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# Hydroxylation of aromatics by $H_2O_2$ catalyzed by mononuclear non-heme iron complexes. Role of triazole hemilability in substrate-induced bifurcation of the $H_2O_2$ activation mechanism

Jean-Noël Rebilly\*, Wenli Zhang, Christian Herrero, Hachem Dridi, Katell Sénéchal-David, Régis Guillot, and Frédéric Banse\*

Dedication ((optional))

Abstract: Rieske dioxygenases are metalloenzymes capable of achieving cis-dihydroxylation of aromatics under mild conditions using O<sub>2</sub> and a source of electrons. The intermediate responsible for this reactivity is proposed to be a cis-Fe<sup>V</sup>(O)(OH) moiety. Molecular models allow generating  $Fe^{III}(OOH)$  species with  $H_2O_2$ , to yield a  $Fe^{V}(O)(OH)$  species with tetradentate ligands, or {Fe<sup>IV</sup>(O)/OH•} pairs with pentadentate ones. We have designed a new pentadentate ligand mtL<sub>4</sub><sup>2</sup> bearing a labile triazole, to generate an "in-between" situation. Two iron complexes [(mtL<sub>4</sub><sup>2</sup>)FeCl](PF<sub>6</sub>) and  $[(mtL_4^2)Fe(OTf)_2])$  were obtained and their reactivity studied towards aromatic substrates in the presence of H<sub>2</sub>O<sub>2</sub>. Spectroscopic and kinetic studies reflect that triazole is bound at the Fe<sup>II</sup> state, but decoordinates in the Fe<sup>III</sup>(OOH). The resulting [(mtL<sub>4</sub><sup>2</sup>)Fe<sup>III</sup>(OOH)(MeCN)]<sup>2+</sup> then lies on a bifurcated decay pathway (end-on homolytic vs side-on heterolytic) depending on the addition of aromatic substrate: in the absence of substrate, it is proposed to follow a side-on pathway leading to a putative  $(N_4)$ Fe<sup>V</sup>(O)(OH), while in the presence of aromatics it switches to an end-on homolytic pathway yielding a  $\{(N_5)Fe^{IV}(O);OH^{\bullet}\}$  reactive species, through recoordination of triazole This switch significantly impacts the reaction regioselectivity.

### Introduction

Finding ways to achieve selective oxidation of organic molecules is of high interest in organic synthesis. Metalloenzymes are capable of doing such conversions under mild conditions using readily available metals as catalysts,  $O_2$  as the oxidant and generating H<sub>2</sub>O as a by-product, and are thus a source of inspiration to develop green processes.<sup>[11]</sup> In particular, nonheme iron enzymes such as Rieske dioxygenases can achieve *cis*-dihydroxylation of aromatics at a mononuclear iron site by activating O<sub>2</sub> using two electrons and two protons.<sup>[2-3]</sup> In the course of dioxygen activation, an Fe<sup>III</sup>(OOH) intermediate has been identified<sup>[4-5]</sup> which is proposed to evolve towards a

 [a] Dr J-N Rebilly\*, W Zhang, Dr C Herrero, Dr H Dridi, Dr K Sénéchal-David, Dr R Guillot, Pr F Banse\*
Institut de Chimie Moléculaire et des Matériaux d'Orsay
Université Paris-Sud, Université Paris-Saclay
91405 Orsay cedex, France
E-mail: jean-noël.rebilly@u-psud.fr; frederic.banse@u-psud.fr

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### Fe<sup>V</sup>(O)(OH) reactive species.<sup>[6]</sup>

Molecular models have been developed to mimic such enzymes by replacing the cofacial triad<sup>[2, 7]</sup> (two imidazoles and a carboxylate from His and Asp residues) by polydentate chelating ligands, mostly based on aza coordination spheres, which allows to ensure stability and mononuclearity for the resulting iron complexes.<sup>[2, 8]</sup> These systems proved capable of achieving biomimetic catalytic activity in the oxidation of alkanes, alkenes and aromatics using the peroxide shunt pathway (H<sub>2</sub>O<sub>2</sub> instead of O<sub>2</sub>, protons and electrons).<sup>[9-16]</sup> For this purpose, at least one exchangeable position must remain in the coordination sphere to generate reactive intermediates. Hence, tetradentate or pentadentate ligands are traditionally used, leaving respectively either two or one labile site(s) at the iron. Hexadentate ligands bearing a labile arm can also give access to pentadentate-like reactivities. Depending on the ligand, different types of activation mechanisms were proposed for the generated Fe<sup>III</sup>(OOH) intermediate, either by homolytic cleavage of the O-O bond, yielding {Fe<sup>IV</sup>(O)/OH•}<sup>[13, 17-20]</sup> or heterolytic cleavage, to yield  $Fe^{V}(O)(OH)^{[9, 21-24]}$  or  $Fe^{V}(O)(OAc)$  when assisted by acetic acid [25-27] The formation of these species is dictated by the ligand backbone, and in turn the reactivity pattern is intimately related to the nature of the reactive species. Formation of the  $Fe^{V}(O)(OH)$  or  $Fe^{V}(O)(OAc)$  motif requires two *cis* labile sites which are found in complexes derived from tetradentate ligands,<sup>[21, 25-26]</sup> while the {Fe<sup>IV</sup>(O)/OH•} pair is often proposed with pentadentate ones.[13, 16, 28-29]

For this reason, we have developed a new pentadentate ligand where one pyridyl group was replaced by a triazole, known to be less donating and more labile than pyridine,<sup>[14, 30]</sup> with the aim of generating a system that could possibly gather the stability and robustness of pentadentate systems while being able to access a tetradentate coordination sphere *in situ* through triazole labilization.

Herein, we report new Fe<sup>II</sup> complexes based on the pentadentate ligand  $mtL_4^2$  (Scheme 1), their characterization in solution and in the solid state, and the evaluation of their catalytic properties towards oxidation of aromatics by  $H_2O_2$  in MeCN. These studies evidence the hemilability of triazole, which allowed to accumulate an Fe<sup>III</sup>(OOH) intermediate under catalytic conditions and get direct insight into the reactive species, which was not possible with parent pentadentate ligand-based complexes.<sup>[13]</sup> The experimental observations suggest that in the absence of aromatic substrate the (mtL\_4<sup>2</sup>)Fe<sup>III</sup>(OOH) intermediate decays along a side on pathway to generate a formally *cis* (*N*<sub>4</sub>)Fe<sup>V</sup>(O)(OH) species, similarly to its (L<sub>4</sub><sup>2</sup>)Fe<sup>III</sup>(OOH) analogue, derived from the tetradentate L<sub>4</sub><sup>2</sup>

ligand. However, addition of aromatic substrates in the medium induces a switch in the Fe<sup>III</sup>(OOH) decay pathway involving recoordination of triazole and the generation of a different reactive intermediate, a { $(N_5)$ Fe<sup>IV</sup>(O)/HO•} caged pair, which significantly impacts the regioselectivity of the reaction.

### Results

The ligand  $mtL_4^2$  (Scheme 1) was synthesized in 77% yield following the CuAAC (Cu-catalyzed alkyne-azide cycloaddition) methodology from ligand  $mpL_4^2$  and the copper sulphate/sodium ascorbate catalytic system in a *t*BuOH/water mixture at 60°C (Supporting Information, Scheme S1).

### Synthesis of the complexes

Complex  $[(mtL_4^2)Fe(OTf)_2]$  was synthesized from  $mtL_4^2$  and  $Fe(OTf)_2$  in methanol and isolated by precipitation with diethyl ether. Complex  $[(mtL_4^2)FeCl](PF_6)$  was synthesized from  $mtL_4^2$  and  $FeCl_2.2H_2O$  in methanol followed by the addition of AgPF<sub>6</sub> to precipitate AgCl. The complex was isolated by precipitation of the filtrate with diethyl ether.



Scheme 1. Structure of the ligands mentioned in this article



**Figure 1.** An ORTEP drawing of compound  $[(mtL_4^2)FeCI]^*$ . Thermal ellipsoids are shown at the 30% level. Fe is in orange-red, C in grey, N in blue, O in dark red, CI in green, F in yellow, P in light orange. Hydrogen atoms are omitted for clarity.

### Solid state studies

Single crystals of  $[(mtL_4^2)FeCl](PF_6)$  were obtained by diffusion of *tert*-butylmethyl ether into a solution of the precipitate

dissolved in MeOH. The crystal structure of the molecular cation  $[(mtL_4^2)FeCI]^*$  is displayed in Figure 1. The metal center sits in a distorted octahedral environment with  $mtL_4^2$  acting as a pentadentate ligand and a chloride anion completing the coordination sphere. The ligand adopts a configuration with the two pyridyl groups lying in *trans* positions oriented perpendicular to each other. Fe-N bond distances sit in the range 2.21-2.29 Å while the Fe-Cl is 2.32 Å, which is consistent with a high spin Fe<sup>II</sup> center.<sup>[14]</sup>





**Figure 2.** (A) UV-vis spectra of  $[(mtL_2^2)Fe(OTf)_2]$  at 298 K in MeCN and MeOH. (B) CV at a GC electrode of  $[(mtL_4^2)Fe(OTf)_2]$ , at 298 K in MeCN-([Fe] = 2 mM, [NBu\_4PF\_6] = 0.1 M, CE = Pt, RE = SCE, scan rate = 0.2 V.s<sup>-1</sup>).

The two complexes  $[(mtL_4^2)Fe(OTI)_2]$  and  $[(mtL_4^2)FeCI](F_6)$ were studied by UV-vis absorption spectroscopy and cyclic voltammetry. The characerizations of  $[(mtL_4^2)FeCI](PF_6)$  are displayed in Figure 2, whereas those of  $[(mtL_4^2)FeCI](PF_6)$  are shown in Supporting Information, Figure S5.

**[(mtL<sub>4</sub><sup>2</sup>)Fe(OTf)<sub>2</sub>]** in MeCN displays an absorption band (MLCT) at  $\lambda = 373$  nm (ε = 7110 M<sup>1</sup>.cm<sup>-1</sup>) while in MeOH it is at  $\lambda = 356$  nm (ε = 2090 M<sup>-1</sup>.cm<sup>-1</sup>) (Figure 2A). The difference in the extinction coefficient suggests a solvent-dependent coordination sphere. The low value in MeOH is consistent with a high spin Fe<sup>II</sup> complex encountered when anion binding occurs and suggests a *N*<sub>5</sub>Fe<sup>II</sup>(OTf)-type-coordination sphere.

In MeCN, the much higher value suggests an Fe<sup>II</sup> complex in a predominantly low spin form in agreement with acetonitrile binding ( $N_5$ Fe<sup>II</sup>(MeCN) coordination sphere). These results are consistent with MeCN acting as a stronger and more competitive ligand than MeOH.

The CV of  $[(mtL_4^2)Fe(OTf)_2]$  in MeCN (Figure 2B) displays a major reversible wave at  $E_p^{\circ} = 1.00 \text{ V}/ E_p^{\circ} = 0.91 \text{ V}$  assigned to the  $[N_5Fe^{\parallel}(MeCN)]^{2^+}$  species and a minor one at  $E_p^{\circ} = 0.65 \text{ V}/ E_p^{\circ} = 0.60 \text{ V}$  assigned to the  $[N_5Fe^{\parallel}(OTf)]^+$  species. The reduction wave at  $E_p^{\circ} = 0.82 \text{ V}$  is tentatively assigned to an isomer of the  $[N_5Fe^{\parallel}(MeCN)]^{3^+}$  species where the triazole and pyridine are exchanged, of to the binding of water instead the MeCN. These assignments are consistent with the CV of 1 + 1 + 1 [(mtL\_4^2)FeCI](PF\_6) in MeCN which reveals an equilibrium

between a  $[N_{\text{s}}\text{Fe}^{\text{II}}\text{CI}]^{*}$  and  $[N_{\text{s}}\text{Fe}^{\text{II}}(\text{MeCN})]^{2*}$  species (Supporting Information, Figure S5).

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Furthermore, the potentials observed for  $[(mtL_4^2)Fe(OTf)_2]$  are very close to those found with complexes derived from ligand  $pL_5^2$   $([N_5Fe^{II/III}(MeCN)]^{2+/3+}$  at  $E_p^a = 1.06V/E_p^c = 0.97$  V,  $[N_5Fe^{II/III}CI]^{+/2+}$  at  $E_p^a = 0.69$  V/  $E_p^c = 0.62$  V).<sup>[14]</sup> Thus, the replacement of a pyridine by a triazole does not affect significantly the donating strength of the overall coordination sphere.

These assignments were confirmed by HR-ESI-MS (Figures S4 and S6).

### **Reactivity studies**

The catalytic properties of the complexes in the oxidation of aromatics were tested on the substrates anisole, benzene and chlorobenzene (Table 1) with PhIO and  $H_2O_2$  as oxidants.

With PhIO (entries 6-10), complexes derived from tetra- ( $N_4$ ), penta- ( $N_5$ ) and hexadentate ( $N_6$ ) ligands are inactive in the oxidation of aromatics (Table 1), in agreement with the formation of a common reactive species ( $N_x$ )Fe<sup>IV</sup>(O) (*vide infra*). It has indeed been frequently reported that non heme Fe<sup>IV</sup>(O) intermediates cannot hydroxylate external aromatic substrates.<sup>[14, 17, 31]</sup>

In contrast, formation of phenol products were observed with  $H_2O_2$ . Comparison of  $[(mtL_4^2)FeC]](PF_6)$  and  $[(mtL_4^2)Fe(OTf)_2]$  shows that the presence of the chloride induces a significant drop in the conversions of anisole (entries 1 and 2). This is in line with the involvement of a Fe<sup>III</sup>(OOH) species (*vide infra*) and the competitive character of chloride (vs HOO<sup>-</sup>) for Fe<sup>III</sup> binding, which lowers the amount of intermediate in solution.

**Table 1**. Oxidation of aromatic substrates by hydrogen peroxide and iodosylbenzene catalyzed by  $[(mtL_4^2)FeCl](PF_6)$  and  $[(mtL_4^2)Fe(OTf)_2]$  at room temperature.<sup>[a]</sup> % Yields are given with respect to the oxidant.

Substrate				Anisole				Benzene	Cl-benzene				
Produc	ts			ο		p	m	PhOH	PhOH	ο	p	m	PhOH
entry	Oxidant	$N_x^{[b]}$	Catalyst										
1	$H_2O_2$	$N_5$	$[(mtL_4^2)FeCI](PF_6)$	34		6	1	5					
2	$H_2O_2$	N <sub>5</sub>	$[(mtL_4^2)Fe(OTf)_2]$	63		13	1	11	50	7	/	6	/
3	$H_2O_2$	N <sub>5</sub>	$[(L_5^2)Fe(OTf)_2]$	66		7	6	10					
4	$H_2O_2$	N <sub>6</sub>	[(TPEN)Fe](PF <sub>6</sub> ) <sub>2</sub>	36		4	1	6					
5	$H_2O_2$	$N_4$	$[(L_4^2)Fe(OTf)_2]$	62		1	1	8					
6	PhIO	$N_5$	$[(mtL_4^2)FeCI](PF_6)$	1		1	1	/					
7	PhIO	$N_5$	$[(mtL_4^2)Fe(OTf)_2]$	1		1	1	/					
8	PhIO	N <sub>5</sub>	$[(L_5^2)Fe(OTf)_2]$	1		1	1	/					
9	PhIO	N <sub>6</sub>	TPENFe(PF <sub>6</sub> ) <sub>2</sub>	1		7	1	/					
10	PhIO	$N_4$	$[(L_4^2)Fe(OTf)_2]$	1		1	1	/					

<sup>[a]</sup> Fe / H<sub>2</sub>O<sub>2</sub> / anisole : 1 / 20 / 3000, Fe / PhIO / anisole : 1 / 2 / 3000. PhOH is phenol, *o*, refer to *o*-methoxyphenol or *o*-chlorophenol, *p* to to *p*-methoxyphenol or *p*-chlorophenol, and *m* to *m*-methoxyphenol or *m*-chlorophenol. Phenol is formed via oxidative demethylation of anisole whereas all other products derive from aromatic hydroxylation. All assays were performed under aerobic conditions. <sup>[b]</sup> Ligand denticity: *N<sub>x</sub>*.

 $(N_5)$  and  $(N_4)$  triflate complexes display very good and similar yields in anisole oxidation products with H<sub>2</sub>O<sub>2</sub> conversions in the range 70-89% (entries 2, 3, 5). The TPEN complex ( $N_6$  ligand, entry 4) shows a strong drop in yield with respect to ( $N_5$ ) and ( $N_4$ ) complexes, despite the formation of a similar ( $N_5$ )Fe<sup>III</sup>(OOH) intermediate.<sup>[32]</sup> Again, this can be ascribed to the better coordinating ability of the pyridyl group with respect to the triflate or the solvent ligand. The efficiency of a hexacoordinated iron catalyst in aromatic hydroxylation has recently been proposed to partly depend on the lability of a pyridine moiety.<sup>[33]</sup>.

It has previously been shown that the complex evolves via oxidative cleavage of the dangling pyridine towards a species which displays an altered reactivity  $vs H_2O_2$  (Figure S20).<sup>[31]</sup>

In anisole oxidation, in all cases the reaction is chemoselective (aromatic hydroxylation is preferred over oxidative demethylation) and displays a significant regioselectivivity (o/(o+m+p), see Table 1) with a preference for o-hydroxylation, far above the statistical ratio of 40%. [( $L_4^2$ )Fe(OTf)<sub>2</sub>] gives the best selectivity for o-hydroxylation. (100% vs 80-85% for the ( $N_5$ ) systems). [(mtL<sub>4</sub><sup>2</sup>)Fe(OTf)<sub>2</sub>] also gave satisfactory results when less reactive aromatic substrates (Table 1) were used such as benzene (50% conversion of H<sub>2</sub>O<sub>2</sub>) and chlorobenzene (13%).

In order to get insight into the reactivity mechanism of  $[(mtL_4^2)Fe(OTf)_2]$ , we carried out spectroscopic and kinetic studies in the presence of  $H_2O_2$  and PhIO.

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### Spectroscopic studies. Characterisation of intermediates



**Figure 3.** UV-vis spectra at 293 K (A) of [(mtL<sub>4</sub><sup>2</sup>)Fe(OTf<sub>2</sub>] 1 mM in MeCN before (black) and immediately after addition of 20 equiv. of hydrogen of hydrogen peroxide (red). EPR spectrum at 20 K (B) of [(mtL<sub>4</sub><sup>2</sup>)Fe(OTI)<sub>2</sub>] 1 mM in MeCN after addition of 20 equiv. of hydrogen peroxide (red). The solution was d awn at the maximum of Fe<sup>III</sup>(OOH) accumulation. Simulated spectrum (grey) as the sum of  $Fe^{III}(OOH)$  (97% of LS signal,  $g_x = 2.210$ ;  $g_y = 2.155$ ,  $g_z = Fe^{III}(OH)$  (3% of LS signal,  $g_x = 2.345$ ;  $g_y = 2.140$ ,  $g_z = 1.915$ ) 1.965) and

Upon addition of 1.2 equiv. of iodosylbenzene to a solution of [(mtL42)Fe(OTf)2] at 253 K in acetonitrile, the solution turned from brown to green. The UV-vis spectrum shows the disappearance of the MLCT band at 373 nm and the prowth of a band at 735 nm typical of other (N<sub>5</sub>)Fe<sup>IV</sup>(O) species (Figure \$14). This latter intermediate exhibits a half-life of 135 mn under these conditions

Upon addition of 20 equiv. H<sub>2</sub>O<sub>2</sub> to a solution of [(mtL<sub>4</sub><sup>2</sup>)Fe(OTf)<sub>2</sub>] in acetonitrile at 293 K (Figure 3), the solution turns from brown to purple. The UV-vis spectrum shows the disappearance of the MLCL band at 373 nm, ascribed to the oxidation of Fe<sup>II</sup>, together with the growth of a new band at 520 nm, which decays in 140 s (Figure S15). Such a chromophore (520 nm) is typical of  $N_x \text{Fe}^{II}$  (OOH) species within this fan OT ligands.[11-14, 34-36]



Scheme 2. Proposed structures of different Fe<sup>III</sup>(OOH) intermediates

Remarkably, such a chromophore can be generated in MeCN similarly to  $[(L_4^2)Fe(OTf)_2]$  (with a maximum at 560 nm, Figure S21) or other Fe<sup>II</sup> complexes with tetradentate ligands.<sup>[37-38]</sup> but cannot be accumulated in MeCN with [TPENFe](PF6)2,  $[(L_5^2)Fe(OTf)_2]$  (Figures S19-S20) and most Fe<sup>II</sup> precursors with pentadentate ligands for which MeOH has to be used instead.<sup>[32,</sup> . 39-41]

To confirm the nature of the transient species, an EPR sample was drawn from the solution at the maximum of accumulation of the 520 nm chromophore and frozen in an EPR tube. The EPR spectrum shows three sets of signals. The signal in the g = 4region (Figure S16) can be ascribed to a non-specific ubiquitous high spin Fe<sup>III</sup> species, whereas the other two correspond to low spin Fe<sup>III</sup> species (Figure 3B). Double integration of the EPR signal allows estimating the high spin Fe<sup>III</sup> / low spin Fe<sup>III</sup> ratio to be 30 / 70 and spectral simulation the relative weight of LS species.

The minor low spin Fe<sup>III</sup> species (2% of total Fe<sup>III</sup>) at g = 2.140, 1.915) corresponds to the  $N_5$ Fe<sup>III</sup>(OH) species resulting from the oxidation of Fe<sup>II</sup> to Fe<sup>III</sup>, and the major one (68% of total  $Fe^{III}$ ) at g = (2.210, 2.155, (1.965), is assigned to an  $Fe^{III}(OOH)$ species.<sup>[13-14, 34, 41-42]</sup> Typical  $N_5$ Fe<sup>III</sup>(OOH) species with aminopyridyl ligands (TPEN or  $L_5^2$ , or  $tL_5^2$ ) display two set s of signals for the hydroperoko species, assigned to two rotarners (Scheme 2),<sup>[34]</sup> as initially proposed for [(N4Py)Fe<sup>III</sup>(OOH)]<sup>2</sup> Feringa, Münck and Que<sup>[39]</sup> By contrast, complexes with L bv or related ligands only show a single signal.<sup>[17, 37]</sup>

The EPR signature of  $[(mtL_4^2)Fe^{III}(OOH)]^{2+}$  is very close to that of  $[(L_4^2)Fe^{III}(OOH)]^{2+}[1^1]$  [This likely results from the decoordination of the labile triazole, leading to a L42-type coordination sphere (Scheme 2). Hence, the different behaviour of  $(mtL_4^2)$  and  $(L_5^2)$  could be assigned to the weaker donating ability and increased lability of trazole (vs pyridine).

### Kinetic Studies in the absence or presence of substrate.

In the absence of substrate, the kinetics for the development and decay of the Fe<sup>III</sup>(OOH) reaction intermediate (formed rom  $(mtL_4^2)Fe(OTf)_2$  and 20 equiv. of  $H_2Q_2$  in MeCN) can described by global fit to a  $A \rightarrow B \rightarrow Q$  model, where A is he the Fa" precursor, B is Fe" (OOH) and C is the decay product, and

rate constants  $k_{1obs}$  and  $k_{2obs}$  extracted (Figure S22) We investigated the dependence of the rate constants on [H2O2] (Fgures 4 and S23) and temperature (Figure S26 \$27 rate of formation of Fe<sup>III</sup>(OOH) (k<sub>1obs</sub>) displays dependence on  $[N_{2}O_{2}]$ , in line with a bimolecular process involving H<sub>2</sub>O<sub>2</sub>, though it is in fact a fast/two-step process:





The decay rate of  $Fe^{III}(OOH)$  ( $k_{2obs}$ ) shows a slight dependence

on  $[H_2O_2]$  reminiscent of a saturation kinetics (Figures 4 and S24). As water does not affect the decay rate (Figure S24-S25), the saturation curve we observed is thus due to excess  $H_2O_2$ . A classical deactivation pathway of the Fe<sup>III</sup>(OOH) intermediate is hydrogen peroxide disproportionation (catalase effect), as reported recently for (N4Py)Fe<sup>III</sup>(OOH).<sup>[41]</sup>

 $\begin{aligned} \mathsf{Fe}^{\text{III}}(\mathsf{OH}) + \mathsf{H}_2\mathsf{O}_2 &\leftrightarrows \mathsf{Fe}^{\text{III}}(\mathsf{OOH}) + \mathsf{H}_2\mathsf{O} \end{aligned} \tag{1} \\ \mathsf{Fe}^{\text{III}}(\mathsf{OOH}) + \mathsf{H}_2\mathsf{O}_2 &\leftrightarrows \mathsf{Fe}^{\text{IIII}}(\mathsf{OH}) + \mathsf{O}_2 + \mathsf{H}_2\mathsf{O} \end{aligned} \tag{2}$ 

This is in line with the turnover experiments which show a drop in the yields of anisole products at higher  $H_2O_2$  concentrations where  $H_2O_2$  disproportionation becomes competitive with substrate hydroxylation (Figure S37).



**Figure 5.** UV-vis spectra (stopped flow, 293 K) of  $[(mtL_4^2)Fe(OTf)_2]$  / benzene 1 / 300 (1mM Fe in MeCN) + 20 equiv. H<sub>2</sub>O<sub>2</sub> monitored in time (A, B, C), and time traces of the characteristic bands observed (D). (A) growth of Fe<sup>III</sup>(OOH), (B) growth of Fe<sup>III</sup>(OPh), (C) decay of Fe<sup>III</sup>(OPh). Simulated spectra (E) and kinetics (F) extracted from the fit to in a ABCD model. A=Fe<sup>II</sup>, B=Fe<sup>III</sup>(OOH), C = Fe<sup>III</sup>(OPh), D = decay product. The raw simulated extinction coefficients and concentrations were corrected to take into account the fact that only 70% of Fe<sup>III</sup> sconverted to Fe<sup>III</sup>OOH (from EPR integration). The corrected values are displayed in panels E and F (see text).

As the system proved to be efficient in aromatic oxidation, we also carried out kinetic studies in the presence of an aromatic

substrate. For simplification, we used benzene as its hydroxylation leads to a single phenol product.

We followed, by stopped-flow methods, the addition of 20 equiv. of  $H_2O_2$  to a solution of  $[(mtL_4^2)Fe(OTf)_2]$  in MeCN in the presence of benzene (Figure 5).

The first observed step (Figure 5A) occurs in the first 5 s and corresponds to the formation of the Fe<sup>III</sup>(OOH) species ( $\lambda_{max} = 520 \text{ nm}$ ). In a second step from 5 to 150 s (Figure 5B), two new broad bands grow up around 650 nm and below 490 nm, which decays in a final step (Figure 5C). With a maximum at 650 nm, this spectrum can be ascribed to the LMCT of a Fe<sup>III</sup>(OPh) adduct (Figure 5E). The kinetics were adjusted to a A  $\rightarrow$  B  $\rightarrow$  C  $\rightarrow$  D model by global fit (A=Fe<sup>III</sup>, B=Fe<sup>III</sup>(OOH), C=Fe<sup>IIII</sup>(OPh), D=decay product), allowing to access simulated spectra of Fe<sup>III</sup>(OOH) and of the transient species formed in the second step.

The rate of formation of  $Fe^{III}(OPh)$  ( $k_{2obs'}$ ) is independent of benzene concentration (Figure S30) and lies in the same order of magnitude as the natural decay rate of  $Fe^{III}(OOH)$  in the absence of substrate ( $k_{2obs}$ ). This suggests that  $Fe^{III}(OOH)$  does not directly react with the substrate but decays in the rate limiting step to generate a species that reacts with benzene.

To get further insight into the Fe<sup>III</sup>(OOH) formation and decay into the reactive species, temperature studies were carried out in the absence of substrate allowing us to access activation parameters *via* Eyring plots (Figure S26-S27).

For the formation step, a relatively high activation enthalpy  $(\Delta H_1^{\dagger})$ = 49 ± 2 kJ.mol<sup>-1</sup>) and negative entropy ( $\Delta S_1^{\neq}$  = -74 ± 5 J.K<sup>-1</sup>.mol<sup>-1</sup> <sup>1</sup>) were found, in line with an associative process, as described in equation (1). With complex  $[(L_4^2)Fe^{II}(MeCN)_2](CIO_4)_2$  ( $\Delta H_1^{\neq}$  = 55 kJ.mol<sup>-1</sup> and  $\Delta S_1^{\neq}$  $= -29 \text{ J.K}^{-1}.\text{mol}^{-1})^{[17]}$ and [(bzTPENFe<sup>III</sup>CI](CIO<sub>4</sub>)<sub>2</sub> ( $\Delta H_1^{\neq}$  = 53 kJ.mol<sup>-1</sup> and  $\Delta S_1^{\neq}$  = -72 J.K<sup>-</sup> .mol<sup>-1</sup>)<sup>[43]</sup>, the same trend is observed. For the decay step (equation 2), the activation enthalpy is low  $(\Delta H_2^{\neq} = 28 \pm 3)$ kJ.mol<sup>-1</sup>), but a strongly negative entropy is obtained ( $\Delta S_2^{\neq} = -$ 193  $\pm$  9 J.K<sup>-1</sup>.mol<sup>-1</sup>), which indicates a strongly organized or associative transition state.  $[(L_4^2)Fe^{III}(OOH)]^{2+}$  decays with very close parameters in MeCN ( $\Delta H_2^{\neq}$  = 32 ± 2kJ.mol<sup>-1</sup> ;  $\Delta S_2^{\neq}$  = -158 ± 7 J.K<sup>-1</sup>.mol<sup>-1</sup>, Figure S32-S34). Thus, it can be concluded that the triazole is likely dangling in  $[(mtL_4^2)Fe(OOH)]^{2+}$  and that it is not involved in the rate determining step of the decay process.

Interestingly, these parameters are far different from those previously reported for  $[(L)Fe^{III}(OOH)]^{2+}$  species (Table 2) and particularly from those determined for the decay of  $[(L_5^2)Fe^{III}(OOH)]^{2+}$  ( $\Delta H_2^{\neq} = 81 \text{ kJ.mol}^{-1}$ ,  $\Delta S_2^{\neq} = -1J.K^{-1}.mol^{-1}$ ).<sup>[13]</sup> With a stronger donor arm, ligand  $(L_5^2)$  remains pentadentate in  $[(L_5^2)Fe^{III}(OOH)]^{2+}$ . With penta-  $(L_5^2)$  or tetradentate ligands  $(L_4^2)^{2+1}$ or mtL<sub>4</sub><sup>2</sup>), Fe<sup>III</sup>OOH thus decays through very different pathways. Kinetic and reactivity studies on  $[(L_5^2)Fe^{III}(OOH)]^{2+}$  showed the intermediate evolved following a homolytic path to yield a {Fe<sup>IV</sup>(O), OH'} caged pair as the reactive species: the strong activation enthalpy reflects the cost of O-O bond breaking in the TS and the near-zero entropy was ascribed to a radical process involving the reaction of the OH moiety with CH<sub>3</sub>CN or another Fe<sup>III</sup>(OOH) species during the decay of the intermediate (Scheme 3).[44]

### In the case of $[(mtL_4^2)Fe^{II}(OOH)]^{2^+}$ , the strongly negative entropy suggests an associative transition state. In the absence of substrate, H<sub>2</sub>O<sub>2</sub> is likely involved in this associative process (leading to catalase effect, *vide supra*). The particularly low activation enthalpy suggests that any O-O bond breaking might be partly compensated by another bond formation. Four scenarii could rationalize these observations (Scheme 3) : i) O-O bond cleavage is concerted with H atom abstraction (HAA) from the *cis* bound MeCN ligand; ii) the activation is assisted by water as proposed by Que and coworkers;<sup>[45-47]</sup> iii) the hydroperoxide binds in a *side-on* fashion to the iron in the transition state, as proposed for many systems based on tetradentate ligands;<sup>[36, 46]</sup> or iv) a second H<sub>2</sub>O<sub>2</sub> molecule is involved in the process.

As already mentioned above, since there is no water dependence on the observed decay rate (Figure S24-S25), hypothesis (ii) can be discarded.

When carried out in  $CD_3CN$  (Figure S29), the decay (step 2) is not significantly slowed down, which is not compatible with HAA from the solvent. Accordingly, the activation parameters obtained in MeOH (Figure S28 and Table 2) are very close to those found in MeCN, suggesting a similar pathway that is compatible with a subordinate role of the solvent and therefore hypothesis (i) can be discarded.



# **Scheme 3.** Proposed decay mechanism for $[(L_5^2)Fe^{III}(OOH)]^{2^*}$ (adapted from ref. 13) and possible transition states for the evolution of $[(mtL_4^2)Fe^{III}(OOH)]^{2^*}$ and $[(L_4^2)Fe^{III}(OOH)]^{2^*}$ .

Hypothesis (iii), O-O bond breaking *via* a side-on transition state, <sup>[36, 46]</sup> appears to be a likely pathway, as tetradentate based systems are often proposed to form *cis* Fe(O)(OH) species. With the solvent playing no important role, it is likely to remain bound, otherwise it would be reflected in a higher activation enthalpy. Additionally, hypothesis (iv) can be considered plausible since it rationalizes the  $[H_2O_2]$  dependence on the decay rate.

Table 2. Activation parameters for	for the decay of v	various Fe <sup>III</sup> (OOH) species
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O-O bond cleavage	O-O bond System		∆S≠ J.mol <sup>-1</sup> .K <sup>-1</sup>	
This work	$[(mtL_4^2)Fe^{III}(OOH)]^{2*}$ in MeCN	28 ± 3	-193 ± 9	
	$[(mtL_4^2)Fe^{III}(OOH)]^{2*}$ in MeOH	33 ± 4	- 176 ± 13	
	[(L4 <sup>2</sup> )Fe <sup>III</sup> (OOH)] <sup>2+</sup> in MeCN	32 ± 2	-158 ± 7	
Á	$[(L_4^2)Fe^{III}(OOH)]^{2+}$ in MeCN + benzene	26.3 ± 2	-178 ± 5	
	$[(mtL_4^2)Fe^{III}(OOH)]^{2+}$ in MeCN + benzene	43.5 ± 4	-133 ± 1.5	
Heterolytic	[(TMC)Fe <sup>III</sup> (OOH)] <sup>2+</sup> + HCIO <sub>4</sub> in MeCN <sup>[48]</sup>	44	-89	
	[(TPA)Fe <sup>lll</sup> (OOH)] <sup>2+</sup> + octene in MeCN <sup>[47]</sup>	45	-95	
	[(PyNMe₃)Fe <sup>III</sup> (OOH)] <sup>2+</sup> in MeCN + H <sup>+[26]</sup>	46	-79	
	(BnTPEN)Fe <sup>III</sup> (OOH) <sup>2+</sup> + HOAc + HOTf in MeCN <sup>[49]</sup>	30	-118	
Homolytic	$[(PyNMe_3)Fe^{III}(OOH)]^{2+}$ + in MeCN <sup>[26]</sup>	43	-137	
	$[(L_5^2)Fe^{III}(OOH)]^{2+}$ in MeCN <sup>[13]</sup>	81	-1	
	[(TMC)Fe <sup>III</sup> (OOH)] <sup>2+</sup> in acetone/CF <sub>3</sub> CH <sub>2</sub> OH <sup>[16]</sup>	56	-75	
	[(N₄Py)Fe <sup>III</sup> (OOH)] <sup>2+</sup> in acetone / CF <sub>3</sub> CH <sub>2</sub> OH <sup>[16]</sup>	53	-121	
	[(bppc)Fe <sup>III</sup> (OOH)] <sup>2+ [28]</sup>	53	-68	

TMC = tetramethylcyclam; TPA = trispyridylamine; PyNMe3 = N,N"-((2,6)dimethylpyridyl)-N,N',N"-trimethyl-diethylenetriamine; N4py = N,N-bis(2pyridylmethyl)-N-(bis-2-pyridylmethyl)amine; bppc = N,N'-dibenzyl-N,N'-bis(2pyridylmethyl)-1,2-cyclohexanediamine

Interestingly, when the reaction is carried out in the presence of 300 equiv. benzene, the Eyring plot gives the activation parameters for the  $[(mtL_4^2)Fe^{III}(OOH)]^{2^+}$  decay  $\Delta H_2^{\,\pm}$  = 43.5  $\pm$  4 kJ.mol<sup>-1</sup> and  $\Delta S_2^{\,\pm}$  = -133  $\pm$  1.5 J.K<sup>-1</sup>.mol<sup>-1</sup> (Figure S31). These parameters are clearly different from those obtained in the absence of substrate and suggest a different activation

mechanism. On the other hand, under the same conditions (300 equiv. benzene), the decay of  $[(L_4^2)Fe^{III}(OOH)]^{2^+}$  is associated to parameters  $\Delta H_2^{\neq} = 26.3 \pm 2 \text{kJ.mol}^{-1}$  and  $\Delta S_2^{\neq} = -178 \pm 5 \text{ J.K}^{-1}$ .mol<sup>-1</sup> (Figure S35-S36), very close to those obtained in the absence of substrate ( $\Delta H_2^{\neq} = 32 \pm 2 \text{kJ.mol}^{-1}$ ;  $\Delta S_2^{\neq} = -158 \pm 7 \text{ J.K}^{-1}$ .mol<sup>-1</sup>, Table 2).

Thus,  $[(L_4^2)Fe^{III}(OOH)]^{2^+}$  decays along an analogous path regardless of the presence or absence of benzene. This path is similar to that of  $[(mtL_4^2)Fe^{III}(OOH)]^{2^+}$  in the absence of benzene and likely involves a side-on transition state to yield a side-on {Fe<sup>IV</sup>(O), OH·  $\leftrightarrow$  Fe<sup>V</sup>(O), OH} species, as proposed by Rybak-Akimova.<sup>[17]</sup> This leaves us with the decay of  $[(mtL_4^2)Fe^{III}(OOH)]^{2^+}$  along a new pathway when in the presence of benzene. The main difference between these two complexes being the dangling triazole, we hypothesize that it is likely that it rebinds during the activation process, preventing a side-on transition state.

To summarize, as decay rates of  $[(mtL_4^2)Fe^{III}(OOH)]^{2+}$  are poorly dependent on benzene concentration, the substrate does not react in the TS. However, given the different sets of activation parameters obtained in the presence and absence of benzene, it induces a switch in the mechanism. This apparent paradox can be solved by considering two competitive pathways for Fe<sup>III</sup>(OOH) activation that are close in energy (Scheme 4): one yields a  $(N_4)$ Fe<sup>V</sup>(O)(OH) species, and the other  $\{(N_5)$ Fe<sup>IV</sup>(O); OH-). In support to this proposition, the activation parameters listed on Table 2 lead to close  $\Delta G^{\neq}(293 \text{ K})$  values of (84.5 ± 6) kJ.mol<sup>-1</sup> and  $(82.5 \pm 5)$  kJ.mol<sup>-1</sup> for the decay of  $[(mtL_4^2)Fe^{III}(OOH)]^{2+}$  in the absence or presence of benzene, respectively. None of these proposed Fe<sup>III</sup>(OOH) activation pathways involve any substrate, hence reaction rates will not depend on substrate concentration. For either Fe<sup>V</sup>(O)(OH) or  $\{Fe^{IV}(O); OH^{\bullet}\}$  intermediate obtained, the subsequent step is the reaction with the aromatic substrate. But if the driving force for the reaction of aromatic substrates with  $\{(N_5)Fe^{iV}(O); OH^{\bullet}\}$  is greater than the driving force for the reaction of substrate with  $(N_4)$ Fe<sup>V</sup>(O)(OH), then by equilibrium displacement, the  $\{(N_5)Fe^{IV}(O); OH^{\bullet}\}$  pathway will preferentially be picked up. It is a plausible hypothesis as aromatic hydroxylation by  $\{(N_5)Fe^{V}(O)\}$ ; OH•} intermediates has been shown to be initiated by the fast interception of OH• by the aromatic ring.<sup>[50]</sup> Conversely, when H<sub>2</sub>O<sub>2</sub> is the subtrate for catalase activity (*i.e.* in the absence of benzene),  $(N_4)$ Fe<sup>V</sup>(O)(OH) is a structurally more suited intermediate, as it can form a transient preorganized 6membered ring intermediate with  $H_2O_2$ , and the ( $N_4$ )Fe<sup>V</sup>(O)(OH) pathway will preferentially be picked up.<sup>[51]</sup> This overall scheme also reflects the two competitive reactions at work (aromatic hydroxylation vs H<sub>2</sub>O<sub>2</sub> disproportionation).

To determine the nature of the O-O bond cleavage, we compared the activation parameters found in this work with other literature systems involving well-characterized homo- and heterolytic pathways (Table 2).

Interestingly, the activation parameters for  $[(mtL_4^2)Fe^{III}(OOH)]^{2+}$ decay in the presence of benzene ( $\Delta H_2^{\pm} = 43.5 \pm 4 \text{ kJ.mol}^{-1}$  and  $\Delta S_2^{\pm} = -133 \pm 1.5 \text{ J.K}^{-1}.\text{mol}^{-1}$ ) are surprisingly close to those reported for the decay of  $[(PyNMe_3)Fe^{III}(OOH)]^{2+}$  in MeCN ( $\Delta H_2^{\pm} = 43 \text{ kJ.mol}^{-1}$ ;  $\Delta S_2^{\pm} = -137 \text{ J.K}^{-1}.\text{mol}^{-1}$ ).<sup>[26]</sup> In this latter example, theoretical studies proposed a homolytic cleavage along an end-on pathway, with the H atom of  $Fe^{III}(OOH)$  being shared between the proximal and distal O atoms in the transition state. A similar pathway, associated to the rebinding of the triazole can thus be proposed (Scheme 4).

To confirm this, we carried out the benzene oxidation reaction with 20 equiv.  $H_2O_2$  starting from a 1:1 mixture of benzene and  $D_6$ -benzene and determined a KIE value of  $1.07\pm0.03$ . If  $Fe^V(O)$  were the reactive species, an inverse KIE would be expected.<sup>[52-53]</sup> Conversely, similar KIE values were reported for a series of complexes involving an { $Fe^{IV}(O) / OH$ ·} caged pair.<sup>[13, 54]</sup>

The magnitude of the activation enthalpy for  $[(mtL_4^2)Fe^{III}(OOH)]^{2+}$  decay in the absence of substrate is relatively small, and its activation entropy very negative compared to most literature parameters. However, literature systems are not ideal references for the proposed side-on decay of the intermediate: homolytic cleavage examples correspond to the cleavage of end-on species, and heterolytic ones involve the addition of acids, which alter the intrinsic decay of Fe<sup>III</sup>(OOH).



**Scheme 4.** Proposed mechanisms for the decay of in the absence or presence of aromatic substrate. Two Fe<sup>III</sup>(OOH) activation pathways are in competition and selectively picked up depending on the subsequent reaction by equilibrium displacement: aromatic oxidation drives the system through the upper pathway, and H<sub>2</sub>O<sub>2</sub> disproportionation through the lower one in the absence of benzene. The reaction is independent on benzene concentration as the Fe<sup>III</sup>OOH activation is the slow step of the mechanism (rds).

### Discussion

Based on their similar activation parameters, we can conclude that both  $[(mtL_4^2)Fe^{III}(OOH)(MeCN)]^{2+}$  and  $[(L_4^2)Fe^{III}(OOH)(MeCN)]^{2+}$  evolve through a similar side-on transition state in the absence of aromatic substrates, yielding a *cis* Fe(O)(OH) which can be described as two {Fe<sup>IV</sup>(O), OH•  $\leftrightarrow$ Fe<sup>V</sup>(O), OH-} electromer forms, the relative weight of each is dependent on the ligand donating ability. In line with this, the highly reactive species resulting from peracid activation by

 $(N_4)$ Fe<sup>II</sup> precursors has been recently described as a mixture of Fe<sup>V</sup>(O)(OC(O)R) / Fe<sup>IV</sup>(O)(•OC(O)R) configurations.<sup>[55-56]</sup>

However, a difference appears in the presence of aromatic substrates: on the one hand,  $[(L_4^2)Fe^{III}(OOH)(MeCN)]^{2+}$  remains on the same pathway to yield *cis*-Fe(O)(OH) which oxidizes the aromatic substrate. The two oxidative equivalents are both metal centered, and the active species can be formally described as a *cis*-Fe<sup>V</sup>(O)(OH) intermediate, which has been proposed to be the active species in  $(N_4)Fe^{II}$  / H<sub>2</sub>O<sub>2</sub> catalytic systems.<sup>[8, 19, 24, 57]</sup>

On the other hand, [(mtL<sub>4</sub><sup>2</sup>)Fe<sup>III</sup>(OOH)(MeCN)]<sup>2+</sup> goes through a new transition state in which triazole rebinds to the metal, prevents the side-on binding of the hydroperoxo and forces a homolytic cleavage of the O-O bond in an end-on arrangement. The resulting reactive species is then a { $(N_5)Fe^{IV}(O), OH \cdot$ } caged pair, as proposed for  $[(L_5^2)Fe^{III}(OOH)]^{2+,[13, 50]}$  and for other Fe<sup>III</sup>(OOH) intermediates in Fenton<sup>[58]</sup> and non heme systems.<sup>[26]</sup> This activation bifurcation between  $[(L_4^2)Fe^{III}(OOH)(MeCN)]^{2+}$ and [(mtL<sub>4</sub><sup>2</sup>)Fe<sup>III</sup>(OOH)(MeCN)]<sup>2+</sup> directly impacts their catalytic performances and selectivities. Whereas [(L<sub>4</sub><sup>2</sup>)Fe<sup>III</sup>(OOH)(MeCN)]<sup>2+</sup> generates a 100% regioselectivity for o-hydroxylation of anisole (Table 1), [(mtL<sub>4</sub><sup>2</sup>)Fe<sup>III</sup>(OOH)(MeCN)]<sup>2+</sup> shows a distribution of products that is closer to that observed for  $[(L_5^2)Fe^{III}(OOH)]^{2^*}$ , where the ligand is pentadentate (Table 1). With  $L_4^2$ , the two oxidizing equivalents are both metal-controlled. The interaction between the OMe substituent of anisole and the OH ligand of Fe(O)(OH) will preferentially expose the ortho position to oxidation initiated by attack of the aromatic  $\pi$  system on the high valent Fe(O), as shown in Scheme 5. Conversely, the spatial arrangement of Fe<sup>IV</sup>(O) and OH• gets looser in the mtL<sub>4</sub><sup>2</sup> system and the regioselectivity becomes altered: aromatic hydroxylation is initiated by the attack on the  $\pi$  system by the hydroxyl radical followed the e<sup>T</sup>/H<sup>+</sup> transfer to the Fe<sup>IV</sup>(O), as demonstrated previously for  $[(L_5^2)Fe^{III}(OOH)]^{2^*}$ .<sup>[13]</sup>

Finally, these bifurcated mechanisms from a similar ( $N_4$ )Fe<sup>III</sup>(OOH) intermediate are also in line with the kinetic isotope effect observed in benzene hydroxylation. A KIE<1 was reported for [( $L_4^2$ )Fe<sup>III</sup>(OOH)(MeCN)]<sup>2+[17]</sup> consistent with the attack on an electrophilic metal-oxo by the  $\pi$  system.<sup>[17, 52]</sup> In contrast, we found KIE >1 in the case of [(mtL<sub>4</sub><sup>2</sup>)Fe<sup>III</sup>(OOH)(MeCN)]<sup>2+</sup> which has been shown to be the signature of {Fe<sup>IV</sup>(O) / OH+} formed from [( $L_5^2$ )Fe<sup>III</sup>(OOH)]<sup>2+</sup> and similar intermediates.<sup>[13, 54]</sup>



Scheme 5. Proposed mechanism for the  $\text{Fe}^{III}(\text{OOH})$  activation and the reactivity on anisole with  $[(L_4^2)\text{Fe}^{III}(\text{OOH})]^{2^+}$  (left) and  $[(\text{mtL}_4^2)\text{Fe}^{III}(\text{OOH})]^{2^+}$  (right).

# **FULL PAPER**

### Conclusions

A new ligand mtL<sub>4</sub><sup>2</sup> was synthesized, in which a pyridyl group was replaced by the less donating triazole group with respect to ligand  $L_5^2$ . Two iron complexes, [(mtL<sub>4</sub><sup>2</sup>)FeCl](PF<sub>6</sub>) and [(mtL<sub>4</sub><sup>2</sup>)Fe(OTf)<sub>2</sub>], were isolated and characterized in solution and in the solid state for [(mtL<sub>4</sub><sup>2</sup>)FeCl](PF<sub>6</sub>). Their catalytic properties in the oxidation of aromatics were tested in acetonitrile using H<sub>2</sub>O<sub>2</sub> and PhIO as oxidants. Spectroscopic studies indicate the formation of intermediates Fe<sup>III</sup>(OOH) and  $Fe^{IV}(O)$  respectively under these conditions. In particular, the Fe/H<sub>2</sub>O<sub>2</sub> system is very efficient in aromatic hydroxylation, reaching an almost quantitative conversion of hydrogen peroxide into anisole oxidation products. The reaction shows a chemoselectivity ratio of 6.9 (aromatic hydroxylation vs demethylation) and regioselectivity for o-hydroxylation of 82% in aromatic hydroxylation. The reaction still occurs with poorer aromatics like benzene and chlorobenzene.

Unlike its pyridyl analogue ( $[(L_5^2)Fe(OTf)_2]$ ), the Fe<sup>III</sup>(OOH) intermediate derived from  $[(mtL_4^2)Fe(OTf)_2]$  can be formed and accumulated in MeCN, which allowed us to study its fate under catalytic conditions.

The intermediate  $[(mtL_4^2)Fe^{III}(OOH)]^{2+}$  displays a signature close to that of  $[(L_4^2)Fe^{III}(OOH)]^{2+}$ . This suggests triazole acts as a labile ligand during the formation process. Kinetic studies show that the decay rate of  $[(mtL_4^2)Fe^{III}(OOH)]^{2+}$  is comparable to the formation rate of the phenol product, indicating the intermediate decay is the rate determining step of the hydroxylation reaction.

In the absence of aromatic substrate, the decay activation parameters are similar to those of  $[(L_4^2)Fe^{II}(OOH)]^{2+}$  and suggest a side-on arrangement of the hydroperoxo in the transition state. This type of transition state can lead to a species described as a mixture of two configurations {Fe<sup>IV</sup>(O)/HO+} and {Fe<sup>V</sup>(O)/(OH)}. Conversely, in the presence of benzene, whereas  $[(L_4^2)Fe^{III}(OOH)]^{2+}$  retains a similar activation mechanism,  $[(mtL_4^2)Fe^{III}(OOH)]^{2+}$  switches to a homolytic O-O bond cleavage assisted by the rebinding of triazole. This constitutes one of the rare examples of a substrate-induced mechanism bifurcation.<sup>[59]</sup>

Consequently, the regioselectivity obtained with [(mtL<sub>4</sub><sup>2</sup>)Fe<sup>III</sup>(OOH)(MeCN)]<sup>2+</sup> is altered with respect to that observed with [(L<sub>4</sub><sup>2</sup>)Fe<sup>III</sup>(OOH)(MeCN)]<sup>2+</sup> and is closer to the one observed with pentadentate ligand systems. This can be rationalized by the formation of a  $\{cis-(N_4)Fe^{IV}(O)(OH^{\bullet}) \leftrightarrow cis (N_4)$ Fe<sup>V</sup>(O)(OH)} species in the case of the (L<sub>4</sub><sup>2</sup>) system and of a  $\{(N_5)Fe^{IV}(O)/HO^{\bullet}\}$  caged pair in the case of  $(mtL_4^2)$ . A direct KIE for benzene oxidation is observed in the case of [(mtL<sub>4</sub><sup>2</sup>)Fe<sup>III</sup>(OOH)(MeCN)]<sup>2+</sup>, whereas an inverse KIE was reported for  $[(L_4^2)Fe^{III}(OOH)(MeCN)]^{2+}$ supporting the assignement of the respective reactive species.

The hemilability of triazole allowed us to accumulate an Fe<sup>III</sup>(OOH) intermediate and fully study the mechanism of aromatic hydroxylation by ( $N_5$ )Fe non-heme complexes under catalytic conditions (MeCN) which was previously impossible with parent systems based on TPEN or  $L_5^2$  ligands.

Finally, this study gives further insight into how ligand denticity affects the nature of the Fe<sup>III</sup>(OOH) reactive intermediate in ironcatalyzed H<sub>2</sub>O<sub>2</sub> oxidations, how it controls its decay pathway (side-on or end-on TS) and into the nature of the resulting reactive species ({*cis*-(*N*<sub>4</sub>)Fe<sup>IV</sup>(O)(OH•)  $\leftrightarrow$  *cis*-(*N*<sub>4</sub>)Fe<sup>V</sup>(O)(OH)} or {( $N_5$ )Fe<sup>IV</sup>(O)/HO•} caged pair), which in turn controls the reaction selectivity.

### **Experimental Section**

Synthesis and characterization of ligands and complexes, detailed spectroscopic and kinetic studies of intermediates and additional information can be found as supplementary material.

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### Entry for the Table of Contents (Please choose one layout)

Layout 1:

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mtL<sub>4</sub><sup>2</sup>Fe<sup>II</sup>(OTf)<sub>2</sub> reacts with H<sub>2</sub>O<sub>2</sub> to yield a (*N*<sub>4</sub>)Fe<sup>III</sup>(OOH)(MeCN) intermediate where triazole remains dangling. The hemilability of triazole then allows for a substrate-triggered switch of the Fe<sup>III</sup>(OOH) activation pathway, yielding a reactive {(*N*<sub>5</sub>)Fe<sup>IV</sup>=O; OH•} species instead (*N*<sub>4</sub>)Fe<sup>V</sup>=O(OH) obtained in the absence of substrate. This significantly impacts the regioselectivity in aromatic hydroxylation.



Jean-Noël Rebilly\*, Wenli Zhang, Christian Herrero, Hachem Dridi, Katell Sénéchal-David, Régis Guillot, and Frédéric Banse\*

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Hydroxylation of aromatics by  $H_2O_2$ catalyzed by mononuclear non-heme iron complexes. Role of triazole hemilability in substrate-induced bifurcation of the  $H_2O_2$  activation mechanism