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ALKANE OXIDATION BY AN IRON COMPLEX-HYDROGEN PEROXIDE SYSTEM IN ACETONITRILE. THE MODEL OF METHANEMONOOXYGENASE *

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The oxidation of methane and other light alkanes in the system iron complex – hydrogen peroxide has been studied. The efficiency of this system of alkane oxidation depends on water concentration. The catalytic methanol formation from methane with respect to the binuclear iron complex has been observed. The role of iron-oxocomplexes in oxidation of alkanes by methanemonooxygenase and model systems is discussed.

1. Introduction

The enzymes monooxygenases catalyze hydroxylation of nonactivated C–H bonds in various organic compounds [1]. The reaction proceeds according to the scheme:

$$\equiv\text{C–H} + \text{O}_2 + 2\bar{e} + 2\text{H}^+ \xrightarrow{\text{monooxygenase}} \equiv\text{C–OH} + \text{H}_2\text{O}.$$

The best known monooxygenase, cytochrome P-450, plays a key role in the oxidative metabolism of exogeneous compounds including alkanes. The active center of this enzyme contains iron porphyrin and $[\text{FeO}]^{3+}$ appears to be a species which transfers the oxygen atom to the substrate reactant [1]. The structure and mechanism of functioning of another very interesting enzyme – methane-monooxygenase (MMO) – is less studied. This non-heme iron-containing enzyme catalyzes methane and other light alkanes hydroxylation and olefin epoxidation. Inspite of its stronger C–H bonds, methane is oxidized faster than other alkanes. The methane hydroxylation was shown [2] to be the rate determining step; the kinetic isotope effect (KIE) is equal to $k_H/k_D = 5 \pm 0.2$ [3]. From the recent work of Dalton et al. [4] we know that the active center of MMO is similar to that of hemerythrine and contains two closely situated iron atoms.

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It has been reported recently that structural analogs of hemerythrine-binuclear iron complexes can catalyze epoxidation of olefins [5] and the oxidation of alkanes [6,7]. However, no evidence has yet been presented that the active particle is an iron complex rather than free radicals such as OH or HO_2. In this paper we describe the oxidation of methane and its homologs by simple oxoferryl complexes formed in acetonitrile solution in the reaction of iron complexes and H_2O_2 [8,9].

2. Experimental section

A Tsvet-100 gas chromatograph equipped with a flame-ionization detector was used for GLC analysis. All liquid alkanes were distilled over Na before use. Acetonitrile was distilled over P_2O_5. Commercial H_2O_2 (30% in H_2O) was used without preliminary treatment. Anhydrous H_2O_2 and $Fe_2O(bpy)_4Cl_4$ were prepared according to literature procedures [9,10], respectively. All other common materials were reagent grade. The concentration of hydrogen peroxide was determined by titration with permanganate.

A mixture of reagents was placed into the reaction vessel and the reaction took place with continuous stirring at room temperature. A steel autoclave was used for the oxidation of gaseous alkanes to be studied. After stirring for 10 min Na_2SO_3 was added to ensure complete decomposition of hydrogen peroxide and then acetonitrile solution was analyzed by GLC. To measure the complete yield of oxidized products, aldehydes and ketones formed were reduced to alcohols by $NaBH_4$ before GLC analysis.

3. Results and discussion

The reaction of H_2O_2 with Fe(II) compounds in acetonitrile differs from the Fenton system in aqueous media [8,9]. The oxidation of alkanes in the system Fe(II)-H_2O_2 in CH_3CN led to the formation of alcohols and ketone (or aldehyde) [11] (table 1). Methane is found to be oxidized with k_H/k_D equal to 5, i.e. the same as in MMO [3]. The ethanol yield in ethane oxidation with respect to H_2O_2 approaches 15% and the reaction is catalytic with respect to the iron complex. The reaction rate appears to be first order on both catalyst and alkane concentrations.

Regioselectivity in n-hexane oxidation is very different from that by cyt. P-450 model systems based on iron porphyrins [12]. 2-Methylbutane oxidation led to the formation of isomeric i-amylic alcohols together with acetone that confirms the cleavage of C–C bond situated in the neighborhood with tertiary C–H bond. The oxidation of methylcyclopropane mainly to cyclopropylmethanol and the

Table 1
The products from Fe(II)-induced oxidation of alkanes by H_2O_2 in acetonitrile [a]

Alkane	Products	$M \times 10^3$
Methane	Methanol [b]	0.85
Methane-$^2H_4$	Methanol [b]	0.17
Ethane	Ethanol [b]	12.0
n-hexane	Hexan-1-ol [b]	1.0
	Hexan-2-ol [b]	7.3
	Hexan-3-ol [b]	10.0
Cyclohexane	Cyclohexanol	7.4
	Cyclohexanone	6.0
Methylcyclopropane	Cyclopropylmethanol	5.8
	Buten-3-ol	0.5
2-methylbutane	3-methylbutan-1-ol [b]	1.9
	3-methylbutan-2-ol [b]	2.0
	2-methylbutan-2-ol [b]	9.0
	Acetone	14.0

[a] Reactions employed 0.8 M alkane, 0.2 M H_2O_2 (30% in H_2O), 10 mM $HClO_4$ and 5 mM $Fe(ClO_4)_2 \cdot 6H_2O$ in CH_3CN and the products were analyzed by gas chromatography;

[b] Aldehyde (or ketone) was reduced by $NaBH_4$ before the GLC analysis.

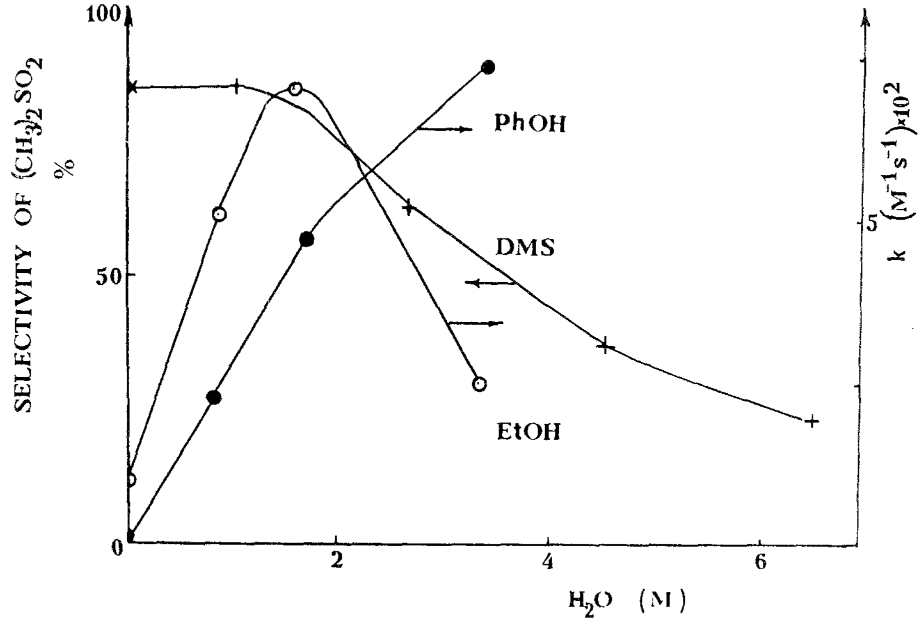

Fig. 1. The dependence of the selectivity of dimethylsulfone (DMS) formation in $(CH_3)_2SO$ oxidation and that of the rate constants of ethanol and phenol formation at ethane and benzene oxidation on water concentration ($[H_2O_2] = 0.2$ M, $[Fe(ClO_4)_2] = 5$ mM in acetonitrile, $[(CH_3)_2SO] = 0.05$ M, $[C_2H_6] = 0.08$ M, $[C_6H_6] = 1$ M).

oxidation of dimethylsulfoxide preferentially to dimethylsulfone indicated that free radicals were not responsible for the main part of the reaction path [9,13].

To check the reaction mechanism in the system Fe(II)-H_2O_2 the dependence of the efficiency of dimethylsulfoxide, ethane and benzene oxidation on water concentration was studied (see fig. 1). Under anhydrous conditions dimethylsulfoxide produced practically only dimethylsulfone, whereas no oxidation of ethane and benzene was observed. The addition of H_2O to this system up to 1.5 M led to the increase in the rate constants of ethanol and phenol formation and did not change the selectivity in dimethylsulfoxide oxidation. At higher H_2O concentrations the yields of sulfone and ethanol diminished, however, that of phenol increased. These data confirmed the suggestion that at high water concentration (with more than 10% H_2O) in acetonitrile this system transformed to the Fenton system generating hydroxyl radicals [9]. Apparently in the system Fe(II)-H_2O_2 there existed the equilibrium between the iron-peroxocomplex under anhydrous condition, iron-oxocomplex in low water concentration and $OH^{\cdot}$ in aqueous media:

$$\mathrm{Fe^{II} + OOH^{-} \rightleftharpoons Fe{-}OOH \overset{H^{+}}{\rightleftharpoons} Fe^{IV}{=}O \overset{H^{+}}{\rightleftharpoons} Fe^{III} + OH^{\cdot}}.$$

The oxidation of alkanes under the conditions shown in table 1 may be due to the presence of iron-oxocomplexes. The catalytic methanol formation from methane was observed in the presence of binuclear iron complex $Fe_2O(bpy)_4Cl_4$ under the following reaction conditions: $[H_2O_2] = 0.84$ M, $[CH_4] = 0.8$ M, and $[Fe_2O(bpy)_4Cl_4] = 0.5$ mM in CH_3CN. The reaction yields approximately 4 mM methanol and 8 mM formaldehyde. Apparently the binuclear iron-oxocomplex may act as an active species in this system.

A similar oxoferryl complex Fe^{IV}–O–Fe^{IV}=O may be expected to be an oxidant formed in the MMO active center. The second iron atom situated near the first one may act as an electron-withdrawing group to increase the electrophilic properties of the reaction center. Preferential oxidation of methane in MMO as compared with other alkanes might be reached by creating a cavity of a definite size, which is stabilized when absorbing the methane molecule (as in clathrate compounds).

Further work on the involvement of binuclear iron complexes to the catalytic methane oxidation is in progress.

References

[1] A.E. Shilov, *Activation of Saturated Hydrocarbons by Transition Metal Complexes* (Reidel, Dordrecht, 1984).
[2] J. Green and H. Dalton, Biochem. J. 236 (1986) 155.
[3] A.I. Pelyashenko-Novokhatnyi, A.N. Grigoryan, A.P. Kovalev, V.S. Belova and R.I. Gvozdev, Dokl. Akad. Nauk SSSR 245 (1979) 1501.

[4] M.P. Woodland, D.S. Patel, R. Cammack and H. Dalton, Biochim. Biophys. Acta 873 (1986) 237.
[5] B.P. Murch, F.C. Bradley and L. Que, Jr., J. Amer. Chem. Soc. 108 (1986) 5027.
[6] N. Kitayama, H. Fukui and Y. Moro-oka, J. Chem. Soc., Chem. Commun. (1988) 485.
[7] J.B. Vincent, J.C. Huffman, G. Christou, Q. Li, M.A. Nanny, D.N. Hendrickson, R.H. Fong and R.H. Fish, J. Amer. Chem. Soc. 110 (1988) 6898.
[8] J.T. Groves and M. van der Puy, J. Amer. Chem. Soc. 98 (1976) 5290.
[9] D.T. Sawyer, L. Spencer and H. Sugimoto, Isr. J. Chem. 28 (1987/88) 3.
[10] D.L. Ghman and D.T. Sawyer, Inorg. Chem. 8 (1969) 900.
[11] V.S. Belova, A.M. Khenkin and A.E. Shilov, Kinetika i Kataliz 29 (1988) 1279.
[12] A.M. Khenkin, O.I. Koifman, A.S. Semeikin, A.E. Shilov and A.A. Shteinman, Tetrahedron Lett. 26 (1985) 4247.
[13] B. Maillard, D. Forrest and K.U. Ingold, J. Amer. Chem. Soc. 98 (1976) 7024.