The Kinetics of Pentoxyl Oxidation by Hypochlorite Ions

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Abstract—The kinetics of pentoxyl (**I**) oxidation in aqueous media under the action of hypochlorite ions was studied at pH 8.8 and 273–298 K. The order of the reaction with respect to both participants was found to be one. The temperature dependence of the reaction rate obeyed the Arrhenius law. The reaction activation parameters were found to be $E_a = 11.08$ kJ/mol, $\Delta H^{\neq} = 8.73$ kJ/mol, $\Delta S^{\neq} = -200.70$ J/(mol K), and $\Delta G^{\neq} = 66.88$ kJ/mol. Reaction stoichiometry was studied, the chemical characteristics of the process considered, and a mechanism of the oxidative transformation of **I** under the action of OCl^- suggested.

INTRODUCTION

This work continues studies of the chemical transformations of biologically active substances under the action of oxidative reagents containing the high-reactivity hypochlorite group [1–8]. Pyrimidine base derivatives, including pentoxyl (6-methyl-5-oxymethyluracil) (**I**), are pharmacologically important substances. They find wide use in medicine. The problems of chemical and biochemical transformations of these compounds [9, 10] and their interactions with various reagents are still a subject of discussion in the literature [11, 12].

The kinetics of oxidative transformations of **I** is of interest for science and practical applications in relation to metabolism problems and the development of methods for controlling the content of **I**. The oxidation of its structural analogues in various objects, including biological materials, is also of interest.

The oxidation of methyluracil with ammonium persulfate in alkaline media according to the Elbs reaction [13–16], sodium hypochlorite [8], and potassium permanganate in acetic acid with the formation of 5-hydroxy-6-methyluracil [17] are well-known reactions. The kinetics and mechanism of the oxidative transformations of pyrimidine base derivatives have scarcely been studied.

In this work, we studied the kinetics and mechanism of the interaction of **I** with hypochlorite ions. The results obtained in this work will be used as a basis and model for further studies of kinetic patterns of reactions involving structural analogues of **I** and for optimizing the corresponding analytic reactions and methods.

EXPERIMENTAL

Solutions were prepared from doubly distilled water. Sodium hypochlorite containing hypochlorite ions OCl^- was synthesized by bubbling chlorine through an aqueous solution of sodium hydroxide. The solutions were stored in dark-glass vessels, and the activity of OCl^- was periodically checked by iodometry. Under the conditions specified, it remained constant for a long time. Solutions of **I** were prepared by dissolving samples in water. The reagents used were either of ch.d.a. (pure for analysis) grade or subjected to the required purification.

Experiments were conducted while maintaining reagent solutions at a constant temperature with an accuracy of ±0.1 K. The kinetics was monitored photometrically by the accumulation of the product of the transformation of **I**. The concentration of the initial solution of **I** was 0.001 M. Reaction medium pH was set at 8.8 using a hydrogen-phosphate buffer. The reaction was performed with OCl^- taken in excess. Excess phenol solution was then added to instantaneously stop the process. The colored product formed was subjected to photometry at $\lambda = 630$ nm. Reaction stoichiometry was determined from the composition of the reaction medium containing various initial concentrations of **I** and OCl^- 24 h after initiating the reaction at ≈20°C.

RESULTS AND DISCUSSION

Data processing was performed using the results of kinetic measurements. The oxidation of **I** under the action of OCl^- occurred at a high rate under our experimental conditions and was complete in ≈2 min (0°C). The concentration of **I** rapidly decreased, and reaction product concentrations increased. The kinetic curves of substrate consumption and product accumulation can be divided into two regions with different rate laws
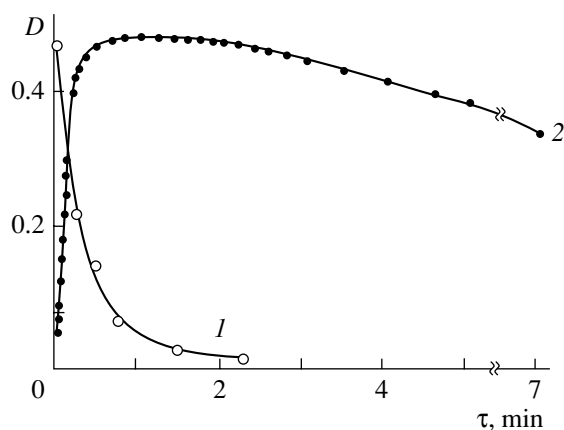
Fig. 1. Kinetic curves of (*1*) consumption of **I** and (*2*) reaction product **II** accumulation.
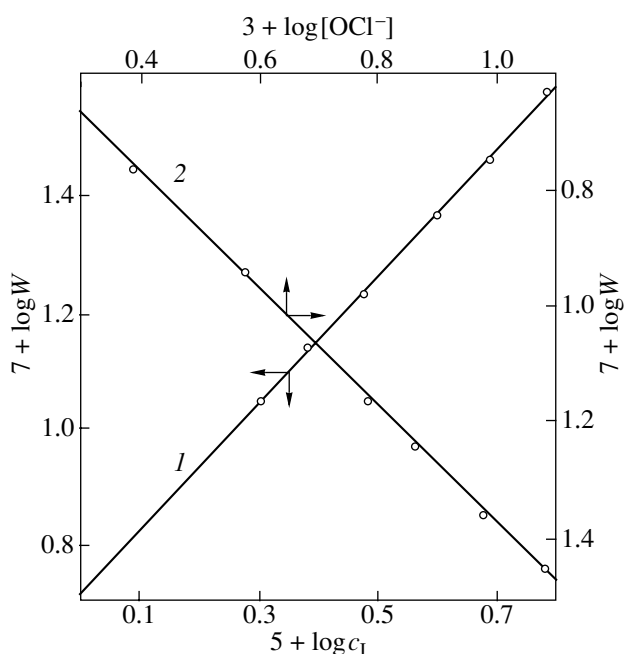

Fig. 2. Logarithm of the rate of reaction product accumulation as a function of the logarithm of the concentration of (*1*) **I** and (*2*) OCl⁻ at 283 K and pH 8.8.

(Fig. 1). The character of the experimental kinetic curves manifests itself most clearly during the first 10–15 s, when a substantial amount of **I** (more than 80%) transforms into reaction products.

An analysis of the kinetic curves obtained when the oxidizer was taken in excess showed that OCl⁻ likely attacked not only **I** but also the reaction product formed. Indeed, we observed a well-defined maximum of product accumulation; that is, the concentration of the product began to decrease starting from a certain time moment (Fig. 1, curve *2*).

The temperature dependence of reaction rate was studied over the temperature range 273–298 K. The

experimental data were well described by the Arrhenius equation.

The dependence of the rate of the reaction on the concentration of **I** at pH 8.8, [OCl⁻] = 1.2×10^{-2} M, and 283 K was as follows:

$c_{\mathrm{I}} \times 10^5$, M	1.0	2.0	3.0	4.0	5.0	6.0
$W \times 10^6$, mol/(l s)	0.5	1.09	1.66	2.29	2.83	3.83

This stationary rate–concentration of **I** dependence is almost linear in the logarithmic coordinates (Fig. 2).

The dependence of the rate of the reaction on the concentration of OCl⁻ at $c_{\mathrm{I}} = 5 \times 10^{-5}$ M, pH 8.8, and 283 K is given below:

[OCl⁻] $\times 10^3$, M	2.4	3.6	4.8	6.0	7.2	9.6	12.0
$W \times 10^6$, mol/(l s)	0.57	0.86	1.15	1.44	1.72	2.35	2.83

This dependence is also linear in the logarithmic coordinates (Fig. 2). The reaction is first-order in both **I** and OCl⁻.

It follows from the data given above that the kinetics of interaction between **I** and OCl⁻ is described by the law

$$dc/dt = kc_{\mathrm{I}}[\mathrm{OCl}^-]. \tag{1}$$

The rate constants calculated by (1) were equal to within measurement errors over the reagent concentration ranges studied. At 283 K, we obtained $k = 4.75 \pm 0.18$ l/(mol s).

The temperature dependence of the rate constant over the temperature range 273–298 K (Fig. 3) is described by the Arrhenius equation

$$k = 5.25 \times 10^2 \exp(-11.08/RT),$$

where $A = 5.25 \times 10^2$ l/(mol s) and activation energy $E_{\mathrm{a}} = 11.08$ kJ/mol. The activation state parameters are: the enthalpy of activation $\Delta H^{\neq} = 8.73$ kJ/mol, the entropy of activation $\Delta S^{\neq} = -200.70$ J/(mol K), and the Gibbs energy of activation $\Delta G^{\neq} = 66.88$ kJ/mol.

The low activation energy and preexponential factor values obtained are characteristic of complex ion-molecular reactions, such as the one considered in this work.

Experiments performed to determine reaction stoichiometry showed that the ratio between the amounts of OCl⁻ consumed and **I** oxidized changed from 1 to 8 as the initial molar ratio [OCl⁻]/c_{I} increased from 0.2 to 10.0. When **I** was taken in excess, the oxidation stopped at intermediate stages. Conversely, in the presence of excess OCl⁻ ions, the reaction yielded strongly oxidized final products such as urea, acetic acid, etc.

The reduction of the hypochlorite ion to Cl⁻ requires the addition of two electrons and two protons. It follows that, in agreement with the experimental data, deep oxidation of 1 mole of **I** requires 6 moles of OCl⁻,

$$6\mathrm{OCl}^- + 12\bar{\mathrm{e}} + 12\mathrm{H}^+ = 6\mathrm{Cl}^- + 6\mathrm{H_2O}. \tag{I}$$
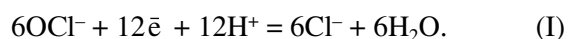
Accordingly, the oxidation of **I** under the action of OCl⁻ is described by the equation

$$\text{(structure of I)} + 6OCl^- = H_2N-\underset{\underset{O}{\|}}{C}-NH_2 + CH_3-C\overset{\nearrow O}{\underset{\searrow OH}{}} + 3CO_2 + 6Cl^-. \qquad (II)$$

Considering our experimental results and the literature data on the transformations of pyrimidine bases [18], the mechanism of reaction (II) can be described as follows. The primary product of the interaction of OCl^- with **I** in an aqueous weakly alkaline medium is likely the 5,6-dioxy derivative of **I**, which rapidly undergoes further oxidation with OCl^- ions to produce a series of heteronuclear ring cleavage products [18].

The saturation of the conjugated π-electronic system of the pyrimidine ring at the $C_5=C_6$ double bond results in the rapid disappearance of characteristic ultraviolet absorption at $\lambda = 260$ nm. After the formation of the 5,6-diol derivative of **I**, sequential stages of pyrimidine ring "disassembly" follow. For instance, urea is formed as a result of the hydrolytic breaking of two bonds, C_4-N_3 and C_6-N_1. The C_4 fragment undergoes decarboxylation. The formation of α,β-dioxybutanol [19–21] occurs as a result of oxidative splitting at the C_6-N_1 and C_5-C_4 bonds. Under the action of OCl^-, α,β-dioxybutanol transforms into α,β-diketobutyric acid and then into acetic and oxalic acids. The latter is oxidized to CO_2.

The addition of OCl^- in greater amounts causes the oxidation of urea formed,

$$H_2N-\underset{\underset{O}{\|}}{C}-NH_2 + 2OCl^- = 2NH_2Cl + CO_3^{2-}. \qquad (III)$$
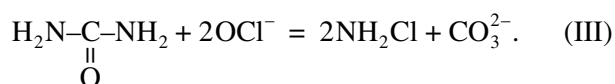
The formation of chloramine was observed photometrically at $\lambda = 244$ nm. Chloramine is rather unstable thermodynamically; curve *2* (Fig. 1) can characterize its accumulation, equilibrium state, and hydrolysis. Figure 1 shows that, first, the concentration of the product increases; next, an equilibrium plateau is observed; and the concentration of the reaction product then begins to decrease gradually.

Aqueous solutions in the reaction system under study contain excess hydroxide ions because of the hydrolysis of OCl^-,

$$OCl^- + HOH \rightleftharpoons HOCl + OH^-. \qquad (IV)$$

The thermodynamic equilibrium constant of the reaction

$$NH_2Cl + OH^- \rightleftharpoons NH_2OH + Cl^- \qquad (V)$$

in alkaline medium is determined by the equation

$$K = a_{NH_2OH} a_{Cl^-} / a_{NH_2Cl} a_{OH^-}, \qquad (2)$$

where a_{NH_2OH}, a_{Cl^-}, a_{NH_2Cl}, and a_{OH^-} are the activities of the corresponding components.

We found in this work that the oxidative transformations of **I** and other uracil derivatives under the action of OCl^- involve several stages and occur at a comparatively high rate at 273–398 K. The formation and composition of intermediate and final products depend on the molar ratio between the substrate and oxidizer, their nature, and reaction conditions.

Further studies of the kinetics and mechanism of oxidative transformations of other pyrimidine derivatives, including nucleosides and nucleotides, under the action of hypochlorite ions would be of interest.
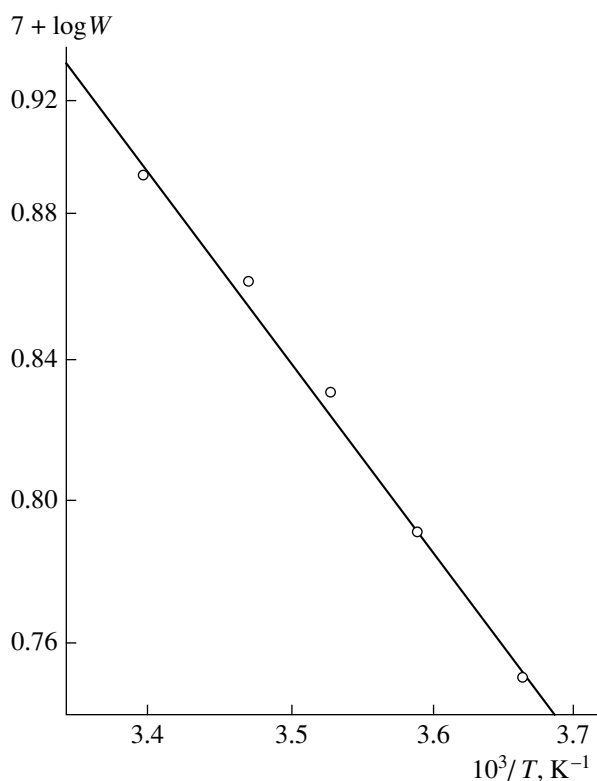
$7 + \log W$

Fig. 3. Reciprocal temperature dependence of the logarithm of the reaction rate at $[OCl^-] = 1.2 \times 10^{-2}$ M, $c_I = 5 \times 10^{-5}$ M, and pH 8.8.

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