A new approach to the synthesis of pyrrolo[1,2-*a*]indole derivatives

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Reactions of 2-(3,3-diamino-2-cyanoprop-2-enylidene)indolin-3-ones with amide acetals afforded derivatives of 3-aminomethyleneamino-2-cyano-9-oxo-9*H*-pyrrolo[1,2-*a*]indole and 3-amino-2-cyano-9-oxo-9*H*-pyrrolo[1,2-*a*]indole. The rate and pathway of the reaction depend on the reagents and solvents. The formation schemes for the compounds obtained were proposed. Their structures were proven by IR and ^{1}H NMR spectroscopy and mass spectrometry and confirmed by independent syntheses.

Key words: 2-(3,3-diaminoprop-2-enylidene)indolin-3-ones, amide acetals, condensation, cyclization, pyrroloindoles, amidines, transamination.

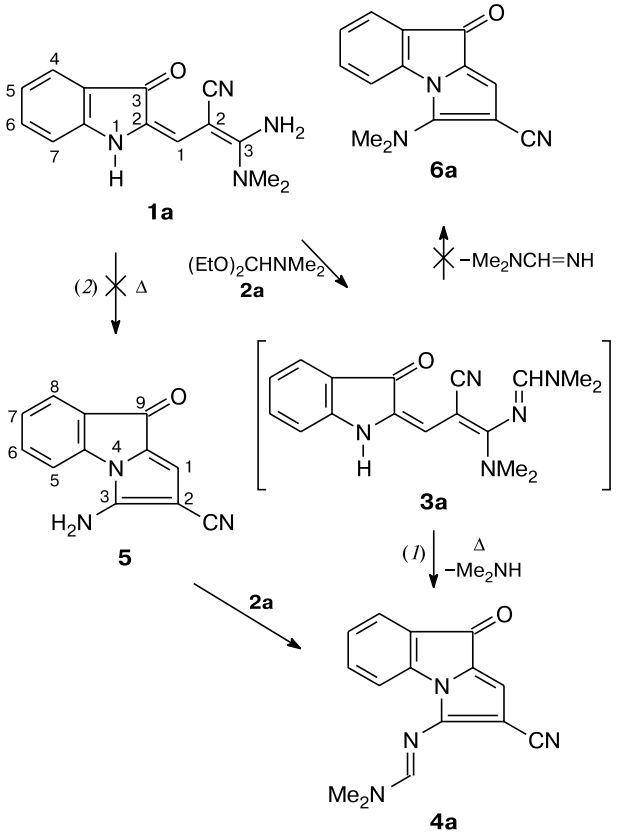
Earlier, we have synthesized new indolin-3-one derivatives, namely, 2-(3,3-diamino-2-cyanoprop-2-enylidene)indolin-3-ones (hereafter, dienediamines) containing various substituents in position 3 of the side chain, and found that they exhibit pronounced antihypertensive activity.[1—3] The chemical properties of these dienediamines remain virtually uninvestigated. It was interesting to study reactions of dienediamines containing the dimethylamino (**1a**), morpholino (**1b**), and piperidino fragments (**1c**) with amide acetals **2a**—**c** to obtain the corresponding amidines **3a**—**c** (Scheme 1).

Our experiments showed that the reaction pathway depends on the substituent in dienediamine, the acetal, and the solvent. However, in all cases, the expected amidines of the general formula **3** were not the final condensation products.

We found that refluxing of 2-(3-amino-2-cyano-3-dimethylaminoprop-2-enylidene)indolin-3-one (**1a**) in ethanol with an excess of dimethylformamide diethyl acetal (**2a**) gives only one compound, namely, 2-cyano-3-dimethylaminomethyleneamino-9-oxo-9*H*-pyrrolo[1,2-*a*]indole (**4a**). The yield of compound **4a** was 83%.

The formation of amidine **4a** can follow two ways. The first one involves cyclization of intermediate **3a** through the indole N atom with release of dimethylamine (see Scheme 1, pathway (*1*)). According to the second one, initial closure of the pyrrole ring leads to the previously described[3] 3-aminopyrroloindole **5**, which reacts with the acetal *via* the NH_2 group to give amidine **4a** (see Scheme 1, pathway (*2*)).

Scheme 1



To determine the actual way to amidine **4a**, we obtained it independently by a reaction of pyrroloindole **5** (see Ref. 3) with acetal **2a**. However, refluxing of a mixture of compounds **5** and **2a** in ethanol (as in the reaction of dienediamine **1a** with acetal **2a**) failed. Amidine **4a** was obtained under substantially more drastic conditions when

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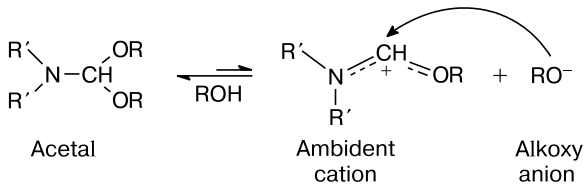
refluxing pyrroloindole **5** and acetal **2a** in DMF or in the acetal itself. Therefore, the formation of amidine **4a** from dienediamine **1a** occurs along pathway (*1*).

Dienediamines **1a,c** undergo cyclization into pyrroloindole[3] under the action of acetic acid and acetic anhydride; the closure of the pyrrole ring is accompanied by elimination of the bulkier substituent. In either case, the resulting product is tricyclic compound **5** containing the primary amino group in position 3.

In the reaction under study, intermediate **3a** has two bulky substituents. Cyclization could be expected to occur with elimination of both dimethylamine (yielding amidine **4a**) and dimethylformamidine (yielding 3-dimethylaminopyrroloindole **6a**). However, dimethylamine was eliminated only, probably because of the equilibrium shift due to removal of dimethylamine from the reaction mixture.

We carried out a reaction of dienediamine **1a** with a double excess of acetal **2a** not only in a protic polar solvent (ethanol) but also in an aprotic polar solvent (DMF, 80 °C) and in an aprotic nonpolar one (benzene, refluxing). It turned out that the solvent substantially affects the reaction rate, which was highest in DMF and lowest in ethanol (Table 1, entries *1—3*). Apparently, this is due to the fact that the reactivity of acetal toward nucleophiles is determined by the equilibrium acetal $\rightleftharpoons$ ambident cation + alkoxy anion. If the reaction is conducted in ethanol, which increases the content of alkoxy anions in the reaction mixture, the above equilibrium is shifted to the left and the nondissociated acetal is much less reactive toward nucleophiles (Scheme 2).

Scheme 2



A reaction of 3-morpholino dienamine **1b** with an excess of acetal **2a** in ethanol gave a mixture of amidine **4a** and 2-cyano-3-morpholino-9-oxo-9*H*-pyrrolo[1,2-*a*]indole (**6b**), which was separated by column chromatography. The yields of compounds **4a** and **6b** were 30 and 22%, respectively. Thus, both morpholine and dimethylformamidine were eliminated in this reaction (Scheme 3).

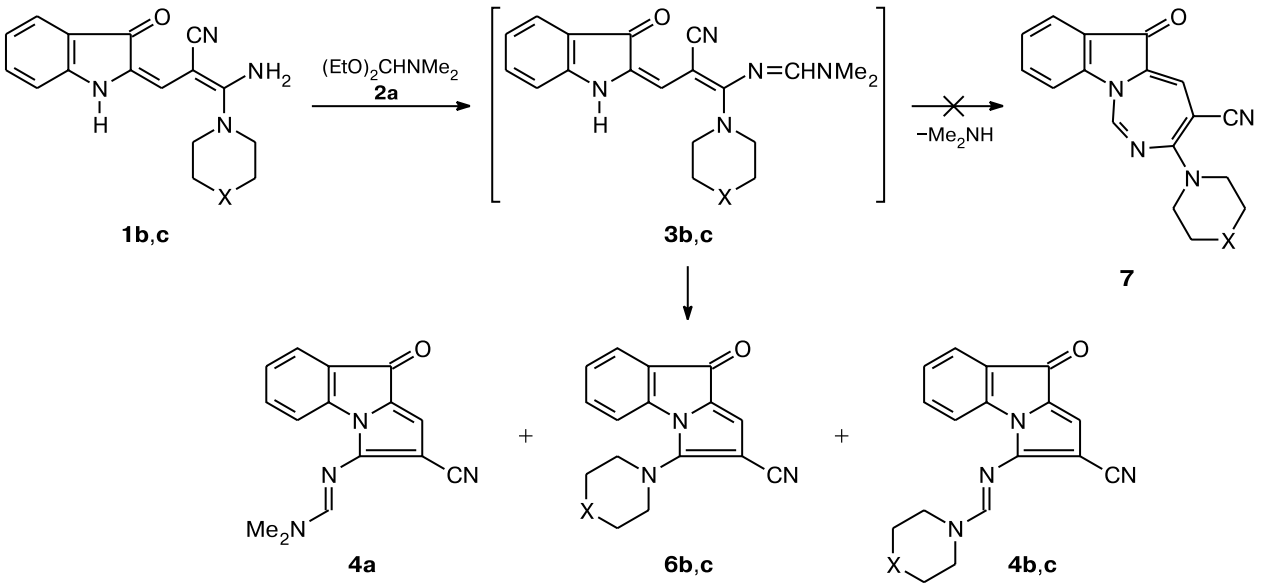
The structures of the compounds obtained were determined by IR and ^{1}H NMR spectroscopy and mass spectrometry (see Experimental). The ^{1}H NMR spectrum of the mixture shows, along with signals for the aromatic protons, signals for the morpholine substituent and the dimethylamino group. The intensities of these signals were used to estimate the ratio of the products (**4a** : **6b** = 60 : 40).

Table 1. Conditions of the reactions of dienediamines **1a—c** with amide acetals **2a—c**, the presence and ratio of the components in the final reaction mixtures (HPLC data), and the yields of the compounds obtained

Entry	Starting reagent	Acetal	Solvent (added amine)	τ^a/h	Components and their ratios[b]	Yields of the products[c]
1	**1a**	**2a**	Ethanol	7	**4a**, **1a**	30 (**4a**)
2	**1a**	**2a**	Benzene	3	**4a**	65
3	**1a**	**2a**[d]	DMF	1[e]	**4a**	64
4	**1a**	**2a**[f]	Ethanol	3.5	**4a**	83
5	**1a**	**2a**	DMF	1	**4a**	60
6	**1a**	**2a**	DMF (piperidine)	1	**4a**, **4b** (41 : 58)	—
7	**1a**	**2b**	DMF	0.5	**4a**, **4c** (19.5 : 76)	—
8	**1b**	**2a**[g]	Ethanol	7	**4a**, **6b**	30 (**4a**), 22 (**6b**)
9	**1b**	**2a**	DMF	1	**4a**, **4b**, **6b** (40 : 37 : 23)	26 (**4b**)
10	**1b**	**2a**	DMF (morpholine)	1	**4a**, **4b**, **6b** (19 : 63 : 18)	39 (**4b**)
11	**1c**	**2a**	Ethanol	7	**4a, 4c**, **6c** (69 : 10 : 20)	54 (**4a**), 7.7 (**4c**), 8.5 (**6c**)
12	**1c**	**2a**	DMF	1	**4a**, **4c**, **6c** — traces (47.5 : 52.5)	13 (**4a**), 39 (**4c**)
13	**1c**	**2b**	DMF	0.5	**4c, 6c** (74.8 : 17.7)	74 (**4c**)
14	**1c**	**2c**	DMF	3.5	**4a, 4c**, **6c** (55 : 16 : 29)	—

[a] τ is the reaction time under reflux.
[b] The components were detected by TLC and their ratios were determined by HPLC.
[c] The yield of the compound obtained.
[d] For all experiments in DMF, a double excess of the acetal was used.
[e] The reaction temperature was 80 °C.
[f] With a sixfold excess of the acetal.
[g] With a ninefold excess of the acetal.

Scheme 3



X = O (**b**), CH_2 (**c**)

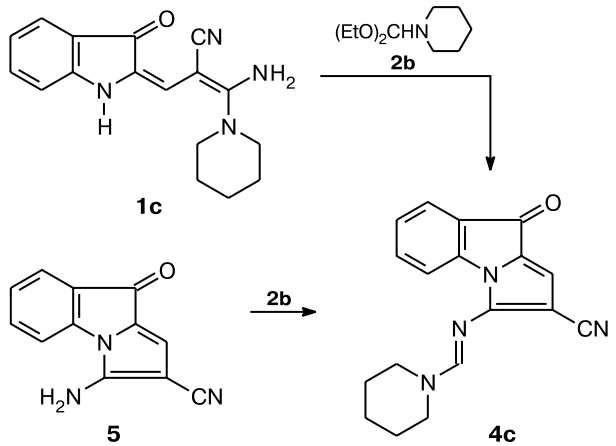
Condensation of morpholino dienamine **1b** with acetal **2a** in DMF gave, along with compounds **4a** and **6b**, a third product (amidine **4b**), which was isolated by chromatography in 26% yield. The ratio of products **4a**, **4b**, and **6b** in the reaction mixture was determined by HPLC (see Table 1). It should be noted that the structure of amidine **4b** was not obvious because of possible alternative cyclization into a 4-cyano-6-oxo-6*H*-[1,3]diazepino[1,7-*a*]indole derivative (**7**) (see Scheme 3). Compounds **4b** and **7** have equal molecular masses and cannot be reliably distinguished from ^{1}H NMR data.

A reaction of 3-piperidino dienamine **1c** with an excess of acetal **2a** in ethanol yielded a mixture of amidines **4a** and **4c** and 2-cyano-9-oxo-3-piperidino-9*H*-pyrrolo[1,2-*a*]indole (**6c**), amidine **4a** being the major product (HPLC; see Table 1, entry *11*). Compounds **4a**, **4c**, and **6c** were isolated in the individual state by column chromatography.

It should be noted that trace amounts of compound **6c** were detected in the reaction of dienediamine **1c** with acetal **2a** in DMF (TLC data), the fraction of amidine **4c** compared to compound **4a** being significantly increased (HPLC; see Table 1, entry *12*). In this case, the yield of amidine **4c** was 39% (versus 7.7% in ethanol).

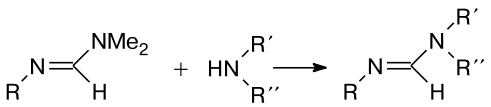
To prove the structure of compound **4c** (and hence **4b**) unambiguously, we tried to synthesize it by condensation of pyrroloindole **5** with *N*-formylpiperidine diethyl acetal (**2b**) and by a reaction of piperidino dienamine **1c** with a double excess of acetal **2b** in DMF. Both the reactions gave the same compound, which was identical with the above amidine **4c** in all physicochemical parameters (Scheme 4).

Scheme 4



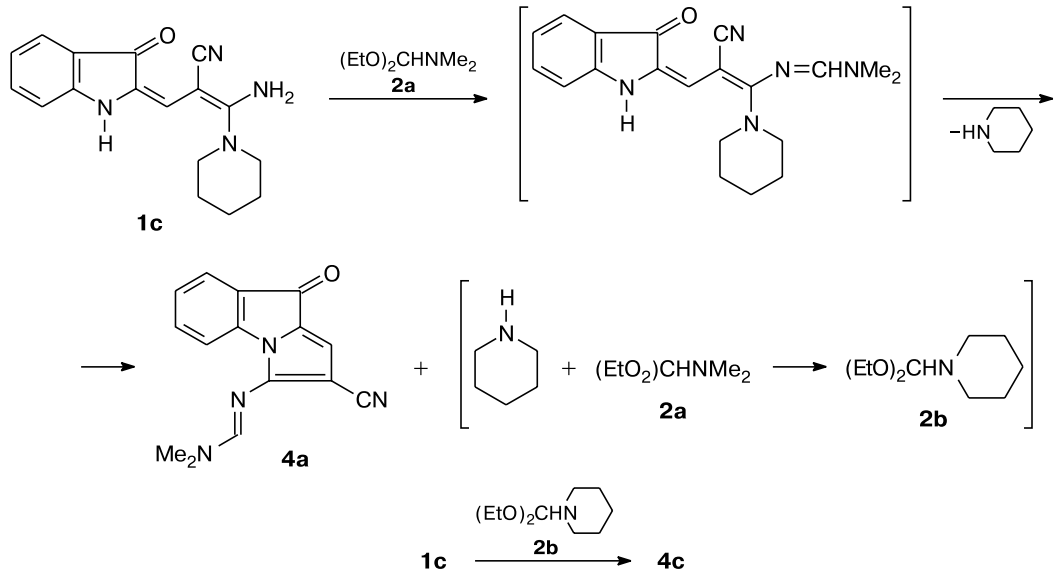
In our opinion, the formation of amidines **4b,c** in the reactions of dienediamines **1b,c** with acetal **2a** can follow three pathways. The first pathway involves transamination of amidine **4a** with morpholine (or piperidine) released during the cyclization of intermediate **3b** (or **3c**). Transamination of amidines has been reported for some amidine derivatives (Scheme 5).[4]

Scheme 5



To verify this possibility, we refluxed a solution of amidine **4a** and piperidine (or morpholine) in DMF for

Scheme 6



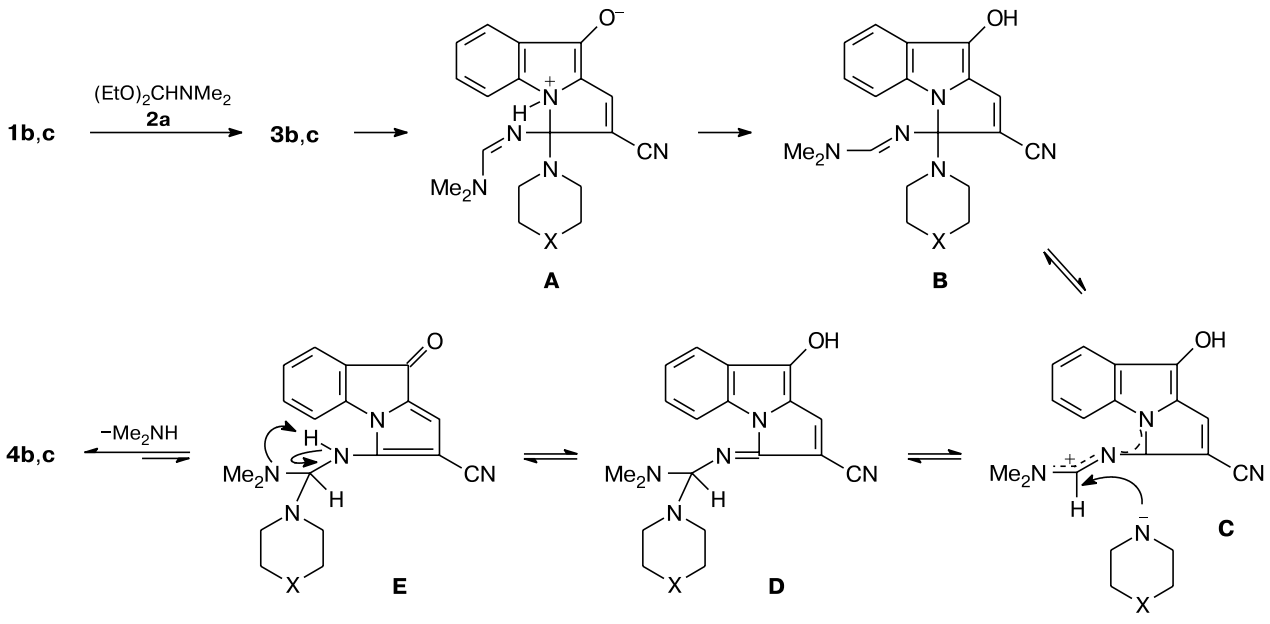
7 h and studied the resulting mixtures by HPLC. It turned out that transamination is insignificant (no more than 2%) in both cases, while over 98—99% of the starting amidine **4a** remain virtually unchanged.

The second pathway involves transamination of acetal **2a** (*e.g.*, with piperidine released during the cyclization of intermediate **3c**);[5] the resulting acetal (*e.g.*, *N*-formylpiperidine acetal **2b**) reacts with dienediamine **1c** to give amidine **4c** (Scheme 6).

To verify this assumption, we refluxed pyrroloindole **5** and acetal **2a** in DMF in the presence of piperidine. The ratio of amidines **4a** and **4c** in the reaction mixture was 87.5 : 12.5 (HPLC), which suggests the possible formation of amidines **4b,c** along this pathway. However, a comparison of these data with the yield of compound **4c** (39%) in the reaction of dienediamine **1c** with acetal **2a** (see Table 1, entry *12*) implies another alternative way to amidines **4b,c**.

Apparently, the third pathway of transamination involves migration of the amine residue when a secondary amino component and the formamidine fragment are geminal in an already cyclic molecule (Scheme 7, **A**→**B**).

Scheme 7



Such a structure is similar to trisaminomethanes, which are characterized, like amide acetals, by dissociation releasing the amide anion and ambident cation **C** (see Refs 6, 7). In cation **C**, the amine fragment is transferred to the amidine meso-position (**D,E**) to form a new amidine group.

If the scheme proposed for the formation of amidines **4b,c** is true, then the fraction of transaminated amidine should increase upon addition of the corresponding amine to the reaction mixture (**1b** or **1c** and **2a**). Indeed, refluxing of morpholino dienamine **1b** with acetal **2a** in DMF in the presence of morpholine gave amidine **4b** in a higher yield (39%). The ratio of products **4a** and **4b** in the reaction mixture noticeable changed: the content of morpholine amidine **4b** approximately doubled (see Table 1, entry *10*). An analogous experiment showed that addition of piperidine to a mixture of dimethylamino dienamine **1a** and dimethylformamide diethyl acetal (**2a**) in DMF leads to the formation of a mixture of two amidines **4a** and **4c**, transaminated product **4c** being dominant (see Table 1, entries *5*, *6*).

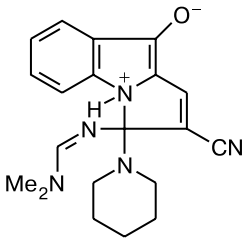
Thus, intramolecular transamination displayed in Scheme 7 seems to be the most likely pathway to amidines **4b,c**, though the second pathway involving the formation of another amide acetal (*e.g.*, such as acetal **2b**) in the reaction mixture is also not improbable.

Diethyl acetal **2a** has been reported to be more reactive than dimethyl acetal **2c** toward nucleophilic reagents (see Ref. 8). Our data for reactions of piperidino dienamine **1c** with acetals **2a,c** agree with the literature data. The reaction time is substantially lower for the reaction of dienediamine **1c** with acetal **2a** than with acetal **2c** (see Table 1, entries *12*, *14*). However, *N*-formylpiperidine diethyl acetal (**2b**) was the most reactive acetal in this reaction (see Table 1, entry *13*). This can be explained by the presence of such bulky substituents as ethoxy and piperidino groups in acetal **2b**, whose sufficiently strong nonbonding interaction destabilizes the ground state. This factor is much less significant for the planar ambident cation; thus, transformations of the substituents in acetals into groups with greater steric demands favor an increase in the cation content and, consequently (of course, to a certain limit), in the reactivity of amide acetal (Scheme 2).

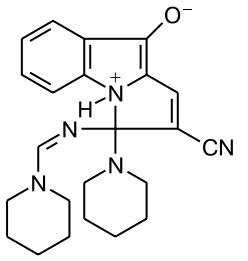
In addition, it can be seen in Table 1 (entries *12*—*14*) that the reactivity of acetal **2a**—**c** affects not only the reaction time but also the reaction pathway, which substantially changes the ratio of the reaction products.

It seems to be reasonable to associate these changes with structural features of cyclic intermediates (**A** for acetals **2a** and **2c** and **A´** for acetal **2b**).

In the reaction of dienediamine **1c** with the most reactive *N*-formylpiperidine acetal (**2b**), two possible transformations of intermediate **A´** include elimination of piperidine or substituted formamidine, giving compounds **4c**



A



A´

and **6c**, respectively; the former product is substantially dominant. The easy and, probably, sufficiently rapid elimination of these fragments is due to a steric strain in intermediate **A´** and predominant elimination of piperidine is favored by a longer conjugation chain in product **4c** than in compound **6c**. In the condensation of dienediamine **1c** with the second most reactive acetal **2a**, the ratio of products **4a** and **4c** was close to 1 : 1 (trace amounts of compound **6c** can be neglected in consideration). Intermediate **A** is sterically less strained than intermediate **A´** (see above) and the formation of more stable conjugated systems characteristic of compounds **4a** and **4c** is dominant in this case. Compound **4c** is a major product, which can be associated with the higher basicity of piperidine compared to dimethylamine (pK_a are 11.22 and 10.78, respectively). This provides an energy gain for piperidine analog **4c** in conjugation.

The pattern is more complicated for the reaction of dienediamine **1c** with the least reactive acetal **2c**. The resulting mixture contains compounds **4a**, **4c**, and **6c**, product **4a** being dominant. At the same time, the content of pyrroloindole **6c** in the mixture is increased. This is probably due to appreciable deceleration of the formation of intermediate amidine **3c** and, accordingly, intermediate **A**, which is then mainly consumed in elimination of piperidine (to product **4a**) and dimethylformamidine (to product **6c**). Apparently, the low rate of formation of intermediate **A** retards the transfer of the piperidine residue to the amidine *meso*-position (Scheme 7); it is not improbable that the transamination of acetals **2a**→**2b** is decisive for the formation of product **4c** in this reaction (Scheme 6). Inhibited formation of intermediate **A´** leads to a lowered amount of amidine **4c**; it seems to be likely that a rather high content of pyrroloindole **6c** is due to superposition of two independent processes, namely, the transformations of both intermediates **A** and **A´**.

Thus, we found that the reactions of dienediamines containing the residues of secondary amines in position 3 of the side chain with amide acetals do not stop at the step of amidine formation. Their subsequent cyclization with elimination of either secondary amine or substituted formamidine give amidines or the corresponding 3-aminopyrroloindoles, respectively. Depending on the reagents (dienediamine and acetal) and the solvent, the above cyclization processes can be accompanied by transamina-

tion leading to modified amidines. The reaction rate and the ratio of the reaction products depend on the reactivity of the acetal and the solvent used. Acetal **2b** was most reactive and acetal **2c** was least reactive. The reaction rate in DMF was higher than in benzene and ethanol.

Experimental

IR spectra were recorded on an FSM-1201 instrument (Nujol). Mass spectra of compounds **4a**, **4c**, and **6c** were recorded on a Waters ZQ-2000 mass spectrometer (positive ESI). Mass spectra of compounds **4b** and **6b** were recorded on a Finnigan SSQ-710 mass spectrometer (EI, direct inlet probe). A solution of a sample in methanol (10 μL, ~0.05 mg mL^{-1}) was introduced into the injector (flow rate of the carrier (methanol) was 0.3 mL min^{-1}) and after separation by column chromatography, part of the eluent flow (0.3 mL min^{-1}) was injected into the mass spectrometer. ^1H NMR spectra were recorded on a Bruker AC-300 spectrometer in DMSO-d_6 according to a Bruker standard procedure. The course of the reactions was monitored and the purity of the products was checked by TLC on Merck 60 F_{254} plates in chloroform—methanol (10 : 1) and benzene—methanol (9 : 1). Spots were visualized under UV light. The reaction mixtures were analyzed by HPLC on the Waters Breeze system consisting of a Waters 1525 gradient pump, a Waters 2487 two-wave detector, and a Rheodyne manual injector. The Empower software was used; a Phenomenex Luna C 18(2) analytical column (150×4.6 mm), a UV 254 detector, flow rate 1 mL min^{-1}, room-temperature separation time 20—30 min.

Products **4a**, **4b**, and **6b** were separated off with MeCN + H_2O (35 : 65, pH 5.2) as a mobile phase; for the mixtures containing compounds **4a**, **4c**, and **6c**, MeOH + H_2O (65 : 35, pH 5.2) was used. A buffer solution was prepared by addition of propylamine to aqueous 0.01% HCOOH to pH 5.2.

2-Cyano-3-dimethylaminomethyleneamino-9-oxo-9*H*-pyrrolo[1,2-*a*]indole (4a). Method ***A***. Acetal **2a** (0.9 mL, 6 mmol) was added to a suspension of dimethylamino dienamine **1a** (0.25 g, 1 mmol) in ethanol (20 mL). The reaction mixture was refluxed with stirring for 3.5 h. The suspension was cooled and the resulting precipitate was filtered off, washed with ethanol, and dried. The yield of amidine **4a*** was 0.22 g (83%), m.p. 244—245 °C (from methanol—acetone (6 : 1)). IR, ν/cm^{-1}: 1673 (CO), 2200 (CN). ^1H NMR (DMSO-d_6), δ: 3.13, 3.18 (both s, 3 H each, $N(CH_3)_2$); 7.27 (s, 1 H, H(1)); 7.26, 7.57, 7.60, 7.75 (all m, 1 H each, H(5)—H(8)); 8.50 (s, 1 H, CH). MS, *m/z*: 265 $[M + H]^+$, 287 $[M + Na]^+$, 551 $[2 M + Na]^+$, 815 $[3 M + Na]^+$. Found (%): C, 68.41; H, 4.59; N, 20.98. $C_{15}H_{12}N_4O$. Calculated (%): C, 68.17; H, 4.58; N, 21.20.

Method ***B***. Acetal **2a** (0.3 mL, 2 mmol) was added to a suspension of dimethylamino dienamine **1a** (0.25 g, 1 mmol) in benzene (5 mL) or DMF (5 mL). The reaction mixture was refluxed with stirring for 3.5 h (in DMF, at 80 °C for 1 h). The suspension was cooled and the resulting precipitate was filtered off, washed with benzene (or DMF) and ethanol, and dried. The yields of amidine **4a** were 0.18 g (65%) and 0.17 g (64%), respectively.

Method ***C***. Acetal **2a** (0.14 mL, 0.68 mmol) was added to a suspension of pyrroloindole **5** (0.07 g, 0.34 mmol) in DMF (5 mL)*. The reaction mixture was refluxed with stirring for 1 h. Then the solvent was removed and the residue was triturated with methanol. The resulting precipitate was filtered off, washed with methanol and ether, and dried. The yield of amidine **4a** was 0.06 g (70%).

Method ***D***. Acetal **2a** (0.3 mL, 2 mmol) was added to a stirred suspension of morpholino dienamine **1b** (0.3 g, 1 mmol) in ethanol (15 mL). The reaction mixture was refluxed with stirring for 2 h. Refluxing was continued with another portion of the acetal (0.3 mL) for 3 h and then with still another portion (0.3 mL) for an additional 2 h. The precipitate that formed was filtered off and washed with ethanol to give a mixture (0.2 g) of compounds **4a** and **6b**. The mixture was separated by column chromatography on SiO_2 eluted with benzene—methanol (50 : 0.1). The yield of amidine **4a** was 0.08 g (30%).

Method ***E***. Acetal **2a** (0.9 mL, 6 mmol) was added to a stirred suspension of piperidino dienamine **1c** (0.25 g, 0.85 mmol) in ethanol (15 mL). The reaction mixture was refluxed for ~5 h. Refluxing was continued with another portion of the acetal (0.25 mL) for 1 h and then with still another portion (0.25 mL) for an additional 1 h. The precipitate was filtered off hot, washed with ethanol, and dried. The yield of amidine **4a** was 0.12 g (54%).

Method ***F***. A mixture of piperidino dienamine **1c** (0.15 g, 0.5 mmol) and acetal **2a** (0.15 mL, 1 mmol) was refluxed in DMF (5 mL) for 1 h. The solvent was removed and the residue was triturated with propan-2-ol to give a mixture (0.12 g) of compounds **4a** and **4c**. The mixture was separated by column chromatography on SiO_2 eluted with chloroform—ethyl acetate (20 : 1). The yield of amidine **4a** was 0.02 g (13%)**.

A mixture of the compounds obtained according to methods ***B***—***F*** with a sample from method ***A*** did not depress the melting point.

2-Cyano-3-morpholinomethyleneamino-9-oxo-9*H*-pyrrolo[1,2-*a*]indole (4b). Method ***A***. A mixture (0.16 g) of compounds **4a**, **4b**, and **6b** was obtained as described for amidine **4a** in method ***F*** from morpholino dienamine **1b** (0.15 g, 0.5 mmol) and acetal **2a** (0.15 mL, 1 mmol) in DMF (5 mL). The mixture was separated by column chromatography on SiO_2 eluted with chloroform—ethyl acetate (9 : 1). The yield of amidine **4b** was 0.04 g (26%), m.p. 247—249 °C. IR, ν/cm^{-1}: 1674 (CO), 2200 (CN). ^1H NMR (DMSO-d_6), δ: 3.60 (2 H), 3.70 (4 H), 3.80 (2 H) (all m, $H_2C(3')$, $H_2C(2')$ and $H_2C(6')$, $H_2C(5')$); 7.28 (s, 1 H, H(1)); 7.26 (1 H), 7.60 (2 H), 7.72 (1 H) (all m, H(5)—H(8)); 8.56 (s, 1 H, CH). MS, *m/z*: 307 $[M + H]^+$, 329 $[M + Na]^+$, 345 $[M + K]^+$, 613 $[2 M + H]^+$, 635 $[2 M + Na]^+$, 651 $[2 M + K]^+$. Found (%): C, 66.60; H, 4.66; N, 17.75. $C_{17}H_{14}N_4O_2$. Calculated (%): C, 66.66; H, 4.61; N, 18.29.

Method ***B***. A mixture (0.18 g) of compounds **4a**, **4b**, and **6b** was obtained analogously from morpholino dienamine **1b** (0.25 g, 0.87 mmol) and acetal **2a** (0.25 mL, 1.69 mol) in DMF (7 mL)

* For **1a** : **2a** = 1 : 2 and a reaction time of 7 h, a mixture (0.22 g) of amidine **4a** and the starting dienediamine **1a** was obtained. Separation of this mixture by column chromatography on SiO_2 eluted with chloroform gave amidine **4a** in 30% yield.

* Heating to boiling of a mixture of dienediamine **1a** and acetal **2a** (without any solvent) gave amidine **4a** in 79% yield.

** Amidine **4a** can also be isolated by column chromatography from a mixture of products obtained under the conditions of entries *6*, *7*, *9*, *10*, and *14* (see Table 1).

in the presence of morpholine (0.15 mL, 1.69 mmol). Separation as described in method ***A*** gave amidine **4b** (0.1 g, 39%).

2-Cyano-9-oxo-3-piperidinomethyleneamino-9*H*-pyrrolo[1,2-*a*]indole (4c). Method ***A***. A mixture of piperidino dienamine **1c** (0.3 g, 1 mmol) and acetal **2b** (0.4 mL, 2 mmol) was refluxed in DMF (10 mL) for 0.5 h. The solvent was removed, the residue was triturated with methanol, and the precipitate was filtered off, washed with methanol, and dried. The yield of amidine **4c** was 0.23 g (74%), m.p. 224—225 °C (from methanol). IR, ν/cm^{-1}: 1676 (CO), 2200 (CN). ^{1}H NMR (DMSO-d_6), δ: 1.67 (br.m, 6 H, $H_2C(3')$—$H_2C(5')$); 3.53, 3.76 (both br.t, 2 H each, $H_2C(2')$, $H_2C(6')$, J = 5.0 Hz); 7.24 (s, 1 H, H(1)); 7.26, 7.58, 7.61, 7.71 (all m, 1 H each, H(5)—H(8)); 8.50 (s, 1 H, CH). MS, *m/z*: 305 $[M + H]^+$, 327 $[M + Na]^+$, 631 $[2 M + Na]^+$, 935 $[3 M + Na]^+$. $C_{18}H_{16}N_4O$. Found (%): C, 71.60; H, 5.34; N, 18.33. Calculated (%): C, 71.03; H, 5.30; N, 18.41.

Method ***B***. A mixture of pyrroloindole **5** (0.09 g, 0.3 mmol) and acetal **2b** (1.5 mL) was refluxed for 5 min and then cooled. The precipitate was filtered off, washed with methanol and ether, and dried. The yield of amidine **4c** was 0.06 g (58%).

Method ***C***. The mother liquor obtained after the isolation of amidine **4a** according to method ***E*** was cooled. The precipitate that formed was filtered off to give a mixture (0.04 g) of amidines **4c** and **4a**. The mixture was separated by column chromatography on SiO_2 eluted with chloroform—ethyl acetate (20 : 1). The yield of amidine **4c** was 0.02 g (7.7%).

Method ***D***. Compound **4c** was isolated by column chromatography from its mixture with compound **4a** (see method ***F*** for the synthesis of amidine **4a**). The yield of amidine **4c** was 0.06 g (39%)*.

A mixture of the compounds obtained according to methods ***B***—***D*** with a sample from method ***A*** did not depress the melting point.

2-Cyano-3-morpholino-9-oxo-9*H*-pyrrolo[1,2-*a*]indole (6b) was isolated by column chromatography from its mixture with compound **4a** (see method ***D*** for the synthesis of amidine **4a**). The yield of compound **6b** was 0.05 g (22%), m.p. 216 °C (from MeOH). IR, ν/cm^{-1}: 1693 (CO), 2216 (CN). ^{1}H NMR (DMSO-d_6), δ: 3.36, 3.85 (both m, 4 H each, $H_2C(2')$—$H_2C(5')$); 7.32 (s, 1 H, H(1); 7.33, 7.40, 7.64, 7.70 (all m, 1 H each, H(5)—H(8)). MS (EI, 70 eV), *m/z* (I_{rel} (%)): 279 $[M]^+$ (100), 221 $[M - CH_2CH_2OCH_2]^+$ (74), 193 $[M - N(CH_2)_2O(CH_2)_2]^+$ (17). Found (%): C, 72.24; H, 5.41; N, 14.92. $C_{17}H_{15}N_3O \cdot 1/4H_2O$. Calculated (%): C, 72.45; H, 5.54; N, 14.91.

2-Cyano-9-oxo-3-piperidino-9*H*-pyrrolo[1,2-*a*]indole (6c). The mother liquor obtained after the isolation of a mixture of amidines **4a** and **4b** (see method ***C*** for the synthesis of amidine **4c**) was concentrated. Column chromatography on SiO_2 with chloroform—ethyl acetate (20 : 1) as an eluent gave pyrroloindole (**6c**) (0.02 g, 8.5%)*, m.p. 177—178 °C (from MeOH). IR, ν/cm^{-1}: 1683 (CO), 2217 (CN). ^{1}H NMR (DMSO-d_6), δ: 1.64 (2 H), 1.76 (4 H) (both m, $H_2C(4')$, $H_2C(3')$ and $H_2C(5')$); 3.33 (m, 4 H, $H_2C(2')$ and $H_2C(6')$); 7.27 (s, 1 H, H(1)); 7.32 (2 H), 7.62 (1 H), 7.68 (1 H) (all m, H(5)—H(8)). MS, *m/z*: 265 $[M + H]^+$, 287 $[M + Na]^+$, 551 $[2 M + Na]^+$, 815 $[3 M + Na]^+$. Found (%): C, 72.24; H, 5.41; N, 14.92. $C_{17}H_{15}N_3O \cdot 1/4H_2O$. Calculated (%): C, 72.45; H, 5.54; N, 14.91.

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* Amidine **4c** can also be isolated by column chromatography from a mixture of products obtained under the conditions of entry *6* (see Table 1).

* Pyrroloindole **6c** can also be isolated by column chromatography from a mixture of products obtained under the conditions of entry *13* (see Table 1).