MECHANISM AND PRODUCTS OF ELECTROCHEMICAL REDUCTION OF 4-NITROPHENYL-2,6-DIMETHYL-3,5-DICYANO-1,4-DIHYDROPYRIDINES IN DIMETHYLFORMAMIDE

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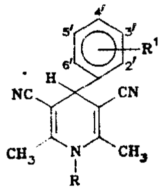
Free anion radicals of the nitrobenzene and nitrosobenzene type, which were identified by EPR spectroscopy, are formed in the electrochemical reduction of isomeric 4-(nitrophenyl)-2,6-dimethyl-3,5-dicyano-1,4-dihydropyridines on mercury and solid electrodes. Reduction of the dihydropyridine ring is observed only for N-substituted p- and m-nitrophenyl derivatives of 1,4-dihydropyridine. An intermediate with a 2-pyridonemethide structure was identified; a set of primary and secondary chemical reactions that are associated with the electrolytic reduction of the investigated compounds is presented.

4-Nitrophenyl derivatives of dihydropyridine (DHP), which display high hypotensive and antioxidant activity, have two electrochemically active centers that are capable of undergoing oxidation [the 1,4-dihydropyridine (DHP) grouping] and reduction (the nitrophenyl group and the DHP grouping). Since a potential intramolecular redox system is possible here, a question arises as to whether the imposition of an external (electrode) voltage initiates intramolecular electron transfer in such molecules or whether it sets up the conditions only for the possibility of the formation of secondary redox systems. We have studied the electrochemical transformations of such compounds by means of a rotating-disk electrode; only the electrolytic oxidation of the DHP part of the molecule was examined in detail [1]. However, considerably less attention was directed to the electrolytic reduction of the nitrophenyl fragment in [1]; in the case of 4-(nitrophenyl)-2,6-dimethyl-3,5-diethoxycarbonyl-1,4-DHP it was examined in [2], in which the formation of a number of free-radical particles as intermediates was revealed.

In connection with the nontraditional character of the occurrence of the electrolytic reduction and the development of several unexpected intermediate free-radical particles that differ from one another it is expedient to make a detailed study of the peculiarities of the electrolytic reduction on a mercury cathode in DMF of related compounds, viz., 4-(nitrophenyl)-1,4-DHP that contain more electronegative (as compared with $COOC_2H_5$) nitrile groups in the 3 and 5 positions of the DHP ring.



I a-f

I a–c $R=CH_3$, d–f $R=H$; Ia,d $R^1=4'\text{-}NO_2$, b,e $R^1=3'\text{-}NO_2$, c,f $R^1=2'\text{-}NO_2$

All of the investigated Ia-f are reduced in a stepwise manner in DMF on a mercury electrode. Redox systems that are due not only to direct transfer of an electron from the electrode to the investigated molecule but also systems that are formed as a consequence of chemical transformations of the intermediate products of electrolytic reduction were detected by means of cyclical voltamperometry. The free-radical particles that develop in these pro-

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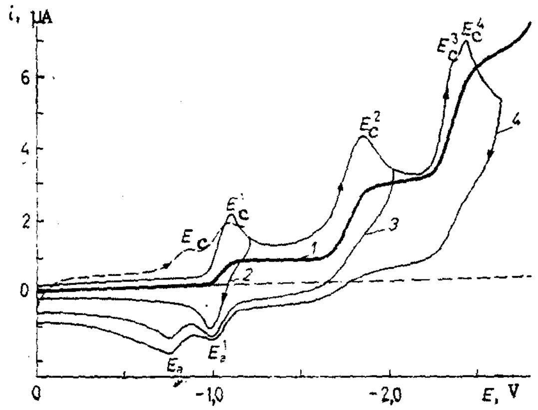


Fig. 1. Classical polarogram (1) and cyclical volt-ampere curves (2-4) in the electrochemical reduction of Ia at various potential scans in DMF: 2) up to −1.2 V; 3) up to −2.0 V; 4) up to −2.6 V.

TABLE 1. Electrochemical Characteristics ($E_{1/2}$, i) of 4-Nitrophenyl-1,4-DHP Derivatives Ia-f and 4-(4'-Nitrophenyl)-3,5-diethoxycarbonyl-2,6-dimethyl-1,4-DHP (Ig) [2] in DMF on a Dropping Mercury Electrode with 0.1 M $(C_4H_9)_4NPF_6$ as the Inert Electrolyte

Compound	$-E^{I}_{1/2}$, V	$-E^{II}_{1/2}$, V	$-E^{III}_{1/2}$, V	$-E^{IV}_{1/2}$, V	i^{I}, μA	i^{II}, μA	i^{III}, μA	i^{IV}, μA
Ia	1,05	1,75	2,32	—	0,65	1,95	3,00	—
Ib	1,04	1,81	2,34	—	0,65	2,00	2,43	—
Ic	1,09	1,84	2,37	2,60	0,65	1,90	0,65	1,30
Id	1,05	1,70	2,23	—	1,15	0,85	2,50	—
Ie	1,03	1,75	2,16	—	0,85	0,55	1,70	—
If	1,07	1,77	2,20	2,59	1,20	0,70	1,70	0,80
Ig	1,18	2,02	2,50		0,65	0,48	1,29	—

cesses were determined by EPR spectroscopy. The number of steps in the electrolytic reduction and their natures for the various representatives of the series differ (Table 1). Thus, p- and m-nitrophenyl derivatives Ia, b, d, e differ in polarographic behavior from ortho derivatives Ic, f. The first wave of N-substituted derivatives Ia-c corresponds to a one-electron process, while the wave for N-unsubstituted derivatives Id-f surpasses the one-electron level. Consequently, the pathways in the reduction of Ia-f in DMF differ as a function of substituent R and the orientation of the nitro group in the benzene ring relative to the heteroring. In view of this, we preferred to thoroughly analyze the mechanisms of the reduction of Ia-f by grouping individual representatives of the series with respect to the most characteristic common features of the electrochemical reduction.

N-Substituted 4-Nitrophenyl-1,4-dihydropyridine Derivatives Ia-c

The first polarographic wave is a one-electron wave for Ia-c. The difference in the potentials (59 mV) between the reduction peaks E_c^1 and the oxidation peaks E_a^1 on the cyclical volt-ampere curves of these compounds constitutes evidence for the reversibility of electron transfer [reaction (1)]. The classical polarogram and the cylical volt-ampere curves at various potential scans for Ia recorded in DMF with 0.1 M $(C_4H_9)_4NPF_6$ as the inert electrolyte are presented in Fig. 1.

Relatively stable primary anion radicals IIa-c, which are formed in the course of the electrochemical generation (ECG) of Ia-c at the potential of the first polarographic wave, were identified by EPR spectroscopy. The EPR spectrum of IIa anions radicals is presented in Fig. 2a. It follows from an analysis of the hyperfine structure (hfs) of the EPR spectra that the unpaired electron is delocalized primarily over the nitrophenyl fragment of the molecule. However, the existence of an $a_{H,4}$ hfs constant due to coupling of the unpaired

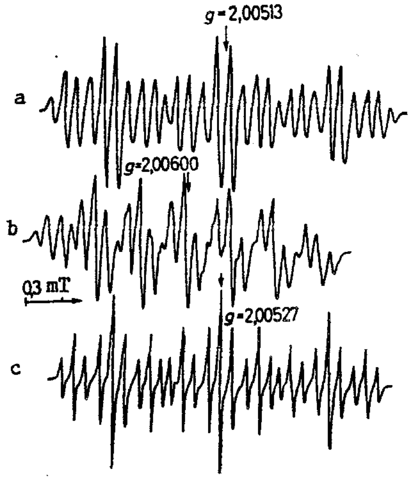


Fig. 2

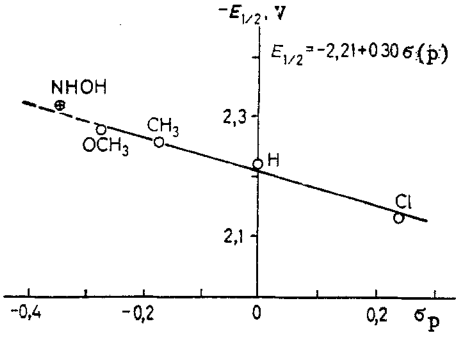


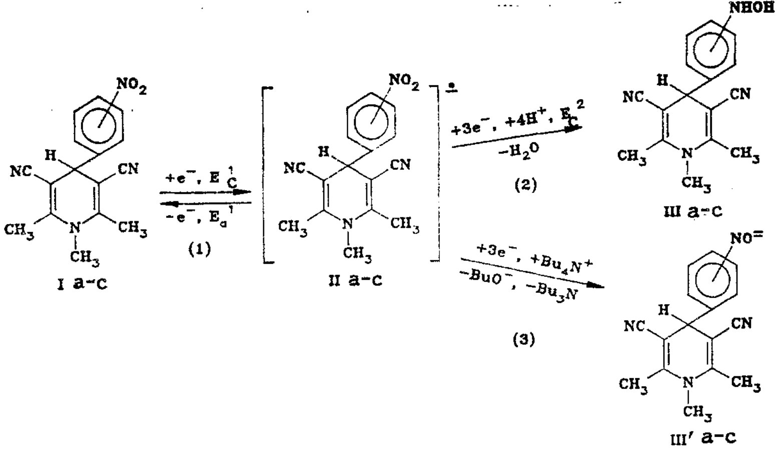
Fig. 3

Fig. 2. EPR spectra of the free-radical particles formed in the electrochemical generation of Ia: a) primary anion radical IIa; b) nitrosophenyl derivative anion radical VIIa; c) 2-pyridonemethide derivative anion radical IXa.

Fig. 3. Relationship between the potentials of the electrochemical reduction ($E_{1/2}$) of p-substituted 1,2,6-trimethyl-3,5-dicyano-4-(4'-phenyl)-1,4-DHP and the Hammett σ_p constants.

electron with the proton in the 4 position of the heteroring constitutes evidence that the 1,4-DHP structure of the heteroring is retained in the IIa-c anion radicals. Thus, in the case of Ia-c only the nitrobenzene fragment of the molecule is reduced in the first step, and the heteroaromatic part remains unchanged.

The second wave in the electrolytic reduction of Ia-c is irreversible and corresponds to the transfer of three electrons. It is known [3] that in an aprotic medium such as DMF nitrobenzene is reduced with the formation of two polarographic waves: anion radicals of the starting compound are formed in the first one-electron step, while hydroxyaminobenzene, which does not undergo further reduction, is formed in the second three-electron step. Il'yasov and coworkers [4] assume that, in the absence of protons, the three-electron reduction of nitrobenzene anion radicals proceeds with the participation of the cation of the inert salt and leads to the nitrosobenzene dianion. The proton concentration is low in dry DMF, and we therefore assume that in our case both reduction processes — reduction to both the hydroxyamino derivative IIIa-c [reaction (2)] and to the nitrosophenyl derivative dianion III'a-c [reaction (3)] — can be realized. The presence of a significant amount of tributylamine among the products of electrolysis formed at the potential of the second polarographic wave and isolated by liquid chromatography constitutes evidence in favor of the occurrence of reaction (3). The tributylamine was identified by mass spectroscopy (the spectrum was identical to the spectrum presented in a catalog [5]).



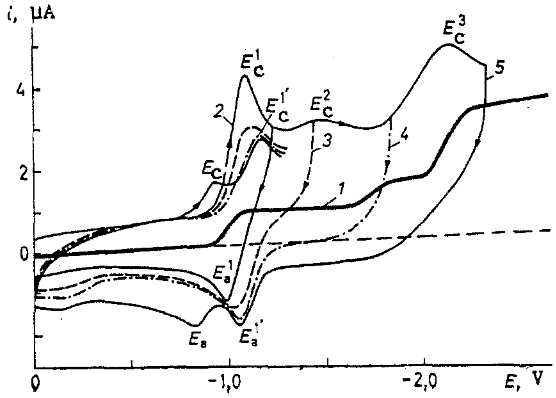
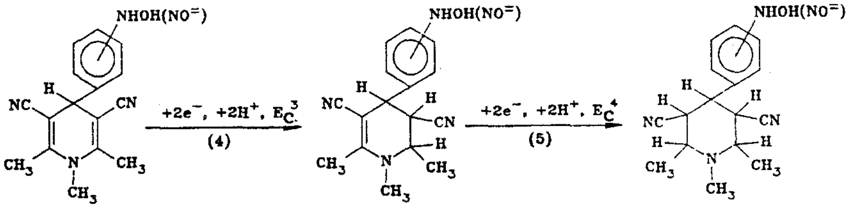


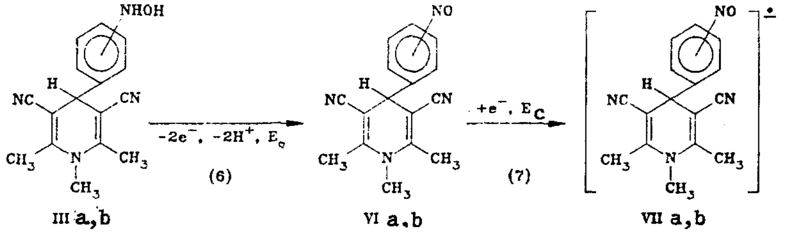
Fig. 4. Classical polarogram (1) and cyclical volt-ampere curves (2-5) of the electrochemical reduction of Ie at various potential scans: 2) up to −1.2 V; 3) up to −1.5 V; 4) up to −1.8 V; 5) up to −2.3 V.

The third polarographic wave for Ia, b is close in height to a four-electron wave; the two closely situated $E_c{}^3$ and $E_c{}^4$ peaks correspond to it on the cyclical volt-ampere curve of Ia (Figs. 1-4). To confirm the assumption that the third wave is due to reduction of the DHP part of the 4-(hydroxyaminophenyl)-1,4-DHP we determined the potentials of the electrochemical reduction of a number of 4-phenyl-1,4-DHP that contain Cl, H, CH_3, and OCH_3 substituents in the para position of the phenyl ring. A linear relationship between the potential of electrochemical reduction $E_{1/2}$ and the Hammett σ_p constant is observed (Fig. 3), and $E^{III}{}_{1/2}$ of Ia lies satisfactorily on the correlation line for the point corresponding to the NHOH substituent. Consequently, the third wave in the polarograms of Ia, b is due to the reduction of the two C=C bonds of the DHP ring [reactions (4) and (5)].

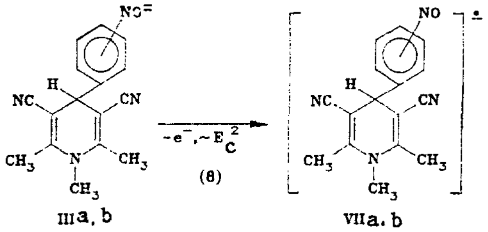


III(III')a, b
IV(IV')a, b
V(V')a, b

A new oxidation peak ($E_a \approx -0.7$ V) is observed on the anode branch on the cyclical volt-ampere curves recorded for Ia (Figs. 1-3) and Ib in the case of scanning up to the potential of the second polarographic wave, while on the cathode branch in the case of rescanning of the potential one observes the corresponding cathode peak at $E_c \approx -0.8$ V, i.e., in a more positive range of potentials than the potential of the first polarographic wave. This redox system was not observed for Ic. Additional EPR signals develop in the process of electrochemical generation (ECG) at the potential of the second polarographic wave for Ia (Fig. 2b) and Ib on the background of the primary anion radicals. The intensity of these signals increases significantly; the signals of the primary EPR spectrum vanish completely if the ECG potential is decreased sharply to 0 V and then increased to −0.8 V. It follows from an analysis of the hfs that this EPR spectrum corresponds to anion radicals of a p-substituted nitrosobenzene [6]. Lower density of the unpaired electron on the nitrogen atom of the nitroso group as compared with the nitro group and nonequivalence of the hfs constants due to the protons in the ortho positions relative to the nitroso group are observed. One should note the low stability of these particles and the increase in the g factor; this is also characteristic for nitrosobenzene anion radicals as compared with nitrobenzene anion radicals. Thus, for Ia, b the redox system at ≈ −0.7 V is formed as a result of oxidation of hydroxyaminophenyl derivatives IIIa, b to nitrosophenyl derivatives VIa, b [reaction (6)], which can then be reduced to the corresponding anion radicals VIIa, b [reaction (7)].



However, the development of anion radicals VIIa, b at the potential of the limiting current of the second polarographic wave is due to one-electron oxidation of dianions III'a, b [reaction (8)], which proceeds at a considerably more negative potential than the potential of oxidation of hydroxyamino derivatives IIIa, b, as demonstrated in the case of unsubstituted nitrobenzene [4].



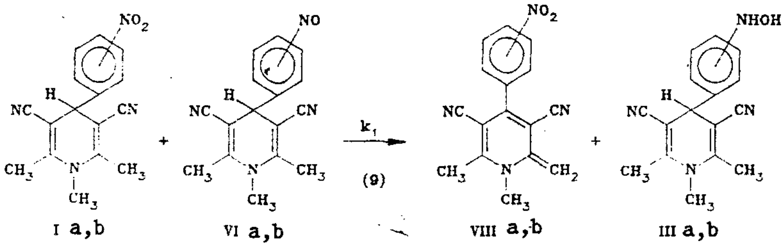
The hfs constants of the anion radicals VIIa and VIIb of 1,4-DHP 4-nitrosophenyl derivatives are presented in Table 2. The existence of an $a_{H,4}$ hfs constant due to the proton of the heteroring in the 4 position constitutes evidence for retention of the 1,4-DHP structure of the heteroring of these anion radicals. Thus, one can exclude the intramolecular transfer of electrons and protons from the DHP part of the molecule to the nitrophenyl fragment in the electrochemical reduction of the nitro group.

However, simultaneously with an increase in the intensities of the EPR signals of anion radicals VII at −0.8 V other lines that do not belong to either the primary or secondary free-radical particles described above also appear in the spectrum. The signals of anion radicals VII vanish completely with an increase in the ECG potential to −1.1 V, and the sharp increase in the intensities of the new signals constitutes evidence for an increase in the amount of free-radical particles with a different structure. Their maximum concentration is reached at ECG potentials from −1.2 to −1.5 V. From the common structure of the distribution of the density of the unpaired electron it may be assumed that this is the EPR spectrum of the anion radicals of a p-substituted nitrobenzene without, however, an hfs constant that attests to the presence of a proton in the 4 position of the heteroring. The new EPR spectrum for Ia is presented in Fig. 1c. A product, the structure of which, determined by

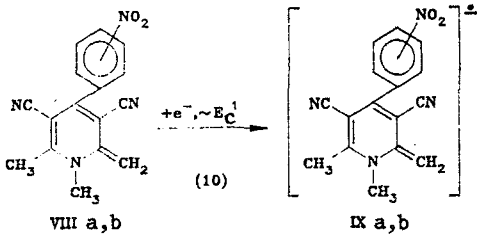
TABLE 2. Hyperfine Structure (hfs) Constants (*a*) of the Free-Radical Products Formed in the Electrochemical Generation (ECG) of Ia-f and Ig [2] in DMF

Compound	Product	ECG potential, V	$a \cdot 10^4$ (T)					
			$a_{2'}$	$a_{3'}$	$a_{4'}$	$a_{5'}$	$a_{6'}$	$a_{H,4}$
Ia	IIa	−1,1	1,07(H)	3,22(H)	9,28(N)	3,22(H)	1,07(H)	1,07
	VIIa	−0,8	0,97(H)	3,65(H)	7,42(N)	2,73(H)	0,97(H)	0,97
	IXa	−1,2	0,97(H)	3,19(H)	8,99(N)	3,19(H)	0,97(H)	—
Ib	IIb	−1,1	3,31(H)	9,05(N)	3,31(H)	1,04(H)	3,89(H)	0,35
	VIIb	−0,8	hfs not deciphered					
	IXb	−1,2	3,19(H)	9,51(N)	3,19(H)	1,04(H)	3,83(H)	—
Ic	IIc	−1,2	9,40(N)	3,71(H)	0,99(H)	4,64(H)	0,99(H)	0,58
Id	IId	−1,1	0,95(H)	3,19(H)	9,74(N)	3,19(H)	0,95(H)	0,95
	XIId	−1,5	1,05(H)	3,31(H)	10,15(N)	3,31(H)	1,05(H)	1,05
	XVd	−0,9	1,05(H)	3,77(H)	7,77(N)	2,90(H)	1,05(H)	1,05
Ie	IIe	−1,1	3,13(H)	9,05(N)	3,13(H)	1,04(H)	3,54(H)	0,35
	XIIe	−1,5	3,19(H)	9,63(N)	3,19(H)	1,04(H)	3,54(H)	0,33
	XVe	−0,9	3,77(H)	7,37(N)	2,84(H)	1,04(H)	3,77(H)	0,29
If	IIf	−1,2	hfs not deciphered					
	XIIf	−1,3	10,09(N)	3,13(H)	1,04(H)	3,60(H)	1,04(H)	0,46
Ig	IIg	−1,2	1,05(H)	3,35(H)	9,85(N)	3,35(H)	1,05(H)	1,05(H)
[2]	XIIg	−2,1	1,10(H)	3,30(H)	10,70(N)	3,30(H)	1,10(H)	1,30(H)

mass spectroscopy, corresponds to 1,6-dimethyl-3,5-dicyano-4-(4'-nitrophenyl)-2-pyridonemethide (VIII) (m/z 292 [$M^{+\cdot}$], 262 [$M^{+\cdot}$ – NO], 236 [$M^{+\cdot}$ – NO, – CN]), was isolated by means of liquid chromatography from the reaction mixture obtained in the electrolysis of Ia at $E_{1/2}^{II}$. The formation of VIIIa can be conceived if and only if it is assumed that molecules of the starting Ia present in solution near the electrode are capable of participating in an intermolecular process involving the transfer of protons and electrons with nitrosophenyl derivative VIa [reaction (9)], which was formed in the oxidation of hydroxyaminophenyl derivative IIIa and is an extremely reactive particle. We assume that VIIIb is formed similarly.



The potential of the electrochemical reduction of VIII should be close to the potential of the corresponding 1,2-DHP. According to the data in [1], $E_{1/2}$ of 4-(4'-nitrophenyl)-3,5-diethoxycarbonyl-1,4-DHP differs from $E_{1/2}$ of the corresponding 1,2-DHP by only 10 mV. This is probably also the reason that redox systems that attest to the formation of a 2-pyridonemethide and its one-electron reduction to anion radical IX [reaction (10)] are not observed on the cyclical volt-ampere curves of Ia (Figs. 1-3) and Ib.



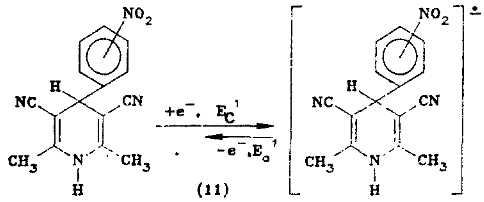
The high stability of anion radicals IX is evidently due to the fact that the nitrophenyl fragment enters into conjugation with the pyridonemethide part of the molecule. The absence in the mass spectrum of VIIIa of a peak with a mass of 170 ([$M^{+\cdot} - C_6H_4NO_2$]) also constitutes evidence in favor of this.

N-Unsubstituted 4-Nitrophenyl-1,4-dihydropyridines Id-f

The pattern of the electrochemical reduction is somewhat different for these compounds. The classical polarogram and the cyclical volt-ampere curves for Ie are presented in Fig. 4, while the EPR spectra of the free radicals formed in its electrochemical reduction are presented in Fig. 5. Freshly prepared samples in dry DMF on a dropping mercury electrode are reduced with the formation of three (or four in the case of If) polarographic waves; however, the heights of these waves differ from those for the corresponding N-substituted derivatives Ia-c (Table 1). The height of the first wave exceeds the one-electron level, and its reversibility is considerably lower as compared with the corresponding N-substituted derivatives. It was established by EPR spectroscopy that extremely unstable free radicals are formed at the potential of the first polarographic wave during electrochemical generation (ECG) (Fig. 5a). In the case of If we were unable to record an EPR spectrum that could be deciphered. In the case of Id, e it was determined from the hfs of the EPR spectra and the hfs constants that these are anion radicals IId, e of substituted nitrobenzenes (reaction (11)]. We suppose that in the case of If also the recorded EPR signals correspond to anion radicals IIf, since their subsequent transformation are similar to the transformations of anion radicals IId, e (see scheme top of next page).

It should be noted that coupling of the unpaired electron with the proton in the 4 position of the heteroring is also observed for anion radicals IId, e (see Table 2).

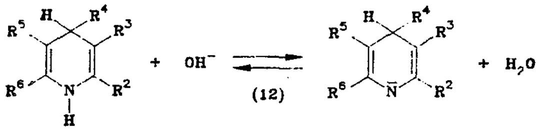
A new oxidation peak $E^{1'}$ was detected on the cyclical volt-ampere curves in the reduction of Id-f up to potentials situated in the interval between the first and second polaro-



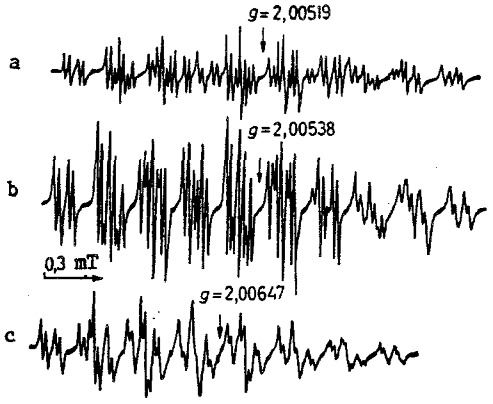
I d-f II d-f

graphic waves, and the reduction peak $E_c^{1'}$ corresponding to it is detected upon scanning of the cycle (see Fig. 4). This constitutes evidence for the formation of a new redox system at more negative potentials that the potential of the electrochemical reduction of the starting molecules. New free-radical particles were also observed during ECG with an increase in the generation potential. With respect to the character of the hfs the two radicals are identical and differ only with respect to the hfs constants (Table 2, Fig. 5b). It is interesting that secondary radicals develop at a potential that does not reach the potential of the second polarographic wave, in contrast to the previously investigated [2] 4-nitrophenyl derivatives of 3,5-diethoxycarbonyl-1,4-DHP. In Tables 1 and 2 for comparison we presented the electrochemical characteristics and hfs of the free radicals for 4-(4'-nitrophenyl)-3,5-diethoxycarbonyl-1,4-DHP (Ig [2]. Whereas in [2] the formation of secondary anion radicals was explained by reduction of the proton attached to the nitrogen atom and the formation of a dianion, which is rapidly protonated in another position such as the 3 position, in our case the reason for the development of secondary anion radicals should be different.

It has been shown [7] that 3,5-dicyano derivatives of 1,4-DHP in a nonaqueous medium can exist in an ionized form, whereas at pH > 10 3,5-diacetyl-1,4-DHP exist in equilibrium (pK = 12-13 [8] [reaction (12)].



We established the possibility of the existence of Id-f in the anionic form in DMF from the difference in the electronic absorption spectra recorded for Ie in the pure solvent and with the addition of benzoic acid or tetrabutylammonium hydroxide (Fig. 6). In the latter case we observed a shift of the absorption maximum to the longer-wave region (425 nm) as compared with the spectrum in the pure solvent (340 nm). This spectral pattern is charac-



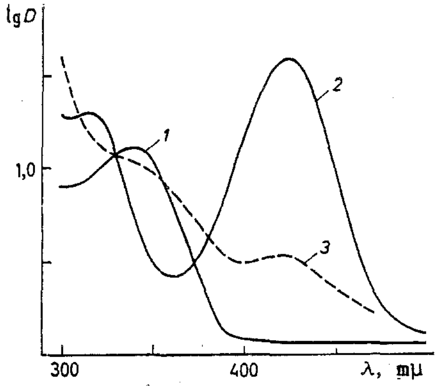
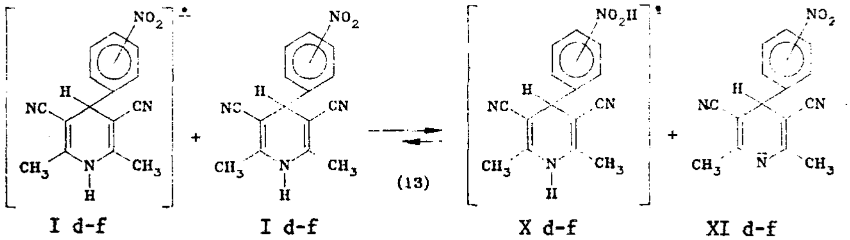


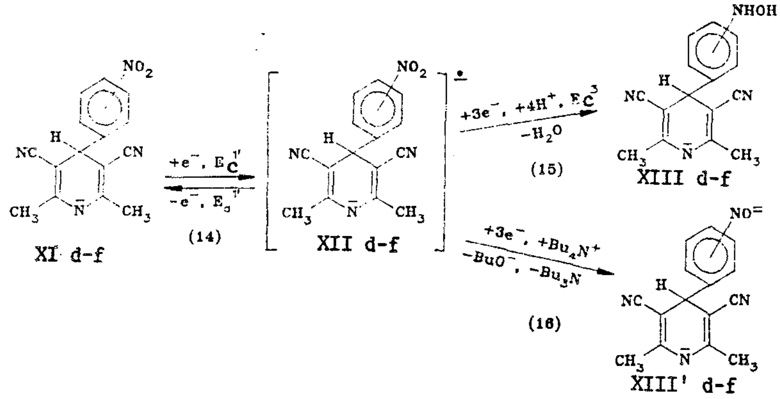
Fig. 5. EPR spectra of the free radicals formed in the electrochemical generation (ECG) of Ie: a) primary anion radical IIe; b) dianion radical XIIe; c) dianion radical XVe of the nitrosophenyl derivative.

Fig. 6. Electronic absorption spectra of Ie: 1) in DMF and DMF with the addition of 0.05 mole/liter benzoic acid or 0.1 mole/liter $(C_4H_9)_4NPF_6$; 2) in DMF with the addition of 0.1 mole/liter tetrabutylammonium hydroxide $(C_4H_9)_4NOH$; 3) in DMF during electrolysis at E = −1.1 V.

teristic for conversion of the substance from the neutral form to the ionized form. However, an anionic form for 4-nitrophenyl-1,4-DHP that contain ester groupings in the 3 and 5 positions of the heteroring was not detected from the electronic spectra. This is in agreement with data on the acidities of the compounds being compared: the transition from the ethoxycarbonyl group to the more electron-acceptor cyano group in the 3 and 5 positions of 1,4-DHP gives rise to an increase in the acidity by 3.4 pK units [9]. We carried out the electrolysis of IE in a quartz cuvette placed in the UV spectrophotometer. Prior to switching on the potential the substance retains the absorption maximum at 340 nm, and, consequently, the inert salt $(C_4H_9)_4NPF_6$ does not affect the protolytic equilibrium of Ie. However, when a voltage of −1.1 V, which corresponds to the potential of the first polarographic wave, is applied, a maximum at 425 nm (Fig. 6, curve 3), which attests to the formation of an anion during electrolysis, appears in the spectrum. The pattern of the formation of an anion is similar for Id and If: in pure DMF and in an acidic medium one observes an absorption maximum at 355 nm for Id and at 330 nm for If, whereas an anion with an absorption maximum at 394 nm (Id) and at 412 nm (If) is formed in an alkaline medium or during electrolysis. Since ionized forms XId-f were not detected in the solutions being subjected to electrolysis without the application of a potential to the electrodes, one should assume that anion radicals IId-f, which are formed at the potential of the first polarographic wave [reaction (13)], act as negatively charged particles that are capable of deprotonating the starting molecules. Neutral radical X and an anion with 1,4-DHP structure XI develop as a result.



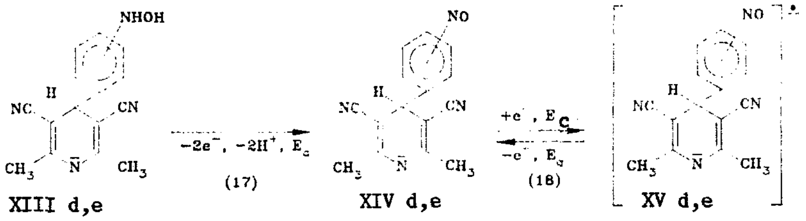
Since the anion is reduced at a more negative potential than the neutral molecule, it might be assumed that the secondary redox system detected on the cyclical volt-ampere curves ($E_a^{1'}$, $E_c^{1'}$; see Fig. 4) and the secondary radical particles in the EPR spectra correspond to the formation of dianion radicals XII of 4-(nitrophenyl)-1,4-dihydropyridines [reaction (14)].



The height of the first polarographic wave of Id-f arbitrarily characterizes the rate of proton transfer, since the potential of the one-electron reduction of the starting molecule $E_c^{1'}$ and the potential of the one-electron reduction of the anion $E_c^{1'}$ are close and appear in the form of a single merged wave $E_{1/2}'$ on the classical polarogram. The height of the first wave increases in the order Ie < Id < If and in the case of If almost reaches the two-electron level (Table 1). The rate of protonation increases in the same order. this explains the extremely low stability of primary anion radicals IIf.

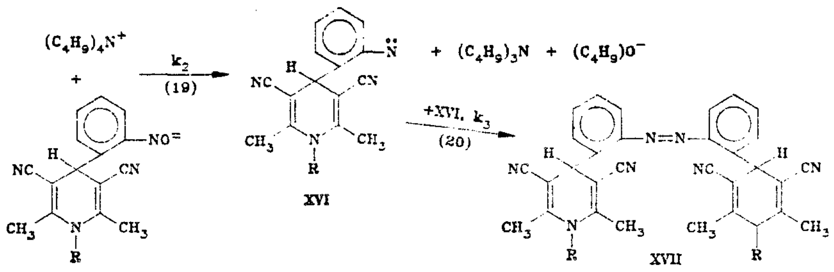
The potentials of the second polarographic wave $E_{1/2}^{II}$ in the electrochemical reduction of Id-f are close, but their heights are significantly lower than the heights of the second wave in the reduction of Ia-c. It might be assumed that this is the wave of the reduction of those anion radicals IId-f that did not have time to be protonated during the period of detachment of a drop of mercury. As in the case of N-substituted derivatives, this process is described by reactions (2) and (3). Evidence for this is provided by the absence on the cyclical volt-ampere curves recorded for Id-f on a stationary mercury or graphite electrode of a reduction peak corresponding to the second polarographic wave. However, a weak E_C^2 peak (see Fig. 4) in the gap between the potentials of the first and second polarographic waves that can be ascribed to three-electron reduction of protonated radical X was observed on the reduction branch.

For Id-f the third polarographic wave corresponds to three-electron reduction of dianion radical XII to the corresponding hydroxyamino (XIII) or nitroso (XIII') derivative [reactions (15) and (16)]. Just as in the case of Ia, b, a redox system at −0.8 V was observed on the cyclical volt-ampere curves of Id, e in the case of rescanning of the potential, and anion radicals of the nitrosobenzene type due to reactions (17) and (18) were recorded by EPR spectroscopy.



In the case of Id electrolysis was carried out at the potential of the third polarographic wave. A product, which, according to mass-spectrometric data, is 4-(4'-hydroxyaminophenyl)-2,6-dimethyl-3,5-dicyano-1,4-DHP (IIId) (m/z 266 [$M^{+\cdot}$], 249 [$M^{+\cdot}$ − OH]), was isolated from the electrolyzate by liquid chromatography. Since the separation of the electrolysis products by liquid chromatography was carried out in 50% aqueous solution, ionic form XIII'd could not be isolated. A significant amount of tributylamine was isolated from this mixture; this constitutes evidence for participation of the tetrabutylammonium ion in the reduction of the nitro group [reaction (16)].

As noted above, the electrochemical reduction of 1,4-DHP o-nitrophenyl derivatives Ic and If has some differences as compared with the electrochemical reduction of the para and meta derivatives. For both Ic and If the potential of the first polarographic wave is shifted to the more negative region (see Table 1); this is probably due to rotation of the nitro group about the C—N bond from the plane of the benzene ring as a consequence of repulsion of the NO_2 group in the phenyl fragment and the CN group in the DHP fragment of the molecule. Another peculiarity of the electrochemical reduction of Ic and If consists in the fact that the products of reduction of the nitro group of IIIc or III'c, just like XIIIf and XIII'f, undergo rapid chemical transformations, as evidenced by the absence on the cyclical volt-ampere curves of a nitrosophenyl derivative redox system in the case of rescanning of the potential after reduction of Ic, f to the second (for Ic) or third (for If) polarographic wave. However, an oxidation peak in the more positive potential range (~ −0.2 V) was observed on the anode branch of the cycle for both Ic and If. We suppose that transformations may proceed either through the detachment of a second oxygen atom in the reaction of nitroso dianions III' and XIII' with the positive ion of the tetraalkylammonium salt [10] with the subsequent formation of azo compound XVII [reactions (19) and (20)] or as a result of the formation of a new heterocyclic system between the hydroxyamino group and the DHP part of the molecule. The hypothetical azo compound can be oxidized at ~ −0.2 V.



The subsequent waves on the polarograms of Ic and If constitute evidence for further reduction of the products of chemical transformations.

The peculiar effect of the DHP fragment on the course of the electrochemical reduction of the nitrophenyl grouping in the series of compounds that we studied is expressed in the formation of secondary free radicals with a nitrosobenzene structure that are sufficiently stable for recording by EPR spectroscopy. As a rule, the formation of such radicals in the course of the electrochemical reduction of nitrobenzenes is not observed by EPR spectroscopy [11].

Whereas it is characteristic for all of the investigated compounds that the nitro group in the phenyl fragment is primarily reduced, regardless of its orientation relative to the dihydropyridine ring, the reduction of the DHP ring itself is observed only for N-substituted p- and m-nitrophenyl derivatives Ia and Ib. It is characteristic for all of the N-unsubstituted derivatives Id-f that the primary anion radicals formed in the first step of electrochemical reduction deprotonate neutral molecules situated near them, which also undergo reduction at the nitro group but in the form of the 1,4-DHP anion. The peculiarity of the electrochemical reduction of o-nitrophenyl derivatives Ic and If consists in the fact that the products of the four-electron reduction of the nitro group undergo fast chemical transformations.

EXPERIMENTAL

The 1,4-DHP derivatives were synthesized by the methods described in [12].

The electrochemical reduction was carried out in anhydrous DMF [13] with tetrabutylammonium hexafluorophosphate (.01 M) as the inert electrolyte. The classical polarograms and cyclical volt-ampere curves were recorded by means of a PAR-170 electrochemical system (USA) using a three-electrode cell. The cathode was a dropping mercury electrode with forced detachment of the drop ($t = 0.5$ sec, $m = 0.90$ mg-sec^{-1}), the anode was a platinum wire, and the reference electrode was an aqueous saturated calomel electrode equipped with a transition bridge for work in nonaqueous solvents. A stationary mercury electrode or a graphite-glass electrode served as the cathode for recording the cyclical volt-ampere curves; the rate of cycle scanning was 0.2 V-sec^{-1}.

The free-radical particles were obtained by electrochemical generation (ECG) via a three-electrode scheme on the surface of a flat platinum electrode (the reference electrode was a silver wire) in a microcell placed in the resonator of an ER-9 spectrometer (Carl Zeiss—Jena) [14]. Samples were selected from the same cell for chromatographic analysis. A diphenylpicrylhydrazyl sample with $g = 2.00410$ was used to determine the g factors.

The mass spectra were recorded with an MS-50 spectrometer (AEI) at an ionizing energy of 70 eV. The samples were introduced directly into the source; the temperature of the ionization chamber was 200°C.

The UV spectra were recorded with a Unicam SP 1800 spectrophotometer; electrolysis was carried out in a quartz cuvette on a platinum-gauze cathode included in a three-electrode scheme (the reference electrode was a silver wire).

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ELECTROPHILIC TRANS QUATERNIZATION OF SUBSTITUTED 2-[2-CYCLOHEXEN-1-YLTHIO(SELENO)]PYRIDINES TO 4a, 10-a-cis-4,4a-trans-1,2,3,4,4a,10a-HEXAHYDROBENZOTHIAZOLO(SELENAZOLO)-[3,2-a]PYRIDINIUM SALTS

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UDC 547.828'821.3'789.6:541.634:543.422.25

It was established that the electrophilic quaternization of substituted 2-[2-cyclohexen-1-ylthio(seleno)]pyridines is a stereoselective process and proceeds as trans quaternization with the formation of 4a,10a-cis-4,4a-trans-1,2,3,4,4a,10a-hexahydrobenzothiazolo(selenazolo)[3,2-a]pyridinium salts.

The study of the mechanism and stereochemistry of electrophilic heterocyclization — quaternization — was associated with its extensive use as a general method in the synthesis of various heterocycles [1-6]. Thus, this reaction was used in the synthesis of annelated pyridinium salts. Imidazo-, oxazolo-, thiazolo-, and selenazolo[3,2-a]pyridinium salts, respectively, were obtained in the bromination or iodination of 2-N-, O-, S-, and Se-allylpyridines [7, 8]. However, the use of 2-N-, O-, S-, and Se-allylpyridines in electrophilic quaternization did not make it possible to form a judgment regarding the stereochemistry of this reaction and its mechanism. In order to develop stereochemical concepts of the investigated reaction we synthesized a number of substituted 2-[2-cyclohexen-1-ylthio(seleno)]pyridines, studied their reaction with various electrophilic reagents, and investigated the structures of the annelated pyridinium salts obtained.

Substituted 2(1H)-pyridinethiones and -selenones Ia-c [9, 10] and 3-bromo-1-cyclohexene (II) were convenient and accessible reagents for the synthesis of IIIa-c; the alkylation of pyridines Ia-c with 3-bromo-1-cyclohexene (II) in DMF in the presence of an equimolar amount of KOH proceeds regioselectively exclusively at the sulfur or selenium atom with the formation of 2-[2-cyclohexen-1-ylthio(seleno)]pyridines IIIa-c.

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