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ESR SPECTRA OF ELECTROCHEMICALLY GENERATED ANION RADICALS OF THE NITROFURAN SERIES

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ABSTRACT

ESR spectra of anion radicals for 29 derivatives of 5-nitrofuran, electrochemically generated in situ, have been obtained and studied. Using spectral HFS constants and quantum chemical model parameters (INDO), the structures of σ- and π-electron systems of 2-nitrofuran and its anion radical have been investigated. Furan ring substituent effects on lone electron distribution have been estimated. On the lone electron level, transmission of substituent effects through the ring has been found to be higher in the case of furan, and lower in the case of thiophene and selenophene, with respect to the benzene ring. Delocalization of the lone electron in various ring-attached substituents has been elucidated. Kinetic studies of radical decay showed a rise in stability with increasing delocalization of the lone electron.

INTRODUCTION

Redox properties of 5-nitrofuran derivatives determine the biological activity of these compounds, thus determining also the possibility of their wide use in medical practice as antibacterial drugs [1], as well as further search for antiblastic [2] and radiosensitizing [3] agents among compounds of this series. Studies of structure and properties of intermediary particles formed during the reduction process of 5-nitrofuran derivatives are therefore of considerable importance.

Electrochemical reduction of these compounds in nonaqueous medium (DMF) leads to formation of anion radicals, dianions of the initial compounds, as well as of nitroso- and *N*-hydroxylamino derivatives of furan [4]. These intermediary particles have, however, so far been detected only by electrochemical methods, hence their more detailed study is difficult. Only in the case of free anion radicals is it possible to investigate the structure of these particles in the reaction mixture by means of ESR spectrometry. Anion radicals of some thirty 5-nitrofuran derivatives were electrochemically generated, ESR spectra were obtained, and the hyperfine structure (HFS) of the latter determined, thus ascertaining the structural peculiarities of these radicals.

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EXPERIMENTAL

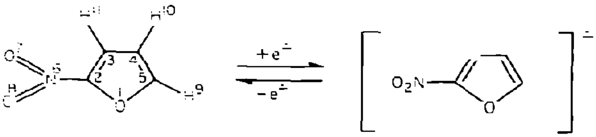
Electrochemical generation (ECG) of free anion radicals was effected in DMF or in DMF- -water mixture. The solutions were deoxygenized by means of dry argon blown through them, or by means of vacuum pumping. The samples contained the substance under investigation in 10^{-3} M concentration, that of the supporting electrolyte being 10^{-1} M. Purity of the compounds was tested by melting point and by means of high-speed liquid chromatography. The DMF was purified according to [5].

The anion radicals of the initial 5-nitrofuran compound molecules were generated in stationary regime on a mercury or platinum electrode at limiting current potential of the first polarographic wave in the ECG cell positioned inside a rectangular resonator H_{102} of an ESR spectrometer ER-9 (Carl Zeiss Jena, G.D.R.) [6], at 0.04 G s^{-1} magnetic field scanning rate, 0.45 s registering time constant, and 0.05—0.9 G depth of high-frequency (100 kHz) modulation of magnetic field. The magnetic field scan was calibrated by means of the ESR spectrum of nitrobenzene anion radical [7]. g-Factor values of free radicals were found after [8]. Stability of anion radicals was determined according to [9], using the method of ECG of radicals inside the ESR spectrometer resonator or outside the latter [10]. Mathematical treatment of the ESR spectra (simulation, cepstral analysis) was done on a HP 2116 C mini-computer coupled to an ER-9 spectrometer to form an on-line system [11]. INDO calculations were conducted as previously described [12].

RESULTS AND DISCUSSION

Anion radicals of 2-nitrofuran

At the first stage of electrochemical reduction of 2-nitrofuran molecules, primary anion radicals, products of one-electron transfer, are formed



as indicated by the appearance of corresponding anodic and cathodic peaks on cyclic voltammetric curves [4].

These radicals, obtained during ECG process, can be registered by ESR without difficulties. The signals obtained in the ESR spectra of these radicals are of sufficiently high intensity, and the spectrum itself reveals well resolved HFS due to interaction between the lone electron with all paramagnetic nuclei present in the anion radical (^{1}H, ^{14}N) (Fig. 1). An analysis of this ESR spectrum shows that the HFS is due to $3_N \cdot 2_H \cdot 2_H \cdot 2_H$. The HFS constant

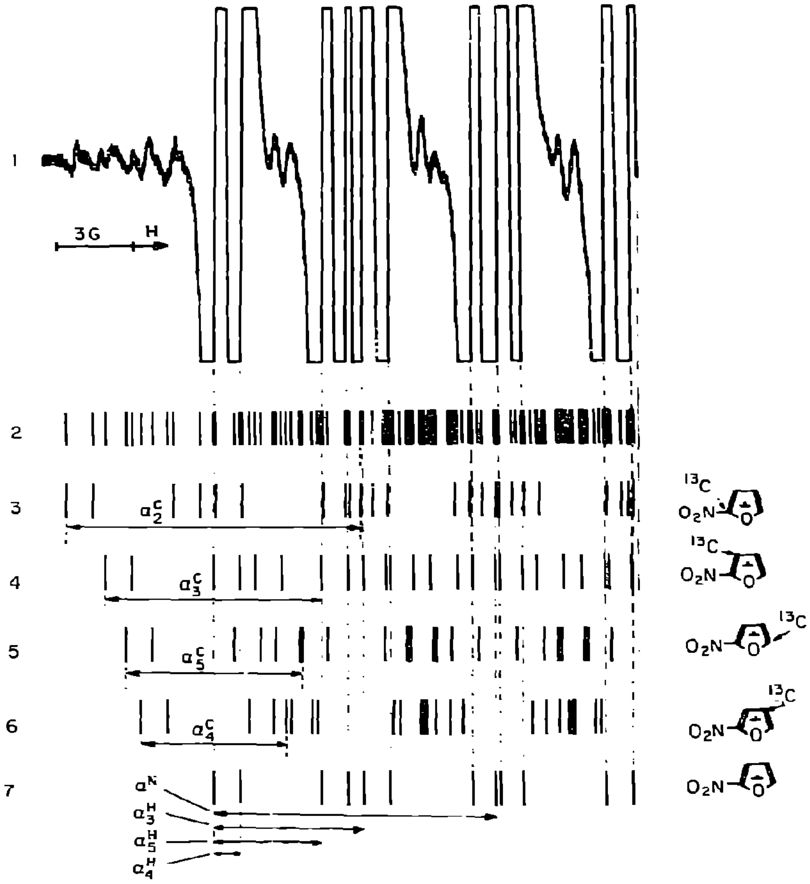


Fig. 1. Full experimental and reconstructed line-spectra of 2-nitrofuran anion radical ESR spectra in DMF. Supporting electrolyte, $(C_4H_9)_4NI$: 1, Full experimental spectrum; 2, Full line-spectrum; 3, 4, 5, 6, ESR line-spectra, corresponding to anion radicals, containing ^{13}C in position 2, 3, 4 and 5, respectively; 7, ESR line-spectrum devoid of splitting due to ^{13}C nuclei.

of triple splitting a_N = 10.2 G is due to the nitro group nitrogen atom. However, from the shape of the spectrum alone it is not possible to assign the other constants a_H = 5.42, 4.13 and 0.97 G unequivocally to separate hydrogen atoms.

For independent assignment of proton HFS constants a quantum chemical model of 2-nitrofuran radicals has been constructed using the INDO approach. Table 1 presents parameters of the spatial structure for electron spin in the frontier orbital, π- and σ-systems. The HFS constants obtained by

TABLE 1

Values of electron density on frontal level ($c^2_{\alpha,22}$), or s- and π-electron densities (ρ_s, ρ_π), as calculated ($a_{\text{theor.}}$, G), and experimental HFS constants for anion radical of 2-nitrofuran in DMF ($a_{\text{exp.},1}$, G), DMF + H_2O (10 M) ($a_{\text{exp.},2}$, G), acetonitrile ($a_{\text{exp.},3}$, G). Supporting electrolyte $(C_4H_9)_4NI$

Atom	$c^2_{\alpha,22}$	ρ_π	ρ_s	$a_{\text{theor.}}$	$a_{\text{theor.}}$ [12]	$a_{\text{exp.},1}$	$a_{\text{exp.},2}$	$a_{\text{exp.},3}$
1	0.034	0.047	0.0015	−1.35	—	—	—	—
2	0.017	−0.097	−0.109	−8.96	—	11.3	12.4	—
3	0.132	0.198	0.0104	8.53	—	8.3	9.2	—
4	0.000	−0.098	−0.0072	−5.91	—	6.6	6.8	—
5	0.070	0.144	0.0078	6.38	—	5.6	5.8	—
6	0.334	0.374	0.0218	8.09	7.28	10.2	13.2	11.25
7	0.213	0.204	0.0048	−4.26	—	—	—	—
8	0.208	0.228	0.0051	−4.55	—	—	—	—
9	—	—	−0.0062	−3.33	−3.63	4.1	4.4	4.12
10	—	—	0.0036	1.96	2.06	1.0	1.0	1.00
11	—	—	−0.0085	−4.61	−5.21	5.4	5.7	5.65

the INDO approach are in qualitative agreement with the corresponding experimental values. (Table 1). This is characteristic of both the model calculated by means of a set of standard initial parameters [12], and of the energy-optimized geometry of the anion radical [13]. Since the experimental values of HFS constants are considerably medium-dependent (Table 1), one cannot expect better coincidence between calculated and experimental HFS constant values, the INDO calculations having been performed for an isolated (not interacting with medium) anion radical. Better agreement between calculated and experimental HFS constants (Table 1) has been obtained for media with lower dielectric permeability than that of water (DMF, acetonitrile).

In the case of an anion radical of 2-nitrofuran (not enriched by ^{13}C isotope) weak signals of four different kinds have been registered, in addition to the spectrum discussed above. Each of them can be attributed to interaction with a paramagnetic nucleus ^{13}C (with its natural contents) of a single carbon atom in different positions of the furan ring. Anion radicals of 2-nitrofuran containing two or more ^{13}C nuclei in samples with natural ^{13}C nuclei content, have not been recorded, the expected signal intensity being less than 2.5×10^{-5} that of anion radicals not containing ^{13}C.

Deconvolution of the total ESR spectrum of 2-nitrofuran anion radical into HFS line-spectra of different varieties differing in the position of ^{13}C in the radical (Fig. 1) made it possible to determine HFS constants due to eight of the eleven atoms (except three ^{17}O atoms) of the 2-nitrofuran system. The HFS constants due to the carbon atoms of 2-nitrofuran anion radicals are as follows: 5.6; 6.6; 8.3; 11.3 G. These constants have been assigned (Table 1) to certain positions in the furan ring according to the quantum chemical model of the 2-nitrofuran anion radical ([13], after [14]).

The qualitative agreement between the calculated and experimental paramagnetic parameters (Table 1) permits comparison between such models of the anion radical and the initial 2-nitrofuran molecule (Table 2). This, in turn, makes it possible to obtain a qualitative, experimentally hardly attainable description of changes in the fine electronic structure of the 2-nitrofuran molecule in the process of its one-electron reduction. Addition of a lone electron to the 2-nitrofuran molecule and the formation of an anion radical leads to an increase in electron density mainly at the nitrogroup atoms in the π-electron system, amounting to ca. 0.75 of an electron. Since this process is accompanied by a decrease in electron density in the σ-system of the nitro group, the total increase in electron density at the nitro group is ca. 0.6 of an electron, evenly distributed over all atoms of the nitro group. The most significant changes in electron density take place at the nitrogen atom of the nitro group: a density increase of ca. 0.33 of an electron in the π-system is accompanied by a decrease of ca. 0.15 of an electron in the σ-system of this atom.

Addition of one electron to the π-system of the 2-nitrofuran molecule leads to strengthening of the C—N bond in the anion radical formed. Although electron density at the nitro group is higher by ca. 0.6 of an electron in the anion radical than in the initial molecule, the population of the N—O bond in the anion radical is diminished by 20% with respect to the initial molecule.

Effects of substituents and heteroatom in the ring on anion radicals

The HFS in the ESR spectra of electrochemically generated (in DMF) anion radicals of 5-nitrofurans, substituted by simple substituents in the 2-position, can be comparatively easily assigned (Table 3). The average signal density of these spectra lies between 0.8 and 2.4 signal G^{-1}.

The nature of the HFS in the ESR spectra recorded, indicating interaction between the lone electron with all paramagnetic nuclei in the conjugated π-electron system confirms the primary structure of the anion radicals as

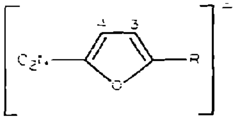
TABLE 2

Charges (in electron charge units) on atoms of 2-nitrofuran molecule (Z) and on atoms of its anion radical ($Z^{\dot{-}}$), their σ- and π-components (Z_σ, Z_π, $Z^{\dot{-}}_\sigma$, $Z^{\dot{-}}_\pi$) as calculated by the INDO method

Type of charge	Atom							
	1	2	3	4	5	6	7	8
Z	−0.16	+0.15	+0.02	−0.05	+0.19	+0.54	−0.38	−0.35
Z_σ	−0.44	+0.28	+0.02	+0.03	+0.20	−0.48	+0.17	+0.17
Z_π	+0.28	−0.13	0	−0.08	−0.01	+1.02	−0.55	−0.52
$Z^{\dot{-}}$	−0.21	+0.19	−0.13	−0.03	+0.09	+0.36	−0.58	−0.57
$Z^{\dot{-}}_\sigma$	−0.45	+0.21	+0.08	+0.03	+0.23	−0.33	+0.19	+0.17
$Z^{\dot{-}}_\pi$	+0.24	−0.02	−0.21	−0.06	−0.14	+0.69	−0.76	−0.74

TABLE 3

g-Factor and HFS constants (a, G) of ESR spectra of anion radicals



in DMF. Supporting electrolyte, $(C_2H_5)_4NBr$

R	Nature of splitting	a_{N,NO_2}	$a_{H,4}$	$a_{H,3}$	a_R	g
H	$3_N \cdot 2_H \cdot 2_H \cdot 2_H$	10.20	5.42	0.97	4.13	2.0053
CH_3	$3_N \cdot 2_H\ 2_H \cdot 4_H$	10.50	5.85	0.85	4.06	2.0052
COO^-	$3_N \cdot 2_H \cdot 2_H$	9.91	5.18	1.02	—	2.0055
CN	$3_N \cdot 2_H \cdot 2_H \cdot 3_N$	7.08	4.53	1.10	0.88	2.0054
CF_3	$3_N \cdot 2_H \cdot 2_H \cdot 4_F$	8.52	5.16	1.09	8.52	2.0055
$COOCH_3$	$3_N \cdot 2_H \cdot 2_H \cdot 4_H$	7.07	4.18	1.08	0.42	2.0056
$COOC_2H_5$	$3_N \cdot 2_H \cdot 2_H \cdot 3_H$	7.14	4.18	1.07	0.36	2.0059
$COCH_3$	$3_N \cdot 2_H \cdot 2_H \cdot 4_H$	6.07	3.52	0.92	1.34	—
CHO	$3_N \cdot 2_H \cdot 2_H \cdot 2_H$	5.16	3.16	0.71	1.96	2.0061
NO_2	$5_N \cdot 3_H$	1.94	1.09	1.09	1.94	—

products of 1e addition to the parent compounds. The primary character of the anion radicals is proved also by the results of cyclic voltammetry.

The *g*-values of the ESR spectra of anion radicals of substituted 5-nitrofurans increase with a rise in electron accepting properties of substituents in the 2-position. The increase in *g*-value is probably due to lowering of the energy level of the lone electron orbital in the anion radical under the effect of such substituents [8].

The HFS constant values (Table 3) yield information on changes in electron density of the frontier orbital in the series of anion radicals of substituted 5-nitrofurans, as they are dependent on the properties of the substituent in 2-position. In particular, a rise in electron accepting properties of substituents leads, according to the McConnell equation [15] to lowering of lone electron density in the 4-position of these radicals. A quantitative estimate of substituent effect (CH_3, H, COO^-, CF_3, CN, $COOCH_3$, $COCH_3$, CHO, NO_2) on HFS constants of anion radicals of 5-nitrofuran derivatives can be obtained through Hammett σ_p constants of substituents from equations

$$a_{N,NO_2} = 10.2 - 4.7\,\sigma_p \quad (r = -0.99, n = 9) \tag{1}$$

$$a_{H,4} = 5.6 - 2.3\,\sigma_p \quad (r = -0.95, n = 9) \tag{2}$$

Constant $a_{H,3}$ is only slightly sensitive to substituent changes in the 2-position, and the correlation coefficient for $a_{H,3}$ and σ_p constants of substituents is extremely low ($r = -0.77$).

An attempt to separate the total substituent effect into a resonance and field component using corresponding Swain and Lupton constants R and F [16] of substituents H, CH_3, $COOC_2H_5$, CN, $COCH_3$, and NO_2 for HFS constants of anion radicals of 5-nitrofuran derivatives has lead to the following equations

$$a_{N,NO_2} = 10.2-5.0\,F + 0.1\,R \;(r = 0.90; n = 6) \tag{3}$$

$$a_{H,4} = 5.9-4.0\,F + 4.1\,R \;(r = 0.82; n = 6) \tag{4}$$

$$a_{H,3} = 0.9-0.1\,F + 0.2\,R \;(r = 0.80; n = 6) \tag{5}$$

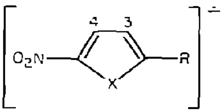
The substituent effect on HFS constants $a_{H,3}$ and $a_{H,4}$ appears to be determined to an equal extent by both field and resonance effect of substituents; however, the correlation coefficient of such correlations is low. Unlike constants a_H, the constant a_{N,NO_2} is subject to substituent effects, mainly by way of field action. Absence of sensitivity to conjugation effects has been observed in studying substituent effects on the one-electron reduction potential of 5-nitrofuran derivatives [4], as well as in ^{14}N NMR studies of the nitro group in these compounds [17].

Redistribution of the lone electron in anion radicals of the 5-nitrofuran compounds, as compared to their benzene and heterocyclic analogues (in case of heteroatom changes) (Table 4), proceeds basically in the same way as changes in polarographic potential of electroreduction of the initial compounds [4].

The value of the HFS constant a_N of nitro group nitrogen decreases with an increase in electron affinity of the heteroatom in the sequence $a_N^O > a_N^S > a_N^{Se}$, whilst constants a_H of ring hydrogen nuclei ^1H change in the opposite sense. It appears that lowering of the a_N constant is due to attraction of the

TABLE 4

HFS constants (a, G) of ESR spectra of anion radicals



(X = O, S, Se, CH = CH; R = H, COO^-, CHO)
Medium, DMF; supporting electrolyte $(C_4H_9)_4ClO_4$

X \ R	H				COO^-			CHO			
	a_N	$a_{H,4}$	$a_{H,3}$	$a_{H,2}$	a_N	$a_{H,4}$	$a_{H,3}$	a_N	$a_{H,4}$	$a_{H,3}$	$a_{H,R}$
O	10.20	5.42	0.97	4.13	9.91	5.18	1.02	5.16	3.16	0.71	1.96
S	9.27	5.88	1.34	4.91	9.06	5.49	1.32	4.87	3.52	0.52	2.06
Se	9.06	6.61	1.46	5.44	8.44	5.98	1.51	4.50	3.98	0.38	1.99
CH=CH	9.88	3.47	1.11	4.09	9.64	3.31	1.06	5.28	3.04	0.40	1.42

lone electron from the nitro group towards the heterocycle, and such electrophility of heterocycles increases with increase in electron affinity of the heteroatom. The changes in HFS constants reflect the lower mobility of the lone electron in the benzene ring, as compared to that in the furan ring: introduction of an aldehyde group produces stronger changes in a_N value in the anion radical of 5-nitrofuran, than in that of nitrobenzene.

Quantitative relationships between HFS constants of anion radicals of nitroheterocyclic series (a^x) and HFS constants of the nitrobenzene radicals (Table 4) can be obtained from linear equations (here the benzene ring is treated as an analogue of a five-membered heterocycle in which the heteroatom is replaced by the group $\mathrm{CH}\overset{..}{-}\mathrm{CH}$)

$$a_N^{O} = 1.08\, a_N^{\mathrm{CH}\overset{..}{-}\mathrm{CH}} - 0.52 \qquad (r = 0.99) \tag{6}$$

$$a_N^{S} = 0.95\, a_N^{\mathrm{CH}\overset{..}{-}\mathrm{CH}} - 0.11 \qquad (r = 0.99) \tag{7}$$

$$a_N^{Se} = 0.94\, a_N^{\mathrm{CH}\overset{..}{-}\mathrm{CH}} - 0.46 \qquad (r = 0.99) \tag{8}$$

$$a_{H,4}^{O} = 2.01\, a_{H,0}^{\mathrm{CH}\overset{..}{-}\mathrm{CH}} - 1.52 \qquad (r = 0.99) \tag{9}$$

$$a_{H,4}^{S} = 2.05\, a_{H,0}^{\mathrm{CH}\overset{..}{-}\mathrm{CH}} - 1.26 \qquad (r = 0.99) \tag{10}$$

$$a_{H,4}^{Se} = 2.20\, a_{H,0}^{\mathrm{CH}\overset{..}{-}\mathrm{CH}} - 1.16 \qquad (r = 0.99) \tag{11}$$

A comparison of coefficients in eqns. (6—8) leads to the conclusion that on the lone electron level the furan ring is a better conductor of electronic effects of substituents than the benzene ring, whilst, on the other hand, the conductivity of thiophene and selenophene are worse than that of benzene. Conductivity of heterocycles decreases with increase in main quantum number value of valence electrons of the heteroatom, and with electron affinity of the latter. The relative conductivity through the furan (1.08) and thiophene (0.95) ring are close to mean values (1.15 and 0.99 respectively) obtained in reactivity studies of these heterocycles in various chemical and electrochemical reactions [18].

The relative ability for transfer of substituent effect from position 2 to position 4 can be estimated from linear correlation equations for values of $a_{H,4}^{x}$ in anion radicals of 5-nitroheterocyclic compounds, and those of $a_{H,0}^{\mathrm{CH}\overset{..}{-}\mathrm{CH}}$ for *p*-substituted nitrobenzene anion radicals. Such transfer values are more than twice as high in the case of anion radicals of nitrofuran and other heterocycles under study, compared with those of the benzene cycle. In the heterocycle series its value also depends on electron affinity of the heteroatom, but inversely with respect to a_N, i.e., with an increase in electron affinity of the heteroatom, the substituent effect on position 4 of the heterocycle also increases. The HFS constants of the anion radicals under consideration may change with a change in properties of the medium [19]. However, even passing from DMF to water, a medium with higher dielectric permeability and proton donating properties, the nature of the change in HFS constants is the same for nitro derivatives of all heterocycles studied, and the sequence of HFS constant values, as established in DMF, remains unchanged in aqueous medium.

Anion radicals of the 5-nitrofuran series with a developed conjugated system of the substituent in position 2

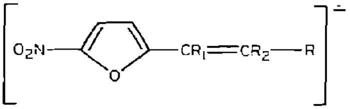
The general rules of change in lone electron density in anion radicals of the nitrofuran series with lengthening of their π-electron system by introduction of a vinylene group is reflected in their HFS constant values (Table 5). An analysis of ESR spectra of anion radicals of 2-vinylene derivatives of 5-nitrofuran has been performed according to [20]. Inclusion of a —CH=CH— group between the furan ring and the substituent R leads to lowering of HFS constant values, both of those due to the nitrogen atom of the nitro group and the proton on position 4 of the furan ring, and of the HFS constants due to nuclei of substituent R atoms. Such a change is caused by delocalization of the lone electron along the vinylene group. Lone electron density on the vinylene group itself equals ca. 0.1 of an electron. The lone electron is distributed unevenly over the vinylene group: electrophility of the β-position (with respect to the furan ring) exceeds more than threefold that of the α-position. Relative electrophility of separate positions of the anion radicals under study also changes depending on the nature of substituents R_1 and R_2 in the vinylene group (Table 4, 5).

The relation

$$a^{\text{vin}} = 0.73\,a + 0.91 \quad (r = 0.99, n = 5) \qquad (12)$$

TABLE 5

HFS constants (a, G) of ESR spectra of anion radicals



in DMF. Supporting electrolyte $(C_4H_9)_4NBr$

R	R_1	R_2	Nature of splitting	a_{N,NO_2}	$a_{H,4}$	$a_{H,3}$	$a_{H,R}$	a_{H,R_1}	a_{H,R_2}
COO^-	H	H	$3_N \cdot 2_H \cdot 2_H \cdot 2_H \cdot 2_H$	7.95	4.96	1.37	—	0.93	3.06
COO^-	Br	H	$3_N \cdot 2_H \cdot 2_H \cdot 2_H$	8.60	4.90	1.20	—	—	2.30
COO^-	H	Cl	$3_N \cdot 2_H \cdot 2_H \cdot 2_H$	8.30	4.70	1.30	—	1.30	
COO^-	H	CH_3	$3_N \cdot 2_H \cdot 2_H \cdot 2_H \cdot 4_H$	9.00	5.00	1.60	—	1.60	2.70
CHO	H	H	$3_N \cdot 2_H \cdot 2_H \cdot 2_H \cdot 2_H \cdot 2_H$	5.02	3.19	0.89	0.51	0.89	3.37
$COOC_2H_5$	H	H	$3_N \cdot 2_H \cdot 2_H \cdot 2_H \cdot 3_H$	5.80	3.72	1.20	0.30	—	3.72
$COOCH_3$	H	H	$3_N \cdot 2_H \cdot 2_H \cdot 2_H \cdot 4_H$	5.80	3.84	1.19	0.34	—	3.84
CF_3	H	H	$3_N \cdot 2_H \cdot 2_H \cdot 2_H \cdot 2_H \cdot 4_F$	7.58	4.68	1.45	7.83	0.59	3.84

between constants $a^{\text{vin}}_{\text{N,NO}_2}$ and $a^{\text{vin}}_{\text{H,4}}$ of anion radicals of 2-vinylene derivatives of 5-nitrofuran and the corresponding values $a_{\text{N,NO}_2}$ and $a_{\text{H,4}}$ of the same HFS constants of anion radicals devoid of vinylene group shows that the vinylene group weakens the substituent effect R on lone electron density distribution in the nitrofuran group. Weakening of the substituent effect by the vinyl group by a factor of 2 has also been observed by comparison of polarographic reduction potentials of the initial molecules [21].

Table 6 presents data on hydrazone-type anion radicals of compounds which, incidentally, have found wide medical application.

Owing to the developed π-electron system of the substituent conjugated with the nitrofuran ring, the ESR spectra of these anion radicals possess a rather complex HFS which is difficult to decipher (Fig. 2). For an analysis of ESR spectra with such complex HFS the cepstral analysis method has been employed [11, 22, 23]. Under the given experimental conditions it has, however, been possible to decipher completely the HFS only for such anion radicals in which interaction of the lone electron takes place with not more than six spectroscopically non-equivalent atomic nuclei. The mean value of limiting signal density for deciphering such spectra under given experimental conditions does not exceed 10 signals G^{-1}. More complex ESR spectra of anion radicals have only been partly deciphered; HFS constants due to the nitrogen atom of the nitro group have been determined. For compounds presented in Table 6, at ECG potentials close to those of the first polarographic wave, formation of free radicals has not been observed, with structure indicating bond cleavage in the hydrazone fragment, as noted in the case of *p*-nitrophenylhydrazones [24]. In this work, cleavage of the N—N bond in the hydrazone group has been observed only at higher potentials. At potentials exceeding that of the second polarographic wave of Furacilin (Nitrofurazone), HFS of the ESR spectrum obtained does not belong to its anion radical, presenting a splitting of structure $3_{\text{N}} \cdot 2_{\text{H}} \cdot 3_{\text{N}}$.

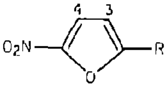
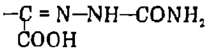
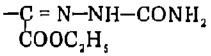
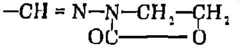
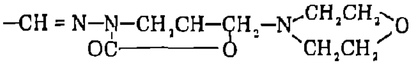
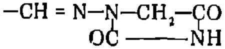
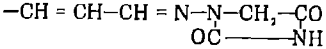
The lone electron is distributed over the 5-nitrofuran and hydrazone group in all anion radicals of the hydrazone series studied. The highest lone electron density concentrated on the nitrofuran fragment. The overall density concentration of the lone electron on the hydrazone group amounts to ca 0.1 of an electron.

Stability of anion radicals of the nitrofuran series

A study of the decay of ESR signals of anion radicals of the nitrofuran series in the non-aqueous medium DMF and in mixed water—DMF media shows that the decay of anion radicals can formally be described as a second order reaction under these conditions. Stability of the anion radicals is, to a large extent, dependent on their structure and on conditions of medium. For instance, the half-life period of anion radicals of 2-nitrofuran, at initial concentration 5×10^{-5} M, may change from a few seconds to half an hour, depending on the water content in DMF.

TABLE 6

Half-wave potential values ($E_{1/2}$, V) for 5-nitro-2-furfurylidenehydrazones and HFS constants (a, G) of ESR spectra of their anion radicals. Medium, DMF; supporting electrolyte $(C_4H_9)_4NI$

 R =	Trivial names of pharmaceuticals	$-E_{1/2}$	a_{N,NO_2}	$a_{H,4}$	$a_{H,3}$	$a_{H,CH=N}$	$a_{N,CH=N}$	$a_{N_\beta,=N-N_\beta}$
$-CH=N-NH-COCH_3$	Acylnydrazone	0.84	8.1	–	–	–	–	–
$-CH=N-NH-CONH_2$	Furacilin (Nitrofurazone)	0.84	7.4	–	–	–	–	–
 $-\underset{COOH}{C}=N-NH-CONH_2$	–	0.92	7.74	4.62	1.36	–	2.10	0.26
 $-\underset{COOC_2H_5}{C}=N-NH-CONH_2$	–	0.79	8.94	4.95	1.22	–	1.22	0.41
$-CH=N-N(CH_2CH_2Cl)_2$	–	0.96	7.9	–	–	–	–	–
 $-CH=N-\underset{OC}{N}-CH_2-\underset{O}{CH_2}$	Furazolidone (Furoxone)	0.82	7.00	4.35	1.19	0.89	1.98	0.40
 $-CH=N-\underset{OC}{N}-CH_2CH-\underset{O}{CH_2}-N\langle^{CH_2CH_2}_{CH_2CH_2}\rangle O$	Furazoline (Altafur)	0.82	7.16	4.50	1.18	0.90	2.10	0.59
 $-CH=N-\underset{OC}{N}-CH_2-\underset{NH}{CO}$	Furadonin (Nitrofurantoin)	0.82	7.25	4.50	1.20	0.80	2.06	0.41
 $-CH=CH-CH=N-\underset{OC}{N}-CH_2-\underset{NH}{CO}$	Furagin	0.78	6.3	–	–	–	–	–

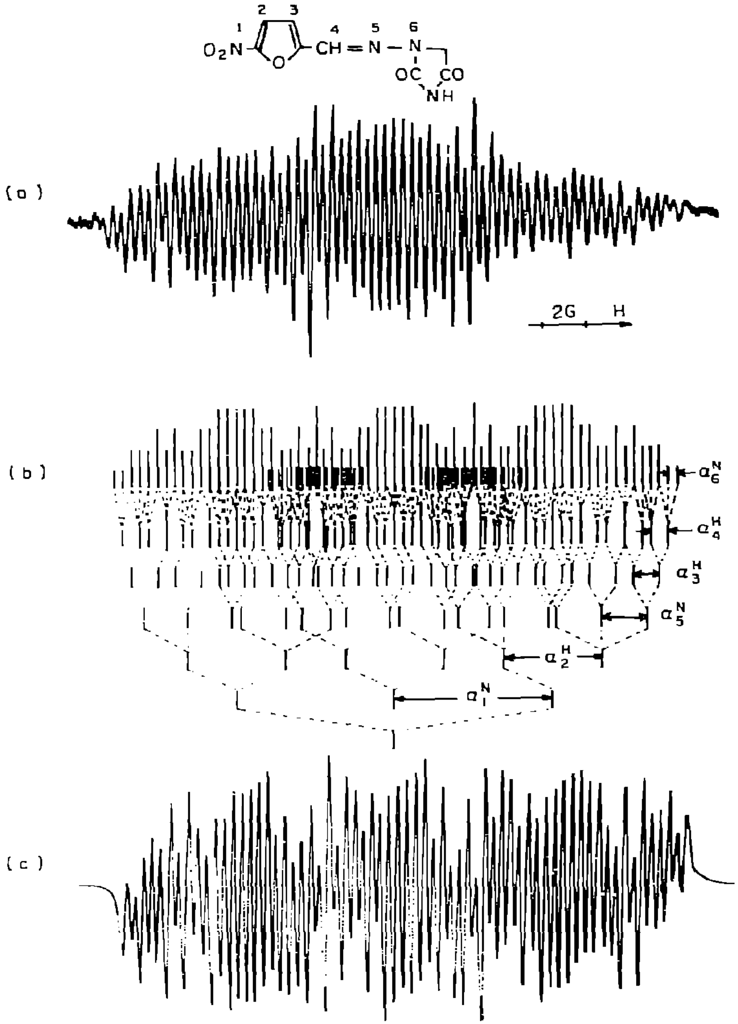


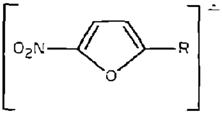
Fig. 2. (a) Experimental ESR spectrum of anion radicals of Furadonin (Nitrofurantoin) in DMF; (b) its reconstructed line-spectrum; (c) simulated ESR spectrum. Supporting electrolyte $(C_2H_5)_4NI$.

Studying stability of anion radicals in DMF in relation to their structure, one may note that of all anion radicals studied (Table 7), anion radicals of unsubstituted 2-nitrofuran are least stable. Substitution of the hydrogen atom in position 2 of the furan ring raises stability of anion radicals of the nitrofuran series in DMF (Table 7). However, the degree of stabilization of the anion radicals depends largely on the nature of the substituent. Whilst substitution by a methyl group affects stability of the anion radical only inconsiderably, substituents possessing a π-electron system conjugated with the nitrofuran system raise stability of the anion radicals in DMF by 1—2 orders of magnitude, as compared to the stability of anion radicals of unsubstituted 2-nitrofuran. The stabilizing properties of the substituent increase with widening of its π-electron system. This appears to be due to increased delocalization of the lone electron over the π-electron system and to lowering of its density on the nitrofuran group, the latter being the more probable reacting centre of lone electron recombination.

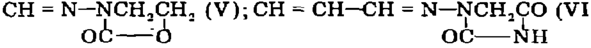
Such a comparatively simple dependence of stability of 5-nitrofuran anion radicals on substitution and on the nature of substituent manifests itself in media of low proton donating ability. With increasing water content in DMF destabilization of the anion radicals takes place. Such destabilization of anion radicals is higher in the case of unsubstituted 2-nitrofuran or in the case of substituents possessing a π-electron system. In case of substitution by a methyl group stability of the anion radical against destabilization by aqueous medium increases. As a result the decay rate constant k_2 increase

TABLE 7

Decay rate constants ($M^{-1}s^{-1}$) of anion radicals



R = CH_3 (I); H(II); CHO (III); CH = N—NHCONH$_2$ (IV);



$CH = N-\underset{OC—O}{NCH_2CH_2}$ (V); $CH = CH-CH = N-\underset{OC—NH}{NCH_2CO}$ (VI).

Medium, DMF; supporting electrolyte, $(C_4H_9)_4NPF_6$

Water content in DMF (M)	Anion radical					
	I	II	III	IV	V	VI
0	8	10	3	2	0.3	—
1	10	15	15	—	—	—
2	—	—	20	10	4	0.03
5	25	40	250	30	20	—
8	—	—	—	—	40	1
10	30	150	8000	100	90	4
20	90	2000	—	500	400	20

for 2-methyl-5-nitrofuran anion radicals is slowed down by an order of magnitude or more with increase in water content in mixed solution as compared to the rate increase for other 5-nitrofuran anion radicals. Destabilization of anion radicals possessing a π-electron system in the substituent R is probably due to additional reaction centres brought in by the substituent. A higher rate of increase of values k_2 with increase in water content in DMF can also be observed for anion radicals of compounds IV, V and VI (Table 7), in the same sequence as the increase in complexity of structure of their substituents.

As a result, stability of anion radicals under the described conditions is determined by destabilizing effect of added water, as well by stabilization due to delocalization of the lone electron. In the case of substituent R = CHO, destabilization of anion radicals by addition of water ($\geqslant$5 M) leads to lower stability of this radical compared to that of an anion radical of unsubstituted 5-nitrofuran. However, in the case of other studied anion radicals possessing a wider π-electron system, destabilization caused by addition of water is compensated by the stabilizing effect of increased delocalization of the lone electron in the substituent. Hence, even at 20 M water content in DMF stabilization of the anion radical, as compared to its unsubstituted analogue takes place. Destabilization of anion radicals by increase of water content in DMF is, apparently, a result of the participation of these radicals in complex chemical processes. One stage of these processes consists of protonization of anion radicals. The complex nature of such processes can, for instance, be seen from the fact that even in the case of such a structurally homogeneous radical as that of anthracene, the simple mechanism of protonization has not yet been clarified [25].

Under conditions of ECG no ESR signal has been registered in protonated media of pH < 4. At the same time, ESR spectra of these radicals have been registered, under conditions of pulse radiolysis, even in media with pH = 0 [26]. Anion radicals of one of the pharmaceuticals of the nitrofuran series (Nitrofurantoin) have been registered also at biochemical reduction of this compound in microsomal medium [27]. These results indicate the possibility of the radicals discussed above taking part in processes determining radiosensitizing and antibacterial properties of nitrofuran compounds. This lends particular interest to further studies of structure and properties of these anion radicals.

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