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REACTIONS OF CINNOLINE, CINNOLINE N-OXIDES, AND THEIR CHLORO DERIVATIVES WITH ALKYLAMINES: THE FIRST CASE OF NUCLEOPHILIC SUBSTITUTION OF HYDROGEN IN THE CINNOLINE SERIES*

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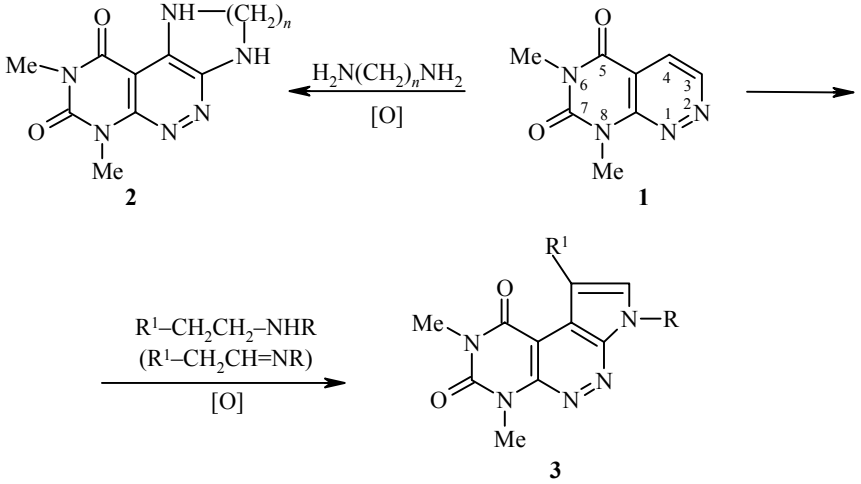
In contrast to cinnoline and cinnoline $N_{(1)}$-oxide, cinnoline $N_{(2)}$-oxide reacts with primary and secondary amines on prolonged heating or in the presence of oxidants to give 3-alkylaminocinnolines.

Keywords: 3-alkylaminocinnolines, 4-alkylaminocinnolines, 4-chlorocinnoline $N_{(1)}$-oxide, 4-chlorocinnoline $N_{(2)}$-oxide, cinnoline, cinnoline $N_{(1)}$-oxide, cinnoline $N_{(2)}$-oxide, aminodehalogenation, nucleophilic substitution of hydrogen, oxidative amination.

We have recently discovered that not only does 6,8-dimethylpyrimido[4,5-*c*]pyridazin-5,7(6H,8H)-dione (**1**) undergo oxidative monoamination [1], which is general for neutral diazines, but it also has the unprecedented capability to undergo tandem S_N^H-S_N^H reactions under the influence of bifunctional nucleophiles [2, 3]. Thus oxidative amination of the pyridazinouracil **1** with α,ω-diaminoalkanes to form polynuclear diamines **2** [2], and its reactions with alicyclic dialkylamines or aliphatic aldimines in the presence of an oxidizing agent is accompanied by annelation of a pyrrole ring to the heterocyclic starting material to give compound **3** [3].



2 **1** **3**

* Dedicated to Professor S. Gronowitz on his 75th Birthday.

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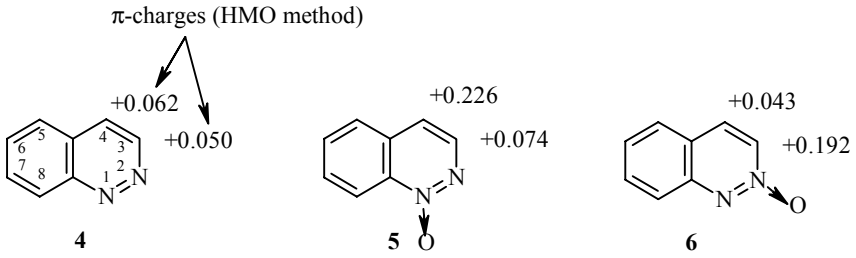
It seemed interesting to extend these reactions to other substrates which, like molecule **1**, have two neighbouring electron-deficient carbon atoms in the pyridazine ring. In this work the simplest of the condensed pyridazines, cinnoline **4**, and its $N_{(1)}$- and $N_{(2)}$-oxides (**5** and **6**) were used as substrates.



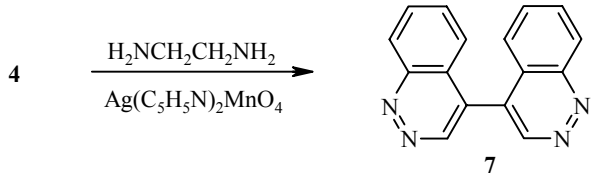
The starting N-oxide **5** and **6** were obtained by oxidation of cinnoline with peracetic acid. It was previously reported [4, 5] that a mixture of the mono N-oxides **5** (mp 110.5-111.5°C) and **6** (mp 125-126°C) and the cinnoline 1,2-dioxide was produced in this reaction with yields of 26, 49, and 0.3% respectively. We have established from a comparative analysis of the ^{1}H NMR spectra of cinnoline, and its N-oxides (Table 1) that the predominant product was erroneously ascribed the structure of the $N_{(2)}$-oxide. Evidently that the protons adjacent to the N→O group, H(3) in the $N_{(2)}$-oxide **6** and H(8) in the $N_{(1)}$-oxide **5**, should experience its shielding anisotropic effect, leading to a shift of the corresponding signals to stronger field in comparison with the spectrum of cinnoline (δ H(3) 9.28, δ H(8) 8.51 ppm). In the spectrum of the N-oxide with mp 125-126°C the H(8) signal (δ 7.90 ppm) is noticeably shifted to stronger field, which corresponds to structure **5**, while in the spectrum of the compound with mp 110-111°C the signal of H(3) (δ 8.28 ppm) shows the greatest shift, which corresponds to compound **6**. We used the N-oxide with mp 110-111°C as the starting material in the synthesis of 3-alkylaminocinnolines.

To our surprise there are no reports in the literature of nucleophilic substition of hydrogen in cinnoline (e.g., in the reviews [6, 7]).

We have found that cinnoline has an unexpectedly low reactivity with respect to amines in contrast with most condensed and monocyclic diazines [6, 8, 10]. It did not react with potassium amide in the $KNH_2/NH_3/KMnO_4$ system nor with methyl-, benzyl-, and cyclohexylamines in the presence of $Ag(C_5H_5N)_2MnO_4$. Cinnoline reacted very slowly with an excess of ethylenediamine in the presence of an oxidant and after 5 days gave only 4,4'-bicinnolyl (**7**) in 2.5% yield. Dimerization of this type is evidently an indication of the formation of anion radicals of the substrate *in situ*. The reason for the low activity of cinnoline in the oxidative amination reaction may be its low π-deficiency [12], comparable with pyridine, which is also inert to the amide ion and other aminating agents in these conditions [13].

TABLE 1. ^{1}H NMR Spectra of Cinnoline N-Oxides

Compound	Proton chemical shifts ($CDCl_3$), δ, ppm (J, Hz)			
	H(3), d	H(4)	H(5), H(6), H(7)	H(8)
4	9.28 (J_{34} = 5.9)	7.70-7.86 (m)		8.51 (d, J_{78} = 8.2)
5	8.16 (J_{34} = 6.9)	7.96 (d, J_{34} = 6.9)	7.57 (dd, J_{56} = 8.5; J_{67} = 8.3) 7.74 (d, J_{56} = 8.5) 7.77 (dd, J_{67} = 8.3; J_{78} = 8.5)	7.90 (d, J_{78} = 8.5)
6	8.28 (J_{34} = 6.2)	7.41 (d, J_{34} = 6.2)	7.70-7.85 (m)	8.64 (m)
Cinnoline 1,2-dioxide	8.15 (J_{34} = 7.3)	7.50 (d, J_{34} = 7.3)	7.67-7.81 (m)	8.39 (d, J_{78} = 8.7)

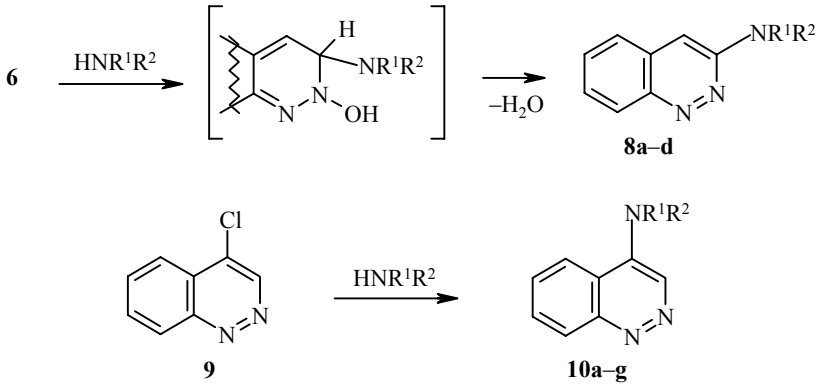


It is known that the introduction of the N-oxide function into the azine ring increases its π-deficiency and frequently facilitates nucleophilic substitution reactions [6, 12]. In fact according to quantum-chemical calculations (the HMO method) the positive charges on atoms C(3) and C(4) in the cinnoline $N_{(1)}$- and $N_{(2)}$-oxides (**5** and **6**) are greater than in molecule **4**. Therefore, despite the report cinnoline $N_{(2)}$-oxide reacts with phenylmagnesium bromide to give a mixture of products of destruction of the heterocycle [14], we studied the reactions of compounds **5** and **6** with alkylamines, assuming that reactions with nucleophiles under milder condition should be more selective.

We established that the $N_{(2)}$-oxide **6** reacted with an excess of primary or secondary amines on prolonged heating (25-100 h) to give 3-aminocinnolines **8a-d** in 26-98% yields (Scheme 1). The lowest yields corresponded to the bulkiest amines. When benzyl- and cyclohexylamines and ethylenediamine were used complex mixtures of products were obtained which could not be separated or identified.

According to the quantum-chemical calculation, the greatest positive charge in the molecule of the $N_{(2)}$-oxide (in comparison with cinnoline) is concentrated at C(3) which is attacked by the nucleophile. This conclusion is based on a comparison of compound **8** with 4-alkylaminocinnolines **10** (Table 2), which we obtained by aminodehalogenation of 4-chlorocinnoline (**9**). For example, the 4-amino derivatives are colourless (λ_{max} 349-370 nm) while the 3-aminocinnolines **8** are bright-yellow (λ_{max} 400-417 nm). In the ^{1}H NMR spectra of compounds **10** the signal of the H(3) proton is found at δ 8.5-8.9 ppm, whereas the signal of proton H(4) of the 3-amino derivatives **8** is shifted by about 1 ppm to strong field (δ 7.6-7.9 ppm). The signals of the NH protons of the 3-alkylamino group are somewhat deshielded and appear at weaker field (δ 5.2-6.5 ppm) in comparison with the signals of analogous protons in the 4-alkylamino derivatives **10** (δ 5.3-5.7 ppm).

Scheme 1



8 a NHR^1R^2 = NHPr, **b** NHR^1R^2 = NHPr-*i*, **c** NHR^1R^2 = pyrrolidino, **d** NHR^1R^2 = piperidino; **10 a** NR^1R^2 = NHPr, **b** NR^1R^2 = cyclohexylamino, **c** NR^1R^2 = = $NHCH_2Ph$, **d** NR^1R^2 = pyrrolidino, **e** NR^1R^2 = piperidino, **f** NR^1R^2 = morpholino, **g** NR^1R^2 = $NHCH_2CH_2NH_2$

It is known [6, 15] that the addition of an oxidizing agent considerably accelerates the reactions of azine N-oxides with amines to give amino derivatives either with or without retention of the N-oxide function. Reaction of cinnoline $N_{(2)}$-oxide with propylamine and pyrrolidine in the presence of $Ag(C_5H_5N)_2MnO_4$ proceeds efficiently under mild conditions (20°C) to give exclusively the desoxy 3-aminocinnolines **8a** and **8c** in yields of 60 and 95% respectively.

TABLE 2. Spectral Characteristics of Compounds **8**, **10**, **13**, and **14**

Compound	IR spectrum, ν, cm^{-1}			^1H NMR spectrum($CDCl_3$), δ, ppm (*J*, Hz)*							UV spectrum, λ_{max}, nm (lg ε)
	Ring	C–H arom	N–H	H(3), s	H(5)	H(6)	H(7)	H(8)	NH, br. s	R	
1	2	3	4	5	6	7	8	9	10	11	12
8a	1572, 1599, 1626	3075	3168	—	8.20 (d, J_{56} = 8.0)	7.66-7.80 (m)		8.63 (d, J_{78} = 8.7)	6.40	1.03 (3H, t, *J* = 7.4, $CH_2CH_2\underline{CH_3}$); 1.82 (2H, m, $CH_2\underline{CH_2}CH_3$); 3.38 (2H, m, $\underline{CH_2}CH_2CH_3$)	281 (3.83), 408 (4.12)
8b	1575, 1610, 1630	3083	3200	—	7.95 (d, J_{56} = 7.8)	7.65-7.77 (m)		8.69 (d, J_{78} = 8.9)	5.20	1.38 (6H, d, *J* = 6.3, $CH(\underline{CH_3})_2$); 3.87 (1H, m, $\underline{CH}(CH_3)_2$)	277 (3.65), 410 (4.10)
8c	1526, 1580, 1606	—	—	—	8.22 (d, J_{56} = 8.6)	7.64-7.74 (m)		8.72 (d, J_{78} = 8.8)	—	2.07 (4H, t, *J* = 6.5, β-CH_2 pyrrolidino); 3.68 (4H, t, *J* = 6.5, α-CH_2 pyrrolidino)	276 (3.83), 416 (4.22)
8d	1530, 1590, 1602	—	—	—	7.98 (m)	7.71-7.75 (m)		8.68 (m)	—	1.72 (2H, m, γ-CH_2 piperidino); 1.84 (4H, m, β-CH_2 piperidino); 3.16 (4H, m, α-CH_2 piperidino)	301 (3.62), 400 (3.92)
10a	1553, 1600, 1646	3100	3220	8.65	7.83 (d, J_{56} = 8.4	7.54 (dd, J_{56} = 8.4, J_{67} = 8.1)	7.70 (dd, J_{67} = 8.1, J_{78} = 8.5)	8.27 (d, J_{78} = 8.5)	5.53	1.04 (3H, t, *J* = 7.4, $CH_2CH_2\underline{CH_3}$); 1.77 (2H, m, $CH_2\underline{CH_2}CH_3$); 3.38 (2H, m, $\underline{CH_2}CH_2CH_3$)	234 (4.05), 351 (4.14)
10b	1550, 1600, 1646	3072, 3100	3229	8.65	7.82 (d, J_{56} = 8.4)	7.55 (dd, J_{56} = 8.4, J_{67} = 7.9)	7.71 (dd, J_{67} = 7.9, J_{78} = 8.4)	8.28 (d, J_{78} = 8.4)	5.26	1.39 (6H, m, $3CH_2$, C_6H_{11}); 1.81 (2H, m, CH_2, C_6H_{11}); 2.16 (2H, m, CH_2, C_6H_{11}); 3.61 (1H, m, CH, C_6H_{11})	351 (4.01)
10c	1540, 1590, 1630	3119	3250	8.67	7.84 (d, J_{56} = 8.4)	7.57 (dd, J_{56} = 8.4, J_{67} = 8.2)	7.73 (dd, J_{67} = 8.2, J_{78} = 8.4)	8.32 (d, J_{78} = 8.4)	5.70	4.60 (2H, d, *J* = 3.6, $NH\underline{CH_2}$); 7.33-7.39 (5H, m, Ph)	347 (4.13)

TABLE 2 (continued)

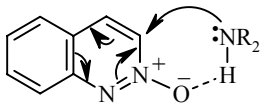
1	2	3	4	5	6	7	8	9	10	11	12
10d	1513, 1553, 1606	—	—	8.51	8.17 (d, J_{56} = 8.6)	7.43 (dd, J_{56} = 8.6, J_{67} = 8.2)	7.65 (dd, J_{67} = 8.2, J_{78} = 8.6)	8.25 (d, J_{78} = 8.6)	—	2.06 (4H, t, J = 6.45, β-CH_2 pyrrolidino); 3.78 (4H, t, J = 6.45, α-CH_2 pyrrolidino)	363 (3.20)
10e	1535, 1580, 1633	—	—	8.84	7.89 (d, J_{56} = 8.5)	7.60 (dd, J_{56} = 8.5, J_{67} = 8.3)	7.72 (dd, J_{67} = 8.3, J_{78} = 8.5)	8.39 (d, J_{78} = 8.5)	—	1.74 (2H, m, γ-CH_2 piperidino); 1.83 (4H, m, β-CH_2 piperidino); 3.33 (4H, m, α-CH_2 piperidino)	328 (3.79), 370 (3.95)
10f	1533, 1580, 1635	—	—	8.88	7.95 (d, J_{56} = 8.2)	7.65 (dd, J_{56} = 8.2, J_{67} = 7.9)	7.76 (dd, J_{67} = 7.9, J_{78} = 8.4)	8.45 (d, J_{78} = 8.4)	—	3.35 (4H, t, J = 4.2, $N(CH_2)_2$); 3.97 (4H, t, J = 4.2, $O(CH_2)_2$)	328 (3.87), 363 (3.89)
10g	1550, 1600, 1646	3100	3200-3400	8.76	8.13 (d, J_{56} = 8.5)	7.66 (dd, J_{56} = 8.5, J_{67} = 8.4)	7.79 (dd, J_{67} = 8.4, J_{78} = 8.5)	8.37 (d, J_{78} = 8.5)	8.25	3.13 (2H, t, J = 6.3, $C\underline{H}_2NH_2$); 3.67 (2H, t, J = 6.3, $C\underline{H}_2NH$); 7.80-8.10 (br. s, NH_2)	353 (3.90)
10h	1530, 1565, 1616	3105	3220, 3345	8.62	8.05 (d, J_{56} = 8.6)	7.59 (dd, J_{56} = 8.6, J_{67} = 8.5)	7.78 (dd, J_{67} = 8.5, J_{78} = 8.6)	8.24 (d, J_{78} = 8.6)	7.43	—	350 (4.02)
13a	1540, 1600	—	3100-3400	7.77	8.46 (m)	7.84-7.88 (m)		8.46 (m)	8.18	3.14 (2H, m, $C\underline{H}_2NH_2$); 3.60 (2H, m, $C\underline{H}_2NH$); 7.56 (br. s, NH_2)	—
13b	1565, 1606	—	3100-3400	7.81	7.60 (d, J_{56} = 8.4)	7.49 (dd, J_{56} = 8.4, J_{67} = 7.4)	7.72 (dd, J_{67} = 7.4, J_{78} = 8.4)	8.28 (d, J_{78} = 8.4)	7.90-8.20	1.93 (2H, m, $CH_2C\underline{H}_2CH_2$); 2.90 (2H, t, J = 6.8, $C\underline{H}_2NH_2$); 3.40 (2H, t, J = 6.8, $C\underline{H}_2NH$)	—
14a	1525, 1625	—	3100-3400	7.88	7.62 (d, J_{56} = 7.9)	7.50 (dd, J_{56} = 7.9, J_{67} = 7.2)	7.74 (dd, J_{67} = 7.2, J_{78} = 8.0)	8.28 (d, J_{78} = 8.0)	8.02	3.07 (2H, t, J = 6.1, $C\underline{H}_2NH_2$); 3.61 (2H, t, J = 6.1, $C\underline{H}_2NH$)	—
14b	1535, 1605	—	3100-3400	7.80	7.60 (d, J_{56} = 8.4)	7.50 (dd, J_{56} = 8.4, J_{67} = 7.8)	7.73 (dd, J_{67} = 7.8, J_{78} = 8.2)	8.23 (d, J_{78} = 8.2)	8.00	1.92 (2H, m, $CH_2C\underline{H}_2CH_2$); 2.90 (2H, t, J = 7.2, $C\underline{H}_2NH_2$); 3.38 (2H, t, J = 7.2, $C\underline{H}_2NH$)	—

* ^{1}H NMR spectra ($CDCl_3$): **8a** – 7.60 (H(4), s) , **8b** – 7.63 (H(4), s), **8c** – 7.61 (H(4), s), **8d** – 7.87 (H(4), s).

TABLE 3. Conditions for the Amination of Compounds **5** and **6** and the Physicochemical Characteristics of Compounds **8**, **10**, **13**, and **14**

Compound	Empirical formula	Found, % / Calculated, %			mp, °C	R_f of product	Reaction conditions (method A)			Yield, %
		C	H	N			Amine	V, ml	Time, h	
8a	$C_{11}H_{13}N_3$	70.8 / 70.6	7.2 / 6.9	22.3 / 22.5	182-184	0.1	$PrNH_2$	2	25.5	53
8b	$C_{11}H_{13}N_3$	70.4 / 70.6	7.3 / 6.9	22.7 / 22.5	208-210	0.1	*i*-$PrNH_2$	6	100	26
8c	$C_{12}H_{13}N_3$	72.3 / 72.4	6.6 / 6.6	21.2 / 21.1	178-180	0.15	Pyrrolidine	2	60	98
8d	$C_{13}H_{15}N_3$	73.1 / 73.2	6.8 / 7.0	20.0 / 19.8	125-127	0.25	Piperidine	13	100	70
10a	$C_{11}H_{13}N_3$	70.7 / 70.6	6.7 / 6.9	22.6 / 22.5	158-160	0.1	$PrNH_2$	2	24	69
10b	$C_{14}H_{17}N_3$	74.1 / 74.0	7.3 / 7.5	18.6 / 18.5	160-162	0.11	Cyclohexylamine	5	144	60
10c	$C_{15}H_{13}N_3$	76.8 / 76.6	5.4 / 5.6	17.7 / 17.9	193-195	0.2	$PhCH_2NH_2$	4	144	57
10d	$C_{12}H_{13}N_3$	72.6 / 72.4	6.3 / 6.6	21.3 / 21.1	166-168	0.23	Pyrrolidine	3	0.01	96
10e	$C_{13}H_{15}N_3$	73.4 / 73.2	7.1 / 7.0	20.0 / 19.8	134-136	0.2	Piperidine	2	0.08	90
10f	$C_{12}H_{13}N_3O$	66.7 / 67.0	6.2 / 6.0	19.3 / 19.5	140-142	0.15	Morpholine	2	24	75
10g	$C_{10}H_{12}N_4$	63.7 / 63.8	6.5 / 6.4	29.6 / 29.8	260 (dec.)	0.05	$NH_2(CH_2)_2NH_2$	2.5	24	53
10h	$C_8H_7N_3$	66.3 / 66.2	5.0 / 4.8	29.2 / 29.0	210 (dec.)	0.15	KNH_2		5	6.5
13a	$C_{10}H_{12}N_4O$	58.6 / 58.8	5.7 / 5.9	27.3 / 27.4	252-254 (dec.)	0.1	$NH_2(CH_2)_2NH_2$	2	168	95
13b	$C_{11}H_{14}N_4O$	59.8 / 60.0	6.2 / 6.4	25.2 / 25.7	>250 (dec.)	0.1	$NH_2(CH_2)_3NH_2$	4	168	94
14a	$C_{10}H_{12}N_4O$	58.7 / 58.8	5.4 / 5.9	27.6 / 27.4	258-260 (dec.)	0.01	$NH_2(CH_2)_2NH_2$	2	24	89
14b	$C_{11}H_{14}N_4O$	60.2 / 60.5	6.5 / 6.4	25.6 / 25.7	275-277 (dec.)	0.01	$NH_2(CH_2)_3NH_2$		24	90

In contrast to compound **6**, cinnoline $N_{(1)}$-oxide **5** does not react with alkylamines either on prolonged heating or in the presence of an oxidizing agent. It is possible that in the case of the $N_{(2)}$-oxide additional activation of the substrate occurs in the form of an intermediate of type **11**, which facilitates nucleophilic attack at position 3.



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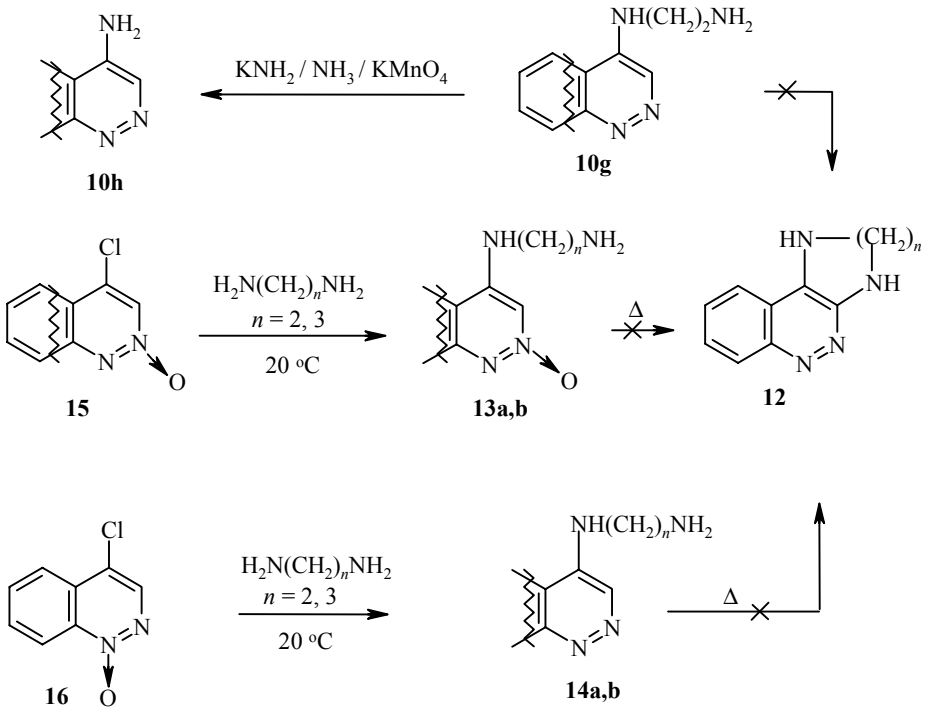
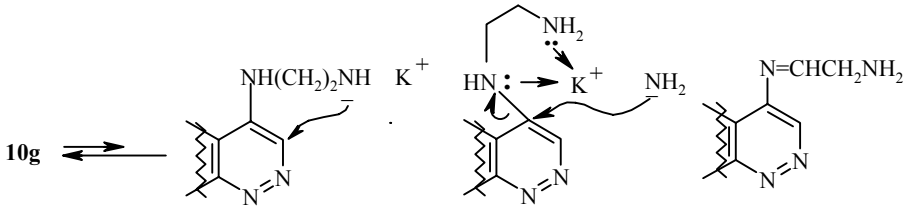
Since we had not succeeded in carrying out tandem S_N^H-S_N^H conversions in cinnoline and its N-oxides, we attempted to synthesize polynuclear systems of type **12** from 4-(β-aminoethylamino)cinnoline **10g** and the N-oxides **13** and **14** (the latter were obtained from chlorides **15** and **16** by scheme 2). Amine **10g** was treated with potassium amide and $KMnO_4$ in liquid ammonia. We had thought that in these conditions it would be possible to form an equilibrium concentration of the N-anion **17** which would undergo intermolecular amination. But instead of the expected piperazinocinnoline (**12**, n = 2), only 4-aminocinnoline (**10h**) was isolated in 6.5% yield. It is possible that during the reaction the diaminoethylene substituent coordinates potassamide, causing attack of the amide anion at C(4) *via* the intermediate complex **18**. But it is more likely that the starting amine **10g** is oxidized to the imine **19**, hydrolysis of which leads to **10h.** Attempts to convert the N-oxides **13** and **14** into the cyclic amines **12** by heating for many hours in DMSO (100 h, 90-100°C) or with excess α,ω-diaminoalkanes were unsuccessful, the starting materials remaining unchanged.

Scheme 2



13, **14** **a** n = 2, **b** n = 3



17 **18** **19**

So, in contrast to pyridazinouracil **1**, cinnoline **4** and its $N_{(1)}$-oxide **5** do not participate in oxidative amination and tandem conversions of the S_N^H-S_N^H type. Direct alkylamination is characteristic only for cinnoline $N_{(2)}$-oxide **6**. This is the first example of nucleophilic substitution of hydrogen in the cinnoline series.

EXPERIMENTAL

^{1}H NMR spectra were recorded on a Bruker-250 (250 MHz) spectrometer, UV spectra of ethanol solutions on a Specord M-40 spectrophotometer, and IR spectra of nujol mulls on Specord IR-71 spectrometer. Chromatography was carried out on Al_2O_3 (Brockman activity IV-V). Melting points were measured in glass capillaries with a PTP apparatus and were not corrected.

The physicochemical and spectral characteristics of the compounds synthesized are cited in Tables 2 and 3.

4,4'-Bicinnoline (7). The oxidizing agent $Ag(C_5H_5N)_2MnO_4$ (0.38 g, 1 mmol) was added in small portions to a solution of compound **4** (0.38 g, 3 mmol) in ethylenediamine (5 ml) cooled to 10°C. The reaction mixture was kept at 20°C for 5 days and was then evaporated to dryness. The residue was extracted with chloroform, the extract was concentrated to about 3 ml and passed through an Al_2O_3 column with $CHCl_3$ as eluent. The first fraction collected was a colorless fraction with R_f 0.32, containing the starting material **4**, then a yellow fraction with R_f 0.12 was collected. The solvent was evaporated and the residue crystallized when treated with diethyl ether, yield 0.019 g (2.5%). Compound **7** consisted of clear yellow crystals, mp 235-236°C, which corresponded to literature data [16]. Mass spectrum, *m/z* (I_{rel}, %): 258 (100) $[M]^+$, 229 (12) $[M - 1 - N_2]^+$, 200 (81) $[M - 2 - 2N_2]^+$, 176 (18), 150 (15), 126 (12), 100 (13), 86 (8), 75 (18), 62 (12), 50 (34), 39 (23), 26 (3). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 9.35 (2H, s , 2H(3)); 8.74 (2H, d, J_{78} = 8.6, 2H(8)); 7.95 (2H, dd, J_{67} = 8.5, J_{78} = 8.6, 2H(7)); 7.72 (2H, dd, J_{56} = 8.5, J_{67} = 8.5, 2H(6)); 7.47 (2H, d, J_{56} = 8.5, 2H(5)). Found, %: C 74.6; H 3.7; N 21.6. $C_{16}H_{10}N_4$. Calculated, %: C 74.4; 3.9; N 21.7.

3-Alkylaminocinnolines (8a-d) (General Method A). A solution of compound **6** (0.1 g, 0.6 mmol) in an alkylamine was refluxed for the time reported in Table 3. The bright-yellow solution was evaporated to dryness, the residue was dissolved in a minimum amount of $CHCl_3$ and chromatographed on an alumina column with $CHCl_3$ as eluent (10:1 $CHCl_3$–Et_2O for compound **8c**). The first fraction collected (R_f 0.3) contained starting material **6**, was followed by a clear yellow solution of the aminocinnoline (see Table 3 for R_f). Bright-yellow crystals of compounds **8a-d** were obtained after recrystallization from benzene (petroleum ether for compound **8c**).

General Method B. Small portions of $Ag(C_5H_5N)_2MnO_4$ (0.42 g, 1.1 mmol) were added to a solution of compound **6** (0.1 g, 0.7 mmol) in 2-5 ml of the corresponding alkylamine, cooled to 10°C. The reaction mixture was kept for 10 days at 20°C (20 days for **8a**). The mixture was evaporated and the residue extracted with $CHCl_3$ (10 ml), then concentrated to about 3 ml and chromatographed on an Al_2O_3 column with $CHCl_3$ as eluent. Bright-yellow fraction with R_f shown in Table 3 was collected. In the case of compound **8a**, a fraction containing unreacted compound was first collected (R_f 0.3). The products were recrystallized from benzene: yields **8a** 60, **8c** 95%.

4-Alkylaminocinnolines (10a-g) (General Method). A solution of compound **9** (0.17 g, 1 mmol) in alkylamine was kept at 20°C for the time given in Table 3, and then evaporated to dryness. The residue was treated with water (10 ml), neutralized with NH_4OH, and evaporated again. The product was recrystallized from benzene (**10e,f** from petroleum ether, and **10g** was washed out of the mixture with hot methanol until colorless). Amine **10b** was chromatographed on an Al_2O_3 column with $CHCl_3$ as eluant (for R_f see Table 3) before recrystallization. Compounds **10a-g** consist of colorless or bright-yellow crystals.

4-Aminocinnoline (10h). Compound **10g** (0.2 g, 1 mmol) was added to a solution of potassium (0.156 g, 4 mmol) in liquid ammonia (30 ml) at -60°C. After 10 min $KMnO_4$ (0.158 g, 1 mmol) was added to the bright-yellow solution. The solution was stirred for 5 h while the temperature was raised stepwise to 20°C. The ammonia evaporated. The residue was extracted with methanol (20 ml), the extract was concentrated to 5 ml and chromatographed on an Al_2O_3 column with $CHCl_3$ as eluent. The fraction collected had the R_f shown in Table 3. Compound **10h** consists of creamy crystals; mp 210°C (dec.), which corresponds to data from [17].

4-(ω-Aminoalklylamino)cinnoline $N_{(2)}$-Oxides (13a,b). A solution of compound **15** [18] (0.2 g, 1 mmol) in 2-4 ml of the corresponding diaminoalkane was kept for 7 d at 20°C and then evaporated to dryness. The residue was dissolved in methanol (5 ml) and chromatographed on an Al_2O_3 column with 1:1 $CHCl_3$–CH_3OH as eluent. The bright-yellow fraction was collected (for R_f see Table 3). Compounds **13a,b** consist of bright-yellow crystals.

4-(ω-Aminoalklylamino)cinnoline $N_{(1)}$-Oxides (14a,b). A solution of compound **16** (0.1 g, 0.5 mmol) in the corresponding diaminoalkane (2-3 ml) was kept for 1 d at 20°C and then evaporated to dryness. The residue was washed clean from impurities with boiling methanol until colorless. Compounds **14a,b** are colorless crystals.

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