3-Carbamoyl-6-methyl-2-keto-4-phenyl-1,2,3,4-tetrahydropyridine (VIa). Diamide (IIIa) (2.5 g) was boiled for 5 h in acetic acid (20 ml). After cooling, the solution was diluted with water and extracted with chloroform. The chloroform was evaporated and the residue was crystallized from ethanol. Yield was 0.93 g (40%), mp 204-205° (from ethanol). Found: C 67.6; H 6.1; N 11.9%. $C_{13}H_{14}N_2O_2$. Calculated: C 67.9; H 6.1; N 12.2%. IR spectrum: 1645, 1692, 3270, 3442 cm^{-1}.

3-Carbamoyl-2-keto-4,6-diphenyl-1,2,3,4-tetrahydropyridine (VIb). A. mixture of diamide (IIIb) (0.25 g) in conc. HCl was kept at room temperature for 2 h 30 min. The solid was filtered off and washed with water. Yield was 75%, mp 170-171°C (from ethanol). The reaction product was identical with that described in [1].

B. The same compound was obtained in a similar manner to A from the hydroxypiperidone (IVb) using 20% HCl. Yield was 60%.

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NITROPYRROLOQUINOLINES

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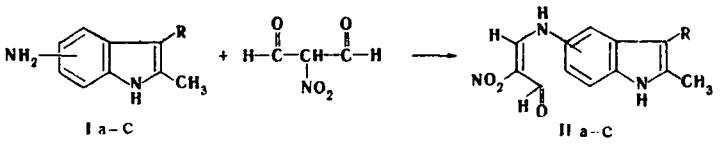
UDC 547.759.3'836.3.07

The condensation of nitromalonic dialdehyde with aromatic amines is known as a synthesis of 3-nitroquinoline derivatives (see [1], for example). In a search for convenient methods of obtaining nitropyrroloquinolines we investigated the behavior of 5- and 6-aminoindoles (Ia-c) in this reaction. Heating these amines with nitromalonic dialdehyde led to the enaminoaldehydes (IIa-c) which cyclized under the action of acid reagents into nitropyrroloquinolines.



I a-c II a-c

I–II a 5-NH_2; R=CH_3; b 5-NH_2; R=H; c 6-NH_2; R=CH_3

Here, as in the case of the enaminoketones in [2], a problem arose in closing the ring, viz., the direction of cyclization. In the analogous condensation with 1,3-diketones steric factors showed a decisive influence on the direction of ring formation [2]. In the present case these factors are reduced to a minimum and the condensation product from formylenaminoindole (IIa) proved to be a mixture of the linear (IIIa) and angular (IVa) isomers in a 4:1 ratio according to PMR spectral data.

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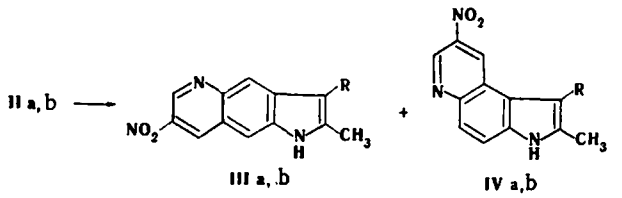
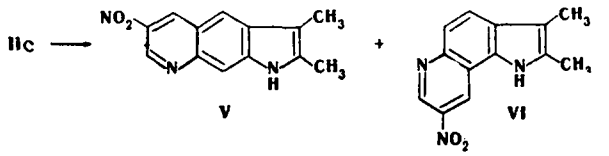


III a, b IV a, b

a R = CH_3; b R = H

The pyrroloquinoline of angular structure with an unprotected β-position of the pyrrole ring should have been even more favored. However cyclization of enaminoaldehyde (IIb) occurred with the predominant formation of the linear isomer (IIIb). The angular pyrroloquinoline (IVb) was detected in only trace amounts, unreacted aminoindole remained, and resinification was observed. The explanation of this change of direction of cyclization as being due to protonation of the pyrrole ring is less probable (see below concerning this). It is more reasonable to suppose that the C_4 atom is deactivated by the influence of the nitro group. As a result of this the rate of intramolecular electrophilic attack was low and the competing intermolecular attack at the free β-position of the indole ring occurred with the formation of an alkylidene derivative, and then a dimer which aided closing to compound (IIIb) or (IVb). However, the steric requirements of the latter are significantly greater. Cyclization of the dimer must occur with the splitting of initial amine and nitrodialdehyde. Consequently after making the reaction mixture alkaline they were detected chromatographically even on increasing the reaction time severalfold.

For amine (Ic), where the reactivity of the C_3 atom is small, the reaction proceeds with the formation of both the linear and the angular isomers (V and VI). They were isolated in the ratio 3:1.



V VI

In the PMR spectra of the linear isomers (III, V) the signals of the benzene protons appeared as two singlets. In the spectra of the angular isomers (IVb and VI) the AB system was poorly resolved. In the UV spectrum of the linear compound (IIIa) a bathochromic shift of 26 nm was observed in the long wave band in comparison with the maximum of the same band of the angular isomer (IVa). In addition the intensity of the maximum at 323 nm increased very sharply in the spectrum of the linear isomer and may be assigned to a $\pi \rightarrow \pi^*$ transition in the aromatic system. Consequently the linear isomer possesses more conjugation than the angular where, evidently due to the close disposition of the peri-substituents, partial disturbance of coplanarity occurs. In reality if only protons are in the peripositions, as, for example, in compound (IIIb), then the bathochromic shift of the long wave band in comparison with the angular compound (IVb) is reduced to 17 nm, although the intensity of the band close to 320 nm is preserved at the same level as in the spectrum of compound (IIIa). The same regularities were also observed in the spectra of pyrroloquinolines (V and VI) although they were expressed more weakly.

The molecular ions of compounds (III-VI) formed by electron impact fairly readily eliminated the nitro group with subsequent ejection of a molecule of HCN. Thus the first process of dissociative ionization of these compounds is linked with decomposition of the pyridine ring. The ions formed along this direction together with the molecular ion comprised as a rule more than half the total ions of the mass spectrum (Table 1). The intensity of the $[M - NO]^+$ peaks was extremely low, which indicates the insignificant probability of processes of nitro—nitrite rearrangement with the presence of a nitro group in the pyridine series. It has been shown previously [3] that loss of an NO fragment from the molecular ion is characteristic of nitroindoles. It was not possible to detect clear differences be-

TABLE 1. Intensities of Peaks of Characteristic Ions in the Mass Spectra of Compounds (III-VI) (%, Σ_{41})

Compound	W_M	$[M-NO_2]^+$	$[M-NO_2-HCN]^+$	$[M-CH_3]^+$	$[M-NO]^+$
IIIa	28,6	22,6	9,2	1,5	0,7
IIIb	29,4	11,7	3,5	—	1,1
IVa	22,5	12,2	1,5	0,5	0,6
IVb	22,6	12,0	14,8	—	0,9
V	31,9	18,3	3,8	1,6	0,8
VI	41,9	12,8	2,7	0,9	0,9

TABLE 2. Enaminoaldehydes (IIa-c)

Compound	Name	mp, °C	R_f[a]	UV spectra λ_{max}, nm	UV spectra lg ε	Found element, %	Found M[b]	Empirical formula	Calc. element, %	Calc. M	Yield, %
IIa	2-Nitro-3-(2,3-dimethyl-5-indolylamino)prop-2-enal	216–217	0,54	228 285 382	4,29 4,14 4,18	C 60,5 H 4,9	259	$C_{13}H_{13}N_3O_3$	C 60,2 H 5,0	259	79
IIb	2-Nitro-3-(2-methyl-5-indolylamino)-prop-2-enal	230–231	0,50	218 288 382	4,31 4,17 4,24	N 17,4	245	$C_{12}H_{11}N_3O_3$	N 17,1	245	86
IIc	2-Nitro-3-(2,3-dimethyl-6-indolylamino)prop-2-enal	210–211[c]	0,57	227 288 407	4,29 3,93 4,16	C 60,0 H 5,2	259	$C_{13}H_{13}N_3O_3$	C 60,2 H 5,0	259	80

[a]Silufol, benzene–ethyl acetate, 3:1. [b]Mass spectroscopically. [c]With decomposition.

tween the stabilities of the molecular ions of the linear and angular isomers; however, it was conspicuous that the angular compound (VI) was almost twice as stable as the isomeric angular compound (IVa). This difference is possibly linked with the enhanced stabilization of the pyridine ring in the ion of compound (VI) due to its close spatial disposition with the electron-donating pyrrole ring. It should also be mentioned that in the mass spectra of compounds containing no methyl group in the 3 position the peaks of $[M-CH_3]^+$ ions were completely absent, which indicates the high probability of loss of a CH_3 group from the 3 position in the mass spectra of pyrroloquinolines (IIIa, IVa, V, and VI).

Thus the condensation of aminoindoles with nitromalonic dialdehyde led to nitropyrroloquinolines of both angular and linear structure. The described condensation was carried out under the action of trifluoroacetic acid. As in the case of enaminoketones in [2] the formation of the pyridine ring occurred onto a molecule unprotonated on the pyrrole ring, which was confirmed by PMR spectral data. Attempts to carry out cyclization in concentrated sulfuric acid, where the enaminoaldehydes were protonated at the β-position of the pyrrole ring, did not lead to the formation of pyrroloquinolines.

EXPERIMENTAL

PMR spectra were taken on a Varian S-100 XL instrument in DMSO (internal standard was TMS). Mass spectra were obtained on an MX-1303 mass spectrometer with direct insertion into the ion source at an ionization energy of 50 eV, emission current was 1.5 mA, and temperature was 100-250°C. UV spectra were taken on a Cary-15 instrument in ethanol.

The sodium salt of nitromalonic dialdehyde* was obtained according to the method in [4], aminoindoles were synthesized as described previously [2, 5].

General Method of Obtaining Enaminoaldehydes (II). A mixture of aminoindoles (0.5 mmole), nitromalonic dialdehyde sodium salt (0.9 mmole), and acetic acid (3-5 drops) in ethyl alcohol (10 ml) was boiled for 5-10 min. The cooled reaction mixture was diluted with

*Attention! The dry salt explodes on storage.

TABLE 3. Nitropyrroloquinolines (III-VI)

Compound	Name	Decomp. pt., °C	R_f[a]	UV spectra λ_{max}, nm	UV spectra lg ε	PMR spectrum, ppm	Found element, %	Found M[b]	Empirical formula	Calculated element, %	Calculated M[b]	Yield, %
IIIa	2,3-Dimethyl-7-nitropyrrolo-[2,3-g]quinoline	275	0,45	233 248 323 365[c] 473	4,22 4,37 4,23 4,74 3,76	11,34 (s, N—H), 9,38 (s, 2H, 6- and 8-H), 8,16 (s, 2H, 4- and 9-H)	C 64,5 H 4,9	241[d]	$C_{13}H_{11}N_3O_2$	C 64,7 H 4,6	241	34
IVa	1,2-Dimethyl-8-nitropyrrolo-[3,2-f]quinoline	240	0,29	225 256 319 380 447	4,16 4,34 3,85 3,53 3,76	11,66 (s, N—H), 9,33 (s, 2H, 7- and 9-H), 7,99 (d, 5-H, $J_{5,4}$=9 Hz), 7,73 (d, 4-H, $J_{4,5}$=9 Hz)	C 64,4 H 4,8	241	$C_{13}H_{11}N_3O_2$	C 64,7 H 4,6	241	11
IIIb	2-Methyl-7-nitropyrrolo[2,3-g]quinoline	244	0,38	227 244 316 360[c] 452	4,27 4,33 4,24 3,72 3,76	11,77 (s, N—H), 9,35 (q, 2H, 6- and 8-H; J=1,5 Hz), 8,16 (s, 2H, 4- and 9-H)	C 63,6 H 4,0	227	$C_{12}H_9N_3O_2$	C 63,4 H 4,0	227	18
IVb	2-Methyl-8-nitropyrrolo[3,2-f]quinoline	265	0,31	219 253 310 369 435	4,16 4,34 3,82 3,50 3,62			227	$C_{12}H_9N_3O_2$		227	3
V	2,3-Dimethyl-6-nitropyrrolo-[3,2-g]quinoline	270	0,21	229 250 325 370[c] 424	4,32 4,19 4,41 3,75 3,29	11,24 (s, N—H), 9,20 (s, 2H, 5- and 7-H), 8,14 (s, 4-H), 7,82 (s, 9-H)	C 64,8 H 4,8	241	$C_{13}H_{11}N_3O_2$	C 64,7 H 4,6	241	14
VI	2,3-Dimethyl-8-nitropyrrolo-[2,3-f]quinoline	225	0,40	210 253 317 394	4,30 4,19 4,06 3,62			241	$C_{13}H_{11}N_3O_2$		241	5

[a] Silufol, benzene—ethyl acetate, 3:1. [b] Mass spectroscopically. [c] Shoulder.

water. The precipitated solid was filtered off, washed with water, and air-dried. The obtained enamine was purified by recrystallization from alcohol or on a column of Al_2O_3 (of activity Brockmann grade 2, eluent was benzene–ethyl acetate, 1:1). Yields and constants of substances are given in Table 2.

General Method of Obtaining Nitropyrroloquinolines (III-VI). Compound (II) (0.38 mmole) was boiled in trifluoroacetic acid (5 ml) for 8 to 10 h. The cooled reaction mixture was poured into a diluted 10% solution of aqueous ammonia. The precipitated solid was filtered off, washed with water, and air-dried. The obtained mixture was separated on a binder-free thick layer of Al_2O_3 (activity Brockmann grade 2, benzene–ethyl acetate, 3:2). Yields and constants of substances are given in Table 3.

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ISOMERIZATION OF THE PYRIDINE RING IN SALTS OF 1,2-DIALKYLISOQUINOLINE

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The pyridine ring of salts of N-alkyl- and N-arylisoquinoline are readily attacked by nucleophilic reagents. It has been shown by PMR spectroscopy that different anions [1-3] add to the C_1 atom while under forcing conditions strong nucleophiles open the pyridine ring [4]. For example, hydrazine and substituted hydrazines open the pyridine nucleus, which cyclizes once again, giving the corresponding pyrazole [5]. In a similar manner hydroxylamine, while interacting with 2-(2,4-dinitrophenyl)isoquinolinium chloride, forms o-[2-(2,4-dinitrophenylamino)vinyl]benzaldoxime, which is readily cyclized once more, giving the isoquinoline N-oxide [6].

By analogy with the conversions of 1,2-dialkylpyridinium salts which are able to recyclize under the action of bases into N-alkylanilines [7], we proposed the possibility of rearranging 1,2-dialkylisoquinolinium salts into N-alkylnaphthylamines, having in view that under the action of bases the pyridine ring will be opened with subsequent closure onto a methylene group of the side chain possessing significant CH acidity. Such a conversion of the isoquinoline structure into a naphthalene nucleus, occurring with fission of a carbon–nitrogen bond and the formation of a new carbon–carbon bond, must be thermodynamically effective. It has been reported that 1-benzyl-2-methylisoquinolinium iodide is converted on extended heating with alcoholic alkali into 2-phenyl-1-naphthol [8] but this process goes with partial breakdown of the molecule and loss of methylamine.

To suppress the undesired process of solvolysis we used an alcoholic solution of methylamine as reagent. In this way 1-methylamino-2-phenylnaphthalene (IIa) was obtained in 65% yield from 1-benzyl-2-methylisoquinolinium iodide (Ia) (10 h at 85°C) and on increasing the temperature to 150°C the yield of amine (IIa) reached 91%. In the mass spectrum of amine (IIa) the molecular ion peak of m/e 233 was the greatest. In addition there were peaks at m/e 232, 230, 217, and 202 corresponding to the assigned structure. A peak was also observed for a doubly charged molecular ion, decomposition of which proceeded in a manner similar to that of the singly charged ion. The UV and PMR spectra of compound (IIa) corresponded to the assigned structure.

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