REDUCTION OF NITRO DERIVATIVES OF AZOLO[5,1-*c*][1,2,4]TRIAZINES

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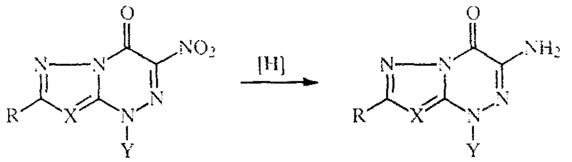
Reduction of 6-nitro-7-oxo-4,7-dihydroazolo[5,1-c][1,2,4]triazines into the corresponding amines with sodium dithionite takes place smoothly in neutral aqueous solutions. The structural effects in reduction of nitroazoloazines were evaluated electrochemically.

Chemical and electrochemical reduction of nitro derivatives of the poorly studied polynitro condensed systems — 6-nitro-7-oxo-4,7-dihydro-1,2,4-triazolo[5,1-*c*][1,2,4]triazines(I,III)and6-nitro-7-oxo-4,7-dihydropyrazolo[5,1-*c*][1,2,4]triazines (V, VII) [1, 2] — was investigated in the present study. It was found that the nitroazines studied are smoothly reduced to the corresponding amines with sodium dithionite in neutral aqueous medium.



I a-d , III a-d , V, VII   II, a-d , IV a-d , VI

I—IV a-d X=N, I a-d Y=Na, II a-d Y=H, I, II a R=H, b R=Me, c R=SMe, d R=SEt; III a-c, IV a-c Y=Me; III, IV a R=H, b R=Me, c R=SMe; III, IV d Y=$(CH_2)_4OAc$, R=H; V, VI, X=CH, Y=Me, R=Me; VII X=CH, Y=Na, a R=H, b R=Me

The process is characterized by the softness of the conditions and the ease of separation of the products of reduction.

The structure of the compounds obtained was confirmed by the IR, ESR, and ^{13}C NMR spectra (Table 1). The IR spectra of the products of reduction contained no bands of vibrations of nitro groups [1, 2] and new absorption was identified at 3300-3500 cm^{-1} caused by amino groups. All parameters of the ESR and ^{13}C NMR spectra (number, multiplicity, and chemical shifts of the signals) were in agreement with the assigned structure of aminoazoloazines. The signals of cyclic carbon atoms in amines IIa, c, d and IVc were assigned based on a comparative analysis of their ^{13}C NMR spectra. The spectra of 2-substituted derivatives IIc, d contained weak-field multiplet signals at ~ 166 ppm ($C_{(2)}$, $^3J = 4.9$ Hz), singlet signals at ~ 144 ppm ($C_{(7)}$), and two broad signals in the region of 145 and 152 ppm ($C_{(3a)}$, $C_{(6)}$). The last signals were assigned by comparison with the analogous signals of N-methylated derivative IVc. The quartet splitting of absorption at ~ 145 ppm ($^3J = 2.4$ Hz) and slight shift to the strong field ($\Delta\delta = 0.4$ Hz) indicate that its $C_{(3a)}$ atom is involved.

Their tendency to decompose in the basic conditions is a special feature of the synthesized amino derivatives. This is probably the cause of the unsuccessful attempts to reduce nitroazoloazines with sodium dithionite in basic medium (in the conditions described for a series of nitroazines [3, 4]) and sodium borohydride in ethanol and hydrazine hydrate in the presence of Raney nickel. Reduction with tin chloride in acid conditions was only successful in isolated cases (compound Ic, see

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TABLE 1. Properties of Aminoazoloazines IIa-d, IVa-d, and VIa

Compound	Empirical formula	Mp, °C	IR spectrum, ν, cm^{-1}		UV spectrum, λ_{max}, nm (log ε)	ESR spectrum δ, ppm	^{13}C NMR spectrum, δ, ppm (J, Hz)					Yield, %
			C=O	NH$_2$, NH			$C_{(2)}$	$C_{(6)}$	$C_{(3a)}$	$C_{(7)}$	R(X)	
IIa*	$C_4H_4N_6O$	>350 (decomp.)	1730	3140, 3330, 3432	227 (3,97), 262 (3,82)	6,36 (2H, s, NH$_2$); 8,17 (1H, s, 2-H)	154,2	151,2	146,7	143,3		66
IIb	$C_5H_6N_6O$	284...286	1727	3340, 3450	229 (4,14), 262 (3,83), 327 (3,85)	2,33 (3H, s, CH$_3$); 6,25 (2H, s, NH$_2$); 13,2 (1H, br.s NH)						45
IIc	$C_5H_6N_6OS$	314...316	1735	3366, 3487	251 (4,54), 327 (4,23)	2,6 (3H, s, SCH$_3$); 6,35 (2H, s, NH$_2$) 13,1 (1H, br.s., NH)	166,2 (q, ^3J=4,9)	151,6 (br.s)	145,3 (br.s)	143,6 s	13,3 (q, SCH$_3$, ^1J=142,8)	50
IId	$C_6H_8N_6OS$	268...270	1720	3300, 3466	252 (4,54), 329 (4,24)	1,38 (2H, q, SCH$_2$); 3,17 (3H, t, CH$_3$); 6,35 (2H, s, NH$_2$); 13,2 (1H, br.s, NH)	165,5 (t, ^3J=4,9)	151,5 (br.s)	145,3 (br.s)	143,6 s	14,9 (q, CH$_3$, ^1J=127,0); 24,8 (t, SCH$_2$, ^1J=142,2)	52
IVa	$C_5H_6N_6O$	196...197	1720	3340		3,72 (3H, s, CH$_3$); 6,33 (2H, s, NH$_2$); 8,00 (1H, s, 2-H)						56
IVb	$C_6H_8N_6O$	210...212	1730	3320	336 (2,48), 272 (2,76), 249 (2,71)	2,33 (3H, s, 2-CH$_3$); 3,73 (3H, s., N—CH$_3$); 6,36 (2H, s, NH$_2$)						65
IVc	$C_6H_8N_6OS$	248...251	1730	3350	334 (2,94), 254 (3,23)	2,59 (3H, s, SCH$_3$); 3,69 (3H, s., N—CH$_3$); 6,49 (2H, s, NH$_2$)	165,9 (q, ^3J=4,9)	151,3 (br.s)	144,9 (q., J=2,4)	143,7 s	13,3 (q, SCH$_3$, ^1J=142,4); 39,9 (q, NCH$_3$, ^1J=142,0)	70
IVd	$C_{10}H_{14}N_6O_3$	121...122	1720, 1730	3320	337 (2,55), 266 (2,52)	1,40...2,00 (4H, m, —(CH$_2$)$_2$—); 2,00 (3H, s, CH$_3$CO); 4,01 (2H, t, OCH$_2$); 4,13 (2H, t, N—CH$_2$); 6,52 (2H, s, NH$_2$); 8,19 (1H, s, 2-H)						72
VI	$C_7H_9N_5O$	178...180	1710	3310		2,41 (3H, s, 2-CH$_3$); 3,82 (3H, s, N—CH$_3$); 5,83 (1H, s, 3-H); 6,37 (2H, s, NH$_2$)						50

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*The ^{13}C NMR spectrum was made with suppression of the spin-spin interaction with protons.

TABLE 2. Half-wave Potentials of Polarographic Reduction of Nitroazoloazines Ia-d, IIIa-c, and VIIa, b

Compound	$-E_{1/2}$, V	Compound	$-E_{1/2}$, V	Compound	$-E_{1/2}$, V	Compound	$-E_{1/2}$, V
Ia	1,38	Ic	1,42	IIIa	0,72; 1,51	VIIa	1,57
Ib	1,41	Id	1,42	IIIb	0,90; 1,72	VIIb	1,59
				IIIc	0,74; 1,49		

Experimental). The nature of the reducing agent and acidity of the medium used thus significantly affect the result of chemical reduction of these nitroazoloazines.

Electrochemical reduction of nitro derivatives in DMF on a rotating disk platinum electrode was conducted to quantitatively assess the capacity for reduction and the characteristics of the structural effects [5]. One one-electron wave corresponding to the formation of a radical dianion was usually observed in the polarograms of salts Ia-d and VIIa, b. Reduction of alkylated nitroazines IIIa-c takes place in two one-electron stages with the successive formation of radical anions and dianions.

The recording of the cyclic volt-ampere characteristics on a stationary platinum electrode for most of the compounds studied indicated the low stability of the generated particles and consequently the impossibility of studying them by ESR. We obtained the half-wave potentials of polarographic reduction ($E_{1/2}$) of the nitroazoloazines (Table 2).

In N-alkylated nitroazines IIIa-c, transfer of the first electron to the electrochemically active part of the molecule, the nitro group ($E_{1/2} = -0.70$ to -0.90 V) takes place more easily than in nitrobenzene ($E_{1/2} = -1$ V) [6] or nitropyrazolopyridines ($E_{1/2} \sim 1$ V) [7], which is in agreement with the high π-deficiency of the polyazaheterocycle examined. The pronounced difficulty in reducing compounds Ia-d and VIIa, b ($E_{1/2} = -1.38$ to -1.59 V) is probably due to the anionic character of the substrates. It follows from the evaluation of the effect of substituents on the ease of reduction of nitroazoloazines that incorporation of substituents (methyl, alkylthio groups) in position 2 of both nitrotriazolotriazine (Ia-d) and nitropyrazolotriazine salts (VIIa, b) only insignificantly alters the electron-acceptor properties of the molecules. However, the methyl substituent (in contrast to the methylthio group) in analogous position 2 in many neutral substrates — azoloazines IIIa-c — significantly complicates reduction ($\Delta E \approx 0.2$ V). In turn, substitution of the nitrogen atom by a CH group in position 3 of the azole ring (compounds Ia-c, VIIa, b) has approximately the same effect.

EXPERIMENTAL

The IR spectra were made on a UR-20 spectrometer in petrolatum, and the UV spectra were made on a Specord UV-vis in ethanol. The ESR spectra were recorded on a Perkin—Elmer R-12B (60 MHz) in DMSO-D_6, and the ^{13}C NMR spectra were made on a Bruker WP-80 in DMSO-D_6; TMS was the internal standard. The purity of the compounds obtained and course of the reactions were monitored by TLC on Silufol UV-254 plates and developed in UV light. The electrochemical studies were conducted in DMF, using tetrabutylammonium perchlorate as the background. The concentration of the solutions tested was $5 \cdot 10^{-4}$ *M*. A rotating disk platinum electrode was used for recording the polarograms.

The data from elemental analysis of the synthesized aminoazoloazines and amine hydrochloride IIc for C, H, N, and Cl corresponded to the calculations.

Nitroazoloazines Ia-d and VIIa, b were prepared according to [1], and IIIa-d and V were prepared according to [2].

6-Amino-7-oxo-4,7-dihydroazolo[5,1-*c*][1,2,4]triazines (IIa-d, IVa-d, VI) (general method). Here 2 mmole of the corresponding nitroazoloazine was mixed with a solution of 1.0 g (6 mmole) of sodium dithionite in 15 ml of water. After holding for 10 min, the reaction mass was cooled, the sediment was filtered off and washed several times with small portions of cold water. It was recrystallized from acetone—water mixture, 2:1, and dried for 1 h at 100°C.

Reduction of nitroazoloazine Ic with tin chloride. A solution of 1.5 g of $SnCl_2 \times 2H_2O$ in a mixture of 2 ml conc. HCl and 2 ml of water was added to a solution of 0.5 g (2 mmole) of compound Ic in 3 ml of water. The reaction mass was stirred, cooled, and the sediment was filtered off and washed with a small portion of cold water. It was dried over P_2O_5, yielding 0.35 g of amine hydrochloride Ic (74.6%). Mp > 200°C (decomp.). IR spectrum: 3400-3050 (NH_3^+, br. s), 1715 cm^{-1} (C—O).

LITERATURE CITED

1. E. N. Ulomskii, V. L. Rusinov, O. N. Chupakhin, G. L. Rusinov, A. I. Chernyshov, and G. G. Aleksandrov, Khim. Geterotsikl. Soedin., No. 11, 1543 (1987).
2. V. L. Rusinov, A. Yu. Petrov, and I. Ya. Postovskii, Khim. Geterotsikl. Soedin., No. 9, 1283 (1980).
3. A. Aydin and H. Feuer, Chim. Acta Turc., **2**, 113 (1980).
4. Weigand-Hilgetag, Experimental Methods in Organic Chemistry [Russian translation], Khimiya, Moscow (1968), p. 522.
5. I. M. Sosonkin, V. A. Subbotin, and N. V. Fedyainov, Zh. Org. Khim., **15**, 344 (1979).
6. S. G. Mairanovskii, Ya. P. Stradyn', and V. D. Bezuglyi, Polarography in Organic Chemistry [in Russian], Khimiya, Leningrad (1975), p. 238.
7. L. Kh. Baumane, R. A. Gvar, Ya. P. Stradyn', O. N. Chupakhin, V. L. Rusinov, and A. Yu. Petrov, Khim. Geterotsikl. Soedin., No. 5, 689 (1985).