trifluoride etherate in 20 ml of methanol are added. After 5 min, the reaction mixture is concentrated to 30-50 ml and the remainder then diluted with three times the amount of water. The solution is made alkaline to pH 8 with sodium carbonate solution and extracted with ether (4 × 20 ml). After the ether solution has been dried over sodium sulfate and the solvent removed, the oily residue isolated is a diastereomeric mixture of XXVIIa and b.

3-Acetoxy-2-methyl-2-methoxy-6-phenyl-5,6-epoxyhexan-4-one (XXVIIIa,b). After 0.01 mole of compounds XXVIIa,b is boiled for 1 h with 7 ml of acetic anhydride, compounds XXVIIIa,b are isolated as described above for pyranone XIX.

1,2-Dihydroxy-2-methyl-5-(4-nitrophenyl)pentan-3,4-dione (XXX). After 1.3 ml (0.01 mole) of boron trifluoride etherate in 10 ml of methanol is added to 2.49 g (0.01 mole) of diepoxyketone XXIXa or XXIXb in 50 ml of methanol, the reaction mixture is treated as described above for compounds VII-IX. Compound XXX is crystallized from 1:2 ether/hexane.

1,2-Diacetoxy-2-methyl-5-(4-nitrophenyl)pentan-3,4-dione (XXXI). After 1.71 g (5 mmole) of diol XXX is dissolved in 10 ml of acetic anhydride, the solution is boiled for 2 h. Compound XXXI is then isolated as described for acetates XIX and XX. Diacetate XXXI is crystallized from ether.

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DETECTION OF NITROSOFURAN ANION RADICALS IN THE ELECTROCHEMICAL REDUCTION OF 5-NITROFURAN. EPR INVESTIGATIONS AND QUANTUM-CHEMICAL CALCULATIONS

T. S. Isichenko, L. M. Baider, and V. B. Luzhkov

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Previously unknown radicals that are associated with the 5-N-furylhydroxylamine–5-nitrosofuran redox system were detected by EPR spectroscopy in the electrochemical reduction of 5-nitrofuran. The electron structures of the free-radical products of the reduction of 5-nitrofuran were calculated by the INDO method. On the basis of the hyperfine structures (hfs) of the EPR spectra and the results of quantum-chemical calculations it was concluded that 5-nitrosofuran anion radicals and the nitrosofuran dimer were recorded.

The metabolic reduction of the nitro group is responsible for the high biological activity of compounds of the 5-nitrofuran series [1]. The study of the structures and properties of the unstable intermediate products of the reduction of nitrofurans, which, it is assumed, play a substantial role in the mechanisms of the carcinogenic, mutagenic, and cytotoxic action of nitrofurans [2], gives rise to particular interest. The structures and properties of the free-radical products of one-electron reduction – the anion radicals – for a large number of 5-nitrofuran derivatives that contain substituents with different chemical natures in the 2

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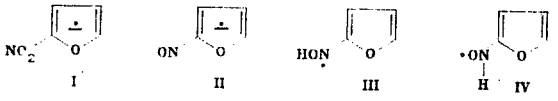
position of the furan ring were studied in detail in papers by Stradyn' and coworkers [3, 4]. The formation of anion radicals in the reduction of compounds of the 5-nitrofuran series in biological systems was demonstrated by Mason and coworkers [5, 6]. A secondary redox system that is associated with more profound reduction steps, viz., the 5-N-furylhydroxylamine–5-nitrosofuran system, was first detected in [7, 8] by a polarographic method in the electrical reduction of 5-nitrofuran. More positive (as compared with the reduction of 5-nitrofuran) redox potentials and low stabilities of the intermediate compounds are peculiarities of the secondary redox system. In the reduction of 5-nitrofuran one should have expected the formation of products of a free-radical nature also at the level of the secondary redox system. However, such experimental data are not available in the literature, evidently because of the low stabilities of the corresponding radicals even in an aprotic medium.

In the present paper we give the results of an investigation of the intermediate free-radical products of the secondary redox system of 5-nitrofuran. The reduction of 5-nitrofuran to 5-N-furylhydroxylamine in an aprotic medium suggests the formation of several intermediates of a free-radical nature; in our opinion, I-IV are the most likely intermediates:



I II III IV

The electron structure of radical I has been previously studied theoretically and experimentally [3, 9]. It was shown that the spin densities and hyperfine structure constants (HFSC) calculated within the framework of the INDO method reflect qualitatively correctly the distribution of the unpaired electron over the 5-nitrofuran molecule in the anion radical state. The best agreement between the calculated and experimental HFSC is observed when interaction with the solvent molecules is taken into account [10]. Solvation should also play a substantial role for radicals II-IV. However, because calculation of the structure of the solvation shell of radicals is a complex problem, for carrying out a comparative analysis in the I-IV series on a qualitative level we were restricted to calculation of the isolated radicals.

For the calculation of the electron structures of radicals I and II we used the structural parameters obtained by the semiempirical MNDO method with complete optimization of the geometries of the 5-nitrofuran and 5-nitrosofuran molecules (Figs. 1 and 2). Complete optimizaton of the geometries of these molecules showed that the parameters of the heteroring change only slightly. For radicals III and IV we carried out partial optimization of the geometries by the MNDO method: the aminyl and nitroxyl fragments were optimized, while the geometry of the furan ring was selected as in the 5-nitrosofuran molecule (Fig. 3). In contrast to the I and II molecules, radical IV, according to the results of the optimization, is not planar. The angles of deviation of the $N_{(9)}$–$O_{(10)}$ and $N_{(9)}$–$H_{(11)}$ bonds from the plane of the furan ring (Fig. 3) are, respectively, 21.1° and 6.9° for isomer IVa and 15.2° and 18.1° for IVb; the $O_{(10)}$ and $H_{(11)}$ atoms are located on the same side of the plane of the ring. In radical III only the $O_{(10)}$–$H_{(11)}$ bond deviates from the plane of the furan ring (Fig. 3). In the IIIa conformation the angle of deviation is 0.9°, whereas it is 0.4° in the IIIb conformation, i.e., radical III has an almost planar structure. Calculation of the electron structures of radical isomers IIa-IVa and IIb-IVb by the INDO method showed that the stereochemistry of the radicals has an appreciable effect on the character of the distribution of the spin density only in radical IV. The spin densities for the most stable isomers of the radicals were calculated by the INDO method (Tables 1 and 2). It follows from the calculation that the bulk of the spin density in these radicals is localized in the p_z orbitals of the nitrogen and oxygen atoms of the substituent in the 5 position of the furan ring, i.e., radicals I-IV are π radicals. For radicals I, II, and IV spin density ρ_O on the $O_{(10)}$ atom [on the $O_{(10)}$ and $O_{(11)}$ atoms for the I molecule] is greater than density ρ_N on the $N_{(9)}$ atom. Redistribution of the spin density between the $N_{(9)}$ and $O_{(10)}$ atoms occurs in radical III in such a way that $\rho_N > \rho_O$. The a_N and a_H values in the I-IV series were calculated from the formula [11]

$$a = 10^{-4} \cdot K \cdot \rho^s, \qquad (1)$$

where ρ^s is the spin density in the s orbital of the atom, and K is a constant, which is equal to 379.34 for N and 539.86 for H. For radicals I and IV we also calculated the a_N values from semiempirical equations (2) and (3), which were obtained, respectively, for nitro compounds in acetonitrile [12] and for aromatic nitroxyl radicals [13]:

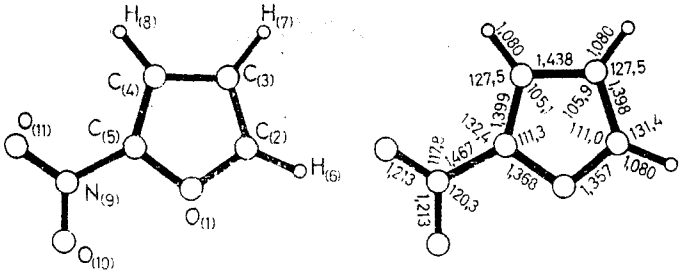
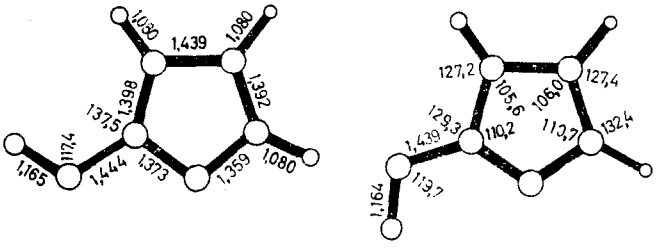


Fig. 1. Numbering of the atoms, bond lengths (Å), and bond angles (deg) in radical I.



IIa IIb

Fig. 2. Bond lengths (Å) and bond angles (deg) in radical II.

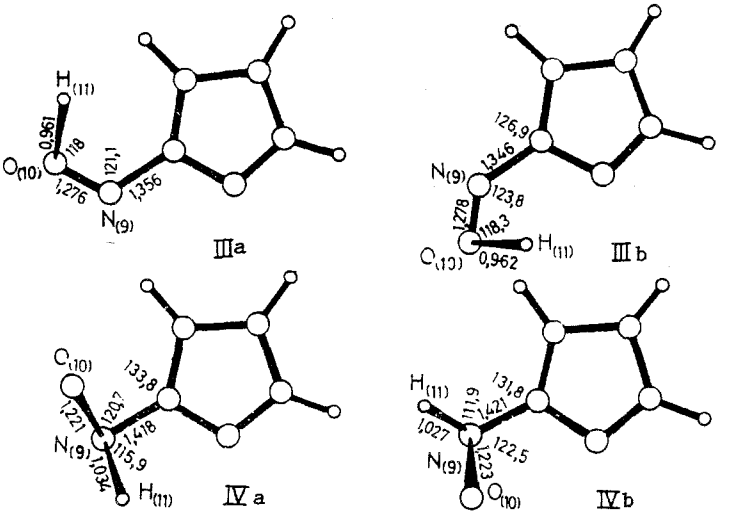


Fig. 3. Bond lengths (Å) and bond angles (deg) in radicals III (isomers IIIa and IIIb) and IV (isomers IVa and IVb).

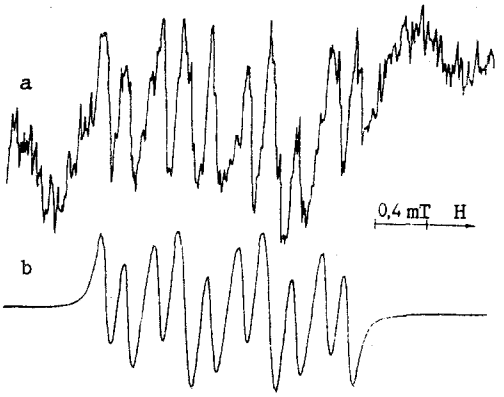


Fig. 4. EPR spectrum of the 5-nitrosofuran anion radical: a) experimental spectrum, modulation amplitude 0.1 mT, 10 signal accumulations; b) theoretical spectrum with constants a_N = 0.67, a_{H-1} = 0.42, a_{H-2} = 0.18 mT, ΔH_{lor} = 0.08 mT, modulation 0.1 mT.

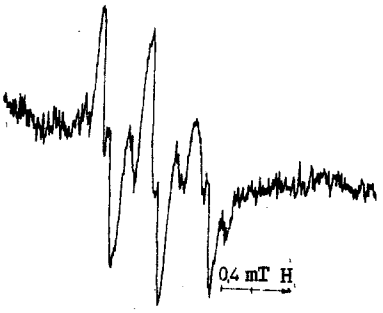


Fig. 5

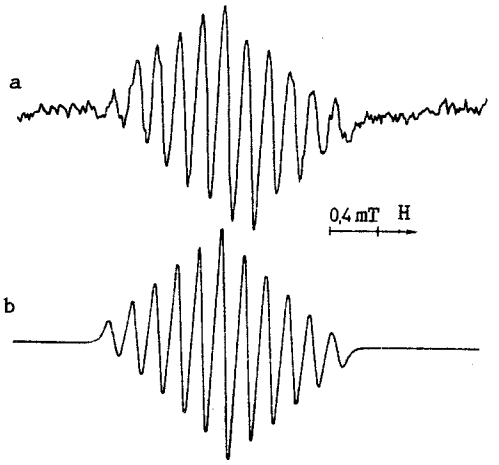


Fig. 6

Fig. 5. Experimental EPR spectrum of radical B: modulation amplitude 0.1 mT, 10 signal accumulations, constants a_N = 0.72, a_H = 0.20 mT.

Fig. 6. EPR spectrum of the anion radical of the 5-nitrosofuran dimer: a) experimental spectrum, modulation amplitude 0.1 mT, 10 signal accumulations; b) theoretical spectrum with constants $a_{2\text{-}N}$ = 0.37 and $a_{2\text{-}H}$ = 0.19 mT, ΔH_{lor} = 0.05 mT, modulation 0.1 mT.

$$a = 10^{-4} \cdot 14.2 \cdot (\rho_N^{\pi} + 2 \cdot \rho_O^{\pi}), \quad (2)$$

$$a = 10^{-4} \cdot (35 \cdot 6\rho_N^{\pi} - 0.93 \cdot \rho_O^{\pi}). \quad (3)$$

The substantial decrease in the a_N value in anion radical II as compared with the value in I is associated with an appreciable decrease in spin density ρ_N^S (Table 1).

Under electrochemical-reduction conditions we recorded the EPR spectrum of radical I, which consists of 24 lines of a single intensity. The character of the hfs is 3N·2H·2H·2H with constants a_N = 1.14, $a_{H\text{-}1}$ = 0.57, $a_{H\text{-}2}$ = 0.41, and $a_{H\text{-}3}$ = 0.09 mT. It should be noted that the a_N value calculated taking into account the nature of the solvent from formula (2) (Table 1) is in good agreement with the experimental value. The highest steady-state concentration of radical I is achieved under the experimental conditions at potentials applied to the cathode of −1.0 to −1.2 V. A reversible change in the potential of the working electrode over the range 0 to −2.8 V, which also includes a second three-electron reduction step, is accompanied only by a corresponding change in the concentration of I radicals. If the electrolysis of a solution of 5-nitrofuran (10^{-3} M) is carried out for a long time (no less than 1 h) at a high cathode potential (−2.8 V), after which oxidation is accomplished, intensive destruction of radical I and the development of EPR signals of, successively, radical A (Fig. 4) and radical B (Fig. 5) are observed at a potential on the working electrode of 0.3 to 0.5 V. The spectra of radicals A and B show up distinctly only in the case of a tenfold accumulation of the signal. The low concentrations of the observed radicals A and B made it impossible to record the EPR spectra under conditions of the best resolution of the signals and to ascertain HFSC below 0.1 mT. An analysis of the hfs for radical A shows that the unpaired electron couples with the nucleus of the nitrogen atom (a_N = 0.67 mT) and two protons ($a_{H\text{-}1}$ = 0.42, $a_{H\text{-}2}$ = 0.18 mT). The character of the hfs in radical B is 3N·2H with constants a_N = 0.72 and a_H = 0.20 mT. The significant decrease in a_N in radical A as compared with a_N of radical I, which, according to the calculations, should occur in the nitrosofuran anion radical, and the ratio of the proton constants make it possible to propose that radical A is the nitrosofuran anion radical. Experimental data [14] also provide evidence for a significant decrease in a_N in the nitrosobenzene anion radical (a_N = 0.79 mT) with respect to the nitrosobenzene anion radical (a_N = 1.15 mT). As regards radical B, an unambiguous interpretation of its structure from the available experimental data is difficult. One of the possible structures that could have been proposed on the basis of a comparison of the experimental HFSC with the calculated values (Table 2) is the structure of a nitroxyl radical of the IV type. Another hypothetical structure of radical B is shown below:

TABLE 1. Spin Densities ρ^S and ρ^π on the s and p_z Orbitals, Total Spin Densities ρ, and Calculated Hyperfine Structure Constants (HFSC) a for Radicals I and IIb

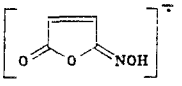
Atom	ρ^s	ρ^π	ρ	a, mT*	ρ^s	ρ^π	ρ	a, mT*
	Radical I				Radical IIb			
$O_{(1)}$	−0.0018	−0.0582	−0.0593		−0.0014	−0.0571	−0.0564	
$C_{(2)}$	−0.0092	−0.1770	−0.1957		−0.0072	−0.1303	−0.1448	
$C_{(3)}$	0.0082	0.1210	0.1434		0.0066	0.1001	0.1185	
$C_{(4)}$	−0.0092	−0.1920	−0.2159		−0.0075	−0.1497	−0.1679	
$C_{(5)}$	0.0122	0.0964	0.1297		0.0098	0.0653	0.0882	
$H_{(6)}$	0.0072		0.0072	0.39	0.0058		0.0058	0.31
$H_{(7)}$	−0.0043		−0.0043	−0.23	−0.0034		−0.0034	−0.18
$H_{(8)}$	0.0080		0.0080	0.43	0.0061		0.0061	0.33
$N_{(9)}$	−0.0200	−0.3714	−0.4141	−0.76 (−1.12)	−0.0087	−0.2843	−0.2933	−0.33
$O_{(10)}$	−0.0031	−0.2157	−0.2059		−0.0106	−0.5350	−0.5434	
$O_{(11)}$	−0.0049	−0.2031	−0.1933					

*The HFSC were calculated from formula (1); the value calculated from formula (2) is presented in parentheses.

TABLE 2. Spin Densities ρ^S and ρ^π on the s and p_z Orbitals, Total Spin Densities ρ, and Hyperfine Structure Constants (HFSC) for Radicals IIIb and IVa

Atom	ρ^s	ρ^π	ρ	a, mT*	ρ^s	ρ^π	ρ	a, mT*
	Radical IIIb				Radical IVa			
$O_{(1)}$	−0.0005	−0.0270	−0.0263		−0.0007	−0.0085	−0.0120	
$C_{(2)}$	−0.0138	−0.2643	−0.2933		−0.0034	−0.0636	−0.0708	
$C_{(3)}$	0.0111	0.1530	0.1857		0.0029	0.0413	0.0497	
$C_{(4)}$	−0.0181	−0.3474	−0.3917		−0.0044	−0.0829	−0.0940	
$C_{(5)}$	0.0190	0.2522	0.3017		0.0044	0.0763	0.0941	
$H_{(6)}$	0.0108		0.0108	0.58	0.0024		0.0024	0.13
$H_{(7)}$	−0.0060		−0.0060	−0.33	−0.0017		−0.0017	−0.09
$H_{(8)}$	0.0141		0.0141	0.76	0.0039		0.0039	0.19
$N_{(9)}$	−0.0246	−0.6462	−0.6912	−0.94	−0.0256	−0.2297	−0.2698	−0.97 (−0.76)
$O_{(10)}$	−0.0045	−0.1203	−0.1094		−0.0123	−0.6417	−0.6867	
$H_{(11)}$	−0.0057		−0.0057	−0.31	0.0049		0.0049	0.26

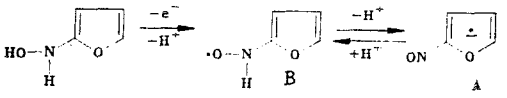
*The HFSC were calculated from formula (1); the value calculated from formula (3).

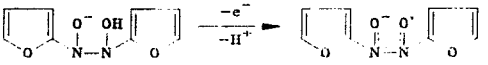


The formation of quinoneimines along with amines was previously detected [15] in the disproportionation of aromatic nitroxyl radicals.

When we increased the starting 5-nitrofuran concentration to $2 \cdot 10^{-3}$ M under the above-described oxidation conditions we recorded the spectrum of a third radical C (Fig. 6), the hfs of which is due to coupling of the unpaired electron with two equivalent nitrogen nuclei (a_N = 0.37 mT) and two equivalent protons (a_H = 0.19 mT). This symmetrical structure may most likely be due to the nitrosofuran dimer anion radical. The ability of aromatic nitroso compounds to dimerize, for example, was observed in the course of the electrolytic reduction of nitrosobenzene [16].

Since radicals A, B, and C are recorded only in the oxidation process, which was preceded by the reduction of 5-nitrofuran to 5-N-furylhydroxylamine [18], one may propose the following mechanism of formation of secondary radicals in the system:





C

EXPERIMENTAL

The reduction of 5-nitrofuran was carried out by an electrochemical method in the aprotic solvent acetonitrile. The 5-nitrofuran concentrations were 10^{-3} and $2 \cdot 10^{-3}$ mole/liter, and the concentration of the background electrolyte (tetrabutylammonium perchlorate) was 10^{-1} mole/liter. Oxygen was removed from the system by bubbling argon through the system. The electrochemical reduction and oxidation were carried out under steady-state conditions on a platinum-foil electrode in a two-electrode cell, which was placed in the resonator of a Bruker ER-220D EPR spectrometer equipped with an Aspekt-2000 minicomputer; this made it possible to accomplish the accumulation of signals and thereby increase the signal/noise ratio. The construction of the theoretical spectra was also carried out with an Aspekt-2000 minicomputer.

The quantum-chemical calculation of the parameters of the electron structures of the radicals was carried out by the semiempirical INDO method within the unrestricted Hartree–Fock approximation using a complex of programs [17]. The optimization of the geometries of the molecules was carried out by the MNDO method [18].

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