Synthesis and some properties of *N*-unsubstituted pyrrolo[2,1-*c*]-1,3-diazacycloalkano[1,2-*a*]pyrazinones

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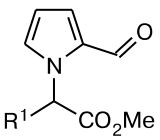
Reactions of methyl 2-(2-formyl-1*H*-pyrrol-1-yl)alkanoates with unsubstituted aliphatic 1,2-, 1,3-, and 1,4-diamines gave *N*-unsubstituted pyrrolo[2,1-*c*]-1,3-diazacycloalkano[1,2-*a*]-pyrazinones. Some of them show ring—chain tautomerism. Transformations of these compounds led to a number of novel heterocyclic systems: 2,10-dihydro-3*H*,5*H*-imidazo[1,2-*a*]-pyrrolo[1,2-*d*]pyrazines, 2,3,4,11-tetrahydro-6*H*-pyrrolo[1′,2′:4,5]pyrazino[1,2-*a*]pyrimidines, 1,2,3,5,6,10b-hexahydroimidazo[1,2-*a*]pyrrolo[2,1-*c*]pyrazines, 1,3,4,6,7,11b-hexahydro-2*H*-pyrrolo[2′,1′:3,4]pyrazino[1,2-*a*]pyrimidines, and 2,3,4,5,6,7-hexahydro-1*H*-pyrrolo[2,1-*c*]-[1,4,7]triazacycloundecin-8(9*H*)-one.

Key words: aliphatic diamines, formyl-containing acid esters, amino lactams, reduction, quantum chemical calculations, keto-enol tautomerism, ring—chain tautomerism, pyrrole-containing heterocyclic systems, X-ray diffraction analysis, NMR spectroscopy.

Earlier,[1] it has been found that reactions of methyl 2-(2-formyl-1*H*-pyrrol-1-yl) carboxylates (**1**) with *N*-substituted diamines afford novel heterocyclic structures **2a**. The goal of the present work was to obtain their *N*-unsubstituted analogs **2b** and examine some of their chemical properties.



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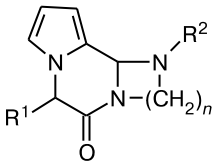

2a,b

2: R^2 = Alk, CH_2Ar (**a**), H (**b**)

For the synthesis of heterocycles **2b**, we employed formyl-containing acid esters **1** and unsubstituted aliphatic diamines as the starting materials. Tricyclic structures **3** were obtained from esters **1** and 1,2-diaminoethane (Scheme 1). The reaction mixtures containing a 10% molar excess of the diamine were refluxed in ethanol for 1 h. The products were isolated by crystallization at −4 °C.

The ^{1}H NMR spectra of structures **3** show a characteristic doublet at δ 3.8—5.2 due to the H(10b) ($^3J_{H(10b),NH}$ = = 11.3—12.4 Hz). Structure **3a** was examined by X-ray diffraction (Fig. 1).

Reactions of esters **1** with 1,3-diaminopropanes under the same conditions as for the synthesis of compounds **3** gave heterocycles **4** (see Scheme 1). A thorough study of these pyrrole derivatives revealed that the ^{1}H NMR spectra of some of them contain, apart from the main set of signals corresponding to the tricyclic forms **4a**—**d**, a second set of signals due to bicyclic imino lactams **5**. The characteristic signal for tricyclic forms **4** is a broadened singlet or a doublet at δ 5.2—5.3 due to the H(11b) proton. The characteristic signals for compounds **5** are a singlet at δ 8.0—8.2 for the imine H(1) proton and a triplet at δ 7.5—7.7 ($^3J_{H(6),C(5)H_2}$ = 6.1 Hz) for the amide proton (H(6)). The coexistence of tri- and bicyclic forms **4** and **5** in solutions suggests that these compounds undergo ring—chain tautomerism, which has not been documented hitherto for such systems. According to the ^{1}H NMR data for some of compounds **4**, the ratio of the tautomers depends on the chemical structures of the compounds, only slightly varying with the solvent (DMSO and $CDCl_3$ were used) (Table 1). In solutions of compounds **4a** and **4b** (with an unsubstituted pyrazine ring, R^1 = H) in DMSO at room temperature, the percentage of the imine form **5** is somewhat higher (10—13%) than that in solutions of heterocycles **4c** and **4d** (R^1 = Me). For compound **4d** in DMSO, the imino lactam percentage is ~5%, while a solution of compound **4c** contains the tricyclic form only. Nearly the same ratios were observed in $CDCl_3$. It should

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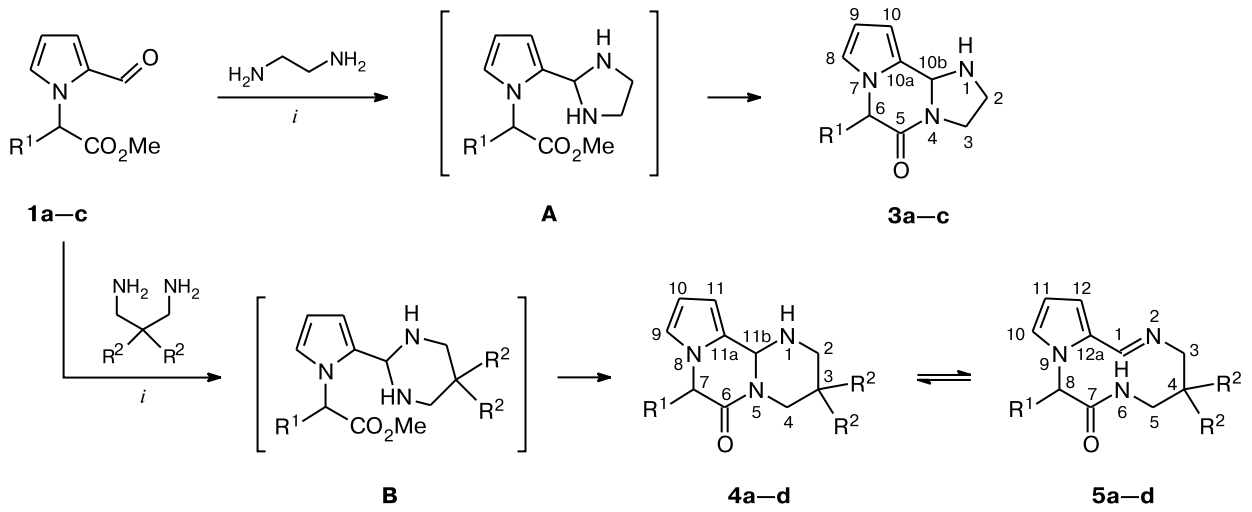
Scheme 1



1, 3: R^1 = H (**a**), Me (**b**), CH_2Ph (**c**)
4, 5: $R^1 = R^2$ = H (**a**); R^1 = H, R^2 = Me (**b**); R^1 = Me, R^2 = H (**c**); $R^1 = R^2$ = Me (**d**)

Reagents and conditions: *i*. EtOH, reflux, 1 h.

also be noted that the ratio of tautomers **4** and **5** is independent of the exposure time of the solutions (*i.e.*, an equilibrium ratio of these forms is reached immediately upon the dissolution of the corresponding solids).

Although compounds **4a**,**b**,**d** in solutions are actually mixtures of tautomers **4** and **5**, there is convincing evidence that their crystals contain tricyclic forms only. For compound **4b**, this was unambiguously confirmed by X-ray diffraction (Fig. 2). For the other compounds **4**, the presence of pure tricyclic forms in the crystals is suggested by their definite melting points. In addition, the IR spectra of crystalline compounds **4** in KBr pellets are very similar to the IR spectra of compounds **3** and **4c**, which show no tautomerism in solutions.

According to ^{1}H NMR data, heterocyclic compounds **3** and **4** with $R^1 \neq H$ are formed as pure diastereomers. Interconversions of the diastereomers, which have been observed[1] for substituted heterocycles **2a**, occurred under neutral conditions only for structure **4c** in $CDCl_3$. For compounds **3b** and **4d**, they were detected in the corresponding solutions only in the presence of a protic (CF_3COOH) or Lewis acid ($AlCl_3$). The interconversions of the diastereomers can be explained by two types of tautomerism (Scheme 2): keto-enol (pathway *a*) and ring—chain

Table 1. Ratio of tautomers **4** and **5** (**4** : **5**) from the ^{1}H NMR spectra of their solutions in DMSO-d_6 and $CDCl_3$ **4**, **5**

4, **5**	**4** : **5**	
	DMSO-d_6	$CDCl_3$
a	9 : 1	10 : 1
b	7 : 1	8 : 1
c	*	*
d	18 : 1	18 : 1

* Only tricyclic tautomer **4**.

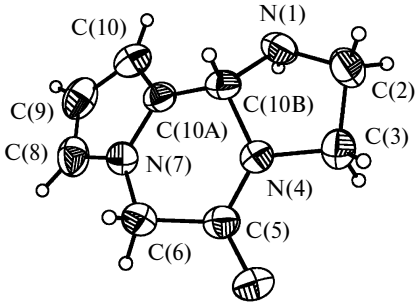


Fig. 1. General view of structure **3a** in the crystal with atomic thermal displacement ellipsoids (p = 50%).

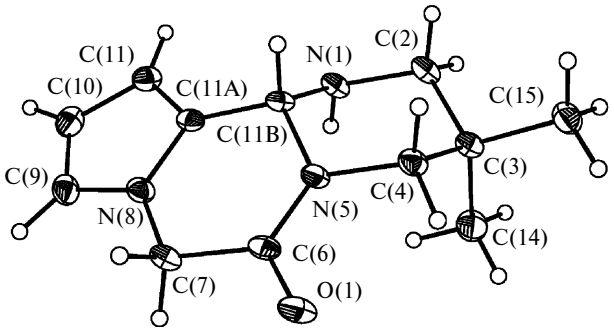
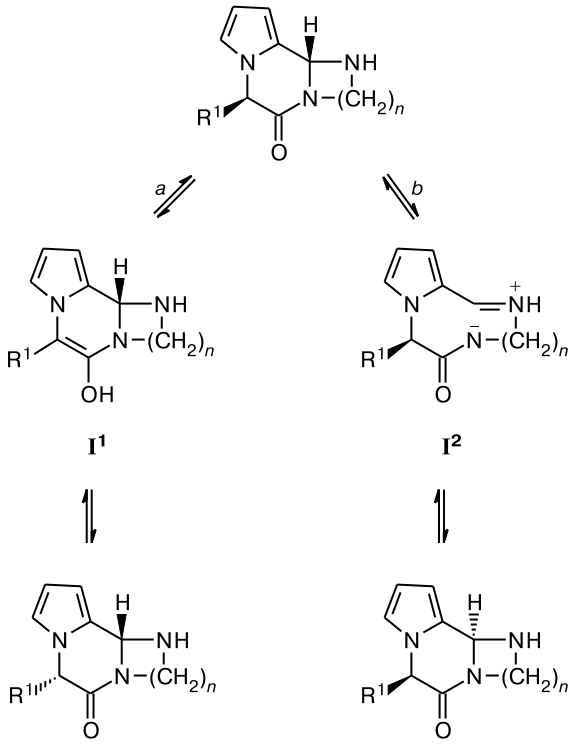


Fig. 2. General view of structure **4b** in the crystal with atomic thermal displacement ellipsoids (p = 50%).

Scheme 2

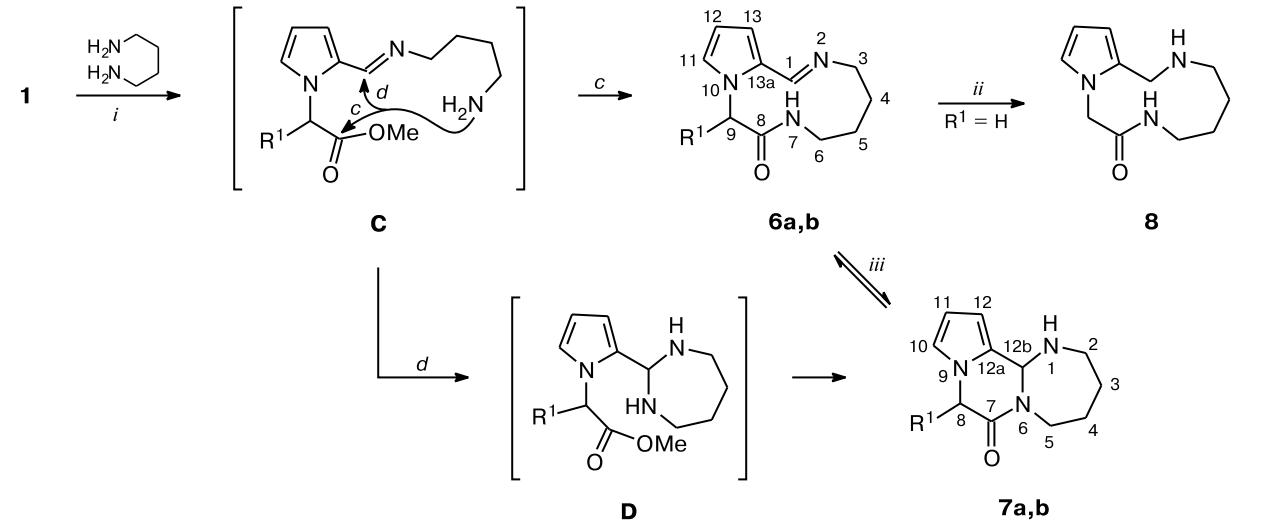


(pathway *b*). In the case of keto-enol tautomerization, which is facilitated by possible conjugation of the enol with the aromatic pyrrole ring (intermediate **I[1]**), a change in the configuration occurs at the asymmetric center bound to the pyrrole N atom. Ring—chain tautomerization involves cleavage of the interior aminal bond with presumable formation of zwitterionic intermediate **I[2]**; a change in the configuration occurs at the center bound to the pyrrole C atom. The final ratios of the diastereomers in solutions kept for two weeks were always about 1 : 1. Compound **3c** containing a bulky benzyl substituent undergoes no such interconversions, probably because of the relatively larger energy difference between its diastereomers compared to compounds **3b** and **4c**,**d** with R^1 = Me. Note that determination of the relative configurations of the diastereomers in question was beyond the scope of this study.

Reactions of esters **1** with 1,4-diaminobutane in ethanol followed a pathway that is substantially different from that observed in the reactions with 1,2- and 1,3-diamines. We found that the reaction mixtures should be refluxed for 4—6 h for completion of the reaction. The major products from 1,4-diaminobutane were bicyclic (**6**) rather than tricyclic structures (**7**) (Scheme 3). For instance, a reaction of ester **1a** with 1,4-diaminobutane yielded bicyclic product **6a** only, tricyclic compound **7a** being detected only in trace amounts. Compound **6a** was isolated in the individual state. Its ^{1}H NMR spectrum show the following characteristic signals: a singlet at δ 8.10 for the imine proton and a triplet at δ 7.61 for the amide proton. The IR spectrum of this compound in the carbonyl absorption range contains two bands at 1657 (C=O) and 1640 cm^{-1} (C=N), while the spectra of heterocyclic products **3** and **4** each exhibit only one band (C=O).

The structure of bicyclic compound **6a** was also confirmed chemically: its palladium-catalyzed hydrogenation at an atmospheric pressure gave 2,3,4,5,6,7-hexahydro-1*H*-pyrrolo[2,1-*c*][1,4,7]triazacycloundecin-8(9*H*)-one (**8**).

Scheme 3



6, 7: R^1 = H (**a**), Me (**b**)

Reagents and conditions: *i*. EtOH, reflux, 4—6 h; *ii*. H_2, 10% Pd/C, EtOH; *iii*. $CHCl_3$ (or DMSO), 25 °C, one month.

We demonstrated that the pathway of the reaction with 1,4-diaminobutane strongly depends on the structure of the starting esters **1**. For instance, a reaction with ester **1b** (R^1 = Me) gave a 2 : 1 mixture of imino lactam **6b** and tricyclic product **7b**, the latter consisting of diastereomers in a ratio of 1 : 1.5.

The aforesaid different pathways of the reactions of esters **1** with unsubstituted 1,2-, 1,3-, and 1,4-diamines is probably due to the different rates of formation of intermediate aminals **A**, **B**, and **D** (see Schemes 1 and 3). The rate of formation of seven-membered aminal **D** is much lower than those for analogous five- and six-membered aminals **A** and **B**.[2,3] That is why the preferential pathway of the reaction with 1,4-diaminobutane is intramolecular N-acylation with the ester group in intermediate **C** (pathway *c*). Apparently, pathway *d* is followed, to some degree, only in the case of ester **1b**: the yield of tricyclic product **7b** is ~33%.

A study of the ^{1}H NMR spectra of the reaction products obtained from esters **1a,b** and 1,4-diaminobutane in $CDCl_3$ and DMSO revealed that tricyclic forms **7** gradually accumulate in their solutions with time for a period of about a month (Fig. 3). The percentages of compounds **7a** and **7b** increase to 45 and 79%, respectively.

To explain the observed trends associated with the presence or the absence of ring—chain tautomerism in compounds **3**—**7**, as well as with the dependence of the ratio of the tricyclic and bicyclic structures on the size of the diazacycloalkane fragment and the presence of the substituent at the pyrazine ring of compounds **3**, **4**, and **7**, we analyzed X-ray diffraction data for compounds **3a** and **4b** and performed quantum chemical calculations for six pairs of tautomers $\mathbf{T^1}$ and $\mathbf{T^2}$ (Scheme 4).

According to X-ray diffraction data, the crystals of compounds **3a** and **4b** can show the stereoelectronic interactions lp—N—C—N (lp stands for lone electron pair), which is evident from the pseudotorsion angles lp—N(1)—C(10B)—N(4) (156°) and lp—N(1)—C(11B)—N(5) (171°)

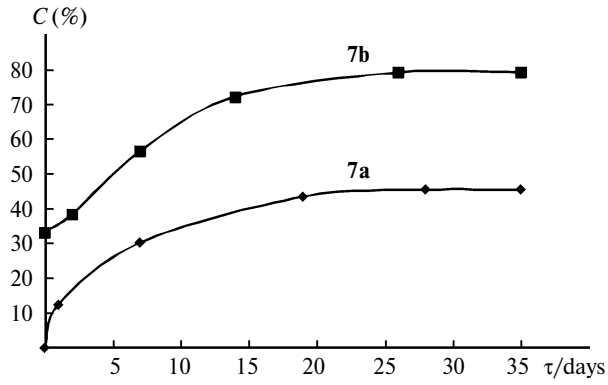
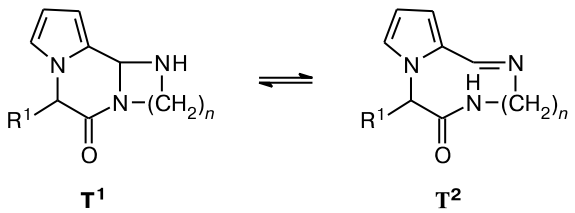


Fig. 3. Plots of the percentages *C* of the tricyclic forms **7a** and **7b** *vs.* the exposure time of solutions of a mixture of the corresponding tautomers **6** and **7**.

Scheme 4



$\mathbf{T^1}$ $\mathbf{T^2}$

n = 2—4

corresponding to the antiperiplanar arrangement of the lone electron pair of the N(1) atom and the polar C—N bond. Such interactions in the system lp—X—C—Y should involve electron transfer from the lone pair of the donating heteroatom X to the antibonding orbital of the polar C—Y bond, thus strengthening the X—C bond and weakening the C—Y bond.[4] Indeed, in the crystal of compound **3a**, the N(1)—C(10B) bond (1.4460(14) Å) is shorter by 0.022(3) Å than the N(1)—C(2) bond (1.4684(15) Å), while the N(4)—C(10B) bond (1.4843(13) Å) is longer by 0.023(3) Å than the N(4)—C(3) bond (1.4613(15) Å). Similar differences in bond lengths are observed for compound **4b**: the N(1)—C(11B) bond (1.4477(19) Å) is shorter by 0.021(4) Å than the N(1)—C(2) bond (1.4683(18) Å), while the N(5)—C(11B) bond (1.4807(18) Å) is longer by 0.013(4) Å than the N(4)—C(3) bond (1.4677(17) Å). Thus, the stereoelectronic interactions lp—N—C—N occur in both structures **3a** and **4b** and are comparable in strength. The resultant weakening of the N(4)—C(10B) and N(5)—C(11B) bonds can facilitate the ring—chain tautomerization discussed above.

Quantum chemical calculations of structures $\mathbf{T^1}$ and $\mathbf{T^2}$ were performed using the B3LYP/6-311++G(d,p)//B3LYP/6-311++G(d,p) method. The geometrical parameters calculated for the tricyclic forms with $n = 2$ and 3 approximate to those observed in the crystals of compounds **3a** and **4b**, respectively; the difference in the bond lengths does not exceed 0.01 Å.

Our calculations (Table 2) showed that the ratio of the tricyclic and bicyclic forms can be entirely explained by the energy differences between these products. Indeed, for $n = 2$, tricyclic structures $\mathbf{T^1}$ are thermodynamically much more favorable than the corresponding bicyclic structures $\mathbf{T^2}$. Ring expansion by a unit ($n = 3$) reduces the energy difference between structures $\mathbf{T^1}$ and $\mathbf{T^2}$, the difference being smaller for compounds with R^1 = H than for those with R^1 = Me. Finally, for $n = 4$, bicyclic form $\mathbf{T^2}$ is substantially more favorable for R^1 = H and has nearly the same energy as tricyclic form $\mathbf{T^1}$ for R^1 = Me. Thus, the experimental and calculated data for structures $\mathbf{T^1}$ and $\mathbf{T^2}$ are in good agreement.

The next part of our study was devoted to some transformations of heterocyclic compounds **3** and **4**. We found that catalytic hydrogenation of these compounds on 10%

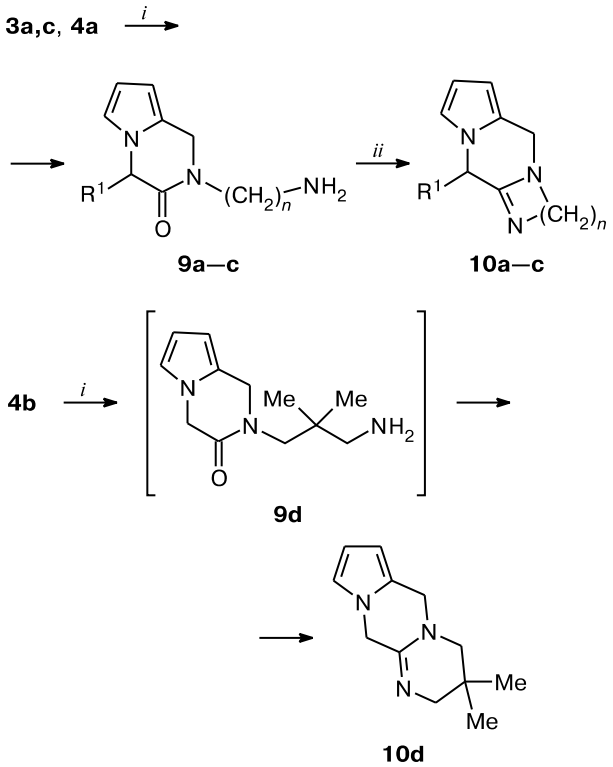
Table 2. Correlation of the B3LYP/6-311++G(d,p)//B3LYP/6-311++G(d,p)-calculated total energy differences for pairs of tautomers $\mathbf{T^1}$ and $\mathbf{T^2}$ with the observed $\mathbf{T^1}$: $\mathbf{T^2}$ ratio in their equilibrium solutions in $CDCl_3$

R^1	*n*	$\mathbf{T^1}$: $\mathbf{T^2}$	Δ*/kcal mol^{-1}
H	2	**	15.9
	3	8 : 1	8.1
	4	1 : 1.2	−1.8
Me	2	**	16.9
	3	**	9.1
	4	3.8:1	−0.4

* The energy difference is cited with allowance for the energy of zero-point vibrations.
** Only $\mathbf{T^1}$.

Pd/C at an atmospheric pressure occurs only in the presence of equimolar amounts of acetic acid but fails under neutral conditions. The reaction gave 2-aminoalkyl-1,2-dihydropyrrolo[1,2-*a*]pyrazin-3(4*H*)-ones **9** (Scheme 5) *via* hydrogenolysis of the aminal fragments in structures **3** and **4** (see Ref. 1). When refluxed in xylene, amino lactams **9** underwent cyclization into 2,10-dihydro-3*H*,5*H*-imidazo[1,2-*a*]pyrrolo[1,2-*d*]pyrazines and 2,3,4,11-tetrahydro-6*H*-pyrrolo[1′,2′:4,5]pyrazino[1,2-*a*]pyrimidines (**10**), which were isolated as hydrooxalates. Earlier,[5,6] such ring closure transformations of amino lactams into amidines have been conducted in boiling aromatic solvents in the presence of Lewis acids. Here we found that the formation of amidines **10** is a sufficiently rapid process requiring no catalysts and that the catalytic hydrogenation of compound **4b** is followed by *in situ* cyclization of the corresponding amino lactam **9d** (see Scheme 5).

Scheme 5



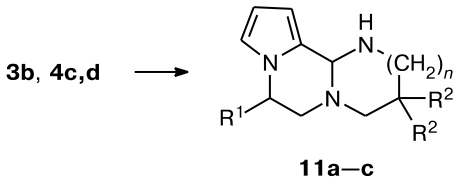
9, 10: R^1 = H, *n* = 2 (**a**); R^1 = CH_2Ph, *n* = 2 (**b**); R^1 = H, *n* = 3 (**c**)

Reagents and conditions: *i*. H_2, 10% Pd/C, EtOH, AcOH; *ii*. *o*-xylene, reflux, 8 h.

Apparently, the formation of amidine **10d** is facilitated by the presence of two methyl groups in the aminoalkyl chain of compound **9d**, which makes its molecular configuration most favorable for this reaction. The ^{1}H NMR spectra of amidines **10** with R^1 = H show a singlet at δ 4.24—4.28 (CH_2 group at the pyrrole C atom) and a singlet at δ 4.50—4.77 (CH_2 group at the pyrrole N atom).

Reduction of heterocyclic compounds **3** and **4** with $LiAlH_4$ gave cyclic aminals **11** (Scheme 6). When comparing the ^{1}H NMR spectra of compounds **11** with those of structures **3** and **4**, one should note that the signal for the proton at the aminal C atom is shifted upfield (δ 3.8—4.7) and that the methylene group resulting from the reduction of the carbonyl function is manifested as a multiplet at δ 2.5—3.2. In addition, the ^{1}H NMR data for products **11** suggest that compound **11a** is diastereomerically pure, while compounds **11b** and **11c** are 3.3 : 1 and 2 : 1 mixtures of diastereomers, respectively. Apparently, the partial racemization of the diastereomerically pure starting compounds **4** results from ring—chain tautomerization, either during their reduction or in final products **11**.

Scheme 6



11: R^1 = Me, R^2 = H (**a**, **b**); R^1 = R^2 = Me; *n* = 0 (**a**), 1 (**b**, **c**)

Reagents and conditions: $LiAlH_4$, anhydrous Et_2O, 10 min.

To sum up, we obtained a number of heterocyclic structures **3**—**7**. Some of them show ring—chain tautomerism, which has not been observed previously in such systems. We demonstrated that the palladium-catalyzed hydrogenation of compounds **3** and **4** occurs in the presence of acetic acid and, *via* hydrogenolysis of the aminal fragment, yields lactams **9**. When heated, the latter undergo cyclization into novel heterocyclic structures **10**. Catalytic hydrogenation of bicyclic compound **6a** occurs under neutral conditions, giving macrocyclic amino lactam **8**. The

carbonyl group in tricyclic compounds **3** and **4** was selectively reduced with $LiAlH_4$, the aminal fragment remaining intact. The results obtained are promising for preparative organic and medicinal chemistry.

Experimental

^{1}H NMR spectra were recorded on a Bruker AC-250 spectrometer in DMSO-d_6 and $CDCl_3$ with the signals for the residual protons of the solvents as the internal standards (δ 2.50 and 7.24, respectively). IR spectra were recorded on a Vertex-70 spectrometer (Bruker) in KBr pellets. Melting points were determined on a Kofler hot stage and are given uncorrected. Mass spectra were measured on a Kratos MS-300 instrument (EI, 70 eV). The course of the reactions was monitored and the purity of the products was checked by TLC in toluene—acetone—heptane—triethylamine (14 : 9 : 3 : 1) on Kieselgel 60 F_{254} plates; spots were visualized under UV light. Quantum chemical calculations were performed with the Gaussian 03 program.[7] The starting compounds methyl 2-(2-formyl-1*H*-pyrrol-1-yl)alkanoates (**1**) were prepared as described earlier.[1]

Reactions of methyl 2-(2-formyl-1*H*-pyrrol-1-yl)alkanoates (1) with 1,2- and 1,3-diamines (general procedure). A solution of methyl 2-(2-formyl-1*H*-pyrrol-1-yl)alkanoate (**1**) (20 mmol) and 1,2-diaminoethane or 1,3-diaminopropane (22 mmol) in ethanol (30 mL) was refluxed for 1 h. The reaction mixture was kept at −4 °C for 48 h. The crystals that formed were filtered off, washed with cold ethanol, and recrystallized (if needed).

1,2,3,10b-Tetrahydroimidazo[1,2-*a*]pyrrolo[2,1-*c*]pyrazin-5(6*H*)-one (3a) was obtained from ester **1a** and 1,2-diaminoethane. Yield 83%, white crystals, m.p. 175—177 °C. Found (%): C, 60.93; H, 6.52; N, 23.73. $C_9H_{11}N_3O$. Calculated (%): C, 61.00; H, 6.26; N, 23.71. ^{1}H NMR (DMSO), δ: 2.91—3.23 (m, 2 H, $H_2C(2)$); 3.23—3.64 (m, 2 H, $H_2C(3)$); 4.55, 4.64 (both d, 1 H each, $H_2C(6)$, ^2J = 16.0 Hz); 5.15 (d, 1 H, H(10b), ^3J = 11.7 Hz); 6.04 (m, 1 H, H(10)); 6.12 (m, 1 H, H(9)); 6.79 (m, 1 H, H(8)). IR, ν/cm^{-1}: 3242 (NH); 3112, 3094 (pyrrole); 2976, 2959, 2882, 2857 (CH_2, CH); 1643 (C=O).

6-Methyl-1,2,3,10b-tetrahydroimidazo[1,2-*a*]pyrrolo[2,1-*c*]pyrazin-5(6*H*)-one (3b) was obtained from ester **1b** and 1,2-diaminoethane. Yield 70%, white crystals, m.p. 154—156 °C. Found (%): C, 62.92; H, 6.94; N, 22.03. $C_{10}H_{13}N_3O$. Calculated (%): C, 62.81; H, 6.85; N, 21.97. ^{1}H NMR (DMSO; the signals for the pairs of diastereomers, which were detected upon the addition of CF_3COOD or $AlCl_3$ to a solution of compound **3b** in DMSO and used to determine the ratio of these diastereomers, are italicized), δ: 1.46 (*1.53* and *1.67*) (d, 3 H, Me, ^3J = 7.1 Hz); 3.00, 3.13 (both m, 1 H each, $H_2C(2)$); 3.20—3.34 (m, 2 H, $H_2C(3)$); 4.68 (q, 1 H, H(6), ^3J = 7.1 Hz); 5.19 (*5.86* and *5.93*) (d, 1 H, H(10b), ^3J = 11.3 Hz); 6.02 (m, 1 H, H(10)); 6.10 (m, 1 H, H(9)); 6.83 (*7.00* and *7.05*) (m, 1 H, H(8)). IR, ν/cm^{-1}: 3258 (NH); 3124, 3097 (pyrrole); 2990, 2978, 2949, 2886 (Me, CH_2, CH); 1649 (C=O).

6-Benzyl-1,2,3,10b-tetrahydroimidazo[1,2-*a*]pyrrolo[2,1-*c*]pyrazin-5(6*H*)-one (3c) was obtained from ester **1c** and 1,2-diaminoethane. Yield 63%, white crystals, m.p. 82—84 °C. Found (%): C, 72.21; H, 6.30; N, 15.73. $C_{16}H_{17}N_3O$. Calculated (%): C, 71.89; H, 6.41; N, 15.72. MS, *m/z*: 267 $[M]^+$, 176 $[M - CH_2Ph]^+$. ^{1}H NMR (DMSO), δ: 2.69, 2.97 (both m, 1 H each, $H_2C(2)$); 3.06—3.29 (m, 4 H, $H_2C(3)$, C<u>H</u>$_2$Ph); 3.83 (d, 1 H, H(10b), ^3J = 12.4 Hz); 4.95 (t, 1 H, C<u>H</u>CH$_2$Ph, ^3J = 5.0 Hz); 5.88 (m, 1 H, H(10)); 6.09 (m, 1 H, H(9)); 6.75 (m, 3 H, H(8), $H_{Ph}(2)$, $H_{Ph}(6)$); 7.09—7.25 (m, 3 H, $H_{Ph}(3)$, $H_{Ph}(4)$, $H_{Ph}(5)$). IR, ν/cm^{-1}: 3281 (NH); 3119, 3099, 3054 (pyrrole, Ph); 2947, 2920, 2887, 2842 (CH_2, CH); 1657 (C=O).

1,3,4,11b-Tetrahydro-2*H*-pyrrolo[2′,1′:3,4]pyrazino[1,2-*a*]-pyrimidin-6(7*H*)-one (4a) was obtained from ester **1a** and 1,3-diaminopropane. Yield 82%, white crystals, m.p. 165—167 °C. Found (%): C, 62.66; H, 7.22; N, 21.91. $C_{10}H_{13}N_3O$. Calculated (%): C, 62.81; H, 6.85; N, 21.97. ^{1}H NMR (DMSO), δ: 1.43—1.57 (m, 2 H, $H_2C(3)$); 2.76—2.95 (m, 2 H, $H_2C(2)$); 3.09 (d, 1 H, $H^aC(4)$, $^2J_{4a,4b}$ = 13.0 Hz); 4.55 (d, 1 H, $H^bC(4)$, $^2J_{4b,4a}$ = 13.0 Hz); 4.61 (s, 2 H, $H_2C(7)$); 5.29 (br.s, 1 H, H(11b)); 6.02 (m, 1 H, H(11)); 6.10 (m, 1 H, H(10)); 6.65 (m, 1 H, H(9)). IR, ν/cm^{-1}: 3284 (NH); 3117, 3091 (pyrrole); 2947, 2933, 2865, 2828 (CH_2, CH); 1643 (C=O).

<u>3,4,5,6-Tetrahydropyrrolo[2,1-*c*][1,4,7]triazecin-7(8*H*)-one (**5a**), a bicyclic tautomer of compound **4a**.</u> ^{1}H NMR (DMSO), δ: 1.67 (m, 2 H, $H_2C(4)$); 3.32 (m, 2 H, C<u>H</u>$_2$NH); 3.48 (m, 2 H, $H_2C(3)$); 4.86 (s, 2 H, $H_2C(8)$); 6.06 (m, 1 H, H(11)); 6.44 (m, 1 H, H(12)); 6.89 (m, 1 H, H(10)); 7.67 (t, 1 H, NH, ^3J = 6.1 Hz); 8.06 (s, 1 H, H(1)).

3,3-Dimethyl-1,3,4,11b-tetrahydro-2*H*-pyrrolo[2′,1′:3,4]-pyrazino[1,2-*a*]pyrimidin-6(7*H*)-one (4b) was obtained from ester **1a** and 1,3-diamino-2,2-dimethylpropane. Yield 68%, white crystals, m.p. > 250 °C. Found (%): C, 65.70; H, 7.90; N, 19.05. $C_{12}H_{17}N_3O$. Calculated (%): C, 65.73; H, 7.81; N, 19.16. ^{1}H NMR (DMSO), δ: 0.84, 0.89 (both s, 3 H each, 2 Me); 2.55—2.86 (m, 3 H, $H_2C(2)$, $H^aC(4)$); 4.24 (d, 1 H, $H^bC(4)$, $^2J_{4b,4a}$ = 12.7 Hz); 4.56, 4.63 (both d, 1 H each, $H_2C(7)$, ^2J = 17.8 Hz); 5.22 (d, 1 H, H(11b), ^3J = 11.0 Hz); 6.03 (m, 1 H, H(11)); 6.13 (m, 1 H, H(10)); 6.67 (m, 1 H, H(9)). IR, ν/cm^{-1}: 3295 (NH); 3120, 3104 (pyrrole); 2972, 2952, 2932, 2870 (Me, CH_2, CH); 1637 (C=O).

<u>4,4-Dimethyl-3,4,5,6-tetrahydropyrrolo[2,1-*c*][1,4,7]triazecin-7(8*H*)-one (**5b**), a bicyclic tautomer of compound **4b**.</u> ^{1}H NMR (DMSO), δ: 0.74 (s, 6 H, 2 Me); 3.03 (d, 2 H, C<u>H</u>$_2$NH, ^3J = 6.1 Hz); 3.11 (s, 2 H, $H_2C(3)$); 4.97 (s, 2 H, $H_2C(8)$); 6.10 (m, 1 H, H(11)); 6.48 (m, 1 H, H(12)); 6.95 (m, 1 H, H(10)); 7.50 (t, 1 H, NH, ^3J = 6.1 Hz); 8.03 (s, 1 H, H(1)).

7-Methyl-1,3,4,11b-tetrahydro-2*H*-pyrrolo[2′,1′:3,4]pyrazino[1,2-*a*]pyrimidin-6(7*H*)-one (4c) was obtained from ester **1b** and 1,3-diaminopropane. Yield 81%, white crystals, m.p. 92—95 °C. Found (%): C, 64.31; H, 7.38; N, 20.61. $C_{11}H_{15}N_3O$. Calculated (%): C, 64.37; H, 7.37; N, 20.47. ^{1}H NMR ($CDCl_3$; the signals for the diastereomer detected in a solution of compound **4c** after its keeping for two weeks are italicized), δ: 1.52—1.85 (m and d (1.64, *1.74*), 5 H, $H_2C(3)$ and Me, ^3J = 6.9 Hz); 2.89 (ddd, 1 H, $H^aC(4)$, $^2J_{4a,4b}$ = $^3J_{4a,3b}$ = 12.9 Hz, $^3J_{4a,3a}$ = 3.8 Hz); 3.01 (ddd, 1 H, $H^aC(2)$, $^2J_{2a,2b}$ = 11.9 Hz, $^3J_{2a,3b}$ = 11.7 Hz, $^3J_{2a,3a}$ = 3.5 Hz); 3.25 (dm, 1 H, $H^bC(2)$, $^2J_{2b,2a}$ = 11.9 Hz); *4.65*, 4.69 (q, 1 H, C<u>H</u>Me, ^3J = 6.9 Hz); 4.82 (dm, 1 H, $H^bC(4)$, $^2J_{4b,4a}$ = 12.9 Hz); *5.33*, 5.35 (br.s, 1H, H(11b)); 6.21 (m, 1 H, H(11)); 6.25 (m, 1 H, H(10)); 6.63 (m, 1 H, H(9)). IR, ν/cm^{-1}: 3302 (NH); 3122, 3101 (pyrrole); 2994, 2960, 2948, 2852 (Me, CH_2, CH); 1640 (C=O).

3,3,7-Trimethyl-1,3,4,11b-tetrahydro-2*H*-pyrrolo[2′,1′:3,4]-pyrazino[1,2-*a*]pyrimidin-6(7*H*)-one (4d) was obtained from ester **1b** and 1,3-diamino-2,2-dimethylpropane. Yield 74%, white crystals, m.p. 66—69 °C. Found (%): C, 66.79; H, 8.27; N, 17.88. $C_{13}H_{19}N_3O$. Calculated (%): C, 66.92; H, 8.21; N, 18.01. MS,

m/z: 233 $[M]^+$, 218 $[M-Me]^+$, 203 $[M-2Me]^+$, 189 $[M-3Me]^+$. ^{1}H NMR (DMSO; the signals for the pairs of diastereomers, which were detected upon the addition of CF_3COOD or $AlCl_3$ to a solution of compound **4d** in DMSO and used to determine the ratio of these diastereomers, are italicized), δ: 0.84, 0.87 (*1.04* and *1.15*, *1.19*) (both s, 3 H each, $Me_2C(3)$); 1.53 (*1.75* and *1.92*) (d, 3 H, MeCH, ^3J = 7.0 Hz); 2.53—2.75 (m and d (2.61), 3 H, $H_2C(2)$ and $H^aC(4)$, $^2J_{4a,4b}$ = 12.7 Hz); 4.20 (d, 1 H, $H^bC(4)$, $^2J_{4b,4a}$ = 12.7 Hz); 4.70 (*4.74* and *5.16*) (q, 1 H, HC(7), ^3J = 7.0 Hz); 5.22 (d, 1 H, H(11b), ^3J = 9.8 Hz); 6.05 (m, 1 H, H(11)); 6.14 (m, 1 H, H(10)); 6.80 (m, 1 H, H(9)). IR, ν/cm^{-1}: 3260 (NH); 3119, 3107 (pyrrole); 2976, 2953, 2927, 2872 (Me, CH_2, CH); 1627 (C=O).

4,4,8-Trimethyl-3,4,5,6-tetrahydropyrrolo[2,1-*c*][1,4,7]-triazecin-7(8*H*)-one (**5d**), a bicyclic tautomer of compound **4d**. ^{1}H NMR (DMSO; the signals that are not masked by those of major tautomer **4d** are cited only), δ: 1.60 (d, 3 H, MeCH, ^3J = 7.0 Hz); 5.73 (q, 1 H, HC(8), ^3J = 7.0 Hz); 6.20 (m, 1 H, H(11)); 6.57 (m, 1 H, H(12)); 7.20 (m, 1 H, H(10)); 7.71 (t, 1 H, NH, ^3J = 6.1 Hz); 8.19 (s, 1 H, H(1)).

Reaction of methyl 2-(2-formylpyrrol-1-yl)acetate (1a) with 1,4-diaminobutane. A solution of methyl 2-(2-formyl-1*H*-pyrrol-1-yl)acetate **1a** (1.67 g, 10 mmol) and 1,4-diaminobutane (0.97 g, 11 mmol) in ethanol (15 mL) was refluxed for 4 h. The reaction mixture was diluted with water (10 mL) and kept at −5 °C for two weeks. The precipitate that formed was filtered off and washed with ethanol. The yield of **4,5,6,7-tetrahydro-3*H*-pyrrolo[2,1-*c*][1,4,7]triazacycloundecin-8(9*H*)-one (6a)** was 1.25 g (61%), light yellow powder, m.p. 128—132 °C. Found (%): C, 64.16; H, 7.22; N, 20.18. $C_{11}H_{15}N_3O$. Calculated (%): C, 64.37; H, 7.37; N, 20.47. MS, *m/z*: 205 $[M]^+$. ^{1}H NMR ($CDCl_3$), δ: 1.35—1.80 (m, 4 H, $H_2C(4)$, $H_2C(5)$); 3.19 (dt, 2 H, $H_2C(6)$, $^3J_{6,NH}$ = 6.0 Hz, $^3J_{6,5}$ = 7.1 Hz); 3.47 (t, 2 H, $H_2C(3)$, $^3J_{3,4}$ = = 6.4 Hz); 4.88 (s, 2 H, $H_2C(9)$); 6.20 (dd, 1 H, H(12), $^3J_{12,13}$ = = 3.8 Hz, $^3J_{12,11}$ = 2.7 Hz); 6.49 (dd, 1 H, H(13), $^3J_{13,12}$ = 3.8 Hz, $^3J_{13,11}$ = 1.7 Hz); 6.88 (dd, 1 H, H(11), $^3J_{11,12}$ = 2.7 Hz, $^3J_{11,13}$ = 1.7 Hz); 7.61 (t, 1 H, NH, $^3J_{NH,6}$ = 6.0 Hz); 8.10 (s, 1 H, H(1)). IR, ν/cm^{-1}: 3294 (NH); 3098 (pyrrole); 2927, 2856 (CH_2); 1657 (C=O); 1640 (C=N); 733 ($(CH_2)_4$).

1,2,3,4,5,12b-Hexahydropyrrolo[2´,1´:3,4]pyrazino[1,2-*a*]-[1,3]diazepin-7(8*H*)-one (7a). ^{1}H NMR ($CDCl_3$; the spectrum was obtained by subtracting the spectrum of compound **6a** from the spectrum of **6a+7a** recorded after a solution of compound **6a** in $CDCl_3$ had been kept for a month), δ: 1.47—1.90 (m, 4 H, $H_2C(3)$, $H_2C(4)$); 2.76—3.04 (m, 2 H, $H_2C(2)$); 3.06—3.15 (m, 1 H, $H^aC(5)$); 4.40 (m, 1 H, $H^bC(5)$); 4.57, 4.67 (both d, 1 H each, $H_2C(8)$, ^2J = 17.2 Hz); 5.40 (s, 1 H, H(12b)); 6.14 (m, 1 H, H(12)); 6.21 (m, 1 H, H(11)); 6.60 (m, 1 H, H(10)).

Reaction of methyl 2-(2-formyl-1*H*-pyrrol-1-yl)propionate (1b) with 1,4-diaminobutane. A solution of compound **1b** (10 mmol) and 1,4-diaminobutane (11 mmol) in ethanol (15 mL) was refluxed for 6 h. The reaction mixture was diluted with water (15 mL). The oil that formed on the bottom of the reaction vessel was separated by decanting the supernatant. The oil with the residual amounts of the supernatant was evaporated to dryness to give a light orange viscous oil containing a 2 : 1 mixture of bicyclic form **6b** and tricyclic form **7b** (a pair of diastereomers) (^{1}H NMR, $CDCl_3$). The yield was 90%. Found (%): C, 65.60; H, 7.92; N, 19.32. $C_{12}H_{17}N_3O$. Calculated (%): C, 65.73; H, 7.81; N, 19.16.

9-Methyl-4,5,6,7-tetrahydro-3*H*-pyrrolo[2,1-*c*][1,4,7]triazacycloundecin-8(9*H*)-one (6b). ^{1}H NMR ($CDCl_3$), δ: 1.42—1.85 (m and d (1.62), 7 H, $H_2C(4)$, $H_2C(5)$, Me, ^3J = 7.0 Hz); 2.90—3.60 (m, 4 H, $H_2C(3)$, $H_2C(6)$); 5.80 (q, 1 H, CHMe, ^3J = 7.0 Hz); 6.19 (m, 1 H, H(12)); 6.44 (m, 1 H, H(13)); 7.06 (m, 1 H, H(11)); 7.97 (t, 1 H, NH, $^3J_{NH,6}$ = 6.0 Hz); 8.08 (s, 1 H, H(1)).

8-Methyl-1,2,3,4,5,12b-hexahydropyrrolo[2´,1´:3,4]pyrazino[1,2-*a*][1,3]diazepin-7(8*H*)-one (7b). ^{1}H NMR ($CDCl_3$; the signals for the minor diastereomer are italicized), δ: 1.37—1.88 (m and d (1.58, *1.74*), 7 H, $H_2C(3)$, $H_2C(4)$, Me, ^3J = 7.1 Hz); 2.61—3.19 (m, 3 H, $H_2C(2)$, $H^aC(5)$); 4.32 (m, 1 H, $H^bC(5)$); *4.59*, 4.67 (q, 1 H, CHMe, ^3J = 7.1 Hz); *5.32*, 5.39 (s, 1 H, H(12b)); *6.10*, 6.13 (m, 1 H, H(12)); 6.19 (m, 1 H, H(11)); 6.62 (m, 1 H, H(10)).

2,3,4,5,6,7-Hexahydro-1*H*-pyrrolo[2,1-*c*][1,4,7]triazacycloundecin-8(9*H*)-one (8). A catalyst (10% Pd/C, 0.2 g) was added to a solution of compound **6a** (0.51 g, 2.5 mmol) in DMF (30 mL). Hydrogen was bubbled through the reaction mixture until its theoretical amount was consumed. The catalyst was filtered off and the solution was evaporated to dryness. The residue was chromatographed on alumina with chloroform (150 mL) as an eluent. The eluate was evaporated to dryness and the residue was recrystallized from ethanol (7 mL). Yield 80%, white crystals, m.p. 147—151 °C. Found (%): C, 61.22; H, 8.66; N, 19.60. $C_{11}H_{17}N_3O \cdot 1/2H_2O$. Calculated (%): C, 61.09; H, 8.39; N, 19.43. ^{1}H NMR ($CDCl_3$), δ: 1.45 (m, 5 H, $H_2C(4)$, $H_2C(5)$, NH); 2.65 (t, 2 H, $H_2C(3)$, ^3J = 6.1 Hz); 3.16 (m, 2 H, $H_2C(6)$); 3.67 (s, 2 H, $H_2C(1)$); 4.50 (s, 2 H, $H_2C(9)$); 6.04 (dd, 1 H, H(13), $^3J_{13,12}$ = 3.4 Hz, $^4J_{13,11}$ = 1.7 Hz); 6.10 (dd, 1 H, H(12), $^3J_{12,13}$ = 3.4 Hz, $^3J_{12,11}$ = 2.8 Hz); 6.70 (dd, 1 H, H(11), $^3J_{11,12}$ = 2.8 Hz, $^4J_{11,13}$ = 1.7 Hz); 7.91 (t, 1 H, CONH, ^3J = 5.3 Hz). IR, ν/cm^{-1}: 3270 (NH); 3088 (pyrrole); 2921, 2858 (CH_2); 1656 (C=O); 719 ($(CH_2)_4$).

Catalytic hydrogenation of pyrrolo[2,1-*c*]-1,3-diazacycloalkano[1,2-*a*]pyrazinones (3 and 4) (general procedure). Acetic acid (7.2 mL, 120 mmol) and 10% Pd/C (0.5 g) were added to a solution of compound **3** or **4** (20 mmol) in ethanol (90 mL). Hydrogen was bubbled through the reaction mixture until its theoretical amount was consumed. The catalyst was filtered off and the solution was evaporated to dryness. A 40% aqueous solution of NaOH (10 mL) was added to the residue and the product was extracted with chloroform (2×20 mL). The combined organic extracts were washed with water (8 mL), filtered through a folded filter, and evaporated to dryness.

2-(2-Aminoethyl)-1,2-dihydropyrrolo[1,2-*a*]pyrazin-3(4*H*)-one (9a) was obtained in 76% yield by catalytic hydrogenation of compound **3a**. The physical constants and ^{1}H NMR spectrum of compound **9a** agree with the literature data.[1]

2-(2-Aminoethyl)-4-benzyl-1,2-dihydropyrrolo[1,2-*a*]pyrazin-3(4*H*)-one (9b) was obtained by catalytic hydrogenation of compound **3c**. Yield 73%, light yellow powder, m.p. 98—100 °C. Found (%): C, 71.47; H, 7.02; N, 15.59. $C_{16}H_{19}N_3O$. Calculated (%): C, 71.35; H, 7.11; N, 15.60. ^{1}H NMR ($CDCl_3$), δ: 1.93 (br.s, 2 H, NH_2); 2.86 (m, 2 H, CH_2NH_2); 3.13—3.42 (m, 3 H, CH_2Ph, $H^aC(1)$); 3.54 (m, 2 H, $CH_2CH_2NH_2$); 4.05 (d, 1 H, $H^bC(1)$, ^2J = 15.4 Hz); 4.96 (t, 1 H, HC(4), ^3J = 4.2 Hz); 5.78 (m, 1 H, H(8)); 6.24 (m, 1 H, H(7)); 6.62 (m, 1 H, H(6)), 6.65—7.22 (m, 5 H, Ph).

2-(3-Aminopropyl)-1,2-dihydropyrrolo[1,2-*a*]pyrazin-3(4*H*)-one (9c) was obtained in 80% yield by catalytic hydrogenation of

compound **4a**. The physical constants and ^{1}H NMR spectrum of compound **9c** agree with the literature data.[1]

Cyclization of 2-aminoalkyl-1,2-dihydropyrrolo[1,2-*a*]pyrazin-3(4*H*)-ones (9) (general procedure). A solution of compound **9** (20 mmol) in *o*-xylene (30 mL) was refluxed for 8 h and evaporated to dryness. The residue was distilled when needed.

2,10-Dihydro-3*H*,5*H*-imidazo[1,2-*a*]pyrrolo[1,2-*d*]pyrazine (10a) was obtained by cyclization of compound **9a**. Yield 62%, colorless viscous oil, b.p. 136—137 °C (1.5 Torr). ^{1}H NMR ($CDCl_3$), δ: 3.41 (t, 2 H, $H_2C(3)$, ^3J = 9.4 Hz); 3.84 (t, 2 H, $H_2C(2)$, ^3J = 9.4 Hz); 4.26 (s, 2 H, $H_2C(5)$); 4.77 (s, 2 H, $H_2C(10)$); 5.96 (m, 1 H, H(6)); 6.20 (m, 1 H, H(7)); 6.61 (m, 1 H, H(8)).

Hydrooxalate: m.p. 209—212 °C. Found (%): C, 52.38; H, 5.30; N, 16.53. $C_9H_{11}N_3 \cdot C_2H_2O_4$. Calculated (%): C, 52.59; H, 5.22; N, 16.73.

10-Benzyl-2,10-dihydro-3*H*,5*H*-imidazo[1,2-*a*]pyrrolo[1,2-*d*]pyrazine (10b) was obtained by cyclization of compound **9b**. Yield 49%, light yellow oil. ^{1}H NMR ($CDCl_3$), δ: 2.67 (d, 1 H, $H^aC(5)$, ^2J = 13.4 Hz); 2.90 (m, 1 H, $H^aC(3)$); 3.18—3.40 (m, 3 H, $H^bC(3)$, $C\underline{H}_2Ph$); 3.67—4.02 (m and d (3.85), 3 H, $H_2C(2)$, $H^bC(5)$, ^2J = 13.4 Hz); 5.23 (t, 1 H, H(10), ^3J = 4.0 Hz); 5.76 (m, 1 H, H(6)); 6.21 (m, 1 H, H(7)); 6.61—7.22 (m, 6 H, H(8), Ph).

Hydrooxalate: m.p. 192—194 °C. Found (%): C, 63.09; H, 5.79; N, 12.56. $C_{16}H_{17}N_3 \cdot C_2H_2O_4$. Calculated (%): C, 63.33; H, 5.61; N, 12.31.

2,3,4,11-Tetrahydro-6*H*-pyrrolo[1′,2′:4,5]pyrazino[1,2-*a*]pyrimidine (10c) was obtained by cyclization of compound **9c**. Yield 54%, light yellow oil, b.p. 150—153 °C (1.5 Torr). ^{1}H NMR ($CDCl_3$), δ: 1.87 (m, 2 H, $H_2C(3)$); 3.29, 3.36 (both t, 2 H each, $H_2C(2)$, $H_2C(4)$, ^3J = 6.1 Hz, ^3J = 5.5 Hz); 4.24 (s, 2 H, $H_2C(6)$); 4.50 (s, 2 H, $H_2C(11)$); 5.92 (m, 1 H, H(7)); 6.13 (m, 1 H, H(8)); 6.59 (m, 1 H, H(9)).

Hydrooxalate: m.p. 187—189 °C. Found (%): C, 54.45; H, 5.63; N, 15.77. $C_{10}H_{13}N_3 \cdot C_2H_2O_4$. Calculated (%): C, 54.33; H, 5.70; N, 15.84.

3,3-Dimethyl-2,3,4,11-tetrahydro-6*H*-pyrrolo[1′,2′:4,5]pyrazino[1,2-*a*]pyrimidine (10d) was obtained by catalytic hydrogenation of compound **4b** as described above. The reaction product was distilled. Yield 55%, colorless oil, b.p. 152—154 °C (1.5 Torr). ^{1}H NMR ($CDCl_3$), δ: 0.95 (s, 6 H, 2 Me); 2.94, 3.04 (both s, 2 H each, $H_2C(2)$, $H_2C(4)$); 4.28 (s, 2 H, $H_2C(6)$); 4.62 (s, 2 H, $H_2C(11)$); 5.93 (m, 1 H, H(7)); 6.14 (m, 1 H, H(8)); 6.60 (m, 1 H, H(9)).

Hydrooxalate: m.p. 193—195 °C. Found (%): C, 57.18; H, 6.69; N, 14.59. $C_{12}H_{17}N_3 \cdot C_2H_2O_4$. Calculated (%): C, 57.33; H, 6.53; N, 14.33.

Reduction of pyrrolo[2,1-*c*]-1,3-diazacycloalkano[1,2-*a*]-pyrazinones (3 and 4) with $LiAlH_4$ (general procedure). Lithium aluminum hydride (0.15 g, 4 mmol) was added to a solution of compound **3** or **4** (1 mmol) in toluene (6 mL) and anhydrous ether (6 mL). The reaction mixture was stirred at room temperature for 10 min, whereupon 20% aqueous NaOH (0.3 mL) and water (2 mL) were added. The precipitate that formed was separated by decanting the supernatant. Ether (5 mL) was added to the precipitate and the mixture was stirred for 5 min. Then the ether was decanted from the precipitate. The combined solutions were evaporated to dryness.

6-Methyl-1,2,3,5,6,10b-hexahydroimidazo[1,2-*a*]pyrrolo-[2,1-*c*]pyrazine (11a) was obtained by reduction of compound **3b**. Yield 90%, yellow oil. Found (%): C, 67.84; H, 8.71; N, 23.51. $C_{10}H_{15}N_3$. Calculated (%): C, 67.76; H, 8.53; N, 23.71. ^{1}H NMR

Table 3. Crystallographic parameters and the data collection statistics for compounds **3a** and **4b**

Parameter	**3a**	**4b**
Molecular formula	$C_9H_{11}N_3O$	$C_{12}H_{17}N_3O$
Molecular weight	177.21	219.29
T/K	293	100
Crystal system	Monoclinic	Monoclinic
Space group	$P2_1/c$	$P2_1/c$
Z	4	4
a/Å	9.6221(19)	18.478(5)
b/Å	7.1615(14)	5.7428(14)
c/Å	14.445(5)	11.247(3)
β/deg	120.05(2)	107.043(5)
V/Å^3	861.6(4)	1141.1(5)
d_{calc}/g cm^{-3}	1.366	1.276
μ/cm^{-1}	0.94	0.84
F(000)	376	472
$2\theta_{max}$/deg	60	60
Number of measured reflections	2655	7077
Number of independent reflections	2522	3316
Number of reflections with $I > 2\sigma(I)$	1631	2426
R_{int}	0.0192	0.0339
Number of parameters refined	118	151
R_1	0.0378	0.0515
wR_2	0.0992	0.1173
GOOF	1.001	1.003
Residual electron density, e Å^{-3}(d_{max}/d_{min})	0.146/−0.156	0.415/−0.260

($CDCl_3$), δ: 1.48 (d, 3 H, Me, ^3J = 6.5 Hz); 2.25 (br.s, 1 H, NH); 2.65 (dd, 1 H, $H^aC(5)$, ^2J = 11.5 Hz, ^3J = 8.0 Hz); 2.88—3.18 (m, 5 H, $H_2C(2)$, $H_2C(3)$, $H^bC(5)$); 4.17 (m, 1 H, H(6)); 4.70 (s, 1 H, H(10b)); 6.16 (m, 2 H, H(9), H(10)); 6.68 (m, 1 H, H(8)).

7-Methyl-1,3,4,6,7,11b-hexahydro-2*H*-pyrrolo[2´,1´:3,4]pyrazino[1,2-*a*]pyrimidine (a mixture of diastereomers in a ratio of 3.3 : 1) (11b) was obtained by reduction of compound **4c**. Yield 98%, white powder, m.p. 63—65 °C. Found (%): C, 68.83; H, 9.14; N, 21.83. $C_{11}H_{17}N_3$. Calculated (%): C, 69.07; H, 8.96; N, 21.97. ^{1}H NMR ($CDCl_3$; the signals for the minor diastereomer are italicized), δ: 1.42, *1.47* (d, 3 H, Me, ^3J = 6.5 Hz); 1.53—1.87 (m, 3 H, NH, $H_2C(3)$); 2.27—3.23 (m, 6 H, $H_2C(2)$, $H_2C(4)$, $H_2C(6)$); 3.96 (s, 1 H, H(11b)); 4.19 (m, 1 H, H(7)); *6.04*, 6.08 (m, 1 H, H(11)); 6.14 (m, 1 H, H(10)); *6.55*, 6.67 (m, 1 H, H(9)).

3,3,7-Trimethyl-1,3,4,6,7,11b-hexahydro-2*H*-pyrrolo[2´,1´:3,4]pyrazino[1,2-*a*]pyrimidine (a mixture of diastereomers in a ratio of 2 : 1) (11c) was obtained by reduction of compound **4d**. Yield 97%, colorless oil. Found (%): C, 71.27; H, 9.45; N, 19.01. $C_{13}H_{21}N_3$. Calculated (%): C, 71.19; H, 9.65; N, 19.16. ^{1}H NMR ($CDCl_3$; the signals for the minor diastereomer are italicized), δ: 0.84 and 1.08 (*1.11*) (both s, 3 H each, $Me_2C(3)$); 1.41, *1.51* (d, 3 H, MeC(7), ^3J = 6.4 Hz); 2.04—2.81 (m, 6 H, $H_2C(2)$, $H_2C(4)$, $H_2C(6)$); 3.81 (s, 1 H, H(11b)); 4.18 (m, 1 H, H(7)); *6.08*, 6.13 (m, 1 H, H(11)); 6.17 (m, 1 H, H(10)); *6.56*, 6.69 (m, 1 H, H(9)).

X-ray diffraction studies. Single crystals of compounds **3a** and **4b** suitable for crystallographic experiments were obtained by recrystallization from ethanol. Low-temperature X-ray diffraction from compound **3a** was measured on a Syntex $P2_1$ diffractometer (MoKα radiation, graphite monochromator, θ/2θ scan mode). Analogous studies for compound **4b** were carried out on a SMART APEX II CCD diffractometer (MoKα radiation, graphite monochromator, ω scan mode). The structures were solved by the direct methods and refined by the least-squares method in the anisotropic full-matrix approximation on F^2_{hkl}. The hydrogen atoms were located from difference electron-density maps and refined using a riding model. Selected crystallographic parameters and the data collection statistics for structures **3a** and **4b** are given in Table 3. All calculations were performed with the SHELXTL PLUS program package.[8]

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