Directing a Non-Heme Iron(III)-Hydroperoxide Species on a Trifurcated Reactivity Pathway

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**Directing a Non-Heme Iron(III)-Hydroperoxide Species on a Trifurcated Reactivity Pathway**


In memory of Professor John J. McGarvey

**Abstract:** The reactivity of [Fe^{III}][tpena]]^{2+} (tpena = N,N,N'-tris(2-pyridylmethyl)ethylenediamine-N'-acetate) as a catalyst for oxidation reactions depends on its ratio to the terminal oxidant H\textsubscript{2}O\textsubscript{2} and presence or absence of sacrificial substrates. The outcome can be switched between: 1) catalysed H\textsubscript{2}O\textsubscript{2} disproportionation, 2) selective catalytic oxidation of methanol or benzyl alcohol to the corresponding aldehyde, or 3) oxidative decomposition of the tpena ligand. A common mechanism is proposed involving homolytic O–O cleavage in the detected transient purple low-spin (S = 1/2) [(tpenaH)][Fe^{IV}O(OH)]\textsuperscript{2-}. The resultant iron(IV) oxo and hydroxyl radical both participate in controllable hydrogen-atom transfer (HAT) reactions. Consistent with the presence of a weaker O-donor carboxylate ligand, the most pronounced difference in the spectroscopic properties of [Fe(OO)(tpenaH)]^{2+} and its conjugate base, [Fe(OO)(tpenaH)]\textsuperscript{+}, compared to non-heme iron(III) peroxide analogues supported by neutral multidentate N-only ligands, are slightly blue-shifted maxima of the visible absorption band assigned to ligand-to-metal charge-transfer (LMCT) transitions and, corroborating this, lower Fe^{III}/Fe\textsuperscript{I} redox potentials for the pro-catalysts.

**Introduction**

Oxygen-coordinated iron complexes, such as iron(III)-O\textsubscript{2} (dioxigen), iron(III)-O\textsubscript{2} (peroxido), iron(III)-OO\textsubscript{H} (hydroperoxido), and iron(III)-OOH (alkylperoxido), along with high-valent iron(IV) and iron(V) oxides formed upon homolytic or heterolytic cleavage of the O–O bond in these complexes, have been proposed as key catalytically competent intermediates in oxidations catalysed by heme and non-heme iron(IV) and iron(V) oxides. The oxygen binding site, we can reasonably expect that the introduction of anionic oxygen donors into the coordination sphere of an iron ion will stabilize higher oxidation states. Concomitantly, the O–O bond of peroxide ligands coordinated to the same iron centre will be weakened. This hypothesis is supported by the fact that many oxidation processes catalysed by non-heme iron O\textsubscript{2}-activating enzymes, such as Rieske dioxygenases, tetrahydropterin-dependent hydroxylases, and 2-oxoglutarate-dependent dioxygenases and hydroxylases, possess an active site consisting of two histidine residues and one carboxylate group from Asp or Glu (Scheme 1). The reaction pathways followed by these enzymes proceed through cleavage of the O–O bond of peroxide/superoxide ligands derived from O\textsubscript{2} to form high-valent iron-oxido species, followed by direct oxidation of a substrate by the generated non-heme iron(IV)\textsuperscript{2}.\textsuperscript{3,4} Despite the biological precedence, the weakening of the O–O bond of an iron-coordinated peroxide ligand by the proximity of a carboxylato group has, to our knowledge, not yet been evaluated through systematic studies in model complexes.

Iron(III)-hydroperoxido and -peroxido complexes based on neutral pentadentate (NS) aminopolypyrrolid ligands with an ethylenediamine backbone as the supporting scaffold, N-alkyl-N'/N'-tris(2-pyridylmethyl)ethylenediamine (Rtpen; Scheme 2a) were the first systems for which peroxide derivatives were spectroscopically characterized, and these have been extensively studied.\textsuperscript{[5–8]} Typically, these are generated by the reaction of air-stable iron(II) precursor complexes with H\textsubscript{2}O\textsubscript{2}, a prerequisite for which is oxidation of the iron centre from the Fe\textsuperscript{II} to the Fe\textsuperscript{II} oxidation state prior to formation of the Fe\textsuperscript{III}-OOH...
step and coordination of a deprotonated H$_2$O$_2$ ligand). Kinetic studies with [Fe$^{III}$(Rtpen)]$^{2+}$ precursors have indicated that the reaction is essentially instantaneous when the metal pre-oxidation step is circumvented.[11] The Rtpen ligands also support iron(IV) oxo species. However, although their formation by homolytic cleavage of the O–O bond of peroxide precursors has been proposed, it is important to note that such species have not actually been prepared using H$_2$O$_2$ as the terminal oxidant, but instead by reaction of the Fe$^6$ precursor with PhIO, m-CPBA, or ClO$_2$. [19]

Since monodentate carboxylate ligands are strong O donors, we reasoned that iron(III) precursor compounds suitable for the rapid preparation of peroxido adducts would be accessed if one of the pyridyl arms were to be substituted by a biomimetic glycinate group. Our initial foray using this strategy produced the N4O ligands N-R-N'$'$-bis(2-pyridylmethyl)ethylenediamine-N'$'$-acetate (Rbpena), R = methyl, benzyl (Scheme 2b), which indeed favoured the formation of iron(III) complexes.[16] Reactions of these iron(III) complexes with H$_2$O$_2$ (and alkyl peroxides or O$_2$ plus ascorbic acid) did not, however, produce detectable peroxide adducts, but instead oxygenation of the Rbpena ligands was observed. Aryl C–H oxidation of rbpena gave the iron(III) complex, in which an O atom was installed in the ligand, N-(2-oxidobenzyl)-N'$'$-bis(2-pyridylmethyl)ethylenediamine-N'$'$-acetate, and O atom insertion into an Fe–N$_{amine}$ bond provided an N-oxide ligand, 2-(N'(2-(methylpyridin-2-ylmethyl)amino)ethyl)-oxido(pyridin-2-ylmethyl)azanyl)acetate (Scheme 2c), for the iron(III) complex of the mepena ligand. These O atom C–H and Fe–N insertion reactions provide circumstantial evidence for the in situ formation of Fe$^6$-peroxide adducts and subsequent heterolytic Fe$^6$–O–O(H) bond cleavage to give putative high-valent Fe$^6$ o xo species capable of engaging in selective two-electron oxygen-atom transfer (OAT) reactions.

By adding a sixth heteroatom donor to replace the alkyl/aryl group in the N4O Rbpena ligand systems, namely a third pyridine group to give the NSO ligand N,N'$'$-bis(2-pyridylmethyl)ethylenediamine-N$'$-acetate (tpena, Scheme 2d), we demonstrate here that the ability to generate detectable transient iron(III)-peroxide adducts is reinstated. In other words, behaviour similar to that observed for the iron(III) complexes of N5 Rtpen can be observed, and this contrasts with that for the iron(III) complexes of N4O Rbpena. However, the Fe$^{III}$-OOH species formed from the tpena-iron complex has a significantly shorter lifetime than those derived from the corresponding Rtpen-based systems. At first sight, it might seem surprising that the ostensibly coordinatively saturated iron(III) precursor [Fe(tpena)]$^{2+}$ can form heterolytic complexes with co-ligand peroxide donors. However, we have previously demonstrated that external substrates can be selectively oxidized using the terminal oxygen-atom-transfer reagents iodosylbenzene and N-morpholine-N-oxide catalysed by [Fe(tpena)]$^{2+}$, and a seven-coordinated intermediate heteroleptic Fe$^6$-oxido adduct was isolated.[22,23]

Herein, we demonstrate the formation and characterization of the species [(tpenaH)Fe$^{III}$(OOH)]$^{2+}$ and [(tpenaH)Fe$^{III}$(OO)]$^+$ and show that the reactivity of these complexes is highly de-
Results and Discussion

Fe⁷⁺/Fe⁶⁺ redox potentials for analogous iron complexes of NSO and N₆ ligands

Solutions of [Fe⁷⁺(tpena)]²⁺ in acetonitrile are obtained by the dehydration of [(tpenaH)Fe(μ-O)Fe(tpenaH)]⁺⁺ upon dissolution. [(tpenaH)Fe(μ-O)Fe(tpenaH)]⁺⁺ → 2 [Fe(tpena)]²⁺ + H₂O.

The cyclic voltammogram of [Fe⁷⁺(tpena)]²⁺ in acetonitrile shows a broad wave due to overlapping reversible Fe⁶⁺/Fe⁷⁺ redox couples at 0.02 V and 0.06 V vs FC/FC' (Figure 1 a). The redox waves are associated with the high-spin (S = 5/2) mer-py₃- [Fe(tpena)]²⁺/²⁻ and the low-spin (S = 1/2) fac-py₃⁻[Fe(tpena)]²⁺/²⁻ diastereoisomers (Figure 1 b). Both the mer-py₃ and fac-py₃ isomers have been previously identified in both the solid and solution states by Mössbauer spectroscopy and in the frozen-solution state by EPR spectroscopy. The potentials are 0.38 and 0.43 V lower compared to that for the Fe⁵⁺/Fe⁶⁺ couple of [Fe(tpen)]¹⁺/²⁺ (0.40 V vs FC/FC'). These results are consistent with our expectation that the binding of a negatively charged carboxylate group in place of a pyridyl moiety will stabilize higher iron oxidation states. It is also consistent with the tendency, in the presence of air, for the tpen and neutral N₅ Rtpen ligands to form iron(II) complexes, whereas iron(III) complexes are formed with tpen, irrespective of the oxidation state of the precursor iron ion starting salt (+2 or +3). The minor redox wave at 0.46 V is due to the oxo-bridged precursor, [(tpenaH)Fe(μ-O)Fe(tpenaH)][ClO₄]₂.

Reaction of HCl and H₂O₂ with [Fe(tpena)]²⁺ to form [FeX-(tpena)]²⁺ (X = Cl⁻, OOH⁻)

Addition of concentrated HCl to solutions of either the brown complex [(tpenaH)Fe(μ-O)Fe(tpenaH)]⁺⁺ (in water/EtOH) or of the red-orange complex [Fe(tpena)]²⁺ (in acetonitrile) resulted in immediate formation of [Fe(Cl)(tpenaH)]²⁺, as manifested by a colour change to yellow, λ_max = 312 and 361 nm [Eqs. (1 a) and (1 b), respectively].

[Fe(tpenaH)Fe(μ-O)Fe(tpenaH)]²⁺ + 2HCl → 2 [Fe(Cl)(tpenaH)]²⁺ + H₂O

fac/mer-[Fe(tpena)]²⁺ + HX → FeX(tpenaH)]²⁺ \[X = Cl⁻, OOH⁻\]

The single-crystal X-ray structure of [Fe(Cl)(tpenaHH)₂ClO₄]·EtOH·2H₂O (Figure 2 a) shows that the iron(III) ion is pentacoordinated by tpenH, with a chlorido ligand occupying the sixth site. The pyridine arm attached to the same amine group, as the glycyl arm does not coordinate to the iron(III)
Addition of H2O2 to [Fe(tpena)]2+ in acetonitrile resulted in an immediate colour change from red to purple, indicative of the formation of an Fe(III)-hydroperoxido adduct structurally analogous to the HCl adduct, namely [Fe(III)(OOH)(tpenaH)]2+ [Eq. (1b)]. The concentration of the transient peroxido complex in acetonitrile is maximized under conditions that minimize the concentration of the hemihydrate, ([tpenaH]Fe(μ-O)OFe(tpenaH)]2+, supporting the view that the anhydrate [Fe(tpena)]2+ is the immediate precursor for reaction with H2O2. Purple solutions of [Fe(III)(OOH)(tpenaH)]2+ in acetonitrile, decay over 30 s at room temperature and over several hours at −40 °C. The rate of decay for [Fe(III)(OOH)(tpenaH)]2+ is significantly faster than that for [Fe(III)(OOH)(metpen)]2+ generated in methanol from [Fe(metpen)Cl](PF6) with 50 equiv of H2O2 at room temperature. Of relevance to the oxidizing ability of [Fe(III)(OOH)(tpenaH)]2+ (see below) is that it cannot be observed in methanol; this is stark contrast to the [Fe(III)(OOH)(Rtpen)]2+ complexes, for which methanol is the favoured solvent for generation.

Spectroscopic properties of [Fe(III)(OOH)(tpenaH)]2+

The transient purple species, assigned as [Fe(III)(OOH)(tpenaH)]2+ shows an absorption band at 520 nm (ε = 465 M−1·cm−1), consistent with an Fe(III) ← ROO· charge-transfer transition (Figure 3a, red curve). The Raman spectrum elicited at λexc = 532 nm shows resonantly enhanced bands at 613 and 788 cm−1 (Figure 3b), which can be assigned to Fe–O and O–O stretching modes, respectively, by comparison with previous literature; see Table 1. The EPR spectrum of a frozen solution shows a rhombic signal (g = 2.21, 2.15, 1.96; Figure 3c). The frozen-solution-state Mössbauer spectrum displays a doublet with δ = 0.21 mm s−1 and ΔE0 = 2.08 mm s−1 (14%, Figure 3d), which is consistent with a low-spin Fe(III) species. The spectrum also shows the presence of the EPR-silent starting complex ([tpenaH]Fe–O–Fe(tpenaH)]2+ (δ = 0.43 mm s−1, ΔE0 = 1.63 mm s−1, 14%)[21] The structure of [Fe(III)(OOH)(tpenaH)]2+ can be any of six diastereoisomers (Scheme 4). However, the simplicity of the Raman, Mössbauer, and EPR spectra implies that one of these isomers dominates, notwithstanding the possibility that the differences between the stereoisomers is insufficient to cause significant changes in the vibrational, nuclear, and spin characteristics. In the present study, the precise stereochemistry of the intermediate is not of specific concern and for simplicity of the data analyses, it is assumed that a single diastereoisomer of [Fe(III)(OOH)(tpenaH)]2+ is formed, cor-

Figure 2. a) Crystal structure of [Fe(III)(tpenaH)]2+. b) The hydrogen-bonded 1D helical chain of cations parallel to the b-axis. Thermal ellipsoids are drawn at 50% probability and the protons are omitted for clarity. The intermolecular hydrogen bond is shown with dashed lines (C=O–H...Npy·1.845 Å).

centre and is protonated. The structure is consistent with the chlorido ligand taking the position that the dangling pyridine had occupied in fac-[Fe(tpena)]2+. The chlorido ligand is trans to the tertiary amine bearing the two methylpyridyl groups and cis to the carboxylato moiety. This structure is one (A) of the six possible diastereoisomers depicted in Scheme 4. Intermolecular hydrogen bonding (Figure 2b) between the non-coordinated carboxylato oxygen and the protonated pyridine results in 1D homochiral chains of the cations parallel to the b-axis. These chains are separated by stacks of ClO4− anions, and water and ethanol molecules occupy pockets between the cationic chains. The solid-state Mössbauer spectrum of [Fe(III)(Cl)(tpenaH)](ClO4)2·EtOH·2H2O shows a broad singlet at δ = 0.46 mm s−1, consistent with a high-spin (S = 5/2) iron(III) complex. [Fe(III)(tpenaH)](ClO4)2·EtOH·2H2O is hygroscopic, and we have speculated that this could be associated with hydrolysis and loss of HCl to form the pseudo aquo complex [Fe(III)(tpenaH)]2+, which has been identified in aqueous solutions at low pH.[23,24]

Scheme 4. Possible diastereoisomers of [Fe(X)(tpenaH)]2+: X = Cl−, OH−, OOH−.
responding to that observed in the crystal structure of the HCl adduct, Figure 2 (i.e., A in Scheme 4).

Deprotonation of \([\text{Fe(OOH)(tpenaH)}]^2+\)

The addition of \(\text{NET}_3\) (30 equiv) to solutions of \([\text{Fe}^{III}(\text{OOH})(\text{tpenaH})]^2+\) and excess \(\text{H}_2\text{O}_2\) in acetonitrile results in an instant colour change from purple to blue and the appearance of a new absorption band at 675 nm (Figure 3 a, blue line). The lifetime of the new species is about 10 min at 0 °C when generated from 50 equiv of \(\text{H}_2\text{O}_2\) and 30 equiv of \(\text{ET}_3\text{N}\). Immediate loss of the Fe/C0 and O/C0 bands of the end-on \(\text{Fe}^{III}-\text{OOH}\) in the Raman spectrum is accompanied by the appearance of the corresponding bands of a side-on peroxido complex at 473 and 815 cm⁻¹ (Figure 3 b), consistent with assignment of the species as \([\text{Fe}^{III}(\text{OO})(\text{tpenaH})]^+\). The band positions are close to those reported for \([\text{Fe}^{III}(\text{OO})(\text{tpen})]^+\) and \([\text{Fe}^{III}(\text{OO})(\text{metpen})]^+\) (Table 1). A high-spin signal \((g^\text{eff} = 8.8, 5.0, 4.3, 4.2, 3.5)\) appears in the EPR spectrum (Figure 4 a). The Mössbauer spectrum (Figure 4 b) of a sample composed of \(\text{Fe}^{57}\text{-labelled}[\text{Fe}^{III}(\text{OO})(\text{tpenaH})]^2+\) (microwave frequency 9.31542 GHz, 110 K, \([\text{Fe}] = 2 \text{ mm}\)) shows a doublet with \(\Delta = 0.48 \text{ mm s}^{-1}\) and \(\Delta E_Q = 1.21 \text{ mm s}^{-1}\) (47 %), which is consistent with a high-spin \(\text{Fe}^{III}\) species. The doublet due to \([\text{Fe}(\text{OO})(\text{tpenaH})]^+\) is not observed, and the spectrum also shows the presence of a significant amount of the EPR-silent starting material \([\text{Fe}^{II}(\text{tpena})]^2+\) (14 %), \([\text{Fe}^{III}(\text{OO})(\text{tpenaH})]^+\) (14 %), and unidentified species (72 %) \(([\text{Fe}] = 2 \text{ mm})\).

Figure 3. Solution-state spectroscopic characterization of \([\text{Fe}^{III}(\text{OO})(\text{tpenaH})]^2+\) and \([\text{Fe}(\text{OO})(\text{tpenaH})]^+\). Colour coding: \([\text{Fe}(\text{tpena})]^2+\) in black, \([\text{Fe}(\text{OO})(\text{tpenaH})]^+\) in blue, \([\text{Fe}(\text{O}(\text{tpenaH}))]^+\) in green. Unidentified species depicted in orange (see text). The sum of the fitted data is coloured in grey. \([\text{Fe}(\text{OO})(\text{tpenaH})]^2+\) was generated by addition of 50 equiv of \(\text{H}_2\text{O}_2\) to \([\text{Fe}(\text{tpena})]^2+\) in MeCN, and subsequent addition of 30 equiv of \(\text{ET}_3\text{N}\) gave \([\text{Fe}(\text{OO})(\text{tpenaH})]^+\). a) UV/Vis absorption spectra (RT, \([\text{Fe}] = 1.5 \text{ mm}\)). b) Resonance Raman spectra (−30 °C, \([\text{Fe}] = 3 \text{ mm}\), \(\lambda_{\text{exc}} = 532 \text{ nm}\)) for \([\text{Fe}(\text{OO})(\text{tpenaH})]^+\) and \(\lambda_{\text{exc}} = 691 \text{ nm}\) for \([\text{Fe}(\text{OO})(\text{tpenaH})]^+\). All spectra were normalized to the solvent band at 750 cm⁻¹. * = solvent bands. c) X-band EPR spectrum of \([\text{Fe}(\text{OO})(\text{tpenaH})]^+\) (microwave frequency 9.31542 GHz, 110 K, \([\text{Fe}] = 2 \text{ mm}\)). d) Mössbauer spectrum of a mixture containing \([\text{Fe}(\text{OO})(\text{tpenaH})]^+\) (14 %), \([\text{Fe}(\text{OO})(\text{tpenaH})]^+\) (14 %), and unidentified species (72 %) \(([\text{Fe}] = 2 \text{ mm})\).

Figure 4. Frozen-solution-state spectroscopic characterization of \([\text{Fe}(\text{OO})(\text{tpenaH})]^+\) (blue). a) EPR spectrum (microwave frequency 9.315392 GHz, 110 K, 2 mm \([\text{Fe}(\text{tpena})]^2+\) and 50 equiv of \(\text{H}_2\text{O}_2\) followed by 30 equiv of \(\text{ET}_3\text{N}\)). b) Mössbauer spectrum of a solution containing \([\text{Fe}(\text{OO})(\text{tpenaH})]^+\) (blue, 47 %) and \([\text{Fe}(\text{O}(\text{tpenaH}))]^+\) (green, 53 %). Fitting in grey \(([\text{Fe}] = 2 \text{ mm}, 30 \text{ equiv of \(\text{ET}_3\text{N}\) followed by 50 equiv of \(\text{H}_2\text{O}_2\)})\).
followed by rapid freezing in liquid $N_2$. This protocol meant that the presumably more labile [Fe(OOH)(tpenaH)]$^{2+}$ did not get the chance to form in any significant concentration.

Spectroscopic data for [Fe(tpena)]$^{2+}$ peroxide adducts are consistent with a side-on bound peroxide $Fe$ complex in [Fe(tpa)(tpenaH)]$^{2+}$ by comparison with iron complexes of $R$tpen (Table 1, $R$ = $\text{Me}$, $\text{BzCH}_2$, $\text{PyCH}_2$). This species is potentially intramolecularly (Scheme 5) or intermolecularly H-bonded, with the solid-state structure of [Cr(n$_2$O)(tpenaH)]$^{2+}$ furnishing a structural analogue for the latter. The pendant pyridinium moiety of the tpena ligand is a second site available for deprotonation by a base, and [Fe(tpa)(tpena)] is a plausible product from the reaction of [Fe(tpena)(tpenaH)]$^{2+}$ with two equivalents of base (Scheme 5). However, in this situation, the pyridine is expected to re-coordinate to the iron atom to form a seven-/eight-coordinated product for $\eta^1$- and $\eta^2$-O$^2$O$^2$-, respectively. This is not expected to be sterically too demanding, because the N-Fe-N angles for multidentate ligands with ethylenediamine backbones are generally less than 90°, thereby providing a relatively open face on the opposite side of the metal ion. Indeed, heptacoordination has been structurally characterized in the high-spin d$^5$ metal ion complexes [Fe(OIPh)(tpena)(ClO$_4$)$_2$] and [Mn(OH)$_2$(tpena)(ClO$_4$)$_2$]. The relatively open face presented by tpena in these structures suggests that formation of a heteroleptic complex with an $\eta^1$-diatomic ligand is also a reasonable structure for the peroxido complex, especially since $\eta^2$-O$^2$O$^2$- ligands are no more sterically demanding than monodentate oxide (O$_2^-$) ligands. Addition of further base leads to the formation of yellow solutions, with vigorous decomposition of H$_2$O$_2$ and ultimately decomposition of the complex (see below), such that the precise details of the protonation state cannot be readily determined experimentally.

Consideration of Table 1 shows that the most significant spectroscopic difference is that the Fe$^{3+}$ -- OOH$^-$ and Fe$^{3+}$ -- O$^2$ LMCT bands for the end-on hydroperoxido and side-on peroxido Fe$^{3+}$-tpena complexes are at shorter wavelengths than those for the analogous Rtpen-based complexes. The
\[ \lambda_{\text{max}} \text{ for } [\text{Fe(OO)}(\text{tpenaH})]^{2+} \text{ is hypsochromically shifted by about 20 nm, and the } \lambda_{\text{max}} \text{ for } [\text{Fe}^0(\text{OO})(\text{tpenaH})]^+ \text{ is shifted by 60, 75, and 95 nm compared to those reported for } [\text{Fe}^0(\text{OO})(\text{tpen})]^+, [\text{Fe}^0(\text{OO})(\text{metpen})]^+, \text{ and } [\text{Fe}^0(\text{OO})(\text{ibztpen})]^+, \text{ respectively.} \]

The larger difference for the peroxido complexes may be related to the intramolecular H-bonding.

**Competition between H$_2$O$_2$ disproportionation and ligand decomposition**

A large excess (20–50 equiv with respect to iron) of H$_2$O$_2$ is required to generate maximum steady-state concentrations of [Fe(OOH)(tpenaH)]$^{2+}$ and [Fe(OO)(tpenaH)]$^+$, under which conditions evolution of gas is observed. Analysis of the dissolved and evolved volatiles by means of membrane mass spectrometry (MIMS) and head-space Raman spectroscopy (HS-RS; \( \lambda_{\text{max}} = 532 \text{ nm} \)) confirmed that the gas evolved was predominantly O$_2$. Addition of $^{18}$O-labelled water in a 1:1:1 ratio of H$_2$O$_2$:H$_2$O:$^{18}$O mixture, confirmed that the O$_2$ evolved did not contain $^{18}$O and hence that the two oxygen atoms in the evolved O$_2$ were derived from H$_2$O$_2$. Thus, [Fe(tpena)]$^{2+}$ catalyses H$_2$O$_2$ disproportionation rather than a more demanding oxidation of water.$^{[26]}$ To the best of our knowledge, H$_2$O$_2$ disproportionation catalysed by exclusively N-donor Rtpen-supported iron(III) peroxides (Scheme 2, R = CH$_2$PyCH$_2$) has not been reported.$^{[10, 11, 17, 29]}$ Since it seemed plausible that this reaction had simply been overlooked (because bubbles were not visible) in previous studies of the generation of non-heme Fe$^{III}$ peroxides, we checked for this possible reaction in the present study by applying MIMS to monitor the reactions of [Fe(ClIImetpen)]$^+$ and [Fe(tpen)]$^{2+}$ with 50 equiv of H$_2$O$_2$. We can verify that O$_2$ evolution, and hence catalase activity, does not occur as a side reaction when these exclusively N-donor ligands support the peroxido complexes.

In further contrast to the exclusively N-donor-supported iron peroxido complexes, the hydperoxido species, [Fe(OOH)(tpenaH)]$^{2+}$, is not regenerated by the addition of a second portion (50 equiv) of H$_2$O$_2$ after the cessation of O$_2$ evolution, nor does catalytic H$_2$O$_2$ disproportionation resume. These observations indicate that either the catalyst is decomposed by H$_2$O$_2$ when the concentration of H$_2$O$_2$ is sufficiently low for competing C–H oxidation of the tpena ligand to become kinetically competent, or the increase in water concentration (introduced with and formed from H$_2$O$_2$) drives the formation of a kinetically inert oxido-bridged species [(tpenaH)Fe(µ-O)Fe(tpenaH)]$^{4+}$.$^{[24, 30]}$ To determine which of these pathways is pertinent, two equivalents of H$_2$O$_2$ were added to solutions of [Fe(tpena)]$^{2+}$ in acetonitrile. A colour change to purple was not observed. Head-space infrared spectroscopy (HS-IRS), however, showed that CO$_2$ was produced. The only carbon sources available for CO$_2$ production were the solvent acetonitrile and/or tpena. Monitoring both the O$_2$ and CO$_2$ releases by MIMS (Figure 5a) following the addition of 50 equiv of H$_2$O$_2$ revealed that O$_2$ was predominantly released in the early stages of the reaction. Quantitative analysis of the CO$_2$ release by HS-IRS showed that approximately seven CO$_2$ molecules per iron centre (Figure 5b) were produced. Increasing the amount of H$_2$O$_2$ added did not result in an increase in CO$_2$ formation, and it can therefore be concluded that the source of CO$_2$ was degradation of tpena rather than oxidation of acetonitrile. Specifically, the CO$_2$ must be derived from the aliphatic and carboxylate carbon atoms of tpenaH$_2$, as would be expected for aliphatic C–N oxidative cleavage/hydrolysis reactions.

The changes in iron speciation after the addition of 50 equiv of H$_2$O$_2$ were monitored by UV/Vis absorption, Raman, EPR, and Mössbauer spectroscopies. The band at 520 nm due to the purple [Fe$^{IV}$(OO)(tpenaH)]$^{2+}$ chromophore decayed completely, and then a new and more intense band appeared at 469 nm (Figure 6a). The absence of an isosbestic point suggests that the conversion between these iron-based chromophores involves relatively long-lived intermediates that do not absorb in the visible region. Time-resolved head-space FTIR and UV/Vis absorption data indicated that the growth of the band at 469 nm was concomitant with the release of CO$_2$ and the consequent growth of the absorbance at 2360 cm$^{-1}$ in the HS-IR spectra. A fit of an EPR spectrum recorded from a reac-
2.44, 2.29, 1.86, and a signal at 469 nm. For simplicity, this was fitted to a broad asymmetric doublet with $\Delta = 0.20 \text{ mm s}^{-1}$ and $\Delta E_q = 1.90 \text{ mm}^{-1}$ (72\%, orange fit). Such asymmetric doublets are commonly seen in spectra of high-spin iron(III) species with paramagnetic relaxation times on the order of a nanosecond. The low intensity of the signal in corresponding EPR spectra suggests that the electron spin relaxation in this dominant non-integer spin component is too rapid for the EPR timescale. Other potential decomposition products, integer spin Fe$^3$ and Fe$^2$ monomers and the strongly anti-ferromagnetically coupled starting material, [Fe$^3$(tpena)$_2$]$^{4+}$, are expected to be EPR silent. Bands at $\nu = 634, 1192,$ and $2094 \text{ cm}^{-1}$ appeared in the Raman spectrum ($\lambda_{exc} = 532 \text{ nm}$) of equivalently treated solutions (Figure 6c).

The band at $\nu = 2094 \text{ cm}^{-1}$ is consistent with the presence of Fe$^4$-coordinated acetonitrile.$^{[31]}$ A $^1$H NMR spectrum of the reaction mixture in CD$_2$CN recorded after 16 h (and hence coinciding with the presence of the EPR-silent species with an absorption at 469 nm showed the characteristic signal of NH$_3$ (three resonances of equal intensity centred at $\delta = 6.61 \text{ ppm}$, $J_{\text{NH} \text{- H}} = 52 \text{ Hz}$; Supporting Information, Figure S2). This demonstrated that the production of NH$_3$ occurred concomitantly with the production of tpenaH-derived CO$_2$. The signals remaining in the aromatic region (7–9 ppm) suggested that the pyridine groups remained intact. Positive- and negative-ion ESI-MS did not provide evidence for the formation of a complex with pyridine ligands that might be associated with the species at 469 nm. Indirectly, however, the ESI-MS data provide further evidence that all of the aliphatic C atoms of the ligands were converted into CO$_2$ through the absence, for example, of picolinato complexes that have previously been observed to form through the reaction of aminopyridyl-metal complexes with peroxides.$^{[32]}$

Overall, the data lead to the conclusion that reaction of [Fe(tpena)$_2$]$^{3+}$ with a large excess of H$_2$O$_2$ results primarily in H$_2$O$_2$ disproportionation, but is accompanied by concurrent oxidative decomposition of the tpena ligand, which occurs primarily when the concentration of H$_2$O$_2$ is low. A mixture of heterogeneous iron(II) complexes of pyridine, ammonia, and/or acetonitrile ligands is ultimately formed through the oxidative decomposition of [Fe$^3$(tpena)$_2$]$^{3+}$. Catalytic alcohol oxidation overrides catalase activity and ligand decomposition

In stark contrast to the reactions of [Fe$^3$(Cl)(Rtpena)$_2$]$^{3+}$ with excess H$_2$O$_2$ in methanol,$^{[10,11,17]}$ the addition of 50 equiv of H$_2$O$_2$ to solutions of [Fe$^3$(tpena)$_2$]$^{3+}$ in methanol does not give rise to detectable amounts of purple [Fe$^3$(OOH)(tpena)$_2$]$^{4+}$. This is because methanol is oxidized. Analysis using the Hantsche reaction$^{[33]}$ and UV/Vis absorption spectroscopy showed that formaldehyde was produced in approximately 35\% yield based on the initial H$_2$O$_2$ concentration. Thus, the activation of H$_2$O$_2$ by Fe$^3$(tpena)$_2$$^{3+}$ can be directed to perform substrate oxidation. This observation inspired us to examine a more readily oxidizable substrate, benzyl alcohol, in acetonitrile (bond dissociation energies for H–CH$_2$OH and H–CH(OH)Ph are 96 and 79 kcal mol$^{-1}$, respectively$^{[34]}$). The addition of 50 equiv of H$_2$O$_2$ to Fe(tpena)$_2$$^{3+}$ in the presence of 500 equiv of benzyl alcohol did not result in either O$_2$ or CO$_2$ evolution, and hence
neither H2O2 disproportionation nor tpena decomposition occurred. In contrast to the reactions performed in methanol, under these conditions, [FeIII(OOH)(tpenaH)]2+ was observed spectroscopically due to the lower concentration of the oxidant substrate. The addition of a second portion of H2O2 (50 equiv) resulted in reappearance of the absorption band of [FeIII(OOH)(tpenaH)]2+ with the same intensity as after the first addition (Figure 7). Continued batchwise addition of H2O2 eventually led to decomposition of the ligand, that is, the band at 469 nm intensified and the purple colour, due to [FeIII(OOH)(tpenaH)]2+, was lost. Thus, tpenaH oxidation competes with alcohol oxidation and the presence of a large excess of alcohol, or its use as the solvent delays the onset of ligand oxidation. 1H NMR spectroscopic analysis showed, after five additions of 50 equiv of H2O2 over 10 min, 50% conversion of benzyl alcohol to benzaldehyde and hence near-stoichiometric conversion with respect to the oxidant. A control reaction in the absence of [Fe(tpena)]2+ showed that, under otherwise identical conditions, benzyl alcohol was oxidized by H2O2 with only 32% conversion after 20 h. 

Mechanistic considerations

The reaction of [(tpenaH)Fe-O-Fet(tpenaH)]2+ with CeIV in water produces the iron(IV) oxo complex, [FeIV(O)(tpenaH)]2+,[24] and recently we have generated this same species electrochemically, also in water.[25] In both of these studies, we demonstrated [FeIV(O)(tpenaH)]2+ to be a promiscuous oxidant in the absence of hydroxyl radicals. It attacks a broad range of C–H bonds by hydrogen-atom transfer. Thus, [FeIV(O)(tpenaH)]2+ displays radical character. Calculations by Faponle et al. show that [FeIV=O(metpen)]2+ can be generated by homolytic cleavage of [FeOOH](metspen)]2+, and it is the FeIV oxo species that reacts with substrates.[26] This reaction has been demonstrated in the gas phase.[27] However, the phase of the reaction medium (and second coordination sphere) is likely to tune the O–O bond-cleavage reaction. With these facts in mind, we propose that the H2O2 activation and reactivity described in the present study can be rationalized in terms of homolytic O–O bond cleavage of the hydroperoxide ligand in [FeIII(OOH)(tpenaH)]2+.

This reactivity is in contrast to the behaviour of FeIV-OOH based on neutral N5 donor systems. In fact, peroxide dissociation is a highly competitive pathway for the decomposition of (NS)FeIV-OOH species. It can thus be concluded that for the iron-tpena system, homolytic O–O bond cleavage occurs in [FeIV(OOH)(tpenaH)]2+, resulting in the formation of [FeIV(O)(tpenaH)]2+ and a hydroxyl radical. Both are aggressive hydrogen-atom abstractors and will react with methanol, benzyl alcohol, and hydrogen peroxide to form the methanol, benzoyl, and hydroperoxide (CH2OH, CH3H6CHOH, ‘OOH) radicals, respectively. In turn, these radicals will propagate chain reactions and radical terminations to give the detected products, CH3O, CH3CHO, and O2. Interconnected catalytic cycles for H2O2 disproportionation and alcohol oxidation are proposed in Scheme 6.

Perspective on the tunability by varying the supporting ligand in H2O2 activation by non-heme iron complexes

Compared to analogous iron(III)-hydroperoxide complexes based on supporting N5 and N6 ligands containing exclusively pyridine and tertiary amine donors (Scheme 2a) and analogous N,N-bis(2-pyridylmethyl)-N-bis(2-pyridyl)methylamine(N4py) systems, the influence of a biomimetic carboxylato donor is demonstrated by the significant difference in FeIV/FeII redox potentials of the parent [Fe(tpen)]2+ and [Fe(tpena)]2+ complexes. The latter is shifted to lower values by an average of 360 mV for the diastereoisomers in acetonitrile. A practical consequence of the lower redox potential is that tpena-FeII complexes are isolated, and these are redox-stable in the +3 oxidation state in all solvents examined.[20] This result stands in contrast to observations for the complexes of tpen and related N5 neutral pentadentate ligands (Scheme 2a), for which the iron(III) complexes are most readily isolated, especially in solvents such as acetonitrile. These are thermodynamic sinks,
retarding their reactivity with H$_2$O$_2$. This tendency towards greater stability in higher iron oxidation states will have a significant impact on the chemistry of the iron-tpena complexes and hence on the construction of proposed catalytic cycles. The pro-catalyst and resting state is iron(III) and not iron(II). As such, the process of peroxide adduction formation does not require a prior oxidation step from iron(II) to iron(III). The Fe$^{IV}$/Fe$^{III}$ couple can be reasonably expected to follow this trend towards lower potentials, and this will favour promotion of the oxidation of benzaldehyde from the [Fe(tpena)]$^{2+}/C_0$ and its conjugate base [Fe(OOH)(tpenaH)]$^{2+}$ and [Fe(OO)(tpenaH)]$^{+}$ compared to the corresponding systems based on N5/N6 Rtpen ligands. A further contrast to the N5/N6 donor-supported systems for the reaction of H$_2$O$_2$ with the resting state iron(III) in [Fe(tpena)]$^{2+}/C_0$ is that no deprotonation of the H$_2$O$_2$ is needed. It is an addition reaction accompanied by charge separation due to concomitant pyridine decoordination and pyridinium formation. The ligand is converted from monoanionic hexadentate (tpena) to zwitterionic pentadentate (tpenaH). With one carboxylato donor and a second base in the coordination sphere, [Fe(OOH)(tpenaH)]$^{2+}$ and its conjugate base [Fe(OO)(tpenaH)]$^{+}$ are particularly germane biomimics for non-heme iron(III) peroxides. The peroxide activation chemistry that we have observed is pertinent to elucidating mechanisms for O$_2$-activating enzymes in which Gly/Asp groups are coordinated to the O$_2$-binding site on iron.$^{[30]}$ In particular, we note that the non-heme 1 Asp/3 His-coordinated iron superoxide dismutase$^{[30]}$ evolves O$_2$ in a similar manner to the Fe-tpena system studied here (although the disproportionate substrates is O$_2$ and not H$_2$O$_2$). The basic amino acid residues found in the second coordination sphere of non-heme active sites are proposed to facilitate proton-coupled redox reactions, and a similar role for the dangling pyridine/pyridinium groups of the tpena system is feasible. The contrast in peroxide activation reactivity between [Fe(tpena)]$^{2+}/C_0$ and the parent pentadentate N4O Rbpena-based Fe$^{	ext{III}}$ systems (Scheme 2b) described in the Introduction is also worth noting: ligand oxygenations result from reactions of the iron(III) starting complexes with H$_2$O$_2$ without the detection of iron(IV) species (Scheme 2 b). The two types of O atom insertions observed are consistent with heterolytic O–O cleavage of a putative (Rbpena)Fe$^{IV}$O–O(H) intermediate to form a putative Fe$^{III}$ oxo species. This reactive species can then transfer [O] to the aromatic C–H or N in bzbpena and mebpena, respectively. The iron(III) complexes of the modified “RbpenaO” ligands may be unable to activate H$_2$O$_2$, and are therefore stable towards oxidative decomposition, in contrast to the iron complex of tpena.$^{[18]}$ Interestingly, the manganese complexes of Rbpena and tpena can withstand thousands of equivalents of organic peroxides without decomposition or ligand modification.$^{[26,28]}$

**Conclusions**

Methanol oxidation to formaldehyde and stoichiometric yields of benzaldehyde from the [Fe(tpena)]$^{2+}/C_0$-catalysed oxidation of benzyl alcohol by H$_2$O$_2$ have been realized in the present study. In the absence of a large excess of a second substrate, H$_2$O$_2$ disproportionation is catalysed by [Fe(tpena)]$^{2+}/C_0$ through a related mechanism. However, in the absence of other oxidizable substrates (methanol, benzyl alcohol, and H$_2$O$_2$), oxidative decay of [Fe(tpena)]$^{2+}$ occurs through the spectroscopically detectable intermediate [Fe(OOH)(tpenaH)]$^{2+}$.$^{[29]}$ Release of all of the aliphatic carbon atoms and amine groups as CO$_2$ and NH$_3$, respectively, has been demonstrated. The reactivity patterns observed (catalysis of the oxidation of alcohols, catalase activity, and tpena degradation, Scheme 3) reflect the higher C–H bond strength in MeCN compared to MeOH, the aliphatic C–H bonds in tpena, and the O–H bond in H$_2$O$_2$, respectively. Overall, the H$_2$O$_2$ activation chemistry described here stands in contrast to that reported previously for the pentadentate N5/N6 supporting ligands [Fe$^{IV}$][OOH](Rtpen)$^{2+}$ and [Fe$^{IV}$][OOH](N4py)$^{2+}$ and a carboxylate-containing N4O pentadentate supporting ligand [Fe$^{IV}$][OOH](Rbpena)$^{2+}$. We have shown: 1) facile homolytic Fe$^{IV}$O–OH cleavage in solution to produce two aggressive H-atom abstractors, Fe$^{IV}$=O and HO, 2) catalytic H$_2$O$_2$ disproportionation, 3) catalytic alcohol oxidation with stoichiometric yields, and 4) total destruction of the aliphatic part of tpena in the presence of low concentrations of H$_2$O$_2$. By tuning the penta- and hexadentate ethylenediamine-backboned ligands (Scheme 2), a tendency towards the limiting reaction types depicted in Equations (2), (3), and (4) for Fe$^{IV}$-peroxide adducts has been exposed. It seems that H$_2$O$_2$ activation is more effective for the carboxylato ligands and the difference in reactivity seen for the N4O (Rbpena) and N5O (tpena) ligand systems must be due to the availability of a second base in the coordination sphere for the latter. The proximity of this group suggests that it may participate at many stages, from its decoordination to allow adduct formation by charge-separated H$_2$O$_2$ addition to H-bonding in the peroxide intermediates. In turn, this electronic modulation may effect a homolytic O–O cleavage rather than the heterolytic cleavage and intramolecular oxygenation that occurs with the otherwise stereochemically and electronically similar N4O Rbpena as a supporting ligand.

Dissociation:

\[
\text{Fe}^{IV}([\text{OOH}](\text{Rtpen}))^{2+} + \text{HX} \rightleftharpoons [\text{Fe}^{IV}(\text{X})(\text{Rtpen})]^{2+} + \text{HOOH} \quad (2)
\]

O–O heterolysis:

\[
[\text{Fe}^{IV}([\text{OOH}](\text{Rbpena}))^{2+} \rightarrow [\text{Fe}^{IV}(\text{RbpenaO})]^{2+} + \text{OH}^- \quad (3)
\]

O–O homolysis:

\[
[\text{Fe}^{IV}([\text{OOH}](\text{tpenaH}))^{2+} \rightarrow [\text{Fe}^{IV}(\text{O})(\text{tpenaH})]^{2+} + \text{OH}^+ \quad (4)
\]

Our work not only presents a germane mimic for non-heme iron chemistry, especially in terms of the carboxylato group and the second coordination sphere base, but also adds to our knowledge of the ligand design features important for activating H$_2$O$_2$, demonstrates controllable bifurcation in catalysed external substrate oxidation reactions, and indicates that destruct-
tive oxidation of the supporting ligand can be avoided through appropriate experimental design [Eqs. (2–4)].

Experimental Section

Materials and preparations

N,N,N-Tris-(2-pyridylmethyl)ethylenediamine-N’-acetic acid (tpenaH),[40] [(tpenaH)Fe-O-Fe(tpenaH)](ClO4)2(H2O)2,[20] [(tpenaH)Fe-O-Fe(tpenaH)]4(ClO4)4(H2O)2,[20] [Fe(Cl)(tpenaH)](ClO4)2, [Fe(Cl)(metpen)](PF6),[17] [Fe(tpen)](ClO4)2, and [Fe(tpen)][ClO4]2·2H2O (702 mg, 54 %) were deposited after two weeks. ESI-MS (MeCN): m/z: 446.1 ([Fe(tpenaH)]+, 34 %), 454.1 ([tpenaFe-O-Fe(tpena)]+, 100 %), 463.1 ([Fe(OH)-tpena]+, 85 %); IR (KBr): 1610 (C–O, s), 1098 cm⁻¹ (ClO4–, s); elemental analysis calc (%) for C20H26N4O4Fe: 2.78; found: 2.68. This solution was then treated with 50 equiv of H2O2 (50 % in water, w/w) to give [Fe(OOH)(tpenaH)]2+. This solution was then treated with 10 min until [(tpenaH)Fe-O-Fe(tpenaH)]4+ had dehydrated to [Fe(tpenaH)]2+. This solution was then treated with 50 equiv of H2O2 (50 % in water, w/w) to give [Fe(OOH)-tpenaH]+, and [Fe(OO)(tpenaH)]+ was formed by the subsequent addition of 30 equiv of Et,N.

[Fe(Cl)(tpenaH)][ClO4]2·(EtOH)-2(H2O): [FeCl3]-H2O (773 mg, 1.7 mmol) was added to tpenaH (655 mg, 1.7 mmol) in acetonitrile (5 mL), water (5 mL), and ethanol (5 mL), and the mixture was adjusted to pH 3 with HCl(aq.). Upon slow evaporation of the volatiles, yellow crystals of [Fe(Cl)(tpenaH)][ClO4]2·EtOH-2H2O (702 mg, 54 %) were deposited after two weeks. ESI-MS (MeCN): m/z: 479.1 ([Fe(tpenaH)-2H2O]+, 78 %), 481.1 ([Fe(tpenaH)+, 81 %), 482.1 ([Fe(tpenaH)]+, 100 %); ESI-MS (H2O): m/z: 466.1 ([Fe(tpenaH)+], 34 %), 454.1 ([tpenaFe-O-Fe(tpena)]+, 100 %), 463.1 ([Fe(OH)-tpena]+, 85 %); IR (KBr): ν = 1610 (C–O, s), 1098 cm⁻¹ (ClO4–, vs); elemental analysis calc (%) for C20H26N4O4Cl4Fe: 2.78; found: 2.68. C 36.21, H 3.65, N 9.27.

Instrumentation and methods

UV/Vis spectra were recorded from solutions in 1 cm quartz cuvettes on either an Agilent 8453 spectrophotometer with a UNISOKU CoolSpek UV USP-203 temperature controller or an Analytik Jena Spectord S600 with a Quantum Northwest TC 125 temperature controller. Raman spectra were recorded from samples in 1 cm quartz cuvettes at either 532 nm (300 mW at source, Cobolt Lasers). The solutions were cooled with a Quantum Northwest Instrumentation and methods temperature controller and the spectra were obtained at 100 K. Cyclic voltammetry was performed on an Eco Chemie Autolab PGSTAT10 potentiostat/galvanostat using a standard three-electrode set-up with a Pt disc as the working electrode, a Pt wire as the counter electrode, and Ag/AgCl as the reference electrode (0.01 M AgNO3 in 0.1 M TBAClO4 in MeCN; TBA: tert-butylammonium). The electrolyte was also 0.1 M TBAClO4 in MeCN. The working electrode was cleaned by polishing with 0.05 μm alumina followed by sonication, and the solutions were purged with nitrogen prior to measurements. The oxidation potential of Fe(III)/Fe(II) in the absence of Ag/AgCl was measured as 0.08 V, and all oxidation potentials were converted accordingly.

CCDC 1559278 ([Fe(tpenaH)][ClO4]2·(EtOH)-2(H2O)) contains the supplementary crystallographic data for this paper. These data are provided free of charge by The Cambridge Crystallographic Data Centre.

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Conflict of interest

The authors declare no conflict of interest.

Keywords: H2O2 activation · high-valent iron · hydroxyl radical · iron(IV) · N2O ligands · peroxides
Peroxide activation at Fe: A transient Fe(III)-hydroperoxide intermediate has been spectroscopically identified during [Fe(III)(tpena)]^2+ -catalysed H_2O_2 disproportionation in acetonitrile (see graphic). If benzyl alcohol is present, or methanol is used as solvent, H_2O_2 disproportionation is inhibited in favour of high-yielding alcohol oxidation to the corresponding aldehyde. In the absence of excess substrate (alcohol or H_2O_2), tpena is oxidatively degraded.