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Catalytic Oxidative Deformylation of Polyethylene Glycols with the Participation of Molecular Oxygen

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Abstract—The kinetics of oxidation of diethylene glycol, triethylene glycol, and polyethylene glycols (PEGs) with molecular weights ranging from 400 to 2000 in the presence of Cu(II) ions and bases was studied. It was found that ethylene glycols can be oxidized by molecular oxygen in anhydrous media in a temperature range of 30–60°C at anomalouosly high rates which are higher than the rates of chain-radical PEG autoxidation by several orders of magnitude. Only terminal hydroxyl groups were subjected to oxidation. The reaction occurs with the cleavage of a C–C bond and results in the formation of formic acid and a PEG with the number of $–(CH_2CH_2O)–$ groups lower than that in the parent compound by unity. The rate and selectivity of PEG oxidation were found to strongly depend on the molecular weight of the polymer; from diethylene glycol to PEG 2000, the specific rate of oxidation increased by a factor of 60 in terms of terminal hydroxyl groups. An oxidation mechanism was suggested, which involves the formation of ternary complexes $[Cu^{2+}\cdots A^{-}\cdots O_2]$, which undergo further degradation by a many-electron concerted mechanism to form formic acid and, probably, an unstable hemiacetal $\{RO–CH_2OH\}$. The rapid oxidative degradation of the latter leads to the formation of PEG with a lower molecular weight.

INTRODUCTION

Previously [1], we found that the catalytic system $\{Cu(II)L_2 + \text{base}\}$ is responsible for the selective oxidation of alcohols (to aldehydes or acids) and ketones (to acids) with molecular oxygen at temperatures from 20 to 60°C; the target product yields are high (up to 90–98%). The main parameters that characterize the efficiency of catalysis by copper compounds in alkaline media, the turnover frequency TOF = 1–10 s^{-1} and the turnover number TON = 10^4, are very similar to analogous characteristics of the enzyme catalysis of oxidation processes [2].

Depending on the reaction conditions and the structure of oxidized substrates, the catalytic system $\{Cu(II)L_2 + \text{base}\}$ simulates the action of oxidase or oxygenase enzymes, and it can be considered as a biomimetic system [3].

It is well known that cytochrome P-450 is a family of monooxygenases, the main function of which consists in the catalysis of hydroxylation, epoxidation, and demethylation of various xenobiotics and steroids [4]. It is believed that the demethylation of 14α-lanosterol takes place consecutively by the oxidation of a methyl group to form an alcohol and subsequently an aldehyde. The participation of cytochrome P-450 as a catalyst in the reaction of aldehyde oxidation results in the cleavage of a C–C bond and in the formation of formic acid [5]. More recently [6], it was found that iron complexes (cytochrome P-450 models) catalyze the oxidative deformylation of aldehydes; in this case, a peroxo complex of Fe(III) acts as an active species.

Recently, we found that a new nontrivial route—oxidative deformylation—appeared in the oxidation of primary alcohols on varying the conditions of oxidation in the presence of the catalytic system $\{Cu^{2+} + \text{base}\}$. This reaction was first discovered using the oxidation of fluorinated alcohols $H(CF_2CF_2)_nCH_2OH$ as an example [7]. The oxidation of these alcohols with oxygen in the presence of ionic copper salts in aprotic solvents resulted in the simultaneous formation of formic acid and dihydroperfluoroalkanes $H(CF_2CF_2)_nH$ (to almost 100% yields under optimum conditions). An analogous oxidative deformylation reaction of polyethylene glycols (PEGs) with the formation of HCOOH as the major reaction product was reported previously [8].

This work was devoted to a study of the kinetics and mechanism of the oxidative deformylation of PEGs of different molecular weights with oxygen in the presence of the catalytic system $\{CuCl_2 + \text{inorganic base}\}$.

EXPERIMENTAL

The oxidation of diethylene glycol (reagent grade); triethylene glycol (reagent grade); and PEGs (Merck) with molecular weights of 400, 600, 1000, 1500, and

2000 by molecular oxygen in the presence of alkalis and copper salts was studied.

The oxidation of the ethylene glycols in solutions was performed in a gas-tight 50-ml glass reactor equipped with a mechanical stirrer with the use of a manometric system [9]. The volume of the oxidized mixture was 10 ml.

The reaction was performed at 30–60°C. A PEG (300 g/l) was added to 1×10^{-4}–2×10^{-2} M solutions of a copper salt ($CuCl_2 \cdot 2H_2O$ of analytical grade) in *tert*-butanol (analytical grade), dimethylformamide (DMF; analytical grade), or acetonitrile (analytical grade). An alkali (NaOH or KOH of analytical grade from Chemapol) was introduced into the reactor as a solution or as pellets. The reactor was thoroughly purged with oxygen and heated to a specified temperature. The reaction was started at the instant the mechanical stirrer was turned on (at ~1000 rpm). The reaction rate was monitored by measuring the rates of oxygen, base, and PEG consumption.

The concentration of the alkali was determined by titration with a 0.1 M H_2SO_4 solution. The amount of consumed oxygen per unit volume of the liquid phase was expressed in mol/l. The products of PEG oxidation were analyzed by high-performance liquid chromatography (HPLC) on a Waters liquid chromatograph with UV (at $\lambda = 210$ nm) and refractometric detectors and a 5-μm ZORBAX SAX column (4.66 × 250 mm; series A2783). An aqueous 0.025 M KH_2PO_4 solution was used as an eluant at a flow rate of 0.5 ml/min. Low-molecular-weight PEGs and nonacid products of their oxidation were determined by gas–liquid chromatography (GLC) (5% Silicone DC 550 on Chromaton N-AW-DMCS from Chemapol). The concentration of CO_2 in oxidation products was determined volumetrically by measuring the released gas amount after acidifying the solution.

RESULTS AND DISCUSSION

Neutral PEG solutions are almost inert toward oxygen in all of the test solvents, and they can be oxidized with detectable rates at 70–90°C only in the presence of initiators [10]. At the same time, the presence of acidic OH groups, which can undergo deprotonation in sufficiently basic media, allowed us to expect the oxidation of these substrates at high rates in the presence of the catalytic system $\{Cu^{2+} + \text{base} + O_2\}$, which was proposed previously for the oxidation of aliphatic primary alcohols [1].

Figure 1 demonstrates the kinetic curve of oxygen consumption in the reaction of PEG 600 oxidation in DMF at 30°C in the presence of $CuCl_2 \cdot 2H_2O$ with the intermittent introduction of pelletized KOH. As can be seen in Fig. 1, PEG 600 was oxidized at room temperature at a very high rate ($w_{O_2} \sim 5 \times 10^{-4}$ mol l^{-1} s^{-1}). The reaction rate was limited by the rate of dissolution of potassium hydroxide. The use of a finely divided alkali in place of the pelletized alkali as a base increased the rate of oxygen consumption several times. The PEG oxidation resulted in the formation of acids as major reaction products. The consumption of oxygen was completely stopped (see Fig. 1) after the dissolution of the alkali added to the reaction mixture and its neutralization with the acids formed. The addition of fresh portions of the alkali (indicated with arrows in Fig. 1) resulted in resumed oxygen consumption at a rate almost equal to the initial rate of oxidation. The PEG conversion depends on the added amount of the alkali. At a very deep oxidation, the oxidation process was strongly inhibited because of catalyst deactivation due to the formation of an aqueous phase. Copper salts passed into the alkaline aqueous phase and formed catalytically inactive polyhydroxo compounds.

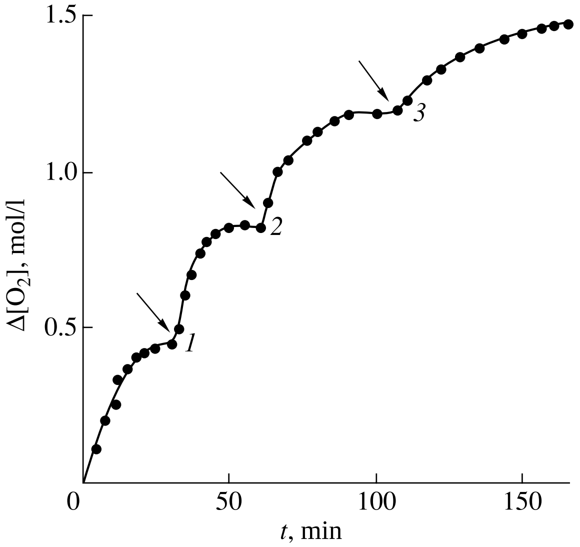

Fig. 1. Kinetic curve of oxygen consumption in the oxidation reaction of PEG 600 (30 wt %) in DMF. $[CuCl_2 \cdot 2H_2O]_0 = 5 \times 10^{-3}$ mol/l; $[KOH]_0 = 0.55$ mol/l; 30°C. Arrows indicate points in time at which additional amounts of pelletized KOH were introduced into the reaction mixture. The concentrations of KOH after dissolution in the reaction mixture were (*1*) 0.55, (*2*) 0.60, and (*3*) 1.00 mol/l.

For the most part, the kinetic experiments were performed with the use of *tert*-butanol as a solvent. Although the rate of PEG oxidation in this solvent is much lower than that in DMF, the use of this solvent makes it possible to introduce an alkali into the reaction mixture not only as pellets but also as a solution and, hence, to exclude the effect of an alkali dissolution process on the kinetics of PEG oxidation.

A study of the oxidizability of PEGs with different molecular weights in the presence of bases and copper salts (Fig. 2) demonstrated that in all cases the oxidation took place at rates higher by a factor of hundreds

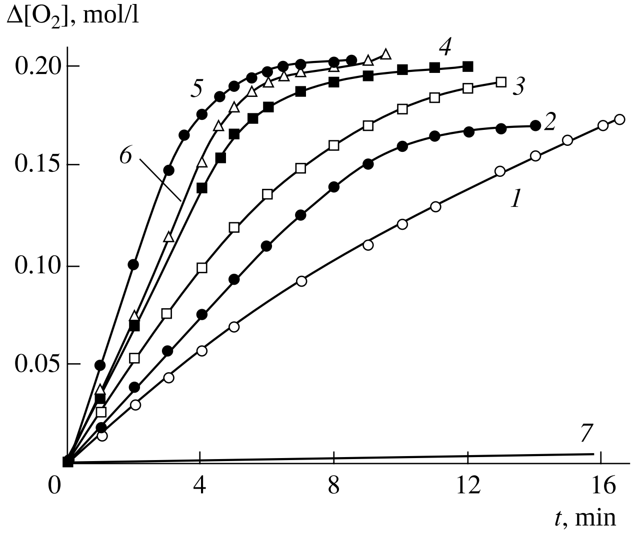

Fig. 2. Kinetic curves of oxygen consumption in the oxidation of (*1*) diethylene glycol, (*2*) triethylene glycol, (*3*) PEG 400, (*4*) PEG 600, (*5*) PEG 1000, (*6*) PEG 2000, and (*7*) diethylene glycol dimethyl ether. Solvent, *tert*-butanol; [PEG] = 300 g/l; $[CuCl_2 \cdot 2H_2O]_0 = 5 \times 10^{-3}$ mol/l; $[KOH]_0 = 0.25$ mol/l; 60°C.

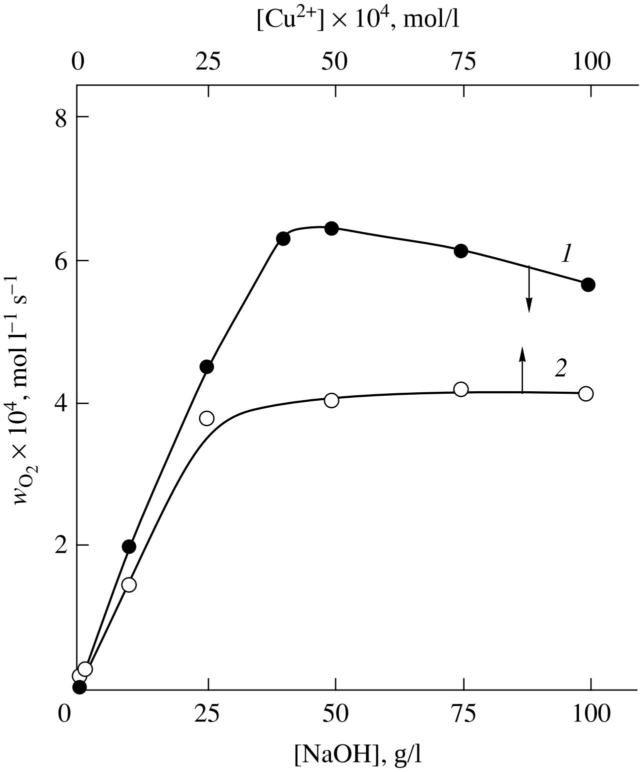

Fig. 3. Rate of oxygen consumption in the reaction of PEG oxidation at 60°C as a function of the initial concentration of (*1*) NaOH or (*2*) $CuCl_2 \cdot 2H_2O$ in *tert*-butanol: (*1*) [PEG 400] = 300 g/l and $[CuCl_2 \cdot 2H_2O]_0 = 5 \times 10^3$ mol/l; (*2*) [PEG 2000] = 300 g/l and $[NaOH]_0 = 0.25$ mol/l.

than the rates of initiated PEG autoxidation [10] at the same temperatures.

As mentioned above, a base is an important component of the catalytic system. In the absence of an alkali, copper compounds do not catalyze the oxidation of ethylene glycols under the test conditions. The oxidizability of PEGs results from the presence of primary hydroxyl groups, which are readily deprotonated under the action of bases. Diethylene glycol dimethyl ether, which is incapable of deprotonation, was not oxidized under the test conditions (Fig. 2, curve *7*). Similarly to the oxidation of primary alcohols, the highest rates of oxygen consumption were observed in the oxidation of PEGs in anhydrous media. The rate of oxygen consumption increased by a factor of dozens from water to nonaqueous solvents (DMF, acetonitrile, and *tert*-butanol).

Figure 3 (curve *1*) demonstrates the rate of oxygen consumption as a function of the amount of an alkali using the oxidation of PEG 400 as an example. It can be seen that an increase in the basicity of the solution resulted in a proportional increase in the reaction rate. This fact suggests that a PEG anionic species is the active form of the substrate in the course of oxidation. It is likely that a detectable decrease in the rate of oxidation in highly alkaline media is due to catalyst deactivation by the formation of the hydroxo complexes of Cu(II). The highest rates of oxidation were attained in DMF because this solvent exhibits the highest polarity in the absence of protonating ability. This resulted in the highest rates of substrate deprotonation and in the highest concentration of the PEG anionic species (A^-) in this solvent.

As in the oxidation of unsubstituted low-molecular-weight primary alcohols [1], the rate of oxygen consumption by PEG solutions linearly increased with copper ion concentration within a range from 0 to 5×10^{-3} mol/l (Fig. 3, curve *2*). The reaction rate remained almost unchanged as the copper concentration in solution was further increased, and it was limited by the rate of PEG deprotonation.

The activation energy of PEG oxidation is almost independent of the PEG molecular weight. This energy is $E_a = (10.0 \pm 1.5)$ kcal/mol for triethylene glycol and PEG 2000 within the temperature range of 30–70°C.

A study of the oxidizability of diethylene glycol, triethylene glycol, and PEGs of different molecular weights exhibited an unusual relationship between the rate of oxidation and the molecular weight. The solutions of PEGs with the same weight concentration (300 g/l) of the substrates were oxidized; thus, the concentrations of –(O–CH_2–CH_2) – groups in the solutions were equal. In this case, the concentration of terminal hydroxyl groups in solution decreased as the molecular weight of PEGs increased.

A decrease in the rate of oxidation with increasing molecular weight of the polymer should be expected because, as mentioned above, terminal hydroxyl groups take part in the oxidation. However, on the contrary, an increase in the molecular weight of PEGs up to PEG 1000 resulted in a significant increase in the rate of oxygen consumption, as can be seen in Fig. 2 and Table 1. A more than tenfold decrease in the concentration of hydroxyl groups in solution from diethylene glycol to PEG 1000 resulted in an increase in the rate of oxygen consumption in oxidation by a factor of 4.

The effect of the degree of polymerization on the rate of oxidation can be demonstrated most clearly by a comparison between the specific rates of oxidation on a basis of 1 g-equiv of OH groups (Table 1). Table 1 indicates that the specific rate of PEG oxidation ($w_{O_2}^{sp}$) increased by a factor of 40–60 as the molecular weight of the substrate increased from 106 (diethylene glycol) to 2000.

Evidently, the observed effect results from an increase in the degree of order of solutions with increasing molecular weight of PEGs and from the ensuing increase in the degree of specific solvation of copper ions with high-molecular-weight PEGs. This solvation can be accompanied by an increase in the donating ability of the substrate anionic form coordinated to copper ions because of a decrease in the polarity of the medium. Such behavior was observed previously in the oxidation of all monohydric alcohols and monatomic ketones in the presence of the catalytic system in use [6]. Thus, it is believed that high-molecular-weight PEGs generate the most favorably organized microenvironments. In turn, this increases the reactivity of the substrate anionic species in [$Cu^{2+}\cdots A^-$] adducts toward molecular oxygen.

The rate of oxidation almost linearly increased with O_2 concentration in the gas phase for all PEGs. Thus, for example, the rate of PEG 600 oxidation increased by a factor of 4.5 going from air to pure oxygen.

It is likely that the oxidation of PEGs in the presence of alkali and Cu(II) ions takes place without considerable degradation of the polymer chain, as supported by the GLC analysis of the oxidation products. Thus, the oxidation of a 0.4 M PEG 600 solution in DMF did not result in the formation of low-molecular-weight PEGs (diethylene glycol, triethylene glycol, or tetraethylene glycol) even upon the consumption of 1.5 mol/l oxygen (the reaction conditions are specified in Fig. 1). The absence of polymer chain degradation was supported by data on the viscosity of solutions. Thus, the viscosity of PEG 2000 solutions in *tert*-butanol at a concentration of 300 g/l (0.15 mol/l) after the oxidation to a degree that corresponds to the formation of 0.07 mol/l acids even increased from 3.9 to 4.6 mPa/s (60°C). Therefore, it is believed that the oxidation of PEGs involves only terminal groups.

As mentioned above, the oxidation of PEGs resulted in the selective formation of acids. The HPLC analysis of the acids demonstrated that formic acid was formed as the main acidic product in all cases. Higher molecular weight acids were detected in insignificant amounts. Formic acid is the primary product of PEG oxidation, and it was detected at the earliest steps of the reaction. In addition to formic acid, considerable amounts of

Table 1. Rates of oxidation of polyethylene glycols depending on the molecular weights. $[Cu^{2+}] = 5 \times 10^{-3}$ mol/l; $[KOH]_0$ = 0.25 mol/l; [PEG] = 300 g/l; solvent, *tert*-butanol; 60°C

Substrate	Molecular weight	$w_{O_2} \times 10^4$, mol l^{-1} s^{-1}	[–OH], g-equiv/l	$w_{O_2}^{sp} \times 10^4$, s^{-1}	Relative rate of oxidation
Diethylene glycol	106	2.0	5.6	0.36	1
Triethylene glycol	150	3.0	4.0	0.75	2.1
PEG 400	400	4.2	1.5	2.8	7.8
PEG 600	600	5.3	1.0	5.3	14.7
PEG 1000	1000	8.3	0.6	13.8	38.3
PEG 1500	1500	7.2	0.4	18.0	50.0
PEG 2000	2000	6.0	0.3	20.0	55.6

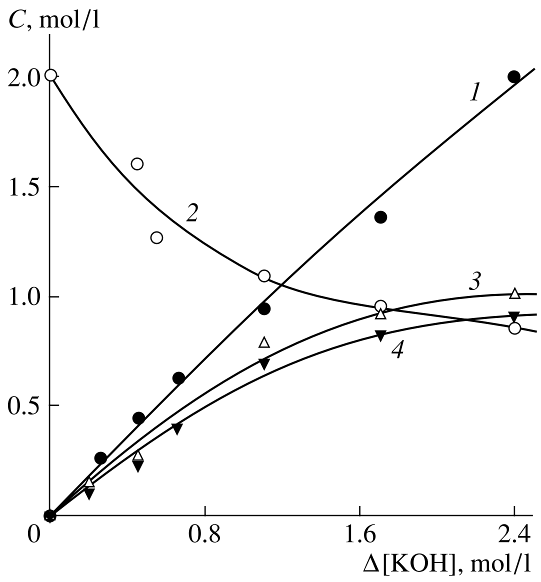

Fig. 4. (*1*) Amount of consumed oxygen and concentrations of (*2*) triethylene glycol, (*3*) HCOOH, and (*4*) diethylene glycol as functions of the amount of consumed KOH. Solvent, *tert*-butanol; [TEG] = 300 g/l; $[CuCl_2 \cdot 2H_2O]_0 = 5 \times 10^{-3}$ mol/l; 60°C.

CO_2 (as K_2CO_3) were detected in the reaction products. The relation $[HCOOH] = 2[K_2CO_3]$ remained unchanged in the course of oxidation in almost all cases.

Table 2. Diethylene glycol oxidation. A comparison between the experimental and calculated yields of ethylene glycol formation and diethylene glycol consumption. $[CuCl_2 \cdot 2H_2O]_0 = 5 \times 10^{-3}$ mol/l; $[DEG]_0$ = 300 g/l; solvent, *tert*-butanol; 50°C (KOH was added intermittently to the reaction mixture as the alkali was consumed)

Reaction characteristics	[KOH], M			
	0.23	0.65	0.90	1.80
$\Delta[O_2]$, mol/l	0.22	0.55	0.90	1.45
$[EG]_{expt}$, mol/l	0.12	0.16	0.26	0.30
[HCOOH], mol/l	0.13	0.40	0.73	1.25
$[K_2CO_3]$, mol/l	0.05	0.10	0.18	0.25
S_{HCOOH}, %*	56.5	61.5	63.5	69.5
$\Delta[DEG]_{calc}$, mol/l	0.1	0.2	0.36	0.5
$[EG]_{calc}$, mol/l	0.12	0.26	0.42	0.67

* The selectivity of HCOOH formation in mol % was determined with respect to the total alkali consumption.

Using the oxidation of diethylene glycol and triethylene glycol as examples, we found that, along with HCOOH, ethylene glycols with the number of ether groups lower than that in the parent PEG by unity were formed as main nonacid products. Figure 4 demonstrates the absorption of O_2 (curve *1*), the consumption of parent triethylene glycol (curve *2*), the accumulation of HCOOH (curve *3*), and the accumulation of diethylene glycol (curve *4*) in the reaction of triethylene glycol oxidation as functions of the consumed amount of KOH (the alkali was added intermittently to the reaction mixture). It can be seen in Fig. 4 that diethylene glycol and formic acid are the main products of triethylene glycol oxidation, and these products are accumulated in equal concentrations at the early stages of the process.

Similarly to triethylene glycol, the oxidation of diethylene glycol resulted in the formation of HCOOH and ethylene glycol (Table 2).

Table 2 indicates that the amount of ethylene glycol formed is close to the amount of formic acid formed only at relatively low diethylene glycol conversions (small alkali additives). It is likely that the subsequent considerable unbalance on the amounts of formed ethylene glycol and HCOOH resulted from a reasonably high rate of ethylene glycol consumption in a mixture with diethylene glycol. Table 2 also summarizes data on the amounts of K_2CO_3 (CO_2) formed and oxygen consumed as functions of the alkali amount consumed in the course of diethylene glycol oxidation.

The oxidation of ethylene glycol in nonaqueous media, as distinct from diethylene glycol and other PEGs, does not result in the formation of CO_2. Formic acid, the yield of which was 200% on a consumed ethylene glycol basis, was the only product of ethylene glycol oxidation under these conditions:

$$HOCH_2\text{–}CH_2OH + 3/2O_2 \xrightarrow{Cu^{2+},\ OH^-} 2HCOOH + H_2O.$$

Consequently, the formation of ethylene glycol in the oxidation of diethylene glycol (DEG) increases the selectivity for HCOOH formation in the course of diethylene glycol oxidation, as observed experimentally (see Table 2).

As stated above, $[HCOOH] = 2[K_2CO_3]$ and $\Delta[PEG] = \Delta[HCOOH]$ in the oxidation of all PEGs. Therefore, the amount of K_2CO_3 formed can serve as a measure of the amount of consumed triethylene glycol. Table 2 gives the values of $\Delta[DEG]_{calcd}$ calculated in this manner. On the other hand, taking into account that the difference $[HCOOH] - 2[K_2CO_3]$ corresponds to the amount of formic acid formed in the oxidation of ethylene glycol and that $\Delta[HO(CH_2CH_2O)_2H] = 2[HCOOH]$, the amount of formed ethylene glycol (EG) can be calculated by the equation

$$[EG]_{calc} = [EG]_{expt} + ([HCOOH] - 2[K_2CO_3])/2\,.$$

Table 2 demonstrates that the amounts of consumed diethylene glycol and formed ethylene glycol thus calculated are close to each other. The observed difference (~20%) can be due to the fact that the amount of CO_2 formed in the oxidation of diethylene glycol is somewhat lower than the amount of formed HCOOH.

Mechanism of the Catalytic Oxidation of PEGs in Alkaline Media

The above experimental data and the kinetics of oxidation of PEGs and their low-molecular-weight analogs with molecular oxygen in the presence of the catalytic system {copper compound + alkali} are inconsistent with a chain-radical mechanism of the reaction:

(1) The oxidation rates were higher than the rates of chain-radical PEG oxidation by several orders of magnitude, and they were close to the rates of enzyme oxidation with molecular oxygen at 40–60°C (TOF ~1–5 s^{-1}; TON > 1000).

(2) The high selectivity of oxidation accompanied by the formation of PEGs with lower molecular weights was retained up to conversions >50%.

(3) The oxidation was characterized by unusual relations between the oxidation rate (w) or selectivity (S) and the molecular weight of the polymer (an increase in w and S with decreasing concentration of terminal hydroxyl groups participating in the reaction) and by the fact that the rate and selectivity of oxidation strongly depended on the nature of the solvent.

(4) The activation energy of the catalytic oxidation of PEGs in alkaline solutions was calculated from the initial rates of oxidation to be E_a = 10 kcal/mol, whereas E_a = 22–24 kcal/mol for chain-radical autoxidation reactions [11].

The above set of experimental data suggests that the process is developed by a nonradical mechanism. By analogy with the oxidation of low-molecular-weight alcohols [1], the PEG derivatives of copper $[Cu^{2+}\cdots A^-]$ are the active species of the substrate. In these derivatives, the substrate anionic form A^- is activated toward oxygen because of partial electron transfer to the copper ion.

In the oxidation of PEGs, as well as in the oxidation of polyols, the highest reaction rates were attained with the use of copper ions as a catalyst [12]. The addition of *ortho*-phenanthroline to the reaction mixture of PEG oxidation weakly affected and even somewhat decreased the efficiency of catalysis and the rate of the process, probably because of the degradation of catalyst–substrate complexes.

The oxidation in the presence of copper compounds and an alkali can simulate enzymic oxidation with molecular oxygen catalyzed by two types of enzymes—oxidases and oxygenases [1]. Copper(I) and copper(II) compounds simulate the oxidase (alcohol oxidation to carbonyl compounds) and oxygenase (alcohol oxidation to acids) functions of enzymes. The formation of acids as the main products of PEG oxygenation suggests that Cu(II) ions are catalytically active in this reaction.

Because of the structural configuration of PEGs, the anionic forms of these substrates can produce polydentate complexes with Cu(II) ions by strong ion–dipole interactions between PEG ether bonds and Cu^{2+} cations [13].[1] These complexes are not prone to redox transformations, as judged from the fact that the visible spectra and absorption intensities of blue Cu(II) complexes remained unchanged under anaerobic conditions. The formation of Cu(I) was also not detected by adding *ortho*-phenanthroline, which forms stable bright red bis(phenanthroline) complexes with Cu(I) ions ($[Cu(o\text{-phen})_2]^+$, λ_{max} = 430 nm [14]), to the system in the course of the reaction and under anaerobic conditions. It is also well known that Cu(II) complexes oxidize redox active compounds such as pyrocatechol [15]. However the rate of this reaction is much lower than the rate of the copper salt-catalyzed oxidation of polyethylene glycolates that have no reductive properties in alkaline solutions.

Thus, the role of Cu^{2+} in the oxidative deformylation of PEGs cannot be reduced to the direct oxidation of the anionic form of the substrate followed by the reoxidation of low-valent copper species to Cu^{2+} by oxygen.

It is likely that, as well as the oxidation of low monohydric alcohols, the oxidation of PEGs proceeds via a step of the formation of the ternary complexes $[Cu^{2+}\cdots A^-\cdots O_2]$, which incorporate a catalyst, a substrate, and oxygen.

The participation of Cu(II) ions in electron transfer from the anion A^- to the oxygen molecule in the ternary complex allows the reaction to proceed via a step of oxygen reduction to form a peroxo complex of Cu(II). Next, the substrate undergoes oxidation by a thermodynamically favorable many-electron mechanism.

Formally, it is believed that, at the first reaction step, a hydride ion is transferred to an oxygen atom of the peroxo complex coordinated to the copper ion with the formation of aldehyde **B** (scheme (I), step 1).

Next, this aldehyde is oxidized by the hydroperoxo complex of copper without leaving the coordination sphere of the metal by a mechanism analogous to the Baeyer–Villiger rearrangement. This results in the cleavage of a C–C bond and in the oxidative deformylation of $H(OCH_2CH_2)_nOH$ with the formation of HCOOH and a labile formaldehyde hemiacetal (**C**) (step 2) [8]. The decomposition of this hemiacetal results in the accumulation of a lower molecular weight PEG and formaldehyde. Previously [16], it was found

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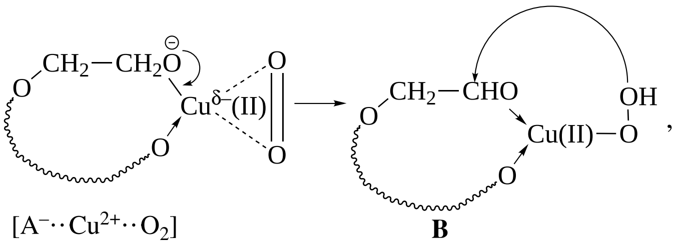
[1] The importance of the formation of polydentate complexes with the participation of a terminal OH group is evident from the fact that the oxidation of monomethylated PEG 600, as distinct from the unmethylated species, resulted in the cleavage of a polymer chain and in the formation of a wide variety of oxidation products in addition to HCOOH.

that under these conditions formaldehyde almost instantaneously undergoes condensation. The subsequent oxidation of the condensation products with oxygen does not form formic acid.

1. 

$$2.\ \mathbf{B} \longrightarrow \mathrm{HCOOH} + \underset{\mathbf{C}}{\mathrm{H(OCH_2CH_2)_{\mathit{n}-1}OCH_2OH}},$$

$$3.\ \mathbf{C} \longrightarrow \mathrm{H(OCH_2CH_2)_{\mathit{n}-1}OH + HCHO + CO_2}. \qquad \text{(I)}$$

Thus, we can state that an unusual route is observed in the reaction of PEG oxidation: direct oxidative deformylation of the substrate takes place at an extremely high rate even at room temperature. It is believed that the reaction of enzymic demethylation [5] also occurs by the direct oxidative deformylation of alcohols without a step of aldehyde formation in solution.

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