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Hydroxylation of aromatics by H₂O₂ catalyzed by mononuclear non-heme iron complexes. Role of triazole hemilability in substrate-induced bifurcation of the H₂O₂ 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 O₂ and a source of electrons. The intermediate responsible for this reactivity is proposed to be a *cis*-Fe^V(O)(OH) moiety. Molecular models allow generating Fe^{III}(OOH) species with H₂O₂, to yield a Fe^V(O)(OH) species with tetradentate ligands, or {Fe^{IV}(O)/OH•} pairs with pentadentate ones. We have designed a new pentadentate ligand mtL₄² bearing a labile triazole, to generate an “in-between” situation. Two iron complexes [(mtL₄²)FeCl](PF₆) and [(mtL₄²)Fe(OTf)₂] were obtained and their reactivity studied towards aromatic substrates in the presence of H₂O₂. Spectroscopic and kinetic studies reflect that triazole is bound at the Fe^{II} state, but decoordinates in the Fe^{III}(OOH). The resulting [(mtL₄²)Fe^{III}(OOH)(MeCN)]²⁺ 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 follows a *side-on* pathway leading to a putative (N₄)Fe^V(O)(OH), while in the presence of aromatics it switches to an *end-on* homolytic pathway yielding a {(N₅)Fe^{IV}(O);OH•} 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, O₂ as the oxidant and generating H₂O as a by-product, and are thus a source of inspiration to develop green processes.^[1] In particular, non-heme iron enzymes such as Rieske dioxygenases can achieve *cis*-dihydroxylation of aromatics at a mononuclear iron site by activating O₂ using two electrons and two protons.^[2-3] In the course of dioxygen activation, an Fe^{III}(OOH) intermediate has been identified^[4-5] which is proposed to evolve towards a

Fe^V(O)(OH) reactive species.^[6]

Molecular models have been developed to mimic such enzymes by replacing the cofacial triad^[2, 7] (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.^[2, 8] These systems proved capable of achieving biomimetic catalytic activity in the oxidation of alkanes, alkenes and aromatics using the peroxide shunt pathway (H₂O₂ instead of O₂, protons and electrons).^[9-16] 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^{III}(OOH) intermediate, either by homolytic cleavage of the O-O bond, yielding {Fe^{IV}(O)/OH•}^[13, 17-20] or heterolytic cleavage, to yield Fe^V(O)(OH)^[9, 21-22] or Fe^V(O)(OAc) when assisted by acetic acid.^[23-25] 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,^[21, 23-24] while the {Fe^{IV}(O)/OH•} pair is often encountered with pentadentate ones.^[13, 16, 26-27]

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,^[14, 28] 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^{II} complexes based on the pentadentate ligand mtL₄² (Scheme 1), their characterization in solution and in the solid state, and the evaluation of their catalytic properties towards oxidation of aromatics by H₂O₂ in MeCN. These studies evidence the hemilability of triazole, which allowed to accumulate an Fe^{III}(OOH) intermediate under catalytic conditions and get direct insight into the reactive species, which was not possible with parent pentadentate ligand-based complexes.^[13] The experimental observations suggest that in the absence of aromatic substrate the (mtL₄²)Fe^{III}(OOH) intermediate decays along a *side-on* pathway to generate a formally *cis* (N₄)Fe^V=O(OH) species, similarly to its (L₄²)Fe^{III}(OOH) analogue, derived from the tetradentate L₄²

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ligand. However, addition of aromatic substrates in the medium induces a switch in the $\text{Fe}^{\text{III}}(\text{OOH})$ decay pathway involving recoordination of triazole and the generation of a different reactive intermediate, a $\{(\text{N}_5)\text{Fe}^{\text{IV}}(\text{O})/\text{HO}\cdot\}$ 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 $[(\text{mtL}_4^2)\text{Fe}(\text{OTf})_2]$ was synthesized from mtL_4^2 and $\text{Fe}(\text{OTf})_2$ in methanol and isolated by precipitation with diethyl ether. Complex $[(\text{mtL}_4^2)\text{FeCl}](\text{PF}_6)$ was synthesized from mtL_4^2 and $\text{FeCl}_2 \cdot 2\text{H}_2\text{O}$ in methanol followed by the addition of AgPF_6 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 $[(\text{mtL}_4^2)\text{FeCl}]^+$. Thermal ellipsoids are shown at the 30% level. Fe is in orange-red, C in grey, N in blue, O in dark red, Cl in green, F in yellow, P in light orange. Hydrogen atoms are omitted for clarity.

Solid state studies

Single crystals of $[(\text{mtL}_4^2)\text{FeCl}](\text{PF}_6)$ were obtained by diffusion of *tert*-butylmethyl ether into a solution of the precipitate dissolved in MeOH. The crystal structure of the molecular cation

$[(\text{mtL}_4^2)\text{FeCl}]^+$ 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. Bond distances sit in the range 2.20–2.35 Å, which is consistent with a high spin Fe^{II} center.^[14]

Solution studies

Figure 2. (Top) UV-vis spectra of $[(\text{mtL}_4^2)\text{Fe}(\text{OTf})_2]$ (A) and $[(\text{mtL}_4^2)\text{FeCl}](\text{PF}_6)$ (B) at 298 K in MeCN and MeOH. (Bottom) CVs at a GC electrode of $[(\text{mtL}_4^2)\text{Fe}(\text{OTf})_2]$ (C) and $[(\text{mtL}_4^2)\text{FeCl}](\text{PF}_6)$ (D) at 298 K in MeCN ($[\text{Fe}] = 2 \text{ mM}$, $[\text{NBu}_4\text{PF}_6] = 0.1 \text{ M}$, CE = Pt, RE = SCE, scan rate = 0.2 $\text{V}\cdot\text{s}^{-1}$).

The two complexes were studied by UV-vis absorption spectroscopy and cyclic voltammetry (Figure 2).

$[(\text{mtL}_4^2)\text{FeCl}](\text{PF}_6)$ displays MLCT absorption bands (Figure 2A) at $\lambda = 349 \text{ nm}$ ($\epsilon = 1875 \text{ M}^{-1}\cdot\text{cm}^{-1}$) and $\lambda = 382 \text{ nm}$ ($\epsilon = 1765 \text{ M}^{-1}\cdot\text{cm}^{-1}$) in MeCN and at $\lambda = 360 \text{ nm}$ ($\epsilon = 1540 \text{ M}^{-1}\cdot\text{cm}^{-1}$) in MeOH. The relatively low extinction coefficient values observed in all cases are in agreement with a common coordination sphere leading to a high spin Fe^{II} complex, e.g. $\text{N}_5\text{Fe}^{\text{II}}\text{Cl}$, in agreement with the bond length observed in the solid state. The cyclic voltammogram (CV) of $[(\text{mtL}_4^2)\text{FeCl}](\text{PF}_6)$ in MeCN (Figure 2C) displays two poorly reversible main waves at $E_p^a = 0.63 \text{ V}$ / $E_p^c = 0.59 \text{ V}$ (assigned to a $[\text{N}_5\text{Fe}^{\text{II}}\text{Cl}]^+$ species) and $E_p^a = 1.00 \text{ V}$ / $E_p^c = 0.84 \text{ V}$ (assigned to a $[\text{N}_5\text{Fe}^{\text{II}}(\text{MeCN})]^{2+}$ species), and an irreversible reduction wave at $E_p^c = 0.28 \text{ V}$ (assigned to a $[\text{N}_4\text{Fe}^{\text{III}}\text{Cl}_2]^+$ species).^[14] Upon increase of the scan rate (Figure S5) the waves assigned to $[\text{N}_5\text{Fe}^{\text{III}}(\text{MeCN})]^{2+/3+}$ and $[\text{N}_4\text{Fe}^{\text{III}}\text{Cl}_2]^+$ species decrease in favor of the wave corresponding to $[\text{N}_5\text{Fe}^{\text{III}}\text{Cl}]^{+/2+}$ which becomes reversible. This indicates an

equilibrium in solution between a $[N_5Fe^II Cl]^+$ and $[N_5Fe^II(MeCN)]^{2+}$ species, with the former being predominant, as observed by UV-vis spectroscopy.

$[(mtL_4^2)Fe(OTf)_2]$ in MeCN displays an absorption band (MLCT) at $\lambda = 373$ nm ($\epsilon = 7110$ M⁻¹.cm⁻¹) while in MeOH it is at $\lambda = 356$ nm ($\epsilon = 2090$ M⁻¹.cm⁻¹) (Figure 2B). The difference in the extinction coefficient suggests a solvent-dependent coordination sphere. The low value in MeOH is consistent with a high spin Fe^{II} complex encountered when anion binding occurs and suggests a $N_5Fe^II(OTf)$ -type coordination sphere.

In MeCN, the much higher ϵ value suggests an Fe^{II} complex in a predominantly low spin form in agreement with acetonitrile binding ($N_5Fe^II(MeCN)$ 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 2D) displays a major reversible wave at $E_p^a = 1.00$ V / $E_p^c = 0.91$ V assigned to the $[N_5Fe^II(MeCN)]^{2+}$ species and a minor one at $E_p^a = 0.66$ V / $E_p^c = 0.60$ V assigned to the $[N_5Fe^II(OTf)]^+$ species. The reduction wave at $E_p^c = 0.82$ V is tentatively assigned to an isomer of the $[N_5Fe^III(MeCN)]^{3+}$ species where the triazole and pyridine are exchanged, or to the binding of water instead of MeCN.

The potentials are very close to those found with complexes derived from ligand pL_5^2 ($[N_5Fe^III(MeCN)]^{2+/3+}$ at $E_p^a = 1.06$ V / $E_p^c = 0.97$ V, $[N_5Fe^III Cl]^{+/2+}$ at $E_p^a = 0.69$ V / $E_p^c = 0.62$ V).^[14] 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 H₂O₂ 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^{IV}(O) (*vide infra*). It has indeed been frequently reported that non heme Fe^{IV}(O) intermediates cannot hydroxylate external aromatic substrates.^[14, 17, 29]

In contrast, formation of phenol products were observed with H₂O₂. Comparison of $[(mtL_4^2)FeCl](PF_6)$ 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^{III}(OOH) species (*vide infra*) and the competitive character of chloride (vs HOO⁻) for Fe^{III} binding, which lowers the amount of intermediate in solution.

(N_5) and (N_4) triflate complexes display very good and similar yields in anisole oxidation products with H₂O₂ conversions up to ca 90% (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^{III}(OOH) intermediate.^[30] Again, this can be ascribed to the better coordinating ability of the pyridyl group with respect to the triflate or the solvent ligand, but also to the fragility of its dangling pyridyl arm in the oxidizing intermediate.

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.^[a] % Yields are given with respect to the oxidant.

Substrate				Anisole				Benzene	Cl-benzene			
Products				<i>o</i>	<i>p</i>	<i>m</i>	PhOH	PhOH	<i>o</i>	<i>p</i>	<i>m</i>	PhOH
entry	Oxidant	N_x ^[b]	Catalyst									
1	H ₂ O ₂	N_5	$[(mtL_4^2)FeCl](PF_6)$	33.8	6	1.32	5.45					
2	H ₂ O ₂	N_5	$[(mtL_4^2)Fe(OTf)_2]$	63.3	12.6	1.1	11.2	50	7.3	/	5.9	/
3	H ₂ O ₂	N_5	$[(L_5^2)Fe(OTf)_2]$	66	7.1	6.3	10.2					
4	H ₂ O ₂	N_6	$[(TPEN)Fe](PF_6)_2$	36	4	1	6					
5	H ₂ O ₂	N_4	$[(L_4^2)Fe(OTf)_2]$	62.0	/	/	8.0					
6	PhIO	N_5	$[(mtL_4^2)FeCl](PF_6)$	/	/	/	/					
7	PhIO	N_5	$[(mtL_4^2)Fe(OTf)_2]$	/	/	/	/					
8	PhIO	N_5	$[(L_5^2)Fe(OTf)_2]$	/	/	/	/					
9	PhIO	N_6	TPENFe(PF ₆) ₂	/	/	/	/					
10	PhIO	N_4	$[(L_4^2)Fe(OTf)_2]$	/	/	/	/					

^[a] Fe / H₂O₂ / anisole : 1 / 20 / 3000, Fe / PhIO / anisole : 1 / 2 / 3000. PhOH is phenol, *o*, refer to *o*-methoxyphenol or *o*-chlorophenol, *p* to *p*-methoxyphenol or *p*-chlorophenol, and *m* to *m*-methoxyphenol or *m*-chlorophenol. All assays were performed under aerobic conditions. ^[b] Ligand denticity: N_x .

It has previously been shown that the complex evolves via oxidative cleavage of this moiety towards a species which displays an altered reactivity vs H_2O_2 (Figure S20).^[29] In anisole oxidation, in all cases the reaction is chemoselective (aromatic hydroxylation is preferred over oxidative demethylation) and regioselective with a preference for *o*-hydroxylation, far above the statistical ratio of 40%.

$[(\text{L}_4^2)\text{Fe}(\text{OTf})_2]$ gives the best selectivity for *o*-hydroxylation. (100% vs 82–83% for the (N_5) systems). $[(\text{mtL}_4^2)\text{Fe}(\text{OTf})_2]$ also gave satisfactory results when less reactive aromatic substrates (Table 1) were used such as benzene (50% conversion of H_2O_2) and chlorobenzene (13%).

In order to get insight into the reactivity mechanism of $[(\text{mtL}_4^2)\text{Fe}(\text{OTf})_2]$, we carried out spectroscopic and kinetic studies in the presence of H_2O_2 and PhIO.

Spectroscopic studies. Characterisation of intermediates

Upon addition of 1.2 equiv. of iodosylbenzene to a solution of $[(\text{mtL}_4^2)\text{Fe}(\text{OTf})_2]$ 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 growth of a band at 735 nm typical of other $(\text{N}_5)\text{Fe}^{\text{IV}}(\text{O})$ species (Figure S14). This latter intermediate exhibits a half-life of 135 min under these conditions.

Upon addition of 20 equiv. H_2O_2 to a solution of $[(\text{mtL}_4^2)\text{Fe}(\text{OTf})_2]$ in acetonitrile at 293 K (Figure 3), the solution turns from brown to purple. The UV-vis spectrum shows the disappearance of the MLCT band at 373 nm, ascribed to the oxidation of Fe^{II} , 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 $\text{N}_5\text{Fe}^{\text{III}}(\text{OOH})$ species within this family of ligands.^[11–14, 31–33]

Figure 3. UV-vis spectra at 293 K (A) of $[(\text{mtL}_4^2)\text{Fe}(\text{OTf})_2]$ 1 mM in MeCN before (black) and immediately after addition of 20 equiv. of hydrogen peroxide (red). EPR spectrum at 20 K (B) of $[(\text{mtL}_4^2)\text{Fe}(\text{OTf})_2]$ 1 mM in MeCN after addition of 20 equiv. of hydrogen peroxide (red). The solution was drawn at the maximum of $\text{Fe}^{\text{III}}(\text{OOH})$ accumulation. Simulated spectrum (grey) as the sum of $\text{Fe}^{\text{III}}(\text{OOH})$ (97% of LS signal, $g_x = 2.210$; $g_y = 2.155$, $g_z = 1.965$) and $\text{Fe}^{\text{III}}(\text{OH})$ (3% of LS signal, $g_x = 2.345$; $g_y = 2.140$, $g_z = 1.915$).

Scheme 2. Proposed structures of different $\text{Fe}^{\text{III}}(\text{OOH})$ intermediates

Remarkably, such a chromophore can be generated in MeCN similarly to $[(\text{L}_4^2)\text{Fe}(\text{OTf})_2]$ (with a maximum at 560 nm, Figure S21) or other Fe^{II} complexes with tetradentate ligands,^[34–35] but cannot be accumulated in MeCN with $[\text{TPENFe}](\text{PF}_6)_2$, $[(\text{L}_5^2)\text{Fe}(\text{OTf})_2]$ (Figures S19–S20) and most Fe^{II} precursors with pentadentate ligands for which MeOH has to be used instead.^[30, 36–38]

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 $g = 4$ region (Figure S16) can be ascribed to a non-specific ubiquitous high spin Fe^{III} species, whereas the other two correspond to low spin Fe^{III} species (Figure 3B).

The minor one, estimated at 3 % by spectral simulation, at $g = (2.345, 2.140, 1.915)$ corresponds to the $\text{N}_5\text{Fe}^{\text{III}}(\text{OH})$ species resulting from the oxidation of Fe^{II} to Fe^{III} , and the major one (97 %) at $g = (2.210, 2.155, 1.965)$, is assigned to an $\text{Fe}^{\text{III}}(\text{OOH})$ species.^[13–14, 31, 38–39] Typical $\text{N}_5\text{Fe}^{\text{III}}(\text{OOH})$ species with aminopyridyl ligands (TPEN or L_5^2 , or tL_5^2) display two sets of signals for the hydroperoxo species, assigned to two rotamers (Scheme 2),^[31] as initially proposed for $[(\text{N}4\text{Py})\text{Fe}^{\text{III}}(\text{OOH})]^{2+}$ by Feringa, Münck and Que.^[36] By contrast, complexes with L_4^2 or related ligands only show a single signal.^[17, 34]

The EPR signature of $[(\text{mtL}_4^2)\text{Fe}^{\text{III}}(\text{OOH})]^{2+}$ is very close to that of $[(\text{L}_4^2)\text{Fe}^{\text{III}}(\text{OOH})]^{2+}$.^[17] This likely results from the decoordination of the labile triazole, leading to a L_4^2 -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 triazole (vs pyridine).

Kinetic studies.

In the absence of substrate, the kinetics for the development and decay of the $\text{Fe}^{\text{III}}(\text{OOH})$ reaction intermediate (formed from $[(\text{mtL}_4^2)\text{Fe}(\text{OTf})_2]$ and 20 equiv. of H_2O_2 in MeCN) can be adjusted by global fit to a $\text{A} \rightarrow \text{B} \rightarrow \text{C}$ model, where A is the Fe^{II} precursor, B is $\text{Fe}^{\text{III}}(\text{OOH})$ and C is the decay product, and the rate constants $k_{1\text{obs}}$ and $k_{2\text{obs}}$ extracted (Figure S22).

We investigated the dependence of the rate constants on $[\text{H}_2\text{O}_2]$ (Figures 4 and S23) and temperature (Figure S26–S27). The rate of formation of $\text{Fe}^{\text{III}}(\text{OOH})$ ($k_{1\text{obs}}$) displays a linear dependence on $[\text{H}_2\text{O}_2]$, in line with a bimolecular process involving H_2O_2 , though it is in fact a fast two-step process:

Figure 4. Time traces for the formation (left) and decay (right) absorption band at 520 nm from the UV-vis spectra (293 K) of $[(\text{mtL}_4^2)\text{Fe}(\text{OTf})_2]$ 1 mM in MeCN upon addition of x equiv. of H_2O_2 .

The decay rate of $\text{Fe}^{\text{III}}(\text{OOH})$ ($k_{2\text{obs}}$) shows a slight dependence on $[\text{H}_2\text{O}_2]$ 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 $\text{Fe}^{\text{III}}(\text{OOH})$ intermediate is hydrogen peroxide disproportionation (catalase effect), as reported recently for $(\text{N}4\text{Py})\text{Fe}^{\text{III}}(\text{OOH})$.^[38]

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).

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, the addition of 20 equiv. of H_2O_2 to a solution of $[(\text{mtL}_4^2)\text{Fe}(\text{OTf})_2]$ 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 $\text{Fe}^{\text{III}}(\text{OOH})$ species ($\lambda_{\text{max}} = 520$ 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 $\text{Fe}^{\text{III}}(\text{OPh})$ adduct (Figure 5E). The kinetics were adjusted to a $A \rightarrow B \rightarrow C$ model by global fit ($A = \text{Fe}^{\text{III}}$, $B = \text{Fe}^{\text{III}}(\text{OOH})$, $C = \text{Fe}^{\text{III}}(\text{OPh})$, $D = \text{decay product}$), allowing to access simulated spectra of $\text{Fe}^{\text{III}}(\text{OOH})$ and of the transient species formed in the second step.

The rate of formation of $\text{Fe}^{\text{III}}(\text{OPh})$ ($k_{2\text{obs}}$) is independent of benzene concentration (Figure S30) and lies in the same order of magnitude as the natural decay rate of $\text{Fe}^{\text{III}}(\text{OOH})$ in the absence of substrate ($k_{2\text{obs}}$). This suggests that $\text{Fe}^{\text{III}}(\text{OOH})$ 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 $\text{Fe}^{\text{III}}(\text{OOH})$ 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 ($\Delta H_1^\ddagger = 49 \pm 2$ kJ.mol⁻¹) and negative entropy ($\Delta S_1^\ddagger = -74 \pm 5$ J.K⁻¹.mol⁻¹) were found, in line with an associative process, as described in equation (1). With complex $[(\text{L}_4^2)\text{Fe}^{\text{III}}(\text{MeCN})_2](\text{ClO}_4)_2$ ($\Delta H_1^\ddagger = 55$ kJ.mol⁻¹ and $\Delta S_1^\ddagger = -29$ J.K⁻¹.mol⁻¹)^[17] and $[(\text{bzTPEN})\text{Fe}^{\text{III}}\text{Cl}](\text{ClO}_4)_2$ ($\Delta H_1^\ddagger = 53$ kJ.mol⁻¹ and $\Delta S_1^\ddagger = -72$ J.K⁻¹.mol⁻¹)^[40], the same trend is observed. For the decay step (equation 2), the activation enthalpy is low ($\Delta H_2^\ddagger = 28 \pm 3$ kJ.mol⁻¹), but a strongly negative entropy is obtained ($\Delta S_2^\ddagger = -193 \pm 9$ J.K⁻¹.mol⁻¹), which indicates a strongly organized or associative transition state. $[(\text{L}_4^2)\text{Fe}^{\text{III}}(\text{OOH})]^{2+}$ decays with very close parameters in MeCN ($\Delta H_2^\ddagger = 32 \pm 2$ kJ.mol⁻¹; $\Delta S_2^\ddagger = -158 \pm 7$ J.K⁻¹.mol⁻¹, Figure S32-S34). Thus, it can be concluded that the triazole is likely dangling in $[(\text{mtL}_4^2)\text{Fe}(\text{OOH})]^{2+}$ and that it is not involved in the rate determining step of the decay process.

Figure 5. UV-vis spectra (stopped flow, 293 K) of $[(\text{mtL}_4^2)\text{Fe}(\text{OTf})_2]$ / benzene 1 / 300 (1mM Fe in MeCN) + 20 equiv. H_2O_2 monitored in time (A, B, C), and time traces of the characteristic bands observed (D). (A) growth of $\text{Fe}^{\text{III}}(\text{OOH})$, (B) growth of $\text{Fe}^{\text{III}}(\text{OPh})$, (C) decay of $\text{Fe}^{\text{III}}(\text{OPh})$. Simulated spectra (E) and kinetics (F) extracted from the fit to a ABCD model. $A = \text{Fe}^{\text{III}}$, $B = \text{Fe}^{\text{III}}(\text{OOH})$, $C = \text{Fe}^{\text{III}}(\text{OPh})$, $D = \text{decay product}$.

Interestingly, these parameters are far different from those previously reported for $[(L)Fe^{III}(OOH)]^{2+}$ species (Table 3) and particularly from those determined for the decay of $[(L_5^2)Fe^{III}(OOH)]^{2+}$ ($\Delta H_2^\ddagger = 81 \text{ kJ.mol}^{-1}$, $\Delta S_2^\ddagger = -1 \text{ J.K}^{-1}.\text{mol}^{-1}$).^[13] 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 or mtL_4^2), $Fe^{III}OOH$ 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 $\{Fe^{IV}=O, OH^\bullet\}$ 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 $OH^\bullet$ moiety with CH_3CN or another $Fe^{III}(OOH)$ species during the decay of the intermediate (Scheme 3).^[41]

In the case of $[(mtL_4^2)Fe^{III}(OOH)]^{2+}$, the strongly negative entropy suggests an associative transition state. In the absence of substrate, H_2O_2 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 scenarios 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;^[42-44] 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;^[33] or iv) a second H_2O_2 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 3) 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.

Hypothesis (iii), O-O bond breaking *via* a side-on transition state, 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.

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 $\Delta H_2^\ddagger = 43.5 \pm 4 \text{ kJ.mol}^{-1}$ and $\Delta S_2^\ddagger = -133 \pm 1.5 \text{ J.K}^{-1}.\text{mol}^{-1}$ (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 $\Delta H_2^\ddagger = 26.3 \pm 2 \text{ kJ.mol}^{-1}$ and $\Delta S_2^\ddagger = -178 \pm 5 \text{ J.K}^{-1}.\text{mol}^{-1}$ (Figure S35-S36), very close to those obtained in the absence of substrate ($\Delta H_2^\ddagger = 32 \pm 2 \text{ kJ.mol}^{-1}$; $\Delta S_2^\ddagger = -158 \pm 7 \text{ J.K}^{-1}.\text{mol}^{-1}$).

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 $\{Fe^{IV}=O, OH^\bullet \leftrightarrow Fe^V=O, OH^\bullet\}$ species, as proposed by Rybak-Akimova.^[17] 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.

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

Scheme 4. Proposed mechanisms for the $Fe^{III}(OOH)$ decay pathways in hypotheses (iii) and (iv).

To summarize, as decay rates of $[(\text{mtL}_4^2)\text{Fe}^{\text{III}}(\text{OOH})]^{2+}$ 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. Therefore, two different pathways can be proposed (Scheme 4) associated to different substrates, either benzene or H_2O_2 , reflecting the two competitive reactions (aromatic hydroxylation vs H_2O_2 disproportionation).

Table 3. Activation parameters for the decay of various $\text{Fe}^{\text{III}}(\text{OOH})$ species

O-O bond cleavage	System	$\Delta H^\ddagger$ kJ.mol ⁻¹	$\Delta S^\ddagger$ J.mol ⁻¹ .K ⁻¹
This work	$[(\text{mtL}_4^2)\text{Fe}^{\text{III}}(\text{OOH})]^{2+}$ in MeCN	28 ± 3	-193 ± 9
	$[(\text{mtL}_4^2)\text{Fe}^{\text{III}}(\text{OOH})]^{2+}$ in MeOH	33 ± 4	-176 ± 13
	$[(\text{L}_4^2)\text{Fe}^{\text{III}}(\text{OOH})]^{2+}$ in MeCN	32 ± 2	-158 ± 7
	$[(\text{L}_4^2)\text{Fe}^{\text{III}}(\text{OOH})]^{2+}$ in MeCN + benzene	26.3 ± 2	-178 ± 5
	$[(\text{mtL}_4^2)\text{Fe}^{\text{III}}(\text{OOH})]^{2+}$ in MeCN + benzene	43.5 ± 4	-133 ± 1.5
Heterolytic	$[(\text{TMC})\text{Fe}^{\text{III}}(\text{OOH})]^{2+} + \text{HClO}_4$ in MeCN ^[45]	44	-89
	$[(\text{TPA})\text{Fe}^{\text{III}}(\text{OOH})]^{2+} + \text{octene}$ in MeCN ^[44]	45	-95
	$[(\text{PyNMe}_3)\text{Fe}^{\text{III}}(\text{OOH})]^{2+}$ in MeCN + H^+ ^[24]	46	-79
Homolytic	$[(\text{PyNMe}_3)\text{Fe}^{\text{III}}(\text{OOH})]^{2+}$ + in MeCN ^[24]	43	-137
	$[(\text{L}_5^2)\text{Fe}^{\text{III}}(\text{OOH})]^{2+}$ in MeCN ^[13]	81	-1
	$[(\text{TMC})\text{Fe}^{\text{III}}(\text{OOH})]^{2+}$ in acetone/ $\text{CF}_3\text{CH}_2\text{OH}$ ^[16]	56	-75
	$[(\text{N}_4\text{Py})\text{Fe}^{\text{III}}(\text{OOH})]^{2+}$ in acetone / $\text{CF}_3\text{CH}_2\text{OH}$ ^[16]	53	-121
	$[(\text{bppc})\text{Fe}^{\text{III}}(\text{OOH})]^{2+}$ ^[26]	53	-68

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

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 3). The magnitude of the activation enthalpy for $[(\text{mtL}_4^2)\text{Fe}^{\text{III}}(\text{OOH})]^{2+}$ decay in the absence of substrate is relatively weak, and its activation entropy very

negative compared to literature parameters. However, heterolytic cleavage examples involve the addition of acids or substrates, and homolytic ones correspond to the cleavage of end-on species, and are not suitable references for a side-on decay of the intermediate.

More interestingly, the activation parameters for $[(\text{mtL}_4^2)\text{Fe}^{\text{III}}(\text{OOH})]^{2+}$ decay in the presence of benzene ($\Delta H_2^\ddagger = 43.5 \pm 4$ kJ.mol⁻¹ and $\Delta S_2^\ddagger = -133 \pm 1.5$ J.K⁻¹.mol⁻¹) are surprisingly close to those reported for the decay of $[(\text{PyNMe}_3)\text{Fe}^{\text{III}}(\text{OOH})]^{2+}$ in MeCN ($\Delta H_2^\ddagger = 43$ kJ.mol⁻¹; $\Delta S_2^\ddagger = -137$ J.K⁻¹.mol⁻¹).^[24] In this latter example, theoretical studies proposed a homolytic cleavage along an end-on pathway, with the H atom of $\text{Fe}^{\text{III}}(\text{OOH})$ 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).

Figure 6. Dissociation pathways of $\text{Fe}^{\text{III}}\text{-OO-Cm}$, the cumene hydroperoxo intermediate (top). Product distribution and percentage of heterolytic and homolytic pathways calculated from product distribution (e.g. % ([Phenol]+[Cumene alcohol]) and % ([acetophenone])) after decay of the intermediate $[(\text{mtL}_4^2)\text{Fe}^{\text{III}}(\text{OOCm})]^{2+}$ generated *in situ* by the addition of CnOOH (1 equiv.) to a solution of $[(\text{mtL}_4^2)\text{Fe}^{\text{III}}(\text{OTf})_3]$ (1mM, V = 1 mL) and 1 equiv. NEt_3 in MeCN, under various conditions: such as the presence of 1.7 μL water; 300 equiv. benzene, 300 equiv. anisole or 300 equiv. chlorobenzene.

The nature of the O-O bond cleavage can also be probed by analyzing the decomposition of $[(\text{mtL}_4^2)\text{Fe}^{\text{III}}(\text{OOCm})]^{2+}$, serving as a model to mimic its $\text{Fe}^{\text{III}}(\text{OOH})$ analog. Due to significant steric hindrance, the $\text{Fe}^{\text{III}}(\text{OOCm})$ is expected to adopt an end-on configuration and the products resulting from the O-O cleavage are unlikely to bind the metal center, e.g. If homolytic cleavage occurs acetophenone is produced together with $\text{Fe}^{\text{IV}}\text{O}$ whereas heterolytic cleavage leads to cumene alcohol $\text{Ph-C}(\text{Me})_2\text{OH}$ (and Fe^{VO}), which can further evolve to yield acetone and phenol (Figure 6).^[46]

$[(\text{mtL}_4^2)\text{Fe}^{\text{III}}(\text{OOCm})]^{2+}$ was prepared by reacting $[(\text{mtL}_4^2)\text{Fe}^{\text{III}}(\text{OTf})_3]$ (see Supporting Information) with 1 equiv. cumene hydroperoxide and 1 equiv. triethylamine. In the absence of substrate, acetophenone is the main product, indicating a predominant homolytic pathway (82% of the decay) (Figure 6). Addition of water in the same amount as in the H_2O_2 catalytic runs does not affect the product distribution (homolytic pathway represents 80% of the decay). In the presence of aromatic substrates, the homolytic cleavage remains the main decay pathway (80% for benzene, 84% for anisole, 87% for chlorobenzene).

In the presence of benzene (*vide supra*), $[(\text{mtL}_4^2)\text{Fe}^{\text{III}}(\text{OOH})]^{2+}$ is likely to decay along an end-on cleavage pathway due to the rebinding of triazole. The decay of its $[(\text{mtL}_4^2)\text{Fe}^{\text{III}}(\text{OOCm})]^{2+}$ analogue under the same conditions suggests $\text{Fe}^{\text{III}}\text{OOH}$ follows a homolytic pathway with an Fe^{V} state attained more easily than the Fe^{V} one. 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 ± 0.03 . If $\text{Fe}^{\text{V}}\text{O}$ were the reactive species, an inverse KIE would be expected.^[47-48] Conversely, similar KIE values were reported for a series of complexes involving an $\{\text{Fe}^{\text{IV}}\text{O} / \text{OH}\cdot\}$ caged pair.^[13, 49]

In the absence of substrate, $[(\text{mtL}_4^2)\text{Fe}^{\text{III}}(\text{OOH})]^{2+}$ is proposed to go through a side-on transition state. Thus, the analogy with the decay of end-on $[(\text{mtL}_4^2)\text{Fe}^{\text{III}}(\text{OOCm})]^{2+}$ must be made cautiously: the $\text{Fe}^{\text{III}}(\text{OOH})$ decay would lead to a *cis* species described as two electromer forms $\{\text{cis-Fe}^{\text{IV}}(\text{O})(\text{OH}\cdot) \leftrightarrow \text{cis-Fe}^{\text{V}}(\text{O})(\text{OH})\}$, whereas cleavage of the O-O bond of $[(\text{mtL}_4^2)\text{Fe}^{\text{III}}(\text{OOCm})]^{2+}$ yields an iron intermediate with a well-defined oxidation state and an unbound $\text{CmO}\cdot$ or CmO^- fragment (Figure 6). In the absence of substrate, the CmOOH experiment only indicates that the *cis-Fe}^{\text{IV}}(\text{O})(\text{OH}\cdot) must be an early form along the reaction coordinate. Similar conclusions can be drawn for the analogous $[(\text{L}_4^2)\text{Fe}^{\text{III}}(\text{OOCm})]^{2+}$ species (Figure S39).*

Discussion

Based on activation parameters and CmOOH experiments (Figure S39 and Figure 6), we can conclude that both

$[(\text{mtL}_4^2)\text{Fe}^{\text{III}}(\text{OOH})(\text{MeCN})]^{2+}$ and $[(\text{L}_4^2)\text{Fe}^{\text{III}}(\text{OOH})(\text{MeCN})]^{2+}$ evolve through a similar side-on transition state in the absence of aromatic substrates, yielding a *cis* $\{\text{Fe}^{\text{IV}}\text{O}, \text{OH}\cdot \leftrightarrow \text{Fe}^{\text{V}}\text{O}, \text{OH}\cdot\}$ species. However, a difference appears in the presence of aromatic substrates: on the one hand, $[(\text{L}_4^2)\text{Fe}^{\text{III}}(\text{OOH})(\text{MeCN})]^{2+}$ remains on the same pathway to yield *cis* $\text{Fe}=\text{O}(\text{OH})$ 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}^{\text{V}}(\text{O})(\text{OH}) intermediate, which has been proposed to be the active species in $(\text{N}_4)\text{Fe}^{\text{II}} / \text{H}_2\text{O}_2$ catalytic systems even though it has not been accumulated and spectroscopically characterized in solution.^[8, 19, 50-51] Therefore, O-O bond cleavage in these $(\text{N}_4)\text{Fe}^{\text{III}}(\text{OOH})$ intermediates leads to a *cis* species described as two $\{\text{cis-Fe}^{\text{IV}}(\text{O})(\text{OH}\cdot) \leftrightarrow \text{cis-Fe}^{\text{V}}(\text{O})(\text{OH})\}$ 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 $(\text{N}_4)\text{Fe}^{\text{II}}$ precursors has been recently described as a mixture of $\text{Fe}^{\text{V}}(\text{O})(\text{OC}(\text{O})\text{R}) / \text{Fe}^{\text{V}}(\text{O})(\cdot\text{OC}(\text{O})\text{R})$ configurations.^[52-53]*

On the other hand, $[(\text{mtL}_4^2)\text{Fe}^{\text{III}}(\text{OOH})(\text{MeCN})]^{2+}$ 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 $\{(N_5)\text{Fe}^{\text{IV}}\text{O}, \text{OH}\cdot\}$ caged pair, as proposed for this $[(\text{L}_5^2)\text{Fe}^{\text{III}}(\text{OOH})]^{2+}$ intermediate.^[13, 54] This activation bifurcation between $[(\text{L}_4^2)\text{Fe}^{\text{III}}(\text{OOH})(\text{MeCN})]^{2+}$ and $[(\text{mtL}_4^2)\text{Fe}^{\text{III}}(\text{OOH})(\text{MeCN})]^{2+}$ directly impacts their catalytic performances and selectivities. Whereas $[(\text{L}_4^2)\text{Fe}^{\text{III}}(\text{OOH})(\text{MeCN})]^{2+}$ generates a 100% regioselectivity for *o*-hydroxylation of anisole (Table 1), $[(\text{mtL}_4^2)\text{Fe}^{\text{III}}(\text{OOH})(\text{MeCN})]^{2+}$ shows a distribution of products that is closer to that observed for $[(\text{L}_5^2)\text{Fe}^{\text{III}}(\text{OOH})]^{2+}$, 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 $\text{Fe}(\text{O})(\text{OH})$ will preferentially expose the ortho position to oxidation initiated by attack of the aromatic π system on the high valent $\text{Fe}(\text{O})$, as shown in Scheme 5. Conversely, the spatial arrangement of $\text{Fe}^{\text{IV}}(\text{O})$ and $\text{OH}\cdot$ gets looser in the mtL_4^2 system and the regioselectivity becomes altered: aromatic hydroxylation is initiated by the attack on the π system by the hydroxyl radical followed the e^-/H^+ transfer to the $\text{Fe}^{\text{IV}}(\text{O})$, as demonstrated previously for $[(\text{L}_5^2)\text{Fe}^{\text{III}}(\text{OOH})]^{2+}$.^[13]

Finally, these bifurcated mechanisms from a similar $(\text{N}_4)\text{Fe}^{\text{III}}(\text{OOH})$ intermediate are also in line with the kinetic isotope effect observed in benzene hydroxylation. A $\text{KIE} < 1$ was reported for $[(\text{L}_4^2)\text{Fe}^{\text{III}}(\text{OOH})(\text{MeCN})]^{2+}$ ^[17] consistent with the attack on an electrophilic metal-oxo by the π system.^[17, 47] In contrast, we found $\text{KIE} > 1$ in the case of $[(\text{mtL}_4^2)\text{Fe}^{\text{III}}(\text{OOH})(\text{MeCN})]^{2+}$ which has been shown to be the signature of $\{\text{Fe}^{\text{IV}}(\text{O}) / \text{OH}\cdot\}$ formed from $[(\text{L}_5^2)\text{Fe}^{\text{III}}(\text{OOH})]^{2+}$ and similar intermediates.^[13, 49]

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

Conclusions

A new ligand mtL_4^2 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, $[(\text{mtL}_4^2)\text{FeCl}](\text{PF}_6)$ and $[(\text{mtL}_4^2)\text{Fe}(\text{OTf})_2]$, were isolated and characterized in solution and in the solid state for $[(\text{mtL}_4^2)\text{FeCl}](\text{PF}_6)$. Their catalytic properties in the oxidation of aromatics were tested in acetonitrile using H_2O_2 and PhIO as oxidants. Spectroscopic studies indicate the formation of intermediates $\text{Fe}^{\text{III}}(\text{OOH})$ and $\text{Fe}^{\text{IV}}(\text{O})$ respectively under these conditions. In particular, the $\text{Fe}/\text{H}_2\text{O}_2$ 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 ($[(\text{L}_5^2)\text{Fe}(\text{OTf})_2]$), the $\text{Fe}^{\text{III}}(\text{OOH})$ intermediate derived from $[(\text{mtL}_4^2)\text{Fe}(\text{OTf})_2]$ can be formed and

accumulated in MeCN, which allowed us to study its fate under catalytic conditions.

The intermediate $[(\text{mtL}_4^2)\text{Fe}^{\text{III}}(\text{OOH})]^{2+}$ displays a signature close to that of $[(\text{L}_4^2)\text{Fe}^{\text{III}}(\text{OOH})]^{2+}$. This suggests triazole acts as a labile ligand during the formation process. Kinetic studies show that the decay rate of $[(\text{mtL}_4^2)\text{Fe}^{\text{III}}(\text{OOH})]^{2+}$ 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 $[(\text{L}_4^2)\text{Fe}^{\text{III}}(\text{OOH})]^{2+}$ 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 $\{\text{Fe}^{\text{IV}}(\text{O})/\text{HO}^\bullet\}$ and $\{\text{Fe}^{\text{V}}(\text{O})/(\text{OH}^\bullet)\}$. Conversely, in the presence of benzene, whereas $[(\text{L}_4^2)\text{Fe}^{\text{III}}(\text{OOH})]^{2+}$ retains a similar activation mechanism, $[(\text{mtL}_4^2)\text{Fe}^{\text{III}}(\text{OOH})]^{2+}$ 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.^[55]

Consequently, the regioselectivity obtained with $[(\text{mtL}_4^2)\text{Fe}^{\text{III}}(\text{OOH})(\text{MeCN})]^{2+}$ is altered with respect to that observed with $[(\text{L}_4^2)\text{Fe}^{\text{III}}(\text{OOH})(\text{MeCN})]^{2+}$ and is closer to the one observed with pentadentate ligand systems. This can be rationalized by the formation of a $\{cis-(N_4)\text{Fe}^{\text{IV}}(\text{O})(\text{OH}\cdot) \leftrightarrow cis-(N_4)\text{Fe}^{\text{V}}(\text{O})(\text{OH})\}$ species in the case of the (L_4^2) system and of a $\{(N_5)\text{Fe}^{\text{IV}}(\text{O})/\text{HO}\cdot\}$ caged pair in the case of (mtL_4^2) . A direct KIE for benzene oxidation is observed in the case of $[(\text{mtL}_4^2)\text{Fe}^{\text{III}}(\text{OOH})(\text{MeCN})]^{2+}$, whereas an inverse KIE was reported for $[(\text{L}_4^2)\text{Fe}^{\text{III}}(\text{OOH})(\text{MeCN})]^{2+}$, supporting the assignment of the respective reactive species.

The hemilability of triazole allowed us to accumulate an $\text{Fe}^{\text{III}}(\text{OOH})$ intermediate and fully study the mechanism of aromatic hydroxylation by $(N_5)\text{Fe}$ 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 $\text{Fe}^{\text{III}}(\text{OOH})$ reactive intermediate in iron-catalyzed H_2O_2 oxidations, how it controls its decay pathway (side-on or end-on TS) and into the nature of the resulting reactive species ($\{cis-(N_4)\text{Fe}^{\text{IV}}(\text{O})(\text{OH}\cdot) \leftrightarrow cis-(N_4)\text{Fe}^{\text{V}}(\text{O})(\text{OH})\}$ or $\{(N_5)\text{Fe}^{\text{IV}}(\text{O})/\text{HO}\cdot\}$ 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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