Pergamon

Tetrahedron Letters 42 (2001) 5663–5667

TETRAHEDRON LETTERS

Novel syntheses of densely functionalized indolizines, di- and tetrahydroindolizines from 2-formyl-1,4-dihydropyridine systems based on cascade process

Štefan Marchalín,[a] Katarína Cvopová,[a] Duy-Phong Pham-Huu,[a] Miloslav Chudík,[a] Jozef Kozisek,[b] Ingrid Svoboda[c] and Adam Daïch[d,*]

[a]*Department of Organic Chemistry, Faculty of Chemical Technology, Slovak University of Technology, SK-812 37 Bratislava, Slovak Republic*

[b]*Department of Physical Chemistry, Faculty of Chemical Technology, Slovak University of Technology, SK-812 37 Bratislava, Slovak Republic*

[c]*Materials Science, Darmstadt University of Technology, Petersenstrasse 23, D-64287 Darmstadt, Germany*

[d]*Laboratoire de Chimie, URCOM, EA 3221, Faculté des Sciences & Techniques de l'Université du Havre, 25 Rue Philippe Lebon, BP 540, F-76058 Le Havre Cedex, France*

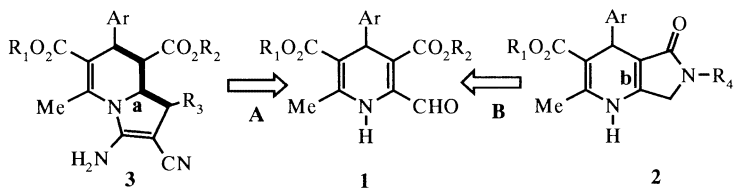
Received 1 June 2001; revised 15 June 2001; accepted 16 June 2001

Abstract—Several indolizines, di- and tetrahydroindolizines have been synthesized successfully in a one-pot procedure, in two or three steps from 2-formyl-1,4-dihydropyridine derivatives and malonitrile in 57–87% yield. The general mechanism leading to these azacyclic compounds, involving 2-dicyanovinyl-1,4-dihydropyridines, is discussed.

The indolizine skeletons with different degrees of unsaturation are present in a wide variety of natural and unnatural azacyclic compounds. The latter are of interest as biologically active products (channel calcium antagonists[1] and cardiovascular agents[2] for example) and constitute key intermediates for the syntheses of electron-enriched cycloazines.[3] Because of the exceptional potential of these species, notable advances on their synthesis and biological evaluation continue to be made.[4]

So, three general methods have been reported for their preparation: the Tschitschibabin reaction,[3a,4b,5] the α-unsaturated pyridine condensation with allyl derivatives, and finally the reaction of pyridinium ylides with acetylenic or olefinic compounds.[3a,6] In all these reported methods, substituted pyridine was used as a starting material.

Because we are interested in developing new methodology to access azabicyclic compounds in the dihydropyridine (DHP) range, our ongoing work showed dialkyl 4-aryl-2-formyl-6-methyl-1,4-DHP-3,5-dicarboxylate (**1**)[7] to be an effective synthon; subsequent reactions with amine followed by borohydride reduction furnished substituted pyrrolo[3,4-*b*]-1,4-DHP lactams **2** resulting in formation of a junction **b** (Scheme 1). These



Scheme 1. (A) Cascade process; (B) thermal amino-ester cyclization (Ref. 7).

Keywords: stereoselectivity; dihydropyidines (DHP); indolizines; dihydroindolizines; tetrahydroindolizines; cascade process.

* Corresponding author. Tel.: (+33) 02-32-74-44-03; fax: (+33) 02-32-74-43-91; e-mail: adam.daich@univ-lehavre.fr

0040-4039/01/$ - see front matter
PII: S0040-4039(01)01054-1

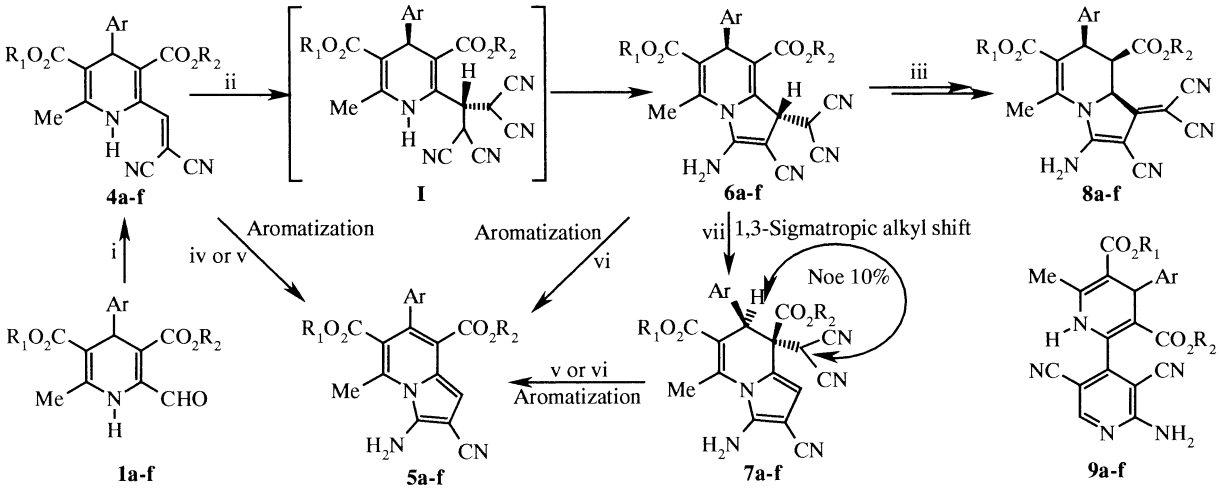
synthons (**1**) have now led to novel routes (cascade process) to the highly functionalized indolizines and their corresponding dihydroindolizines and tetrahydroindolizines **3** obtained by formation of a junction **a**.

In this perspective, we have reported recently a simple synthesis of substituted 3-amino-2-benzoylindolizine derivatives via the reaction of 2-formyl-1,4-DHPs (**1**) with 3-phenyl-3-oxopropanenitrile.[8] In this continuation we wish to report herein our preliminary finding towards reaction of 2-formyl-1,4-DHPs (**1**) and malonitrile as an activated methylene reagent.

As depicted in Scheme 2, the requisite 2-formyl-1,4-DHPs **1a–f** were easily prepared in 75–94% yield by acidic hydrolysis of the corresponding 2,2-dimethoxymethyl-1,4-DHPs according to the procedure reported by us,[7] and were subjected to the Knoevenagel reaction with various amounts of malonitrile and a catalytic amount of piperidine at room temperature. So, with a 2:1 ratio of malonitrile and 2-formyl-1,4-DHPs **1a–f** the reaction afforded neither the intermediate 2-dicyanovinyl-1,4-DHPs **4a–f** nor the 3-amino-2-cyanoindolizines **5a–f** and a pyridine derivatives **9a–f** as indicated in the literature.[9] In all cases, the reaction led to formation of crystalline products as a single stereoisomer, which were identified as the 3-amino-2-cyano-1-dicyanomethylene-1,7,8,8a-tetrahydroindolizines **8a–f** (Scheme 2) in 57–69% yield (Table 1).[10]

On the other hand, when the same reactions were conducted in refluxing ethanol, the latter tetrahydroindolizines **8a–f** were not observed and the reactions gave only the dark violet crystalline product which corresponds to the expected 3-amino-2-cyanoindolizines **5a–f** in 58–87% yield (Table 1).[11] Interestingly, these latter products were shown to be more stable to related aminoindolizines as reported in the literature.[12]

These reactions, leading in a one-pot procedure to indolizines **5a–f** and tetrahydroindolizines **8a–f**,[13] seem to proceed with a tandem Knoevenagel condensation/amino–nitrile cyclization followed by departure or not of one molecule of malonitrile, respectively. In order to rationalize the formation of the tetrahydroindolizines **8a–f** and the corresponding indolizines **5a–f**, our efforts were directed from the outset at adjusting the reaction conditions to prepare 2-dicyanovinyl-1,4-DHPs **4a–f**. In fact, treatment of 2-formyl-1,4-DHP derivatives **1a–f** with 1 equiv. of malonitrile in the absence of the alkaline catalysis (see conditions i, Scheme 2) afforded the expected Knoevenagel products **4a–f** in good yields. Amino–nitrile cyclization with additional piperidine as a catalyst at room temperature or reflux (see conditions

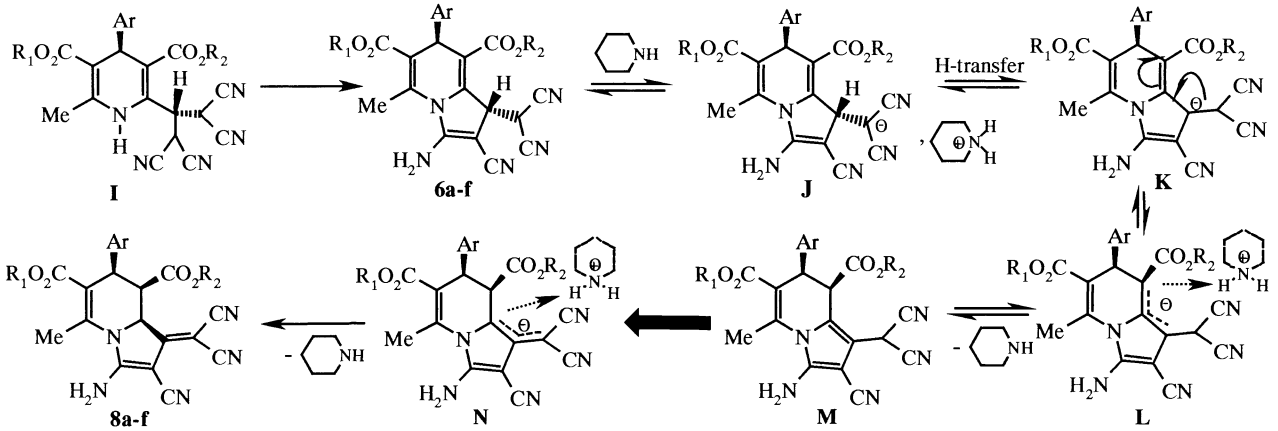


Scheme 2. *Reagents and conditions*: (i) 1 equiv. of $CH_2(CN)_2$, ethanol, rt, 2 h; (ii) 1 equiv. of $CH_2(CN)_2$, catalytic piperidine, ethanol, rt, 10 min; (iii) catalytic piperidine, ethanol, rt, 6 h; (iv) 1 equiv. of $CH_2(CN)_2$, catalytic piperidine, ethanol, rt, 3 h; (v) 1 equiv. of $CH_2(CN)_2$, catalytic piperidine, ethanol, reflux, 30 min; (vi) ethanol, reflux, 5 h; (vii) ethanol, rt, 3 h.

Table 1. Indolizines **5** and tetrahydroindolizines **8** obtained by reaction of malonitrile with 2-formyl-1,4-DHPs **1a–f** in alkaline catalysis

Compd	Aryl	R_1	R_2	Yield of **5** (%)[a]	Yield of **8** (%)[a]
a	3-NO_2Ph	*i*-Pr	Me	75	64
b	3-NO_2Ph	Et	Me	80	69
c	2-NO_2Ph	*i*-Pr	Me	87	57
d	2-NO_2Ph	Et	Me	83	65
e	2-C_4H_3S	Et	Et	60	64
f	3-Me-2-C_4H_2S	Me	Me	58	65

[a] The indicated yields were obtained after recrystallization from ethanol.



Scheme 3. Plausible sequential mechanism leading to tetrahydroindolizines **8** based on the intermediates *trans*-1,7-dihydroindolizines **6**.

ii, iii or v, Scheme 2) furnished dihydroindolizines **6a–f** and indolizines **5a–f** (in this case, the second equivalent of malonitrile was not necessary). These latter products were also obtained in the best manner by the elimination process from dihydroindolizines **6a–f** and **7a–f** in refluxing ethanol and in the presence or the absence of a catalyst (see conditions v or vi, Scheme 2).

At this stage, it is important to note that the diastereoselective transformations of *trans*-dihydroindolizines **6a–f** to *cis*-dihydroindolizines **7a–f**[14] (conditions vii, Scheme 2) suggested 1,3-sigmatropic migration involving an alkyl group shift. Moreover, on the basis of the proximity between H_7 and the proton of the dicyanomethyl group borne by C_8, which was established by NOE measurements (10%) (Scheme 2), we assess that the migrating dicyanomethyl fragment remains associated with the same face of the π system during the course of the migration. This feature, similar to those reported in the literature, is commonly known as a suprafacial process.[15]

If the formation of indolizines **5a–f** and dihydroindolizines **6a–f** could be explained easily by intramolecular amino–nitrile cyclization and/or malonitrile thermal or alkaline elimination (Scheme 1), Scheme 3 demonstrates a plausible mechanism of the formation of tetrahydroindolizines **8a–f**. So, because the methylene proton at C_1 of the common intermediates **6a–f** is readily acid, the resulting stable anionic charge in **J** is in rapid equilibrium with **K**. This latter intermediate, after a conjugation with **L**, is protonated stereoselectively to give the *cis*-dihydroindolizine **M**. At the present time, this structure has not been isolated, but it is probably converted rapidly to **8** in the same manner by proton transfer with piperidine assistance. It is worth mentioning that only the nitrogen bases, such as piperidine, morpholine, DABCO and triethylamine, constitute the catalyst of choice for these cascade-type reactions. Finally, for total clarification of this mechanism, studies using other bases and activated methylene reagents are now under investigation and the results will be reported in due course.

The structure elucidation of (7*S**,8*R**,8a*S**)-tetrahydroindolizines **8a–f** and 3-amino-2-cyanoindolizines **5a–f** was established by spectroscopic analyses, ^{1}H NMR (including DEPT, COSY and HETCOR programs), ^{13}C NMR and IR. The ^{1}H NMR spectra of **5a–f** showed a proton signal at $\delta = 6.6$–6.9 ppm,[13] typical for H_1 of 3-aminoindolizines.[16] No signal for the proton in position 4 of the 1,4-DHP system appearing classically at about $\delta = 5$ ppm was observed in these cases. Furthermore, the proton chemical-shift value of the amino group in compounds **8a–f** appeared 3 ppm downfield in comparison to the same one in the corresponding indolizines **5a–f**.[13] Especially diagnostic was also the appearance of the amino group stretch at 3260–3400 cm^{-1} and those of the cyano group at 2190–2230 cm^{-1} in the IR spectra of all compounds **8a–f** and **5a–f**.[13] This group was also indicated by the isolated signals at $\delta = 114$–116 ppm in ^{13}C NMR spectra of **8a–f** and **5a–f**. These data, the microanalyses, and the coupling GC–MS clearly confirm the proposed structure of products **8a–f** and **5a–f**.

On the other hand, the *cis* ring junction and relative stereochemical relationship within bicycles **8a–f** were established using selective NOE difference measurements. Large NOE enhancement between C_7, C_{8a} and C_8 methine hydrogens, and *o*-hydrogens of *m*-nitrophenyl group is in corroboration of our relative configuration determination.

The identity of the (7*S**,8*R**,8a*S**)-3-amino-2-cyano-1,7,8,8a-tetrahydroindolizines **8a–f** and 3-amino-2-cyanoindolizines **5a–f** was finally secured through an X-ray crystallographic determination of representative derivatives **8f**[17] (Fig. 1) and **5c**[18] (Fig. 2), respectively.

Furthermore, the *cis*-configuration of the three hydrogen atoms H_7, H_8 and H_{8a} of **8f** was additionally confirmed by X-ray analysis (Fig. 1). The crystal bond lengths C_1–C_2 of 1.389(3) Å, C_2–C_3 of 1.422(3) Å and C_3–N_4 of 1.351(2) Å indicated partly the multiple character for the C_1–C_2 and C_3–N_4 bonds allowing the existence of two mesomer forms of **8f** in crystalline state as illustrated in Fig. 3.

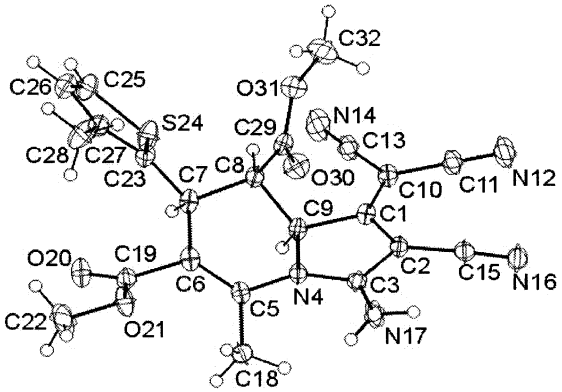


Figure 1. ORTEP view of the molecular structure of the tetrahydroindolizine **8f** (50% probability thermal ellipsoids).

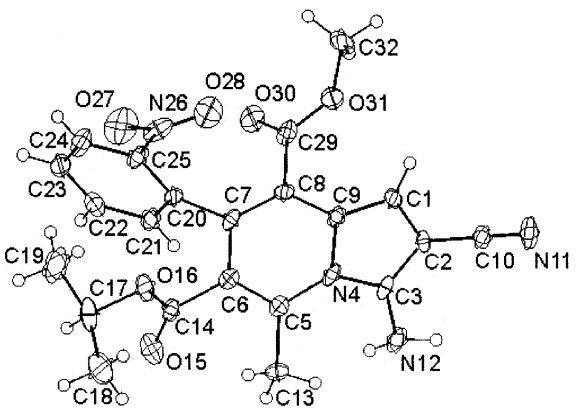


Figure 2. ORTEP view of the molecular structure of the indolizine **5c** (50% probability thermal ellipsoids).

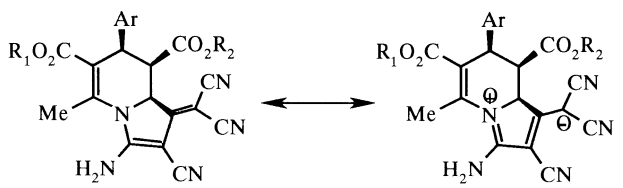


Figure 3. The two mesomer forms, neutral and dipolar, of structure **8f**.

In summary we have described in one (two or three) step(s) a new, short, straightforward and stereoselective access to functionalized indolizines with different degrees of unsaturation such as 7-aryl(or heteroaryl)-3-amino-2-cyanoindolizines, 7-aryl(or heteroaryl)-3-amino-2-cyano-1-dicyanomethylene-1,7-dihydroindolizines and 7-aryl(or heteroaryl)-3-amino-2-cyano-1-dicyanomethylidene - 1,7,8,8a - tetrahydroindolizines derivatives from easily available 2-formyl-1,4-DHPs. A probable mechanism for these cascade reactions is proposed and discussed.

Supplementary material

The data including chemical and physical characteristics of all products not described herein may be obtained at the following e-mail address: adam.daich@univ-lehavre.fr

Acknowledgements

The authors thank the Grant Agency of Slovak Republic, Grant No. 1/6095/99 and the Scientific Council of University of Le Havre for their financial support.

References

1. 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*, 1425–1433 and references cited therein.
2. Gubin, J.; Descamps, M.; Chatelain, P.; Nisato, D. Eur. Pat. Appl. EP 0,235,111, 1987; *Chem. Abstr.* **1988**, *109*, 6405b.
3. (a) Uchida, T.; Matsumoto, K. *Synthesis* **1976**, 209–236; (b) Dick, J. W.; Gibson, W. K.; Leaver, D.; Roff, J. E. *J. Chem. Soc., Perkin Trans. 1* **1981**, 3150–3157; (c) Daïch, A.; Ohier, P.; Decroix, B. *Tetrahedron Lett.* **1995**, *36*, 83–86.
4. For recent reports, see: (a) Katritzky, A. R.; Qiu, G.; Yang, B.; He, H. Y. *J. Org. Chem.* **1999**, *64*, 7618–7621 and references cited therein; (b) Kostik, E. I.; Abiko, A.; Oku, A. *J. Org. Chem.* **2001**, *66*, 2618–2623 and references cited therein; (c) Settambolo, R.; Caiazzo, A.; Lazzaroni, R. *Tetrahedron Lett.* **2001**, *42*, 4045–4048.
5. Chichibabin, A. E. *Ber. Dtsch. Chem. Ges.* **1927**, *60*, 1607–1617.
6. (a) Wei, X.; Hu, Y.; Li, T.; Hu, H. *J. Chem. Soc., Perkin Trans. 1* **1993**, 2487–2489; (b) Kakehi, A.; Ito, S.; Suga, H.; Yasuraoka, K. *Heterocycles* **2001**, *54*, 185–200.
7. (a) Chudík, M.; Marchalín, Š.; Knesl, P.; Daïch, A.; Decroix, B. *J. Heterocyclic Chem.* **2000**, *37*, 1549–1554; (b) Chudík, M.; Marchalín, Š.; Daïch, A.; Decroix, B. *Res. Adv. Synth. Org. Chem.* **2000**, *1*, 1–7.
8. (a) Pham-Huu, D. P.; Chudík, M.; Marchalín, Š. *Chem. Papers* **1997**, *51*, 242–243; (b) Chudík, M.; Marchalín, Š.; Havrilová, K. *Collect. Czech. Chem. Commun.* **1998**, *63*, 826–830; (c) Chudík, M.; Marchalín, Š.; Pham-Huu, D. P.; Humpa, O.; Friedl, Z. *Monatsh. Chem.* **1999**, *130*, 1241–1252.
9. Marco, J. L.; Chinchon, P. M. *Heterocycles* **1999**, *51*, 1130–1140.
10. General procedure for preparation of 3-amino-2-cyano-1,7,8,8a-tetrahydroindolizines **8a–f**. To a stirred mixture of **1a–f** (1 mmol) and malononitrile (2 mmol) in ethanol (10 mL) was added piperidine (1 drop). The mixture was stirred for 3 h at room temperature and after cooling to 0°C, the precipitate was filtered off and recrystallized from ethanol to afforded crystalline **8a–f** in 57–69% yield.
11. General procedure for preparation of 3-amino-2-cyanoindolizines **5a–f**. To a stirred mixture of **1a–f** (1 mmol) and piperidine (1 drop) in refluxing ethanol (5 mL) was added dropwise a solution of malononitrile (1 mmol) in ethanol (15 mL) over a period of 45 min. The reflux was continued for 2 h and after standing overnight in a fridge, the dark violet solid crystallized from ethanol. The expected indolizines **5a–f** were isolated in 58–87% yield.

12. (a) Hurst, J.; Melton, T.; Wibberley, D. G. *J. Chem. Soc.* **1965**, 2948–2955; (b) Melton, T.; Wibberley, D. G. *J. Chem. Soc. C* **1967**, 983–988.
13. Selected data for (7*S**,8*R**,8a*S**)-3-amino-2-cyano-1-dicyanomethylene-5-methyl-7-thiophen-2′-yl-1,7,8,8a-tetrahydroindolizine-6,8-dicarboxylic acid 6-isopropyl-8-methyl diester (**8a**): mp 298–300°C; ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.87 (bb, 2H, NH_2), 8.14 (d, 1H, $J_{4',5'}=7.4$ Hz, $H_{4'}$), 7.97 (s, 1H, $H_{2'}$), 7.69 (d, 1H, $J_{5',6'}=7.4$ Hz, $H_{6'}$), 7.64 (dd, 1H, $J_{4',5'}=J_{5',6'}=7.8$ Hz, $H_{5'}$), 5.44 (d, 1H, $J_{1,8a}=3.4$ Hz, H_{8a}), 4.90 (d, 1H, $J_{7,8}=8.0$ Hz, H_7), 4.71 (sept., 1H, $J=6.2$ Hz, CH of *i*-Pr), 3.90 (dd, 1H, $J_{7,8}=8.0$ Hz, $J_{8,8a}=3.7$ Hz, H_8), 3.30 (s, 3H, OMe), 3.16 (s, 3H, C_6-Me), 1.00, 0.59 (2d, 6H, Me of *i*-Pr); ^{13}C NMR (80 MHz, DMSO-d_6): δ 168.0, 165.0 (2 CO), 163.4 (C_1), 162.1 (C_3), 147.5 ($C_{1'}$), 141.7 ($C_{3'}$), 140.3 (C_5), 135.0 ($C_{6'}$), 130.1 ($C_{5'}$), 122.4 ($C_{4'}$), 122.0 ($C_{2'}$), 118.5 (C_6), 116.2, 114.2 (2CN), 112.0 (C_2), 76.0 (C=C(CN)$_2$), 67.9 (CH of *i*-Pr), 65.2 (C_{8a}), 51.7 (OMe), 46.1 (C_8), 42.4 (C_7), 21.3, 20.4 (2Me of *i*-Pr), 17.7 (Me); IR (KBr), ν/cm^{-1}: 3394, 3260 (NH), 3010, 2989, 2209, 2198 (CN), 1719, 1715 (C=O); EIMS *m*/*z* 502 ($M^{\bullet+}$). Anal. calcd for $C_{25}H_{22}N_6O_6$: C, 59.76; H, 4.41; N, 16.72. Found: C, 59.83; H, 4.52; N, 16.51%.
Selected data for 3-amino-2-cyano-5-methyl-7-thiophen-2′-ylindolizine-6,8-dicarboxylic acid 6-isopropyl-8-methyl diester (**5a**): mp 209–211°C; ^{1}H NMR (300 MHz, DMSO-d_6): δ 8.14 (d, 1H, $J_{4',5'}=7.5$ Hz, $H_{4'}$), 7.94 (s, 1H, $H_{2'}$), 7.70 (dd, 1H, $J_{4',5'}=J_{5',6'}=7.8$ Hz, $H_{5'}$), 7.60 (d, 1H, $J_{5',6'}=7.2$ Hz, $H_{6'}$), 6.75 (s, 1H, H_1), 5.87 (bb, 2H, NH_2), 4.70 (sept., 1H, $J=6.3$ Hz, CH of *i*-Pr), 3.57 (s, 3H, OMe), 2.87 (s, 3H, C_6-Me), 1.05, 0.88 (2d, 6H, Me of *i*-Pr); ^{13}C NMR (80 MHz, DMSO-d_6): δ 165.8, 165.0 (2CO), 147.3 ($C_{3'}$), 142.6 (C_3), 138.6 (C_5), 136.0 ($C_{1'}$), 135.3 ($C_{6'}$), 129.9 ($C_{2'}$), 125.7 (C_7), 123.3 (C_8), 122.8 ($C_{4'}$, $C_{5'}$), 121.8 (C_6), 119.7 (C_{8a}), 116.2 (CN), 102.0 (C_1), 84.6 (C_2), 69.2 (CH of *i*-Pr), 52.1 (OMe), 20.8 (2Me of *i*-Pr), 17.3 (Me); IR (KBr), ν/cm^{-1}: 3362, 3319 (NH), 2998, 2226 (CN), 1723, 1709 (C=O); EIMS *m*/*z* 436 ($M^{\bullet+}$). Anal. calcd for $C_{22}H_{20}N_4O_6$: C, 60.55; H, 4.62; N, 12.84. Found: C, 60.39; H, 4.57; N, 12.69%.
14. Selected data for *trans*-(7*R**,8*R**)-3-amino-2-cyano-8-cyanomethyl-5-methyl-7-thien-2′-yl-7,8-dihydroindolizine-6,8-dicarboxylic acid diethyl ester (**7e**): mp 182–185°C; ^{1}H NMR (300 MHz, DMSO-d_6): δ 1.06–1.24 (t, 3H, $J=7.2$ Hz, CH_3CH_2O), 2.72 (s, 3H, 5-CH_3), 4.11–4.18 (q, 2H, $J=7.2$ Hz, CH_3CH_2O), 5.01 (s, 1H, $CH(CN)_2$), 5.54 (s, 1H, H_7), 6.50 (bb, 2H, NH_2), 6.59 (s, 1H, H_1), 6.70 (d, 1H, $J_{4',5'}=3.0$ Hz, $H_{3'}$), 6.86 (1H, dd, $J_{3',4'}=J_{4',5'}=3.0$ Hz, $H_{4'}$), 7.35 (d, 1H, $J_{3',4'}=3.0$ Hz, $H_{5'}$); ^{13}C NMR (80 MHz, DMSO-d_6): δ 13.4–14.0 (CH_3CH_2O), 17.7 (5-CH_3), 31.1 (C-4), 41.7 ($CH(CN)_2$), 53.1 (C_8), 61.0–62.7 (CH_3CH_2O), 74.1 (C_2), 111.6–112.3 (C_6-C_{8a}), 114.2 (C_1-CN), 114.5–116.6 (CN), 126.4 ($C_{4'}$-$C_{5'}$), 127.2 ($C_{3'}$), 138.2 ($C_{2'}$), 145.4 (C_5), 148.6 (C_3), 164.9–166.7 (CO_2Et); IR (KBr), ν/cm^{-1}: 3365, 3365 (NH), 2989, 2877, 2205 (CN), 1708, 1639 (C=O); EIMS *m*/*z* 463 ($M^{\bullet+}$). Anal. calcd for $C_{23}H_{21}N_5O_4S$: C, 59.60; H, 4.57; N, 15.11. Found: C, 59.46; H, 4.51; N, 15.06%.
15. Hess, Jr., B. A.; Schaad, L. J.; Pancir, J. *J. Am. Chem. Soc.* **1985**, *107*, 149–154.
16. Troll, T.; Beckel, H.; Lentner-Bohm, C. *Tetrahedron* **1997**, *53*, 81–90.
17. Crystal structure of **8f**. Pale-yellow, 0.20×0.24×0.28 mm block, $C_{22}H_{21}N_5O_5S$, triclinic, $P\bar{1}$, $a=9.095(3)$, $b=9.187(3)$, $c=15.296(5)$ Å, $\alpha=74.61(2)$, $\beta=73.50(2)$, $\gamma=76.08(1)°$, $Z=2$. Stoe Stadi-4 diffractometer using Mo Kα radiation, $T=302(2)$ K, 9112 reflections measured up to $2\theta=52°$, 4562 independent data ($R_{int}=1.67\%$) for 310 refined parameters. The structure was refined on the basis of absorption-corrected data ($T_{min}=0.9508$, $T_{max}=0.9645$), using standard methods[19] with constraints for hydrogen atoms. Final *R* indices: $R_1=4.63\%$ for 3635 data having $I>2\sigma(I)$ and $wR_2=13.89\%$ for all data.
18. Crystal structure of **5c**. Dark-red, rod crystal, 0.55×0.075×0.075 mm, $C_{22}H_{20}N_4O_6$, monoclinic, $P2_1/c$, $a=9.712(2)$, $b=10.193(1)$, $c=20.943(2)$ Å, $\beta=96.17(1)°$, $Z=4$. Stoe Stadi-4 diffractometer using Mo Kα radiation, $T=301(2)$ K, 5120 reflections measured up to $2\theta=52°$, 4012 independent data ($R_{int}=2.71\%$) for 298 refined parameters. The structure was refined on the basis of absorption-corrected data ($T_{min}=0.9447$, $T_{max}=0.9922$), using standard methods[19] with constraints for hydrogen atoms. Final *R* indices: $R_1=7.34\%$ for 1747 data having $I>2\sigma(I)$ and $wR_2=19.77\%$ for all data.
19. Sheldrick, G. N. SHELX-97 User's Manual, University of Göttingen, Germany, 1997.