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EPR SPECTROSCOPY AND POLAROGRAPHY OF NITROAZOLES.

3.* NITROPYRAZOLES

T. I. Vakul'skaya, L. I. Larina,
O. B. Nefedova, and V. A. Lopyrev

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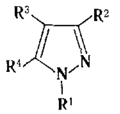
The results of an EPR investigation are presented with polarographs of electrochemical excitation of nitropyrazoles in acetonitrile. It is shown that 3- and 4-nitropyrazoles are excited in two single-electron stages with formation of dianion radicals. Upon excitation, N-alkylnitropyrazoles form stable anion radicals. 1-Nitro- and 1,4-dinitropyrazoles are excited upon splitting off of the NO_2 anion. Excitation potentials of the nitropyrazoles and hyperfine interaction constants for the corresponding ion radicals are given.

Pyrazole derivatives have found extensive application as medicinal preparations (antipyrine, pyramidon, and analgin) [2]. The nitro derivatives of heterocycles have the most clearly expressed biological activity [3]. There is no doubt that the mechanism of their action includes a step involving one-electron transfer [4]. The study of the behavior of nitropyrazoles in redox processes and the structure of their free radicals and the distribution of spin density in them is therefore extremely timely.



I-VI

I $R^1=R^3=R^4=H$, $R^2=NO_2$; II $R^1=R^2=R^4=H$, $R^3=NO_2$; III $R^1=CH_3$, $R^2=R^4=H$, $R^3=NO_2$; IV $R^1=C_2H_5$, $R^2=R^4=H$, $R^3=NO_2$; V $R^1=NO_2$, $R^2=R^3=R^4=H$; VI $R^1=R^3=NO_2$, $R^2=R^4=H$

In a continuation of our research on nitroazoles [1, 5] we studied the electrochemical reduction of C- and N-nitropyrazoles I-VI in acetonitrile by EPR spectroscopy and polarography.

Nitrogen-unsubstituted 3(5)-nitro- and 4-nitropyrazoles are reduced in two one-electron steps in acetonitrile. The first wave in the polarogram corresponds to irreversible one-electron transfer, while the second wave corresponds to reversible one-electron transfer. Although the solutions remain colorless during electrolysis, at the potentials of the second half waves we were able to record EPR signals, the character and hyperfine structure (hfs) of which correspond to interaction of the unpaired electron with all of the magnetic nuclei of the molecule, in addition to one proton (Table 1 and Fig. 1). As we have previously shown [5], these EPR signals are related to dianion radicals of the corresponding nitropyrazoles, which are probably formed via Scheme 1 (top, following page).

It is apparent from Scheme 1 that cleavage of the primary anion radical at the polar covalent N—H bond with the ejection of atomic hydrogen occurs during transfer of the first electron to the nitropyrazole molecule with an unsubstituted nitrogen atom. The half-wave potentials and the parameters of the EPR signals of the ion radicals of nitropyrazoles I-VI are

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*See [1] for Communication 2.

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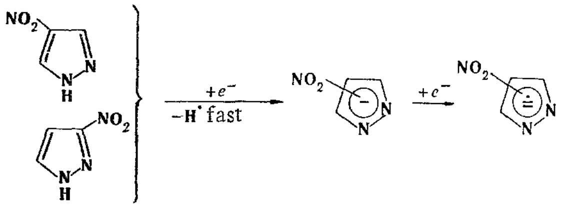
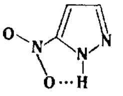


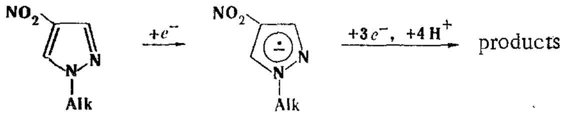
(1)

presented in Table 1. It follows from Table 1 that 3(5)-nitropyrazole (I) is reduced more readily than the 4-nitro isomer (II); this is evidently explained by the contribution of the 1H-5-nitro tautomer, in which an intramolecular hydrogen bond can be realized.



Facilitation of reduction by the formation of an intramolecular hydrogen bond was previously observed in the case of o-nitrophenols [6] and 4(7)-nitrobenzimidazoles [7]. The potentials of the second half-waves for pyrazoles I and II are virtually identical, which is in complete agreement with the insignificant differences in the structures of their anions. It should be noted that 4-nitropyrazole (II) undergoes reduction to give an anion radical with a symmetrical structure, to which a symmetrical distribution of the spin density in it corresponds (Table 1). The assignment of the hfs constants was made on the basis of quantum-chemical calculations [8] by the CNDO/2 method in the Pople parametrization. It follows from the calculated data that the larger doublet constant in dianion radical I is related to the proton that is closest to the NO_2 group.

N-Alkylnitropyrazoles III and IV are also reduced in two steps; the first step corresponds to reversible one-electron transfer. As compared with nitropyrazoles with an unsubstituted nitrogen atom, the potentials of the first half waves of N-alkylnitropyrazoles are shifted substantially to the cathode region. The second reduction wave of pyrazoles III and IV is similar to the second wave of nitrobenzene obtained under identical conditions (Scheme 2).



(2)

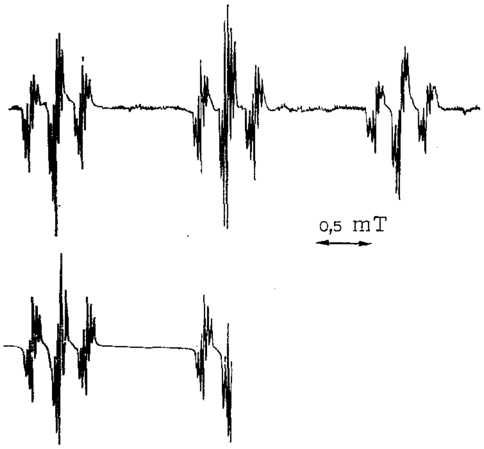
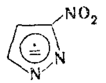
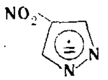
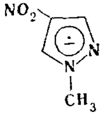
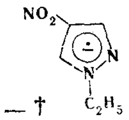
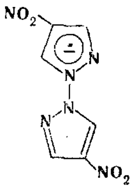


Fig. 1. EPR spectra of the 4-nitropyrazole dianion radical. (The experimental spectrum is shown at the top of the figure, while the theoretical spectrum is shown at the bottom.)

TABLE 1. Reduction Potentials of Nitropyrazoles in Acetonitrile and Parameters of the EPR Signals of Their Ion Radicals

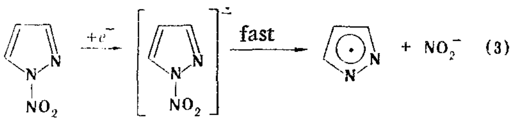
Compound	$-E_{1/2}$, V	Reduction product recorded in the EPR spectrum	Character of the hfs of the EPR signal	hfs constants of the theoretical EPR spectra, mT							ΔH, mT
				$a_N^{NO_2}$	a_1	a_2	a_3	a_4	a_5	a_6	
I	1,46 2,18		$3_N^{NO_2}\times 2_{H(4)}\times 3_{N(2)}\times 3_{N(1)}\times 2_{H(5)}$	1,510	0,084	0,164	—	0,230	0,015	—	0,020
II	1,55 2,17		$3_N^{NO_2}\times 3_{H(3,5)}\times 5_{N(1,2)}$	1,620	0,026	0,026	0,251	—	0,251	—	0,015
III	1,72 2,54		$3_N^{NO_2}\times 2_{H(5)}\times 2_{H(3)}\times 4_H^{CH_3}\times 3_{N(2)}\times 3_{N(1)}$	1,400	0,032	0,038	0,208	—	0,398	0,06 *	0,025
IV	1,73 3,10		$3_N^{NO_2}\times 2_{H(5)}\times 3_{N(2)}\times 2_{H(3)}\times 2_{H(6)}\times 3_{N(1)}$	1,507	0,010	0,080	0,047	—	0,525	0,047*	0,030
V	0,95 1,73	—†	—	—	—	—	—	—	—	—	—
VI	0,55 1,25 1,70 2,20 2,75		$3_N^{NO_2}\times 2_{H(5)}\times 2_{H(3)}\times 3_{N(2)}\times 3_{N(1)}\times 3_{N(6)}$	1,430	0,032	0,046	0,170	—	0,470	0,02 ‡	0,028

*The $a_H^{N\text{-}Alk}$ hfs constant. †An EPR signal was not observed. ‡ The a_N constant.

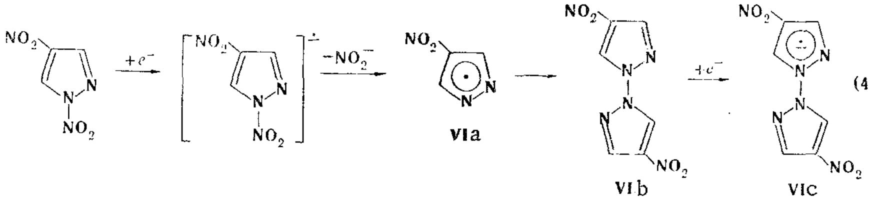
In fact, signals corresponding to primary anion radicals are observed at the potentials of the first half waves in the EPR spectra of N-alkylnitropyrazoles (Fig. 2 and Table 1). In the case of electrolysis at the potentials of the first half-waves the solutions have a yellow-green coloration that becomes reddish-brown at higher potentials, and the solutions gradually lose their paramagnetism.

A comparison of the potentials of the first half waves of II-V (Table 1) provides evidence for their high sensitivity to the electronic effects of substituents.

N-Nitropyrazole (V) is a structural isomer of I and II. However, the presence of an $N-NO_2$ bond substantially facilitates electrochemical reduction. It is known that the NO_2 group has the strongest effect in nitropyrazole when it is adjacent to the pyridine nitrogen atom [9], i.e., in the 1 and 3 positions. In addition, the $N-NO_2$ bond in 1-nitropyrazole is extremely labile, and migration of the NO_2 group to the 3 position to give 1H-3-nitropyrazole is observed under certain conditions [10]. The polarogram of V in acetonitrile contains two waves (Table 1). The first wave corresponds to one-electron irreversible transfer, while the second wave is ~3.5 times higher with a deep drop prior to discharge of the base electrolyte. Electron paramagnetic resonance signals cannot be detected at any of the reduction potentials. In a study of the dependence of the reduction potentials of 1-nitropyrazole on the pH of the medium it was shown [11] that the second reduction wave in neutral and alkaline media corresponds to reduction of the NO_2^- anion (or HNO_2). Taking this fact into account, one may propose the following scheme for the reduction of 1-nitropyrazole in acetonitrile:



The polarogram of 1,4-dinitropyrazole (VI) is considerably more complex and has five waves (Table 1). It follows from Table 1 that VI is the most readily reduced of all of the investigated compounds. The first wave corresponds to irreversible one-electron transfer. As in the case of 1-nitropyrazole (V), an unstable anion radical that is cleaved at the $N-NO_2$ bond is evidently formed in this step. This suggests the formation of a neutral 4-nitropyrazolyl radical and an NO_2 anion, to the reduction of which the wave with $E_{1/2} = -1.7$ V is evidently related. However, we were able to record an EPR signal for this compound only at a potential close to discharge of the base electrolyte. The character of the hfs of the EPR signal (Table 1) does not make it possible to assign it to a neutral 4-nitropyrazolyl radical, since the nitrogen atoms and the protons of the heterocyclic ring in the latter should be equivalent. Considering the fact that azolyl radicals have a high tendency to undergo dimerization [12] and the fact that with respect to its principal hfs constants, the recorded EPR signal is most similar to the signals of the anion radicals of 1-alkyl-4-nitropyrazoles III and IV, one may propose the following scheme for the reduction of 1,4-dinitropyrazole:



The spin density in the hypothetical anion radical VIc is concentrated primarily in one heterocyclic ring. This may be due to the noncoplanar orientation of the nitropyrazolyl fragments. Thus the transfer of one electron is characteristic for all of the investigated C- and N-nitropyrazoles in the first step of reduction in acetonitrile. The anion radicals of NH- and N-nitropyrazoles undergo rapid decomposition either with ejection of atomic hydrogen (I, II) or with splitting out of a nitrite anion (V, VI); this is a consequence of the strongly and differently polarized N–H and $N-NO_2$ bonds.

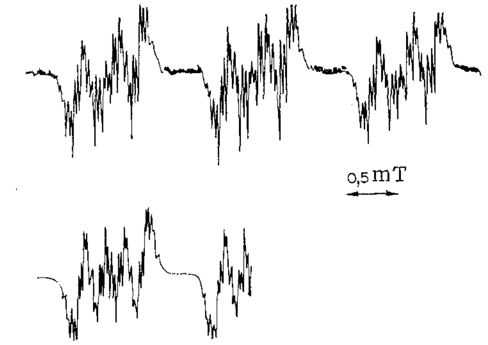


Fig. 2. EPR spectra of the 1-methyl-4-nitropyrazole anion radical. (The experimental spectrum is given at the top of the figure, while the theoretical spectrum is presented at the bottom.)

EXPERIMENTAL

The nitropyrazoles were obtained and purified by known methods [9, 10, 13, 14]. Chromatographic-grade acetonitrile was used as the solvent. The electrochemical generation of the ion radicals was carried out in special cells, which were previously freed of oxygen by successive freezing and thawing of the solutions *in vacuo* and were then filled with argon that had been purified over a potassium-sodium alloy. The EPR spectra were recorded with THN-252 (Thomson, France) and Rubin spectrometers. The theoretical spectra were calculated with an M4030 computer by means of a modified EPR-3 program with allowance for the Lorentzian form of the line [15]. The polarograms were recorded with an ON-102 polarograph (Hungary) with tetra-n-butylammonium perchlorate as the base electrolyte relative to the mercury sludge by means of a dropping mercury electrode ($m = 2.0$ mg/sec, $t = 3.5$ sec). Freshly distilled nitrobenzene ($E_{1/2} = -1.50$ V) was used as the standard substance.

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