Facile Coupling of 2-(1-Ethylthioethenyl)pyrroles with Amines: A Route to 2-(1-Aminoethenyl)pyrroles and 1-Amino-3-iminopyrrolizines

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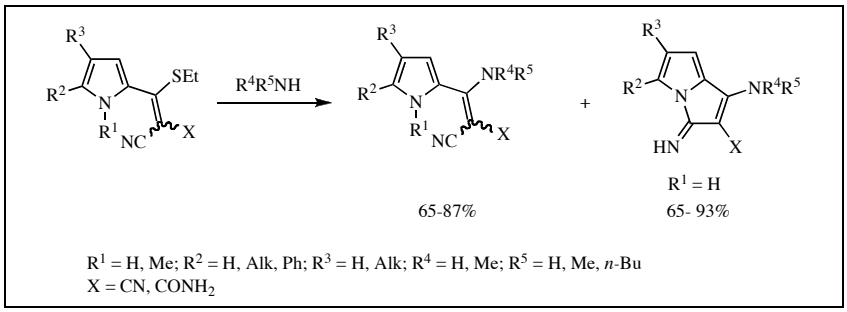

2-(2-Cyano-1-ethylthioethenyl)pyrroles are readily coupled (50-55°) with primary and secondary amines at the position 1 of the ethenyl moiety to eliminate ethanethiol and afford 2-(1-amino-2-cyanoethenyl)pyrroles and/or their cyclic isomers – functionalized 1-amino-3-iminopyrrolizines, in good to high yields.

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INTRODUCTION

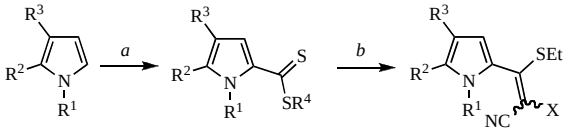
Functionalized vinylpyrroles are important building blocks in heterocyclic chemistry [1-3]. Among them, there are just a few [4] representatives with amino function at the double bond. Meanwhile, such pyrroles offer wide opportunities in design of new drugs and materials for optoelectronics, including porphyrine-like systems [3]. Their close derivatives and, in certain cases, cyclic isomers, pyrrolizines, are a scaffold of numerous alkaloids and some pheromones, though still remain a synthetic challenge [5].

Herein, we describe an approach to the synthesis of 2-(1-aminoethenyl)pyrroles and their cyclic isomers, 1-amino-3-iminopyrrolizines, by a non-catalyzed unusually mild coupling of 2-(2-cyano-1-ethylthioethenyl)pyrroles with primary and secondary amines.

We focus on the peculiarities and general features of this reaction and its further development to an expedient synthesis of so far inaccessible and mostly unknown but highly synthetically attractive 2-(1-aminoethenyl)pyrroles with strong electron-withdrawing substituents at the double bond and their cyclization products, functionalized pyrrolizines.

Starting 2-(2-cyano-1-ethylthioethenyl)pyrroles **1a-h**, including previously unknown **1g**,**h**, are available through 2-pyrrolecarbodithioates (Scheme I) [6-8].

Scheme I



a: for **1a-f**: CS_2, KOH, DMSO (20-25°, 2 hours), then EtI (20-25°, 2 hours) [6]; for **1g**,**h**: *n*-BuLi, CS_2, MeI [7]

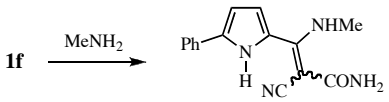
b: XCH_2CN, KOH, DMSO (110°, 1.5 hour), then EtI (20-25°, 2 hours) [8]

Pyrrole	R^1	R^2	R^3	X
1a	H	$(CH_2)_4$		CN
1b	H	Ph	H	CN
1c	H	*n*-Pr	Et	$CONH_2$
1d	H	*n*-Bu	*n*-Pr	$CONH_2$
1e	H	$(CH_2)_4$		$CONH_2$
1f	H	Ph	H	$CONH_2$
1g	Me	H	H	CN
1h	Me	H	H	$CONH_2$

RESULTS AND DISCUSSION

We found that 2-(2-carbamoyl-2-cyano-1-ethylthioethenyl)-5-phenylpyrrole **1f** with aqueous methylamine (50-55°, 0.5 hour) exchanges the ethylthio group for methylamine moiety to give 2-(2-carbamoyl-2-cyano-1-methylaminoethenyl)-5-phenylpyrrole **2f** in 74% yield (Scheme II).

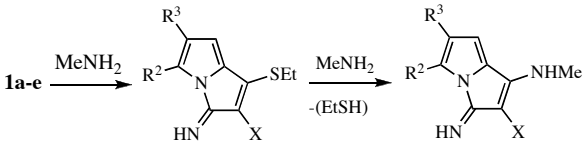
Scheme II



2f 74%

Meanwhile, pyrroles **1b-d**, as well as preliminarily reported [9] pyrroles **1a**,**e**, under the same conditions form 1-methylamino-3-iminopyrrolizines **4a-e** in 77-93% yield (Scheme III). The TLC monitoring (Silufol, eluent – diethyl ether) of the reaction indicates that its first stage is the cyclization of ethenylpyrroles **1a-e** to 1-ethylthio-3-imino-pyrrolizines **3a-e**. The second step is the coupling of pyrrolizines **3a-e** with methylamine to eliminate ethan-ethiol. Correspondingly, 1-aminopyrrolizines **4a-e** are synthesized from 1-ethylthio-3-iminopyrrolizines **3a-e**, readily prepared by cyclization of pyrroles **1a-e** in the presence of triethylamine [10], under the above conditions in 78-83% yield (Scheme III).

Scheme III

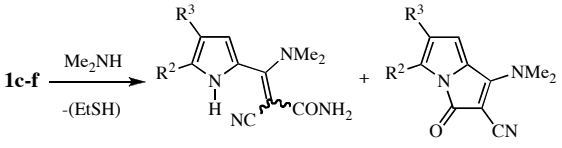


3a-e

4a-e
from **1a-e** - 77-93%
from **3a-e** - 78-83%

With dimethylamine, the major (or in the case of pyrrole **1f** exclusive) pathway is the coupling to yield 2-(1-amino-2-carbamoyl-2-cyanoethenyl)pyrroles **5c-f** along with minor amount of 3-pyrrolizinones **6c-e** (the **5c-e**: **6c-e** ratio is ~3-19:1, ^{1}H NMR) (Scheme IV).

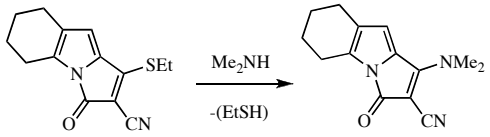
Scheme IV



5c-f 68-87% **6c-e**

The latter result from the intramolecular cyclization of pyrroles **5c-e**, that follows from the fact that the content of 3-pyrrolizinones **6c-e** in the reaction mixture increases. Thus, percentage of 3-pyrrolizinone **6d** in 15, 30 and 90 minutes changes from 0 to 5 and 25%, respectively. Apparently, the coupling of the intermediate 1-ethylthio-3-pyrrolizinones, which are products of intramolecular cyclization of pyrroles **1c-e** with dimethylamine, is not ruled out. The ease of such an exchange (35°, 5 minutes) is demonstrated by the synthesis of 1-dimethylamino-3-pyrrolizinone-2-carbonitrile **6e** from corresponding 1-ethylthio-3-pyrrolizinone-2-carbonitrile **7** (Scheme V), available from 4,5,6,7-tetrahydroindole-2-carbodithioate and ethyl cyanoacetate [10].

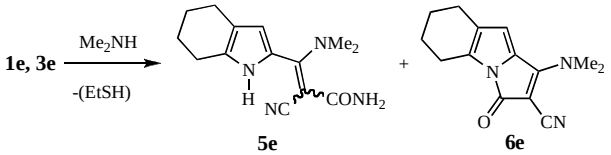
Scheme V



7 **6e** 85%

Pyrrolizine **3e**, when allowed to react with dimethyl-amine, undergoes ring-opening (50-55°, 0.5 hour) affording aminoethenylpyrrole **5e** and aminopyrrolizinone **6e** in the same ratio (7:1) as in the reaction of pyrrole **1e** with dimethylamine (Scheme VI).

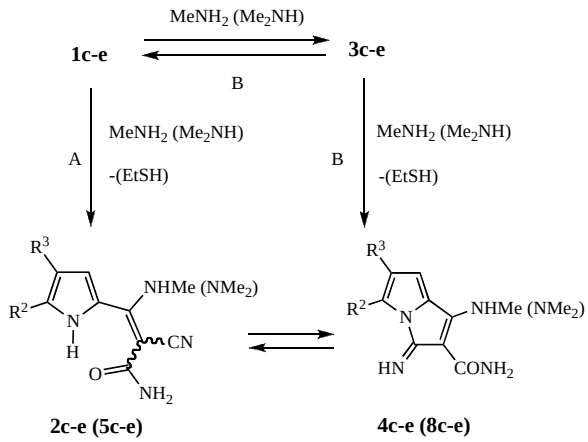
Scheme VI



5e **6e**

Thus, pyrroles **1c-e** react with aqueous methyl- and dimethylamine differently: with the former first the cyclization to 1-ethylthiopyrrolizines **3c-e** takes place and afterwards the exchange with amine occurs, whereas with the latter the ring-closure is not the case. Evidently, there are two competing pathways of the coupling: the direct ethylthio-amino exchange in ethenylpyrroles **1c-e** to form aminoethenylpyrroles **2c-e**, **5c-e** (A) and intramolecular cyclization of ethenylpyrroles **1c-e** to 1-ethylthio-3-iminopyrrolizines **3c-e** followed by the ethylthio-amino exchange (B) (Scheme VII).

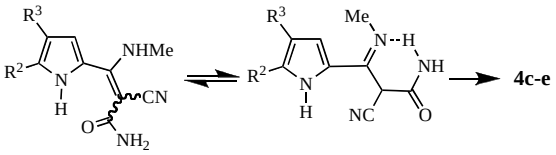
Scheme VII



2c-e (5c-e) **4c-e (8c-e)**

Pyrroles **2c-e** are capable of cyclization to pyrrolizines **4c-e** in their tautomeric form (Scheme VIII).

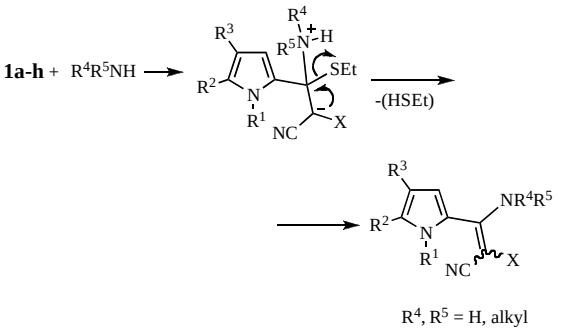
Scheme VIII



2c-e

The most likely mechanism of the coupling observed seems to be zwitter-ion formation in the first step by the nucleophilic attack of amine at the electron-deficient site of the vinyl group, *i.e.* position 1, and the further intramolecular thiol elimination *via* four-membered transition state or in an intermolecular manner with the participation of another molecule of the zwitter-ion or/and with electrophilic assistance of the solvent (alcohol, water) (Scheme IX).

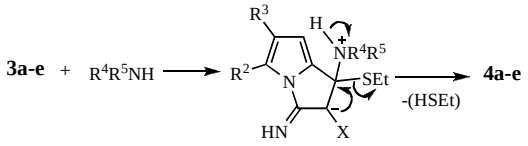
Scheme IX



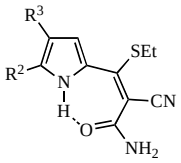
A similar mechanism may be operative in the coupling of amines with 1-ethylthio-3-pyrrolizines **3a-e** to yield pyrrolizines **4a-e** (Scheme X).

An obvious driving force of the coupling is a known stronger p-π-conjugation of the lone electron pare of the amine nitrogen with the double bond than that of the sulfide sulfur.

Scheme X



The difference in behavior of 2-(2,2-dicyanoethenyl)-pyrroles **1a**,**b** and 2-(2-carbamyl-2-cyanoethenyl)pyrroles **1c-f** is due to the existence of the latter solely in *E*-configuration with *syn*-disposition of the carbamoyl and NH groups (^{1}H NMR) stabilized by the intramolecular H-bond, which is unfavorable for cyclization:



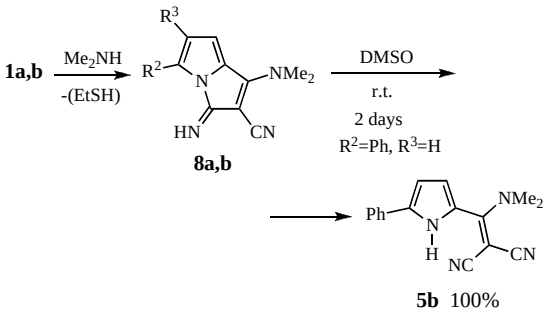
1c-f

2-(2-Carbamoyl-2-cyano-1-ethylthioethenyl)pyrroles **1c-f** cyclize not as easy as the corresponding dicyanoethenyl-pyrroles **1a**,**b** [10].

The fact that pyrrole **1f** couples with both methyl- and dimethylamine to furnish only corresponding 2-(1-aminoethenyl)pyrroles **2f**, **5f** indicates its lower reactivity in the intramolecular cyclization. Actually, it does not cyclize on reflux in methanol with triethylamine (under these conditions pyrroles **1a**,**c-e** are converted to pyrrolizines within 0.5-4 hours).

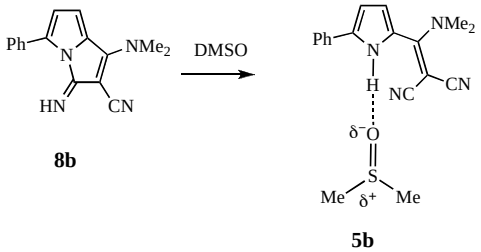
Pyrroles **1a**,**b** with dimethylamine form 1-dimethyl-amino-3-iminopyrrolizines **8a**,**b** in 90 and 85% yield, respectively (Scheme XI).

Scheme XI



Interestingly, pyrrolizine **8b**, which is stable upon storage in crystalline state, when dissolved in DMSO-d_6, undergoes the ring-opening to 2-(1-dimethylamino-2,2-dicyanoethenyl)-pyrrole **5b** (2 days, r.t., 100% conversion). A partial ring-opening **8b**→**5b** is also observed on recrystallization of **8b** from ethanol, while pyrrolizine **8a** is stable under analogous conditions. Evidently, the role of DMSO in the complete conversion of **8b** to **5b** is the H-bonding with pyrrole and the stabilization of highly polar [11] open form **5b** by dipole-dipole interaction with the polar solvent (Scheme XII).

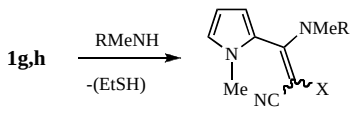
Scheme XII



Incomplete transformation **8b→5b** in ethanol is explained by a lower basicity and polarity of the latter as compared to DMSO. A better stabilization of the 2-phenyl-substituted **5b** than **5a** (Schemes XI, XII) agrees with a higher acidity of its pyrrole NH function (stronger H-bonding) [12].

2-(2-Cyano-1-ethylthioethenyl)-1-methylpyrroles **1g**,**h** with aqueous methyl- and dimethylamine (50-55°, 0.5 hour) afford 2-(1-amino-2-cyanoethenyl)-1-methylpyrroles **2h**, **5g**,**h** in 65-73% yield (Scheme XIII).

Scheme XIII



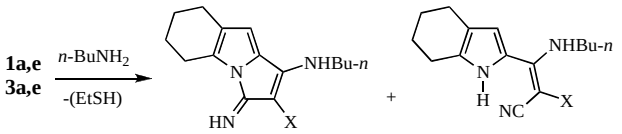
2h, 5g,h

2h: R = H, X = $CONH_2$;
5: R = Me; X = CN (**g**), $CONH_2$ (**h**)

In the case of pyrrole **1g**, the reaction is accompanied by hydrolysis of one of the nitrile groups to yield 2-(2-carbamoyl-2-cyano-1-methylaminoethenyl)-1-methyl-pyrrole **2h**.

The reaction of pyrroles **1a**,**e** with *n*-butylamine in aqueous ethanol (1:1, v/v) is slower (reflux, 2-4 hours) and less selective than that with methylamine. Thus, pyrrole **1a** and its cyclic isomer, pyrrolizine **3a**, give a mixture of 1-*n*-butylaminopyrrolizine **9a** and 2-(1-*n*-butylamino-2,2-dicyanoethenyl)pyrrole **10a**, 19:1 (Scheme XIV).

Scheme XIV

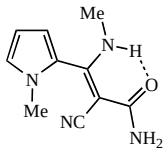


9a,e **10a,e**

When the reaction is carried out in ethanol, only pyrrolizine **9a** is formed (80% yield). Likewise (ethanol-water, 1:1,v/v, 4 hours), pyrrole **1e** gives aminopyrrolizine **9e** (65% yield) and aminoethenylpyrrole **10e**, 5:1 (Scheme XIV)

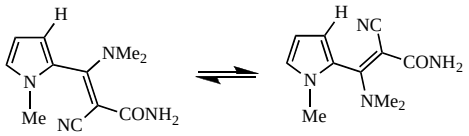
Di(*n*-butyl)amine, due to its bulky substituents, does not couple neither with ethenylpyrrole **1e** nor with imino-pyrrolizine **3e**. Its reaction with pyrrole **1e** (ethanol-water, 1:1, v/v, reflux, 4 hours) results in pyrrolizine **3e**, *i.e.* this amine acts just as a basic catalyst. Under the same conditions, when reacting with di(*n*-butyl)amine, pyrrolizine **3e** is recovered almost quantitatively.

Pyrroles **1h** and **5h** consisted of *E*- and *Z*-isomers (1:5, and 1:3 respectively), while pyrrole **2h** was isolated as the *Z*-isomer only, probably due to stabilization by the intramolecular hydrogen bonding which can not be formed in pyrrole **5h**:



2h

The isomers of **2h** and **5h** were assigned using the ^1H NMR spectra: in *Z*-**5h**, signals of H-3 and the pyrrole Me are downfield shifted due to the CN bond anisotropy and their values are close to those of the same hydrogen in pyrrole **5g**:



***Z*-5 h**

In *E*-**1h**, a downfield shift due to CN bond anisotropy is observed for the CH_2 hydrogens of the ethylthio group. Their chemical shift (2.70 ppm) corresponds to that of pyrrole **1g**.

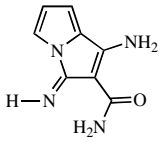
Aminoiminopyrrolizines **4a-e**, **9a**,**e** were isolated in the form of the individual isomers with the unknown configuration at the C=N bond. In view of the further synthetic interest to iminopyrrolizines, the potential building blocks capable of stereo-dependendent heterocylization to highly condensed heterocycles, it was a rewarding task and a structural challenge to determine the configuration of **9e** as an illustrative representative of this series.

To solve this problem we used a method [13] based on the measurement of the one-bond ^{13}C-^{13}C spin-spin coupling constants, $^1J(C,C)$, showing marked stereochemical dependence upon the orientation of the nitrogen lone pair in azomethines.

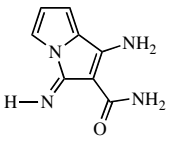
Experimental measurement of $^1J(C,C)$ involving the α-imino carbon of the individual isomer of **9e** has been carried out from the INADEQUATE spectrum accumulated overnight while calculations of this coupling in the four possible forms of **9e** were performed at the SOPPA (*Second-Order Polarization Propagator Approach*) level [14] taking into account all four coupling contributions, namely, Fermi contact, J_{FC}, spin–dipolar, J_{SD}, diamagnetic spin–orbital, J_{DSO}, and paramagnetic spin–orbital, J_{PSO} (Table 1). The model structure of **9e** was used since the original molecule is too large for the high-level *ab initio* calculations.

Table 1

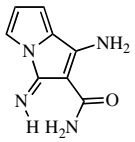
Spin-spin coupling constants $^1J(C,C)$ of the model of 2-carbamoyl-3-iminopyrrolizines calculated at the SOPPA level [a]



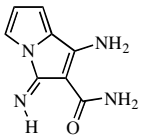
Z-s-cis



Z-s-trans



E-s-cis

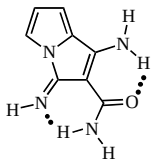


E-s-trans

Isomer	Conformation	Relative energy, kcal/mol	J_{DSO}	J_{PSO}	J_{SD}	J_{FC}	J	J experimental
Z	*s-cis*	0.0	0.4	-2.4	0.5	74.2	72.7	71.0
	s-trans	12.4	0.4	-1.9	0.5	79.9	78.9	
E	*s-cis*	2.9	0.4	-2.2	0.5	61.9	60.6	
	s-trans	4.5	0.4	-1.9	0.5	63.4	62.4	

[a] All couplings and their contributions are in Hz. In the calculations of $^1J(C,C)$ the coupled carbons were specified with the cc-pVDZ-Cs basis set [15-17] while the rest of the elements were assigned with cc-pVDZ [15] with no polarization *p*-functions on hydrogens. The equilibrium HF/6-311G** geometries were used throughout. All calculations were performed without symmetry constraints assuming the C_1 symmetry point group.

It is obvious from the data presented in Table 1 that calculated $^1J(C,C)$ expectedly show marked stereospecificity in respect to the orientation of the nitrogen lone pair being 10-15 Hz larger in *Z*-isomer. On the other hand, $^1J(C,C)$ also depends upon the orientation of the C=O bond of the $CONH_2$ group in different conformations of both isomers being 2-6 Hz larger in *s-trans* conformations. Comparison of these theoretical results with experiment leaves no doubt that 1-*n*-butylaminopyrrolizine **9e** obtained as shown in Scheme XIV is the individual isomer with *Z* configuration at the C=N bond adopting predominant *s-cis* conformation of the $CONH_2$ moiety. These results are in line with the thermodynamic reasoning based on the fact that it is this form, *Z-s-cis*, which is most favorable, *i.e.* having the lowest total energy calculated at the MP2//HF/6-311G** level (see Table 1). It is noteworthy that predominant *Z-s-cis* form is ideally planar while the higher-energy other three, *Z-s-trans*, *E-s-cis* and *E-s-trans*, show noticeable out-of-plane deviations (*ca* 15-30°). The stabilization of the *Z-s-cis* form is likely due to the following multiple H-bonding:



CONCLUSION AND OUTLOOK

Thus, an efficient route to earlier inaccessible aminoethenylpyrroles and aminopyrrolizines through a facile non-catalyzed coupling of available 2-(2-cyano-1-ethylthioethenyl)pyrroles with primary and secondary amines has been developed. No obvious limitation are envisaged for this approach to be valid for coupling of the functionalized ethenylpyrrole moiety with molecules of pharmacologically and synthetically important functionalized amines, including aminoacids and amino-substituted heterocycles.

EXPERIMENTAL

IR spectra of compounds synthesized (400-4000 cm^{-1}) were recorded on a Bruker IFS-25 instrument in potassium bromide pellets. ^1H and ^{13}C NMR spectra were taken on Bruker DPX 250 [250.13 (^1H) and 62.9 (^{13}C) MHz, respectively] and Bruker DPX 400 [400 (^1H) MHz] spectrometers in dimethylsulfoxide-d_6 and deuteriochloroform with HMDS as internal reference.

Structure of compounds synthesized was determined by ^1H and ^{13}C NMR spectroscopy with the use of 2D NMR techniques. Assignment of ^{13}C resonances was done using 2D heteronuclear HSQC [18] and HMBC [19] correlation methods.

In 2D HMBC pulse sequence, the delays optimized for the direct coupling constant $^1J(H,C)$ = 145 Hz and long-distance coupling constant $^nJ(H,C)$ = 5 Hz were used.

Methyl- and dimethylamines were used as 2 *M* aqueous solutions.

Analyses of reaction mixtures and purity control of compounds obtained were carried out using TLC on Silufol UV-254 plates, eluent: diethyl ether:ethanol, 10:1. Carbon–carbon coupling constants were measured at 25° in deuteriochloroform using the INADEQUATE [20] pulse sequence adjusted for J = 70 Hz on a Bruker AVANCE 400 MHz spectrometer in a 10 mm broadband probe at 300 K in deuteriochloroform with HMDS as an internal standard. Settings for the INADEQUATE experiments were as follows: 90° pulse length, 12–14 μs; spectral width, 10–15 kHz; acquisition time, 4–6 s; relaxation delay, 6–10 s; characteristic delay τ = 1/4J, 3.6 ms; digital resolution 0.05–0.1 Hz/pt; accumulation time, 12 h.

Geometrical optimizations were performed with the GAMESS code [21] while calculations of spin–spin coupling

constants have been carried out using the DALTON package [22] as described in the text.

2-(2,2-Dicyano-1-ethylthioethenyl)-1-methylpyrrole (1g). To a suspension of malononitrile (600 mg, 9 mmoles) and KOH (500 mg, 9 mmoles) in DMSO (30 ml) stirred at room temperature for 0.5 hour, methyl 1-methyl-2-pyrrolecarbodithioate (1030 mg, 6 mmoles) was added. The reaction mixture was heated at 110° for 1.5 hour, cooled to room temperature, then ethyl iodide (940 mg, 6 mmoles) was added. The mixture was stirred for 2 hours, diluted with brine (100 ml) and extracted with ether. After removal of ether, the residue was recrystallized from ethanol to give 1110 mg (85%) of pyrrole **1g** as yellow solid, mp 68°; ir (potassium bromide): 2217, 1533, 1481, 1472, 1454, 1402, 1374, 1306, 1267, 1246, 1054, 945, 750, 688, 605 cm^{-1}; ^1H nmr (400 MHz, deuteriochloroform): δ 1.22 (t, 3H, Me, J = 7.3 Hz); 2.79 (q, 2H, SCH_2, J = 7.3 Hz), 3.75 (s, 3H, NMe), 6.30 (dd, 1H, H-4, J = 3.9, 2.6 Hz), 6.69 (dd, 1H, H-3, J = 3.9, 1.7 Hz), 7.00 ppm (dd, 1H, H-5, J = 2.6, 1.7 Hz); ^{13}C nmr (62.5 MHz, deuteriochloroform): δ 14.4, 29.7, 35.4, 76.3, 110.8, 113.4, 114.0, 118.9, 125.2, 131.8, 168.6 ppm. *Anal.* Calcd. for $C_{11}H_{11}N_3S$: C, 60.80; H, 5.10; N, 19.34; S, 14.76. Found C, 60.52; H, 5.06; N, 19.02; S, 14.81.

2-(2-Carbamoyl-2-cyano-1-ethylthioethenyl)-1-methylpyrrole (1h). To a suspension of cyanoacetamide (660 mg, 9 mmoles) and KOH (500 mg, 9 mmoles) in DMSO (30 ml) stirred at room temperature for 0.5 hour, methyl 1-methyl-2-pyrrolecarbodithioate (1030 mg, 6 mmoles) was added. The reaction mixture was heated at 110° for 1.5 hour, cooled to room temperature, then ethyl iodide (940 mg, 6 mmoles) was added. The mixture was stirred for 2 hours and then diluted with brine (100 ml). The crystals formed were collected by filtration, dried and recrystallized from ethanol to give 1060 mg (75%) of pyrrole **1h** (*E*/*Z*, 1:5) as yellow solid, mp 192°; ir (potassium bromide): 3394, 3296, 3176, 2210, 1681, 1617, 1546, 1501, 1382, 1306, 1236, 939, 793, 732 cm^{-1}; *E*-isomer: ^1H nmr (400 MHz, deuteriochloroform): δ 1.17 (t, 3H, Me, J = 7.5 Hz), 2.70 (q, 2H, SCH_2, J = 7.5 Hz), 3.55 (s, 3H, NMe), 5.46 (br s, 2H, $CONH_2$), 6.28 (dd, 1H, H-4, J = 3.8, 2.6 Hz), 6.42 (dd, 1H, H-3, J = 3.8, 1.7 Hz), 6.90 ppm (dd, 1H, H-5, J = 2.6, 1.7 Hz); ^{13}C nmr (62.5 MHz, deuteriochloroform): δ 14.6, 28.5, 34.5, 102.5, 112.1, 114.7, 116.7, 124.5, 128.4, 161.3, 162.8 ppm. *Z*-isomer: ^1H nmr (400 MHz, deuteriochloroform): δ 1.13 (t, 3H, Me, J = 7.5 Hz), 2.38 (q, 2H, SCH_2, J = 7.5 Hz), 3.61 (s, 3H, NMe), 5.65 (br s, 1H, $CONH_2$), 6.17 (br s, 1H, $CONH_2$), 6.23 (dd, 1 H, H-4, J = 3.8, 2.7 Hz), 6.29 (dd, 1H, H-3, J = 3.8, 1.7 Hz,), 6.80 ppm (dd, 1H, H-5, J = 2.7, 1.7 Hz); ^{13}C nmr (62.5 MHz, deuteriochloroform): δ 13.6, 28.1, 34.2, 101.7, 109.0, 112.1, 117.3, 125.6, 126.0, 163.9, 168.4 ppm. *Anal.* Calcd. for $C_{11}H_{13}N_3OS$: C, 56.15; H, 5.57; N, 17.86; S, 13.62. Found: C, 56.12; H, 5.60; N, 17.68; S, 13.41.

General procedure for coupling of 2-(2-cyano-1-ethylthioethenyl)pyrroles 1a-f with methylamine. A suspension of 2-(2-cyano-1-ethylthioethenyl)pyrrole **1a-f** (0.40 mmoles) in aqueous methylamine solution (5 ml) was heated at 50-55° for 0.5 hour. The suspension turned homogeneous and then crystalline precipitate formed. The crystals were collected by filtration, washed with water and dried. Recrystallization from ethanol gave 3-imino-1-methylaminopyrrolizine **4a-e** and 2-(2-carbamoyl-2-cyano-1-methylaminoethenyl)-5-phenylpyrrole (**2f**). The TLC monitoring (Silufol, eluent – diethyl ether) of the reaction indicates that its first stage is the cyclization of ethenylpyrroles **1a-e** to 1-ethylthio-3-iminopyrrolizines **3a-e** [yellow spots of ethenylpyrroles **1a-e** (R_f 0.90) turn to red spots of 1-ethylthio-3-iminopyrrolizines **3a-e** (R_f 0.95 for pyrrolizines **3a**,**b** and R_f 0.15 for pyrrolizines **3c-e**)]. Then red spots (eluent – diethyl ether : ethanol, 10:1 (v/v) of 1-ethylthio-3-iminopyrrolizines **3a-e** turn to orange spots of 1-amino-3-iminopyrrolizines **4a-e** (R_f 0.5-0.6).

2-(2-Carbamoyl-2-cyano-1-methylaminoethenyl)-5-phenylpyrrole (2f). This compound was obtained as white solid, 79 mg (74%), mp 176-177°; ir (potassium bromide): 3483, 3382, 3248, 2185, 1651, 1599, 1357, 790, 759 cm^{-1}; ^1H nmr (400 MHz, deuteriochloroform): δ 3.15 (d, 3H, NMe, J = 4.9 Hz), 5.49 (br s, 2H, $CONH_2$), 6.60 (dd, 1H, H-3, J = 3.7, 2.1 Hz), 6.70 (dd, 1H, H-4, J = 3.7, 2.1 Hz), 7.30 (m, 1H, Ph-H_p), 7.40 (m, 2H, Ph-H_m), 7.55 (m, 2H, Ph-H_o), 9.18 (br s, 1H, N*H*Me), 10.78 ppm (br s, 1H, NH); ^{13}C nmr (62.5 MHz, dimethylsulfoxide-d_6): δ 32.0, 70.9, 106.9, 114.7, 121.1, 122.2, 124.4, 126.8, 128.8, 131.8, 134.8, 161.9, 170.2 ppm. *Anal.* Calcd for $C_{15}H_{14}N_4O$: C, 67.65; H, 5.30; N, 21.04. Found: C, 67.51; H, 5.14; N 20.82.

3-Imino-1-(methylamino)-5,6,7,8-tetrahydro-3*H*-pyrrolo-[1,2-*a*]indole-2-carbonitrile (4a). This compound was obtained as yellow solid, 80 mg (88%), mp 215-216°; ir (potassium bromide): 3276, 3292, 2190, 2205, 2179, 1653, 1576, 1536, 1297, 791, 760 cm^{-1}; ^1H nmr (400 MHz, deuteriochloroform): δ 1.75 (m, 2H, CH_2-6), 1.82 (m, 2H, CH_2-7), 2.49 (m, 2H, CH_2-8), 2.85 (m, 2H, CH_2-5), 3.23 (br s, 3H, NMe), 6.09 (br s, 1H, =NH), 6.26 (s, 1H, H-3), 7.66 ppm (br s, 1H, N*H*Me). *Anal.* Calcd. for $C_{13}H_{14}N_4$: C, 69.00; H, 6.24; N, 24.76. Found: C, 68.78; H, 6.15; N, 24.96.

3-Imino-1-(methylamino)-5-phenyl-3*H*-pyrrolizine-2-carbonitrile (4b). This compound was obtained as yellow solid, 76 mg (77%), mp 202-203°; ir (potassium bromide): 3375, 3292, 2206, 2189, 2179, 1651, 1615, 1536, 1297, 1157, 758 cm^{-1}; ^1H nmr (400 MHz, dimethylsulfoxide-d_6): δ 3.27 (br s, 3H, NMe), 6.60 (d, 1H, H-4, J = 4.0 Hz), 6.85 (d, 1H, H-3, J = 4.0 Hz), 7.31 (m, 1H, Ph-H_p), 7.40 (m, 2H, Ph-H_m), 7.55 (m, 2H, Ph-H_o), 7.80 (br s, 1H, N*H*Me), 9.54 ppm (br s, 1H, =NH); ^{13}C nmr (100 MHz, deuteriochloroform): δ 32.84, 81.70, 108.13, 117.4, 124.1, 124.9, 127.6, 128.9, 131.2, 137.4, 159.5, 166.8 ppm. *Anal.* Calcd. for $C_{15}H_{12}N_4$: C, 72.56; H, 4.87; N, 22.57. Found: C, 72.47; H, 4.79; N, 22.62.

6-Ethyl-3-imino-1-(methylamino)-5-*n*-propyl-3*H*-pyrrolizine-2-carboxamide (4c). This compound was obtained as yellow solid, 97 mg (93%), mp 191-192°; ir (potassium bromide): 3358, 3263, 1653, 1625, 1589, 1570, 1426, 1280, 1153, 821, 797, 769 cm^{-1}; ^1H nmr (400 MHz, deuteriochloroform): δ 1.00 (m, 3H, CH_3 of propyl), 1.16 (m, 3H, CH_3 of ethyl), 1.65 (m, 2H, CH_2-2 of propyl), 2.39 (m, 2H, CH_2 of ethyl), 2.71 (m, 2H, CH_2-1 of propyl), 3.21 (d, 3H, NMe, J = 5.4 Hz), 5.10 (br s, 1H, $CONH_2$), 6.23 (s, 1H, H-3), 7.15 (br s, 1H, =NH), 8.12 (br s, 1H, $CONH_2$), 8.96 ppm (br s, 1H, N*H*Me); ^{13}C nmr (100 MHz, deuteriochloroform): δ 14.0, 15.4, 18.7, 21.2, 26.7, 31.8, 89.5, 110.9, 126.6, 129.4, 131.9, 157.1, 157.8, 168.8 ppm. *Anal.* Calcd. for $C_{14}H_{20}N_4O$: C, 64.59; H, 7.74; N, 21.52. Found: C, 64.47; H, 7.56; N, 21.62.

5-*n*-Butyl-3-imino-1-(methylamino)-6-*n*-propyl-3*H*-pyrrolizine-2-carboxamide (4d). This compound was obtained as yellow solid, 104 mg (90%), mp 154-155°; ir (potassium bromide): 3364, 3268, 1623, 1584, 1571, 1425, 1273, 1153, 773 cm^{-1}; ^1H nmr (400 MHz, deuteriochloroform): δ 0.95 (m, 6H, CH_3 of butyl and propyl), 1.41 (m, 2H, CH_2-3 of butyl), 1.58 (m, 4H, CH_2-2 of butyl and propyl), 2.33 (m, 2H, CH_2-1 of propyl), 2.72 (m, 2H, CH_2-1 of butyl), 3.20 (d, 3H, NMe, J = 5.1 Hz), 5.07 (br s, 1H, $CONH_2$), 6.21 (s, 1H, H-3), 7.15 (br s, 1H, =NH),

8.17 (br s, 1H, $CONH_2$), 8.94 ppm (1H, br s, N*H*Me); ^{13}C nmr (100 MHz, deuteriochloroform): δ 13.8, 14.0, 22.7, 24.1, 24.6, 27.6, 30.0, 31.7, 89.6, 111.5, 126.6, 127.5, 132.7, 157.1, 157.9, 168.9 ppm. *Anal.* Calcd. for $C_{16}H_{24}N_4O$: C, 66.64; H, 8.39; N, 19.43. Found: C, 66.42; H, 8.23; N, 19.65.

3-Imino-1-(methylamino)-5,6,7,8-tetrahydro-3*H*-pyrrolo-[1,2-*a*]indole-2-carboxamide (4e). This compound was obtained as orange solid, 89 mg (91%), mp 210-211°; ir (potassium bromide): 3330, 3149, 1636, 1620, 1589, 1574, 1523, 1478, 1427, 1272, 1137, 787, 738 cm^{-1}; ^1H nmr (400 MHz, deuteriochloroform): δ 1.76 (m, 2H, CH_2-6), 1.88 (m, 2H, CH_2-7), 2.49 (m, 2H, CH_2-8), 2.77 (m, 2H, CH_2-5), 3.19 (d, 3H, NMe, J = 5.1 Hz), 5.09 (br s, 1H, $CONH_2$), 6.17 (s, 1H, H-3), 7.12 (br s, 1H, =NH), 8.03 (br s, 1H, $CONH_2$), 8.90 ppm (br s, 1H, N*H*Me); ^{13}C nmr (100 MHz, deuteriochloroform): δ 22.5, 22.7, 22.9, 23.1, 31.8, 89.4, 110.5, 124.7, 126.2, 130.5, 156.9, 158.2, 168.8 ppm. *Anal.* Calcd. for $C_{13}H_{16}N_4O$: C, 63.92; H, 6.60; N, 22.93. Found: C, 63.57; H, 6.34; N, 22.62.

General procedure for coupling of 2-(2-carbamoyl-2-cyano-1-ethylthioethenyl)pyrroles 1c-e with dimethylamine. A suspension of 2-(2-carbamoyl-2-cyano-1-ethylthioethenyl)-pyrrole **1c-e** (0.40 mmoles) in aqueous dimethylamine (5 ml) was heated at 50-55° for 0.5 hour. The suspension turned homogeneous and then gave crystalline precipitate. The crystals were immediately collected by filtration, washed with water and dried, then washed with ether and recrystallized from ethanol to produce 3-pyrrolizinones **6c**,**e**. This procedure was invalid to isolate pure 3-pyrrolizinone **6d**, so it was characterized in the reaction mixture by its ^1H nmr. The filtrate was extracted with chloroform, washed with water and dried over $MgSO_4$. The residue after chloroform removal was recrystallized from aqueous acetone (1:1, v/v) to give 2-(1-dimethylaminoethenyl)pyrrole **5c-e**.

2-(2-Carbamoyl-2-cyano-1-dimethylaminoethenyl)-4-ethyl-5-*n*-propylpyrrole (5c). This compound was obtained as cream-colored solid (acetone:H_2O, 1:1, v/v), 73 mg (68%, purity 98%), mp 135-136°; ir (potassium bromide): 3423, 3201, 2185, 1630, 1609, 1549, 1386, 835, 772 cm^{-1}; ^1H nmr (400 MHz, deuteriochloroform): δ 0.95 (t, 3H, CH_3 of propyl, J = 7.1 Hz), 1.15 (t, 3H, CH_3 of ethyl, J = 7.5 Hz), 1.62 (m, 2H, CH_2-2 of propyl), 2.40 (q, 2H, CH_2 of ethyl, J = 7.5 Hz), 2.56 (t, 2H, CH_2-1 of propyl, J = 7.1 Hz), 3.17 (s, 6H, NMe_2), 5.34 (br s, 2H, $CONH_2$), 6.44 (d, 1H, H-3, J = 2.4 Hz), 8.89 ppm (1H, br s, NH); ^{13}C nmr (62.5 MHz, deuteriochloroform): δ 13.8, 15.3, 18.8, 23.1, 27.9, 43.9, 69.1, 117.6, 120.4, 123.2, 125.4, 136.7, 161.0, 167.9 ppm. *Anal.* Calcd for $C_{15}H_{22}N_4O$: C, 65.67; H, 8.08; N, 20.42. Found: C, 65.33; H, 8.00; N 20.21.

1-(Dimethylamino)-6-ethyl-3-oxo-5-*n*-propyl-3*H*-pyrrolizine-2-carbonitrile (6c). This compound was obtained as yellow solid, 10 mg (10%), mp 174-175°; ir (potassium bromide): 2194, 1716, 1617, 1506, 1409, 1299, 747 cm^{-1}; ^1H nmr (400 MHz, dimethylsulfoxide-d_6): δ 0.86 (t, 3H, CH_3 of propyl, J = 7.1 Hz), 1.10 (t, 3H, CH_3 of ethyl, J = 7.5 Hz), 1.66 (m, 2H, CH_2-2 of propyl), 2.33 (q, 2H, CH_2 of ethyl, J = 7.5 Hz), 2.67 (t, 2H, CH_2-1 of propyl, J = 7.1 Hz), 3.33 (s, 3H, NMe_2), 3.47 (s, 3H, NMe_2), 6.71 ppm (s, 1H, H-3); ^{13}C nmr (62.5 MHz, deuteriochloroform): δ 13.6, 15.2, 18.0, 21.7, 25.5, 41.6, 43.4, 66.1, 117.2, 117.5, 124.0, 129.9, 134.3, 157.2, 164.1 ppm. *Anal.* Calcd. for $C_{15}H_{19}N_3O$: C, 70.01; H, 7.44; N, 16.33. Found: C, 69.78; H, 7.39; N, 16.69.

5-*n*-Butyl-2-(2-carbamoyl-2-cyano-1-dimethylaminoethenyl)-4-*n*-propylpyrrole (5d). This compound was obtained as cream-colored solid (acetone:H_2O, 1:1, v/v), 105 mg (87%), mp 164-165°; ir (potassium bromide): 3391-3183, 2190, 2172, 1651, 1630, 1605, 1538, 1485, 1389, 1377, 1269, 1009 cm^{-1}; ^1H nmr (400 MHz, deuteriochloroform): δ 0.95 (m, 6H, CH_3 of butyl and propyl) 1.32 (m, 2H, CH_2-3 of butyl), 1.55 (m, 4H, CH_2-2 of butyl and propyl), 2.38 (m, 2H, CH_2-1 of propyl), 2.60 (m, 2H, CH_2-1 of butyl), 3.18 (s, 6H, NMe_2), 5.37 (br s, 2H, $CONH_2$), 6.46 (d, 1H, H-3, J = 2.7 Hz), 9.00 ppm (br s, 1H, NH); ^{13}C nmr (62.5 MHz, dimethylsulfoxide-d_6): δ 13.9, 22.4, 24.1, 25.8, 27.9, 31.9, 44.0, 68.8, 118.5, 120.5, 123.3, 123.8, 137.0, 161.0, 167.5 ppm. *Anal.* Calcd. for $C_{17}H_{26}N_4O$: C, 67.52; H, 8.67; N, 18.53. Found: C, 67.39; H, 8.49; N, 18.23.

5-*n*-Butyl-1-(dimethylamino)-3-oxo-6-*n*-propyl-3*H*-pyrrolizine-2-carbonitrile (6d). ^1H nmr (400 MHz, deuteriochloroform): δ 0.95 (m, 6H, CH_3 of butyl and propyl), 1.32 (m, 2H, CH_2-3 of butyl), 1.55 (m, 4H, CH_2-2 of butyl and propyl), 2.38 (m, 2H, CH_2-1 of propyl), 2.76 (m, 2H, CH_2-1 of butyl), 3.38 (s, 3H, NMe_2), 3.59 (s, 3H, NMe_2), 6.25 (s, 1H, H-3).

2-(2-Carbamoyl-2-cyano-1-dimethylaminoethenyl)-4,5,6,7-tetrahydroindole (5e). This compound was obtained as white solid, 70 mg (68%), mp 219-220°; ir (potassium bromide): 3360, 3231, 3173, 2184, 1644, 1611, 1541, 1490, 1362, 1155, 1103, 812 cm^{-1}; ^1H nmr (400 MHz, deuteriochloroform): δ 1.77 (4H, m, CH_2-5,6), 2.51 (m, 2H, CH_2-4), 2.65 (m, 2H, CH_2-7), 3.21 (s, 6H, NMe_2), 6.42 (d, 1H, H-3, J = 2.4 Hz), 8.56 ppm (br s, 1H, NH); ^{13}C nmr (62.5 MHz, dimethylsulfoxide-d_6): δ 21.7, 21.9, 22.3, 22.4, 41.6, 43.5, 71.5, 115.8, 116.9, 118.5, 121.7, 133.6, 160.0, 166.3 ppm. *Anal.* Calcd. for $C_{14}H_{18}N_4O$: C, 65.09; H, 7.02; N, 21.69. Found: C, 65.39; H, 6.89; N, 21.44.

1-(Dimethylamino)-3-oxo-5,6,7,8-tetrahydro-3*H*-pyrrolo-[1,2-*a*]indole-2-carbonitrile (6e). A suspension of 3-pyrrolizinone **7** (103 mg, 0.40 mmoles) in aqueous dimethylamine (5 ml) was heated for 5 min at 30-35° and then cooled to room temperature. Crystals formed were filtered off, washed with water, dried and recrystallized from aqueous acetone (1:1) to give 82 mg (85%) of **6e** as yellow crystals, mp 185-186°; ir (potassium bromide): 3116, 2201, 2190, 1710, 1611, 1505, 1429, 1289, 742 cm^{-1}; ^1H nmr (400 MHz, deuteriochloroform): δ 1.75 (m, 4H, CH_2-6,7), 2.43 (m, 2H, CH_2-8), 2.79 (m, 2H, CH_2-5), 3.35 (s, 3H, NMe_2), 3.57 (s, 3H, NMe_2), 6.19 ppm (s, 1H, H-3); ^{13}C nmr (100 MHz, deuteriochloroform): δ 21.5, 21.9, 22.2, 22.4, 42.1, 43.4, 68.2, 116.1, 117.1, 124.4, 125.6, 134.5, 158.7, 164.0 ppm. *Anal.* Calcd. for $C_{14}H_{15}N_3O$: C, 69.69; H, 6.27; N, 17.41. Found: C, 69.48; H, 6.19; N, 17.19.

2-(2-Carbamoyl-2-cyano-1-dimethylaminoethenyl)-5-phenylpyrrole (5f). A suspension of 2-(2-cyano-1-ethylthioethenyl)-pyrrole **1f** (119 mg, 0.40 mmoles) in aqueous dimethylamine (5 ml) was heated for 0.5 hour at 50-55°. The suspension turned to a homogeneous solution, from which crystals were then formed. The latter were filtered off, washed with water and dried to give 77 mg (69%) of pyrrole **5f** as white solid, mp 228-229°; ir (potassium bromide): 3364, 3248, 3169, 2184, 1642, 1611, 1538, 1517, 1477, 1366, 1134, 799, 759 cm^{-1}; ^1H nmr (400 MHz, dimethylsulfoxide-d_6): δ 2.96 (br s, 6H, NMe_2), 6.69 (br s, 4H, H-3,4, $CONH_2$), 7.26 (m, 1H, Ph-H_p), 7.41 (m, 2H, Ph-H_m), 7.79 (m, 2H, Ph-H_o), 11.79 ppm (br s, 1H, NH); ^{13}C nmr (62.5, MHz, dimethylsulfoxide-d_6): δ 43.2, 73.47, 107.8, 117.9, 122.8, 124.6, 127.1, 128.8, 131.6, 136.3, 159.1, 165.9 ppm. *Anal.* Calcd. for $C_{16}H_{16}N_4O$: C, 68.55; H, 5.75; N, 19.99. Found: C, 68.39; H, 5.49; N, 20.18.

General procedure for coupling of 2-(2-cyano-1-ethylthioethenyl)pyrroles 1a,b with dimethylamine. A suspension of 2-(2-cyano-1-ethylthioethenyl)pyrrole **1a,b** (0.40 mmoles) in

aqueous dimethylamine solution (5 ml) was heated for 0.5 hour at 50-55°. During that time, the suspension turned to a homogeneous solution, from which a crystalline precipitate was then formed. The crystals were collected by filtration, washed with water and dried. Recrystallization from ethanol gave 1-dimethylamino-3-iminopyrrolizine **8a,b**.

1-(Dimethylamino)-3-imino-5,6,7,8-tetrahydro-3*H*-pyrrolo-[1,2-*a*]indole-2-carbonitrile (8a). This compound was obtained as yellow solid, 87 mg (90%), mp 197-198°; ir (potassium bromide): 3248, 2201, 2195, 1641, 1609, 1511, 1439, 1418, 1278, 1184, 1002, 901, 885, 713 cm^{-1}; ^1H nmr (250 MHz, deuteriochloroform): δ 1.72 (m, 4H, CH_2-6,7), 2.46 (m, 2H, CH_2-8), 2.78 (m, 2H, CH_2-5), 3.28 (s, 3H, NMe_2), 3.41 (s, 3H, NMe_2), 6.15 (s, 1H, 3-H), 7.95 ppm (br s, 1H, NH); ^{13}C nmr (62.5 MHz, deuteriochloroform): δ 22.4, 23.1, 23.4, 41.8, 42.8, 68.1, 112.4, 118.2, 125.1, 126.1, 133.2, 155.6, 159.3 ppm. *Anal.* Calcd for $C_{14}H_{16}N_4$: C, 69.97, H, 6.71; N, 23.31. Found: C, 69.78; H, 6.65; N, 23.66.

1-(Dimethylamino)-3-imino-5-phenyl-3*H*-pyrrolizine-2-carbonitrile (8b). This compound was obtained as yellow solid, 89 mg (85%), mp 167-168°; ir (potassium bromide): 3254, 2190, 1642, 1609, 1470, 1447, 1421, 1166, 896, 788, 756, 714, 694 cm^{-1}; ^1H nmr (250 MHz, dimethylsulfoxide-d_6): δ 3.39 (s, 3H, NMe_2), 3.47 (s, 3H, NMe_2) 6.57 (d, 1H, H-4, J = 4.0 Hz), 6.81 (d, 1H, H-3, J = 4.0 Hz), 7.35 (m, 3H, Ph-$H_{m,p}$), 7.90 (m, 2H, Ph-H_o), 8.19 ppm (br s, 1H, NH); ^{13}C nmr (62.5 MHz, dimethylsulfoxide-d_6): δ 42.1, 42.8, 69.9, 112.9, 116.2, 117.8, 124.9, 127.7, 129.0, 130.4, 131.2, 138.1, 154.6, 159.3 ppm. *Anal.* Calcd for $C_{16}H_{14}N_4$: C, 73.26; H, 5.38; N, 21.36. Found: C, 73.09; H, 5.49; N, 21.69.

2-(2,2-Dicyano-1-dimethylaminoethenyl)-5-phenylpyrrole (5b). ^1H nmr (400 MHz, dimethylsulfoxide-d_6): δ 3.15 (s, 6H, NMe_2); 6.39 (m, 1H, H-3), 6.71 (m, 1H, H-4), 7.32 (m, 1H, Ph-H_p), 7.45 (m, 2H, Ph-H_m), 7.78 (m, 2H, Ph-H_o), 11.98 ppm (br s, 1H, NH); ^{13}C nmr (62.5 MHz, dimethylsulfoxide-d_6): δ 43.4, 69.9, 108.4, 118.0, 118.8, 119.2, 122.3, 128.0, 128.6, 128.9, 131.2, 137.8, 162.4 ppm.

General procedure for coupling of 2-(2-cyano-1-ethylthio-ethenyl)-1-methylpyrroles 1g,h with aqueous methyl- and dimethylamine. A suspension of 2-(2-cyano-1-ethylthio-ethenyl)-1-methylpyrrole **1g,h** (0.40 mmoles) in aqueous amine solution (5 ml) was heated for 0.5 hour at 50-55°. Then the reaction mixture was cooled to room temperature and extracted with chloroform. After removal of chloroform, the residue was recrystallized from ethanol to give 2-(2-cyano-1-aminoethenyl)-1-methylpyrrole **2h, 5g,h**.

2-(2-Carbamoyl-2-cyano-1-methylaminoethenyl)-1-methyl-pyrrole (2h). This compound was obtained as white solid, 60 mg (73%), mp 212-213°; ir (potassium bromide): 3469-3185, 2189, 1635, 1583, 1488, 1461, 1417, 1401, 1354, 1334, 1290, 870, 835, 736 cm^{-1}; ^1H nmr (400 MHz, deuteriochloroform): δ 2.85 ppm (d, 3H, NH*M*e, J = 5.0 Hz), 3.64 (s, 3H, NMe), 5.23 (br s, 1H, $CONH_2$), 5.78 (br s, 1H, $CONH_2$), 6.23 (dd, 1H, H-4, J = 3.8, 2.7 Hz), 6.35 (dd, 1H, H-3, J = 3.8, 1.7 Hz), 6.79 (dd, 1H, H-5, J = 2.7, 1.7 Hz), 10.48 (br s, 1H, N*H*Me) ppm; ^{13}C nmr (62.5 MHz, deuteriochloroform): δ 31.9, 34.5, 73.9, 109.0, 112.5, 120.4, 122.9, 125.6, 163.2, 170.2 ppm. *Anal.* Calcd. for $C_{10}H_{12}N_4O$: C, 58.81; H, 5.92; N, 27.43. Found: C, 59.09; H, 5.79; N, 27.41.

2-(2,2-Dicyano-1-dimethylaminoethenyl)-1-methylpyrrole (5g). This compound was obtained as white solid, 52 mg (65%), mp 116-117°; ir (potassium bromide): 2206, 2193, 1556, 1535, 1480, 1465, 1444, 1403, 1304, 1114, 1058, 750, 716 cm^{-1}; ^1H nmr (400 MHz, deuteriochloroform): δ 2.99 (br s, 3H, NMe_2), 3.43 (br s, 3H, NMe_2), 3.67 (s, 3H, NMe), 6.25 (dd, 1H, H-4, J = 3.9, 2.7 H,), 6.49 (dd, 1H, H-3, J = 3.9, 1.7 Hz), 6.88 ppm (dd, 1H, H-5, J = 2.7, 1.7 Hz); ^{13}C nmr (62.5 MHz, deuteriochloroform): δ 34.6, 43.1, 53.1, 109.8, 116.5, 116.6, 117.2, 123.4, 128.6, 163.1 ppm. *Anal.* Calcd. for $C_{11}H_{12}N_4$: C, 65.98; H, 6.04; N, 27.98. Found: C, 65.79; H, 6.23; N, 28.14.

2-(2-Carbamoyl-2-cyano-1-dimethylaminoethenyl)-1-methyl-pyrrole (5h). This compound was obtained as white solid, 60 mg (69%), mp 174-175°; ir (potassium bromide): 3427, 3140, 2181, 1659, 1608, 1554, 1534, 1437, 1394, 1341, 1205, 1122, 1058, 779, 732, 642, 608 cm^{-1}; *E*-isomer: ^1H nmr (deuteriochloroform): δ 3.19 (br s, 6H, NMe_2), 3.57 (s, 3H, NMe), 5.19 (br s, 2H, $CONH_2$), 6.24 (dd, 1H, H-4, J = 3.8, 2.6 Hz), 6.37 (dd, 1H, H-3, J = 3.8, 1.4 Hz), 6.85 ppm (1H, dd, H-5, J = 2.6, 1.4 Hz); ^{13}C nmr (deuteriochloroform): δ 34.6, 43.3, 75.9, 109.4, 115.3, 122.3, 125.1, 128.1, 160.4, 167.2 ppm. *Z*-isomer: ^1H nmr (deuteriochloroform): δ 3.08 (s, 6H, NMe_2), 3.69 (s, 3H, NMe), 5.53 (br s, 2H, $CONH_2$), 6.24 (dd, 1H, H-4, J = 3.8, 2.6 Hz), 6.50 (dd, 1H, H-3, J= 3.8, 1.7 Hz), 6.87 ppm (dd, 1H, H-5, J = 2.6, 1.7 Hz); ^{13}C nmr (deuteriochloroform): δ 34.6, 43.9, 74.5, 109.5, 117.0, 120.4, 126.1, 128.4, 160.4, 165.5 ppm. *Anal.* Calcd. for $C_{11}H_{14}N_4O$: C, 60.53; H, 6.47; N, 25.67. Found: C, 60.29; H, 6.33; N, 25.36.

General procedure for coupling of 2-(2-cyano-1-ethylthio-ethenyl)pyrroles 1a,e and 1-ethylthio-3-iminopyrrolizines 3a,e with *n*-butylamine. A mixture of 2-(2-cyano-1-ethylthio-ethenyl)pyrrole **1a,e** or 1-ethylthio-3-iminopyrrolizine **3a,e** (0.39 mmoles) and *n*-butylamine (142 mg, 1.94 mmoles) in 20 ml of ethanol (or in a water-ethanol solution, 1:1, v/v) was heated at 70° for 4 hours. After cooling, the crystals that formed were collected by filtration, dried and recrystallized from benzene to give pyrrolizine **9a,e**.

1-(*n*-Butylamino)-3-imino-5,6,7,8-tetrahydro-3*H*-pyrrolo-[1,2-*a*]indole-2-carbonitrile (9a). This compound was obtained as yellow solid, 84 mg (80%), mp 148°; ir (potassium bromide): 3255, 2205, 2188, 1646, 1610, 1575, 1408, 1182, 805 cm^{-1}; ^1H nmr (400 MHz, deuteriochloroform): δ 0.97 (m, 3H, Me), 1.45 (m, 2H, CH_2-3 of butyl), 1.69 (m, 2H, CH_2-2 of butyl), 1.71 (m, 2H, CH_2-6), 1.82 (m, 2H, CH_2-7), 2.48 (m, 2H, CH_2-8), 2.85 (m, 2H, CH_2-5), 3.50 (m, 2H, NCH_2), 5.54 (br s, 1H, =NH), 6.22 (s, 1H, H-3), 7.70 ppm (br s, 1H, N*H*Bu); ^{13}C nmr (400 MHz, deuteriochloroform): δ 13.7, 20.0, 22.4, 23.1, 23.2, 23.4, 31.5, 45.8, 95.5, 111.9, 124.8, 125.3, 133.8, 157.5, 158.4 ppm. *Anal.* Calcd for $C_{16}H_{20}N_4$: C, 71.61; H, 7.51; N, 20.88. Found: C, 71.49; H, 7.67; N, 20.62.

1-(*n*-Butylamino)-3-imino-5,6,7,8-tetrahydro-3*H*-pyrrolo-[1,2-*a*]indole-2-carboxamide (9e). This compound was obtained as yellow solid, 73 mg (65%), mp 184°; ir (potassium bromide): 3326, 3157, 1634, 1617, 1586, 1569, 1520, 1471, 1272, 1167, 1146, 973, 952, 780 cm^{-1}; ^1H nmr (400 MHz, deuteriochloroform): δ 0.95 (3H, m, Me) 1.44 (2H, m, CH_2-3 of butyl), 1.68 (2H, m, CH_2-2 of butyl), 1.76 (2H, m, CH_2-6), 1.86 (2H, m, CH_2-7), 2.46 (2H, m, CH_2-8), 2.82 (2H, m, CH_2-5), 3.42 (2H, m, NCH_2), 5.01 (1H, br s, $CONH_2$), 6.12 (1H, s, H-3), 7.12 (1H, br s, =NH), 8.00 (1H, br s, $CONH_2$), 9.05 ppm (1H, br s, N*H*Bu); ^{13}C nmr (100 MHz, deuteriochloroform): δ 13.8, 20.1, 22.5, 22.6, 22.9, 23.1, 31.9, 45.1, 89.2, 110.0, 124.3, 126.1, 129.9, 156.7, 157.1, 168.7 ppm. *Anal.* Calcd for $C_{16}H_{22}N_4O$: C, 67.11; H, 7.74; N, 19.56. Found: C, 66.73; H, 7.92; N, 19.48.

Reaction of 1e, 3e with di(*n*-butyl)amine. A mixture of pyrrole **1e** or pyrrolizine **3e** (107 mg, 0.39 mmoles) and di(*n*-

butyl)amine (251 mg, 1.94 mmoles) in 20 ml of ethanol (or in a water-ethanol solution, 1:1, v/v) was heated at 70° for 4 hours. After cooling, the reaction mixture was diluted with water and extracted with chloroform. The extracts were washed with water and dried over $CaCl_2$. The residue left after chloroform removal had ^1H nmr spectra identical to those of 1-ethylthio-3-iminopyrrolizine **3e** [10].

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