ANODE VOLT—AMPEROMETRY OF AMINOPYRIDINES AND AMINOPICOLINES

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The electrochemical behavior of amino derivatives of pyridine — 2-, 3-, and 4-aminopyridines, 2-amino-3-methylpyridine, 2-amino-4-methylpyridine, 4-amino-3-methylpyridine, and 2,6-diaminopyridine — during their oxidation on a rotating platinum microanode in acetonitrile and aqueous alcohol was investigated. Differences associated with the electronic effect of the substituent were uncovered during the electrical oxidation of the indicated compounds. The data obtained make it possible to conclude that the magnitude of the current strength in the oxidation of aminopyridines is determined by the rate of diffusion of the depolarizer to the electrode.

Numerous studies [1-9] have been devoted to the electrochemical oxidation of heterocyclic nitrogen-containing compounds. However, no data pertaining to aminopyridines and aminopicolines are available. The study of these compounds by means of anode voltamperometry is of considerable interest, since the establishment of the specific values of the electrical oxidation (EO) potentials provides a possibility for making a comparative evaluation of the reactivities of derivatives of the heterocyclic series; this cannot always be done by other methods when there are several substituents. In addition, electrochemical oxidation can be used for modeling the individual redox steps of biochemical processes. Amines of the pyridine series often serve as substrates, inhibitors, and components of enzyme systems and their synthetic analogs [10].

The present research includes a study of the oxidation of pyridine, 2-, 3-, and 4-aminopyridine, 2-amino-4-, 2-amino-3-, and 4-amino-3-methylpyridine, and 2,6-diaminopyridine on a rotating platinum microelectrode.

It should be noted that distinct volt—ampere curves are obtained for all the investigated compounds (except pyridine). The curves are poorly expressed in the case of pyridine, since the oxidation wave of pyridine is found at potentials >1.8 V and is overlapped by discharge of the base electrolyte.

It is apparent from Table 1 that aminopyridines and aminopicolines are oxidized at potentials ranging from +0.70 to 1.30 V, whereas pyridine is oxidized when $E_{1/2} \sim +1.82$ V. 3-Aminopyridine is oxidized more readily than 2- and 4-aminopyridines; the latter undergo electrochemical oxidation almost identically. For 2-aminopyridine as compared with 3-aminopyridine, $\Delta E_{1/2}$ is 160 mV, as compared with 180 mV for 4-aminopyridine.

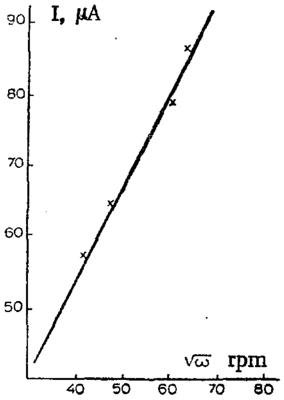

Fig. 1. Effect of the rate of rotation (ω) of the platinum electrode on the current strength (i) in the study of $4 \cdot 10^{-4}$ M solution of 2,6-diaminopyridine.

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TABLE 1. Peak Potentials (E_p), Half-Wave Potentials ($E_{1/2}$), and Limiting Currents (i) of Aminopyridines and Aminopicolines in Acetonitrile with a 1 M $LiClO_4$ Base Electrolyte

Compound No.	Compound	$E_{1/2}$, V	$E_{p \cdot ox}$, V	ΔE*, mV	$E_{1/2}$†, V	i, μA
1	2-Aminopyridine	1,22	1,24	610	1,06	2.2
2	3-Aminopyridine	1,06	1,08	770	0,88	1,9
3	4-Aminopyridine	1,24	1,26	590	1,07	2.1
4	2-Amino-3-methylpyridine	1,19	1,21	—	1,03	2,3
5	2-Amino-4-methylpyridine	1,20	1,22	—	1,04	2,0
6	4-Amino-3-methylpyridine	1,22	1,24	—	1,02	2,4
7	2,,6-Diaminopyridine	0,75	0,75	1100	0,65	4,2
8	Pyridine	1,82‡	1,85	—	—	
9	p-Phenylenediamine [16]	0,18	—	—	—	

*ΔE = E_p of pyridine — E_p of the corresponding aminopyridine; i (in microamperes) is the limiting diffusion current in a 1 M $LiClO_4$ base electrolyte.

†The base electrolyte was a 0.1 M solution of $(CH_3)_4NClO_4$ in 96% ethanol.

‡Indistinct wave.

It must be noted that, in addition to the indicated distinct waves on the EO polarograms of aminopyridines, subsequent indistinct waves at 1.5-1.7 V, which correspond to a greater degree of oxidation, were observed. The presence of another amino group gives rise to a further shift of the potential of the peak to less positive values ($E_{1/2}$ = 0.75 V). It should be noted that only one wave and one peak corresponding to it were observed on the polarograms pertaining to the EO of 2,6-diaminopyridine. Since the height of this wave (i = 4.2 μA) is almost twice the height of the wave for monosubstituted 2-aminopyridine (i = 2.2 μA), it may be assumed that this wave reflects the overall electrical oxidation of both amino groups.

A rough calculation of the number of electrons (n) from the equation of the limiting current on a rotating disk electrode [13, 14] for monoaminopyridines showed that n = 2.

All of the investigated compounds have electron-donor properties in aqueous alcohol media (in a 0.1 M solution of tetramethylammonium chloride in 96% ethanol), and their potentials in these media are less positive (by 100-200 mV) than in acetonitrile; this is evidently explained by the different acid—base properties of the solvents used.*

An important characteristic for the study of the mechanism of the electrochemical oxidation is the nature of the limiting current. The results obtained in this research show that a directly proportional dependence between the limiting current and the concentration of the corresponding aminopyridine is observed at $1 \cdot 10^{-4}$ M to $1.2 \cdot 10^{-3}$ M. We established that a linear dependence of the current strength (i) on the square root of the angular rate of rotation is observed over the investigated range of rates of rotation of the electrode (800-4000 rpm) (Fig. 1). We also experimentally determined that a slight increase in the limiting current as the temperature is raised is characteristic for all of the investigated aminopyridines. The temperature coefficient for the investigated compounds ranges from 1.5 to 2.0% per degree Centigrade. This can evidently be explained by the temperature changes in the diffusion coefficient [15]. All of the data listed above make it possible to conclude that the magnitude of the current strength in the oxidation of aminopyridines is determined by the rate of diffusion of the depolarizer to the electrode. Primarily the amino groups are involved in the electrical oxidation of the investigated pyridine derivatives. This is confirmed by the twofold increase in the height of the wave when a second amino group is introduced and also by the greater ease of EO of 3-aminopyrimidine as compared with the EO of 2- and 4-aminopyrimidines; this is probably explained by the presence of a conjugation effect for 2- and 4-aminopyridines and the absence of a conjugation effect for 3-aminopyridine.

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*Although the dielectric constant (ε) of acetonitrile (37.45) exceeds ε of ethanol (24.3), the aqueous alcohol medium has a considerably higher ε value, since the dielectric constant of water is 83.

Similar relationships between the structure and the polarographic characteristics ($E_{1/2}$ of the anode waves) are displayed by aromatic amines [12].*

EXPERIMENTAL

The research was carried out with an LP-7 recording polarograph. The volt–ampere curves were recorded under integral (with a sensitivity of 1/10) and differential (with a sensitivity of unity) recording conditions. A rotating platinum microdisk anode (d = 1.2 mm, angular rate of rotation 800-5000 rpm) was used as the indicator electrode. The polarization rates were 200 and 400 mV/min. The comparison electrode (cathode) was an external saturated calomel electrode. To obtain reproducible results the polarizable Pt microanode was washed after each experiment with distilled water, cleaned with fine emery paper (000), and washed again with distilled water prior to recording of the curves. The electrode was dried successively with filter paper and "Fen."

A 1 M solution of $LiClO_4$ in acetonitrile (base electrolyte I) and a 0.1 M solution of $(CH_3)_4NClO_4$ in 96% C_2H_5OH (base electrolyte II) were used as the base electrolytes. The acetonitrile was purified by the method in [10] and monitored polarographically for the absence of oxidation waves in the positive region of polarization of the platinum electrode.

The cell was thermostated at 25 ± 0.2°C.

The investigated aminopyridines were used either in the form of the commercial compounds after appropriate purification or were synthesized by known methods [16, 12].

Prior to preparation of the base electrolyte the $LiClO_4$ was dried at 200°C for 10 h. The $(CH_3)_4NClO_4$ was dried in vacuo at 50°C for 12 h. The experimentally found E_p and $E_{1/2}$ values were measured relative to a saturated calomel electrode with an accuracy of ±20–40 mV.

All of the above-listed amino derivatives were studied at a depolarizer concentration of $4 \cdot 10^{-4}$ M with the same platinum electrode and constant electrode parameters. Acetonitrile or $LiClO_4$ in acetonitrile or 0.1 M $(CH_3)_4NClO_4$ in C_2H_5OH was introduced into the cell as argon was blown through it continuously, after which the substance under investigation was added. The oxygen was then removed from the solution by blowing in dry argon (for 10 min), which had previously been saturated with acetonitrile vapors. Dry argon saturated with acetonitrile vapors was blown in continuously through the cell above the solution during recording of the polarograms. The diffusion coefficients were calculated from the Stokes–Einstein equation [17].

LITERATURE CITED

1. W. Bladel and R. H. Haar, Anal. Chem., 42, 918 (1970).
2. Ya. P. Stradyn', G. Ya. Dubur, Yu. I. Beilis, Ya. R. Uldrikis, and A. F. Korotkova, Khim. Geterotsikl. Soedin., No. 1, 84 (1972).
3. Ya. P. Stradyn', Yu. I. Beilis, Ya. R. Uldrikis, G. Ya. Dubur, A. E. Sausin', and B. S. Chekavichus, Khim. Geterotsikl. Soedin., No. 12, 1525 (1975).
4. Ya. P. Stradyn', G. Ya. Dubur, Yu. I. Beilis, Ya. R. Uldrikis, A. E. Sausin', and B. S. Chekavichus, Khim. Geterotsikl. Soedin., No. 12, 1530 (1975).
5. Yu. I. Beilis, L. F. Korotkova, A. F. Shikarev, and M. I. Rutkevich, Novel Features in the Electrochemistry of Organic Compounds [in Russian], Kazan (1970), p. 15.
6. Yu. I. Vainshtein, I. N. Palant, L. N. Yakhontov, D. M. Krasnokut-skaya, and M. V Rubtsov, Khim. Geterotsikl. Soedin., No. 8, 1106 (1969).
7. Yu. I. Beilis, O. N. Chupakhin, V. L. Rusinov, and V. D. Bezuglyi, Zh. Obshch. Khim., 65, 606 (1975).
8. K. K. Barnes, Electrochemical Reactions in Nonaqueous Systems (ed. by C. K. Mann), Marcel Dekker (1970).
9. A. P. Tomilov, S. G. Mairanovskii, M. Ya. Fioshin, and V. A. Smirnov, Electrochemistry of Organic Compounds [in Russian], Khimiya, Moscow (1968), pp. 362, 363.
10. G. K. Skryabin and L. A. Golovleva, Utilization of Microorganisms in Organic Synthesis [in Russian], Nauka, Moscow (1976), pp. 41, 264.
11. A. R. Katritzky (editor), Physical Methods in the Chemistry of Heterocyclic Compounds, Academic Press (1963).

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*Unfortunately, a rigorous comparative analysis is impossible because of the absence in the literature of data obtained under identical conditions.

12. S. G. Mairanovskii, Ya. P. Stradyn', and V. D. Bezuglyi, Polarography in Organic Chemistry [in Russian], Khimiya, Moscow (1975), p. 225.
13. Electrochemistry of Organic Compounds [in Russian], Mir, Moscow (1976).
14. Yu. V. Pleskov and V. Yu. Filinovskii, The Rotating Disk Electrode [in Russian], Nauka, Moscow (1972), p. 41.
15. I. P. Wibaut, S. Herzberg, and I. Schlatmen, Rec. Trav. Chim., 73, 140 (1954).
16. Yu. I. Chumakov, Pyridine Bases [in Russian], Kiev (1965), p. 94.
17. Ya. P. Stradyn', The Polarography of Organic Nitro Compounds [in Russian], Riga (1961), p. 12.

STEREOCHEMISTRY OF THE SYNTHESIS OF 1,2,3,4-TETRAHYDROCINNOLINES FROM ARYLDIAZENIUM SALTS AND OLEFINS

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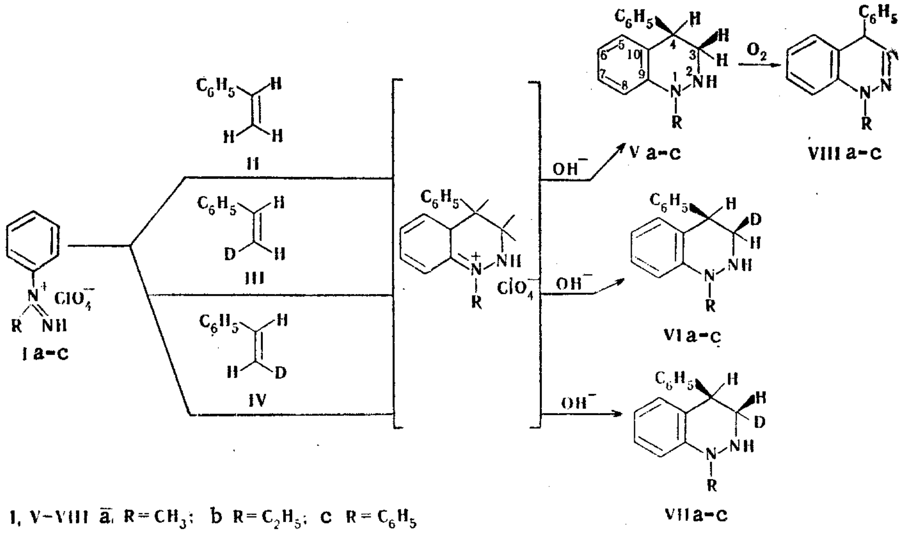
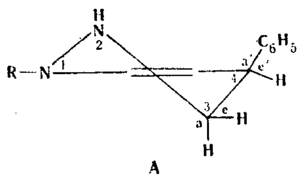
It follows from the PMR spectra that the reaction of 1-methyl-, 1-phenyl-, 1-ethyl-, 1-phenyl-, and 1,1-diphenyldiazenium salts with cis- and trans-d-styrenes, which leads to the corresponding 3-d-4-phenyl-1,2,3,4-tetrahydrocinnolines, takes place with retention of the configuration in the starting styrenes. It is therefore proposed that this reaction be regarded as a special case of $[4^+\pi_s + 2\pi_s]$-cycloaddition.

A new and promising method for the synthesis of cinnoline derivatives was recently proposed [1, 2]; this method consists in the reaction of nucleophilic alkenes with diazenium salts. An unconfirmed mechanism with the participation of intermediate ionic particles in which the (1-C)—(9-C) and (4-C)—(10-C) bonds are formed separately and the reaction is consequently nonstereospecific, was adopted for this transformation [2]. However, this trans-



I, V-VIII a $R=CH_3$; b $R=C_2H_5$; c $R=C_6H_5$



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