Non-heme iron polyazadentate complexes as catalysts for aromatic hydroxylation by H_2O_2: Particular efficiency of tetrakis(2-pyridylmethyl) ethylenediamine–iron(II) complexes

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ABSTRACT

Two iron(II) complexes with ligands related to TPEN, *N,N,N′,N′*-tetrakis-(2-pyridylmethyl)ethane-1,2-diamine, were prepared, characterized and compared as catalysts for the hydroxylation of aromatic compounds by H_2O_2. The (TPEN)Fe^{II} complex gave the best yields ever reported for such iron polyazadentate catalysts with yields up to 86, 59, 59 and 38% for the hydroxylation of anisole, benzene, chlorobenzene and ethylbenzene, respectively.

Experiments using $H_2{}^{18}O_2$ and $H_2{}^{18}O$ clearly showed that the oxygen atom incorporated in the aromatic substrates almost exclusively comes from H_2O_2. Preliminary experiments on the effects of O_2 and spin-traps on the reactions suggested a minor contribution of uncontrolled radicals such as •OH. From the presently available data, a tentative mechanism based on the hydroxylation of substrates by a Fe^{III}OOH intermediate or, more probably, by a species resulting from the O–O bond cleavage of this intermediate, such as [Fe^{IV}O + •OH], is proposed.

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1. Introduction

Several systems based on iron-porphyrins have been shown to efficiently mimic alkene epoxidation and alkane hydroxylation by cytochrome P450-dependent monooxygenases [1–7]. More recently, non-heme iron complexes, that were developed as models of non-heme iron-containing monooxygenases, have been found to act as good catalysts for the epoxidation or *cis*-dihydroxylation of alkenes by H_2O_2 [8–13]. Cytochromes P450 and some non-heme iron monooxygenases also catalyze the efficient and selective hydroxylations of aromatic compounds [14,15]. However, reproducing these enzymatic hydroxylations of aromatic substrates appears to be much more difficult, presumably because of the very easy further oxidation of the expected phenol products in the oxidizing medium [6,7,16,17]. Recently, we have 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 by H_2O_2, but was an efficient catalyst for the hydroxylation of aromatic compounds by

H_2O_2 [18]. In fact, this catalyst gave satisfactory hydroxylation yields in the case of electron-rich aromatic compounds such as anisole (53% yield based on H_2O_2, 10.6 turnovers (TON) of the catalyst), however, it was less efficient for less electron-rich aromatics such as benzene and chlorobenzene (respective yields of 22 and 13%, respective TON of 4.4 and 2.6) [18]. Iron(II) complexes of the 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] (Fig. 1) exhibited comparable properties, i.e. they were poor catalysts for alkene epoxidation and alkane hydroxylation by H_2O_2, but gave satisfactory results for aromatic hydroxylation by H_2O_2 [19]. In the case of the two latter complexes, addition of an appropriate reducing agent, such as a hydroquinone, thiophenol, or a tetrahydropterin, led to marked increases of the yields of hydroxylation of aromatic compounds such as anisole, ethylbenzene or benzene. Such systems catalyzed the transfer of an oxygen atom from H_2O_2 into anisole, as shown by experiments using $H_2{}^{18}O_2$, with yields based on starting H_2O_2 up to 69% (TON of 13.8) [19].

In our search of more potent non-heme iron complexes as aromatic hydroxylation catalysts, we have prepared and completely characterized iron(II) complexes with ligands related to TPEN [*N,N,N′,N′*-tetrakis-(2-pyridylmethyl)ethane-1,2-diamine]

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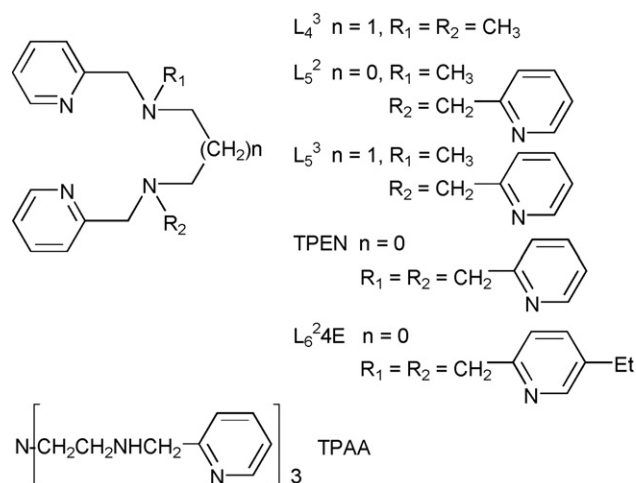
Fig. 1. Structure of the polyazadentate ligands present in the iron catalysts compared in this study.

(Fig. 1) [20]. We have also compared the catalytic properties of [(TPEN)Fe](PF$_6$)$_2$ and [(L$_6^2$4E)Fe](PF$_6$)$_2$, a complex obtained with the new hexaazadentate ligand L$_6^2$4E, [N,N'-bis-(5-ethyl-2-pyridylmethyl)-N, N'-bis-(2-pyridylmethyl)ethane-1,2-diamine] (Fig. 1). This paper shows that, when used in the presence of an appropriate reducing agent, the [(TPEN)Fe](PF$_6$)$_2$ complex acts as a remarkable catalyst for the hydroxylation of aromatic compounds by H$_2$O$_2$, as not only electron-rich aromatics such as anisole but also much less reactive aromatics such as benzene and chlorobenzene are hydroxylated with yields between 40 and 60%.

2. Experimental

2.1. Catalysts and reactants

The ligand L$_6^2$4E was synthesized as described in the Supplementary material. Both Fe^{II} complexes were synthesized according to the procedure described for [(TPEN)Fe](PF$_6$)$_2$ by Chang et al. [21] but without heating the reaction mixture. Crystals of the two complexes were obtained from methanolic solutions of the crude red powders at 4 °C. 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. X-ray crystallography

X-ray diffraction data for [(TPEN)Fe](PF$_6$)$_2$ and [(L$_6^2$4E)Fe](PF$_6$)$_2$ were collected by using a Kappa X8 APPEX II Bruker diffractometer with graphite-monochromated Mo Kα radiation (λ = 0.71073 Å). The temperature of the crystal was maintained at the selected value (100 K) by means of a 700 series Cryostream cooling device within an accuracy of ±1 K. The data were corrected for Lorentz polarization, and absorption effects. The structures were solved by direct methods using SHELXS-97 [22] and refined against F^2 by full-matrix least-squares techniques using SHELXL-97 [23] with anisotropic displacement parameters for all non-hydrogen atoms. Hydrogen atoms were located on a difference Fourier map and introduced into the calculations as a riding model with isotropic thermal parameters. All calculations were performed by using the crystal structure crystallographic software package WINGX [24].

The drawing of the two molecules was realised with the help of ORTEP32 [25].

Crystal data for [(TPEN)Fe](PF$_6$)$_2$. C$_{30}$H$_{34}$F$_{12}$FeN$_8$P$_2$, M = 852.44, monoclinic, a = 20.5330(10) Å, b = 14.2133(7) Å, c = 26.0786(16) Å, α = 90°, β = 109.2940(10)°, γ = 90°, V = 7183.4(7) Å^3, T = 100(1) K, space group C2/c (no. 15), Z = 8, μ(Mo Kα) = 0.607 mm^{-1}, 53378 reflections measured, 8269 unique (R_{int} = 0.0485), 5968 (I > 2σ(I)) which were used in all calculations. The final $R(F2)$ = 0.0493. Crystal data for [(L$_6^2$4E)Fe](PF$_6$)$_2$. C$_{34}$H$_{44}$F$_{12}$FeN$_6$P$_2$, M = 882.54, monoclinic, a = 11.7790(14) Å, b = 15.9414(16) Å, c = 20.208(3) Å, α = 90°, β = 91.311(4)°, γ = 90°, V = 3793.5(8) Å^3, T = 100(1) K, space group P2$_1$/c (no. 14), Z = 4, μ(Mo Kα) = 0.576 mm^{-1}, 23011 reflections measured, 9132 unique (R_{int} = 0.0502), 5238 (I > 2σ(I)) which were used in all calculations. The final $R(F2)$ = 0.0636. CCDC 653820 and 653821 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

2.3. Typical procedure for catalytic oxidations

The oxidant (H$_2$O$_2$; 20 μmol) was added to a CH$_3$CN/CH$_2$Cl$_2$ (1/1, v/v) solution of the Fe^{II} catalyst (1 μmol), the substrate (3 mmol) and eventually the reducing agent (10 μmol, see Tables 1 and 2), the total volume of the solvents being 1 mL. After 2 h at 20 °C, an internal standard (PhCOCH$_3$ or PhI, 10 μmol) was added and the reaction mixture was analyzed by gas chromatography.

Reactions under anaerobic conditions were performed by "freeze–thaw cycles" of a vial containing a solution of all the reactants except H$_2$O$_2$ and of a second vial containing the H$_2$O$_2$ solution.

Table 1
Effects of various reducing agents on aromatic hydroxylations by H$_2$O$_2$ catalyzed by [(TPEN)Fe](PF$_6$)$_2$ and [(L$_6^2$4E)Fe](PF$_6$)$_2$[a]

Catalyst ± reductant	Products (yields %)[b]												
	Anisole				Benzene	Chlorobenzene			Ethylbenzene				
	o-OH	p-OH	PhOH	Total	PhOH	o-OH	m + p-OH	Total	o-OH	m-OH	p-OH	PhCHOHCH$_3$	PhCOCH$_3$
[(L$_6^2$4E)Fe]$^{2+}$	14.5	1.5	2	18	25	10.5	9	19.5	1	<1	1	11	23
+1-naphthol	18	3	3	24	26	14	16	30	10	2	3.5	6	10
+triMeHQ	21	2.5	3	26.5	15	7.5	6.5	14	4	<2	2	9	20
+PhSH	30	8	3	41	31	23	17	40	8	3	3	14.5	27
[(TPEN)Fe]$^{2+}$	32	4	5	41	46	24	20	44	9	4	4	19	34
+1-naphthol	60	26	8	94	59	24	18	42	20	9	9.5	15	17
+triMeHQ	32	6	4.5	42.5	37	20	14	34	5	3.5	3	13	23
+PhSH	30	4	5	39	30	17	16	33	9	4	4	12	22

[a] Conditions: catalyst/H$_2$O$_2$/substrate/±reducing agent molar ratio = 1/20/3000/±10 in CH$_3$CN/CH$_2$Cl$_2$ (1/1) for 2 h at 20 °C; [catalyst] = 1 mM. o-OH, m-OH and p-OH are used for ortho, meta and para-substituted phenols, respectively. In the case of anisole, meta-methoxyphenol corresponded to less than 5% of total methoxyphenols.

[b] Yields are based on starting H$_2$O$_2$.

Table 2
Comparison of the efficiency of the hydroxylation of aromatic compounds by H_2O_2 in the presence of various (polyazadentate)iron catalysts[a]

Catalyst[b] ± reductant	Products (yields %)[c]											
	Anisole			Benzene	Ethylbenzene				Chlorobenzene			Ref.
	o-OH	*p*-OH	Total		*o*-OH	*m*-OH	*p*-OH	Total	*o*-OH	*m* + *p*-OH	Total	
$[(L_4{}^3)FeCl_2] +$ triMeHQ	20	13	33		3.5	0.7	1	5.2				[19]
$[(L_5{}^3)FeCl]^+ +$ triMeHQ	37	16	53		9	2	3	14	8	8	16	[19][d]
$[(L_5{}^2)FeCl]^+ +$ triMeHQ	43	18	61	31	11	3	4	18	3.5	4	7.5	[19][d]
$[(TPAA)Fe]^{2+}$	26	27	53	22	9	4	11	24	6	7	13	[18]
$[(L_6{}^24E)Fe]^{2+} +$ PhSH	30	8	38	31	8	3	3	14	23	17	40	This work
$[(TPEN)Fe]^{2+} +$ 1-naphthol	60	26	86	59	20	9	9.5	38.5	29	30	59	This work

[a] Best yields obtained so far for each substrate and catalyst (the reducing agent used to obtain these yields is indicated). Conditions are described in Refs. [18,19], and Table 1; they correspond, in most cases, to catalyst/H_2O_2/substrate molar ratio = 1/20/3000 in CH_3CN/CH_2Cl_2 (1/1) for 2 h at 20 °C. Results concerning chlorobenzene and $[(TPEN)Fe](PF_6)_2$ were obtained under the conditions of Table 1, except for the use of CH_3CN as solvent instead of CH_3CN/CH_2Cl_2.

[b] All the complexes were used as their $PF_6{}^-$ salts, except for the TPAA complex that was used as its $ClO_4{}^-$ one.

[c] Yields are based on starting H_2O_2.

[d] Yields indicated in the case of chlorobenzene were obtained under identical conditions, except for the absence of a reducing agent [35].

The content of the first vial was then transferred onto the H_2O_2 solution under argon.

2.4. Product analysis and identification

Gas chromatographic analyses were done using either a packed 5% FFAP column for most substrates, or a capillary BP20 (polar) column for 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 gas chromatography–mass spectrometry analysis, using a Hewlett-Packard 5890 Series II GC coupled with a HP5972 mass selective detector.

The *ortho*-, *meta*- and *para*-chlorophenol could be separated and then quantitatively analyzed after silyl derivatization [26]. In the oxidation of chlorobenzene using $H_2{}^{18}O_2$ or $H_2{}^{18}O$, either in aerobic or in anaerobic conditions, the levels of ^{18}O incorporation into chlorobenzene were measured on the basis of an analysis of the peaks at *m/z* 187 corresponding to the molecular ion $(Cl–Ph–OSi(CH_3)_2{}^+)$ obtained after silyl derivatization of the chlorophenols.

3. Results and discussion

3.1. Spectrophotometric and structural characterizations of the Fe^{II} complexes

Solutions, in methanol or acetonitrile, of the $[(TPEN)Fe](PF_6)_2$ and $[(L_6{}^24E)Fe](PF_6)_2$ complexes exhibited similar UV–vis spec-

tra characterized by an Fe^{II}-to-pyridine charge transfer at 417 ($\varepsilon = 10500\,M^{-1}\,cm^{-1}$, in MeOH and CH_3CN) or 419 nm ($\varepsilon = 8020\,M^{-1}\,cm^{-1}$, in MeOH and $8480\,M^{-1}\,cm^{-1}$ in CH_3CN), respectively (spectra not shown). The position and high intensity of these bands indicated that these complexes contained low spin (S = 0) Fe^{II} centers [27]. The X-ray structures of the complexes $[(TPEN)Fe](PF_6)_2$ and $[(L_6{}^24E)Fe](PF_6)_2$ were very similar (Fig. 2). They also were similar to that previously reported by Chang et al. [21] for $[(TPEN)Fe](ClO_4)_2$. Both complexes involved hexacoordinate iron with a distorted octahedral geometry [28]. The Fe–N(pyridine) and Fe–N(amine) distances are slightly shorter in the $[(TPEN)Fe](PF_6)_2$ complex (mean values of 1.976 and 1.993 Å, instead of 1.981 and 2.000 in the $[(L_6{}^24E)Fe](PF_6)_2$ complex). The bond distances are characteristic of a low spin Fe^{II} site for both complexes [27]. On the basis of these data and on the above-mentioned UV–vis signatures, it seems that the structures observed in the solid state (Fig. 2) are retained in solution.

3.2. Comparison of $[(TPEN)Fe](PF_6)_2$ and $[(L_6{}^24E)Fe](PF_6)_2$ complexes as H_2O_2-dependent aromatic hydroxylation catalysts

The $[(L_6{}^24E)Fe](PF_6)_2$ and $[(TPEN)Fe](PF_6)_2$ complexes were active catalysts for the hydroxylation of aromatic compounds by H_2O_2 (entries 1 and 5 of Table 1). These catalytic oxidations, as well as all the aromatic hydroxylations described in the following, were performed under our standard experimental conditions (with an iron catalyst/H_2O_2/substrate molar ratio = 1/20/3000 in most experiments) for an immediate comparison with our previ-
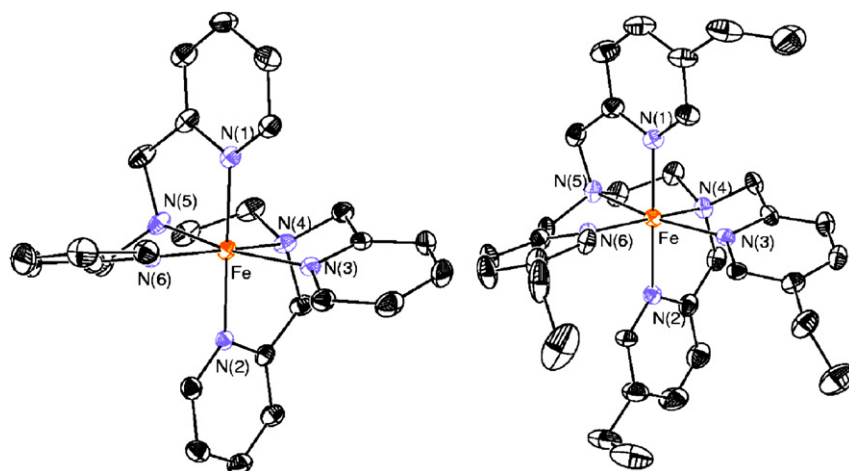

Fig. 2. Structures of the molecular complex cations of $[(TPEN)Fe](PF_6)_2$ (left) and $[(L_6{}^24E)Fe](PF_6)_2$ (right).

ous systems [18,19]. These reactions were conducted 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 catalytic systems to transfer an oxygen atom from H_2O_2 to the substrate. Table 1 clearly shows that [(TPEN)Fe]$(PF_6)_2$ is a better aromatic hydroxylation catalyst than [$(L_6{}^2 4E)$Fe]$(PF_6)_2$, and leads to good yields of hydroxylation not only of electron-rich aromatics such as anisole (36% yield of methoxyphenols) but also of benzene and chlorobenzene (46 and 44% yield, respectively).

As shown in Table 1, addition of a reducing agent, such as 1-naphthol, 2,3,5-trimethylhydroquinone (triMeHQ) or thiophenol, to the [$(L_6{}^2 4E)$Fe]$(PF_6)_2$-H_2O_2 system led in most cases to an increase of the yields of aromatic hydroxylation of anisole, benzene, chlorobenzene and ethylbenzene. The best results were obtained with thiophenol with an increase of the yields of aromatic hydroxylation of these substrates by a factor of 2.4, 1.2, 2 and 6, respectively. The effects of the addition of a reducing agent on the [(TPEN)Fe]$(PF_6)_2$-H_2O_2 system on the hydroxylation of the same substrates was less clear (Table 1). Actually, only 1-naphthol led to a significant increase of the hydroxylation yields with most substrates. Thus, in the presence of this reducing agent, hydroxylation of the aromatic ring of anisole, benzene, and ethylbenzene, occurred with yields of 86, 59 and 38.5%, respectively. Such large differences in the effects of reducing agents on the aromatic hydroxylation yields of iron polyazadentate ligands-H_2O_2 systems, as a function of the nature of the reducing agent and of the iron catalyst, have already been reported in the case of the [(TPAA)Fe]$(ClO_4)_2$, [$(L_5{}^2)$FeCl]PF_6, [$(L_5{}^3)$FeCl]PF_6 and [$(L_4{}^3)$FeCl$_2$] complexes [19].

3.3. Comparison of the efficiency of [(TPEN)Fe]$(PF_6)_2$ and [$(L_6{}^2 4E)$Fe]$(PF_6)_2$ complexes with other H_2O_2-dependent hydroxylation catalysts

Table 2 compares the best aromatic hydroxylation yields, either described in this article, or that we have previously reported [18,19], for iron(II) polyazadentate ligands-H_2O_2 systems. It gives the best yields obtained for each aromatic substrate/iron catalyst couple, and indicates the nature of the reducing agent used, when its use was necessary to optimize the aromatic hydroxylation yield. For all substrates, the best oxidation catalyst was [(TPEN)Fe]$(PF_6)_2$. With anisole as substrate, it led to a 86% yield in the presence of 1-naphthol; this yield is much better than the one obtained with [$(L_5{}^2)$FeCl]PF_6 in the presence of triMeHQ (61%). With benzene and ethylbenzene as substrates, [(TPEN)Fe]$(PF_6)_2$ in the presence of 1-naphthol was largely superior to the other catalysts, with aromatic hydroxylation yields of 59 and 38.5, respectively, whereas the second best systems only gave yields of 31 and 24, respectively. With most oxidizing systems, benzylic oxidation is by far the most favored reaction occurring on ethylbenzene [29,30], and Table 1 shows that the aromatic hydroxylation/benzylic oxidation ratio was 0.06 in the case of the [$(L_6{}^2 4E)$Fe]$(PF_6)_2$-H_2O_2 system. Interestingly, the hydroxylation of the aromatic ring of ethylbenzene by the [(TPEN)Fe]$(PF_6)_2$-H_2O_2-1-naphtol system became slightly more important than the oxidation of the benzylic position of this substrate (aromatic hydroxylation/benzylic oxidation = 1.2) (Table 1). Finally, the most spectacular result was observed with chlorobenzene as substrate, whose hydroxylation

by the [(TPEN)Fe]$(PF_6)_2$-H_2O_2 system occurred with a yield of 59% (in CH_3CN in that case), whereas the systems using either [(TPAA)Fe]$(ClO_4)_2$ or [$(L_5{}^2)$FeCl]PF_6 led to yields lower than 13% [18,19].

3.4. Preliminary experiments to further characterize the iron(II) polyazadentate/H_2O_2/reducing agent systems and their mechanism of aromatic hydroxylation

All the results described in Tables 1 and 2 were obtained after a single addition of H_2O_2 (20 equivalents relative to iron) to a substrate/catalyst/reducing agent mixture in CH_3CN/CH_2Cl_2. In order to know whether the catalyst turnover number for aromatic hydroxylation may increase upon further additions of H_2O_2, four successive additions of 20 eq. of H_2O_2 and 5 eq. of PhSH were done every 2 h on a solution of [$(L_6{}^2 4E)$Fe]$(PF_6)_2$ and chlorobenzene (3000 eq.) in CH_3CN/CH_2Cl_2. Product analysis after each addition showed that the turnover number of the iron catalyst for chlorophenols formation progressively increased from 6.2 to 13 after the first three additions, and slightly decreased to 12 after the fourth addition. This could be due to the disappearance of the phenol products because of further oxidations and/or to a progressive inactivation of the catalyst. A study of the oxidation of a mixture of *ortho-* and *para-*chlorophenol and benzene (5, 5 and 2220 eq. based on iron) by the [$(L_6{}^2 4E)$Fe]$(PF_6)_2$-H_2O_2-PhSH system under the conditions of Table 1, showed that, as expected, benzene was hydroxylated to phenol (22% yield based on H_2O_2) [31] and also that 25% of the starting chlorophenols disappeared, which indicate that further oxidations of the phenol products do occur.

Preliminary experiments were done to start to understand the mechanism of these complex oxidation systems. As far as the origin of the oxygen atom inserted in the aromatic substrates is concerned, experiments using either $H_2{}^{18}O_2$ or $H_2{}^{18}O$ were performed under conditions identical to those described in Table 1, except for the use of CH_3CN instead of CH_3CN/CH_2Cl_2. Oxidation of chlorobenzene by $H_2{}^{18}O_2$ in the presence of either [$(L_6{}^2 4E)$Fe]$(PF_6)_2$ or [(TPEN)Fe]$(PF_6)_2$ led to chlorophenols containing more than 95% ^{18}O. Identical experiments performed under anaerobic conditions led to $99 \pm 2\%$ incorporation of ^{18}O. By contrast, the same experiments using H_2O_2 in $CH_3CN/H_2{}^{18}O$ (9/1) led to chlorophenols containing less than 1% ^{18}O.

Free radicals not to tightly controlled by the iron catalyst, such as the $^{\bullet}OH$ radical deriving from a Fenton reaction between the Fe^{II} complex and H_2O_2, could possibly be involved in the aromatic hydroxylations. Two series of experiments were performed in order to test this hypothesis. In the first series of experiments, the spin trap 5,5-dimethyl-1-pyrroline-*N*-oxide (DMPO) was added to a [$(L_5{}^2)$FeCl]PF_6-H_2O_2–anisole mixture in CH_3CN/CH_2Cl_2 and aliquots were studied by EPR spectroscopy at 100 and 292 K. The usual 1:2:2:1 quartet signal that is expected for the DMPO-$^{\bullet}OH$ adduct could not be detected. Moreover, the addition of DMPO (30 eq. vs. Fe) did not stop the formation of phenol products and only led to a moderate decrease of their yields (23% instead of 33% in absence of a reducing agent, or 33% instead of 46% in the presence of PhSH) [32]. In the second series of experiments, several catalytic oxidations were performed either under aerobic (see Tables 1 and 2) or anaerobic conditions. The presence of O_2 had only minor effects on the aromatic hydroxylation yields and regioselectivity. In general, it only led to a small increase of the yields. For instance, in the case of the hydroxylation of chlorobenzene by the [$(L_6{}^2 4E)$Fe]$(PF_6)_2$- or [(TPEN)Fe]$(PF_6)_2$-H_2O_2 systems operating in CH_3CN without a reducing agent, yields of 22 and 56% were obtained respectively for the two catalysts in the presence of O_2, instead of 18 and 53% in its absence. Such a minor influence of O_2 seems to be general for the aromatic hydroxylations catalyzed by

our iron(II) polyazadentate-H_2O_2 systems since similar observations were done with iron(II) complexes of TPAA and L_5^2 [19].

3.5. Discussion

The aforementioned data clearly show that the $[(TPEN)Fe](PF_6)_2$-H_2O_2 system, in the presence of 1-naphthol when necessary, is particularly efficient for the hydroxylation of the aromatic ring of a variety of substrates, with yields between 38.5 and 86% for ethylbenzene and anisole, respectively. From all the analogous iron(II) polyazadentate complexes that have been tested so far (see Table 2), $[(TPEN)Fe](PF_6)_2$ is the best catalyst for such aromatic hydroxylations. It should be useful for the preparation of metabolites deriving from the aromatic hydroxylation of drugs, which are difficult to obtain by other methods.

Presently, it is too early to give a detailed mechanism for the aromatic hydroxylations performed by these complex systems. However, the preliminary experiments that we have done in that purpose definitely show that the oxygen atom incorporated in the aromatic substrates almost exclusively comes from H_2O_2. The experiments using $H_2^{18}O_2$ and $H_2^{18}O$ described above show that this is true for the $[(TPEN)Fe](PF_6)_2$ and $[(L_6^24E)Fe](PF_6)_2$ complexes. Similar previous experiments have demonstrated that this was also true for $[(L_5^2)FeCl](PF_6)_2$ [19]. Taking into account the very easy overoxidation of the phenol products, as shown by the experiments performed on a benzene/chlorophenols mixture (see Section 3.4), the yields of transfer of an oxygen atom from H_2O_2 to the aromatic substrates (see Table 1, 86, 59 and 44% in the case of anisole, benzene and chlorobenzene, with $[(TPEN)Fe](PF_6)_2$ as catalyst) are presumably underestimated.

The preliminary mechanistic experiments described in Section 3.4 on the effects of O_2 or spin-traps such as DMPO on the reactions suggest a minor contribution of uncontrolled free radicals such as $^\bullet OH$ in the aromatic hydroxylations.

It was shown that reaction of H_2O_2 with the iron(II) polyazadentate complexes used in this study led to $Fe^{III}OOH$ complexes [33–37]. In the case of $[(L_5^2)FeOOH](PF_6)_2$, a microcrystalline powder could be isolated at low temperature [37]. This isolated complex was found to react with aromatic substrates [38] with regioselectivities close to those we reported for the corresponding system using the $[L_5^2Fe(Cl)](PF_6)_2$ catalyst [19]. These chemo- and regioselectivities are definitely different from those observed for the oxidations of the same substrates by $Fe^{IV}O$ intermediates prepared from the same Fe^{II} starting complexes [39,40]. Thus, it is tempting to speculate that the aromatic hydroxylations described throughout this paper are due to the oxidation of the substrates either by $Fe^{III}OOH$ intermediates or, more probably, by species resulting from the O–O bond cleavage of these intermediates such as $[Fe^{IV}O + {}^\bullet OH]$. Such a pair of caged reactive species has already been proposed to be responsible for the stoichiometric intramolecular oxidation of an aromatic ligand of an iron complex in the presence of H_2O_2 [11]. Here, reaction of aromatic substrates with $^\bullet OH$ within the $[Fe^{IV}O + {}^\bullet OH]$ cage would generate substrate-derived cyclohexadienyl radicals that should be very rapidly oxidized to the corresponding phenols by the $Fe^{IV}O$ species before to diffuse out from the cage. Such a mechanism would explain the relatively weak effects of DMPO and O_2 on the aromatic hydroxylations.

The molecular origin of the particular efficiency of the $[(TPEN)Fe](PF_6)_2$ complex remains to be elucidated. It has been shown that, in the $[(L_4^3)FeCl_2]$, $[(L_5^2)FeCl]PF_6$, $[(L_5^3)FeCl]PF_6$, and $[(TPAA)Fe](ClO_4)_2$ series, and in the absence of a reducing agent, there was a correlation between the redox potential and the catalytic efficiency of these iron complexes [18,19]. However, the redox potential (Fe^{III}/Fe^{II} couple) of the $[(TPEN)Fe](PF_6)_2$ complex (+760 mV vs. SCE) is lower than that of $[(TPAA)Fe](ClO_4)_2$ (1023 mV

vs. SCE), whereas the former is a better aromatic hydroxylation catalyst. Thus, more relevant parameters, such as the redox potential of the hydroxylating species, should be considered. The greater efficacy of $[(TPEN)Fe](PF_6)_2$, when compared to $[(L_6^24E)Fe](PF_6)_2$, as catalyst of aromatic hydroxylation by H_2O_2, could be due to a less easy access of the substrates to the iron-containing hydroxylating species in the latter catalyst because of the presence of the ethyl substituents on the pyridyl rings (see Fig. 2).

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.molcata.2008.03.006.

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[32] Experiments performed under the conditions of Table 1. Fe/H$_2$O$_2$/anisole/±PhSH/±DMPO: 1/20/3000/±10/±30; (−PhSH/−DMPO) *o*-OH 28, *p*-OH 5, PhOH 6; (−PhSH/+DMPO) *o*-OH 19, *p*-OH 4.3, PhOH 2; (+PhSH/−DMPO) *o*-OH 35, *p*-OH 11.3, PhOH 5.4; (+PhSH/+DMPO) *o*-OH 26, *p*-OH 6.7, PhOH 4.

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