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Non-heme iron polyazadentate complexes as catalysts for oxidations by H_2O_2: particular efficiency in aromatic hydroxylations and beneficial effects of a reducing agent

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Abstract

Four iron(II) complexes, bearing hexa-, penta- or tetra-azadentate ligands, whose redox potentials (for the Fe^{III}/Fe^{II} couple) vary from +280 to +1023 mV (versus saturated calomel electrode), were compared as catalysts for the oxidation of various substrates by H_2O_2. These complexes were bad catalysts for alkene epoxidation or alkane hydroxylation, whereas those exhibiting the highest redox potentials were interesting catalysts for the hydroxylation of aromatic compounds. For most of them, addition of an appropriate reducing agent, such as hydroquinones, PhSH or tetrahydropterins, in the medium, led to spectacular increases of the yields of hydroxylation of aromatic compounds such as anisole, toluene, ethylbenzene, benzene and naphthalene (with final yields based on H_2O_2 up to 69, 33, 18, 40 and 47%, respectively). Such systems catalyzed the transfer of an oxygen atom from H_2O_2, as shown by experiments using $H_2{}^{18}O_2$ and $H_2{}^{18}O$, into anisole with yields based on starting H_2O_2 up to 69%.

Keywords: Tetrahydropterins; Hydroquinones; Anisole; Monooxygenation; Polypyridinic ligands

1. Introduction

Several systems based on iron porphyrins have been shown to efficiently mimic alkene epoxidation and alkane hydroxylation by cytochrome P450-dependent monooxygenases [1–6]. More recently, non-heme iron complexes that were developed as mimics of non-heme iron-containing monooxygenases, have also been found to act as good catalysts for the epoxidation or *cis*-dihydroxylation of alkenes by H_2O_2 (for recent articles, see for instance [7–12]). Cytochromes P450 and some non-heme iron-containing monooxygenases also catalyze the selective and efficient hydroxylation of aromatic compounds [13]. However, very few iron-based model systems have been described so far for the selective hydroxylation of aromatic compounds [1–6]. In the context of a comparative study of the catalytic properties of iron porphyrins and non-heme iron complexes in the oxidation of hydrocarbons by H_2O_2, we have recently found that the iron(II) complex of the hexaazadentate ligand tris[*N*-(2-pyridylmethyl)-2-aminoethyl]amine (TPAA) (Fig. 1) was a poor catalyst for alkene epoxidation and alkane hydroxylation, but a quite efficient catalyst for the hydroxylation of aromatic compounds [14]. Thus, $[(TPAA)Fe^{II}](ClO_4)_2$ catalyzes the hydroxylation by H_2O_2 of anisole, toluene, ethylbenzene, benzene and chlorobenzene, with respective yields of 53, 17, 24, 22 and 13% based on H_2O_2. Moreover, hydroxylation of the aromatic ring of toluene and ethylbenzene by the $[(TPAA)Fe](ClO_4)_2/H_2O_2$ system is the major reaction, more important than the usually favoured hydroxylation of their benzylic position [15].

Non-heme iron(II) complexes bearing similar polyazadentate ligands, either pentaazadentate ligands $L_5{}^2$, [*N*-methyl-*N*,*N*′,*N*′-tris(2-pyridylmethyl)ethane-1,2-diamine], and $L_5{}^3$, [*N*-methyl-*N*,*N*′,*N*′-tris(2-pyridylmethyl)propane-1,3-diamine], or tetraazadentate ligand $L_4{}^3$, *N*,*N*′-dimethyl-*N*,*N*′-bis(2-pyridylmethyl)propane-1,3-diamine (Fig. 1), have been recently characterized [16–18], and found to react with H_2O_2 with formation of $Fe^{III}OOH$ species that have

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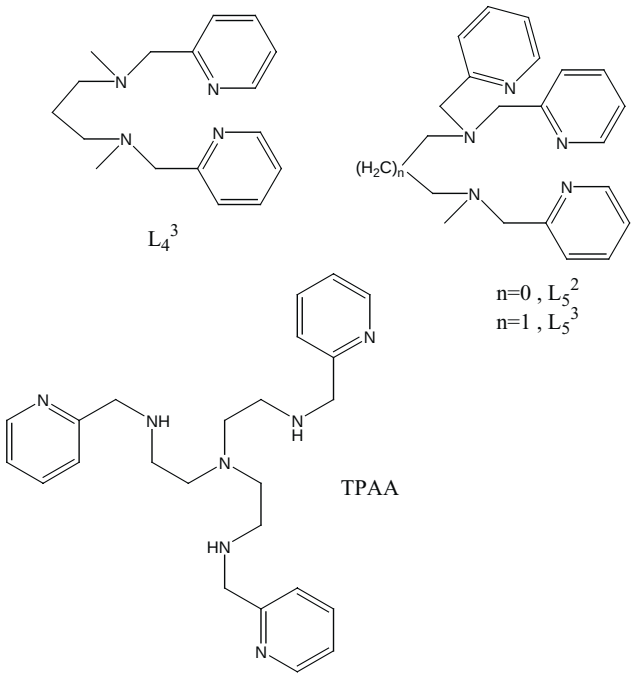


Fig. 1. Formula of the polydentate ligands of the iron complexes used in this study.

been spectrally detected in the case of the (L_5) iron complexes [18,19]. Some of the $L_4{}^3$ iron complexes have been found to act as catalysts of hexane hydroxylation by O_2 in the presence of 2,3,5-trimethylhydroquinone as a reducing agent [16]. Here, we compare the properties of the (L_4) and (L_5) iron(II) complexes to those of [(TPAA)Fe](ClO_4)$_2$, as catalysts for the oxidation of several substrates by H_2O_2. Some of them appear to be very efficient for the hydroxylation of aromatic compounds, particularly in the presence of reducing agents, such as hydroquinones or tetrahydropterins.

2. Experimental

2.1. Catalysts and reactants

The iron complexes used in this study were prepared as described previously [16–18,20]. All the reactants and products were commercially available and used without further purification. $H_2{}^{18}O_2$ (95% enriched in ^{18}O, 2.5% in $H_2{}^{16}O$) was purchased from ICON (NJ, USA); $H_2{}^{18}O$ (98% enriched in ^{18}O) was purchased from EURISO-TOP (Saclay, France).

2.2. Typical procedure for catalytic oxidations

H_2O_2 (20 μmol, 40% in H_2O, 1.45 μl) was added to a CH_2Cl_2/CH_3CN solution (1/1 v/v) of the iron catalyst (1 μmol) and the substrate (3 mmol), the total volume of the solvents being calculated to obtain a 1.5 mM concentration of the catalyst. For most reactions performed in the presence of a reducing agent (conditions of Tables 2 and 3), the CH_2Cl_2/CH_3CN solution also contained 20 μmol of the reducing agent. Slightly different conditions were used for the experiments corresponding to the results of Tables 1 and 4 (changes in the nature of the solvents and on the relative amounts of the reducing agent). After 2 h at 20 °C, an internal standard ($PhCOCH_3$ or PhI, 10 μmol), was added and the reaction mixture was analysed by gas chromatography.

Reactions under anaerobic conditions were done by "freeze–thaw cycles" of a vial containing a solution of all the reactants except H_2O_2 and of a second vial containing the H_2O_2 solution. The content of the first vial was then transferred onto the H_2O_2 solution under argon.

2.3. Product analysis and identification

Gas chromatographic analyses were done using either a packed 5% FFAP column for anisole and naphthalene as substrates, or a capillary BP20 (polar) column for toluene and ethylbenzene, with detection with a flame ionization detector. The products formed were analyzed by comparison of their retention time with those of authentic samples, and by gaz chromatography-mass spectrometry analysis, using a Hewlett-Packard 5890 Series II GC coupled with a HP5972 mass selective detector.

In the oxidations of anisole using either $H_2{}^{18}O_2$ or $H_2{}^{18}O$, the levels of ^{18}O incorporation into anisole were measured on the basis of an analysis of the peaks at $m/z = 124$ and 126 (molecular ion) and at $m/z = 109$ and

Table 1
Comparison of various iron complexes bearing different polyazadentate ligands as catalysts of hydroxylation of anisole and toluene by H_2O_2[a]

Catalyst	Product (yields %)[b]							
	Anisole			Toluene				
	o-OH	*p*-OH	PhOH	*o*-OH	*m*-OH	*p*-OH	$PhCH_2OH$	PhCHO
(TPAA)Fe(ClO_4)$_2$	26	27	3	8	2	7	0.5	1
($L_5{}^2$FeCl)PF_6	23	7	3	3	1.5	1.5	3	5
($L_5{}^3$FeCl)PF_6	24	7	6	4.5	2	2	1	0.8
$L_4{}^3FeCl_2$	2	2	1	2.5	1	1.5	0.5	0.6

[a] Conditions: catalyst/H_2O_2/substrate molar ratio = 1/20/3000 in CH_3CN/H_2O (9/1) for 2 h at 20 °C; [catalyst] = 2 mM. *o*-OH, *p*-OH and *m*-OH are used for *ortho*, *para* and *meta*-substituted phenol products. In the case of anisole, *meta*-methoxyphenol corresponded to less than 5% of total methoxyphenols.

[b] Yields are based on starting H_2O_2; those obtained with (TPAA)Fe(ClO_4)$_2$ came from ref [14].

111 $(M-15)^+$ observed in the mass spectra of the *ortho*-, *meta*- and *para*-methoxyphenol products. In all reactions, the levels of ^{18}O incorporation calculated either from the 124/126 or from the 109/111 peaks of the mass spectra of the three regioisomers of methoxyphenol were in excellent agreement (equal values ±1%).

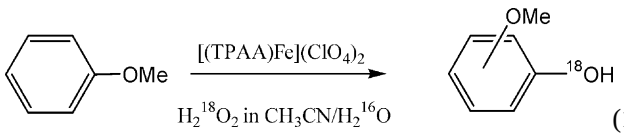
3. Results and discussion

3.1. Comparison of iron complexes bearing tetra-, penta-, or hexa-azadentate ligands as H_2O_2-dependent oxidation catalysts

The possible roles of the $L_4{}^3Fe^{II}Cl_2$, $(L_5{}^2Fe^{II}Cl)PF_6$ and $(L_5{}^3Fe^{II}Cl)PF_6$ complexes as catalysts for the oxidation of hydrocarbons by H_2O_2 were compared to those previously reported [14] for the $[(TPAA)Fe^{II}](ClO_4)_2$ complex. These three complexes were found to act as poor catalysts for the epoxidation of alkenes by H_2O_2. Under identical conditions (catalyst/H_2O_2/substrate molar ratio = 1/40/800 in CH_2Cl_2/CH_3CN), they exhibited characteristics very similar to those previously described for $[(TPAA)Fe^{II}](ClO_4)_2$ [14]: (i) yields lower than 20% for the epoxidation of cyclooctene, (ii) major formation of allylic oxidation products when using cyclohexene as a substrate, and (iii) major formation of benzaldehyde and only minor formation of epoxides (<10%) in the case of *cis*-stilbene.

In a similar manner, these three iron(II) complexes were bad catalysts for the hydroxylation of cyclohexane by H_2O_2 (yields based on H_2O_2 in the presence of cyclohexane in excess lower than 20%).

The four complexes $L_4{}^3Fe^{II}Cl_2$, $(L_5{}^2Fe^{II}Cl)PF_6$, $(L_5{}^3Fe^{II}Cl)PF_6$ and $[(TPAA)Fe^{II}](ClO_4)_2$ exhibited a very different behaviour as catalysts for the hydroxylation of anisole by H_2O_2. Table 1 shows that, in the presence of anisole in excess (iron catalyst/H_2O_2/anisole molar ratio = 1/20/3000 in CH_3CN/H_2O (90/10)), all these iron complexes, except $L_4{}^3FeCl_2$, were active catalysts for the formation of methoxyphenols with yields (based on H_2O_2) between 30 and 53%, the oxidative demethylation of anisole being a minor reaction with all catalysts. This catalytic oxidation of anisole, as all the aromatic hydroxylations described in the following, were performed by using the substrate in excess, in order to avoid as much as possible further oxidations of the phenol products in the oxidizing medium. This is usually done in aromatic hydroxylations by bioinspired systems because of the great reactivity of the phenol products towards the oxidizing species. Under these conditions, yields are expressed relative to the limiting reactant in the medium, here H_2O_2. These yields give an estimation of the ability of the systems to transfer an oxygen atom to the substrate. In that regard, experiments using $H_2{}^{18}O_2$ or $H_2{}^{18}O$ were performed to determine the origin of the oxygen atom inserted in the substrate. Oxidation of anisole by $H_2{}^{18}O_2$ (containing 95% ^{18}O) in the presence of $[(TPAA)Fe^{II}](ClO_4)_2$ under conditions identical to those described in Table 1 (in $CH_3CN/H_2{}^{16}O$) led to *ortho*-, *meta*- and *para*-methoxyphenols bearing a phenolic oxygen atom containing 95 ± 1% of ^{18}O isotope, as shown by mass spectrometry coupled to gaz chromatography. When the same reaction was performed with $H_2{}^{16}O_2$ in $CH_3CN/H_2{}^{18}O$ (98% enriched), the methoxyphenol products contained less than 1% ^{18}O. These data clearly show that the oxygen atom incorporated into anisole almost exclusively came from H_2O_2 (Eq. (1)). Since most of the oxidation reactions were done under aerobic conditions, the above data also show that the incorporated oxygen atom did not come from O_2. Accordingly, the same reactions performed under anaerobic conditions (under Ar, see Section 2) led to almost identical results.



(1)

Similar reactions using $H_2{}^{18}O_2$ or $H_2{}^{18}O$, but with the $(L_5{}^2FeCl)PF_6$ catalyst (conditions of Table 1, except for the CH_3CN/H_2O ratio which was 80/20 in these experiments) led to the same results and conclusions concerning the origin of the phenolic oxygen atom in methoxyphenols.

The total yield of methoxyphenols and the regioselectivity of anisole hydroxylation were dependent on the structure of the catalyst; $[(TPAA)Fe](ClO_4)_2$ led to the best total yield and to almost equal amounts of *ortho* and *para*-methoxyphenol [14], whereas $(L_5{}^2FeCl)PF_6$ and $(L_5{}^3FeCl)PF_6$ exhibited a quite identical behaviour, with total yields of ca. 30% and a regioselectivity in favour of *ortho*-hydroxylation. In the hydroxylation of toluene by H_2O_2, $[(TPAA)Fe](ClO_4)_2$ was also the best catalyst, with a total yield of cresols formation of 17%, whereas this yield was only 6% in the case of the $L_5{}^2$ complex. Table 1 also shows very different chemoselectivities (aromatic hydroxylation: benzylic hydroxylation ratios) and regioselectivities for aromatic hydroxylations, as a function of the catalyst structure. Aromatic hydroxylation is largely predominent in the case of $[(TPAA)Fe](ClO_4)_2$, whereas benzylic hydroxylation becomes slightly predominent in the case of the $L_5{}^2$ complex.

3.2. Effects of the presence of a reducing agent in the non-heme iron complexes-catalyzed hydroxylation of aromatic compounds by H_2O_2

In the course of this study of the hydroxylation of aromatic compounds by H_2O_2 catalyzed by non-heme iron complexes, we investigated the possible role of the presence of a reducing agent on the reactions. Preliminary experiments showed us that the presence of such reductants were without marked effects on the $[(TPAA)Fe](ClO_4)_2$-catalyzed aromatic hydroxylations, whereas it led to dramatic effects in the case of the reactions catalyzed by the other complexes. Thus, Table 2 shows that the addition of

Table 2
Effects of the presence of 2,3,5-trimethylhydroquinone on aromatic hydroxylations by H_2O_2 catalyzed by non-heme iron complexes[a]

Catalyst[b]		Products (Yield %)[c]														
		Anisole			Toluene					Ethylbenzene					Naphtalene	
		o-OH	*p*-OH	PhOH	*o*-OH	*m*-OH	*p*-OH	ol	al	*o*-OH	*m*-OH	*p*-OH	ol	one	1-ol	2-ol
$L_5{}^2FeCl^+$	(−)	28	5	6	4	2	1.5	3	6	2	3	1	5	12	<0.2	<0.2
	(+)	43	18	8	23	2.5	7.5	4	4	11	3	4	8	12	23	7
$L_5{}^3FeCl^+$	(−)	15	5	5	2	1	1.5	3	6	1	<0.2	<0.2	8	15	1	<0.2
	(+)	37	16	7	16	5	6	5	9	9	2	3	6	9	22	5
$L_4{}^3FeCl_2$	(−)	2	0.8	2	0.3	<0.1	0.2	1.5	3	<0.2	<0.2	<0.2	4	12	<0.2	<0.2
	(+)	20	13	5	7	1	3	3	4	3.5	0.7	1	9	10.5	10	4

[a] Conditions: catalyst/H_2O_2/substrate molar ratio = 1/20/3000 in CH_3CN/CH_2Cl_2 (1/1) for 2 h at 20 °C. [catalyst] = 1.5 mM. These reactions were done under aerobic conditions. Some of them (anisole and $L_5{}^3FeCl^+$ with or without reductant, anisole and $L_5{}^2FeCl^+$ with reductant) were also done under anaerobic conditions (under Ar, see Section 2), and gave results not significantly different from those obtained under aerobic conditions.

[b] (−) Corresponds to experiments performed without reductant, (+) experiments performed in the presence of 2,3,5-trimethylhydroquinone (20 eq. relative to catalyst).

[c] Yields are based on starting H_2O_2. *o*-, *m*-, *p*-OH are used for *ortho*, *meta* and *para*-hydroxylated substrates, respectively; ol is used for benzyl alcohol in the case of toluene, and for phenyl-1-ethanol in the case of ethylbenzene; al is used for benzaldehyde, and one for acetophenone. 1-ol and 2-ol are used for 1- and 2-naphthol, respectively.

2,3,5-trimethylhydroquinone to the $L_4{}^3FeCl_2/H_2O_2$ system led to a spectacular increase in the yields of anisole hydroxylation (33 instead of 3%) and of naphthalene hydroxylation (14 instead of <1%). The presence of this reducing agent also had a dramatic effect on the chemoselectivity of toluene hydroxylation, as it greatly favours aromatic hydroxylation over benzylic hydroxylation (ratios of 1.6 instead of 0.1). Similar results were observed in the case of the (L_5) iron complexes, with increases of the yields of aromatic hydroxylation of anisole, toluene and ethylbenzene by factors between 2 and 11 (Table 2). The most spectacular increase was observed with naphthalene whatever the catalyst; the yields of α- and β-naphthols reached 30% (in the case of the $L_5{}^2$ complex), whereas they were very low (<2%) in the absence of reductant. Addition of trimethylhydroquinone allowed one to reach yields of aromatic hydroxylation of anisole, toluene and ethylbenzene of 61, 33 and 18%, respectively. In the case of toluene and ethylbenzene, this increase in the aromatic hydroxylation yields was always accompanied by a great increase in the aromatic/benzylic hydroxylation ratio.

This increase of the aromatic hydroxylation yields upon addition of trimethylhydroquinone to the iron catalyst–H_2O_2 systems is not due to supplementary oxidation reactions coming from iron-catalyzed activation of dioxygen, which is present in these aerobic reactions, by the reducing agent, for the two following reasons. Oxidation of anisole by the $L_5{}^2$ (or $L_5{}^3$)$FeCl^+$–H_2O_2–trimethylhydroquinone systems were performed either on aerobic or on anaerobic conditions (see Section 2 and Table 2) and always gave almost identical results. Moreover, oxidation of anisole by $H_2{}^{18}O_2$ in $CH_3CN/H_2{}^{16}O$ (80/20) and in the presence of ($L_5{}^2FeCl$)PF_6 and trimethylhydroquinone (anisole/H_2O_2/catalyst/trimethylhydroquinone molar ratio = 3000/20/1/10) led to methoxyphenols with phenolic oxygen atoms containing 95 ± 1% of ^{18}O isotope. Thus, the presence of trimethylhydroquinone markedly increases the yields of aromatic hydroxylation (Table 2) but does not change the origin (H_2O_2) of the oxygen atom incorporated into the substrates.

Addition of trimethylhydroquinone to the $L_4{}^3FeCl_2$– or $(L_5FeCl)^+$–H_2O_2 systems led not only to an increase in the yields of phenol products but also to an increase in the oxidation rates. For instance, addition of trimethylhydroquinone to the ($L_5{}^3FeCl$)PF_6–H_2O_2 system, under conditions of Table 2, led to a fivefold increase of the initial rates of anisole oxidation to methoxyphenols (11 turnovers per min instead of 2.2; data not shown).

Finally, Table 2 also shows that the lower activity of the catalyst in the absence of reductant, the higher the increase of the aromatic hydroxylation yields upon addition of the reductant. Thus, the yields of methoxyphenols derived from anisole hydroxylation increased 1.8-, 2.7- and 11-fold upon addition of trimethylhydroquinone to the systems using ($L_5{}^2FeCl$)PF_6, ($L_5{}^3FeCl$)PF_6 and $L_4{}^3FeCl_2$, respectively. Similarly, addition of this reductant to the three catalytic systems, respectively led to 4.4-, 6- and 20-fold increases of the yields of aromatic hydroxylation of toluene (Table 2).

Table 3 shows that the effects of trimethylhydroquinone on the yields of anisole hydroxylation by the (L_5) iron–H_2O_2 systems were also observed with other reducing agents, such as thiophenol, 3,5-dimethylthiophenol or α-naphthol. Yields of anisole hydroxylation increased up to 66 and 69% upon addition of thiophenol and α-naphthol, respectively. Addition of phenol did not lead to an increase of the anisole hydroxylation yields, and piperidine exhibited an inhibitory effect on this hydroxylation (Table 3).

The level of increase of aromatic hydroxylation upon addition of a reducing agent was dependent on the reducing agent/catalyst ratio used, as shown in Table 4. Thus, the yields of methoxyphenols derived from anisole were 41 and 51% for trimethylhydroquinone/($L_5{}^2FeCl$)PF_6 ratios of 1

Table 3
Compared effects of various reducing agents on the hydroxylation of anisole by H_2O_2 catalyzed by $(L_5{}^2FeCl)PF_6$ and $(L_5{}^3FeCl)PF_6$[a]

Reductant	Products (yield %)[b]					
	$(L_5{}^2FeCl)PF_6$			$(L_5{}^3FeCl)PF_6$		
	o-OH	*p*-OH	PhOH	*o*-OH	*p*-OH	PhOH
Trimethylhydroquinone	43	18	8	37	16	7
Phenol	24	6	–	11	3	–
Thiophenol	45	21	7	40	20	4
3,5-Dimethylthiophenol	46	19	7	43	18	4
α-Naphthol	47	22	7	37	20	8
Piperidine	<1	<1	<1	<1	<1	<1
Without reductant	28	5	6	15	5	5

[a] Conditions as in Table 2.
[b] Yields based on starting H_2O_2. *o*-OH and *p*-OH refer to *ortho*- and *para*- methoxyphenol, respectively. *Meta*-methoxyphenol was formed in very low amounts (<5% of total methoxyphenols).

and 5, respectively. The increase of the yields of cresols derived from toluene was even larger with the same increase in the reductant/catalyst ratio (12.5 and 27%).

In that respect, the most spectacular results were obtained with a reducing agent, $diMeH_4P$, which is a close analogue of the well-known biological reducing cofactor tetrahydrobiopterin, H_4B (Fig. 2). Table 4 shows that the optimal increase of methoxyphenols yields was already obtained with a $diMeH_4P/(L_5{}^2FeCl)PF_6$ ratio of 1. Addition of a stoechiometric amount of $diMeH_4P$ (relative to the catalyst) led to a 48% yield of methoxyphenols instead of 30% in the absence of this reductant, whereas the addition of an excess of $diMeH_4P$ (5 eq. relative to the catalyst) led to a smaller increase of the yield. The most striking beneficial effect of $diMeH_4P$ was observed in the case of naphthalene oxidation. Naphthols were formed in very low yields in the absence of a reducing agent or even in the presence of 5 eq. of trimethylhydroquinone (relative to the catalyst). By contrast, they were formed in a 47% yield in the presence of 5 eq. of $diMeH_4P$. In fact, this is the best yield obtained so far for naphthalene hydroxylation by such non-heme iron complexes/H_2O_2 systems (compare Tables 2 and 4).

The beneficial effects of $diMeH_4P$ was also clear in the case of benzene itself as substrate, as the addition of this reducing agent (5 eq. relative to the catalyst) allowed one to obtain a remarkable yield of 40% for benzene hydroxylation.

3.3. Discussion

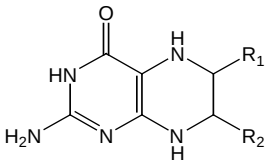
A comparative study of the catalytic properties of iron complexes bearing hexa-, penta-, and tetra-azapolydentate ligands, $[(TPAA)Fe](ClO_4)_2$, $(L_5{}^2FeCl)PF_6$, $(L_5{}^3FeCl)PF_6$ and $L_4{}^3FeCl_2$, towards hydroxylation of hydrocarbons by H_2O_2, showed us that all of them are not efficient catalysts for alkene epoxidation or alkane hydroxylation. However, $(L_5{}^2FeCl)PF_6$ and $(L_5{}^3FeCl)PF_6$ exhibit interesting properties as catalysts for the hydroxylation of aromatic compounds by H_2O_2, even though they are less efficient than $[(TPAA)Fe](ClO_4)_2$ (Table 1). Actually, the efficacy of the four studied catalysts for hydroxylation of anisole by H_2O_2 increases in the following order:

$$L_4{}^3FeCl_2 < (L_5{}^2FeCl)PF_6 \sim (L_5{}^3FeCl)PF_6 < [(TPAA)Fe](ClO_4)_2$$

Table 4
Comparison of the effects of $diMeH_4P$ and 2,3,5-trimethylhydroquinone on the hydroxylation of aromatic compounds by H_2O_2 catalyzed by $(L_5{}^2FeCl)PF_6$[a]

Reductant	Products (yields %)[b]										
	Anisole			Naphthalene		Benzene	Toluene				
	o-OH	*p*-OH	PhOH	1-ol	2-ol	PhOH	*o*-OH	*m*-OH	*p*-OH	$PhCH_2OH$	PhCHO
$diMeH_4P$											
1 eq.	37	11	5	5	4	33	12	4.5	5	1.5	1
5 eq.	29	14	4	30	17	40	16	4.5	6	1	3
Trimethylhydroquinone											
1 eq.	32	9	5	2	1	29	6.5	3	3	2	4
5 eq.	36	15	8	7.5	5	31	16	5	6	3.5	3
Without reductant	23	7	3	<0.5	<0.5	26	3	1.5	1.5	3	5

[a] Conditions: catalyst/H_2O_2/substrate molar ratio = 1/20/3000 in CH_3CN/H_2O (80/20 because of the low solubility of $diMeH_4P$ in organic solvents) for 2 h at 20 °C. [catalyst] = 1.5 mM.
[b] Yields based on starting H_2O_2. Abbreviations for the products as in Table 2



H_4B R_1 = CHOH-CHOH-CH_3 R_2 = H

diMeH_4P $R_1 = R_2 = CH_3$

Fig. 2. Formula of tetrahydropterins H_4B and diMeH_4P.

In [(TPAA)Fe]$(ClO_4)_2$-catalyzed hydroxylation of anisole, 56% of starting H_2O_2 is used for anisole oxidation, resulting in a largely predominant hydroxylation of the aromatic ring (95% of total oxidation) and a minor oxidative demethylation reaction leading to phenol (Table 1). By comparison, the two (L_5) iron complexes lead to a ca. 30% yield of anisole aromatic hydroxylation whereas $L_4{}^3FeCl_2$ gives very low yields. In all these hydroxylations of anisole, the oxygen atom incorporated into the aromatic ring comes from H_2O_2.

It is noteworthy that the redox potentials (Fe^{III}/Fe^{II} couple) of the Fe^{II} complexes used in this study increase in the following order:

$$\underset{+280\,mV[16]}{L_4{}^3FeCl_2} < \underset{+570\,mV[17]}{(L_5{}^2FeCl)PF_6} \sim \underset{+640\,mV[18]}{(L_5{}^3FeCl)PF_6} < \underset{+1023\,mV[21]\,(versus\,SCE)}{(TPAA)Fe(ClO_4)_2}$$

Thus, there is a parallel variation of the redox potential and the catalytic efficiency of these iron catalysts.

Our data also show that the addition of reducing agents, such as trimethylhydroquinone or thiophenol, to the iron catalyst–H_2O_2 systems may lead to a considerable increase of the aromatic hydroxylation yields (Tables 2–4). Such beneficial effects of the addition of a reducing agent to "Fenton-like" systems using ferrous ions and H_2O_2 in the hydroxylation of aromatic compounds have been previously reported [22]. They have been attributed to the fact that the reducing agent regenerates ferrous ions by the reduction of the ferric ions formed during the reactions [22].

Great increases of the aromatic hydroxylation yields were observed in the case of the two (L_5) iron complexes and were particularly important with $L_4{}^3FeCl_2$ since the latter catalyst was almost inefficient in the absence of reductant. Such increases did not significantly occur in (TPAA)Fe$(ClO_4)_2$-catalyzed reactions. The presence of a reducing agent in (L_5) iron complexes-catalyzed oxidation of anisole allows one to reach aromatic hydroxylation yields up to 60–70%, that are markedly better than the best ones reported previously with [(TPAA)Fe]$(ClO_4)_2$ [14]. In the best case (Table 3; case of α-naphthol), 76% of starting H_2O_2 was used to produce anisole oxidation products (69% for aromatic hydroxylation and 7% for oxidative demethylation). This improvement of the yields was observed for all the studied aromatic substrates, allowing us to increase the best yields of aromatic hydroxylation of toluene, ethylbenzene and naphthalene obtained in the absence of reductant (7, 6 and <1%, respectively, Table 2) up to 33, 18 (Table 2) and 47% (Table 4), respectively.

With toluene and ethylbenzene for which aromatic hydroxylation is in competition with benzylic hydroxylation, that is a highly favorable reaction with most oxidizing systems (see for instance [15,23]), the increases of the aromatic hydroxylation yields in the presence of a reductant were always accompanied with an increase in the aromatic/benzylic hydroxylation ratio. Several reducing agents, trimethylhydroquinone, thiophenol, 3,5-dimethylthiophenol, α-naphthol and diMeH_4P exhibit comparable beneficial effects on aromatic hydroxylation yields (Tables 3 and 4). However, diMeH_4P is particularly interesting in that respect, since it causes an important increase of anisole hydroxylation yields when used in stoechiometric amounts relative to the catalyst, and since it leads to a spectacular increase of the yields of naphthalene hydroxylation (from less than 1 to 47%, Table 4) and to the best yields of hydroxylation of this substrate (47%) and of benzene itself (40%, Table 4) observed with the non-heme iron–H_2O_2 systems.

The mechanism of the above described aromatic hydroxylations, as well as the origin of the beneficial effects of reducing agents on some of these reactions, are far from being understood. Such a mechanism should take into account four main results of this work.

(a) The unusual pattern of reactivity of the above described systems, with a low ability to epoxidize alkenes and a particular efficiency for aromatic hydroxylation.
(b) The increase of this efficiency for aromatic hydroxylations with the redox potential of the catalyst.
(c) The beneficial effects of reducing agents on several systems.
(d) The fact that the oxygen atom inserted into anisole almost exclusively comes from H_2O_2 (even in the presence of large amounts of H_2O).

Whatever this mechanism may be, the aforementioned results show that some non-heme iron complexes may act as good catalysts for the hydroxylation of aromatic compounds by H_2O_2, and indicate some ways to improve their efficacy.

References

[1] B. Meunier, Chem. Rev. 92 (1992) 1411.
[2] D. Mansuy, Coord. Chem. Rev. 125 (1993) 129.
[3] J.R. Lindsay Smith, in: R.A. Sheldon (Ed.), Metalloporphyrins in Catalytic Oxidation, Marcel Dekker, New York, 1994, p. 325.
[4] D. Dolphin, T.G. Traylor, L. Xie, Acc. Chem. Res. 30 (1997) 251.
[5] J.T. Groves, Y.Z. Han, in: P. Ortiz de Montellano (Ed.), Cytochrome P450: Structure, Mechanism and Biochemistry, Plenum Press, New York, 1995, p. 3.

[6] B. Meunier, A. Robert, G. Pratviel, J. Bernadou, in: K.M. Kadish, K.M. Smith, R. Guilard (Eds.), The Porphyrin Handbook, vol. 4, Academic Press, New York, 1999, p. 119.
[7] M. Costas, A.K. Tipton, K. Chen, D.H. Jo, L. Que, J. Am. Chem. Soc. 123 (2001) 6722.
[8] K. Chen, M. Costas, J. Kim, A.K. Tipton, L. Que, J. Am. Chem. Soc. 124 (2002) 3026.
[9] M.C. White, A.G. Doyle, E.N. Jacobsen, J. Am. Chem. Soc. 123 (2001) 7194.
[10] Y. Mekmouche, S. Ménage, C. Toia-Duboc, M. Fontecave, J.-B. Galey, C. Lebrun, J. Pécaut, Angew. Chem. Int. Ed. Engl. 40 (2001) 949.
[11] T. Okuno, S. Ito, S. Ohba, Y. Nishida, J. Chem. Soc., Dalton Trans. (1997) 3547.
[12] J.M. Rowland, M. Olmstead, P.K. Mascharak, Inorg. Chem. 40 (2001) 2810.
[13] J. Reedijk, E. Bouwman (Eds.), Bioinorganic Catalysis, Marcel Dekker, New York, 1999.
[14] J.F. Bartoli, F. Lambert, I. Morgenstern-Badarau, P. Battioni, D. Mansuy, C.R. Chimie 5 (2002) 263.
[15] S. Evans, J.R. Lindsay Smith, J. Chem. Soc., Perkin Trans. (2001) 174.
[16] N. Raffard, V. Balland, J. Simaan, S. Létard, M. Nierlich, K. Miki, F. Banse, E. Anxolabéhère-Mallart, J.J. Girerd, C.R. Chimie 5 (2002) 99.
[17] I. Bernal, I.M. Jensen, K.B. Jensen, C.J. McKenzie, H. Toftlund, J.P. Tuchagues, J. Chem. Soc., Dalton Trans (1995) 3667.
[18] V. Balland, F. Banse, E. Anxolabéhère-Mallart, M. Ghiladi, T.A. Mattioli, C. Philouze, G. Blondin, J.J. Girerd, Inorg. Chem. 42 (2003) 2470.
[19] J. Simaan, S. Döpner, F. Banse, S. Bourcier, G. Bouchoux, A. Boussac, P. Hildebrandt, J.J. Girerd, Eur. J. Inorg. Chem. (2000) 1627
[20] I. Morgenstern-Badarau, F. Lambert, J.-P. Renault, M. Cesario, J.-D. Maréchal, F. Maseras, Inorg. Chim. Acta 297 (2000) 338.
[21] A. Deroche, PhD, Université Paris Sud, Orsay, France, 1995: because of the irreversibility of the one-electron oxidation of (TPAA)Fe(ClO_4)$_2$, we have indicated the value of the oxidation potential, E_{pa}.
[22] R.O.C. Norman, J.R. Lindsay Smith, in: T.E. King, M.S. Mason, M. Morrison (Eds.), Oxidases and Related Redox Systems, Wiley, Amherst, 1965, p. 131.
[23] M. Klopstra, R. Hage, R.M. Kellogg, B.L. Feringa, Tetrahedron. Lett. 44 (2003) 4581.