High-Valent Non-Heme Complexes

A Dramatic Push Effect on the Homolysis of Fe^{III}(OOR) Intermediates To Form Non-Heme $Fe^{IV}=O$ Complexes**

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The first synthetic complexes with a mononuclear non-heme $Fe^{IV}=O$ unit have recently been unequivocally identified, thus lending strong credence to the involvement of such species in the postulated oxygen activation mechanisms of enzymes with mononuclear non-heme iron active sites such as isopenicillin *N*-synthase, pterin-dependent phenylalanine hydroxylase, and 2-oxoglutarate-dependent clavaminate synthase.[1–4] Crystallographically characterized $[Fe^{IV}(O)(TMC)(NCCH_3)]^{2+}$[5] is obtained by oxygen-atom transfer from PhIO to $[Fe^{II}(TMC)(OTf)_2]$ in CH_3CN at −40 °C,[6] while $[Fe^{IV}(O)(TPA)]^{2+}$[5] is generated by O–O bond heterolysis in the stoichiometric reaction of $[Fe^{II}(TPA)(OTf)_2]$[5] with CH_3CO_3H in CH_3CN at −40 °C.[7] The availability of these two non-heme $Fe^{IV}=O$ complexes allows us for the first time to identify the intrinsic spectroscopic signatures of the $Fe^{IV}=O$ unit in the absence of a porphyrin. Besides having properties observed for oxoiron(IV) porphyrin complexes,[8] such as an Fe–O bond shorter than 1.7 Å and Mössbauer parameters characteristic of a low-spin ($S=1$; $S=$ spin angular momentum) iron(IV) center, the non-heme complexes are characterized by relatively weak electronic transitions in the near IR region ($\lambda_{max} \sim 700$–800 nm, $\varepsilon_M \sim 300$–400).[6,7] In the course of our efforts to synthesize functional models for non-heme iron enzymes, we have investigated the reaction of *t*BuOOH with iron(II) complexes of tris(2-pyridylmethyl)amine (TPA) and related ligands and obtained indirect evidence of the involvement of corresponding $Fe^{IV}=O$ species in the oxidations of alkanes, dialkyl sulfides, and arenes.[9] In all cases, a transient low-spin $[Fe^{III}(L)(OOtBu)]^{2+}$ intermediate could be observed, which for L = TPA (**1**) is characterized by an absorption band at 600 nm ($\varepsilon_M \sim 2000$),[10] whose intensity could have hampered observation of the pale green $Fe^{IV}=O$ species. Herein we report direct spectroscopic evidence for the formation of $[Fe^{IV}(O)TPA]^{2+}$ (**2**) from **1**. Furthermore the addition of Lewis bases accelerates this conversion and enhances the yield of **2**, thus demonstrating a "push" effect in the O–O bond homolysis of a non-heme iron peroxo species.

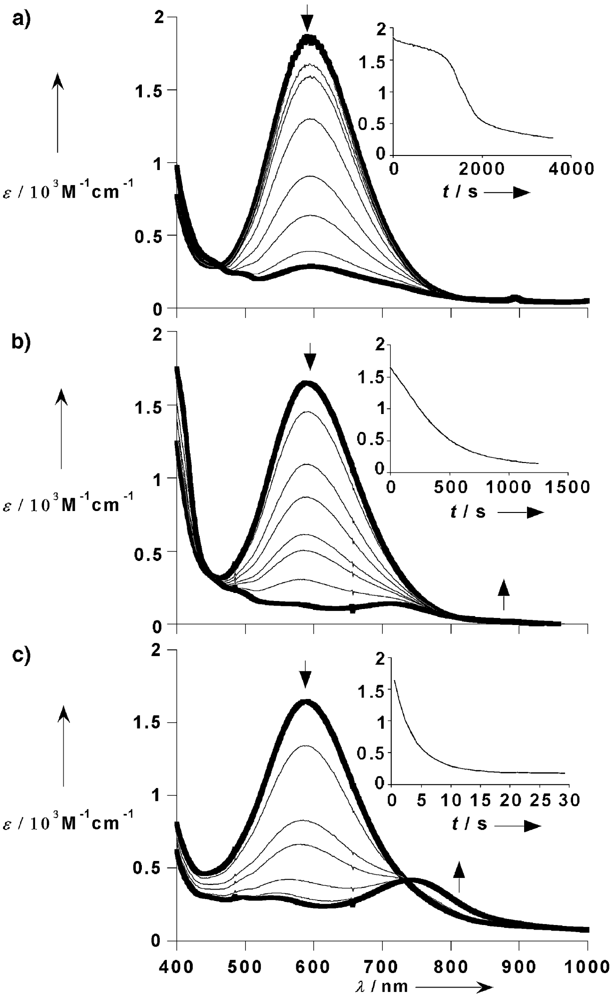

Figure 1. Visible spectral changes for the decay of **1** in acetonitrile at −36 °C formed by adding: a) 10 equiv *t*BuOOH, b) 2 equiv *t*BuOOH, and c) 2 equiv *t*BuOOH with 12 equiv of pyridine *N*-oxide. Insets: time-dependent conversions of **1** under the conditions described above monitored at 593 nm.

Figure 1a shows the time course for the decay of $[Fe^{III}(TPA)(OOtBu)]^{2+}$ (**1**) formed by the addition of ten equivalents of *t*BuOOH (in nonane) to a 1 mM $[Fe^{II}(TPA)(OTf)_2]$ in CH_3CN at −36 °C. Previously, the high conversion of iron(II) precursor to **1** obtained during the steady-state phase immediately after formation facilitated its spectroscopic characterization.[10b] Under these conditions, **1** decomposed without obvious accumulation of a new species with a long-wavelength absorption. However when only two equivalents of *t*BuOOH was used, **1** decayed in a first-order process ($k_{obs} = 2.1(1)\times10^{-3}\,s^{-1}$) to a new species with a weak absorption at 700 nm that reached maximum intensity after 1000 s (Figure 1b). Assuming an ε_M of 300 $M^{-1}cm^{-1}$ found in the CH_3CO_3H oxidation of its iron(II) precursor,[7] then **2** was formed in about 45 % yield.

The addition of various Lewis bases after the formation of **1** accelerated its decay and increased the yield of **2**. For example, addition of 12 equivalents of 4-picoline to **1** increased its first order decay rate tenfold ($k_{obs} = 1.6(1)\times10^{-2}\,s^{-1}$) and resulted in a 90 % yield of **2**. However 2,6-di-*tert*-butylpyridine had no effect, thus showing that the 4-picoline was not acting simply as a Brønsted base. Even more dramatically, the addition of 12 equivalents of pyridine *N*-

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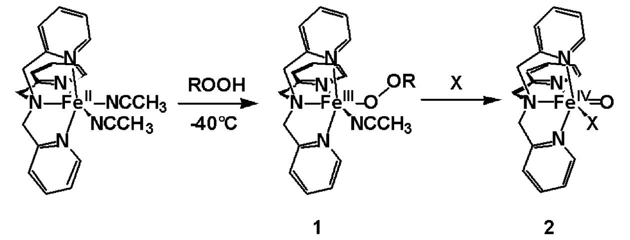
oxide (PyO) to **1** accelerated its decay by another order of magnitude ($k_{obs} = 3.1(1) \times 10^{-1}\,s^{-1}$) affording **2** in >95% yield (Figure 1c)! The Mössbauer spectrum of this last species shows a quadrupole doublet ($\delta = 0.04(2)\,mm\,s^{-1}$; $\Delta E_Q = 0.90(2)\,mm\,s^{-1}$), very similar to that reported for $[Fe^{IV}(O)(TPA)]^{2+}$ derived from the reaction of $[Fe(TPA)(CH_3CN)_2]^{2+}$ with peracetic acid.[7]

Examination of the spectral maximum associated with **2** under these various conditions showed that it was also sensitive to the nature of the Lewis base. While this electronic transition has not yet been unequivocally assigned, its relatively low energy and intensity suggest that it is a ligand field transition. The λ_{max} of the decay product shifted from 700 nm to 718 nm or 742 nm with the respective addition of 4-picoline or PyO either before or after the decomposition of **1**. These observed shifts of the $Fe^{IV}{=}O$ chromophore of **2** suggest that the added Lewis base occupies the sixth site on the $Fe^{IV}{=}O$ center (Scheme 1), displacing the presumed CH_3CN ligand for the species with a λ_{max} of 700 nm. The fact that PyO is known to serve as an oxo transfer agent for some oxidation catalysts[11] raises the question of whether such chemistry occurs in this system. This is in fact not the case for two reasons. First, the addition of PyO to $[Fe^{II}(TPA)(OTf)_2]$ does not elicit the near IR chromophore associated with **2**. Second, the addition of even only one equivalent of PyO promoted the conversion of **1** to **2** to afford a product with the same λ_{max} of 742 nm. If PyO transferred its oxygen atom to form **2**, then the sixth ligand on **2** would have to be pyridine and a λ_{max} of 718 nm should have been observed instead.



Scheme 1. Formation of $[Fe^{IV}(O)(TPA)(X)]$ (**2**) complexes from $[Fe^{II}(TPA)(CH_3CN)_2]^{2+}$.

Kinetic experiments were carried out to put a more quantitative basis on the conversion of **1** to **2** and gain insight into the dynamics of the O–O bond cleavage. The reactions, followed by measuring the absorbance decrease of the ligand-to-metal charge-transfer (LMCT) band of **1** at 593 nm (Figure 1b,c), all afforded a time profile indicating an exponential decay of [**1**]. A straight line was obtained in a plot of the reaction rate versus the initial concentration of **1** to establish a rate law of $-d[\mathbf{1}]/dt = k_{app}[\mathbf{1}]$ for all cases studied. A variation of 4-(dimethylamino)pyridine or PyO concentration revealed saturation behavior with K_{assoc} values of about $20\,M^{-1}$ for both additives (Figure 2). These results support the likely displacement of the CH_3CN ligand in **1** prior to its conversion to **2** (Scheme 1).

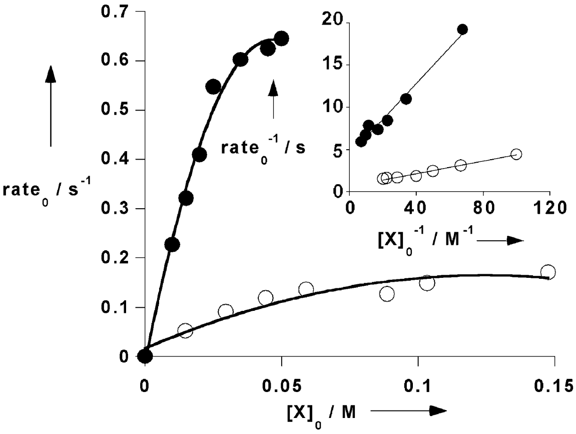


Figure 2. Initial rate of the decay of **1** as a function of [X] (X = PyO (●) or 4-$(CH_3)_2N$-C_5H_4N (○)) at −42 °C in CH_3CN. Inset: Plots of $rate_0^{-1}$ versus $[X]^{-1}$ by using the same points.

Analysis of the temperature dependence of the reaction rates (Table 1) afforded activation parameters at −40 °C of $\Delta H^{\ddagger} = 52(1)\,kJ\,mol^{-1}$ and $\Delta S^{\ddagger} = -74(3)\,J\,mol^{-1}\,K^{-1}$ for the decay of **1** in the absence of any additive and of $\Delta H^{\ddagger} = 50(2)\,kJ\,mol^{-1}$ and $\Delta S^{\ddagger} = -42(10)\,J\,mol\,K$ for its decay in the presence of 10 mM PyO. While the activation entropies differ somewhat, perhaps because of some component arising from the binding of PyO in the latter case, the activation enthalpies are nearly identical. These experimentally determined values in fact approach the enthalpy range estimated by Lehnert et al. ($60–80\,kJ\,mol^{-1}$) from DFT calculations for the homolytic cleavage of the O–O bond in $[Fe^{III}(TPA)(OOt\text{-}Bu)(OH)]^+$ along an O–O bond stretching trajectory.[12] These values are also comparable to the activation parameters for the homolysis of $[(TMP)Fe^{III}OOFe^{III}(TMP)]$[5] reported by Balch and co-workers ($\Delta H^{\ddagger} = 61\,kJ\,mol^{-1}$ and $\Delta S^{\ddagger} = -60\,J\,mol\,K$) to form $[Fe^{IV}(O)TMP]$,[13] but clearly distinct from those associated with the homolysis of $[(TMP)Fe^{III}OOC(O)R]$ in toluene ($\Delta H^{\ddagger} = 31(2)\,kJ\,mol^{-1}$ and $\Delta S^{\ddagger} = -161(7)\,J\,mol\,K$).[14]

Table 1: Activation parameters for homolytic O–O bond cleavage reactions of $Fe^{III}OOR$ complexes.

	$k_{-40°C}$ [s^{-1}]	$\Delta H^{\ddagger}$ [$kJ\,mol^{-1}$]	$\Delta S^{\ddagger}$ [$J\,mol^{-1}\,K^{-1}$]	
1[a]	1.25×10^{-3}	52(1)	−74(3)	This work.
1[a] + 10 equiv PyO	1.81×10^{-1}	50(2)	−42(10)	This work.
[(TMP)Fe-O-O-Fe(TMP)][b]		61	−60	[13]
[Fe(TMP)(O_3CR)][b]	2×10^{-3}	31(2)[c]	−161(7)[c]	[14]
[Fe(TMP)(O_3CR)][b] + 1-PhIm	3.3×10^{-3}	26(1)[c]	−180(5)[c]	[14]

[a] In CH_3CN. [b] In toluene. [c] Calculated from published data [14]. $\Delta H^{\ddagger}$ = enthalpy of activation; $\Delta S^{\ddagger}$ = entropy of activation.

The significant acceleration of the decomposition of **1** upon addition of pyridine or PyO reveals a significant push effect for the sixth ligand. As shown in Figure 3, linear Hammett correlations with ρ values of -0.78 and -1.22 are obtained respectively for a series of 4-substituted pyridines and pyridine *N*-oxides, demonstrating that electron-releasing groups enhance the decay of **1**. Such a push effect has been prominent in proposed mechanisms for oxygen activation by heme enzymes and emphasizes the role the proximal axial ligand can play in promoting O–O bond cleavage.[15] However in a systematic study of the decomposition of $[(TMP)Fe^{III}OOC(O)R]$ complexes, Morishima and co-workers found homolytic O–O bond cleavage to be enhanced by a factor of at most three upon the addition of imidazoles, but, surprisingly, somewhat retarded by electron-donating groups on the porphyrins.[14] Thus, the push effect we have observed for the decomposition of **2** is quite dramatic. This accelerative effect lends credence to the proposed mechanism for O–O bond homolysis proposed by Lehnert et al.[12] that involves electron donation from the Fe d_{xy} orbital to the O–O σ^* orbital. Thus donation of electron density to the low-spin iron(III) center by the ancillary sixth ligand in the plane perpendicular to the incipient Fe=O bond (designated as the z axis) promotes the cleavage of the O–O bond.

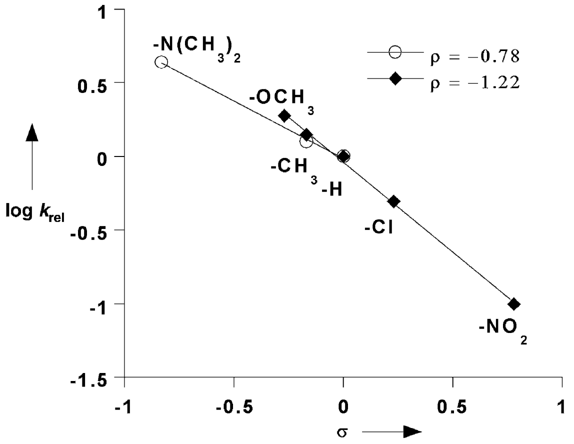


Figure 3. Substituent effects on the rate constants for homolytic O–O bond cleavage reactions of **1** in the presence of 4-substituted pyridine (○) and pyridine *N*-oxide additives (◆) in CH_3CN at −42 °C.

In conclusion, we have shown a significant push effect on homolysis of the FeO–OR bond in non-heme TPA complexes, unlike for heme complexes.[14] Addition of an exogenous Lewis base (Py or PyO) accelerates the decay of **2** by as much as two orders of magnitude, thus providing nucleophilic assistance to the rate-determining step. This push effect has allowed us to trap and observe $[Fe^{IV}(O)(TPA)]^{2+}$ intermediates previously proposed but unobserved in oxidation reactions of Fe(TPA) complexes with ROOH.[9]

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Keywords: high-valent species · iron · kinetics · oxo ligands · push effect

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[5] Abbreviations used: OTf, trifluoromethanesulfonate; 1-PhIm, 1-phenyl-imidazole; PyO, pyridine *N*-oxide; TMC, 1,4,8,11-tetramethylcyclam; TPA, tris(pyridyl-2-methyl)amine; $TMPH_2$, tetramesitylporphyrin.
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