

# Alkane oxidation catalyzed by $\mu$ -oxo bridged diferric complexes: an overall mechanism

Stéphane Ménage, Jean-Marc Vincent, Claude Lambeaux, Marc Fontecave \*

*Laboratoire d'Etudes Dynamiques de la Structure et de la Sélectivité, URA 332, Université Joseph Fourier, BP 53X,  
38041 Grenoble Cedex, France*

## 1. Introduction

Saturated hydrocarbons are among the most difficult substrates to oxidize selectively [1]. However, nature has evolved a host of enzymes which carry out this task [2,3] under mild conditions, with non-heme iron enzymes emerging as a major subclass of this category [4]. Enzymatic oxidations can be effected with either dioxygen, in the presence of a source of electrons, or two-electron oxidants such as hydroperoxides or  $H_2O_2$  [5–7]. As a consequence, alkane oxidation by hydroperoxides catalyzed by non-heme iron model complexes has recently attracted a great deal of interest.

The catalytic system developed in Barton's [8,9] and Sawyer's [10] laboratories, the so-called Gif system and its derivatives, is the most extensively studied one. The key characteristic of this system resides in the solvent, a mixture of pyridine and acetic acid, which is responsible for the selectivity for secondary C–H positions,

with respect to tertiary ones as far as the oxygenated products are concerned, and for the high ketone to alcohol ratio (Table 1). In general, the catalysts are simple iron salts, but the catalytic activity is greatly increased when iron ligands, such as picolinate or dipicolinate, are present in the reaction mixture [11,12]. Representative results of cyclohexane oxidation by *t*-butyl hydroperoxide (TBHP) are shown in Table 1. However, it is now quite clear that such a solvent is a source of a variety of problems and has no future for industrial applications. Moreover, the stability of the catalysts is questionable and has been shown recently to be quite weak [13]. In addition, the structure of the oxidizing species remains unknown.

More recently, Que and co-workers have characterized some non-heme mononuclear iron catalysts with tripodal (2-pyridylmethyl)amine (TPA) ligands and have employed them together with TBHP to oxidize cyclohexane and adamantane in acetonitrile at room temperature [14,15]. Some results are shown in Table 1. Comparable amounts of alcohol and ketone are produced as well as a large amount of cyclohexyl *t*-butyl peroxide.

Methane monooxygenase is one of the most fascinating non-heme iron enzymes. Its dinuclear iron center, which is now structurally characterized [16,17], catalyzes the oxidation of

Abbreviations: TPA, tris(2-pyridylmethyl)amine; tmima, tris(1-methylimidazol-2-yl)amine; TBHP, *t*-butylhydroperoxide; CHP, cumene hydroperoxide; bipy, 2,2'-bipyridine; phen, 1,10-phenanthroline; 4,4'-Me<sub>2</sub>bipy, 4,4'-dimethyl-2,2'-bipyridine; OAc, acetate anion; pym, 2-pyridylimidazole; HQ, 8-hydroxyquinoline; MeCO<sub>2</sub>bipy, 4,4'-dimethoxycarbonyl-2,2'-bipyridine

\* Corresponding author.

Table 1  
Product distributions for the iron catalyzed oxidation of cyclohexane by TBHP

Catalyst(mM) <sup>a</sup>	Ratio: cat/ox/sub	Conditions	Products	TN/h <sup>b</sup>	% yield <sup>c</sup> (reaction time)	Ref.
GoAgg V Fe(NO <sub>3</sub> ) <sub>3</sub> (14.5) + 3PA	1/20/100	pyr/HOAc/air	cyOH cyONE	0.07 1.3	107 (16 h)	[11]
[Fe(TPA)Cl <sub>2</sub> ] <sup>+</sup> (0.7)	1/1100/140	CH <sub>3</sub> CN/Argon	cyOH cyONE cyOObu cyCl	7.5 6 4 0.5	37 (2 h)	[14]
[Fe <sub>2</sub> O(OAc)(TPA) <sub>2</sub> ] <sup>3+</sup> (0.7)	1/1100/140	CH <sub>3</sub> CN/Argon	cyOH cyONE cyOObu	36 44 64	34 (0.25 h)	[20]
[Fe <sub>2</sub> O(H <sub>2</sub> O) <sub>2</sub> (tmima) <sub>2</sub> ] <sup>4+</sup> (1.0)	1/770/100	CH <sub>3</sub> CN/O <sub>2</sub>	cyOH cyONE	3.7 3.8	nr <sup>*</sup>	[21]

<sup>a</sup> PA, picolinic acid; TPA, tris(2-pyridylmethyl)amine; tmima, tris((1-methylimidazol-2-yl)methyl)amine.

<sup>b</sup> TN/h, turnover number (calculated as moles of product per mole of catalyst per hour).

<sup>c</sup> Total yield based on TBHP.

\* No reported.

a variety of alkanes, including methane [18,19]. This led several groups to explore model complexes (containing the Fe–O–Fe unit) as a possible new class of catalysts for the oxidation of saturated hydrocarbons by hydroperoxides. In Table 1 are selected the best results obtained by Que and co-workers, with their Fe<sub>2</sub>O(TPA)<sub>2</sub>(OAc)(ClO<sub>4</sub>)<sub>3</sub> catalyst [20], and by Fish and co-workers, with their Fe<sub>2</sub>O(tmima)<sub>2</sub>(OAc)(ClO<sub>4</sub>)<sub>3</sub> catalyst [21] during oxidation of cyclohexane by TBHP in acetonitrile. The few examples reported in Table 1 raised the question of the necessity to use a dinuclear ferric catalyst (compare di- and mononuclear complexes containing TPA as a ligand).

Recent work from our laboratory demonstrated that simple bipyridine or phenanthroline ligands allowed to prepare a wealth of stable dinuclear iron complexes, with excellent catalytic activities during oxidation of alkanes by TBHP [22]. This report details our investigation into these systems, with special attention to the relation between the structure of the complexes and their reactivity, to the mechanism of peroxide decomposition, substrate oxidation and to the role of molecular oxygen in the reaction.

Previous work [23,24] is extended here also with the comparison of different oxidants, TBHP, CHP and H<sub>2</sub>O<sub>2</sub>.

## 2. Experimental procedures

### 2.1. Physical methods

Visible spectra were recorded on a Uvikon 930 spectrophotometer. <sup>1</sup>H-NMR spectra were recorded on a Bruker WP 200 spectrophotometer at 200 MHz. Chemical shifts (ppm) were referred to residual protic solvent peaks. EPR spectra were recorded with a Varian E102 at *T* = 4 K or a Bruker ESP 300E at *T* = 100 K and ambient temperature (spin trapping experiments). Gas chromatography was performed on a Perkin Elmer Autosystem instrument connected to a Shimadzu chromatopac CR6A with an FID detector using an OV 17 capillary column (30 m). HPLC were performed on a Waters HPLC system using a waters 440 Absorbance detector and a 660 model solvent programmer.

## 2.2. Synthetic methods

The synthesis of all the complexes  $\text{Fe}_2\text{O}(\text{L})_n(\text{X})_m(\text{ClO}_4)_z$  have been previously described [22,24]. They were prepared by self assembly method: an iron salt  $\text{Fe}(\text{ClO}_4)_3 \cdot 9\text{H}_2\text{O}$  was mixed in a polar solvent (MeOH or  $\text{H}_2\text{O}$ ) with the bidentate nitrogen ligands and when required with a carboxylate (acetate or a dicarboxylate, *m*-phenylenedipropionate dianion). Sometimes, a base such as triethylamine was required in order to provide the oxo bridge formation. All these complexes exhibit satisfactory elemental analysis and expected properties of  $\mu$ -oxo diiron(III) complexes (such as high antiferromagnetic coupling, weak oxo to iron LMCT in the visible spectrum, Resonance Raman spectra with enhanced Fe–O vibrations characteristic of mono-, di- or tribridged complexes). Some have been characterized by electrospray mass spectroscopy. In addition, their purity have been checked by EPR spectroscopy, the presence of mononuclear species being detected by this technique.

## 2.3. Oxidation procedure

Standard reactions were carried out under inert atmosphere (Argon) as follows. The complexes (3.5  $\mu\text{mol}$ ) were dissolved in 4.5 ml of  $\text{CH}_3\text{CN}$  containing either 3.83 mmol (1100 eq.) of cyclohexane, cyclooctane, heptane, cumene or 1.9 mmol (550 eq.) of toluene, dimethyl sulfide or 1.05 mmol (300 eq.) of dimethyl sulfoxide and *trans*-stilbene or 0.4 mmol (115 eq.) of adamantane (benzene was added for dissolution of the substrate) or 3.83 mmol or 70  $\mu\text{mol}$  (1100 or 20 eq.) of alcohols (benzyl alcohol, cyclooctanol, 1-phenylethanol) unless specified in the text. The reaction was started by adding 0.5 mmol of TBHP, CHP or  $\text{H}_2\text{O}_2$  (ratio  $\text{Fe}_2$  complex/oxidant = 1 : 140). After 30 min stirring, 50  $\mu\text{mol}$  of an internal standard (acetophenone or naphthalene) were added to the reaction mixture and the products were quantified by GC and verified by GC/MS. Unam-

biguous identification of the products was made by comparison with pure compounds, prepared independently or commercially available. Only in the case of cyclohexane, the mixed dialkyl peroxide was characterized and quantified. Kinetics experiments were carried out as previously [22].

In some experiments, argon was continuously bubbled through the solution during the reaction, reduced pressure (30–40 mmHg) was continuously applied to the reaction mixture or the solutions were saturated with dioxygen.

## 2.4. Primary isotope effect

Under an inert atmosphere, 1.75  $\mu\text{mol}$  of complex dissolved in  $\text{CH}_3\text{CN}$  (2.4 ml) was stirred with 0.92 mmol (100  $\mu\text{l}$ ) each of cyclohexane and cyclohexane- $d_{12}$ . TBHP (0.25 mmol) was then added and the solution stirred for 30 min (ratio of  $\text{Fe}_2$  complex/cyclohexane/cyclohexane- $d_{12}$ /TBHP = 1 : 550 : 550 : 140). The products were quantitated by GC (acetophenone as standard). Overall  $k_{\text{H}}/k_{\text{D}}$  was calculated as the alcohol + ketone/deuteriated alcohol + ketone ratio.

## 2.5. Decomposition of CHP in the presence of $\text{Fe}_2\text{O}(\text{phen})_4(\text{H}_2\text{O})_2(\text{ClO}_4)_4$

The reaction solution was first eluted through a SEP-PAK cartridge in order to separate the catalyst from the organic products. The resulting solution was then injected into a Waters HPLC system and eluted with a methanol/water mixture (50%, v/v, 1 ml/min) through a  $\mu$ Bondapak C18 column. Products were detected by UV absorption at 254 nm. Acetophenone and 2-phenyl-2-propanol were quantitated using benzylacetone as an internal standard, with correction for their respective absorbance at 254 nm.

## 2.6. Spin trapping experiments

In a standard experiment 2  $\mu\text{l}$  of 5,5-dimethylpyrroline 1-oxide (DMPO) per ml of reaction

solution was added before addition of the oxidant (TBHP or CHP) under argon. A multiplet EPR signal was obtained at 100 K corresponding to the alkyl peroxide adduct (DMPO-OOR). In order to obtain a well resolved EPR signal, the same reaction was performed in the presence of water (30%, v/v) and was recorded at room temperature under argon. The isotropic spectrum with a quadruplet signal (relative intensities of 1:2:2:1) unambiguously confirmed the presence of peroxy radicals during the oxidation process (the hyperfine constant were found equal to  $a_N = 14.5$  G;  $a_H = 10.5$  G;  $a_h = 1.3$  G for TBHP).

### 3. Results

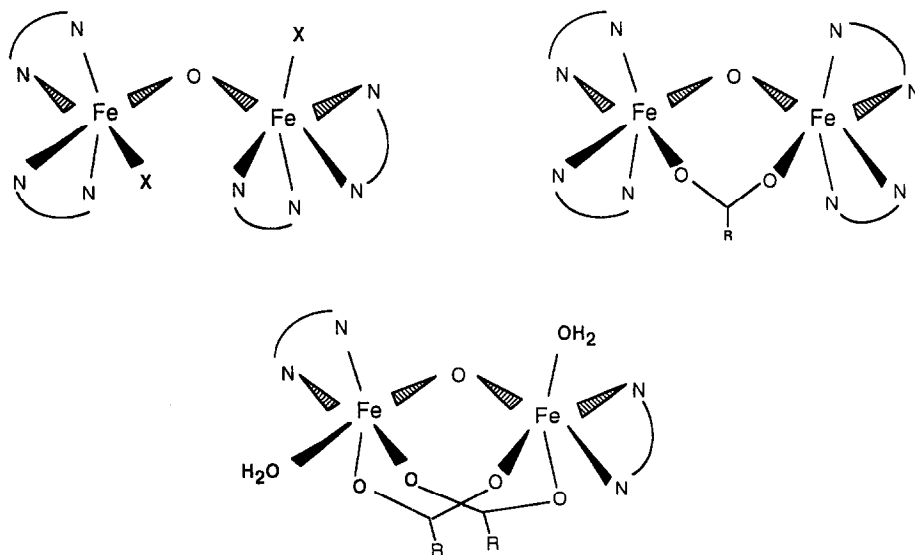
#### 3.1. Structure / reactivity study

We have prepared several series of complexes  $\text{Fe}_2\text{O}(\text{L})_n(\text{X})_m(\text{ClO}_4)_z$ , containing the Fe–O–Fe unit, where a bidentate nitrogen ligand

and noted L and a potentially labile ligand noted X were varied in order to understand how the catalytic activity during oxidation reactions can be modulated by the number of bridges in the diferric unit, the basicity of L and the exchangeability of X. The structures of the catalysts are shown in Scheme 1.

Alkane oxidation has been typically tested in the presence of 0.7 mM of the catalyst with a 1100-fold molar excess of the substrate and a 140-fold molar excess of the oxidant under argon. With cyclohexane as the substrate and *tert*-butyl hydroperoxide as the oxidant, the major results can be summarized as follows (Table 2):

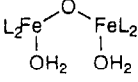
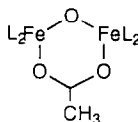
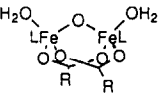
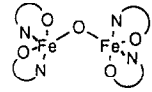
(1) The monobridged  $\text{Fe}_2\text{O}(\text{L})_4(\text{X})_2(\text{ClO}_4)_4$  complexes were very powerful catalysts and their remarkable efficiency greatly depended on the lability of X. The presence of an accessible coordination site allowed the binding of the alkylhydroperoxide to iron. Cyclohexane was oxidized into cyclohexanol, cyclohexanone and



Scheme 1. Molecular structures of the catalysts  $\text{Fe}_2\text{O}(\text{L})_n(\text{X})_m(\text{ClO}_4)_z$ . L stands for a bidentate nitrogen ligand: 2,2'-bipyridine (bipy); 4,4'-dimethyl-2,2'-bipyridine ( $44'\text{Me}_2\text{bipy}$ ); 2-pyridylimidazole (pym); 4,4'-dimethoxycarbonyl-2,2'-bipyridine ( $\text{MeCO}_2\text{bipy}$ ); 1,10-phenanthroline (phen); 8-hydroxyquinoline (HQ).

Table 2

Cyclohexane oxidation catalyzed by TBHP in the presence of various  $\mu$ -oxo diferric  $\text{Fe}_2\text{O}(\text{L})_n(\text{X})_m(\text{ClO}_4)_z$  complexes

catalyst	L/X	products <sup>(a)</sup>			%yield <sup>(b)</sup> (reaction time)	$V_0$ <sup>(c)</sup>
		CyOH	Cy=O	CyOObu		
	bipy/H <sub>2</sub> O	17	19	7	44 (7min)	17
	bipy/OAc	18	15	6	38 (2h)	2
	44'Me <sub>2</sub> bipy/OAc	27	24	7	57 (10min)	8
	pym/OAc	19	21	<1	42 (24h)	0.1
	bipy/OAc	19	16	<1	37 (10h)	0.15
	MeCO <sub>2</sub> bipy/OAc	21	16	<1	40 (24h)	0.10
	bipy/MPDP	17	15	<1	35 (20h)	0.10
	HQ	0	0	0	0	0

<sup>a</sup> Numbers are moles of product/mol of catalyst.<sup>b</sup> Yields based on TBHP; reaction time is the time when all oxidant has disappeared.<sup>c</sup>  $V_0$  is initial rate in turnover numbers per minute.

cyclohexyl *t*-butylperoxide. The yield for cyclohexane oxidation exceeded 50% based on the oxidant and the initial rate is 17 TN · min<sup>-1</sup> with  $\text{Fe}_2\text{O}(\text{bipy})_4(\text{H}_2\text{O})_2(\text{ClO}_4)_4$ , which thus represented the most efficient non-heme iron catalyst reported so far. When water was replaced by less exchangeable ligands such as fluoroacetate, chloride or bromide, the complex was much less active (2% yield after 2 h reaction).

(2) The dibridged  $\text{Fe}_2\text{O}(\text{L})_4(\text{OAc})(\text{ClO}_4)_3$  complexes also afforded very good yields for cyclohexane oxidation but with significantly slower reaction rates [21,22]. It has been well established that the bridging bidentate acetato ligand is readily exchangeable [22].

(3) With the tribridged complexes  $\text{Fe}_2\text{O}(\text{L})_2(\text{OAc})_2(\text{H}_2\text{O})_2(\text{ClO}_4)_2$ , oxidation rates were two orders of magnitude slower than those obtained with the monobridged diiron catalysts.

One should note that the comparison with mono- and dibridged complexes is not obvious since now iron has a very different environment with only one L ligand. With such slow catalysts, the yield of dialkylperoxide formation is very small, when compared to the corresponding yields obtained with the fast monobridged catalysts. Another slow oxidizing system using  $\text{Fe}_2\text{O}(\text{tmima})_2(\text{OAc})(\text{ClO}_4)_3$  as a catalyst did not generate coupled products as well [25].

(4) Reaction yields and, to a much larger extent, reaction kinetics could be smoothly modulated by variations of the bidentate nitrogen L ligand. In the case of the monobridged catalysts, the reaction rates increased as the basicity of L decreased, according to the following order: bipy ( $pK = 4.42$ ) > 44'Me<sub>2</sub>bipy ( $pK = 4.77$ ) > phen ( $pK = 4.93$ ) [26], pointing to the Lewis acidity of the iron center as a key parameter for its reactivity. The situation was

more complicated with one or two additional carboxylato bridges and no correlation between catalytic activity and L basicity could be found. However, imidazole-containing ligands such as 2-pyridylimidazole (Table 2) had a negative effect on the kinetics. Also, the comparison between  $\text{Fe}_2\text{O}(\text{tmima})_2(\text{OAc})(\text{ClO}_4)_3$  and  $\text{Fe}_2\text{O}(\text{TPA})_2(\text{OAc})(\text{ClO}_4)_3$  illustrated this point.

(5) Increasing the number of electron-donating negatively charged oxygen ligands, such as carboxylates and phenolates, thus decreasing the N:O ratio in the iron coordination sphere, decreased the activity of the diiron complexes. This can be rationalized in terms of decreased Lewis acidity of the iron center and decreased positive charge, making TBHP more difficult to bind. It is quite clear that phenoxo ligands have to be excluded, on the basis of the results obtained with hydroxyquinoline as a bidentate ligand.

(6) Under oxidative conditions, all catalysts were inactivated (80% inactivation after one run) whatever the catalyst was (Table 2). Spectroscopic studies ( $^1\text{H}$  NMR, EPR, UV-visible) have shown that, after completion of the reaction catalyzed by  $\text{Fe}_2\text{O}(\text{bipy})_4(\text{H}_2\text{O})_2(\text{ClO}_4)_4$ , a diferric species (half of total iron based on NMR titration) was still present in solution, with a structure slightly different from that of the starting material and with a weaker catalytic efficiency. Moreover, unidentified mononuclear high spin mononuclear species have been detected by EPR. The low spin  $\text{Fe}^{\text{II}}(\text{L})_3$ , as reported earlier [22], was not the major product of catalyst decomposition. We are currently trying to improve the stability of the catalyst by adding bulky groups to the bipyridine.

(7) A high selectivity of the oxidizing system for the tertiary C–H bonds versus secondary ones, determined with adamantane as a substrate, has been observed. A  $C_3/C_2$  ratio value of about 10 was observed for  $\text{Fe}_2\text{O}(\text{bipy})_4(\text{H}_2\text{O})_2(\text{ClO}_4)_4$ ,  $\text{Fe}_2\text{O}(\text{phen})_4(\text{H}_2\text{O})_2(\text{ClO}_4)_4$ ,  $\text{Fe}_2\text{O}(\text{bipy})_4(\text{OAc})(\text{ClO}_4)_3$ ,  $\text{Fe}_2\text{O}(44'\text{Me}_2\text{bipy})_4(\text{H}_2\text{O})_2(\text{ClO}_4)_4$ .

The intermolecular primary isotopic effect

was large, attesting that hydrogen abstraction from the substrate was the limiting step of the reaction. Accordingly, formation of intermediate substrate radicals has been established by the accumulation of chloro adducts when  $\text{CCl}_4$  was present in the reaction mixture. The hydrogen abstracting power of the catalyst is modulated by the iron environment. The overall  $k_{\text{H}}/k_{\text{D}}$  values were 7.1, 7.8, 6.1, 5.9 for  $\text{Fe}_2\text{O}(\text{bipy})_4(\text{H}_2\text{O})_2(\text{ClO}_4)_4$ ,  $\text{Fe}_2\text{O}(\text{phen})_4(\text{H}_2\text{O})_2(\text{ClO}_4)_4$ ,  $\text{Fe}_2\text{O}(\text{bipy})_4(\text{OAc})(\text{ClO}_4)_3$  and  $\text{Fe}_2\text{O}(\text{phen})_4(\text{OAc})(\text{ClO}_4)_3$ , respectively. Then, increasing the number of negatively charged oxygen ligands into the catalyst caused a decrease of its selectivity for tertiary C–H bonds and an increase of its oxidizing power.

(8) The  $\text{Fe}_2\text{O}(\text{bipy})_4(\text{H}_2\text{O})_2(\text{ClO}_4)_4/\text{TBHP}$  system was also efficient for the oxidation of other alkanes (toluene, ethylbenzene, cumene, cyclooctane, adamantane) and sulfides, sulfoxides and alcohols (see Table 3). Toluene was less reactive than cyclohexane or cyclooctane in spite of the lower energy of the C–H bond. This trend is also observed in the Gif chemistry [27]. Linear alkanes were also substrates with the formation of excess ketones over alcohols, with poor regioselectivity. No primary positions were attacked.

The alcohol/ketone ratio depended on the alkane used. The formation of ketone or aldehyde prevailed in the case of cyclooctane or toluene but equimolar amounts of alcohol and ketone were formed during oxidation of cyclohexane or adamantane (considering only the secondary positions). It is interesting to note that cumene was oxidized into equal amounts of 2-phenyl-2-propanol and acetophenone. The latter is a degradation product of the cumoxyl radical.

Alcohol to ketone conversion was very efficient with a 70% yield after 5 min reaction. Even, when the alcohol (cyclooctanol or benzyl alcohol) was the limiting reactant (20 eq.), the yield based on the alcohol was 60% in less than 10 min.

Benzene was not oxidized by TBHP under

Table 3

Products distribution in the oxidation of alkanes, related alcohols and sulfur compounds by TBHP catalyzed by  $\text{Fe}_2\text{O}(\text{bipy})_4(\text{H}_2\text{O})_2(\text{ClO}_4)_4$  under argon <sup>a</sup>

Substrates	Products (TN) <sup>b</sup>	% yield <sup>c</sup>
Cumene	acetophenone (20)	39
	2-phenyl-2-propanol (15)	
Toluene	benzaldehyde (6)	10
	benzylalcohol (1)	
<i>trans</i> -Stilbene	<i>trans</i> -stilbene oxide (8)	19
	benzaldehyde (11)	
Cyclooctane	cyclooctanol (3)	31
	cyclooctanone (20)	
Ethylbenzene	1-phenylethanol (12)	42
	acetophenone (23)	
Adamantane	1-adamantanol (16)	18
	2-adamantanol (2.5)	
	2-adamantanone (2.5)	
Dimethyl sulfide	dimethyl sulfoxide (13)	14
	dimethylsulfone (3)	
Dimethyl sulfoxide	dimethylsulfone (7)	5
Benzylalcohol	benzaldehyde (100)	70
Cyclooctanol (20 eq.)	cyclooctanone (9)	45 <sup>d</sup>
1 phenyl ethanol (40 eq.)	acetophenone (19)	49 <sup>d</sup>
Heptane	4-heptanone (3)	18
	4-heptanol (1)	
	3-heptanone (4)	
	3-heptanol(0.5)	
	2-heptanone (4)	
	2-heptanol (1.5)	

<sup>a</sup> Oxidations were performed under Argon with 0.7 mM of catalyst and 140 eq. of TBHP; see experimental section for the amount of substrates. In the case of alkane oxidations, dialkylperoxides yields have not been determined.

<sup>b</sup> TN (turnover numbers) = moles of product per mole of catalyst after complete reaction.

<sup>c</sup> yield based on the oxidant.

<sup>d</sup> yields are based on the alcohol, in this case the limiting reactant.

our conditions. Phenol was transformed into 1,4-benzoquinone and 1,4-hydroquinone as main products. Competitions between cyclohexane and phenol (1100 and 20 equivalents, respectively) demonstrated that phenol was a strong inhibitor of the alkane functionalization. Moreover, 50 eq. of BHT (2,6-*t*-butyl-4-methylphenol), a well-known radical scavenger [28],

inhibited cyclohexane oxidation under argon (90% inhibition) and was transformed into the BHT radical, as shown by EPR experiments. 2,6-dimethylphenol was transformed into the 3,5,3',5'-tetramethyldiphenoquinone.

Dimethyl sulfide (DMS) was converted to dimethyl sulfoxide together with small amounts of dimethyl sulfone (up to 3 equivalents based on the catalyst), with an overall yield of 14%. Interestingly, DMS oxidation was not affected by the presence of BHT. Dimethyl sulfoxide was poorly oxidized to the sulfone (5% yield).

Cyclohexene gave allylic alcohol and ketone as major products but also cyclohexene oxide (10% yield). *trans*-Stilbene was converted to benzaldehyde and the epoxide with an overall yield of 10% based on TBHP. Cyclooctene was also oxidized to its epoxide with a similar yield.

### 3.2. Variation of the oxidant

The effect of varying the oxidant was studied during cyclohexane oxidation in the presence of  $\text{Fe}_2\text{O}(\text{bipy})_4(\text{H}_2\text{O})_2(\text{ClO}_4)_4$  (0.7 mM). Catalytic oxidations were effective only with TBHP,  $\text{H}_2\text{O}_2$  and CHP (Table 4). No oxidation products could be detected when iodosylbenzene (PhIO) or sodium hypochlorite (NaOCl) were used. The best yields have been obtained with TBHP (up to 50%), followed by CHP (27%) and  $\text{H}_2\text{O}_2$  (12%) (Table 4). The low yield with hydrogen peroxide as the oxidant was due to an efficient catalyzed dismutation [23]. A too large excess of the hydroperoxide favored its dismutation and lowered the overall yields of alkane oxidation products. In the absence of substrate, around 50% of total TBHP and 70% of total  $\text{H}_2\text{O}_2$  was transformed into  $\text{O}_2$  and *t*-butanol and  $\text{H}_2\text{O}$ , respectively. In the presence of cyclohexane, the  $\text{O}_2$  yield dropped to 10% with TBHP but was not significantly changed with  $\text{H}_2\text{O}_2$ . With CHP no  $\text{O}_2$  could be detected in the presence of the substrate, whereas only 10%  $\text{O}_2$  yield was detected in the absence of substrate. Efforts to avoid dismutation of the oxidants is under investigation.

The alcohol/ketone ratio was dependent on the oxidant and not on its concentration. The cyclohexanol/cyclohexanone ratio was found to be 0.5 with CHP and close to 1 with TBHP and  $H_2O_2$ .  $K_H/K_D$  values were also dependent on the oxidant. For example the overall  $K_H/K_D$  value, during cyclohexane oxidation, was 7.1 with TBHP, 5 with CHP and 2.1 with  $H_2O_2$  showing that the H abstracting species generated during the reaction of the complex with TBHP, CHP or  $H_2O_2$  were different and that the third one was more powerful. In addition, the selectivity for tertiary positions increased in the following order: CHP < TBHP <  $H_2O_2$  ( $C_3/C_2 = 7.5, 10, 13$ , respectively).

In general  $H_2O_2$  was less efficient than TBHP and CHP for alkane oxidation. It was thus interesting to note that the contrary is observed for sulfur oxidation (Table 4). Oxidation of dimethylsulfide gave dimethylsulfoxide with a 86% yield (to compare to 31% with CHP and 14%

Table 4  
Oxidation of alkanes and dimethyl sulfide by various oxidants catalyzed by  $Fe_2O(phen)_4(H_2O)_2(ClO_4)_4$ <sup>a</sup>

Oxidant	Substrate	$R_1R_2CH-OH$ <sup>b</sup>	$R_1R_2C=O$ <sup>b</sup>	% yield <sup>c</sup>
	cyclohexane			
TBHP		17	19	39
$H_2O_2$		7.5	5	12
PhIO		0	0	
CHP		8	15	27
	cyclooctane			
TBHP		3	20	31
CHP		12	24	43
$H_2O_2$		2	8	13
	ethyl benzene			
TBHP		12	23	41
$H_2O_2$		14	17	34
	dimethylsulfide			
		$R_1R_2SO$	$R_1R_2SO_2$	
TBHP		13	3.5	14
$H_2O_2$		120	1	86
CHP		40	1.5	31

<sup>a</sup> The concentration of oxidant was 140 eq. for TBHP, CHP and  $H_2O_2$ , and 40 eq. for PhIO. The catalyst concentration was 0.7 mM. In the case of alkane oxidations, dialkylperoxides yields have not been determined.

<sup>b</sup> Numbers are moles of product per mole of catalyst after complete reaction.

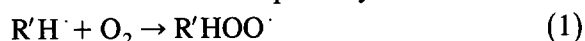
<sup>c</sup> Yield based on the oxidant.

with TBHP). Formation of sulfone from sulfoxide was more efficient with  $H_2O_2$  (17% yield, 24 TN) than with TBHP and CHP (yields around 5%, 7 TN).

TBHP was recovered as *t*-BuOH and mixed dialkylperoxides with no evidence for di-*t*-butylperoxide formation. No quantification of the TBHP-derived products has been carried out except for the mixed dialkylperoxide. This was done more carefully in the case of CHP-dependent reactions. It is known that CHP usually decomposes into acetophenone and 2-phenyl-2-propanol with no evidence of phenol formation. The former product was obtained, together with one molecule of methanol, from the  $\beta$  scission of the cumoxyl radical [29]. Product analysis by HPLC has been performed after incubation of  $Fe_2O(phen)_4(H_2O)_2(ClO_4)_4$  with CHP either in the presence or in the absence of cyclohexane. In the absence of substrate, acetophenone yield was 45% and dropped to 20% in the presence of cyclohexane. The CHP complement was recovered as 2-phenyl-2-propanol. The loss of acetophenone during cyclohexane oxidation perfectly matched the yield of cyclohexane oxidation products (value found: 23%). Clearly cumoxyl radicals were formed during CHP decomposition, by homolysis of the O–O bond, and were likely to be involved in cyclohexane oxidation.

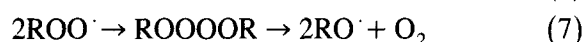
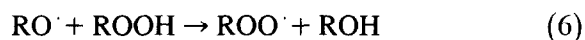
### 3.3. Effect of $O_2$ in the catalytic process

Several authors have suggested that  $O_2$  is a key intermediate during oxidation of alkanes  $R'H_2$  by alkylhydroperoxides catalyzed by  $\mu$ -oxo diferric complexes [8,25,30]. Obviously, when reactions are carried out in aerated solvents,  $O_2$  has to be considered as a key reactant because of its radical nature and its reactivity with free radicals  $R'H\cdot$ . Oxidation products would then derive from the following auto-oxidation mechanism pathways:





However, also in deaerated solvents, O<sub>2</sub> can be present, due to alkylhydroperoxide, ROOH, degradation as follows:



Fish et al. with the Fe<sub>2</sub>O(tmima)<sub>2</sub>(OAc)<sub>2</sub>(ClO<sub>4</sub>)<sub>2</sub>/H<sub>2</sub>O<sub>2</sub> system [31], Barton et al. in the Gif chemistry [8] have detected the presence of alkylhydroperoxides issued from the reaction of O<sub>2</sub> with substrate radicals (reaction 1 and 2). Also with TBHP as the oxidant, dioxygen was absolutely required in their systems and substrate-derived alkylhydroperoxides were suggested as intermediates. Very recently, Arends et al. have shown that the oxidation of cyclooctane by TBHP catalyzed by a mononuclear

[Fe(TPA)Cl<sub>2</sub>](BF<sub>4</sub>), originally tested by Que et al., was strongly inhibited by a vigorous bubbling of argon [30]. The authors then concluded that in the original Que's experiments, the anaerobiosis was partial, and that dioxygen, coming from the decomposition of intermediate tetroxides (reaction 7), participated to the autoxidation of the substrate, with intermediate substrate-derived alkylhydroperoxide and tetroxide.

We have seen earlier that O<sub>2</sub> was formed during incubation of Fe<sub>2</sub>O(bipy)<sub>4</sub>(H<sub>2</sub>O)<sub>4</sub>(ClO<sub>4</sub>)<sub>4</sub> with excess hydroperoxides. With TBHP, O<sub>2</sub> formation (50% yield) was large enough to account for all alkane oxidation products. This was not true anymore with CHP, for which O<sub>2</sub> yield (10% yield) in the absence of substrate, was much lower than the yields of the oxidation products (30%). Four sets of reaction conditions have been investigated in order to determine whether dioxygen plays a role during oxidation reactions: (i) solutions saturated with argon; (ii)

Table 5  
Effect of O<sub>2</sub> on products distribution in the oxidation of alkanes by various oxidants catalyzed by Fe<sub>2</sub>O(bipy)<sub>4</sub>(H<sub>2</sub>O)<sub>2</sub>(ClO<sub>4</sub>)<sub>4</sub><sup>a</sup>

Oxidant	Substrate	Products		Conditions <sup>b</sup>
	Cyclooctane	Cyclooctanol	Cyclooctanone	
TBHP		3	20	O <sub>2</sub> saturation
TBHP		3	20	argon
TBHP		0	11	argon bubbling
CHP		12	24	O <sub>2</sub> saturation
CHP		12	24	argon
CHP		4	18	argon bubbling
	Adamantane	1-ol	2-ol/2-one <sup>c</sup>	
TBHP		16	2.5/2.5	O <sub>2</sub> saturation
TBHP		16	2.5/2.5	argon
TBHP		10	2/2	argon bubbling
CHP		13	3/3	O <sub>2</sub> saturation
CHP		13	3/3	argon
CHP		9	2/2	vacuum
	Cumene	2-Phenyl-2-propanol	Acetophenone	
TBHP		20	15	argon
TBHP		36	35	O <sub>2</sub> saturation

<sup>a</sup> Number are moles of product per mole of catalyst after complete reaction; the concentration of oxidant was 140 eq. for the oxidant and 200 eq. for adamantane, and 600 eq. for cumene, 1100 eq. for cyclooctane. The catalyst concentration was 0.7 mM.

<sup>b</sup> Argon, solution has been degassed before addition of oxidant. O<sub>2</sub> saturation, continuous saturation with O<sub>2</sub>; argon bubbling, argon was flushed vigorously during the course of the reaction; vacuum, the reaction was done under dynamic vacuum (10 mmHg). Except in O<sub>2</sub> saturation experiments, the volume of the solution has decreased by 30%.

<sup>c</sup> 1-ol, 2-ol and 2-one correspond to 1-adamantanol, 2-adamantanol and 2-adamantanone, respectively.

solutions vigorously bubbled through with argon during all the reaction; (iii) solutions continuously saturated with oxygen; (iv) solutions under dynamic vacuum (10 mmHg). Alkanes with limited volatility such as cyclooctane, adamantane and cumene have been used. As shown in Table 5, there was not a single anaerobic experiment in which oxidation was totally abolished. Moreover, saturation with dioxygen had an effect on the reaction only in the case of cumene: both the yield and the alcohol/ketone ratio were increased significantly. In most cases, the variations in reaction yields and products proportions were limited. Only with strong argon bubbling was the alcohol yield greatly decreased. Evaporation, due to the vigorous bubbling, has probably contributed to that loss.

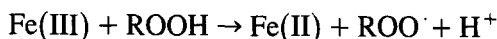
Finally, cyclohexylhydroperoxide CyOOH was searched for during the cyclohexane oxidation but could not be detected and isolated [31]. CyOOH is expected to be a key intermediate of cyclohexane autoxidation. However, it has to be noted that CyOOH was efficiently transformed, in the presence of  $\text{Fe}_2\text{O}(\text{bipy})_4(\text{H}_2\text{O})_2(\text{ClO}_4)_4$ , into cyclohexanol and cyclohexanone in a 1:1 ratio (70% yield based on the alkylperoxide). The same result was obtained in the presence of TBHP.

*In conclusion*, our results unambiguously demonstrate that dioxygen is not absolutely required for alkane oxidation to alcohols and ketones. Since free radicals are generated, it is not surprising that dioxygen can trap some of these radicals but this pathway is a minor one.

#### 3.4. Spectroscopic studies of the alkane oxidation catalyzed by $\text{Fe}_2\text{O}(\text{bipy})_4(\text{H}_2\text{O})_2(\text{ClO}_4)_4$

During oxidation of cyclohexane by TBHP in the presence of  $\text{Fe}_2\text{O}(\text{bipy})_4(\text{H}_2\text{O})_2(\text{ClO}_4)_4$  a new species was transiently formed as shown by the appearance of a broad absorption band at around 640 nm, in the last phase of the reaction (Fig. 1). The transition characteristic of the ferrous inactive species was also observed at 510 nm at the end of the reaction. A possible

pathway for reduction of Fe(III) is the following:



The late appearance of  $[\text{Fe(II)}\text{L}_3]^{2+}$  strongly suggested that the reaction was favored by the accumulation of the alcohol. We actually showed that alone the peroxide or the alcohol could slowly reduce Fe(III) but altogether the reaction was accelerated.

The spectroscopic characteristics (UV-visible, resonance Raman and EPR spectroscopies) of the species absorbing at 640 nm are identical to those of the mononuclear alkylperoxo-iron complex,  $\text{Fe(III)}(\text{OOR})(\text{HOR}')$ , with  $\text{R}'\text{OH}$  corresponds to cyclohexanol and  $\text{ROO}\cdot$  to the alkylperoxide anion, reported earlier [32]. This shows that during catalysis the diiron catalyst generated mononuclear complexes with the ability to bind the hydroperoxide. High concentration of the mononuclear species could be obtained by addition of an excess of alcohol and running the reaction at low temperature. Formation of the iron-peroxo complex followed the formation of the alcohol, explaining its late appearance. Moreover, this intermediate was likely to be involved in the oxidation of the alcohol to ketone. As a matter of fact, after generation of the iron-peroxo complex in the presence of a small excess of alcohol, the kinet-

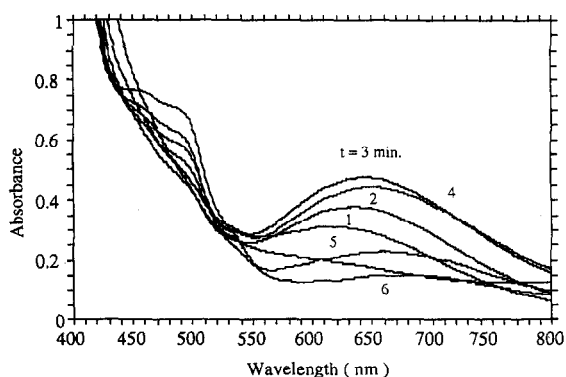


Fig. 1. Cyclohexane oxidation by TBHP catalyzed by  $\text{Fe}_2\text{O}(\text{bipy})_4(\text{H}_2\text{O})_2(\text{ClO}_4)_4$  followed by UV-visible spectroscopy (0.7 mM on catalyst; catalyst/TBHP/cyclohexane = 1:140:1100); reaction time in minutes for each spectrum are included in the figure.

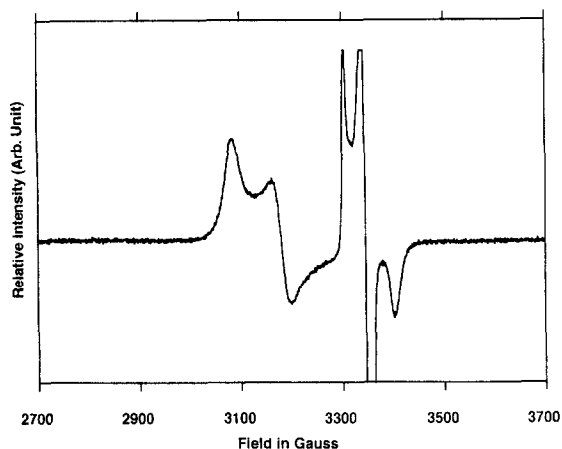


Fig. 2. EPR spectrum at 100 K recorded after 1 min reaction during cyclohexane oxidation by TBHP catalyzed by  $\text{Fe}_2\text{O}(\text{bipy})_4(\text{H}_2\text{O})_2(\text{ClO}_4)_4$ . Experimental conditions:  $T = 100$  K; microwave power = 20 mW; frequency = 9.41 GHz; gain = 5000; modulation = 2.5 mT.

ics of its decomposition was found to follow that of ketone formation (data not shown).

The 100 K EPR spectrum recorded during the course of the reaction is shown in Fig. 2. It is composed of a rhombic signal ( $g_1 = 2.18$ ;  $g_2 = 2.06$ ;  $g_3 = 1.96$ ) attributed to the low spin iron-peroxo complex and a second signal centered at  $g = 2.007$ , characteristic of a free radical. The latter one is observed only with alkylhydroperoxides and not with  $\text{H}_2\text{O}_2$ , with the highest intensities observed with TBHP as the oxidant and alkanes as substrates. Much lower intensities were observed with alcohols as substrates. In order to identify the species responsible for this signal, spin-trapping experiments have been performed with DMPO as the trapping agent under argon. DMPO-OOR ( $R = t$ -butyl or cumyl) was detected as a multiplet ( $a_N = 14.5$  Gauss,  $a_H = 10.5$  G,  $a_h = 1.3$  G for TBHP) [33], which decomposed slowly to DMPO-OH with time. No DMPO-OR could be detected.

#### 4. Discussion

At this point it is tempting to rationalize the various characteristics of the oxidation reactions

reported above in terms of a minimal mechanism.

We will first discuss the nature of the active oxygen species responsible for the abstraction of the hydrogen atom of the alkane  $R'H_2$  substrate. Then we will make suggestions about the reactions of oxygen transfer to the radical  $R'H^\cdot$  intermediate with special emphasis on the role of molecular oxygen. That a substrate radical is formed during the reaction is in agreement with: (i) the formation of high yields of  $R'HCl$  when the reaction is carried out in the presence of  $\text{CCl}_4$ ; (ii) the formation of mixed dialkylperoxides  $\text{ROOR}'$ . The abstraction of the C–H hydrogen atom is the rate limiting step of the reaction as shown from the high  $k_H/k_D$  values.

It is now well established that the function of the iron center is to activate the alkylhydroperoxide into a more reactive oxygen-centered species. This activation requires the presence of a labile site on the catalyst and the binding of the peroxide. Recently, an iron peroxo intermediate has been detected and fully characterized during oxidation of alcohols by TBHP or CHP, in the presence of a dinuclear iron complex [32,34]. Here we report that the same intermediate is formed also during oxidation of alkanes, which became detectable after accumulation of alcohol.

Three reactive oxygen-centered intermediates derived from such an iron peroxo complex are likely to be present in the reaction mixture: an alkoxy radical, a peroxy radical and a high valent iron oxo complex.

The alkoxy radical is formed during homolysis of the O–O bond. The presence of such a radical has been clearly established in the case of CHP, from the detection of acetophenone, a characteristic decomposition product of  $\text{RO}^\cdot$ . The alkoxy radical has the potential for abstracting hydrogen atoms either from the substrate C–H bonds or from a second molecule of hydroperoxide. The second reaction, in a non-basic solvent such as acetonitrile, is rather efficient and would generate  $\text{ROO}^\cdot$  the peroxy radical [28].

Evidence for the presence of the peroxy radicals during TBHP-dependent oxidations comes from: (i) the detection of the mixed dialkylperoxides; (ii) spin trapping experiments with the detection of DMPO-OOR; (iii) the generation of high yields of molecular oxygen. As a matter of fact,  $O_2$  comes from the dimerization of the peroxy radical and decomposition of the intermediate tetroxide.

The peroxy radical is much less reactive than the alkoxy radical for hydrogen abstraction from C–H bonds, more sensitive to the strength of these bonds, and as a consequence is much more selective. The fact that toluene oxidation is slower than cyclohexane oxidation, in spite of the lower energies of the C–H bonds, eliminates the peroxy radical as the H abstracting agent. On the contrary, this is consistent with the alkoxy radical being the active species. The alkoxy radical would be thus the site for three competitive reactions: the spontaneous decomposition to diamagnetic compounds ( $\beta$  scission for example), reaction with the substrate, reaction with the hydroperoxide generating  $O_2$ . The competition is dependent on the starting hydroperoxide:  $RO^\cdot$  from MPPH, 2-methyl-1-phenylpropylhydroperoxide, essentially decomposes giving no alkane oxidation and no dioxygen;  $RO^\cdot$  from CHP, rapidly decomposes, giving only small amounts of dioxygen, but is efficiently trapped by excess substrate;  $RO^\cdot$  from TBHP is rather stable, generates high yields of dioxygen in the absence of substrate, but can be efficiently trapped by an excess of alkane.

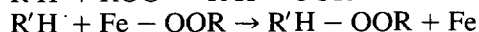
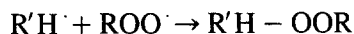
Most studies on oxidations of alkanes by alkylperoxides strongly favor  $RO^\cdot$  as the active species and our system could be just one more example in which alkoxy radicals are involved. However, several results are not consistent with such an hypothesis: (i) oxidation of adamantane by TBHP gives a  $C_3/C_2$  ratio of 10, a value much larger than the  $C_3/C_2$  ratio characteristic of the *t*-buO $^\cdot$  radical ( $C_3/C_2 = 4$ ) [27]. (ii)  $C_3/C_2$  ratios and  $k_H/k_D$  values obtained with a given oxidant are significantly dependent on the nature of the iron catalyst (effects of termi-

nal and bridging ligands), suggesting that the oxidizing center is, at least partly, controlled by the metal/ligand environment. (iii) significant yields of epoxides have been observed during oxidation of alkenes. Recently  $RO^\cdot$  was shown to be unable to epoxidize alkenes [27].

A possible candidate for the H-abstrating species is a high valent iron oxo complex derived from the heterolytic cleavage of the O–O bond of the peroxy complex. This iron oxo complex can abstract a hydrogen atom from the C–H bond but also from the O–H bond of the peroxide thus generating the peroxy radical and then dioxygen. Such a species, in the non-heme chemistry, is still speculative. There is no example of an isolated non-heme iron oxo complex, allowing the investigation of its chemical reactivity. However, Que et al. have characterized an intermediate, during the reaction of  $H_2O_2$  with  $Fe_2O(5-Me-TPA)_2(H_2O)(OH)(ClO_4)_3$ , as a high valent Fe(III)Fe(IV) species in which the iron ions are coupled by two oxo bridges [35]. This complex can be viewed as a di-iron oxo intermediate in which the oxo group is shared by the two iron ions. This provides a strong evidence that high valent iron can be generated during reaction of peroxides with  $\mu$ -oxo diferric species. Based on the oxo iron porphyrin chemistry, such high valent iron complexes are expected to have the ability to transfer oxygen atoms to double bonds or to sulfur atoms, explaining the formation of DMSO and  $DMSO_2$  during oxidation of DMS. However it is clear that if a non-heme iron-oxo complex is formed in our systems, its epoxidizing power is rather limited. Whether this is due to an iron environment greatly different from that of iron porphyrin remains to be elucidated.

We suspect that both mechanisms ( $RO^\cdot$  or iron-oxo) operate in our system (Scheme 2). Our results seem to indicate that, with CHP, the homolytic cleavage of the O–O bond predominates while it is the heterolytic cleavage in the case of TBHP or  $H_2O_2$ . For example, the  $C_3/C_2$  ratio is 7.5 with CHP, 10 with TBHP and 13 with  $H_2O_2$ .

The next step of the reaction is the conversion of the  $R'H\cdot$  radical into alcohol, ketone and mixed dialkylperoxide. The dialkylperoxide can be formed from either following reactions,

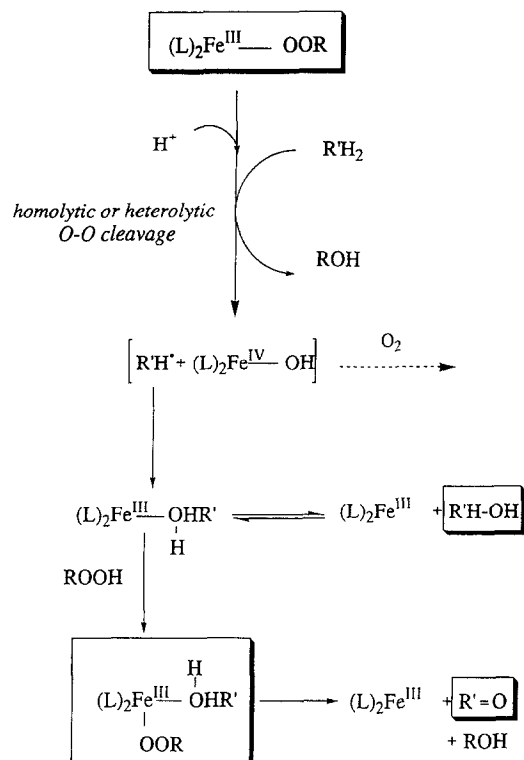


It is generally accepted that oxidations by TBHP catalyzed by non-heme iron requires the presence of dioxygen [8,21,30].  $O_2$  reacts with the substrate radical thus generating the peroxy radical  $R'HOO\cdot$ . This radical is then transformed into either  $R'HOOH$  or the tetroxide  $R'HOOOOR'H$ . Decomposition of these intermediates gives rise to the alcohol and the ketone.

However, we would like to make it clear that, under our reaction conditions,  $O_2$  seems to be only marginally involved. High yields of oxidation products are found when reactions are carried out under anaerobic conditions (vigorous argon bubbling) while saturation with  $O_2$  had only limited effects on these yields.

The origin of the discrepancy with other systems is unclear but probably reflects important differences in terms of the kinetics of the reaction. We suggest that, in slow oxidizing systems, such as those reported by Fish et al. [31] and Arends et al. [30], dioxygen is playing an important role as a trapping agent of intermediate substrate radicals, free in solution. The system based on  $Fe_2O(bipy)_4(H_2O)_2(ClO_4)_4$  is much faster and we presume that dioxygen is only marginally involved in the formation of the oxidation products as a result of an efficient oxygen transfer from a high valent iron hydroxide intermediate to the substrate radical (oxygen rebound mechanism) (Scheme 2). Such an intermediate is the result of both the homolytic and the heterolytic O–O bond cleavage pathway.

In Scheme 2, we summarize our interpretation of the experimental data reported here. In the first step of the reaction, the binding of the oxidant to the iron catalyst probably results in the cleavage of the dinuclear unit into monomers. As a matter of fact, traces of low spin and high spin ferric species, during incuba-



Scheme 2. Putative mechanism for alkane ( $R'H_2$ ) oxidation by alkylperoxides (ROOH) catalyzed by  $\mu$ -oxo diferric complexes.

tion of the diiron complex with TBHP, have been detected by EPR (data not shown). The equilibrium between mononuclear and dinuclear ferric species is further shifted in the direction of the monomer by the binding of alcohols. It thus appears that, even though the catalyst is a diiron complex, the intermediate active species are in all probability mononuclear. It is tempting to suggest that the advantage of the dinuclear structure over the mononuclear one is to allow the preparation of highly stable, easy to handle, iron complexes with highly labile sites, and that the dinuclear complexes serve as a source of very active mononuclear complexes in solution. At the end of the reaction iron is recovered in both the  $[Fe(L)_3]^{2+}$  inactive form and the  $\mu$ -oxo bridged dinuclear iron complex, as shown by the characteristic  $^1H$  NMR spectrum of the reaction solution and the absence of signals in the EPR spectrum.

After cleavage of the O–O bond within the iron-peroxo complex, homolytically or heterolytically as discussed above, and oxygen transfer to the substrate radical, an iron-alkoxo intermediate may be generated from which the alcohol is either released in solution or further oxidized to the ketone. This oxidation may depend on the binding of a second molecule of peroxide to the iron-alkoxo intermediate and on the formation of the iron-peroxo complex, detected during the reaction and characterized by UV-Visible, resonance Raman and EPR spectroscopy.

The catalytic system reported here is now quite well characterized and is shown to be very efficient, in particular for alkane oxidation. It is a suitable tool to study mechanistic aspects of the reaction. We are aware that our present conclusions are rather conflicting with other studies. The existence of high valent non-heme iron complexes and their role during alkane oxidations will require to be investigated with more experiments. However, we think that our results give some indications that non-heme iron may, with the correct coordination environment, induce heterolytic cleavages of peroxides and have the potential to control carbon radicals. One should remember that the iron-porphyrin field has been also controversial for at least 20 years.

## References

- [1] (a) R.A. Sheldon and J.K. Kochi, *Metal Catalyzed Oxidations of organic Compounds*, Academic press, 1981. (b) A.E. Shilov, in: *Activation of Saturated Hydrocarbons by Transition Metal Complexes*, D. Reidel, 1984. (c) C.A. Tolman, J.D. Druher, M.J. Nappa and N. Herron, in *Activation and Functionalization of Alkanes*; C.L. Hill, John Wiley & Sons, 1989.
- [2] T.J. Mc Murry and J.T. Groves, in *Cytochrome P-450*; P.R. Ortiz de Montellano (Ed.), Plenum Press, New York, 1986.
- [3] D. Mansuy and P. Battioni, in *Bioinorganic Catalysis*, J. Reedijk (Ed.), Dekker, New York, 1993.
- [4] (a) L. Que Jr. and A.E. True, in *Progress in Inorganic Chemistry*, S.J. Lippard (Ed.), John Wiley & Sons, New York, 1990, p. 97. (b) J. Sanders-Loehr, in *Iron Carriers and Iron Proteins*; T.M. Loehr (Ed.), VCH, 1989.
- [5] K.K. Andersson, W.A. Froland, S.-K. Lee and J.D. Lipscomb, *New J. Chem.*, 15 (1991) 411.
- [6] M. Fontecave, C. Gerez, M. Atta and A. Jeunet, *Biochem. Biophys. Res. Commun.*, 168 (1990) 659.
- [7] M. Salhin, B.-M. Sjöberg, G. Backes, T. Loehr and J. Sanders-Loehr, *Biochem. Biophys. Res. Commun.*, 167 (1990) 813.
- [8] D.H.R. Barton, S.D. Bévière, W. Chavasiri, E. Cshuai, D. Doller and W.-G. Liu, *J. Am. Chem. Soc.*, 114 (1992) 2147 and references therein.
- [9] D.H.R. Barton and D. Doller, *Acc. Chem. Res.*, 25 (1992) 504.
- [10] C. Sheu, S.A. Richert, P. Cofré, B. Ross, A. Sobkowiak, D.T. Sawyer and J.R. Kanofsky, *J. Am. Chem. Soc.*, 112 (1990) 1936.
- [11] E. About-Jaudet, D.H.R. Barton, E. Cshuai, D. Doller and N. Ozbalik, *Tetrahedron Lett.*, 31 (1990) 1657.
- [12] D.H.R. Barton and W. Chavasiri, *Tetrahedron*, 50 (1994) 19.
- [13] U. Schuchardt, W.A. Carvahlo and E.V. Spinacé, *Synlett* (1993) 713.
- [14] R.A. Leising, R.E. Norman and L. Que Jr., *Inorg. Chem.*, 29 (1990) 2553.
- [15] R.A. Leising, Y. Zang and L. Que Jr., *J. Am. Chem. Soc.*, 113 (1991) 8555.
- [16] (a) A.C. Rosenweig, C.A. Frederick, S.J. Lippard and P. Nordlund, *Nature*, 366 (1993) 537. (b) A.C. Rosenweig, P. Nordlund, P.M. Takahara, C.A. Frederick and S.J. Lippard, *Chem. Biol.*, 6 (1995) 409.
- [17] A.C. Rosenweig and S.J. Lippard, *Account. Chem. Res.*, 27 (1994) 229.
- [18] J.D. Lipscomb, *Annu. Rev. Microbiol.*, 48 (1994) 371.
- [19] M.J. Rataj, J.E. Kauth and M.I. Donnelly, *J. Biol. Chem.*, 266 (1991) 18684.
- [20] R.A. Leising, J. Kim, M.A. Pérez and L. Que Jr., *J. Am. Chem. Soc.*, 115 (1993) 9524.
- [21] R.M. Buchanan, S. Chen, J. Richardson, M. Bressan, L. Forti, A. Morvillo and R.H. Fish, *Inorg. Chem.*, 33 (1994) 3208.
- [22] S. Ménage, J.-M. Vincent, C. Lambeaux, G. Chottard, A. Grand and M. Fontecave, *Inorg. Chem.*, 32 (1993) 4766.
- [23] S. Ménage, J.-M. Vincent, C. Lambeaux and M. Fontecave, *J. Chem. Soc. Dalton Trans.* (1994) 2081.
- [24] S. Ménage, J.-M. Vincent, C. Lambeaux and M. Fontecave, *Tetrahedron Lett.*, 35 (1994) 6287.
- [25] R.H. Fish, K.J. Oberhausen, S. Chen, J.F. Richardson, W. Pierce and R.M. Buchanan, *Cat. Lett.*, 18 (1993) 357.
- [26] R.M. Smith and A.E. Martell, *Critical Stability Constant*, 2, Plenum Press 1990.
- [27] F. Minisci, F. Fontana, S. Araneo, F. Recupero, S. Banfi and S. Quici, *J. Am. Chem. Soc.*, 117 (1995) 226.
- [28] R.A. Sheldon and J.K. Kochi, in *Metal Catalyzed Oxidations of Organic Compounds*, Academic press, 1981.
- [29] T.C. Bruice, P.N. Balasubramanian, R.W. Lee and J.R. Lindsay Smith, *J. Am. Chem. Soc.* 110 (1988) 7890.
- [30] I.W.C.E. Arends, K.U. Ingold and D.D.M. Wayner, *J. Am. Chem. Soc.*, 117 (1995) 4710.
- [31] R.H. Fish, M.S. Konings, K.J. Oberhausen, R.H. Fong, W.M. Yu, G. Christou, J.B. Vincent, D.A.K. Coggin and R.M. Buchanan, *Inorg. Chem.*, 30 (1991) 3002.

- [32] S. Ménage, E.C. Wilkinson, L. Que Jr. and M. Fontecave, *Angew. Chem. Int. Ed. Engl.*, 34 (1995) 203.
- [33] G.R. Buettner, *Free Radical in Biology and Medicine* (1987) 259.
- [34] J. Kim, E. Larka, E.C. Wilkinson and L. Que Jr., *Angew. Chem. Int. Ed. Engl.*, 34 (1995) 2048.
- [35] Y. Dong, H. Fujii, M.P. Hendrich, R.A., Leising, G. Pan, C.R. Randall, E.C. Wilkinson, Y. Zang, L. Que Jr., B.G. Fox, K. Kauffmann and E. Münck, *J. Am. Chem. Soc.*, 117 (1995) 2778.