ELECTROLYTIC OXIDATION OF 2,6-DIMETHYL-3,5-BIS(ETHOXYCARBONYL)-1,2-DIHYDROPYRIDINES IN ACETONITRILE ON PLATINUM ELECTRODES

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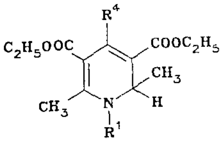
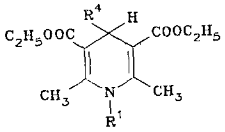
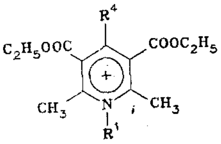
Free cation radicals, which subsequently undergo deprotonation to neutral radicals and disproportionation to give the starting molecules and pyridinium cations, are formed in the electrochemical oxidation of N-substituted 2,6-dimethyl-3,5-bis-(ethoxycarbonyl)-1,3-dihydropyridines on a rotating disk electrode with a ring in solution in acetonitrile. The primary cation radicals were identified by electrochemical generation in a cell placed in the resonator of an EPR spectrometer, and the hyperfine structures of the corresponding EPR spectra were studied.

The goal of this research was to ascertain the mechanism of the electrochemical oxidation of N-substituted 2,6-dimethyl-3,5-bis(ethoxycarbonyl)-1,2-dihydropyridines (I), which are isomers of the previously investigated [1] corresponding 1,4-dihydropyridines II. The electrochemical oxidation of dihydropyridines I and the properties of the resulting cation radicals were studied in an aprotic medium (acetonitrile) on platinum electrodes by means of a rotating ring—disk electrode (RRDE) and by cyclical voltammetry and EPR spectrometry.


Ia-i


IIa-d


IIIa-d

I—III a $R^1=CH_3$, $R^4=C_6H_5$; b $R^1=CH_3$, $R^4=4\text{-}CH_3C_6H_4$; c $R^1=R^4=C_6H_5$, d $R^1=4\text{-}CH_3C_6H_4$, $R^4=C_6H_5$; e $R^1=4\text{-}CH_3OC_6H_4$, $R^4=C_6H_5$; f $R^1=C_6H_5$, $R^4=4\text{-}O_2NC_6H_4$; g $R^1=CH_3$, $R^4=4\text{-}CH_3OC_6H_4$; h $R^1=CH_3$, $R^4=2\text{-}O_2NC_6H_4$; i $R^1=CH_3$, $R^4=4\text{-}O_2NC_6H_4$

One wave of oxidation of the starting compounds, the potentials of which range from +0.6 to +0.8 V, was recorded in potential—current (E—I) coordinates in the electrochemical oxidation of I on the disk electrode, and the following three reduction waves were recorded on the ring electrode: 1) the cathode branch of a mixed anode-cathode wave corresponding to reduction of the primary particles (cation radicals) formed in the electrolytic oxidation of compounds of the I series; 2) a wave of the reduction of the protons formed in the deprotonation of the cation radicals (with a half-wave potential of $\sim$−0.6 V); 3) a wave of reduction of the final product (at −1.3 to −1.5 V) (Fig. 1).

As in [1], the waves of the electrolytic reduction of the protons and final products of electrolytic oxidation on the ring electrode were identified, respectively, by recording, under the same experimental conditions, the curves of electrolytic reduction of solutions of sulfuric acid ($5 \cdot 10^{-5}$ mole/liter) and solutions of the corresponding model compounds III (cations with pyridinium structures), which are the hypothetical final products of the electrolytic oxidation of I and II. The final product was identified not only from the third wave of electrolytic reduction on the ring but also by comparison of the UV spectra of the solutions after prolonged electrolysis of I and II and solutions of the corresponding model compounds III.

To a first approximation, the character of the curves recorded in the electrolytic oxidation of I (Fig. 1) can be explained by the scheme:

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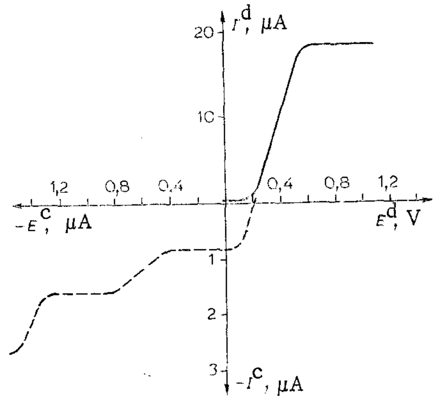


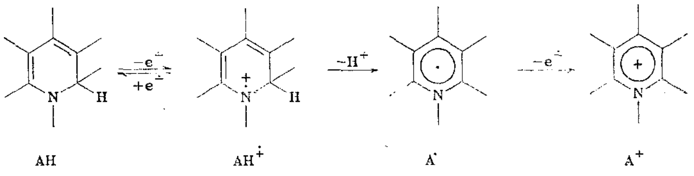
Fig. 1. Volt—ampere curves for the electrolytic oxidation of Ia on a disk electrode (continuous line) and the electrolytic reduction of the intermediate and final products of electrolytic oxidation on a ring electrode (dash line).

TABLE 1. Measured [with a rotating ring—disk electrode (RRDE)] Parameters of the Electrolytic Oxidation of 2,6-Dimethyl-3,5-bis-(ethoxycarbonyl)-1,3-dihydropyridines (I) on Platinum Electrodes in Acetonitrile (depolarizer concentrations $5 \cdot 10^{-4}$ mole/liter, solution temperature 20°C; potentials reduced relative to an $Ag/AgNO_3$ reference electrode)

Parameter	Ia	Ib	Ic	Id
$E_1/_2$ of the wave of electrolytic oxidation on the disk,[a] V	+0,40 (+0,66)	+0,37 (+0,65)	+0,52 (+0,77)	+0,51 (+0,70)
Ht. of the wave of electrolytic oxidation on the disk, μA	18,5	22,2	21,0	22,7
No. of electrons in the electrolytic oxidation	1,0	1,2	1,2	1,2
Ht. of the wave of reduction of the cation radicals on the ring, μA	1,05	0,52	0,3	0,14
$E_1/_2$ of the wave reduction of the final product on the ring,[b] V	−1,43 (−1,45)	−1,46 (−1,45)	−1,34 (−1,34)	−1,34 (−1,35)
Ht. of the wave of reduction of the final product on the ring, μA	0,38	0,55	1,20	1,40
Coefficient of diffusion · 10^5 cm²/sec	1,37	1,34	1,26	1,24

[a] The $E_{1/2}$ values of electrolytic oxidation of II are presented in parentheses for comparison.

[b] The $E_{1/2}$ values of electrolytic reduction of the corresponding III are presented in parentheses for comparison.



It follows from the $E_{1/2}$ potentials for electrolytic oxidation presented in Table 1 that 1,2-dihydropyridines are oxidized 200-300 mV more readily than the corresponding 1,4-dihydropyridines. This is in agreement with data on the relative stabilities of N-methyldihydropyridines (the 1,4 isomers are 2.3 kcal/mole more stable than the 1,2 isomers) [2], which is also understandable if it is assumed that detachment of the first electron in the electrolytic oxidation takes place from the unshared pair of electrons of the nitrogen atom, which in the case of II is included in a more conjugated system, whereas in the case of I it is the terminal atom in an open (relative to the 2 position) conjugated system.

The electrolytic oxidation of I in acetonitrile on a platinum electrode is a one-electron process (one one-electron wave is recorded on the disk electrode) and remains a one-

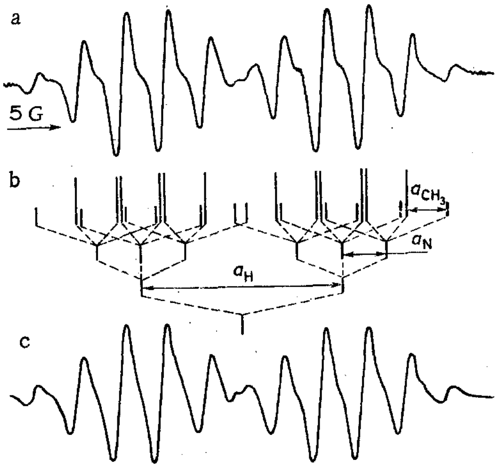


Fig. 2. EPR spectrum of electrochemically generated $AH^{+\cdot}$ cation radicals of Ia in acetonitrile at −35°C: a) experimental spectrum; b) its line reconstruction; c) simulated spectrum.

electron process over a wide range of concentrations (from $2\cdot10^{-5}$ to $1\cdot10^{-3}$ mole/liter) both in the presence of gaseous oxygen dissolved in the electrolysis medium and after removal of the dissolved oxygen. The one-electron character of the electrolytic oxidation is also retained in the presence of water (up to 5% by volume), but in this case the electrolytic oxidation is facilitated by 30-50 mV. For comparison one should, however, note that in the case of II over the indicated concentration range removal of the oxygen or the addition of water up to 1% gives rise to an increase in the height of the electrolytic oxidation wave up to values corresponding to the transfer of 1.5 electrons.

The apparent contradiction between the formation of a product of two-electron oxidation A^+ (detected on the ring) and the one-electron character of the wave of electrolytic oxidation of A on the disk (for I) is explained by disproportionation of the intermediate products of electrolytic oxidation (see below).

An anode—cathode wave is recorded in the electrolytic oxidation of I on the ring electrode even at room temperature (the cathode part corresponds to the reduction of the primary particles, viz., $AH^{+\cdot}$ cation radicals), which indicates the relative stability of the cation radicals (Fig. 1). The stability of $AH^{+\cdot}$ increases substantially when the temperature of the medium is lowered; this is manifested experimentally in an increase in the yield with respect to the current on the disk (Q) [3] for the wave of reduction of the cation radicals (in the case of Ia at −37°C and a rate of revolution of the electrode of 2000 rpm, Q = 94%).

The increase in the stability of the cation radicals at lower temperatures was used to realize the electrochemical generation (ECG) at $AH^{+\cdot}$ particles by carrying out the electrolytic oxidation of compounds of the I type in a cell placed in the resonator of an EPR spectrometer by the method described in [4]. It should be noted that the corresponding EPR signals were not observed in the course of ECG of free radicals of 1,4-dihydropyridines II even at low temperatures (up to −40°C). In contrast to II, we were able to record distinct EPR signals of free-radical particles in the case of the corresponding 1,2-dihydropyridines in the course of their electrochemical oxidation at the potentials of the plateau of the first wave. This difference alone in the behavior of I and II indicates that the recorded radicals do not have the structure of neutral pyridinyl radicals $A^\cdot$, since such radicals should also have been formed in the case of the electrolytic oxidation of 1,4-dihydropyridines, inasmuch as pyridinyl radicals from 1,4- and 1,2-dihydropyridines with identical substituents are not distinguishable.

The EPR spectrum recorded in the electrochemical oxidation of Ia (see Table 2) in acetonitrile at −35°C is presented in Fig. 2. The hyperfine structure (hfs) of this spectrum is due to coupling of the unpaired electron with the lone proton (a_H = 24.05 G), the nucleus of the nitrogen atom (a_N = 4.93 G), and three equivalent protons (a_H = 5.20 G). The latter are the protons of the R^1 substituent (methyl group) attached to the nitrogen atom,

TABLE 2. Constants of the Hyperfine Structure of the EPR Spectra of AH$^{+\cdot}$ Cation Radicals Formed in the Electrolytic Oxidation of I

Compound	Type of splitting	a, G			Generation potential,* V
		a_N	a_H	$a_{H,R}$	
Ia	$2_H \cdot 4_H \cdot 3_N$	4,93	24,05	5,20	1,0
Ib	$2_H \cdot 4_H \cdot 3_N$	5,46	24,46	5,46	1,3
Ic	$2_H \cdot 3_N$	4,80	26,40	—	1,2
Id	$2_H \cdot 3_N$	4,62	26,04	—	1,4
Ie	$2_H \cdot 3_N$	4,81	25,55	—	1,4
If	$2_H \cdot 3_N$	4,41	24,57	—	1,6
Ig	$2_H \cdot 4_H \cdot 3_N$	4,72	23,31	4,99	1,3
Ih	$2_H \cdot 4_H \cdot 3_N$	4,83	23,52	5,09	0,9
Ii	$2_H \cdot 4_H \cdot 3_N$	5,15	23,83	5,15	1,2

*Relative to a silver reference electrode.

since the EPR spectra of the cation radicals of 1,2-dihydropyridines Ic-f, which do not have a methyl group attached to the nitrogen atom (Table 2), do not contain quartet splitting. The absence of splitting also constitutes evidence that the unpaired electron does not couple with the protons of the methyl groups in the 2 and 6 positions of the dihydropyridine ring. Coupling of the unpaired electron with the nucleus of the nitrogen atom and the lone proton is observed for all of the radicals obtained (Table 2).

The appearance of a lone proton in the hfs of the EPR spectra also constitutes evidence that the recorded radicals are AH$^{+\cdot}$ cation radicals of 1,2-dihydropyridines. The values of the constant of doublet splitting due to this proton ($a_H \approx 25$ G) repudiate the possibility that the EPR spectrum is due to pyridinyl radical A$^\cdot$, i.e., a π radical that has an aromatic structure: Such a large proton splitting is characteristic for hyperfine coupling with a proton located outside of the plane of the π-electron system at an sp^3-hybridized carbon atom and is due to overlapping of the 1s orbital of the hydrogen atom with the 2pπ orbitals of the C$_{(3)}$ and N$_{(1)}$ atoms [5].

Considerable positive charge, which is formed not only because of detachment of one electron from the electron pair of the nitrogen atom in the course of oxidation of the starting molecule but also because of significant delocalization of the second electron, is concentrated on the nitrogen atom in the AH$^{+\cdot}$ cation radicals. In fact, it follows from the expression $a_N = 28.6\rho_N$ [6] that the density of the unpaired electron on the nitrogen atom (ρ_N) of the cation radicals obtained amounts to less than 1/5 of an electron, i.e., the resulting unpaired electron is delocalized to a significant extent over the π-electron system as a result of conjugation. The absence in the EPR spectra of an hfs constant due to R^6 = CH$_3$ constitutes evidence for the very low density of the unpaired electron at the C$_{(6)}$ atom ($\rho_{C-6} < 0.01$ of an electron). Evidently because of the higher overall electrophilicity of substituents R^3, R^4, and R^5 as compared with the nitrogen atom in the $1s^2 2\sigma^3 \pi^1$ electronic state, the unpaired π^1 electron is delocalized to the extent of 4/5 over the π-electron system at the ring C$_{(3)}$, C$_{(4)}$, and C$_{(5)}$ atoms. Evidence for this is provided not only by the deficit of the unpaired electron at the nitrogen atom but also by the significant width of the lines of the EPR spectra ($\Delta H \approx 1$ G), which is evidently due to a latent hfs from the protons of the R^3 and R^5 substituents. The cation radicals of 1,2-dihydropyridines that we obtained are unstable intermediates in the electrochemical oxidation of the starting compounds, the recording of which by EPR spectroscopy under the given conditions is possible only at low temperatures. As the temperature is increased, the intensity of the EPR signals decreases until the signals vanish completely at ~ -5°C.

As one of the most probable pathways for the destruction of the investigated AH$^{+\cdot}$ cation radicals one may postulate the formation from them of pyridinyl radicals A$^\cdot$, which, inasmuch as they are usually products of the one-electron reduction of the corresponding pyridinium salts, rapidly lose an unpaired electron at sufficiently high cathode potentials [7, p. 3] under electrochemical oxidation conditions. It should be noted that the stability of their precursors, viz., AH$^{+\cdot}$ cation radicals, is not determined by the properties of the resulting pyridinyl radicals A$^\cdot$, since the same A$^\cdot$ can be formed from cation radicals with different structures and, consequently, different stabilities, for example, from AH$^{+\cdot}$ of 1,2- and 1,4-dihydropyridines. Splitting out of a proton attached to C$_{(2)}$, which is responsible for transition of this atom from the $1s^2 2\sigma^4$ state to the $1s^2 2\sigma^3 \pi^1$ state and tran-

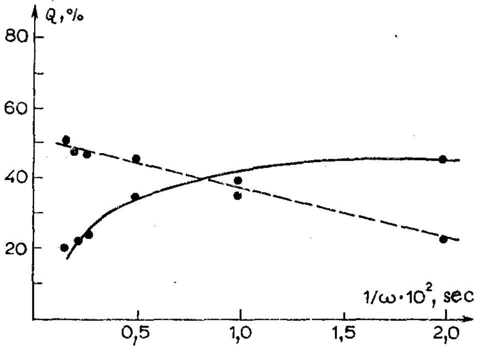


Fig. 3. Dependence of the yield with respect to the current on the disk (Q) on the reciprocal of the angular rate of revolution of the electrode (1/ω) for the wave of electrolytic reduction on the ring electrode of final product A^+ (continuous line) and cation radicals $AH^{+\cdot}$ (dash line) for Ia at a solution temperature of +20°C.

sition of the nitrogen atom from the $1s^22\sigma^3\pi^1$ state to the $1s^22\sigma^3\pi^2$ state, can be assumed as the rate-determining step in the disappearance of the cation radicals of, for example, 1,2-dihydropyridines. The fact that the cation radicals of dihydropyridines that do not have a hydrogen atom attached to a carbon atom in the $1s^22\sigma^4$ state in the ring, viz., 4,4'-disubstituted 3,5-dicyano-1,4-dihydropyridines, could not be recorded by EPR spectroscopy even at room temperature [8] constitutes indirect evidence for this. . It may be assumed that the different stabilities of the cation radicals of 1,2-dihydropyridines investigated in this research and the cation radicals of the corresponding 1,4-dihydropyridines (as indicated above, the latter could not be recorded by EPR spectroscopy) are due to different relative orientations of substituents R^3, R^4, and R^5, the nitrogen atom, and the carbon atom in the $1s^22\sigma^4$ state in the cation radicals of 1,2- and 1,4-dihydropyridines, which determine the competition between the nitrogen atom and the C–H bond for the electron pair.

In principle, dimerization is possible after deprotonation of the cation radicals [7, p. 34]. Disproportionation pathway $AH^{+\cdot} + A^{\cdot}$ is also likely, but the EPR data do not contain unambiguous information regarding this.

We proved deprotonation of $AH^{+\cdot}$ by means of a rotating ring–disk electrode (RRDE) by recording the wave of reduction of H^+ on the ring electrode (Fig. 1). It should be noted that we were unable to detect an $A^{\cdot}$ particle in electrochemical experiments in the electrolytic oxidation of I; this means that it is subsequently transformed at a high rate (i.e., its lifetime is shorter than the time of possible recording by the methods that we used, viz., the RRDE method and cyclical voltammetry).

The following fact established by the RRDE method is of great value for shedding some light on the problem of the mechanism of the electrolytic oxidation of 1,2-dihydropyridine derivatives: The yield with respect to the current on the disk (Q) for the wave of the electrolytic reduction of final product A^+ on the ring increases as the rate of revolution of the electrode is decreased (i.e., as the time during which the product of electrolytic oxidation on the disk reaches the ring electrode increases) and approaches a maximum value, viz., 50% (Fig. 3). This may mean that each particle of final product A^+ is obtained as a result of electrolytic oxidation on the disk electrode of two starting AH particles.*

The yield with respect to the current on the disk (Q) for the wave of the reduction of cation radicals $AH^{+\cdot}$ as the rate of revolution of the electrode is increased (from 500 to

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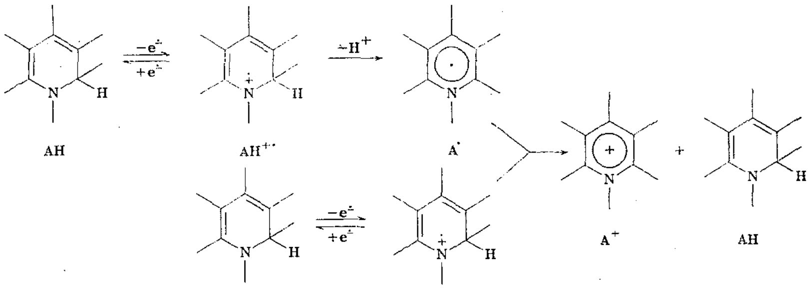
*The fact that a distinct wave, the height of which corresponds to a one-electron process ($n = 1.0 \pm 0.1$), is recorded in the electrolytic reduction of the corresponding model compounds III on the same ring indicates the absence in this case of adsorption phenomena (which could have been the reason for the lowering of the heights of the waves of reduction of A^+).

6000 rpm or ω from 52.4 to 628 sec^{-1}) is described by a straight line in Q and $1/\omega$ coordinates. The rectilinear character of this dependence constitutes evidence for disappearance of $AH^{+\cdot}$ in the course of a slow homogeneous reaction [3]. In our case this may be a process involving deprotonation of $AH^{+\cdot}$ in the volume of acetonitrile between the disk and the ring.

The experimental data presented above make it possible to propose a refined scheme for the electrolytic oxidation of 1,2-dihydropyridines:



The key step in the proposed mechanism is disproportionation, viz., chemical reaction between $A^\cdot$ radicals (which, as we mentioned above, have pronounced reactivity) and those $AH^{+\cdot}$ cation radicals that still did not have time to undergo deprotonation between the disk and the ring.

Thus we assume that the electrolytic oxidation of compounds of the I series on platinum electrodes in acetonitrile proceeds via an ECC mechanism the first step of which is assumed to be detachment of one electron from the starting AH molecule. In principle, according to the scheme presented above, when the rate of revolution of the electrode was decreased, the height of the wave of oxidation of the starting AH molecules should have approached a height corresponding to the transfer of 1.5 electrons (in the case of realization of two cycles) if the newly formed AH still had time to undergo oxidation on the disk electrode, as in the electrolytic oxidation of 1,4-dihydropyridines II (see also [8]). In fact, the height of this wave increases by only 10-20% above the one-electron level. The latter indicates that the cation radicals of I are probably deprotonated more slowly on the surface of the electrode than in the solution (and, consequently, A^+ + AH are formed more slowly). Data from cyclical voltammetry also provide evidence for this — the anode (i_a) and cathode (i_c) peaks of the reversible electrolytic oxidation on a stationary electrode reach the same height at those rates of potential scanning for which the time interval from i_a to i_c is four or more times greater than the time of transit of the particles from the disk to the ring electrode in experiments by the RRDE method (this time is 0.066 sec at the lowest experimental rate of revolution of the electrode of 500 rpm). According to our preliminary calculations, the lifetime of cation radicals $AH^{+\cdot}$ (from experimental data from the RRDE method) of I in the volume of acetonitrile at room temperature is relatively short — it ranges from 2 msec to 0.1 sec. For this reason, cation radicals could be detected and studied by EPR spectroscopy only at substantially lower temperatures.

The shielding coefficients S, which are less than unity (0.65-0.8) for Ia-d investigated by the RRDE method at a rate of revolution of the electrode of 2000 rpm [3], also constitute evidence in favor of the above-indicated assumption that cations A^+ and particles identical to the starting AH are formed as a result of the electrolytic oxidation of I. This shows that particles that are oxidized at the same potentials as the starting compounds (in our case starting AH is newly formed) are formed as a result of a homogeneous reaction (and reach the ring electrode). As the rate of revolution of the electrode is decreased, coefficient S increases for the reason set forth above — in this case the newly formed AH still have time to undergo partial oxidation in the zone of the disk electrode.

EXPERIMENTAL

The electrochemical investigations with the aid of the RRDE method and cylical voltammetry were carried out with an apparatus designed and prepared in the Institute of Organic Synthesis of the Academy of Sciences of the Latvian SSR [9]. The disk and the ring of the electrode were prepared from platinum and had active surface areas of 0.0314 and 0.0177 cm^2, respectively [10]. The coefficient of efficiency of the electrode (N = 0.12) was found from the ratios of the currents of the ring and disk electrodes in two experiments: in the oxidation of p-phenylenediamine and in the reduction of tetracyanoquinodimethane (both reactions were reversible). Prior to each recording, the electrode was polished successively with water-resistant abrasive paper and filter paper and washed with acetone and acetonitrile. All of the potentials were measured relative to an $Ag/AgNO_3$ reference electrode (in acetonitrile). The depolarizer concentration in all cases was $5 \cdot 10^{-4}$ mole/liter, and a solution (0.1 mole/liter) of tetrabutylammonium perchlorate prepared by the method in [11] was used as the inert electrolyte. The coefficient of diffusion of Ia in acetonitrile was calculated from the Stokes—Einstein equation from the pycnometrically measured density of the substance and was found to be $1.37 \cdot 10^{-5}$ cm²/sec. The coefficients of diffusion of the remaining compounds were calculated from the D value for Ia on the basis of the assumption that they are inversely proportional to the corresponding molecular masses of the compounds raised to the $^1/_2$ power. The number of electrons consumed in the oxidation of one molecule of the starting compound was calculated from the equation of the diffusion current on a rotating disk electrode [12]. The UV absorption spectra were recorded with a Pye—Unicam SP-1800 automatic spectrometer.

Investigations by EPR spectroscopy were carried out with an ER-9 spectrometer by electrochemical generation (ECG) of free radicals on a platinum foil electrode in an electrochemical cell placed in the resonator of the spectrometer. The concentration of the solutions of the starting compounds in acetonitrile was $5 \cdot 10^{-3}$ mole/liter; $(C_4H_9)_4NPF_6$ (10^{-1} mole/liter) served as the inert salt. The anode potentials were measured relative to a reference electrode, viz., silver wire. In selecting the anode potential of ECG we took into account the fact that the potential of this reference electrode is 500 mV more positive than that of the $Ag/AgNO_3$ reference electrode (in acetonitrile). The magnetic field sweep rate was 0.04 G/sec, the recording time constant was 0.45 sec, and the degree of high-frequency modulation (100 kHz) of the magnetic field was 0.05-0.15 G. The construction of the theoretical EPR spectra was accomplished by means of an NR 2116S computer linked with the EPR spectrum by an "on-line" system with the aid of the appropriate program [13] adapted to the given system.

The measurements at reduced temperatures by both the RRDE method and in the case of EPR spectroscopy were made in special cells by means of ventilating the latter with a thermostatted stream of nitrogen. The temperature was measured directly in the investigated solution with an accuracy of ±1°C.

1,2-Dihydropyridine derivatives I were obtained by reduction of the corresponding pyridinium salts III with sodium borohydride by the method in [14]. The physicochemical characteristics of the newly synthesized compounds are presented below.

1-(4-Methoxyphenyl)-2,6-dimethyl-4-phenyl-3,5-bis(ethoxycarbonyl)-1,2-dihydropyridine (Ie). This compound had mp 85-87°C (from methanol). PMR spectrum ($CDCl_3$): 0.66 (t, 3H) and 3.66 (q, 2H, $3\text{-}OCH_2CH_3$); 0.82 (t, 3H) and 3.83 (q, 2H, $5\text{-}OCH_2CH_3$); 1.46 (d, 3H, J = 6.5 Hz, $2\text{-}CH_3$); 2.22 (s, 3H, $6\text{-}CH_3$); 3.83 (s, 3H, OCH_3); 4.81 (q, 1H, J = 6.5 Hz, 2-H); 6.90 and 7.20 (d, 2H each, C_6H_4); 7.27 ppm (s, 5H, Ph). UV spectrum (ethanol), λ_{max} (log ε): 203 (4.47), 216 (4.35) (shoulder), 280 (4.36), and 386 nm (3.97).

1,2,6-Trimethyl-4-(2-nitrophenyl)-3,5-bis(ethoxycarbonyl)-1,2-dihydropyridine (Ih). This compound had mp 117-118°C (from methanol). PMR spectrum ($CDCl_3$): 0.63 (t, 3H) and 3.58 (q, 2H, $3\text{-}OCH_2CH_3$); 0.74 (t, 3H) and 3.70 (q, 2H, $5\text{-}OCH_2CH_3$); 1.17 (d, 3H, J = 6.6 Hz, $2\text{-}CH_3$); 2.38 (s, 3H, $6\text{-}CH_3$); 3.28 (s, 3H, $1\text{-}CH_3$); 4.55 (q, 1H, J = 6.6 Hz, 2-H); 6.82-7.06 (m, 1H), 7.14-7.47 (m, 2H), and 7.83-8.06 ppm (m, 1H) (C_6H_4 protons). UV spectrum (ethanol), λ_{max} (log ε): 206 (4.37), 222 (4.33) (shoulder), 292 (4.25), and 378 nm (3.90).

1-Phenyl-2,6-dimethyl-4-(4-nitrophenyl)-3,5-bis(ethoxycarbonyl)-1,2-dihydropyridine (Id). This compound had mp 108-110°C (from methanol). PMR spectrum ($CDCl_3$): 0.67 (t, 3H) and 3.64 (q, 2H, $3\text{-}OCH_2CH_3$); 0.81 (t, 3H) and 3.80 (q, 2H, $5\text{-}OCH_2CH_3$); 1.42 (d, 3H, J = 6.5 Hz, $2\text{-}CH_3$); 2.21 (s, 3H, $6\text{-}CH_3$); 4.88 (q, 1H, J = 6.5 Hz, 2-H); 7.10-7.42 (m, 7H) and 8.10 ppm (d, 2H, aromatic protons). UV spectra (ethanol), λ_{max} (log ε): 204 (4.48), 281 (4.40), 344 (4.01), and 378 nm (3.93) (shoulder).

1,2,6-Trimethyl-4-(2-nitrophenyl)-3,5-bis(ethoxycarbonyl)-1,4-dihydropyridine (IIh). This compound had mp 144-145°C (from ethanol). PMR spectrum ($CDCl_3$): 1.17 (t, 6H) and 3.87-4.27 (m, 4H, 3- and $5\text{-}OCH_2CH_3$); 2.38 (s, 6H, 2- and $6\text{-}CH_3$); 3.19 (s, 3H, $1\text{-}CH_3$), 5.71 (s, 1H, 4-H); 7.02-7.66 ppm (m, 4H, C_6H_4).

1-(4-Methoxyphenyl)-2,6-dimethyl-4-phenyl-3,5-bis(ethoxycarbonyl)pyridinium Perchlorate (IIIe). This compound had mp 235-237°C (from isopropyl alcohol). PMR spectrum (d_6-DMSO): 0.89 (t, 6H) and 4.07 (q, 4H, 3- and $5\text{-}OCH_2CH_3$); 2.29 (s, 6H, 2- and $6\text{-}CH_3$); 3.90 (s, 3H, OCH_3); 7.21-7.42 (m, 4H) and 7.53-7.69 ppm (m, 5H, aromatic protons).

1,2,6-Trimethyl-4-(2-nitrophenyl)-3,5-bis(ethoxycarbonyl)pyridinium Perchlorate (IIIh). This compound had mp 158-159°C (from isopropyl alcohol). PMR spectrum (d_6-DMSO): 0.75 (t, 6H) and 3.90 (q, 4H, 3- and 5-OCH_2CH_3); 2.78 (s, 6H, 2- and 6-CH_3); 4.09 (s, 3H, 1-CH_3), 7.08-7.29 (m, 1H), 7.63-7.86 (m, 2H), and 8.13-8.35 ppm (m, 1H, C_6H_4).

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SYNTHESIS OF 5-HYDROXY- AND 5-ACYLHYDRAZINOPYRAZOLIDINES BY THE REACTION OF β-SUBSTITUTED HYDRAZIDES WITH α,β-UNSATURATED ALDEHYDES AND THEIR BIOLOGICAL ACTIVITY

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The reaction of β-substituted hydrazides with alkenals (acrolein, methacrolein, crotonaldehyde, and cinnamaldehyde) serves as a method for the synthesis of the corresponding 1-acyl-5-hydroxypyrazolidines and, in a number of cases, 1-acyl-5-acylhydrazinopyrazolidines. Some of the 1-acyl-5-hydroxypyrazolidines obtained have antiphlogistic activity.

It is known [1, 2] that 1,2-dimethyl- and 1-methyl-2-phenylhydrazines usually form 3-pyrazolines upon reaction with α,β-unsaturated carbonyl compounds. In individual cases Jacquier and co-workers [3, 4] have observed the formation of hydroxypyrazolidines — cyclic semihydrazinals.

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