C–C Bond Rupture in the Oxidation of Lower (C$_2$–C$_6$) Alcohols with Hydrogen Peroxide Mediated by Iron-Containing Compounds

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Abstract—C–C bond rupture upon the oxidation of alcohols in the Fe(ClO$_4$)$_3$ + H$_2$O$_2$ system in aqueous acetonitrile at room temperature is found. The relative yield of the products of C–C bond rupture is 20–30% under standard conditions for C$_2$ and C$_3$ alcohols and decreases in the series C$_2$ > C$_3$ > C$_4$ > C$_6$. The alkyl radical and carboxylic acid are the products of C–C bond rupture in alcohol oxidation. Cyclohexane is a competitive inhibiting agent for C–H bond oxidation in 1-propanol, and it does not affect the yield of the products of C–C bond rupture. When H$_2$O$_2$ is replaced by *tert*-BuOOH, the fraction of the products of C–C bond rupture decreases by an order of magnitude. Our data suggest that a non-radical intermediate, likely Fe(III) hydroperoxo complex, is responsible for C–C bond rupture in alcohol under the reaction conditions.

INTRODUCTION

It is known that C–H bonds are more reactive in liquid-phase radical oxidation of alkanes at low (<200°C) temperatures, although C–C bonds are substantially weaker than C–H bonds. This is due to steric hindrances when an oxidant interacts with a C–C bond in alkane [1]. Earlier, we found the formation of the products of C–C bond rupture in significant amounts in the oxidation of ethane and propane by hydrogen peroxide with Fe(ClO$_4$)$_3$ in acetonitrile at room temperature [2]. Alkylhydroperoxides, alcohols, and aldehydes with shorter carbon chains were found in the reaction products. In the case of propane, the total amounts of C$_1$ and C$_2$ products were nearly the same: ($P_{C_1} = P_{C_2}$). This suggested that the rupture of the C–C bond in alkanes occurs through the attack of a molecular oxidant, an iron complex containing active oxygen. The formation of these oxidants in the above system (H$_2$O$_2$ + Fe(ClO$_4$)$_3$) has been shown to be possible [3, 4].

However, the study of *n*-hexane oxidation under the same conditions showed a different distribution of the products of C–C bond rupture: $P_{C_1} \gg P_{C_5}$ and $P_{C_2} \gg P_{C_4}$ [5]. Similar results were obtained for *n*-pentane. Based on these data, we suggested that C–C bonds in an oxidation product rather than in an alkane molecule are ruptured to produce unidentified products along with shorter hydroperoxides, alcohols, and aldehydes.

In this work, we studied C–C bond rupture in the oxidation of C$_2$–C$_6$ alcohols in the H$_2$O$_2$ + Fe(ClO$_4$)$_3$ system.

EXPERIMENTAL

Reactions were carried out in acetonitrile, purified using the usual procedure and containing ~1% water, in air at a room temperature. In typical experiments, a reaction volume (2 ml) contained 4 mmol/l Fe(ClO$_4$)$_3$· 6H$_2$O, 400 mmol/l H$_2$O$_2$ (70% aqueous solution), and different alcohols whose concentrations are presented in the text. Duration of the reaction was chosen in such a way that the conversion sumption of hydrogen peroxide was 60–70% (normally, 7–10 min). The reaction was stopped by the addition of Na$_2$S$_2$O$_4$ in a small amount to neutralize unreacted H$_2$O$_2$. To reduce the oxidation products to the corresponding alcohols, a small amount of dry NaBH$_4$ was added to samples before analyses (1–2 h ahead). When *tert*-BuOOH was used as a starting reactant, its 70% aqueous solution was used.

The concentration of hydrogen peroxide in the course of the reaction was monitored by titration with KMnO$_4$. Alcohols and aldehydes were analyzed by GLC using a Hewlett Packard 5880A chromatograph using DB-WAX and OV-1 columns with a length of 60 m. Acetic and butyric acids were analyzed by GLC using an LKhM chromatograph (steel column of 3 mm × 300 mm with Porapac Q, T = 195°C). Formic acid was analyzed by high-efficiency liquid chromatography using a Waters chromatograph (column Zorbax SAX, 4.6 mm × 250 mm). The amount of alkylhydroperoxide was determined by the reaction with P(Ph)$_3$.

RESULTS

The oxidation of alcohols in the system under study leads to aldehydes, ketones, and unidentified products of deep oxidation. Along with the C–H bond oxidation

products, the products of C–C bond rupture were formed in significant amounts and were analyzed (after reduction with sodium borohydride) as alcohols with shorter chain lengths. Table 1 presents experimental data obtained for the oxidation of propanols.

As can be seen from Table 1, in the first minutes of the reaction, the relative yields of the products of C–H and C–C bond oxidation in propanol are higher than those at the end of a run. This indicates that the primary reaction products are unstable and can undergo further oxidation. When cyclohexane was introduced into the reaction medium as a competitive substrate, the amounts of the substrate consumed and the sum of C–H and C–C bond oxidation products matched satisfactorily (at the same extent of hydrogen peroxide decomposition of 65%) and the relative yields of the products of C–C bond rupture increased nearly 4 times, from 19 to 70% (see Table 1). This is due to a decrease in the total alcohol consumption based on consumed hydrogen peroxide. At the same time, the absolute yield of the products of C–C bond rupture changed slightly. As follows from data in Table 1, the yields of ethanol in the

reaction without cyclohexane and with cyclohexane (1 mol/l) added were 13 and 15 mmol/l, respectively.

When aqueous acetonitrile was replaced by the dried solvent, the relative yield of the products of C–C bond rupture substantially decreased in the case of primary alcohols and dropped almost to zero in the case of iso-alcohols. When hydrogen peroxide was replaced by *tert*-BuOOH, the oxidation rate for 1-propanol nearly halved and the fraction of the products of C–C bond rupture decreased by an order of magnitude, the amount of consumed substrate being the same.

Detailed analysis shows that the products of oxidation of 1-propanol and 2-propanol are shorter alkylhydroperoxide, alcohol, and aldehyde; the fractions of ROOH and ROH change from 0 to 100%, and that of R'O is at most 30%. The same features were found for the oxidation of C_4 and C_6 alcohols. In some cases, namely, at a low concentration of $Fe(ClO_4)_3$ (0.4 mmol/l), at concentrations of initial C_4 or C_6 alcohol higher than 1 mol/l, and in the presence of cyclohexane (≥ 0.8 mol/l), lower alkanes were formed in

Table 1. Products of oxidation of propanols in the system $Fe(ClO_4)_3 + H_2O_2$ in acetonitrile at a room temperature. ($[Fe(ClO_4)_3] = 4$ mmol/l, $[H_2O_2] = 0.4$ mol/l)

Conditions	Time, min	Consumption of substrate, mmol/l	Relative yield of the product, %[a]		
			C_1^b	C_2^b	CH_3CH_2CHO or CH_3COCH_3
[1-Propanol] = 130 mmol/l, standard conditions	1.5	20	0[c]	34	51
	10[d]	67	0[c]	19	17
			HCOOH 15		
Cyclohexane additive, 1 mol/l	15[d]	21	0[c]	70	23
Dry acetonitrile as solvent	10	73	0[c]	6	–
Replaced H_2O_2 for *tert*-BuOOH, 400 mmol/l	20	60	0[c]	2	14
[2-Propanol] = 130 mmol/l, standard conditions	1.5	8	40	0[c]	67
	7	38	26	CH_3COOH 22	53
Dry acetonitrile as solvent	1.5	19	0[c]	0[c]	100
	7	31	0[c]	0[c]	42
[2-Propanol] = 1.3 mmol/l, standard conditions	1	–[e]	14 mmol/l[e]	CH_3COOH^e 13.5 mmol/l CH_3CHO 0.5 mmol/l	–

Notes: [a] The yield of products is based on consumed alcohol; the data scatter is 10–25%.
[b] Except for compounds italicized, we show the reaction products, which were analyzed as alcohols after reduction of a sample with $NaBH_4$, that is, those also including the corresponding hydroperoxides and aldehydes.
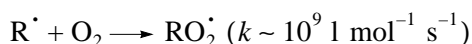[c] The sensitivity of chromatographic analysis allowed for the determination of $[CH_3OH] \geq 1$ mmol/l and $[C_2H_5OH] \geq 0.1$ mmol/l.
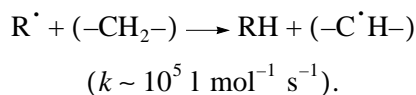[d] $\Delta H_2O_2 = 65\%$.
[e] The substrate consumption is negligible compared to its initial concentration; therefore, the absolute concentrations of the reaction products are presented.

concentrations of $\sim 5 \times 10^{-5}$ mol/l along with the above products.

We conclude from the above data that the alkyl radical is a precursor of the above products. The fact that lower alkylhydroperoxides and the corresponding alkanes are present in the reaction medium under certain conditions provides evidence for that. As was mentioned above, alkanes are formed at either low rates of hydrogen peroxide decomposition (and O_2 formation, respectively) or at a high concentration of methylene groups. It seems that in both cases the reaction

$$R^{\cdot} + O_2 \longrightarrow RO_2^{\cdot} \ (k \sim 10^9 \ l \ mol^{-1} \ s^{-1})$$

becomes noticeable, along with the diffusion-controlled reaction of alkyl radicals with molecular oxygen

$$R^{\cdot} + (-CH_2-) \longrightarrow RH + (-C^{\cdot}H-)$$
$$(k \sim 10^5 \ l \ mol^{-1} \ s^{-1}).$$

Then, we suggested that, when the alkyl radical is eliminated from the alcohol molecule, either aldehyde or carboxylic acid is the product of C–C bond rupture. Analysis showed that, in 1-propanol oxidation, formic acid was formed in addition to propionic acid in the amount comparable with that of ethanol. Acetic acid was found in the products of 2-propanol oxidation in the average amount of 90% with respect to methanol. Special runs with a high concentration (1.3 mol/l) of initial 2-propanol and the analyses of the reaction products, beginning from the first minutes of the run, led to detecting only traces of acetaldehyde (see Table 1). In the case of 3-hexanol, butyric acid was found and its amount grew with time, whereas an intermediate butyric aldehyde was not found.

Data on the composition of the reaction products and the selectivity of C–C bond rupture in C_2–C_6 alcohols are summarized in Table 2. These data show that the C–C bond next to the hydroxyl group undergoes rupture and this rupture in 3-hexanol occurs at the side of the shorter alkyl radical. Among the products of C–C bond rupture formed in the reaction medium, a mixture of alkylhydroperoxide and aldehyde/ketone was found along with carboxylic acid. We also found that, other conditions being equal, the relative yields of the products of C–C bond rupture in primary alcohols decreased in the series $C_2 > C_3 > C_4 > C_6$.
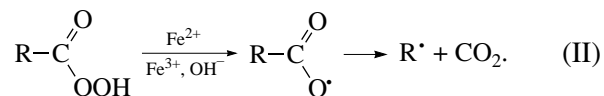
Table 2. Distribution of the products of C–C bond rupture upon the oxidation of C_2–C_6 alcohols in the $Fe(ClO_4)_3$ + H_2O_2 system*

Substrate	C_1	C_2	C_3	C_4	C_5
Ethanol	ROOH ROH R'O HCOOH				
1-Propanol	HCOOH	ROOH ROH R'O			
2-Propanol	ROOH ROH R'O	RCOOH			
1-Butanol	HCOOH		ROOH ROH R'O		
1-Hexanol	**				ROOH ROH R'O
3-Hexanol	**	ROOH ROH R'O		RCOOH	

* The absence of data in the table cell means that the products with such a carbon chain length are either not found or they are present as traces.

** In this case formic acid was not analyzed.

DISCUSSION

It is known that, in the interaction of hydrogen peroxide with iron ions, two types of oxidative species, hydroxyl ($OH^{\cdot}$) and superoxide ($HO_2^{\cdot}$), are formed along with iron complexes containing active oxygen, namely, hydroperoxo, oxo, and other complexes [6].

In the radical oxidation of alcohols, the weakest α-C–H bonds are attacked first and, as a result, hydroxyhydroperoxides, aldehydes/ketones, and other more complicated products of deep oxidation are formed. The radicals thus formed can isomerize through C–C bond rupture. In the oxidation of primary alcohols, the main route of C–C bond rupture producing an alkyl radical is the isomerization of acyl radicals, which are formed in further oxidation of aldehydes:

$$R-C^{\cdot}=O \longrightarrow R^{\cdot} + CO. \tag{I}$$

However, when oxygen is present, its reaction with acyl radical will be dominating because the activation energy of this reaction is close to zero, whereas the activation energy of reaction (I) is ~ 50 kJ/mol [7]. As a result, a peracid is formed from an aldehyde and it can also decompose into an alkyl radical and carbon dioxide under the action of Fe(II) ions [8]:

$$R-C\underset{OOH}{\overset{O}{\big\langle}} \xrightarrow[Fe^{3+},\ OH^-]{Fe^{2+}} R-C\underset{O^{\cdot}}{\overset{O}{\big\langle}} \longrightarrow R^{\cdot} + CO_2. \tag{II}$$

This reaction also seems improbable because the concentration of hydrogen peroxide is higher (0.4 mol/l) than that of peracid, and hydrogen peroxide is quite competitive with peracid for interaction with Fe^{2+}. This conclusion is indirectly confirmed by the sta-

bility of hydroperoxides formed upon the oxidation of alkanes and alcohols in the system under study.

In addition to the above consideration, our experimental data provide evidence against the radical pathway of the formation of the products of C–C bond rupture in this system.

(1) When *tert*-BuOOH is used instead of H_2O_2, C–H bonds in 1-propanol undergo radical oxidation by $RO^\bullet$ radicals, as seen from the consumption of 1-propanol in the reaction and from the simultaneous formation of propanal; the relative yield of the products of C–C bond rupture decreases by an order of magnitude (see Table 1).

(2) Cyclohexane, which is a source of methylene groups, traps hydroxyl radicals and inhibits the oxidation of C–H bonds in the initial alcohol, but this does not change the yield of oxidation products formed by the rupture of C–C bonds. As a result, the relative yields of oxidation products increase depending on the cyclohexane/alcohol ratio to 70% (see Table 1).

The above data suggest that C–C bond rupture occurs with the assistance of oxidants that are incapable of reacting efficiently with cyclohexane. Iron complexes with active oxygen can play this role.

Our findings are in agreement with data reported earlier. Recently, Sakharov and Skibida [9] showed that telomeric fluorinated alcohols are oxidatively deformylated in oxidation by molecular oxygen in the presence of copper salts, that is, the C–C bond in the initial alcohol is broken, leading to formic acid and the corresponding α, ω-dihydroperfluoroalkane.

The highly selective rupture of the C–C bond has been found in the oxidation of α-alkyl-substituted benzyl alcohols in the system iodobenzene + Fe(III)-5,10,15,20-tetrakis(pentafluorophenyl)porphirine in which oxoferryl is the only oxidant [10]. The selective rupture of the C–C bond in aryl-substituted 1,2-ethanediols has been shown [11] in their oxidation with dioxygen in the presence of dihydropyridine and iron porphyrin as a catalyst. Aldehydes and ketones (depending on the substrate structure) were solely obtained by C–C bond rupture in diols. Okamoto *et al.* [11] also concluded that an intermediate diol–Fe(IV) oxo complex preceded the rupture reaction.

One can suggest that in our case the reaction proceeds via a similar mechanism, that is, the C–C bond in alcohol is cleaved through the formation of an alcohol–iron oxo (or peroxo) complex, and this fact substantially changes the reaction selectivity toward the oxidation of C–C bonds. Similar to enzymatic processes, the selectivity in this case is determined by the accessibility of bonds to active oxygen rather than by the bond strength.
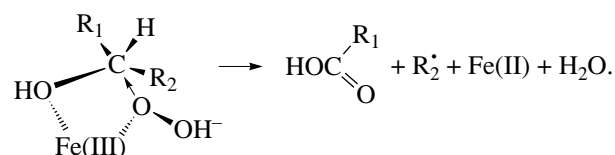
The presence of shortened carboxylic acids in reaction products, which can be formed from the alcohol residue after the elimination of an alkyl radical, gives evidence for the proposed hypothesis. For this mechanism, the three-electron oxidation of alcohol with the

involvement of oxidative intermediate is required. This reaction pathway is more thermodynamically favorable than aldehyde formation, but its realization is possible only for a certain structure of the oxidative intermediate. In our case, it could be Fe(III) hydroperoxo complex or its isoelectron analog, perferryl $Fe^{(III)}(H_2O_2) \rightleftharpoons Fe^{(V)}O(H_2O)$, rather than $Fe^{(IV)}O$, which is a two-electron oxidizing agent.

The participation of Fe(III) hydroperoxo complex in the reaction may be a reason for the influence of water on the efficiency of C–C bond rupture. When a water molecule enters the coordination sphere of iron instead of acetonitrile, it decreases the oxidative potential of the Fe^{3+}/Fe^{2+} pair (from +1.62 V (relative to normal hydrogen element) in dry acetonitrile to +0.4 V in water (at pH 7) [12], thereby increasing the stability of the $Fe^{3+}(OOH)^-$ complex. When H_2O_2 is replaced by *tert*-BuOOH, C–H bond oxidation in alcohol is retained and C–C bond oxidation declines. This fact can also be explained by the involvement of the H_2O_2 molecule in the intermediate that oxidizes mainly C–C bonds.

It is interesting that data reported earlier suggest the participation of iron hydroperoxo complex as an active intermediate in deformylation catalyzed by aromatases, enzymes belonging to the cytochrome P-450 class [13–15], as well as the formation of this complex upon the rupture of C–C bonds in DNA under the action of bleomycine as a catalyst [16–18].

Hence, we can hypothesize that C–C bond rupture occurs in the complex of iron (III) with hydrogen peroxide and alcohol. One of oxygen atoms (active oxygen) can favor C–C bond rupture, forming a complex with the nearest carbon atom (complex with five-coordinated carbon) [19]. Therefore, the C–C bond weakens, the alkyl radical is eliminated, and carboxylic acid is formed from the alcohol residue and the active oxygen according to the following scheme:

Further study is necessary to confirm the above hypothesis.

To conclude, we note that a vast amount of literature is available on the methods of detecting molecular oxidants in the systems based on hydrogen peroxide and iron complex, which are often treated as chemical models for non-heme monooxygenases [20]. Our results show that revealing of the molecular intermediates against the strong background of radical oxidation becomes possible due to the use of substrates capable of coordinating with an iron ion. As a result, the oxidation selectivity becomes unusually high. For example, the rupture of the C–C bond in the presence of weak α-C–H bonds occurs with a high selectivity.

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