NITROAZINES.
15.* CONTRACTION OF THE PYRIMIDINE RING IN 6-NITROAZOLO[1,5-*a*]PYRIMIDINES

V. L. Rusinov, A. V. Myasnikov, O. N.Chupakhin, and G. G. Aleksandrov

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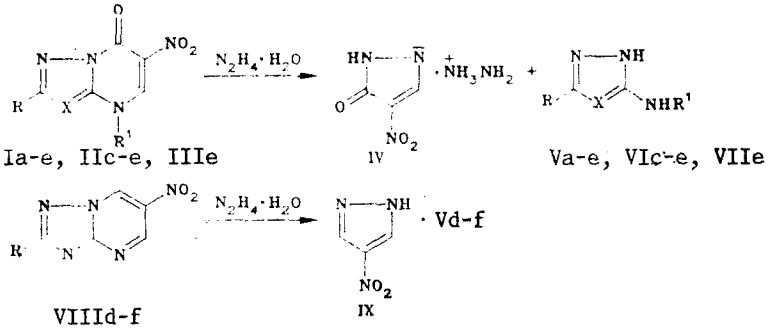
It is shown that contraction of the pyrimidine ring occurs when 6-nitro-7-oxo-4,7-dihydroazolo[1,5-a]pyrimidines are heated with hydrazine hydrate. Complexes of 4-nitropyrazole with 5-aminoazoles, the structures of which were proved by x-ray diffraction analysis, are formed in a similar reaction of nitro-substituted azolopyrimidines that do not contain an oxo function.

The reaction of monocyclic nitro derivatives of pyrimidine, viz., 4-methoxy-5-nitropyrimidine and 1,3,6-trimethyl-5-nitrouracil, with hydrazine leads to contraction of the pyrimidine ring accompanied by the elimination of an N—C—N fragment and the formation of nitropyrazole derivatives [2, 3]. The same compounds were also obtained in the treatment of 2,3-dihydro-6-nitroimidazo[1,2-*a*]pyrimidines with hydrazine [4]. At the same time, in 6-nitropyrazolo- or 1,2,4-triazolo[1,5-*a*]pyrimidines transformation of the azine ring by the action of C,N-dinucleophiles takes place without ejection of the N—C—N group of the pyrimidine ring [5, 6]. In the present research we investigated the behavior of these compounds in reactions with an N,N-dinucleophile, viz., hydrazine.

We established that contraction of the pyrimidine fragment to give a 4-nitro-3-pyrazolone hydrazinium salt (IV) and the corresponding aminoazoles Va-e, VIc-e, and VIIe occurs when 6-nitro-7-oxo-4,7-dihydroazolo[1,5-*a*]pyrimidines Ia-e, IIc-e, and IIIe are heated with hydrazine hydrate in alcohol or without a solvent. 4-Nitro-3-pyrazolone was obtained when hydrazinium salt IV was treated with hydrochloric acid. The use of II and III may serve as a convenient method for obtaining alkylaminopyrazoles and 1,2,4-triazoles. It is known that the synthesis of such compounds by alkylation of the amino derivatives leads to complex mixtures of isomers [7].

The spectral characteristics of azoles IV-VII correspond to the structures assigned, while the melting points are in agreement with the literature data available for some of them.



a R=H, X=CH; b R=CH_3, X=CH; c R=C_6H_5, X=CH; d R=H, X=N; e R=CH_3, X=N; f R=CF_3, X=N; I, V R^1=H; II, VI R^1=CH_3; III, VII R^1=C_3H_7

Heating 6-nitroazolo[1,5-*a*]pyrimidines VIIId-f, which do not contain an oxo function, in propanol with hydrazine hydrate gave crystals, the elementary compositions of which corresponded to the overall empirical formulas, while their PMR spectra contained signals of protons of an azole fragment and a two-proton singlet at 8.4 ppm. It was established by x-ray diffraction analysis that a 1:1 complex (VIIIe) of 4-nitropyrazole with 3-methyl-5-aminotriazole linked in the crystal by intermolecular hydrogen bonds was obtained as a result of this reaction.

*See [1] for Communication 14.

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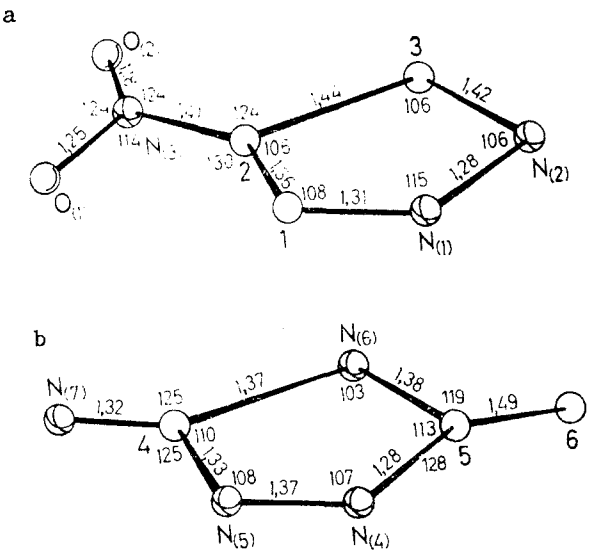

Fig. 1. Bond lengths and bond angles in 4-nitropyrazole (a) and 3-methyl-5-amino-1,2,4-triazole (b); the errors in the determination of the bond lengths and bond angles were 0.02-0.03 Å and 2-3°, respectively.

TABLE 1. Coordinates of the Atoms ($\times 10^3$) and Their $U_{eq} = 1/3\Sigma_i\Sigma_j u_{ij} a^*_i a^*_j a_i a_j$ Values

Atom	x	y	z	U_{eq}	Atom	x	y	z	U_{eq}
$O_{(1)}$	−110(3)	91(1)	178(2)	0,07(1)	$N_{(7)}$	240(3)	353(1)	337(2)	0,05(1)
$O_{(2)}$	−108(2)	211(1)	310(2)	0,07(1)	$C_{(1)}$	178(4)	13(2)	422(3)	0,06(1)
$N_{(1)}$	300(3)	3(1)	560(2)	0,05(1)	$C_{(2)}$	97(3)	97(1)	413(3)	0,04(1)
$N_{(2)}$	318(3)	73(1)	646(2)	0,05(1)	$C_{(3)}$	187(4)	139(2)	560(3)	0,05(1)
$N_{(3)}$	−56(3)	137(1)	298(3)	0,05(1)	$C_{(4)}$	303(3)	275(2)	300(3)	0,05(1)
$N_{(4)}$	474(3)	153(1)	307(2)	0,04(1)	$C_{(5)}$	347(3)	158(2)	176(3)	0,04(1)
$N_{(5)}$	452(3)	229(1)	387(2)	0,04(1)	$C_{(6)}$	314(4)	94(2)	46(3)	0,07(1)
$N_{(6)}$	232(3)	234(1)	160(2)	0,03(1)					

TABLE 2. Possible Hydrogen Bonds in the II Structure

Atoms	d (Å)	Atoms	d (Å)
$N_{(1)}$—H···$N_{(4)}$ (1−x, −y, 1−z)	2,87(3)	$N_{(7)}$—H···$O_{(1)}$ ($^1/_2$+x, $^1/_2$−y, $^1/_2$+z)	3,11(3)
$N_{(4)}$···H—$N_{(1)}$ (1−x, −y, 1−z)	2,87(3)	$N_{(7)}$—H···$O_{(2)}$ (x, y, z)	3,27(3)
$N_{(5)}$—H···$N_{(6)}$ ($^1/_2$+x, $^1/_2$−y, $^1/_2$+z)	2,76(3)	$O_{(1)}$···H—$N_{(7)}$ (−$^1/_2$+x, $^1/_2$−y, $^1/_2$+z)	3,11(3)
$N_{(6)}$···H—$N_{(5)}$ (−$^1/_2$+x, $^1/_2$−y, −$^1/_2$z)	2,76(3)	$O_{(2)}$···H—$N_{(7)}$ (−1+x, y, z)	3,27(3)

The geometrical parameters of the two molecules are the usual values (Fig. 1 and Table 1), and the molecules have planar five-membered heterorings (the errors in the determination of the bond lengths and bond angles were 0.02-0.03 Å and 2-3°, respectively). The nitro group is turned by an angle of 3.3° about the $C_{(2)}$—$N_{(3)}$ bond relative to the plane of the pyrazole ring. Four active protons (one in the nitropyrazole molecule and three in the 3-methyl-5-amino-1,2,4-triazole molecule), which are capable of forming hydrogen bonds, are present in the structure. However, only the ring hydrogen atoms form strong hydrogen bonds (Table 2); the protons of the amino group are located rather far away from the oxygen atoms of the nitro group (N—H···O 3.11 and 3.27 Å) for the formation of a strong hydrogen bond. Due to the strong $N_{(1)}$—H···$N_{(4)}$ hydrogen bond (1 − x, −y, 1 − z) with a length of 2.87 Å, the IX and Ve molecules are bonded together to give bimolecular complexes, which, due to $N_{(5)}$—H···$N_{(6)}$ hydrogen bonds (1/2 + x, 1/2 − y, 1/2 + z), are united to form chains that are stretched out along the (101) direction.

Molecular-ion peaks of the aminoazole and 4-nitropyrazole and, in addition, peaks of [M — 30] and [M — 46] ions, which are characteristic for the nitro group of the latter, were detected in the mass spectra of the investigated complexes.

The UV spectra of the complexes obtained corresponded to the sums of the spectra of 4-nitropyrazole and the corresponding aminoazole. A charge-transfer band could not be detected.

The complexes decompose when they are heated in water, and pure 4-nitropyrazole precipitates on cooling.

EXPERIMENTAL

The PMR spectra of solutions in d_6-DMSO were obtained with a Bruker WH-90 spectrometer at 80 MHz with tetramethylsilane (TMS) as the internal standard. The mass spectra were obtained with a Varian MAT-311A spectrometer; the accelerating voltage was 3 kV, the cathode emission current was 1 mA, and the ionizing-electron energy was 7 eV with direct introduction of the samples into the ion source. The IR spectra of suspensions in mineral oil were recorded with a UR-20 spectrometer. The UV spectra were obtained with a Specord UV-vis spectrophotometer. The crystals of the complex of Ve with nitropyrazole were monoclinic and had the following parameters: a = 7.47(1), b = 14.61(2), c = 9.34(1) Å, β = 109.4(1)°, V = 962(4) Å^3, Z = 4, space group $P2_1/n$. The x-ray diffraction study was carried out with a Syntex-P1 diffractometer with λ_{MoK_α}, a graphite monochromator, $\theta/2\theta$ scanning, and $4° \leq 2\theta \leq 46°$. The structure was decoded by the direct method and refined by the method of least squares within the complete-matrix anisotropic approximation up to R = 0.109 (R_w = 0.106) for 433 reflections with $F^2 \geq 3\sigma$. The final coordinates of the atoms are presented in Table 1.

The results of elementary analysis for C, H, and N were in agreement with the calculated values.

The 6-nitroazolo[1,5-*a*]pyrimidines were obtained by the method in [8], while the 6-nitro-7-oxo-4,7-dihydroazolo-[1,5-*a*]pyrimidines were obtained by the method in [9].

Reaction of 6-Nitro-7-oxo-4,7-dihydroazolo[1,5-*a*]pyrimidines I-III with Hydrazine Hydrate. A 0.01-mole sample of I-III was refluxed with 0.03 mole of hydrazine hydrate in 20 ml of isopropyl alcohol for 30 min, after which the mixture was cooled to 20°C, and the precipitated 4-nitro-3-pyrazolone hydrazinium salt (IV, $C_3H_7N_5O_3$) was removed by filtration to give a product with mp 264°C (from water) in quantitative yield. IR spectrum: 1290, 1460 (NO_2); 1650 (C=O); 3210, 3325 cm^{-1} (NH, NH). PMR spectrum: 6.6 (1H, broad s, NH), 7.5 ppm (1H, s, 5-H). The filtrate was evaporated, and the aminoazoles were extracted from the residue with ethyl acetate. Compound Va was an oil (mp 37-39°C [10]), Vb was an oil (mp 44°C [11]), Vc had mp 124-125°C (mp 121-126° [12]), Vd had mp 157-158°C (mp 159°C [13]), Ve had mp 148-150°C (mp 148°C [14]), Vf had mp 194-196°C (mp 193-194°C [15]), VIc had mp 128-130°C (mp 130°C [16]), VId had mp 188°C (mp 189-190°C [7]), and VIe had mp 209-210°C (mp 210-212°C [17]).

Compound VIIe ($C_6H_{12}N_4$). PMR spectrum: 0.85 (3H, broad t, CH_3), 1.10-1.90 (2H, m, CH_2), 2.05 (3H, s, 3-CH_3), 3.03 (2H, dt, N—CH_2), 5.90 (1H, broad t, NH), 11.90 ppm (1H, broad s, 1-NH). The compound had mp 180-181°C.

4-Nitro-3-pyrazolone. A 0.8-g (0.005 mole) sample of hydrazinium salt IV was dissolved in 5 ml of water, 1 ml of concentrated HCl was added, and the mixture was stirred for 10 min. The precipitate was removed by filtration to give a product with mp 135-136°C. PMR spectrum: 8.40 ppm (1H, s, 5-H). The yield was 0.6 g (92%).

Molecular Complex of 4-Nitropyrazole with 5-Aminotriazole. A 1.65-g (0.01 mole) sample of 6-nitro-1,2,4-triazolo[1,5-*a*]pyrimidine (VIIId) was refluxed with an equimolar amount of hydrazine hydrate in 10 ml of alcohol, after which the mixture was evaporated, and the residue was triturated with ether and crystallized from isopropyl alcohol to give a product with mp 128-130°C. PMR spectrum: 5.70 (2H, broad s, NH_2), 7.45 (1H, s, 3-H_{Vd}), 8.40 ppm (2H, s, 3-H, 5-H_{IX}). The yield of the complex of IX and Vd ($C_5H_7N_2O_2$) was 1.8 g (91%).

A complex of IX and Ve ($C_6H_9N_7O_2$), with mp 161-162°C, was similarly obtained from 2-methyl-6-nitro-1,2,4-triazolo[1,5-*a*]pyrimidine (VIIIe) and hydrazine hydrate. PMR spectrum: 2.12 (3H, s, CH_3), 5.70 (2H, broad s, $NH_{2\,Ve}$), 8.40 ppm (2H, s, 3-H, 5-H_{IX}). The yield was 80%.

A complex of IX and Vf ($C_6H_6F_3N_7O_2$), with mp 108-110°C, was similarly obtained from 2-trifluoromethyl-6-nitro-1,2,4-triazolo[1,5-*a*]pyrimidine (VIIIf) and hydrazine hydrate. PMR spectrum: 5.70 (2H, broad s, $NH_{2\,Vf}$), 8.40 ppm (2H, s, 3-H, 5-H_{IX}). The yield was 60%.

4-Nitropyrazole (IX, $C_3H_3N_3O_2$). A 0.5-g sample of the complex of IX and Vd was refluxed in 5 ml of water, after which the mixture was cooled to 20°C and filtered to give 0.2 g of 4-nitropyrazole with mp 160-161°C (mp 162°C [18]). IR spectrum: 1380, 1520 cm^{-1} (NO_2). PMR spectrum: 8.50 (2H, s, 3-H, 5-H), 14.80 ppm (1H, broad s, NH).

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