.99%); ν_{max}/cm^{-1} 2220, 1666, 1622; δ_H 8.02 (d, *J* 7.8, 2H), 7.94 (d, *J* 8.8, 1H), 7.84 (d, *J* 7.6, 2H), 7.64 (t, *J* 7.3, 1H), 7.58 (t, *J* 7.3, 1H), 7.53–7.50 (m, 3H), 7.48–7.44 (m, 3H), 7.16 (d, *J* 7.1, 1H); *m*/*z* 350 (M$^+$, 31%), 245 (100).

Methyl 3,5-dibenzoylindolizine-1-carboxylate (3b). Yellow needles, mp 198–200 °C (EtOAc–PE) (Found: C, 75.42; H, 4.56; N, 3.87. $C_{24}H_{17}NO_4$ requires: C, 75.18; H, 4.47; N, 3.65%); ν_{max}/cm^{-1} 1690, 1655, 1625; δ_H 8.57 (d, *J* 8.8, 1H), 8.02 (d, *J* 7.8, 2H), 7.85 (d, *J* 7.6, 2H), 7.71 (s, 1H), 7.62 (t, *J* 7.3, 1H), 7.56 (t, *J* 7.4, 1H), 7.51–7.48 (m, 2H), 7.47–7.41 (m, 3H), 7.13 (d, *J* 7.0, 1H), 3.91 (s, 3H); *m*/*z* 384 (M + 1, 11%), 279 (100).

Diethyl 3,5-dibenzoylindolizine-1,2-dicarboxylate (3c). Yellow needles, mp 149–150 °C (EtOAc–PE) (Found: C, 71.82; H, 4.91; N, 2.72. $C_{28}H_{23}NO_6$ requires: C, 71.63; H, 4.94; N, 2.98%); ν_{max}/cm^{-1} 1720, 1690, 1660, 1620; δ_H 8.58 (d, *J* 9.1, 1H), 7.93 (d, *J* 7.4, 2H), 7.78 (d, *J* 7.3, 2H), 7.61 (t, *J* 7.3, 1H), 7.54 (t, *J* 7.3, 1H), 7.49–7.46 (m, 2H), 7.42–7.37 (m, 3H), 7.13 (d, *J* 7.1, 1H), 4.36 (q, *J* 7.2, 2H), 3.64 (q, *J* 7.2, 2H), 1.35 (t, *J* 7.2, 3H), 1.02 (t, *J* 7.2, 3H); *m*/*z* 470 (M + 1, 11%), 364 (100).

McMurry coupling of 3,5-dibenzoylindolizines 3a–c

To a stirred suspension of zinc powder (2.6 g, 40 mmol) in dry THF was added $TiCl_4$ (2.2 cm^3, 20 mmol) under nitrogen and the mixture was refluxed for 2 h. After the mixture had been cooled to room temperature, a solution of indolizine (**3**, 5 mmol) in dry THF was added within 40 min. The resultant mixture was stirred for another 30 min (monitored by TLC) and then the THF was evaporated. The residue was treated with a 1% aqueous solution of HCl and was extracted with CH_2Cl_2. The combined organic layers were washed with brine and dried over $MgSO_4$. The solvent was removed to yield crude product, which was purified by chromatography (silica gel, EtOAc–PE) to give compound **4** as yellow crystals.

3,4-Diphenylpyrrolo[2,1,5-*cd*]indolizine-1-carbonitrile (4a). Yellow crystals, mp 196–197 °C (EtOAc–PE) (Found: C, 86.75; H, 4.51; N, 9.03. $C_{23}H_{14}N_2$ requires: C, 86.77; H, 4.43; N, 8.80%); ν_{max}/cm^{-1} 2200; δ_H 8.16 (d, *J* 7.8, 1H), 8.01 (d, *J* 7.6, 1H), 7.96 (s, 1H), 7.92 (t, *J* 7.7, 1H), 7.62 (d, *J* 7.3, 2H), 7.54 (d, *J* 7.3, 2H), 7.47–7.38 (m, 6H); *m*/*z* 319 (M + 1, 25%), 318 (M$^+$, 100).

Methyl 3,4-diphenylpyrrolo[2,1,5-*cd*]indolizine-1-carboxylate (4b). Yellow crystals, mp 146–147 °C (EtOAc–PE) (Found: C, 82.01; H, 4.84; N, 3.93. $C_{24}H_{17}NO_2$ requires: C, 82.03; H, 4.88; N, 3.99%); ν_{max}/cm^{-1} 1690; δ_H 8.40 (d, *J* 7.6, 1H), 8.20 (s, 1H), 7.94 (d, *J* 7.6, 1H), 7.88 (t, *J* 7.6, 1H), 7.67 (d, *J* 7.6, 2H), 7.55 (d, *J* 7.6, 2H), 7.34–7.45 (m, 6H), 4.03 (s, 3H); *m*/*z* 352 (M + 1, 26%), 351 (M$^+$, 100).

Diethyl 3,4-diphenylpyrrolo[2,1,5-*cd*]indolizine-1,2-dicarboxylate (4c). Yellow crystals, mp 213–214 °C (EtOAc–PE) (Found: C, 76.85; H, 5.35; N, 3.39. $C_{28}H_{23}NO_4$ requires: C, 76.87; H, 5.30; N, 3.20%); ν_{max}/cm^{-1} 1730, 1690; δ_H 8.46 (d, *J* 8.2, 1H), 8.03 (d, *J* 7.9, 1H), 7.94 (t, *J* 8.1, 1H), 7.52–7.47 (m, 4H), 7.42–7.33 (m, 6H), 4.48 (q, *J* 7.1, 2H), 4.28 (q, *J* 7.1, 2H), 1.47 (t, *J* 7.1, 3H), 1.13 (t, *J* 7.1, 3H); *m*/*z* 438 (M + 1, 16%), 437 (M$^+$, 50), 291 (100).

McMurry coupling of 3-benzoylindolizine-5-carbaldehydes 6a–c

By the same procedure as the preparation of compounds **4a**–**c**, the titanium-promoted coupling reaction of 3-benzoylindolizine-5-carbaldehydes **6a**–**c** yielded the corresponding 3-phenylpyrrolo[2,1,5-*cd*]indolizines **7a**–**c** and 3-phenyl-4-hydroxypyrrolo[2,1,5-*cd*]indolizines **8a**–**c**.

3-Phenylpyrrolo[2,1,5-*cd*]indolizine-1-carbonitrile (7a) and 3-phenyl-4-hydroxypyrrolo[2,1,5-*cd*]indolizine-1-carbonitrile (8a). Compound **7a** was obtained as yellow crystals, mp 118–120 °C (EtOAc–PE, lit.[8f] 118–120 °C) (Found: C, 84.77; H, 4.42; N, 11.35. $C_{17}H_{10}N_2$ requires: C, 84.28; H, 4.16; N, 11.56%); ν_{max}/cm^{-1} 2200; δ_H 8.14 (d, *J* 7.6, 1H), 8.10 (s, 1H), 8.00–7.98 (m, 3H), 7.91 (t, *J* 7.7, 1H), 7.66 (s, *J* 7.3, 1H), 7.55 (t, *J* 7.4, 2H), 7.45 (t, *J* 7.4, 1H); *m*/*z* 242 (M$^+$, 100%).

Compound **8a** was obtained as yellow crystals, mp 261–263 °C (EtOAc–PE) (Found: C, 79.35; H, 3.50; N, 10.65. $C_{17}H_{10}N_2O$ requires: C, 79.06; H, 3.90; N, 10.85%); ν_{max}/cm^{-1} 3400, 2200; δ_H 8.04–7.94 (m, 3H), 7.67–7.62 (m, 2H), 7.58–7.47 (m, 4H); *m*/*z* 258 (M$^+$, 100%).

Methyl 3-phenylpyrrolo[2,1,5-*cd*]indolizine-1-carboxylate (7b) and methyl 3-phenyl-4-hydroxypyrrolo[2,1,5-*cd*]indolizine-1-carboxylate (8b). Compound **7b** was obtained as yellow crystals, mp 109–110 °C (EtOAc–PE) (Found: C, 78.53; H, 4.77; N, 4.98. $C_{18}H_{13}NO_2$ requires: C, 78.53; H, 4.76; N, 5.09%); ν_{max}/cm^{-1} 1700; δ_H 8.30 (d, *J* 7.6, 1H), 8.25 (s, 1H), 7.97 (d, *J* 7.3, 2H), 7.83 (d, *J* 7.5, 1H), 7.79 (t, *J* 7.8, 1H), 7.50 (s, 1H), 7.46 (t, *J* 7.3, 2H), 7.35 (t, *J* 7.2, 1H), 3.96 (s, 3H); *m*/*z* 275 (M$^+$, 95%), 244 (100).

Compound **8b** was obtained as yellow crystals, mp 224–226 °C (EtOAc–PE) (Found: C, 74.38; H, 4.50; N, 4.91. $C_{18}H_{13}NO_3$ requires: C, 74.22; H, 4.50; N, 4.81%); ν_{max}/cm^{-1} 3250, 1650; δ_H (DMSO) 11.17 (s, 1H), 8.33 (d, *J* 8.2, 1H), 8.29–8.23 (m, 4H), 7.90 (t, *J* 7.9, 1H), 7.54 (t, *J* 7.4, 2H), 7.36 (t, *J* 7.2, 1H), 3.92 (s, 3H); *m*/*z* 291 (M$^+$, 100%).

Diethyl 3-phenylpyrrolo[2,1,5-*cd*]indolizine-1,2-dicarboxylate (7c) and diethyl 3-phenyl-4-hydroxypyrrolo[2,1,5-*cd*]indolizine-1,2-dicarboxylate (8c). Compound **7c** was obtained as yellow crystals, mp 82–84 °C (EtOAc–PE) (Found: C, 73.30; H, 5.39;

N, 3.84. $C_{22}H_{19}NO_4$ requires: C, 73.11; H, 5.30; N, 3.88%); ν_{max}/cm^{-1} 1720, 1685; δ_H 8.44 (d, *J* 7.6, 1H), 8.00–7.91 (m, 2H), 7.83 (d, *J* 7.3, 2H), 7.53–7.40 (m, 4H), 4.54–4.44 (m, 4H), 1.50 (t, *J* 7.1, 3H), 1.32 (t, *J* 7.1, 3H); *m*/*z* 361 (M^+, 100%).

Compound **8c** was obtained as yellow crystals, mp 187–188 °C (EtOAc–PE) (as its 4-acetate. Found: C, 68.75; H, 5.10; N, 3.29. $C_{24}H_{21}NO_6$ requires C, 68.73; H, 5.05; N, 3.34%); ν_{max}/cm^{-1} 3350, 1720, 1660; δ_H (as its 4-acetate) 8.46 (m, 1H), 7.91 (m, 2H), 7.73 (d, 2H), 7.51 (m, 2H), 7.43 (t, 1H), 4.47 (q, *J* 7.2, 2H), 4.34 (q, *J* 7.2, 2H), 2.42 (s, 3H), 1.47 (t, *J* 7.2, 3H), 1.19 (t, *J* 7.2, 3H); *m*/*z* 377 (M^+, 100%).

Tandem reaction for the preparation of 3-phenyl-5*H*-pyrrolo[2,1,5-*de*]quinolizin-5-ones 15

To a stirred solution of Et_3N (3.0 g, 30 mmol) in DMF was added CrO_3 (650 mg, 6.5 mmol). Five minutes later, alkene (**2**, 25 mmol) and 2-acetyl-*N*-phenacylpyridinium bromide (**13**, 5 mmol) were added and the resultant mixture was stirred for 4–5 hours at 90 °C. The mixture was then cooled to room temperature and poured into 5% aqueous solution of HCl saturated with NaCl. The crude product was collected as a solid, which was purified by chromatography (20% EtOAc in PE) to give pure product **15**.

1-Cyano-3-phenyl-5*H*-pyrrolo[2,1,5-*de*]quinolizin-5-one (15a). Yellow crystals, mp 271–272 °C (acetone–PE) (Found: C, 79.94; H, 3.76; N, 10.32. $C_{18}H_{10}N_2O$ requires: C, 79.98; H, 3.73; N, 10.37%); ν_{max}/cm^{-1} 2200, 1640, 1590; δ_H 8.65 (d, *J* 7.6, 1H), 8.44 (d, *J* 8.4, 1H), 8.02 (t, *J* 7.8, 1H), 7.86 (s, 1H), 7.68–7.67 (m, 2H), 7.60–7.59 (m, 3H), 7.19 (s, 1H); *m*/*z* 271 (M + 1, 21%), 270 (M^+, 100).

Methyl 5-oxo-3-phenyl-5*H*-pyrrolo[2,1,5-*de*]quinolizine-1-carboxylate (15b). Yellow crystals, mp 226–227 °C (acetone–PE) (Found: C, 75.48; H, 4.46; N, 4.75. $C_{19}H_{13}NO_3$ requires: C, 75.23; H, 4.32; N, 4.62%); ν_{max}/cm^{-1} 1700, 1630, 1590; δ_H 8.91 (d, *J* 8.5, 1H), 8.62 (d, *J* 7.5, 1H), 8.05 (s, 1H), 7.98 (t, *J* 7.9, 1H), 7.71–7.70 (m, 2H), 7.59–7.58 (m, 3H), 7.18 (s, 1H), 4.00 (s, 3H); *m*/*z* 304 (M + 1, 22%), 303 (M^+, 100).

Dimethyl 5-oxo-3-phenyl-5*H*-pyrrolo[2,1,5-*de*]quinolizine-1,2-dicarboxylate (15c). Orange crystals, mp 169–171 °C (acetone–PE) (lit.[4d] 168–170 °C); ν_{max}/cm^{-1} 1740, 1710, 1640, 1600; δ_H 8.93 (d, *J* 8.5, 1H), 8.65 (d, *J* 7.7, 1H), 8.01 (t, *J* 8.3, 1H), 7.52–7.49 (m, 5H), 7.02 (s, 1H), 3.97 (s, 3H), 3.42 (s, 3H).

1-Benzoyl-3-phenyl-5*H*-pyrrolo[2,1,5-*de*]quinolizin-5-one (15d). Yellow crystals, mp 200–201 °C (acetone–PE) (Found: C, 82.69; H, 4.37; N, 3.82%. $C_{24}H_{15}NO_2$ requires: C, 82.50; H, 4.33; N, 4.01%); ν_{max}/cm^{-1} 1640, 1620, 1590; δ_H 9.12 (d, *J* 7.4, 1H), 8.70 (d, *J* 7.2, 1H), 8.08 (t, *J* 7.4, 1H), 7.93–7.90 (m, 2H), 7.84 (s, 1H), 7.72–7.69 (m, 2H), 7.63–7.53 (m, 6H), 7.21 (s, 1H); *m*/*z* 350 (M + 1, 27%), 349 (M^+, 100).

Tandem reaction for the preparation of 5-phenyl-3*H*-pyrrolo[2,1,5-*de*]quinolizin-3-ones 17

Compounds **17a**–**d** were obtained from 2-benzoyl-*N*-acetonylpyridinium bromide **16** by the same procedure used for the preparation of **15a**–**d**.

1-Cyano-5-phenyl-3*H*-pyrrolo[2,1,5-*de*]quinolizin-3-one (17a). Deep orange crystals, mp 264–265 °C (acetone–PE) (Found: C, 79.96; H, 3.86; N, 10.40. $C_{18}H_{10}N_2O$ requires: C, 79.98; H, 3.73; N, 10.37%); ν_{max}/cm^{-1} 2210, 1600; δ_H 8.33 (s, 1H), 8.32 (s, 1H), 7.86–7.81 (m, 2H), 7.59–7.54 (m, 5H), 7.34 (s, 1H); *m*/*z* 271 (M + 1, 20%), 270 (M^+, 100).

Methyl 3-oxo-5-phenyl-3*H*-pyrrolo[2,1,5-*de*]quinolizine-1-carboxylate (17b). Yellow crystals, mp 206–207 °C (acetone–PE) (Found: C, 75.74; H, 4.22; N, 4.43. $C_{19}H_{13}NO_3$ requires: C, 75.23; H, 4.32; N, 4.62%); ν_{max}/cm^{-1} 1710, 1600; δ_H 8.77 (d, *J* 7.4, 1H), 8.43 (s, 1H), 7.78–7.75 (m, 2H), 7.55–7.53 (s, 5H), 7.30 (s, 1H), 4.01 (s, 3H); *m*/*z* 304 (M + 1, 22%), 303 (M^+, 100).

Dimethyl 3-oxo-5-phenyl-3*H*-pyrrolo[2,1,5-*de*]quinolizine-1,2-dicarboxylate (17c). Yellow–green crystals, mp 254–255 °C (acetone–PE) (lit.[4d] 252–257 °C); ν_{max}/cm^{-1} 1740, 1710, 1610; δ_H 8.78–8.80 (m, 1H), 7.82–7.78 (m, 2H), 7.56–7.50 (m, 5H), 7.28 (s, 1H), 4.13 (s, 3H), 4.0 (s, 3H).

1-Benzoyl-5-phenyl-3*H*-pyrrolo[2,1,5-*de*]quinolizin-3-one (17d). Yellow crystals, mp 199–200 °C (acetone–PE) (Found: C, 82.59; H, 4.28; N, 3.94. $C_{24}H_{15}NO_2$ requires: C, 82.50; H, 4.33; N, 4.01%); ν_{max}/cm^{-1} 1615, 1590; δ_H 9.07–9.03 (m, 1H), 8.38 (s, 1H), 7.99–7.96 (m, 2H), 7.87 (d, *J* 6.2, 2H), 7.65–7.57 (m, 8H), 7.37 (s, 1H); *m*/*z* 350 (M + 1, 27%), 349 (M^+, 100).

1-Cyano-3-methyl-5*H*-pyrrolo[2,1,5-*de*]quinolizin-5-one (24a) and 1-cyano-5-methyl-3*H*-pyrrolo[2,1,5-*de*]quinolizin-3-one (24b)

Compounds **24a** and **24b** were obtained from 2-acetyl-*N*-acetonylpyridinium bromide (**23**) by the procedure used to prepare **17a**–**d**.

Compound 24a. Yellow needles, mp 290–291 °C (acetone–PE) (Found: C, 74.86; H, 3.70; N, 13.29. $C_{13}H_8N_2O$ requires: C, 74.98; H, 3.87; N, 13.46%); ν_{max}/cm^{-1} 2210, 1640, 1600; δ_H 8.53 (d, *J* 7.2, 1H), 8.37 (s, 1H), 7.95–7.91 (m, 1H), 7.84 (s, 1H), 6.97 (s, 1H), 2.68 (s, 3H); *m*/*z* 209 (M + 1, 15%), 208 (M^+, 100).

Compound 24b. Yellow needles, mp 251–252 °C (acetone–PE) (Found: C, 75.02; H, 3.86; N, 13.53. $C_{13}H_8N_2O$ requires: C, 74.98; H, 3.87; N, 13.46%); ν_{max}/cm^{-1} 2210, 1610; δ_H 8.27 (d, *J* 8.3, 1H), 8.21 (s, 1H), 7.95 (d, *J* 7.55, 1H), 7.88–7.85 (m, 1H), 7.20 (s, 1H), 2.75 (s, 3H); *m*/*z* 209 (M + 1, 15%), 208 (M^+, 100).

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