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Journal of Molecular Catalysis A: Chemical 156 (2000) 85–89

JOURNAL OF MOLECULAR CATALYSIS A: CHEMICAL

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Hydroxylation of alkanes catalysed by a chiral μ-oxo diferric complex: a metal-based mechanism

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Received 27 September 1999; received in revised form 15 October 1999; accepted 28 October 1999

Abstract

The hydroxylation of alkanes by hydrogen peroxide catalysed by a chiral μ-oxo diferric complex has been demonstrated to be stereospecific and partially enantioselective indicating a metal-based mechanism.

Keywords: Hydroxylation; Alkanes; μ-Oxo diferric complex

The selective oxidation of C–H bonds in hydrocarbons is one of the outstanding challenges in catalysis. A biomimetic approach has proved to have the potential to provide new homogeneous complexes with interesting catalytic activities, as shown with model complexes for cytochrome *P*450-dependent monooxygenases or for methane monooxygenase (MMO) [1–5].

MMO is a complex enzymatic system, in which molecular oxygen is reductively activated and alkane oxidation (including methane) is catalysed by a non-heme diiron center [6,7]. Such a center can be chemically reproduced and simple synthetic diferric complexes recently proved to be efficient as catalysts for the oxidation of alkanes by hydrogen peroxide, alkylhydroperoxides and peracids [8–13]. However, little selectivity has been achieved with such systems so far.

Oxidation with alkylhydroperoxides, such as *tert*-butylhydroperoxide (TBHP), catalysed by non-heme iron has probably been the most extensively studied reaction, in the recent past. Its mechanism, which has been a matter of controversy, is now well established [14]. The H-abstracting species is the alkoxyl radical RO° derived from the homolytic cleavage of an alkylperoxo-iron Fe-OOR intermediate. The resulting substrate radical is then believed to react with molecular oxygen, when the reaction is carried out in air, providing the corresponding

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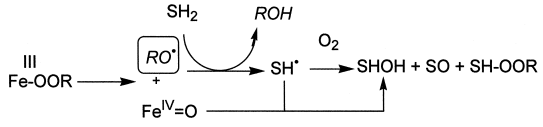
1381-1169/00/$ - see front matter
PII: S1381-1169(99)00402-1

alcohol, ketone and mixed dialkylperoxide. When the reaction is carried out under strictly anaerobic conditions, the substrate radical reacts with the intermediate ferryl intermediate and generates mostly the alcohol (Scheme 2). Since this system involves pure radical chemistry, it is obviously inapt for selective reactions.

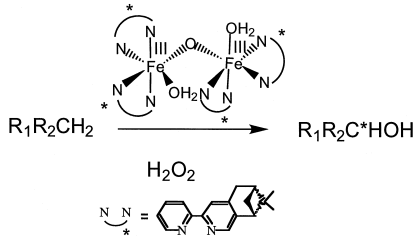


Scheme 2.

It is generally assumed that a combination of a non-heme iron complex and hydrogen peroxide, H_2O_2, also gives radical chemistry, precluding selectivity (Fenton reaction). However, there are a few observations reported that suggest that this assumption might not be true [15–18]. For example, we earlier developed a catalytic system, in which the catalyst is a μ-oxo diferric complex **1**, $Fe_2O(pb)_2(H_2O)_2(ClO_4)_4$, pb = 4,5(−)pinene-2,2′bipyridine [19], which contains a chiral bipyridine derivative as the iron ligand. This complex is able to catalyse an enantioselective oxidation of sulfides into sulfoxides by H_2O_2, with significant enantiomeric excesses [20]. Since this reaction involves an oxygen atom transfer with no covalent bond breakage and no radical intermediate, we reasoned out that enantioselective hydroxylation of alkanes would be a better probe to support the notion that selectivity can be achieved with non-heme iron and H_2O_2-dependent systems. Here we show that with the complex mentioned above, stereospecific and moderate enantioselective hydroxylation could be obtained with H_2O_2 but not TBHP as the oxidant (Scheme 1).

The catalytic properties of complex **1** have been tested during oxidation of a variety of substrates in large excess by using 10 or 20 equivalents of oxidant with respect to the catalyst, in argon-deaerated acetonitrile. This small excess of oxidant was selected to limit molecular oxygen production from dismutation of the oxidant. The results are shown in Table 1 and these allow one to compare H_2O_2- to TBHP-dependent reactions.[1] The mass balance for both systems was calculated in the case of alkane oxidation and found close to quantitative, taking into account the amount of oxygen evolved[2] [21]. The production of molecular oxygen in situ explains why the reactions are not fully anaerobic. Accordingly, ketone formation is the signature for the presence of dioxygen.

With cyclohexane as the alkane probe, TBHP was found to be more efficient than H_2O_2 (compare yields). However, this is a consequence of the production of a large amount of mixed cyclohexyltbutylperoxide, obviously absent from H_2O_2-dependent reactions. With regard to alcohol and ketone formation, the systems are comparable. The presence of air affected the yield of the reaction only in the case of TBHP, for which the yield increased to reach over 100% based on the oxidant (Table 1). Furthermore, H_2O_2 differed from TBHP in terms of kinetic isotopic effects during oxidation of cyclohexane (K.I.E. = 7 and 3.2 for

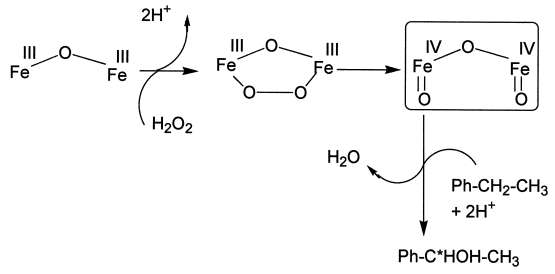


Scheme 1.

[1] Experimental conditions for the catalytic oxidations: **1**/alkane/ROOH(R═H or tBu) = 1:1100:10 or (a) 20 or in acetonitrile; reaction time 15 min. [**1**] = 0.7 mM. 600 equiv. of sulfides are used for the sulfoxidation reaction. Yields are based on the oxidant. Ar corresponds to strict anaerobic conditions, obtained in a glove box. ∗Solvent = EtOH. (b) no cyclohexylperoxide could be detected.

[2] Measurement of dioxygen evolution has been done by volumetry. The presence of O_2 has already been shown in TBHP systems (see Ref. [18]) and in related systems.

TBHP and H_2O_2, respectively). Another difference concerns tertiary to secondary carbon selectivity during oxidation of adamantane (C3/C2 = 10 and 3.5 for TBHP and H_2O_2, respectively). This demonstrates that C–H abstraction is the limiting step of the reaction, in both cases, and suggests that the active abstracting species are different. In the case of H_2O_2 it is interesting to note that the above numbers are clearly different from those obtained with hydroxyl radicals as the abstracting species but close to a recently reported Fe(III) porphyrin/H_2O_2 system [22,23].



Scheme 3.

Table 1
Catalytic properties of complex **1** with peroxides as oxidants

		OH	O	O-Otbu	
	TBHP/Ar	3	1	6	55
	H_2O_2/Ar	3	1	-b)	25
	TBHP/Air	7.2	8.2	2	130
	H_2O_2/Air	2.6	1	-b)	23
		OH	OH	others	
	TBHP	0.8	0.5	2	30
	H_2O_2	2	-	1	33
	H_2O_2	-	0.7	0.8	15
		OH	O	ee%	
	TBHP/Ar	2.1	1.8	0	57
	H_2O_2/Ar	1.8	1.5	15*	48
		OH	O	ee%	
	TBHP/Ar	2.2	0.7	0	36
	H_2O_2/Ar	1.4	1.5	7	44
Br, S		Br, S, O		ee%	
	TBHP/Ar	2		0	20
	H_2O_2/Ar	9		40	90
		O			
	TBHP/Ar[a]	1.2			6
	H_2O_2/Ar[a]	6			30

See Footnote 1 for experimental conditions. (a) 20 equiv. of oxidant; (b): no cyclohexylperoxide could be detected.

The most impressive difference between the two systems concerns the selectivity of the hydroxylation reactions. This property was investigated with 1,2-dimethylcyclohexane (DMC), ethylbenzene and 1,1′dimethylindane as substrate probes. First, as shown in Table 1, only the H_2O_2-dependent system was stereospecific since the *cis* configuration and the *trans* configuration was retained in the tertiary alcohol product during oxidation of *cis*-DMC and *trans*-DMC, respectively. Such a stereospecific oxidation has been observed during oxidation by H_2O_2 catalysed by a mononuclear Fe(II)TPA complex but not with hydroxy radicals [16,24]. Second, only H_2O_2 gave a moderate but significant enantiomeric excess during oxidation of ethylbenzene (7%) and dimethylindane (15%).[3,4] With a sulfide as a substrate, we confirmed that TBHP was unable to give an enantioselective oxidation, whereas H_2O_2 gave an enantiomeric excess of 40%.

[3] Oxidation of alcohols by **1**/H_2O_2 is rather poor precluding kinetic resolution in this case. In addition, the kinetics of oxidation by H_2O_2 for the two enantiomers of 1-phenyl ethanol, were found identical.

[4] The enantiomeric excesses have been measured using a Chiraldex GC column. Racemic mixture of alcohols or the mixture of TBHP-dependent alkane oxidation leads to 1:1 ratio of the respective GC peaks.

With cyclooctene as an olefin probe, we show that H_2O_2 is a much better epoxidizing agent than TBHP, when associated to complex **1**. We did not find evidence for the oxidation at the allylic positions.

This is the first report of an enantioselective catalytic hydroxylation by hydrogen peroxide using a non-heme iron complex, with chiral ligands, as a catalyst. Only few examples of enantiocatalysis of alkane hydroxylation have been reported [25,26]. Although the enantiomeric excesses are still moderate, this unambiguously shows that a non-heme diiron/H_2O_2 combination may not only be a source of hydroxyl radicals (Fenton reaction), precluding selectivity, but also involve metal-based chemistry. The mechanism remains to be established but it probably involves a diiron–peroxo complex as a first intermediate (Scheme 3). Such a peroxo complex has indeed been previously observed during reaction of $H_2O_2$with complex **1**, at low temperature, and characterized by UV–visible and Raman resonance spectroscopy [20]. Furthermore, there is a number of reported μ-peroxo non-heme diiron complexes that have been crystallographically characterised [27–29]. The peroxo complex might be a precursor of a high-valent iron complex able to control the stereochemistry of the reaction, explaining the observed enantioselectivity. However, non-selective hydroxylation reactions involving free radical and dioxygen are competing with the above process.

Our data also clearly confirm the free radical mechanism of the oxidations by the non-heme iron/TBHP system, consistent with Scheme 2. It is a poor epoxidizing agent and does not display any stereospecificity and enantioselectivity during sulfide and alkane oxidation.

The fact that the selectivity of the oxidations by H_2O_2 catalysed by simple iron complexes can be controlled, offers new possibilities for the design of enantioselective catalytic systems. Obviously, further investigation should focus on the improvement of the enantiomeric excesses reported here.

Acknowledgements

This work was financed by the Iron–oxygen protein network (ERBMRFXCT980207) of the T.M.R. program of E.U and The Rhone Alpes Region (Emergence Program).

References

[1] P.R. Ortiz de Montellano (Ed.), Cytochrome *P*-450: Structure, Mechanism and Biochemistry, Plenum, New York, 1986.
[2] B. Meunier, Chem. Rev. 92 (1992) 1411.
[3] D. Dolphin, T. Traylor, L.Y. Xie, Acc. Chem. Res. 30 (1997) 251.
[4] M. Fontecave, S. Ménage, C. Duboc-Toia, in: Coord. Chem. Rev., 1998, p. 1555.
[5] Y. Dong, L. Que Jr., Acc. Chem. Res. 29 (1996) 150.
[6] A.C. Rozenweig, S.J. Lippard, Acc. Chem. Res. 27 (1994) 229.
[7] J.B. Wallar, J.D. Lipscomb, in: Chem. Rev.,1996, p. 2625.
[8] R.M. Buchanan, S. Chen, J.F. Richardson, M. Bressan, L. Forti, A. Morvillo, R.H. Fish, Inorg. Chem. 33 (1994) 3208.
[9] J. Kim, R.G. Harrison, C. Kim, L. Que Jr., J. Am. Chem. Soc. 118 (1996) 4373.
[10] C. Duboc-Toia, S. Ménage, C. Lambeaux, M. Fontecave, Tetrahedron Lett. 38 (1997) 3727, and references herein.
[11] M. Kodera, H. Shimakoshi, K. Kano, in: J. Chem. Soc., Chem. Commun.,1996, p. 1737.
[12] D.T. Sawyer, C. Kang, A. Liobet, C. Redman, J. Am. Chem. Soc. 115 (1993) 5817.
[13] D.H.R. Barton, S.D. Bévière, W. Chavasiri, E. Cshuai, D. Doller, W.-G. Liu, J. Am. Chem. Soc. 114 (1992) 2147.
[14] P.A. MacFaul, K.U. Ingold, D.D.M. Wayner, L. Que Jr., J. Am. Chem. Soc. 119 (1997) 10594.
[15] J.T. Groves, T.E. Nemo, J. Am. Chem. Soc. 105 (1983) 6243.
[16] C. Kim, J. Kim, L. Que Jr., J. Am. Chem. Soc. 119 (1997) 5964.
[17] Y. Kaku, M. Otsuka, M. Ohno, Chem. Lett. (1989) 611.
[18] S. Ménage, J.-M. Vincent, C. Lambeaux, M. Fontecave, J. Mol. Catal. 113 (1996) 61.
[19] P. Hayoz, A. von Zelewsky, H. Stoeckli-Evans, J. Am. Chem. Soc. 115 (1993) 5111.
[20] C. Duboc-Toia, S. Ménage, R.Y.N. Ho, L. Que Jr., C. Lambeaux, M. Fontecave, Inorg. Chem. 38 (1999) 1261.
[21] J. Kim, C. Kim, R.G. Harrison, E.C. Wilkinson, L. Que Jr., J. Mol. Catal A: Chem. 117 (1997) 83.
[22] G.V. Buxton, C.L. Greenstock, W.P. Helman, A.B. Ross, J. Phys. Chem. Ref. Data 17 (1988) 513.
[23] W. Nam, Y.M. Goh, Y.J. Lee, M.H. Lim, C. Kim, Inorg. Chem. 38 (1999) 3238.
[24] A.M. Kenkin, A.E. Shilov, New J. Chem. 119 (1997) 5964.

[25] J.T. Groves, P. Viski, J. Am. Chem. Soc. 111 (1989) 8537.
[26] K. Hamachi, R. Irie, T. Katsuki, Tetrahedron Lett. 37 (1996) 4979.
[27] K. Kim, S.J. Lippard, J. Am. Chem. Soc. 118 (1996) 4914.
[28] T. Ookubo, H. Sugimoto, T. Matsuda, T. Sato, K. Tanaka, Y. Maeda, H. Okawa, Y. Hayashi, A. Uehara, M. Suzuki, J. Am. Chem. Soc. 118 (1996) 4914.
[29] Y. Dong, S. Yan, V.G. Young, L. Que Jr., Angew. Chem., Int. Ed. Engl. 35 (1996) 618.