Raman Evidence for a Weakened O−O Bond in Mononuclear Low-Spin Iron(III)−Hydroperoxides

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Iron−peroxo species have been proposed or demonstrated to be catalytic intermediates in the mechanisms of a number of mononuclear iron enzymes[1,2] and catalysts involved in alkane and arene hydroxylation and olefin epoxidation.[3−5] Among these is a subset that have low-spin iron(III) centers as indicated by rhombic EPR signals at $g = 1.9-2.4$. Four of these have been formulated to be [LFe−OOH] species based on electrospray ionization mass spectral (ESI-MS) data, where L = TPA,[4,6] N4Py,[5] Py5,[7] and the antitumor drug bleomycin[8] and are implicated in hydrocarbon oxidation reactions.[3a−5,9,10] Such low-spin iron(III)−hydroperoxo species are also likely to be involved in the chemistry of heme peroxidases, cytochrome P450, and related heme catalysts.[2,11] To date, no vibrational information has been obtained that provides insight into the relative bond strengths of the O−O and Fe−O bonds because of the short lifetimes of such complexes and their susceptibility to photodecomposition.[3b,5] By excitation into the peroxide-to-iron(III) charge-transfer band at much lower energy, we have obtained resonance Raman spectra of [Fe(III)(TPA)(OOH)]$^{2+}$ (**1**) and [Fe(III)(N4Py)(OOH)]$^{2+}$ (**2**) which shed light into the reactivity of these species.

Previously, we have reported that the addition of excess H_2O_2 to [Fe(II)(TPA)$(CH_3CN)_2$]$^{2+}$ or [Fe(II)(N4Py)(CH_3CN)]$^{2+}$ at low temperatures gives rise to purple low-spin Fe(III)−OOH intermediates, **1** and **2**, with λ_{max}'s at 538 nm[4] ($\epsilon \approx 1000$ M^{-1} cm^{-1}) or 532 nm[5] ($\epsilon \approx 1100$ M^{-1} cm^{-1}), respectively. The Raman spectrum of **1** (Figure 1A), obtained by excitation into the long wavelength tail of its peroxo-to-iron(III) charge-transfer band, shows two resonance-enhanced features at 626 and 789 cm^{-1}, while that of **2** (Figure 1B) shows four features at 632, 651, 672, and 790 cm^{-1}. Excitation profile studies confirm that these vibrations are all associated with the peroxo-to-iron(III) charge-transfer transition. Due to experimental complications,[12] isotope data could only be obtained for **2**. With $H_2{}^{18}O_2$ (Figure 1C), only the features at 632 and 790 cm^{-1} of **2** downshift by 16 and 44 cm^{-1}, respectively, while the 651 and 672 cm^{-1} features are unaffected.[13] The vibrations around 630 and 790 cm^{-1} are thus associated with the Fe−OOH moiety.

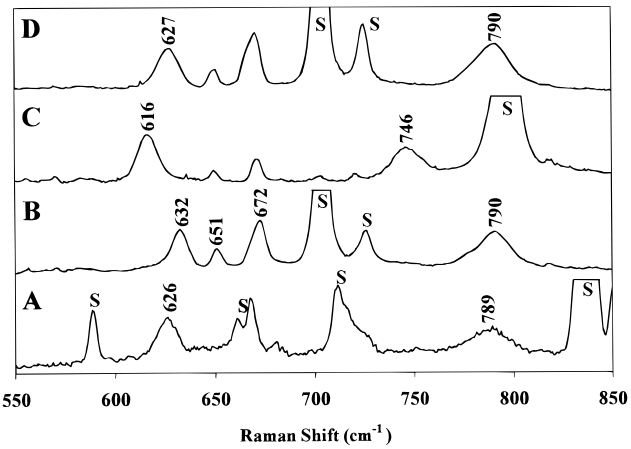

Figure 1. Resonance Raman spectra of **1** and **2**. A. 50 mM H_2O_2 dissolved in CD_3CN was added to 10 mM [Fe(II)(TPA)$(CH_3CN)_2$]$^{2+}$ in 4/1 CD_3CN/THF at −50 °C. The spectrum was obtained with 568.2 nm laser excitation at 20 mW power at the sample. B. 50 mM H_2O_2 was added to 10 mM [Fe(II)(N4Py)(CH_3CN)]$^{2+}$ in d_6-acetone at −10 °C. The spectrum was obtained with 615 nm laser excitation at 20 mW power at the sample. C. Same as B, except $H_2{}^{18}O_2$ and acetone were used. D. Same as B, except H_2O_2 diluted in D_2O was used.

Resonance Raman spectra of iron−peroxide complexes typically exhibit two resonance enhanced features, a ν(O−O) between 800 and 900 cm^{-1} and a ν(M−O) between 400 and 503 cm^{-1} (Table 1). The 790 cm^{-1} feature in **1** and **2** is best assigned as the ν(O−O). This assignment is strongly justified by the −44 cm^{-1} shift for this feature upon ^{18}O substitution in **2** (Figure 1C), which matches well the shift of −45 cm^{-1} predicted by Hooke's law for a diatomic O−O stretch. As shown in Table 1, 790 cm^{-1} is the lowest ν(O−O) of any iron−peroxo species, including the two characterized η^2-peroxo−iron species. This comparison suggests that the O−O bond is significantly weakened in **1** and **2**.

The assignment of the 632 cm^{-1} feature is less certain. While it is initially tempting to assign it to a ν(Fe−O), Fe−O vibrations for other iron−peroxo species are significantly lower in energy and are typically observed between 400 and 503 cm^{-1} (Table 1). Furthermore the use of $H_2{}^{18}O_2$ affords a shift of only −16 cm^{-1}, which is about half that predicted by Hooke's law calculations for a pure Fe−O vibration (−28 cm^{-1}). Calculations for an Fe−OO vibration (−23 cm^{-1}) or an Fe−OOH vibration (−22 cm^{-1}) afford shifts that approach the observed value, but it is clear that this vibration must involve the coupling of a number of modes. Similar complications have been noted in the analysis of Raman

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(6) Abbreviations used: BLM = bleomycin, DFT = density functional theory, EDTA = ethylenediaminetetraacetic acid, N4Py = *N*-(bis(2-pyridyl)-methyl)-*N*,*N*-bis(2-pyridylmethyl)amine, OEP = 2,3,7,8,12,13,17,18-octaethyl-21H,23H-porphine, Py5 = 2,6-bis-(bis(2-pyridyl)methoxymethane)pyridine, T(2-N-Me)PyP = tetrakis(2-*N*-methylpyridiniumyl)-porphinato, TPA = tris-(2-pyridylmethyl)amine.
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(12) $H_2{}^{18}O_2$ is commercially available only as a 2% aqueous solution. Such a solution freezes rapidly when introduced to a 9/1 CH_3CN/THF at −40 to −50 °C and prevents the generation of **1** for Raman studies. With $H_2{}^{16}O_2$, this problem can be avoided by diluting the aqueous 30% H_2O_2 with CH_3CN.
(13) Scrutiny of the spectra in Figure 1 may indicate a downshift for the 672 cm^{-1} feature. However this is only an apparent shift, as the solvent d_6-acetone has a weak feature at 668 cm^{-1} which overlaps with the 672 cm^{-1} feature in **2**. Curve fits of the Raman spectra gave 651 and 672 cm^{-1} for ^{16}O, 650 and 671 cm^{-1} for ^{18}O, and 650 and 671 cm^{-1} for ^{2}H. The 1 cm^{-1} downshifts observed are within the uncertainty of our instrument.

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Table 1. Reported Resonance Raman Features of Iron−Peroxide Complexes

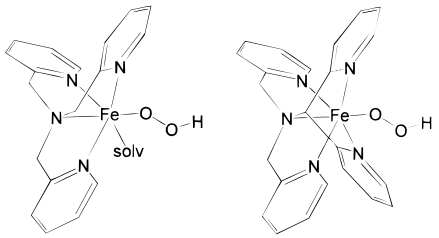
complex	ν_{Fe-L} (cm^{-1})[a]	ν_{O-O} (cm^{-1})	ref
$[Fe(TPA)(OOH)]^{2+}$	626[b]	789	this work
$[Fe(N4Py)(OOH)]^{2+}$	632[b]	790	this work
$[Fe(OEP)(\eta^2\text{-}O_2)]^-$	n.o.	805	14
$[Fe(III)(EDTAH)(\eta^2\text{-}O_2)]^{2-}$	n.o.	815	15
oxyhemerythrin $[Fe(\eta^1\text{-}OOH)]$	503	844	16,17
$Fe_2(\mu\text{-}1,2\text{-}O_2)$ species	415−476	848−900	18

[a] L = O or OOH. [b] Observed feature for the coupled Fe−OOH mode.

data for the related $[Fe(TPA)(OO^tBu)]^{2+}$ species.[19] The 632 cm^{-1} feature also exhibits a 5 cm^{-1} downshift with $^2H_2O_2$ (Figure 1D) compared to a calculated shift of −6 cm^{-1} for a ν(Fe−OOH). This ^2H isotope shift strongly supports the presence of a hydroperoxide ligand initially deduced from ESI-MS data.[5] The sensitivity of the 632 cm^{-1} feature to both ^{18}O and ^2H from H_2O_2 indicates a coupled mode that arises from an Fe−OOH unit.

In contrast to the high spin centers of other characterized iron−peroxo species in Table 1, the iron(III) centers in **1** and **2** are low-spin. This change in the spin state causes a decrease in the ionic radius which may result in the strengthening of the Fe−O bond. The pentadentate N4Py ligand may also promote a stronger Fe−O bond as demonstrated by the very short (1.79 Å) Fe−OMe bond in $[Fe(III)(N4Py)(OMe)]^{2+}$ [20] which is also found in the closely related $[Fe(III)(Py5)(OMe)]^{2+}$.[21] These factors may contribute to the unusually high energy observed for the vibration of the Fe−OOH mode.

The Raman features around 630 and 790 cm^{-1} clearly distinguish **1** and **2** from other metal−peroxide species (Table 1) and may represent the Raman signature for mononuclear low-spin Fe(III)−OOH species. Given the fact that the few structurally characterized M−OOH complexes all have η^1 (end-on) binding modes,[22,23] it is likely that the hydroperoxides in **1** and **2** are similarly bound (Figure 2). The observation that these low-spin Fe(III)−OOH species have a ν(O−O) at least 50 cm^{-1} lower than that of the high-spin peroxo complexes suggests that the low-spin center may weaken the O−O bond. This notion is supported by recent nonlocal DFT calculations on the putative Fe−OOH species in cytochrome P450.[24] This weakened bond would then be primed for O−O bond cleavage to convert the low-spin iron(III) (t_{2g}^5) center with minimal electronic reorganization to low-spin iron(IV) (t_{2g}^4)−oxo or iron(V) (t_{2g}^3)−oxo species, which are generally accepted as the key oxidants in the mechanisms of many heme-catalyzed oxidations.[2,11] Indeed **1** and **2** are the only peroxo species in Table 1 associated with the catalytic oxidation of relatively inert hydrocarbons such as cyclohexane.[4,5] Similar arguments may be applied to rationalize the involvement of low-spin Fe(III)−OOH species in the catalytic cycles of bleomycin[3a,9,10] and several heme enzymes.[2,11] Our Raman data thus shed light into one mechanism by which dioxygen can be activated at mononuclear iron sites, illustrating a common thread that underlies iron metallobiochemistry in both heme and non-heme systems.



1 **2**

Figure 2. Proposed binding mode of the hydroperoxide in **1** and **2**.

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