

Metal Ion Effect on the Switch of Mechanism from Direct Oxygen Transfer to Metal Ion-Coupled Electron Transfer in the Sulfoxidation of Thioanisoles by a Non-Heme Iron(IV)–Oxo Complex

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S Supporting Information

ABSTRACT: The mechanism of sulfoxidation of thioanisoles by a non-heme iron(IV)–oxo complex is switched from direct oxygen transfer to metal ion-coupled electron transfer by the presence of Sc^{3+} . The switch in the sulfoxidation mechanism is dependent on the one-electron oxidation potentials of thioanisoles. The rate of sulfoxidation is accelerated as much as 10^2 -fold by the addition of Sc^{3+} .

Oxygen atom transfer (OAT) from high-valent metal–oxo species to organic or inorganic substrates is ubiquitous in biological and catalytic oxygenation processes.¹ Extensive efforts have been devoted to clarifying the mechanisms of OAT reactions of iron(IV)–oxo complexes bearing heme and non-heme ligands as chemical models of cytochromes P450 (CYP 450) and non-heme iron oxygenases, respectively.² In sulfoxidation reactions, two plausible mechanisms for the oxidation of sulfides by high-valent metal–oxo complexes have been proposed:^{3–5} direct oxygen transfer (DOT) and electron transfer followed by oxygen transfer (ETOT). As shown in Scheme 1, sulfoxide $[\text{ArS}(\text{O})\text{R}]$ is formed either by DOT from a metal–oxo species $[\text{M}^{n+}(\text{O})]$ to sulfide (ArSR) (i.e., DOT mechanism, pathway a) or by electron transfer from ArSR to $\text{M}^{n+}(\text{O})$ followed by OAT from $\text{M}^{(n-1)+}(\text{O})$ to the radical cation ($\text{ArSR}^{\bullet+}$) (i.e., ETOT mechanism, pathways b and c).

Although the mechanisms of the oxidation of sulfides by high-valent iron–oxo intermediates of CYP 450 and model compounds have been extensively investigated experimentally and theoretically,^{4,6} non-heme iron(IV)–oxo species have rarely been explored in the mechanistic studies of sulfoxidation reactions.⁷ We report herein the remarkable effects of a metal ion (i.e., Sc^{3+}) in accelerating the reaction rate and changing the mechanism from DOT to ETOT in the sulfoxidation of thioanisoles by a non-heme iron(IV)–oxo complex, $[(\text{N4Py})\text{Fe}^{\text{IV}}(\text{O})]^{2+}$ [$\text{N4Py} = N,N$ -bis(2-pyridylmethyl)- N -bis(2-pyridyl)methylamine].^{8–10} The role of the metal ion in the sulfoxidation reactions is discussed as well.

Sulfoxidation of para-substituted thioanisoles by $[(\text{N4Py})\text{Fe}^{\text{IV}}(\text{O})]^{2+}$ has been suggested to occur via an electrophilic reaction that quantitatively gives the corresponding methyl phenyl sulfoxides and an Fe^{II} complex as products.⁷ As shown in Figure 1a, the time course of the reaction of $[(\text{N4Py})\text{Fe}^{\text{IV}}(\text{O})]^{2+}$ with *p*-methylthioanisole was readily monitored by the decrease in the absorbance due to $[(\text{N4Py})\text{Fe}^{\text{IV}}(\text{O})]^{2+}$ ($\lambda_{\text{max}} = 695 \text{ nm}$).⁸ In the presence of $\text{Sc}(\text{OTf})_3$

Scheme 1

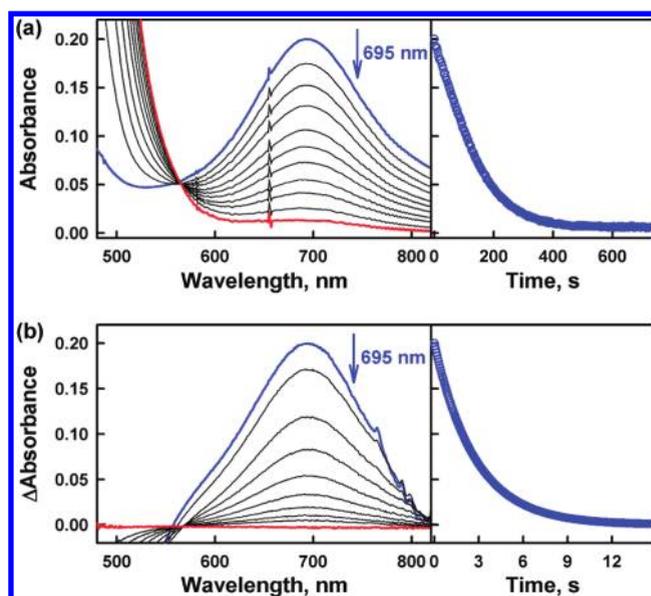
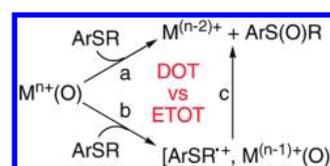


Figure 1. Changes in the visible spectrum observed in the reaction of $[(\text{N4Py})\text{Fe}^{\text{IV}}(\text{O})]^{2+}$ (0.50 mM) with *p*-methylthioanisole (5.0 mM) in the (a) absence and (b) presence of Sc^{3+} (10 mM) in CH_3CN at 298 K (left panels). The right panels show time courses monitored at 695 nm.

($\text{OTf} = \text{CF}_3\text{SO}_3^-$), the reaction was remarkably accelerated, and the time course was monitored using a stopped-flow spectrometer (Figure 1b).¹⁰ The rate obeyed pseudo-first-order kinetics [Figure S1 in the Supporting Information (SI)], and the pseudo-first-order rate constant increased linearly with increasing concentration of *p*-methylthioanisole (Figure S2). The second-order rate constant (k_{obs}) was obtained from the slope of the linear correlation between the

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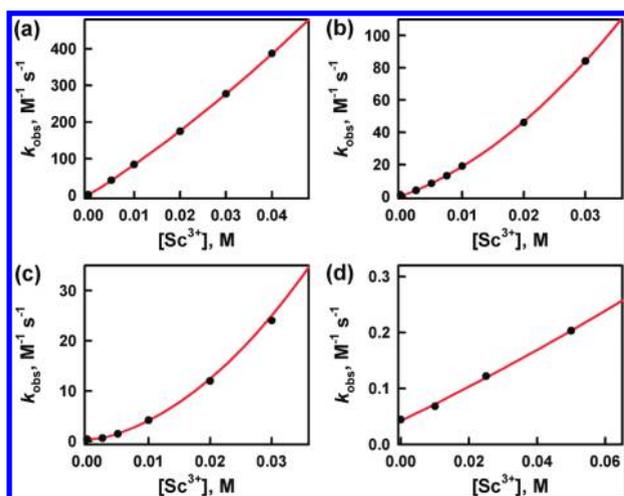


Figure 2. Plots of k_{obs} vs Sc^{3+} concentration in the oxidation of para-*X*-substituted thioanisoles [*X* = (a) Me, (b) H, (c) Cl, (d) CN] by $[(\text{N4Py})\text{Fe}^{\text{IV}}(\text{O})]^{2+}$ in MeCN at 298 K.

pseudo-first-order rate constant and the concentration of *p*-methylthioanisole.

The dependence of k_{obs} on $[\text{Sc}^{3+}]$ for the reaction of $[(\text{N4Py})\text{Fe}^{\text{IV}}(\text{O})]^{2+}$ with *p*-methylthioanisole is shown in Figure 2a. The k_{obs} value increased, exhibiting a first-order dependence on $[\text{Sc}^{3+}]$ at low concentrations and a second-order dependence at high concentrations (eq 1):

$$k_{\text{obs}} = k_0 + [\text{Sc}^{3+}](k_1 + k_2[\text{Sc}^{3+}]) \quad (1)$$

where k_0 is the rate constant for the sulfoxidation of a para-substituted thioanisole derivative by $[(\text{N4Py})\text{Fe}^{\text{IV}}(\text{O})]^{2+}$ (5.0×10^{-4} M) in the absence of Sc^{3+} . The k_1 and k_2 values were determined from the intercept and slope, respectively, of the linear plot of $(k_{\text{obs}} - k_0)/[\text{Sc}^{3+}]$ vs $[\text{Sc}^{3+}]$ (Figure S3). The k_{obs} value *p*-methylthioanisole in the presence of 10 mM Sc^{3+} was $8.4 \times 10 \text{ M}^{-1} \text{ s}^{-1}$, which is $\sim 10^2$ -fold larger than the value determined in the absence of Sc^{3+} . The dependence of the first- and second-order rate constants on the concentration of Sc^{3+} was reported previously for metal ion-coupled electron transfer from one-electron reductants to $[(\text{N4Py})\text{Fe}^{\text{IV}}(\text{O})]^{2+}$, and this was ascribed to binding of one Sc^{3+} ion and two Sc^{3+} ions to $[(\text{N4Py})\text{Fe}^{\text{IV}}(\text{O})]^{2+}$, respectively.^{11–14}

Similar remarkable acceleration effects of Sc^{3+} were observed in the reactions of $[(\text{N4Py})\text{Fe}^{\text{IV}}(\text{O})]^{2+}$ with para-*X*-substituted thioanisoles with *X* = H, Cl, and Br (Figure 2b,c and Figure S4). When a strongly electron-withdrawing substituent (*X* = CN, NO_2) was employed, however, only a small acceleration was observed, as shown for *X* = CN in Figure 2d (see Figure S4 for *X* = NO_2).

The reason that the acceleration effect of Sc^{3+} is quite different depending on the substituent *X* can be explained by plots of $\log k_{\text{obs}}$ versus the driving force for electron transfer from the thioanisole to $[(\text{N4Py})\text{Fe}^{\text{IV}}(\text{O})]^{2+}$ ($-\Delta G_{\text{et}}$) in the absence and presence of Sc^{3+} , as shown in Figure 3. The ΔG_{et} values were obtained from the difference between the one-electron oxidation potentials of the thioanisoles (E_{ox} vs SCE)^{4a} and the one-electron reduction potentials of $[(\text{N4Py})\text{Fe}^{\text{IV}}(\text{O})]^{2+}$ (E_{red} vs SCE) in the absence and presence of Sc^{3+} .^{11,15} It should be noted that the E_{ox} values of the thioanisoles did not change in the presence of Sc^{3+} , whereas the E_{red} value of $[(\text{N4Py})\text{Fe}^{\text{IV}}(\text{O})]^{2+}$ was significantly shifted in the positive direction from 0.51 V vs SCE in the absence of Sc^{3+} to 1.19 V vs SCE

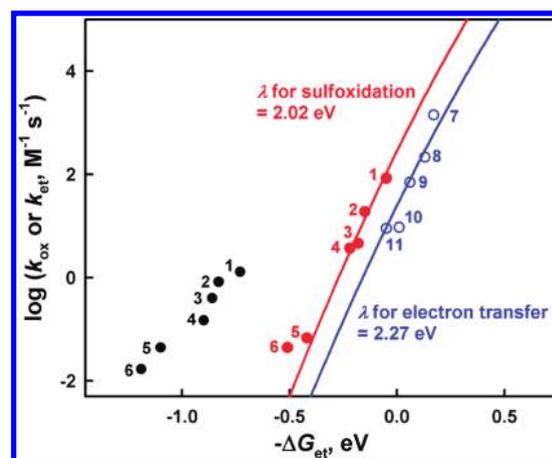


Figure 3. Plot of $\log k_{\text{obs}}$ for oxidation of para-*X*-substituted thioanisoles [*X* = (1) Me, (2) H, (3) Cl, (4) Br, (5) CN, (6) NO_2] by $[(\text{N4Py})\text{Fe}^{\text{IV}}(\text{O})]^{2+}$ in MeCN at 298 K vs the driving force for electron transfer $[-\Delta G_{\text{et}} = e(E_{\text{red}} - E_{\text{ox}})]$ from the thioanisoles to $[(\text{N4Py})\text{Fe}^{\text{IV}}(\text{O})]^{2+}$ in the absence of Sc^{3+} (black ●) and the presence of 10 mM Sc^{3+} (red ●). The blue ○ show the driving-force dependence of the rate constants ($\log k_{\text{et}}$) for electron transfer to $[(\text{N4Py})\text{Fe}^{\text{IV}}(\text{O})]^{2+}$ from the one-electron reductants (7) $[\text{Fe}^{\text{II}}(\text{Ph}_2\text{-Phen})_3]^{2+}$, (8) $[\text{Fe}^{\text{II}}(\text{bpy})_3]^{2+}$, (9) $[\text{Ru}^{\text{II}}(\text{Me}_2\text{-bpy})_3]^{2+}$, (10) $[\text{Fe}^{\text{II}}(\text{Cl-phen})_3]^{2+}$, and (11) $[\text{Ru}^{\text{II}}(\text{bpy})_3]^{2+}$ in the presence of Sc^{3+} (10 mM) in MeCN at 298 K.

in the presence of 10 mM Sc^{3+} .^{11,15a} In the absence of Sc^{3+} , $-\Delta G_{\text{et}}$ is largely negative. This indicates that electron transfer from the thioanisoles to $[(\text{N4Py})\text{Fe}^{\text{IV}}(\text{O})]^{2+}$ is highly endergonic and therefore quite unlikely to occur. In such a case, the DOT pathway (Scheme 1a) predominates over the ETOT pathway (Scheme 1b,c), and the k_{obs} values are only slightly dependent on the $-\Delta G_{\text{et}}$ values.

In contrast, the $\log k_{\text{obs}}$ values obtained in the presence of Sc^{3+} increased remarkably with increasing $-\Delta G_{\text{et}}$. In the case of *p*-methylthioanisole, the free-energy change for electron transfer becomes negative. In such a case, the ETOT pathway (Scheme 1b,c) becomes dominant over the DOT pathway (Scheme 1a). The dependence of $\log k_{\text{obs}}$ on the driving force for electron transfer ($-\Delta G_{\text{et}}$) in the presence of Sc^{3+} (red line in Figure 3) is remarkably parallel to that of $\log k_{\text{et}}$ for actual electron transfer from one-electron reductants to $[(\text{N4Py})\text{Fe}^{\text{IV}}(\text{O})]^{2+}$ (blue line in Figure 3). The driving-force dependence of both the rate constants for sulfoxidation of thioanisoles by $[(\text{N4Py})\text{Fe}^{\text{IV}}(\text{O})]^{2+}$ and electron transfer from one-electron reductants to $[(\text{N4Py})\text{Fe}^{\text{IV}}(\text{O})]^{2+}$ in the presence of 10 mM Sc^{3+} was well-fitted in light of the Marcus theory of adiabatic outer-sphere electron transfer (eq 2):

$$k_{\text{et}} = Z \exp \left[-\frac{\lambda (1 + \Delta G_{\text{et}}/\lambda)^2}{4 k_{\text{B}} T} \right] \quad (2)$$

where Z is the collision frequency (taken as $1 \times 10^{11} \text{ M}^{-1} \text{ s}^{-1}$), λ is the reorganization energy for electron transfer, k_{B} is the Boltzmann constant, and T is the absolute temperature.^{15,16} The best-fit λ value for electron transfer in sulfoxidation of thioanisoles was determined to be 2.02 eV, which agrees reasonably well with the λ value for electron transfer from one-electron reductants (2.27 eV).¹⁷ Such an agreement with the Marcus equation indicates that the sulfoxidation of thioanisoles by $[(\text{N4Py})\text{Fe}^{\text{IV}}(\text{O})]^{2+}$ in the presence of Sc^{3+} proceeds via Sc^{3+} ion-coupled electron transfer from thioanisoles to $[(\text{N4Py})\text{Fe}^{\text{IV}}(\text{O})]^{2+}$, which is the rate-determining step, followed

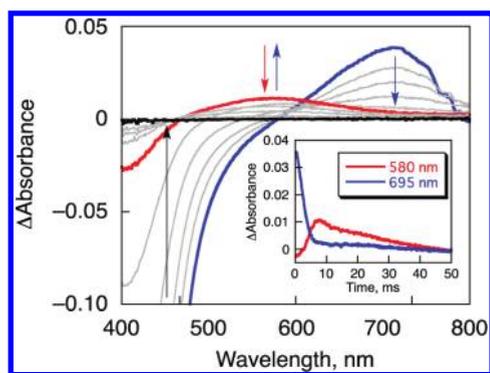


Figure 4. Difference UV-vis spectral changes in the reaction of $[(\text{N4Py})\text{Fe}^{\text{IV}}(\text{O})]^{2+}$ (1.0×10^{-4} M) with *p*-methoxythioanisole (4.0×10^{-3} M) in the presence of Sc^{3+} (4.0×10^{-3} M) in MeCN at 298 K. The inset shows the time courses monitored at 580 nm for *p*-methoxythioanisole radical cation and 695 nm for $[(\text{N4Py})\text{Fe}^{\text{IV}}(\text{O})]^{2+}$.

by rapid OAT from $[(\text{N4Py})\text{Fe}^{\text{III}}(\text{O})]^{+}$ to the radical cation ($\text{ArSR}^{+\bullet}$), as described in Scheme 1b,c.

When the ΔG_{et} value becomes more negative than 0.4 eV, the k_{et} value becomes smaller than the k_{obs} value for DOT. Thus, the borderline between the DOT pathway (Scheme 1a) and the ETOT pathway (Scheme 1b,c) may be determined by the E_{ox} value of the para-*X*-substituted thioanisole, ~ 1.6 V vs SCE, that corresponds to *p*-cyanothioanisole.

The occurrence of electron transfer is clearly shown in the case of *p*-methoxythioanisole in the presence of Sc^{3+} (4 mM), where the driving force for electron transfer is positive ($-\Delta G_{\text{et}} = 0.01$ eV). As shown in Figure 4, the transient absorption band at 580 nm due to *p*-methoxythioanisole radical cation appears, accompanied by a decrease in the absorption band at 695 nm due to $[(\text{N4Py})\text{Fe}^{\text{IV}}(\text{O})]^{2+}$ (for the reference spectrum of *p*-methoxyanisole radical cation, see Figure S5).¹⁸ This result clearly demonstrates that the ETOT pathway becomes dominant over the DOT pathway when the sulfoxidation by the iron(IV)-oxo complex is carried out in the presence of a metal ion (Scheme 1).

In summary, we have demonstrated that Sc^{3+} ion promotes sulfoxidation of thioanisoles significantly via Sc^{3+} ion-coupled electron transfer and that the borderline between a direct oxygen atom transfer pathway (Scheme 1a) and an electron-transfer pathway (Scheme 1b,c) is determined by the E_{ox} value of thioanisole that is ~ 1.6 V vs SCE. Thus, the present study provides a new and rational way to enhance the reactivity of high-valent metal-oxo species by binding of redox-inactive metal ions such as Sc^{3+} . The generality of this idea is under investigation.

■ ASSOCIATED CONTENT

S Supporting Information. Experimental details, second-order rate constants (Table S1), pseudo-first-order kinetics (Figure S1), second-order kinetics (Figures S2), the linear plot of $(k_{\text{obs}} - k_0)/[\text{Sc}^{3+}]$ vs $[\text{Sc}^{3+}]$ (Figure S3), the dependence of k_{obs} on $[\text{Sc}^{3+}]$ for other substrates (Figure S4), and UV-vis spectra for *p*-MeO-PhSMe⁺ (Figure S5). This material is available free of charge via the Internet at <http://pubs.acs.org>.

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