POLAROGRAPHIC OXIDATION OF SOME 5,10-DIHYDROPHENAZINE DERIVATIVES

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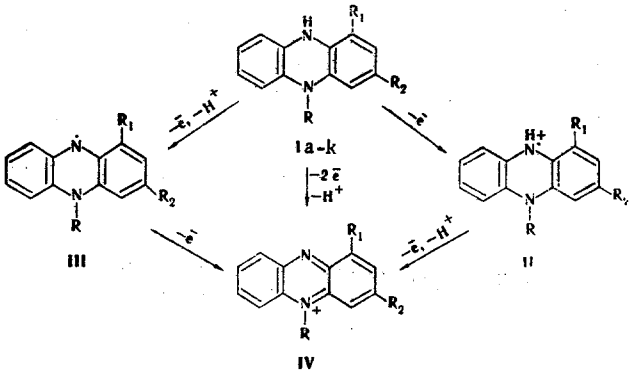
The polarographic anode oxidation of 5-substituted dihydrophenazines in an aprotic medium and an aqueous acetone solution has one-electron or two-electron character. It was shown by means of the electronic and ESR spectra that the intermediates in the anode oxidation of dihydrophenazine and 5-methyldihydrophenazine are cation radicals and that the products of one-electron oxidation of 1,3-dinitro-5-aryl-substituted dihydrophenazines are phenazyl radicals. The final products of anode oxidation are phenazinium salts.

The behavior of phenazine and its derivatives under polarographic reduction conditions has been studied in detail [1-4]. Except for the data in [5], there is no information available regarding similar studies of dihydrophenazines. In a continuation of our study of the structure of 5,10-dihydrophenazine derivatives [6] we investigated the polarographic oxidation of Ia-k.

The polarograms of the investigated compounds are in the form of one-step S-shaped curves (Fig. 1), except for the two-step polarograms for unsubstituted dihydrophenazine (Ia) and 5-methyldihydrophenazine (Ib). All of the polarographic waves obtained have diffusion process on a rotating electrode [7].

The pathways of anode polarographic oxidation of 5-substituted dihydrophenazines can be hypothetically represented by the following scheme:



I a $R=R_1=R_2=H$; b $R=CH_3$, $R_1=R_2=H$; c $R=COC_6H_5$, $R_1=R_2=H$; d $R=CO\text{-}(4\text{-}NO_2C_6H_4)$, $R_1=R_2=H$; e $R=COCH_3$, $R_1=R_2=H$; f $R=Ph$, $R_1=H$, $R_2=NO_2$; g $R=n\text{-}Bu$, $R_1=R_2=NO_2$; h $R=4\text{-}CH_3C_6H_4$, $R_1=R_2=NO_2$; i $R=C_6H_5$, $R_1=R_2=NO_2$; j $R=2,4\text{-}(NO_2)_2C_6H_3$, $R_1=R_2=NO_2$; k $R=2,4,6\text{-}(NO_2)_3C_6H_2$, $R_1=R_2=NO_2$

To determine the number of electrons participating in the electrochemical oxidation we treated the polarographic curves by means of the Nernst equation for a reversible anode wave [7]. It was observed that both waves of 5,10-dihydrophenazine and 5-methyldihydrophenazine obey this equation and correspond to two one-electron oxidation steps.

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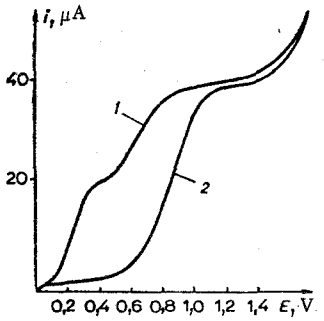

Fig. 1

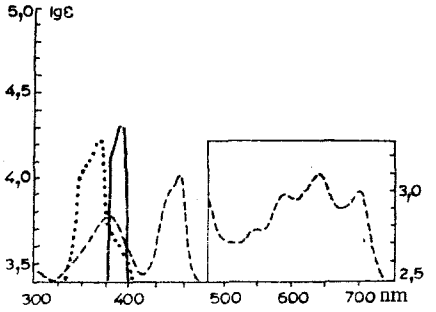

Fig. 2

Fig. 1. Polarograms of anode oxidation: 1) dihydrophenazine (Ia), 5-methyldihydrophenazine (Ib); 2) the remaining 5,10-dihydrophenazine derivatives (Ic-k).

Fig. 2. Electronic absorption spectra (alcohol): The dotted line represents phenazine; the solid line, phenazine methylsulfate; the broken lines, phenazine cation radical.

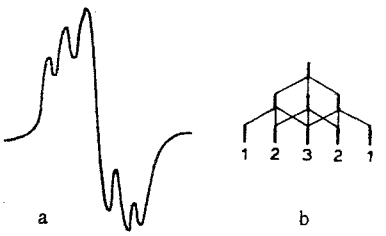

Fig. 3. ESR spectra: a) phenazyl radical (III); b) theoretical spectrum [16].

TABLE 1. Potentials of Anode Oxidation of 5,10-Dihydrophenazine Derivatives

Compound I	$E_{1/2}$, V
a	0,20; 0,52
b	0,25; 0,58
c	0,76
d	0,78
e	0,80
f	0,62
g	0,76
h	0,77
i	0,79
j	0,88
k	0,97

TABLE 2. Oxidation Potentials ($E_{1/2}$) and Number of Electrons (n) for Ii as a Function of the pH of the Medium

pH	1,55	3,10	5,65	6,8	8,0	12,0
$E_{1/2}$, V	0,605	0,575	0,580	0,710	0,555	0,565
n	2,38	2,60	2,30	0,96	1,34	1,03

Preparative electrolysis of a solution of dihydrophenazine Ia at the potential of the first polarographic waves gave a product whose electronic (Fig. 2) and ESR spectra correspond to the phenazine cation radical (IIa) [8, 9]. The electronic spectrum of the final oxidation product coincided completely with the spectrum of phenazine [10, 11] (Fig. 2).

The product of electrolysis of a solution of 5-methyldihydrophenazine Ib at the potential of the first polarographic wave displayed the ESR signal characteristic for the cation radical of 5-substituted phenazine (IIb)

[12]. The final oxidation product was found to be the 5-methylphenazinium salt (IVb), which was identified from its electronic spectrum [9] (Fig. 2).

However, it was found to be impossible to determine the number of electrons by means of the Nernst equation for the one-step polarographic curves. The simultaneous solution of the Levich equation for a rotating electrode and the equation of the diffusion process on a stationary electrode [13] was therefore used for this purpose in the case of the remaining 5,10-dihydrophenazine derivatives (Ic-k). The number of electrons transferred during anode oxidation in an aprotic medium found in this way was two, and phenazinium salt IV should be considered to be a product of the electrode process, as in the case of 5-methyldihydrophenazine.

On comparing the oxidation potentials of dihydrophenazines (Table 1), one may note that acyl substituents, which have an overall electron-acceptor effect, give rise to an increase in the potential. The difference in the oxidation potentials in the series of 5-acyldihydrophenazines Ic-e is insubstantial; this is due to the blocking effect of the carbonyl grouping, which hinders transmission of the effect of the substituent to the reaction center of the dihydrophenazine system. The appreciable shift of the oxidation potential to the positive region in the case of Ig, h, i as compared with Ia, b can be explained by the electron-acceptor effect of the nitro groups in the 1 and 3 positions of the dihydrophenazine molecule. However, the oxidation potentials of Ig, h, i are close to one another, inasmuch as the conjugation of a substituent in the 5 position with the reaction center is weakened because of the noncoplanarity of the dihydrophenazine molecule [14, 15]. The introduction of nitro groups in the 2' and 6' positions of the phenyl ring attached to the nitrogen atom creates additional steric hindrance, which reduces the effect of these strong electron-acceptor substituents (Ii, j, k), whereas a nitro group in the 1 position gives rise to a considerable shift in the potential (If, i).

In order to find the conditions for stabilization of the product of one-electron oxidation we undertook the polarographic oxidation of 1,3-dinitro-5-phenyldihydrophenazine (Ii) in aqueous acetone solution over a broad range of pH values (1.5–12.0) (Table 2).

The number of electrons participating in the oxidation of Ii was also found by simultaneous solution of the equations of the diffusion process on rotating and stationary electrodes. This number was found to be two in an acidic medium, whereas the oxidation has one-electron character in neutral and alkaline media.

The oxidation potentials change only slightly as the pH of the medium changes. The discontinuity in $E_{1/2}$ in the positive region at pH 6.8 accompanies the transition from a two-electron to a one-electron process and the formation of a paramagnetic compound, which can be obtained by preparative electrolysis of Ii in alkaline media (pH 12.0). This is accompanied by a rather persistent green coloration of the solution and a poorly resolved five-component ESR signal (Fig. 3) due to the formation of phenazyl radical IIIi. The structure of this spectrum can be described by coupling of the spin of the unpaired electron primarily with two equivalent nitrogen nuclei [16]. A similar electronic spectrum [6] and a similar ESR signal were observed when radical IIIi was generated in benzene by means of lead dioxide.

A paramagnetic product having the seven-component ESR spectrum characteristic for the phenazine cation radical [8] was unexpectedly detected as a result of the electrolysis of 5-acyldihydrophenazines (Ic-e) in aqueous acetone solution. The electrode reaction in this case apparently precedes hydrolytic splitting out of an acyl substituent [17].

EXPERIMENTAL METHOD

Anode polarographic oxidation was carried out with an LP-7 polarograph (Czechoslovakian SSR) from 0 to +1.3 V relative to a saturated calomel half cell. A rotating graphite disk electrode impregnated with paraffin was used as the anode. The experiments were carried out in a hermetically sealed thermostatted cell at 25° in anhydrous acetone at a depolarizer concentration of 10^{-4} mole/liter with a lithium perchlorate base electrolyte (concentration $5 \cdot 10^{-2}$ mole/liter in solution).

Data on the synthesis of the investigated compounds were presented in our preceding paper [6].

LITERATURE CITED

1. L. V. Varyukhina and Z. V. Pushkareva, Zh. Obshch. Khim., 26, 1740 (1956).
2. Yu. S. Rozum, S. B. Serebryanyi, E. F. Karaban, V. P. Chernetskii, and M. N. Dropkina, Zh. Obshch. Khim., 34, 2599 (1964).
3. L. L. Gordienko, Élektrokhimiya, 1, 1497 (1965).
4. D. N. Bailey, D. M. Hercules, and D. K. Roe, J. Electrochem. Soc., 116, 190 (1969).

5. K. H. Hausser, A. Häbich, and V. Z. Franzen, Naturf., 16a, 836 (1961).
6. Z. V. Pushkareva, I. N. Noskova, and V. F. Gryazev, Khim. Geterotsikl. Soedin., No. 10, 1428 (1970).
7. J. Heyrovsky, and J. Kuta, Fundamentals of Polarography [Russian translation], Mir, Moscow (1965).
8. Y. Matsunaga and C. A. McDowell, Proc. Chem. Soc., 175 (1960).
9. W. S. Zaugg, J. Biol. Chem., 239, 3964 (1964).
10. G. M. Badger, R. S. Pearce, and R. Pettit, J. Chem. Soc., No. 4, 3199 (1951).
11. H. H. Perkumpus, Z. Phys. Chem., No. 6, 18 (1956).
12. G. Cauquis and D. Serve, Tetrahedron Lett., 29, 2695 (1973).
13. V. I. Kravtsov, Electrode Processes in Solutions of Complex Metals [in Russian], Leningrad (1969), p. 100.
14. J. G. M. Campbell, C. G. Le Fevre, R. J. W. Le Fevre, and E. E. Turner, J. Chem. Soc., 404 (1938).
15. J. P. Malrieu, J. Chim. Phys., 62, 485 (1965).
16. F. Gerson, High-Resolution Electron Spin Resonance Spectroscopy, Wiley-Interscience (1970).
17. A. G. Terent'ev, Master's Dissertation, Kiev (1974).

ANALOGS OF PURINE NUCLEOSIDES AND PURINE MONO- AND POLYNUCLEOTIDES

V.* PREPARATION OF 9-(1,5-DIHYDROXY-3-PENTYL)-PURINES

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A number of 6-substituted 9-(1,5-dihydroxy-3-pentyl)purines were obtained from 5-amino-4,6-dichloropyrimidine. 5-Amino-4,6-dichloropyrimidine reacts with 2-hydroxymethylpyrrolidine to give 4-chloro-5-amino-6-(2-hydroxymethylpyrrolidino)pyrimidine.

As previously reported in [2], the synthesis of analogs of oligonucleotides with a modified pentose residue seems of interest in order to study the effect of such oligomers on biologically important systems, the functioning of which is associated with nucleic acids. Replacement of the ribose or deoxyribose of natural polynucleotides by dihydroxyalkyl groups of corresponding length and conformation may lead to analogs of nucleotides that to a greater or lesser extent are capable of complexing with natural polynucleotide matrices.

The synthesis and subsequent polycondensation of 1'5'-diphosphates of 1',5'-dihydroxypentylpurines also seems of definite interest, since it is possible that synthetic polynucleotides containing a pentamethylene chain instead of a ribose (deoxyribose) residue will prove to be conformationally closer to natural prototypes.

9-(1,5-Dihydroxy-3-pentyl)purines, the synthesis of which is possible by two methods – by alkylation of purine derivatives (for example, see [3, 4]) or by adding an imidazole ring to the corresponding pyrimidine derivatives (for example, see [5]) – can be used as the starting materials for the preparation of such compounds.

Our attempts to alkylate 6-fluoropurine with diethyl α- or β-bromoglutarates in the presence of sodium hydride or potassium carbonate [4, 6] in dimethylformamide (DMF) with subsequent reduction of the ester

*See [1] for communication IV.
†Deceased.

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