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CHEMICAL KINETICS AND CATALYSIS

Kinetics of the Electrochemical Oxidation of 1,1-Bis-hydroperoxy-4-methylcyclohexane on Platinum

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Abstract—The electrochemical synthesis of 3,12-dimethyl-7,8,15,16-tetraoxadispiro[5.2.5.2]hexadecane (1,2,4,5-tetraoxane) from 1,1-bis-hydroperoxy-4-methylcyclohexane on platinum electrode in a cell with separated and unseparated cathode and anode space in an aprotic solvent is conducted. The kinetics of electrochemical oxidation of 1,1-bis(hydroperoxy)-4-methylcyclohexane is studied. The current yield of the reaction is determined.

Keywords: 1,1-bis-hydroperoxy-4-methylcyclohexane, electrochemical synthesis, 1,2,4,5-tetraoxane, platinum electrode, cyclic voltammetry.

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INTRODUCTION

Over the last two decades, organic peroxides have been attracting the attention of chemists and researchers in the development of medicinal preparations due to the high antimalarial [1, 2] and antitumor [3] activity found for these compounds. To date, tetraoxanes, ozonides, and trioxanes having activity comparable to or surpassing that of natural peroxide artemisinin have been obtained [4].

Geminal bis-hydroperoxides are initial reagents in the synthesis of peroxides with antimalarial and antitumor activity. Moreover, they are of interest as initiators of radical polymerization [5] and as initial compounds in the synthesis of esters [6]. The reactivity and other properties of geminal bis-hydroperoxides have been actively studied in the last five years after convenient and accessible methods for their synthesis were developed [7].

The electrochemistry of organic peroxides attracts attention in developing methods for their analysis with the aim of investigating the mechanisms of O–O moiety reduction, and when studying structures having antimalarial activity [8–10].

In [11], we studied the electrosynthesis of 1,2,4,5-tetraoxane (**2**) from 1,1-bis-hydroperoxy-4-methylcyclohexane (**1**) under membrane-free conditions. The aim of this work is to study the kinetics of this reaction and of the electrochemical behavior of initial compound **1** and product **2**.

EXPERIMENTAL

Initial compound **1** was obtained via the reaction of 4-methylcyclohexanone with hydrogen peroxide [7]. A 1% $LiClO_4$ (Acros) solution in acetonitrile was used as our background electrolyte. To conduct our preliminary synthesis, 600 mg of **1** were dissolved in 150 mL of the background electrolyte, while 10 mg of **1** were dissolved in 10 mL of the background electrolyte to perform the electroanalytical and kinetics experiments. Preliminary electrolysis was performed in the galvanostatic (50 mA) and potentiostatic modes in a two-electrode glass cell with and without a K-40 ion-exchange membrane. Platinum plates with surface areas of 10 cm^2 were used as electrodes in our preliminary experiments, while platinum plates with surface areas of 1 cm^2 were used for our electroanalytical measurements (working and auxiliary electrodes). Electrochemical measurements were conducted relative to a silver/silver chloride reference electrode (Ag|AgCl|KCl(sat)).

Cyclic voltammograms (CVAs) were recorded using a computer-controlled IPC-Compact potentiostat.

Acetonitrile was distilled over phosphorus pentoxide. Lithium perchlorate was used without additional purification.

Samples were collected and analyzed by means of thin layer chromatography (TLC) in the electrooxidation of **1**. The completion of electrolysis was established based on the disappearance of a spot corresponding to the initial **1**. After the completion of elec-

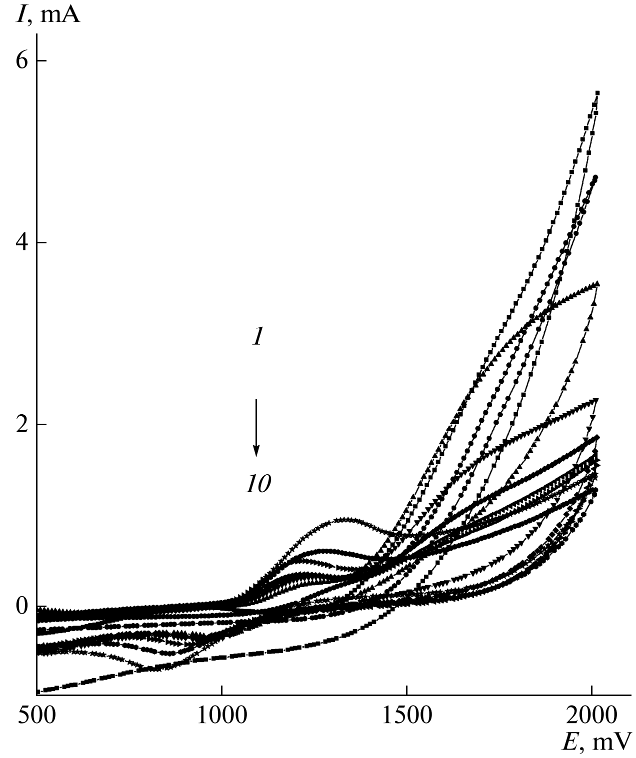


Fig. 1. Change in the cyclic voltammograms of 1,1-bis-hydroperoxy-4-methylcyclohexane on a Pt anode during electrolysis in the potentiostatic mode; *1*–*10* are the numbers of our experiments.

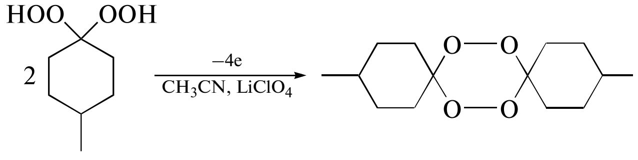
trolysis, acetonitrile was evaporated on a rotary evaporator to yield 3–4 mL of solution to which 15 mL of water were added, followed by extraction with five portions of diethyl ether (5 mL each time). The combined extracts were washed with water (5 mL) and dried over Na_2SO_4. The ether was then evaporated, and the residue was purified via column chromatography on SiO_2. The product was analyzed by means of NMR spectroscopy and TLC using the preliminarily prepared reference.

The ^1H NMR spectra were recorded on a Bruker AM-300 spectrometer ($CDCl_3$ was used as a solvent). Silufol UV-254 plates were used for TLC; column chromatography was performed on silica gel 63–200 mesh (Acros) using a mixture of petroleum ether and ethyl acetate (20 : 1) as an eluent.

A sample of **2** was synthesized according to the procedure described in [12]. The melting point of the sample was 69.5–71°C (mp 71–72°C [4]). The ^1H NMR spectrum (300.13 MHz, δ, ppm) was 0.91 (d, 6H, CH_3, $J = 6.4$ Hz) and 1.08–1.99 (m, 18H, CH_2, CH).

RESULTS AND DISCUSSION

Preliminary experiments on the oxidation of **1** in galvanostatic mode in a cell with separated and unseparated cathode and anode space were performed until the disappearance of spot of **1** in TLC was observed. Analysis of the isolated product by NMR showed that tetraoxane was formed as a product in both cases. No by-products were detected. This agrees with the data of [11] and corresponds to the electrooxidation of the initial compound into **2** according to the reaction:



(1) **(2)**

Compound **2** was isolated in amounts of 314–341 mg from the reaction mass, corresponding to a reaction yield of 68–72% expressed in the weight of isolated product regardless of in which cell (separated or unseparated) the electrolysis was conducted.

To determine the depth to which the reaction of oxidation of **1** into **2** proceeded, the kinetics of this reaction before extraction of the product was studied under potentiostatic conditions in a three-electrode cell. In this experiment, electrolysis was conducted at working electrode potential $E = 2.0$ V for 6 h with control over the electrolysis current. The experiment was interrupted each 30 min, and CVAs were recorded at potential sweep rate of 100 mV/s. The whole experiment was thus split into 12 separate experiments. As can be seen from Fig. 1, the appearance of CVAs varied continuously in the course of electrolysis. Neither anodic nor cathodic branches of the CVAs of the initial **1** have maxima. During electrolysis, however, the formation of **2** results in the emergence of two peaks: an anodic one at $E = 1.35$ V and a cathodic one at $E = 0.85$ V (Fig. 1).

A monotonous decline in the value of electrolysis current at $E = 2.0$ V and an increase in the peak currents belonging to **2** are observed during the oxidation of **1**. The appearance of the CVAs does not change after 5 h of electrolysis, indicating the end of the oxidation of **1**. This is also confirmed by the spot belonging to **1** completely disappearing in the same time of electrolysis, according to TLC of the reaction mixture. Moreover, the CVAs obtained for electrolysis product **1** and those recorded for tetraoxane obtained by counter synthesis [11] are identical, which also indicates the completion of the process within 5 hours of electrolysis and the formation of **2** as a single product.

The dependence of electrolysis current on the duration of the experiment (Fig. 2) shows that the electrolysis current fell substantially over time in each experiment and with respect to each preceding experiment as well. It can be seen from Fig. 2 that the initial current of oxidation for **1** in each experiment and the charge passing through the cell in the experiment and equal to the area enclosed by the kinetics curve both diminish continuously in the course of electrolysis. The current fell to zero after 5 h of electrolysis, and an electric charge equal to 11.99 C was passed through

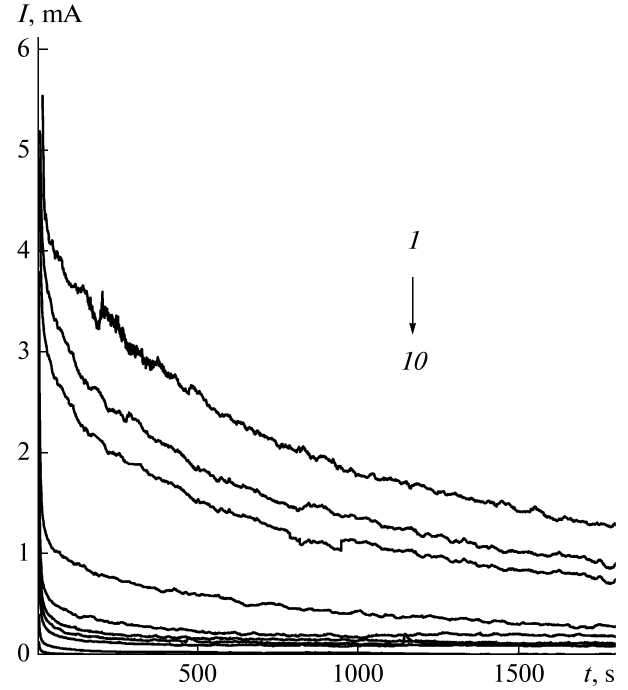


Fig. 2. Kinetics of electochemical oxidation of 1,1-bis-hydroperoxy-4-methylcyclohexane on a Pt anode in the potentiostatic mode; *1–10* are the numbers of our experiments.

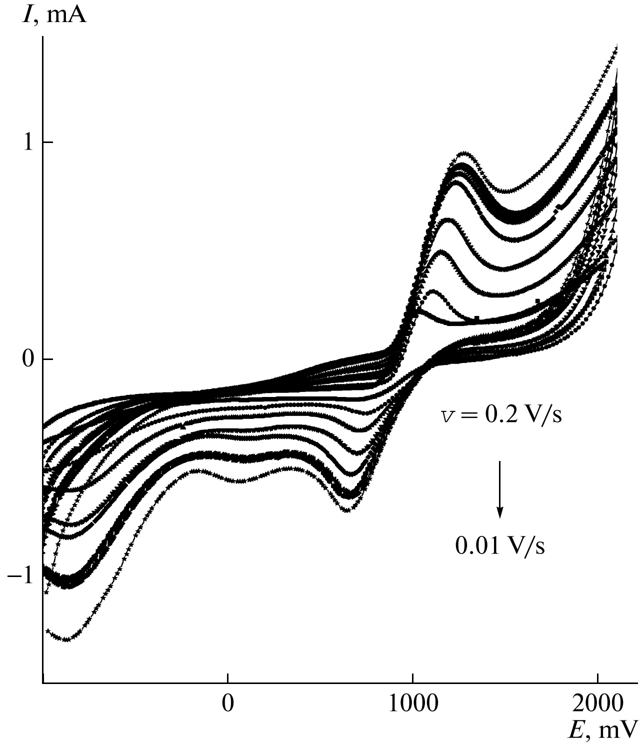


Fig. 3. Cyclic voltammograms for the product of the electochemical oxidation of **1** in an acetonitrile solution on a Pt anode. The electrode potential scanning rates were 0.01, 0.025, 0.050, 0.075, 0.1, 0.125, 0.150, 0.175 V/s.

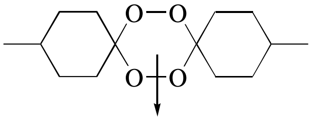
the cell during this time. Calculations using the chemical equation shows that an electric charge equal to 11.91 C is required for the complete oxidation of 10 mg of **1** into **2**. From the ratio of the calculated amount of electricity required for the complete oxidation of **1** and the amount of electricity calculated from the experimental data, it follows that the reaction proceeds with a current yield of no less than 99%. The relatively moderate values of the product yield (no more than 72%) obtained in the preparative experiments were due only to losses of the product at the stage of its isolation from the reaction mass.

Comparison of CVAs of **2** (Fig. 3) and CVAs of **1** shows that the first differ from the second not only in the presence of anodic and cathodic peaks but also in the highest value of anodic current for **2** in CVAs at the potential value E = 2.0 V being considerably lower than that for **1**. The latter indicates the stability of **2** toward anodic oxidation, as was already shown above. It seems that peaks in the region of potentials E = 0.85–1.35 V correspond to a redox pair being formed on the surface of platinum electrode. The interrelation of the values of the anodic peak at E = 1.20–1.35 V and the cathodic peak at E = 0.85–0.90 V (Fig. 3) can be seen from the narrowing of the potential scanning interval to E = 0.0–1.5 V, E = 0.0–1.4 V, and E = 0.0–1.0 V resulting in the simultaneous drop and subsequent complete disappearance of the anodic and cathodic peaks on our CVAs.

Figure 3 shows CVAs of **2** at different potential scanning rates (v). It turns out that the values of the anodic peak ($I_{\mathrm{p,\,a}}$) and the current of the cathodic peak ($I_{\mathrm{p,\,c}}$) grow linearly with an increase in v. The straight-line dependence of $I_{\mathrm{p,\,a}}$ and $I_{\mathrm{p,\,c}}$ on v indicates that **2** participates in the reaction of redox pair formation while in the adsorbed state. The Laviron equation [13] defining the dependence of $I_{\mathrm{p,\,a}}$ on v is applicable here:

$$I_{\mathrm{p,a}} = nFQv/4RT,$$

where v is the potential scanning rate, Q is the electric charge required for trioxane adsorption, F is the Faraday number equal to 96485 C/mol, R is the gas constant equal to 8.315 J/(mol K), and T is the absolute temperature (K) of the experiment. From the experimental data for the range of values of the potential scanning rate v = 0.025–0.1 V/s, it was found that n = 0.88. Keeping in mind the measurement error, we may therefore assume that the formation of the redox pair by tetraoxane proceeds with the transfer of one electron. Considering the possibility of interaction between the unshared electron pair of the peroxide bridge and the metal cations resulting complex formation [15], it is reasonable to assume that the formation of a surface complex between tetraoxane and platinum accompanied by the transfer of one electron occurs in this case:



According to the Laviron equation [13, 14], using the straight-line dependence of $E_{p,a}$ and $E_{p,c}$ on v:

$$E_{p,a} = E^0 + (RT/\alpha nF)[\ln(RTk_s/\alpha nF) - \ln v],$$

where $E_{p,a}$ and E^0 are the potentials of anodic peaks and the standard potential of the reaction, α is an electron transfer coefficient, n is the number of electrons participating in the rate-limiting stage, an k_s is an apparent reaction rate constant, we calculated the α coefficient. It was found to be equal to 0.19 for the anodic branches of CVAs and 0.22 for the cathodic branches. Values of the α coefficient lower than 0.5 indicate a low rate of electron transfer in the assumed charge-transfer complex formation reaction between tetraoxane and platinum on the anodes' surfaces and agree with the above conclusion that the formation of the complex between **2** and Pt is limited by electron transfer.

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