Preparation of indolizine-3-carboxamides and indolizine-3-carbonitriles by 1,3-dipolar cycloaddition of *N*-(cyanomethyl)pyridinium ylides to alkenes in the presence of tetrakispyridinecobalt(II) dichromate or manganese(IV) oxide

Bingxiang Wang,[a] Xuechun Zhang,[a] Jun Li,[a] Xin Jiang,[a] Yuefei Hu *[ab] and Hongwen Hu[ab]

[a] *Department of Chemistry and* [b] *Coordination Chemistry Institute, Nanjing University, Nanjing 210093, People's Republic of China*

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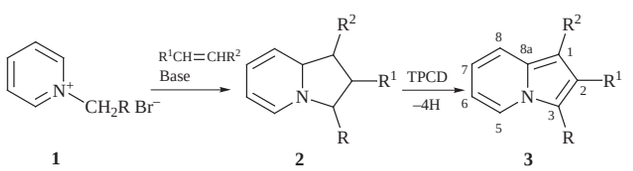
Two selective procedures for the synthesis of potentially important agrochemicals, indolizine-3-carboxamides (**6**) and indolizine-3-carbonitriles (**7**), were developed. In the presence of tetrakispyridinecobalt(II) dichromate (TPCD), compounds **6** are readily synthesized by a one-pot reaction sequence which consists of a 1,3-dipolar cycloaddition of pyridinium *N*-ylides to alkenes, followed by an aromatization and a regiospecific hydration reaction. When MnO_2 instead of TPCD was used in the 1,3-dipolar addition reaction, the nitrile group of the indolizine product was not hydrated and compounds **7** were obtained as final products. Both procedures utilize convenient conditions and inexpensive reagents, and give products in good to high yields.

Introduction

Aromatic indolizines have been prepared previously and derivatives containing a variety of functional groups are used for many different purposes.[1,2] In recent years, some indolizines have been prepared and studied because of their interesting biological activities.[3] In our previous work,[4] several derivatives of indolizine were synthesized for evaluation in agrochemical research studies. In continuation of our studies, a series of indolizine-3-carbonitriles (**7**) were selected for preparation and evaluation.

Many papers have been published on the preparation of indolizine-3-carbonitriles. Methods using 1,3-dipolar cycloadditions of heteroaromatic *N*-ylides with electron-deficient acetylenes[5] or alkenes[6] are most attractive because of their convenience. Usually, indolizines containing C3-nitrile groups are prepared from starting materials which are heteroaromatic *N*-dicyanomethylides. However, there are several drawbacks associated with this general method. The preparation of dicyanomethylides is very expensive and the highly toxic gas hydrogen cyanide is produced during the reactions used to prepare these compounds. Additionally, since most electron-deficient acetylenes are not commercially available, the range of C1 and C2 functionalized indolizine-3-carbonitriles that can be prepared by this is quite limited. Finally, the 1,3-dipolar cycloaddition to alkenes usually gives 1,2,3,8a-tetrahydroindolizines, which are generally not stable because the products are either reversibly converted back to starting materials or to ring opened betaines.[7] Thus only alkenes with "abnormal" structures such as phenylsulfinylethene,[5f] phenyl vinyl sulfoxide,[6a] nitroketene dithioacetal,[6b] α-chloroacrylonitrile[6c] and methoxyethylene derivatives[6d] give good yields of the desired 1,3-dipolar addition products.

We have reported that C1 and C2 functionalized indolizines are conveniently prepared in good yield using "normal" alkenes instead of acetylenes as dipolarophiles in 1,3-dipolar cycloaddition reactions when the reactions are carried out in the presence of tetrakispyridinecobalt(II) dichromate (TPCD).[4a] As demonstrated in Scheme 1, the 1,3-dipolar cycloaddition of a heteroaromatic *N*-ylide (from salt **1**) with alkenes was followed by the *in situ* aromatization of 1,2,3,8a-tetrahydroindolizine (**2**) by



1 **2** **3**

Scheme 1

TPCD. In the present instance, when we used this strategy to prepare indolizine-3-carbonitriles (**7**), we unexpectedly obtained indolizine-3-carboxamides (**6**) as products. Ultimately, indolizine-3-carbonitriles (**7**) were prepared successfully when the 1,3-dipolar cycloaddtion reactions were carried out in the presence of MnO_2. Herein, the methods used for the syntheses of indolizine-3-carboxamides (**6**) and indolizine-3-carbonitriles (**7**) as well as the scopes of the synthetic methods are presented.

Results and discussion

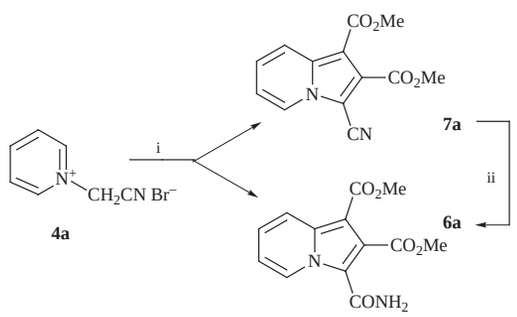
Synthesis of indolizine-3-carboxamide (6)

Following the original procedure described in Scheme 1, a mixture of *N*-(cyanomethyl)pyridinium bromide (**4a**), dimethyl maleate (**5a**), pyridine and TPCD in DMF was heated at 90–95 °C for 3 h to yield a product as white needles. The melting point (mp 156–157 °C) is different from that of the expected product, dimethyl 3-cyanoindolizine-1,2-dicarboxylate (**7a**) (lit.,[5a,b] mp 129–130 °C), and a nitrile group in this product could not be detected spectroscopically. Instead, the IR, ^{1}H NMR, MS spectra and microanalytical analysis results for the product indicated that the compound was dimethyl 3-carbamoylindolizine-1,2-dicarboxylate (**6a**), the nitrile hydration product.

This surprising result is of value to us not only because we are interested in indolizine-3-carboxamides (**6**) as potential agrochemicals, but also because we were unable to find previous methods for such a convenient synthesis of indolizine-3-carboxamide in the literature.[8] By monitoring the reaction for the presence of reaction intermediates, it was found that the reaction proceeded *via* hydration of the expected dimethyl 3-cyanoindolizine-1,2-dicarboxylate (**7a**) intermediate. Long

Table 1 Indolizine-3-carboxamides **6a–j** prepared

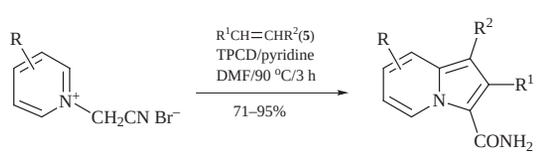
Compd.	R	R^1	R^2	Yield (%)
6a	H	CO_2Me	CO_2Me	73
6b	H	CO_2Et	CO_2Et	77
6c	H	H	CO_2Et	75
6d	H	H	CN	71
6e	7-Me	CO_2Et	CO_2Et	95
6f	7-Me	H	CO_2Et	83
6g	7-Me	H	CN	90
6h	7,8-benzo	CO_2Et	CO_2Et	87
6i	7,8-benzo	H	CO_2Et	79
6j	7,8-benzo	H	CN	76



Scheme 2 *Reagents and conditions*: i) $MeO_2CHC{=}CHCO_2Me$ (**5a**), TPCD, pyridine, DMF, 90–95 °C, 3 h, 73%; ii) TPCD, DMF, 90–95 °C, 3 h.

reaction times favored compound **6a** as the sole product (Scheme 2).

To test the scope of this new method, the reactions of substituted *N*-(cyanomethyl)pyridinium bromides **4b–c** and alkenes **5b–d** were studied. In each case, the corresponding indolizine-3-carboxamides (**6b–j**) were obtained in good to excellent yields (71–95%). It is noteworthy that the nitriles on the indolizines were hydrated regiospecifically. In examples **6d**, **6g**, and **6j**, only the C3-nitrile was hydrated to the amide group. The C1-nitrile group remained unchanged (Scheme 3 and Table 1). When



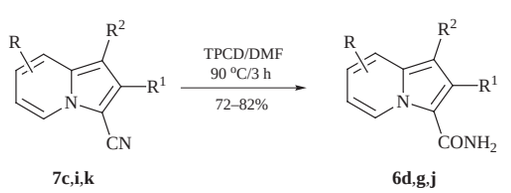
4 **a** R = H
b R = 4-Me
c R = 3,4-benzo
d R = 2-Me

5 **a** $R^1 = R^2 = CO_2Me$
b $R^1 = R^2 = CO_2Et$
c R^1 = H, $R^2 = CO_2Et$
d R^1 = H, R^2 = CN
e R^1 = H, $R^2 = CO_2Me$

6

Scheme 3

indolizine-1,3-dicarbonitriles **7c**, **7i**, and **7k** were treated with TPCD in DMF for 3 h, the corresponding 1-cyanoindolizine-3-carboxamides **6d** (75%), **6g** (82%) and **6j** (72%) were obtained (Scheme 4). Overall, the results show that hydration of a nitrile

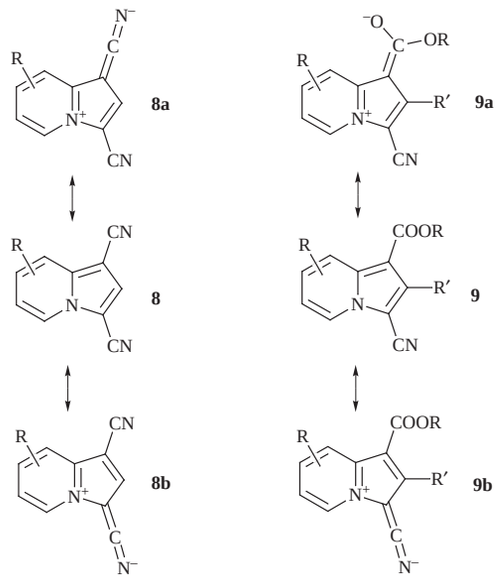


7c,**i**,**k** **6d**,**g**,**j**

Scheme 4

group at position C3, but not at position C1, of indolizines can be achieved with TPCD.

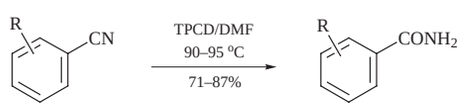
It is well known that the resonance hybrid of indolizine involves a bicycloiminium ylide structure, in which the bridgehead nitrogen carries a positive charge.[9] For the compounds **6a–j**, several resonance structures are possible, and the selective hydration of the C3-nitrile on indolizine can be explained by the resonance structures shown in Scheme 5. Thus, the strong



Scheme 5

electron-withdrawing effect of the positively charged nitrogen attached to C3 will selectively polarize this group and facilitate its hydration in the presence of TPCD. The molecular orbital calculation of indolizine-1,3-dicarbonitrile in a published reference[10] also indicates that the order of electrophilicity of nitriles is 3-CN > 1-CN.

On the basis of this hypothesis, a series of substituted benzonitriles were allowed to react with TPCD under the same reaction conditions. The benzonitriles substituted with electron-withdrawing groups (**10a–d**) were converted smoothly into their corresponding benzenecarboxamides (**11a–d**) in 72–87% yields. 1,3-Dicyanobenzene (**10e**) and 1,4-dicyanobenzene (**10f**) gave the corresponding benzene-1,3-dicarboxamide (**11e**, 76%) and benzene-1,4-dicarboxamide (**11f**, 71%). As was expected, benzonitrile (**10g**), 4-methoxybenzonitrile (**10h**) and aliphatic nitriles, such as acrylonitrile, dodecanenitrile and phenylacetonitrile, were inert to hydration in the presence of TPCD (Scheme 6).



10 **11**

	R		R	Yield (%)
10a	3-Br	**11a**	3-Br	87
10b	4-Cl	**11b**	4-Cl	78
10c	3-NO_2	**11c**	3-NO_2	85
10d	4-NO_2	**11d**	4-NO_2	72
10e	3-CN	**11e**	3-$CONH_2$	76
10f	4-CN	**11f**	4-$CONH_2$	71
10g	H	**11g**	—	—
10h	4-OMe	**11h**	—	—
10i	2-Cl	**11i**	—	—
10j	2-NO_2	**11j**	—	—

Scheme 6

These results provide strong evidence in support of the above presented resonance hypothesis. The fact that 2-chlorobenzonitrile (**10i**) and 2-nitrobenzonitrile (**10j**) were recovered

Table 2 Indolizine-3-carbonitriles **7a**–**k** prepared

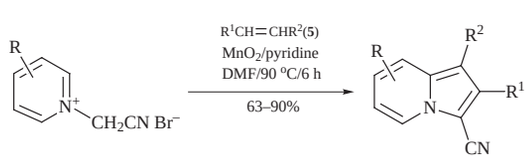
Compd.	R	R^1	R^2	Yield (%)
7a	H	CO_2Me	CO_2Me	72
7b	H	H	CO_2Me	71
7c	H	H	CN	83
7d	5-Me	CO_2Me	CO_2Me	78
7e	5-Me	H	CO_2Me	70
7f	5-Me	H	CN	72
7g	7-Me	CO_2Me	CO_2Me	90
7h	7-Me	H	CO_2Me	86
7i	7-Me	H	CN	84
7j	7,8-benzo	H	CO_2Me	76
7k	7,8-benzo	H	CN	63

unchanged under the same conditions may result from their hindrance effects.

Further experiments showed that $Co(OAc)_2$ or other Cr^{VI} oxidants, such as PCC or PDC do not mediate nitrile hydration. To our surprise, the mixture of PCC and $Co(OAc)_2$ or PDC and $Co(OAc)_2$ can mediate the conversion of **7c** to **6d**. The results imply that the central metal ion Co^{II} in TPCD might play a very important role in this conversion.

Synthesis of indolizine-3-carbonitrile (7)

The results reported for the synthesis of indolizine-3-carboxamides (**6**) are consistent with a reaction sequence that combines an initial 1,3-dipolar cycloaddition reaction with subsequent *in situ* TPCD promoted aromatization and nitrile hydration reactions. Accordingly, indolizine-3-carbonitriles (**7**) should be prepared easily by using MnO_2. This reagent is a good reagent for aromatization as it does not contain a free metal ion that would also facilitate the nitrile hydration reaction. In fact, MnO_2 has been used in 1,3-diploar cycloaddition of heteroaromatic ylides with alkenes for the preparation of indolizines.[11] As was expected, when the mixture of *N*-(cyanomethyl)pyridinium bromide (**4a**), dimethyl maleate (**5a**), pyridine and MnO_2 in DMF was heated at 85–90 °C for 6 h, indolizine-3-carbonitrile (**7a**) was obtained as the sole product in 72% yield. In all cases, when pyridinium *N*-ylides (**4a**–**d**) and alkenes (**5a**, **5d**, **5e**) were reacted in the presence of MnO_2, the corresponding indolizine-3-carbonitriles (**7a**–**k**) were obtained in satisfactory yields (Scheme 7 and Table 2).



4 7

Scheme 7

In conclusion, a TPCD promoted one-pot procedure that combines 1,3-dipolar cycloaddition, aromatization and hydration reactions to synthesize indolizine-3-carboxamides was developed. The procedure is regiospecific for hydration of the C3-nitrile group. MnO_2 can replace TPCD to promote the 1,3-dipolar cycloaddition of heteroaromatic *N*-ylides and alkenes and the subsequent aromatization reaction, but it does not cause nitrile hydration. Both procedures are very valuable new additions to existing methods for the synthesis of indolizines by 1,3-dipolar cycloaddition of heteroaromatic *N*-ylides and alkenes.

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 with KBr pellets. ^{1}H NMR Spectra were recorded on a Bruker ACF-300 spectrometer with TMS as internal reference. *J* Values are given in Hz. Mass spectra were obtained on a ZAB-HS mass spectrometer with 70 eV. Elemental analyses were performed on a Perkin-Elmer 240C instrument. TPCD[12] and MnO_2[13] were prepared according to reported procedures.

Preparation of *N*-(cyanomethyl)pyridinium bromide (4a): a typical procedure

A mixture of pyridine (7.9 g, 100 mmol) and bromoacetonitrile (12 g, 100 mmol) in EtOAc (50 cm^3) was stirred at room temperature for 0.5 h. After it stood for another 48 h, the precipitated solid was collected and rinsed with EtOAc (50 cm^3) to give 17.5 g (88%) of **4a** as a colorless solid, mp 166–168 °C. Salts **4b**–**d** were prepared by the same procedure and they were directly used in the next step without any further purification (**4b**, 86%, mp 178–180 °C; **4c**, 90%, mp 207–209 °C; **4d**, 93%, mp 201–203 °C).

Dimethyl 3-carbamoylindolizine-1,2-dicarboxylate (6a): a typical procedure

A solution of *N*-(cyanomethyl)pyridinium bromide (**4a**, 1.99 g, 10 mmol), dimethyl maleate (**5a**, 5.76 g, 40 mmol), TPCD (4.0 g, 6.5 mmol) and pyridine (2.0 cm^3) in DMF (40 cm^3) was stirred at 90 °C for 3 h (monitored by TLC). It was then cooled to room temperature and poured into 5% aqueous HCl (200 cm^3). The mixture was extracted with Et_2O (2 × 100 cm^3) and the combined extracts were washed with water (2 × 50 cm^3) and dried over Na_2SO_4. The solvent was removed to give a solid, which was purified by chromatography [silica gel, 35% EtOAc in petroleum ether (60–90 °C)] to yield 2.02 g (73%) of dimethyl 3-carbamoylindolizine-1,2-dicarboxylate (**6a**) as yellowish crystals, mp 156–157 °C (from EtOH) (Found: C, 56.50; H, 4.44; N, 10.01. $C_{13}H_{12}N_2O_5$ requires C, 56.52; H, 4.38; N, 10.14%); ν_{max}/cm^{-1} 3401, 3175, 2951, 1726, 1712, 1700, 1250, 1238, 742; δ_H 3.92 (3H, s, OCH_3), 4.01 (3H, s, OCH_3), 6.32 (2H, br, $CONH_2$), 6.98 (1H, m, ArH), 7.34 (1H, m, ArH), 8.25 (1H, d, *J* 8.9, ArH), 9.59 (1H, d, *J* 7.1, ArH); *m*/*z* 276 (M$^+$, 100%), 245 (18), 218 (8), 213 (78), 169 (36). Compounds **6b**–**j** were prepared by the same procedure.

Diethyl 3-carbamoylindolizine-1,2-dicarboxylate (6b). Obtained as yellowish crystals, mp 131–132 °C (from EtOH) (Found: C, 59.07; H, 5.49; N, 9.20. $C_{15}H_{16}N_2O_5$ requires C, 59.20; H, 5.30; N, 9.20%); ν_{max}/cm^{-1} 3384, 3184, 2985, 1721, 1689, 787; δ_H 1.40 (3H, t, *J* 7.0, CH_3), 1.41 (3H, t, *J* 7.0, CH_3), 4.39 (2H, q, *J* 7.0, OCH_2), 4.45 (2H, q, *J* 7.0, OCH_2), 6.48 (2H, br s, $CONH_2$), 6.93–7.33 (2H, m, ArH), 8.26 (1H, m, ArH), 9.59 (1H, m, ArH); *m*/*z* 304 (M$^+$, 100%), 258 (24), 232 (27), 213 (73), 187 (24).

Ethyl 3-carbamoylindolizine-1-carboxylate (6c). Obtained as a yellow solid, mp 250–251 °C (from EtOH) (Found: C, 62.16; H, 5.23; N, 12.01. $C_{12}H_{12}N_2O_3$ requires C, 62.06; H, 5.20; N, 12.05%); ν_{max}/cm^{-1} 3390, 3169, 1661, 775; δ_H 1.42 (3H, t, *J* 7.0, CH_3), 3.09 (2H, br s, $CONH_2$), 4.37 (2H, q, *J* 7.0, OCH_2), 6.89–6.94 (2H, m, ArH), 8.00 (1H, s, ArH), 8.25 (1H, m, ArH), 9.76 (1H, d, *J* 7.2, ArH); *m*/*z* 232 (M$^+$, 100%), 240 (32), 187 (92), 160 (31), 144 (14).

1-Cyanoindolizine-3-carboxamide (6d). Obtained as white crystals, mp 290–292 °C (from EtOH) (Found: C, 64.98; H, 4.04; N, 22.55. $C_{10}H_7N_3O$ requires C, 64.87; H, 3.81; N, 22.68%); ν_{max}/cm^{-1} 3416, 3172, 2218, 1689, 754; δ_H 3.39 (2H, br s, $CONH_2$), 6.98 (1H, m, ArH), 7.33 (1H, m, ArH), 7.68 (1H, m, ArH), 7.90 (1H, s, ArH), 9.79 (1H, m, ArH); *m*/*z* 185 (M$^+$, 100%), 169 (75), 141 (39), 114 (25).

Diethyl 3-carbamoyl-7-methylindolizine-1,2-dicarboxylate (6e). Obtained as a yellowish solid, mp 161–162 °C (from EtOH) (Found: C, 60.22; H, 5.84; N, 8.60. $C_{16}H_{18}N_2O_5$ requires C, 60.37; H, 5.70; N, 8.80%); ν_{max}/cm^{-1} 3391, 3178, 2985, 1734, 1689, 1644; δ_H 1.39 (3H, t, *J* 7.0, CH_3), 1.40 (3H, t, *J* 7.0, CH_3), 2.43 (3H, s, CH_3), 4.36 (2H, q, *J* 7.0, OCH_2), 4.45 (2H, q, *J* 7.0, OCH_2), 6.29 (2H, br s, $CONH_2$), 6.79 (1H, m, ArH), 8.05 (1H, m, ArH), 9.47 (1H, d, *J* 7.5 ArH); *m*/*z* 318 (M^+, 100%), 246 (28), 227 (55), 201 (21), 184 (24).

Ethyl 3-carbamoyl-7-methylindolizine-1-carboxylate (6f). Obtained as a yellow solid, mp 280–281 °C (from EtOH) (Found: C, 63.36; H, 5.67; N, 11.19. $C_{13}H_{14}N_2O_3$ requires C, 63.40; H, 5.73; N, 11.37%); ν_{max}/cm^{-1} 3346, 3107, 1663, 774; δ_H 1.40 (3H, t, *J* 7.0, CH_3), 2.43 (3H, s, CH_3), 3.36 (2H, br s, $CONH_2$), 4.34 (2H, q, *J* 7.0, OCH_2), 6.78 (1H, m, ArH), 7.89 (1H, s, ArH), 8.00 (1H, s, ArH), 9.65 (1H, d, *J* 7.2, ArH); *m*/*z* 246 (M^+, 100%), 218 (38), 201 (89), 174 (39), 158 (13).

1-Cyano-7-methylindolizine-3-carboxamide (6g). Obtained as a white solid, mp 294–297 °C (from EtOH) (Found: C, 66.10; H, 4.85; N, 20.94. $C_{11}H_9N_3O$ requires C, 66.33; H, 4.55; N, 21.09%); ν_{max}/cm^{-1} 3442, 3178, 2211, 1683; δ_H 2.44 (3H, s, CH_3), 3.39 (2H, br s, $CONH_2$), 6.82 (1H, m, ArH), 7.44 (1H, m, ArH), 7.81 (1H, s, ArH), 9.65 (1H, d, *J* 7.2 ArH); *m*/*z* 199 (M^+, 100%), 183 (68), 155 (50), 128 (13).

Diethyl 3-carbamoylpyrrolo[2,1-*a*]isoquinoline-1,2-dicarboxylate (6h). Obtained as white crystals, mp 180–182 °C (from EtOH) (Found: C, 64.61; H, 5.35; N, 7.90. $C_{19}H_{18}N_2O_5$ requires C, 64.40; H, 5.12; N, 7.90%); ν_{max}/cm^{-1} 3300, 3146, 2985, 1728, 1696, 1670, 793; δ_H 1.40 (3H, t, *J* 7.0, CH_3), 1.42 (3H, t, *J* 7.0, CH_3), 4.40 (2H, q, *J* 7.0, OCH_2), 4.47 (2H, q, *J* 7.0, OCH_2), 6.50 (2H, br s, $CONH_2$), 7.06–7.68 (4H, m, ArH), 8.56 (1H, m, ArH), 9.43 (1H, d, *J* 7.8, ArH); *m*/*z* 354 (M^+, 100%), 308 (71), 282 (32), 263 (95), 236 (45).

Ethyl 3-carbamoylpyrrolo[2,1-*a*]isoquinoline-1-carboxylate (6i). Obtained as a white solid, mp 238–240 °C (from EtOH) (Found: C, 67.84; H, 5.00; N, 10.06. $C_{16}H_{14}N_2O_3$ requires C, 68.07; H, 4.99; N, 9.91%); ν_{max}/cm^{-1} 3391, 3184, 2978, 1708, 1631, 806; δ_H 1.03 (3H, t, *J* 7.0, CH_3), 2.98 (2H, br s, $CONH_2$), 3.99 (2H, q, *J* 7.0, OCH_2), 6.70–7.31 (4H, m, ArH), 7.61 (1H, s, ArH), 9.17 (1H, d, *J* 7.5, ArH), 9.33 (1H, m, ArH); *m*/*z* 282 (M^+, 100%), 254 (14), 237 (52), 210 (24), 164 (7).

1-Cyanopyrrolo[2,1-*a*]isoquinoline-3-carboxamide (6j). Obtained as a white solid, mp 285–288 °C (from EtOH) (Found: C, 71.00; H, 3.89; N, 17.40. $C_{14}H_9N_3O$ requires C, 71.48; H, 3.85; N, 17.85%); ν_{max}/cm^{-1} 3444, 3350, 3200, 2219, 1669, 800; δ_H (DMSO-d_6) 3.33 (2H, br s, $CONH_2$), 7.17–7.80 (4H, m, ArH), 7.88 (1H, s, ArH), 8.84 (1H, m, ArH), 9.55 (1H, d, *J* 7.8, ArH); *m*/*z* 235 (M^+, 100%), 219 (30), 191 (9), 164 (19).

Hydration of 3-bromobenzonitrile (10a): a typical procedure

A mixture of 3-bromobenzonitrile (0.91 g, 5.0 mmol) and TPCD (2.0 g, 3.3 mmol) in DMF (30 cm^3) was stirred at 90 °C for 3 h. It was then cooled to room temperature and poured into a solution of 5% aqueous HCl (100 cm^3). The precipitated solid was collected and the crude product was purified by recrystallization from EtOH to give 0.87 g (87%) of 3-bromobenzenecarboxamide (**11a**), mp 153–154 °C. The hydrations of **10b**–**j** were proceeded by the same procedure.

Preparation of dimethyl 3-cyanoindolizine-1,2-dicarboxylate (7a): a typical procedure

A mixture of *N*-(cyanomethyl)pyridinium bromide (**4a**, 1.99 g, 10 mmol), dimethyl maleate (**5a**, 5.67 g, 40 mmol), MnO_2 (3.48 g, 40 mmol) and pyridine (2.0 cm^3) in DMF (30 cm^3) was stirred at 85–90 °C for 6 h (monitored by TLC). Then it was filtered through a cake of silica gel (4.0 g) and the solid was washed with DMF (3 × 10 cm^3). Combined organic layers were treated with 5% aqueous HCl (160 cm^3) and the precipitated solid was collected. The crude product was purified by chromatography [silica gel, 35% EtOAc in petroleum ether (60–90 °C)] to give 1.86 g (72%) of pure compound **7a**, mp 130–131 °C (from EtOH) [lit.,[5b] mp 129–130 °C]. Compounds **7b**–**k** were prepared by the same procedure.

Methyl 3-cyanoindolizine-1-carboxylate (7b). Obtained as white crystals, mp 122–123 °C (from EtOH) (Found: C, 66.03; H, 4.16; N, 13.89. $C_{11}H_8N_2O_2$ requires C, 65.99; H, 4.03; N, 14.00%); ν_{max}/cm^{-1} 3121, 2221, 1700, 864, 779; δ_H 3.91 (3H, s, OCH_3), 7.04 (1H, m, ArH), 7.34 (1H, m, ArH), 7.77 (1H, s, ArH), 8.33 (2H, m, ArH); *m*/*z* 200 (M^+, 53%), 169 (100), 141 (9), 114 (8), 89 (33), 57 (19).

Indolizine-1,3-dicarbonitrile (7c). Obtained as white crystals, mp 250 °C (from EtOH) (Found: C, 72.11; H, 3.12; N, 24.83. $C_{10}H_5N_3$ requires C, 71.85; H, 3.02; N, 25.13%); ν_{max}/cm^{-1} 3107, 2214, 1686, 864, 751; δ_H 7.13 (1H, m, ArH), 7.41 (1H, m, ArH), 7.59 (1H, s, ArH), 7.83 (1H, m, ArH), 8.39 (1H, d, *J* 6.1, ArH); *m*/*z* 167 (M^+, 100%), 140 (17), 113 (10), 88 (25), 78 (29), 62 (37), 51 (39).

Dimethyl 3-cyano-5-methylindolizine-1,2-dicarboxylate (7d). Obtained as white crystals, mp 169–170 °C (from EtOH) (Found: C, 61.58; H, 4.15; N, 10.29. $C_{14}H_{12}N_2O_4$ requires C, 61.76; H, 4.44; N, 10.29%); ν_{max}/cm^{-1} 2959, 2214, 1743, 1693, 850, 800; δ_H 3.03 (3H, s, CH_3), 3.91 (3H, s, OCH_3), 4.02 (3H, s, OCH_3), 6.80 (1H, d, *J* 6.9, ArH), 7.29 (1H, m, ArH), 8.23 (1H, d, *J* 9.0, ArH); *m*/*z* 272 (M^+, 77%), 241 (100), 211 (19), 183 (11), 155 (12), 127 (7), 103 (7), 77 (6).

Methyl 3-cyano-5-methylindolizine-1-carboxylate (7e). Obtained as yellowish crystals, mp 140–141 °C (from EtOH) (Found: C, 67.33; H, 5.12; N, 13.01. $C_{12}H_{10}N_2O_2$ requires C, 67.28; H, 4.71; N, 13.08%); ν_{max}/cm^{-1} 3105, 2207, 1692, 1240, 793, 721; δ_H 3.03 (3H, s, CH_3), 3.91 (3H, s, OCH_3), 6.74 (1H, d, *J* 6.8, ArH), 7.26 (1H, d, *J* 5.8, ArH), 7.86 (1H, s, ArH), 8.26 (1H, d, *J* 8.9, ArH); *m*/*z* 214 (M^+, 62%), 183 (100), 155 (10), 127 (4).

5-Methylindolizine-1,3-dicarbonitrile (7f). Obtained as white crystals, mp 202–203 °C (from EtOH) (Found: C, 72.98; H, 3.90; N, 22.92. $C_{11}H_7N_3$ requires C, 72.91; H, 3.89; N, 23.19%); ν_{max}/cm^{-1} 3114, 2221, 2200, 871, 779; δ_H 3.00 (3H, s, CH_3), 6.82 (1H, d, *J* 7.0, ArH), 7.31 (1H, m, ArH), 7.67 (1H, s, ArH), 7.71 (1H, m, ArH); *m*/*z* 181 (M^+, 100%), 153 (10), 127 (8), 77 (5), 63 (7), 51 (7).

Dimethyl 3-cyano-7-methylindolizine-1,2-dicarboxylate (7g). Obtained as white crystals, mp 123–124 °C (from EtOH) (Found: C, 61.84; H, 4.37; N, 10.27. $C_{14}H_{12}N_2O_4$ requires C, 61.76; H, 4.44; N, 10.29%); ν_{max}/cm^{-1} 2959, 2214, 1735, 1700, 885, 772; δ_H 2.47 (3H, s, CH_3), 3.91 (3H, s, OCH_3), 4.00 (3H, s, OCH_3), 6.94 (1H, d, *J* 7.0, ArH), 8.05 (1H, s, ArH), 8.20 (1H, d, *J* 7.0, ArH); *m*/*z* 272 (M^+, 68%), 241 (100), 211 (22), 155 (16), 127 (8), 103 (9), 77 (8).

Methyl 3-cyano-7-methylindolizine-1-carboxylate (7h). Obtained as white crystals, mp 128–130 °C (from EtOH) (Found: C, 67.19; H, 4.63; N, 12.98. $C_{12}H_{10}N_2O_2$ requires C, 67.28; H, 4.71; N, 13.08%); ν_{max}/cm^{-1} 3135, 2214, 1693, 871, 772; δ_H 2.46 (3H, s, CH_3), 3.90 (3H, s, OCH_3), 6.87 (1H, d, *J* 7.0, ArH), 7.70 (1H, s, ArH), 8.08 (1H, s, ArH), 8.20 (1H, d, *J* 7.0, ArH); *m*/*z* 214 (M^+, 56%), 183 (100), 155 (13), 103 (16), 77 (16), 51 (6).

7-Methylindolizine-1,3-dicarbonitrile (7i). Obtained as white crystals, mp 228–229 °C (from EtOH) (Found: C, 72.93; H, 4.13; N, 23.23. $C_{11}H_7N_3$ requires C, 72.91; H, 3.89; N, 23.19%); ν_{max}/cm^{-1} 3114, 2214, 1721, 842, 765; δ_H 2.49 (3H, s, CH_3), 6.95 (1H, d, *J* 7.0, ArH), 7.53 (1H, s, ArH), 7.57 (1H, s, ArH), 8.26 (1H, d, *J* 7.0, ArH); *m*/*z* 181 (M^+, 100%), 153 (11), 51 (6).

Methyl 3-cyanopyrrolo[2,1-*a*]isoquinoline-1-carboxylate (7j). Obtained as white crystals, mp 155–156 °C (from EtOH) (Found: C, 71.84; H, 4.28; N, 11.12. $C_{15}H_{10}N_2O_2$ requires C, 71.99; H, 4.03; N, 11.20%); ν_{max}/cm^{-1} 3149, 2214, 1700, 864, 786; δ_H 3.97 (3H, s, OCH_3), 7.64–7.78 (4H, m, ArH), 7.86 (1H, s, ArH), 8.13 (1H, d, *J* 7.2, ArH), 9.85 (1H, m, ArH); *m*/*z* 250 (M^+, 77%), 219 (100), 191 (17), 164 (22), 139 (26), 87 (5), 69 (12).

Pyrrolo[2,1-*a*]isoquinoline-1,3-dicarbonitrile (7k). Obtained as white crystals, mp 187–188 °C (from EtOH) (Found: C, 77.31; H, 3.37; N, 19.35. $C_{14}H_7N_3$ requires C, 77.41; H, 3.25; N, 19.34%); ν_{max}/cm^{-1} 3124, 2220, 792; δ_H 7.61 (1H, d, *J* 7.7, ArH), 7.84 (2H, m, ArH), 8.07 (1H, d, *J* 7.7, ArH), 8.23 (1H, s, ArH), 8.43 (1H, d, *J* 7.3, ArH), 8.72 (1H, d, *J* 8.0, ArH); *m*/*z* 217 (M^+, 100%), 190 (11), 164 (7), 163 (8), 108 (6).

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