STUDY OF THE ELECTRICAL OXIDATION OF 2,6-DIMETHYL-3,5-DIETHOXYCARBONYL-1,4-DIHYDROPYRIDINES IN ACETONITRILE BY MEANS OF A ROTATING DISK ELECTRODE WITH A RING

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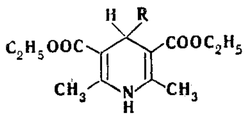
It is shown that the electrochemical oxidation of esters of 2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylic acids in anhydrous acetonitrile takes place as a one-electron process, while the final products of the transformations (pyridines or pyridinium salts) are formed as a result of disproportionation of the intermediate radicals. When 1-2% (by volume) water is added, the oxidation mechanism changes substantially, and the electrochemical process becomes a two-electron process.

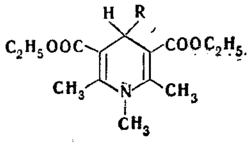
The potentials of the anode oxidation of alkyl esters of 1,4-dihydropyridine-3,5-dicarboxylic acids, which are determined by voltammetry, may serve as a quantitative characteristic of the ability of these compounds to undergo oxidation. The electrochemical oxidation potentials of numerous 1,4-dihydropyridine (1,4-DHP) derivatives on a platinum electrode in acetonitrile were established in [1-4], and the principles of the effect of substituents on the numerical values of the potentials were ascertained. However, the problem as to precisely which step of the electrical oxidation is characterized by the experimentally determined potentials, i.e., what the mechanism of the electrochemical oxidation of these compounds is, remains unsolved.

On the basis of an analysis of the volt—ampere curves, coulometric data, and preparative electrolysis, Volke and co-workers [5] concluded that the electrochemical oxidation of 1,4-DHP in 50% aqueous acetonitrile solution proceeds overall as a two-electron process with the formation of the corresponding pyridine derivatives; a one-electron pathway for the oxidation was established by these authors only in the case of 4,4-disubstituted 3,5-dicyano-1,4-DHP. In turn it was demonstrated [6] that under certain conditions the potential-determining step of the overall two-electron process is detachment of a proton, which evidently takes place as deprotonation of the cation radicals formed after detachment of the first electron from a molecule of the starting 1,4-DHP.

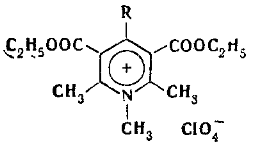
In the present research we attempted to establish the mechanism of the electrical oxidation of 1,4-DHP in acetonitrile by means of a rotating disk (platinum) electrode with a ring (see also [7]). The volt—ampere curves of electrical oxidation of 1,4-DHP derivatives of the I and II type were recorded on the disk. For comparison, the curves of electrical reduction of III, which are the proposed oxidized forms of II, were also recorded on a platinum electrode (they have already been determined on a mercury electrode [8]).



Ia-c



IIa-c



IIIa-c

I-III a $R=H$; b $R=CH_3$; c $R=C_6H_5$

Particular attention was directed to the curves recorded with a ring in order to experimentally establish (and thereby definitively prove) splitting out of hydrogen ions from

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TABLE 1. Parameters of the Electrochemical Transformations of I-III on a Rotating Platinum Disk Electrode with a Ring and Coefficients of Diffusion of I-III in Acetonitrile with 0.5 M Tetrabutylammonium Perchlorate As the Base Electrolyte at a Depolarizer Concentration of $5 \cdot 10^{-4}$ mole/liter

Compound	C, cm^2/sec, 10^{-5}	Oxidation on the disk			Reduction on the ring				
					first wave		second wave		
		$E_{1/2}$, V	i_{lim}, μA	n	$-E_{1/2}$	i_{lim}, μA	$-E_{1/2}$	i_{lim}, μA	n
Ia	1,54	0,54	125	1,1	0,60	60	—	—	
IIa	1,49	0,52	135	1,2	0,61	30	1,40	30	
Ib	1,50	0,71	110	1,0	0,62	60	—	—	
IIb	1,45	0,64	113	1,0	0,62	35	1,60	28	
Ic	1,35	0,80	126	1,2	0,61	60	—	—	
IIc	1,32	0,71	124	1,2	0,60	35	1,45	30	
IIIa	1,34						1,39	125	1,2
IIIb	1,32						1,60	125	1,2
IIIc	1,22						1,44	125	1,3

the 1,4-DHP molecules during their electrical oxidation (similar splitting out of hydrogen ions in the case of 9,10-dihydroacridine was demonstrated in [9]). The development of hydrogen ions in this process can be explained by electrochemical reaction via an ECE mechanism.

A distinct one-electron wave at 0.50-0.80 V was recorded during electrochemical oxidation of both N-unsubstituted (I) and N-methyl-1,4-DHP (II) on a disk.

Two waves, of which the first corresponds to reduction of hydrogen ions, while the second corresponds to reduction of the final oxidation product, i.e., a pyridinium system, were recorded for I and II on a ring. The latter is confirmed by the agreement between the $E_{1/2}$ values recorded for II and the $E_{1/2}$ values characteristic for the electrical reduction of the corresponding model compounds, viz., pyridinium salts III (Table 1). In the case of I the second wave is not distinctly expressed.

The wave of the reduction of H^+ ions recorded on the ring electrode as intermediate particles of the electrode oxidation of 1,4-dihydropyridines on a disk was identified by comparison of this wave with the wave of the electrochemical reduction of sulfuric acid used as an "external" proton donor. For this, under the same experimental conditions we recorded the curves of electrical reduction of standard solutions of chemically pure sulfuric acid solutions with various concentrations ($0.5 \cdot 10^{-4}$, $1 \cdot 10^{-4}$, and $2 \cdot 10^{-4}$ mole/liter) without added 1,4-DHP. A wave of reduction of hydrogen ions, which was also noted on the ring for all of the investigated solutions of I and II without added H_2SO_4 (Table 1), is observed during the recording of the volt—ampere curves of standard solutions at —0.4 to —0.6 V; the half-wave potentials of the standard and investigated solutions with the same depolarizer concentration were virtually the same.

It follows from a calculation of the number of electrons by means of the coefficients of diffusion of the I-III molecules (see the experimental section) that electrochemical oxidation in anhydrous acetonitrile is a one-electron process. However, the final product

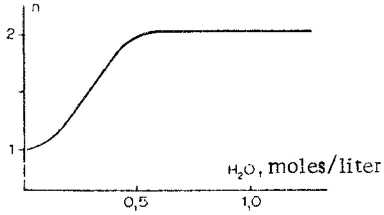
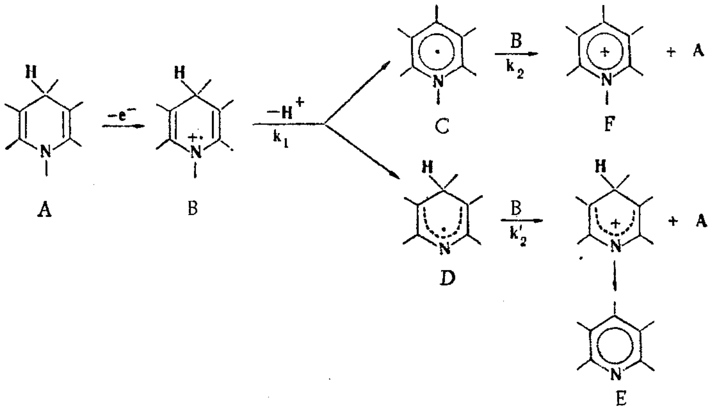


Fig. 1. Dependence of the number of electrons (n) on the molar concentration of water (moles/liter) for Ib (for a Ib concentration of $5 \cdot 10^{-4}$ mole/liter).

of electrical oxidation turns out to be the corresponding substituted pyridine (in the case of I) or the pyridinium cation (in the case of II), i.e., the product of two-electron oxidation. To explain this reaction pathway one should assume that the intermediately formed free radical undergoes disproportionation to the starting DHP (A) and a compound with a pyridine structure (E or F). The overall pathway of the reaction can consequently be represented by the scheme



The process begins with one-electron oxidation of 1,4-DHP (A) to the corresponding cation radical (B), which is recorded in the form of a one-electron oxidation wave. A proton is subsequently split out from the resulting cation radical with the formation of a neutral radical (C or D). The latter undergoes disproportionation to give starting A and free pyridine E or pyridinium cation F by reaction with, most likely, cation radical B. It should be assumed that the rate constant for splitting out of a proton from the cation radical (k_1) is considerably smaller than the rate constant for disproportionation of the neutral radical (k_2 or k'_2), and the electrochemical oxidation of the latter therefore cannot be recorded.

One cannot establish the site or primary detachment of a proton from compounds of the I type on the basis of the experimental data obtained in acetonitrile. It is known that nitrogen-unsubstituted 1,4-DHP is capable of splitting out of a proton from this atom [10]; in our opinion, this ability should be even more pronounced for the cation radicals. The data obtained are in agreement with the assumption that protons are detached in the cation-radical step that was expressed on the basis of the character of the dependence of $E_{1/2}$ on the pH of an aqueous acetonitrile buffer solution [6].

In the case of Ib we found by experiment a dependence of the number of electrons expended in the electrical oxidation of one DHP molecule on the amount of water added to the acetonitrile (Fig. 1). The water was added as a nucleophilic agent for tying up the protons split out from Ib during electrical oxidation. It was established that at a water concentration corresponding to 0.55 mole/liter or 1% (by volume) to the aqueous acetonitrile solution the electrochemical oxidation undergoes complete transformation from a one-electron process to a two-electron process,* which was also observed in [5]. In this case the electrochemical oxidation can be represented by the equation

$$A \xrightarrow[+H_2O]{-e^- \; -H_3O^+} C \text{ (or D)} \xrightarrow[+H_2O]{-e^- \; -H_3O^+} E$$

In this case the anode oxidation process is recorded in the form of a coalesced two-electron wave, the separation of which into two one-electron waves does not occur because of the close potentials of the two steps of electrical oxidation. In this case deprotonation of the cation radical is accelerated significantly under the influence of a nucleophilic reagent, viz., water, and the radical undergoes further oxidation instead of disproportionation.

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*Such a pronounced effect of the addition of even small amounts of water to the acetonitrile should especially be taken into account in the electrochemical oxidation of 1,4-DHP derivatives, since the number of electrons (n) may turn out to be some value other than unity in the case of an inadequate degree of purification of the reagents (acetonitrile and the inert salts).

EXPERIMENTAL

The investigation of the mechanism of the electrochemical oxidation of I-III was carried out by means of a rotating disk electrode with a ring (RDER) designed and manufactured in the Institute of Organic Synthesis of the Academy of Sciences of the Latvian SSR [1]. The apparatus was equipped with a dual potentiostat, which made it possible to maintain the potentials on the disk and ring electrodes (independently of one another) constant values [−4 to +4 V (with respect to the common reference electrode)] or change them in conformity with a linear law with an accuracy of ±10 mV. The rate of change of the potential can be established within the limits of 5 mV/sec to 50 V/sec. A rotating platinum electrode with a ring was fastened securely to the shaft of the motor. The rate of rotation of the electrode can be held constant at 300 to 13,000 rpm with an accuracy of ±2% or changed in conformity with a linear law within the indicated limits. The disk and ring were made of platinum and had active surface areas of 0.20 and 0.22 cm^2, respectively. The electrode characteristics were as follows: $r_1 = 2.52$ mm, $r_2 = 2.65$ mm, $r_3 = 3.90$ mm, and $r_4 = 5.85$ mm. The theoretical coefficient of efficiency (N) was 0.489. Prior to each filling of the electrochemical cell the active surface of the electrode was washed with acetonitrile and acetone and air dried. Prior to each recording of the volt–ampere curve the electrode was additionally cleaned with filter paper as it rotated. This cleaning is completely adequate for the current-recording sensitivities used, and the reproducibility of the recording is not less than ±1% on the disk and ±3% on the ring. The results described above were obtained at electrode rotation rates of 2000 rpm over a three-electrode circuit. A silver electrode was used as the reference electrode.

The specially designed electrochemical cell of the closed type had a working volume of 10 cm^3. During the experiments argon was blown continuously through the investigated solutions. All of the measurements were made at room temperature.

The electrochemical studies of I-III were carried out in anhydrous acetonitrile purified by the method in [12]. A 0.5 M (0.1 M in the case of a study of the effect of the addition of water as a proton acceptor) solution of tetrabutylammonium perchlorate prepared by the method in [13] was used as the base electrolyte. The water was added in concentrations of 0.1, 0.2, 0.5, 1, 5, 10, 20, 30, and 40% by volume. The depolarizer concentration in all cases was $5 \cdot 10^{-4}$ mole/liter.

The coefficients of diffusion of the investigated compounds were determined from pycnometric data from the Stokes–Einstein equation [14]. The number of electrons consumed by the molecule of the compound undergoing oxidation during electrochemical oxidation was calculated from the equation of the limiting diffusion current on a rotating disk electrode [15].

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STERIC EFFECTS IN THE RECYCLIZATION OF NITROPYRIDINIUM SALTS TO NITROANILINES

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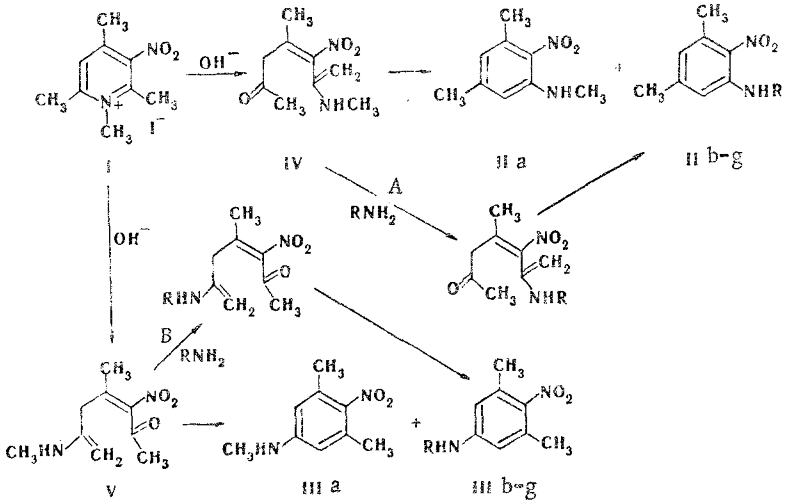
The effect of the degree of branching of alkyl groups attached to the amine nitrogen atom on the recyclization of 1,2,4,6-tetramethyl-3-nitropyridinium iodide to nitroanilines was studied.

1,2-Dimethylpyridinium salts that have a nitro group in the ring (type I) undergo recyclization to N-substituted nitroanilines under the influence of alkali or alkylamines [1]. If an alkylamine with a grouping that differs from that in the starting pyridinium salt is used, transamination to give the other N-alkylnitroaniline hypothetically takes place in the step involving the open intermediate [2]. Consequently, when two methyl groups are present in the α positions of the pyridine ring and with allowance for transamination, one might expect the formation of two pairs of isomeric nitroanilines (II and III) during the recyclization. It is known that acyclic enamino ketones tend to undergo transamination [3-6]; in our case one may therefore assume [1, 2] that the reaction proceeds through enamino ketones IV and V, which are formed by opening of the pyridine ring.



II, III a $R=CH_3$; b $R=n\text{-}C_3H_7$; c $R=n\text{-}C_4H_9$; d $R=n\text{-}C_{15}H_{31}$; e $R=i\text{-}C_4H_9$;

f $R=i\text{-}C_3H_7$; g $R=sec\text{-}C_4H_9$

1,2,4,6-Tetramethyl-3-nitropyridinium iodide (I) is a convenient model for a more detailed study of the transamination reaction. In this case the maximum yields (90%) of

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*Decreased.

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