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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*

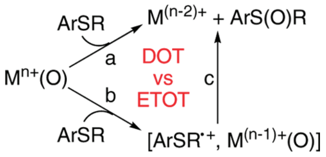
ABSTRACT: The mechanism of sulfoxidation of thioaniosoles by a non-heme iron(IV)−oxo complex is switched from direct oxygen transfer to metal ion-coupled electron transfer by the presence of Sc^{3+}. The switch in the sulfoxidation mechanism is dependent on the one-electron oxidation potentials of thioanisoles. 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 [ArS(O)R] is formed either by DOT from a metal−oxo species [M^{n+}(O)] to sulfide (ArSR) (i.e., DOT mechanism, pathway a) or by electron transfer from ArSR to M^{n+}(O) followed by OAT from $M^{(n-1)+}$(O) to the radical cation ($ArSR^{\bullet+}$) (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, $[(N4Py)Fe^{IV}(O)]^{2+}$ [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.

Sulfoxidaton of para-substituted thioanisoles by $[(N4Py)Fe^{IV}(O)]^{2+}$ 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 $[(N4Py)Fe^{IV}(O)]^{2+}$ with *p*-methylthioanisole was readily monitored by the decrease in the absorbance due to $[(N4Py)Fe^{IV}(O)]^{2+}$ (λ_{max} = 695 nm).[8] In the presence of $Sc(OTf)_3$ (OTf = $CF_3SO_3^-$), 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

Scheme 1



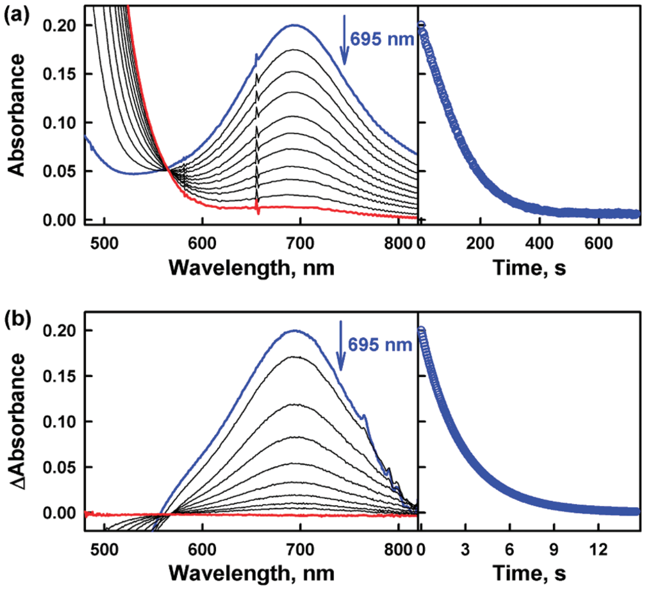


Figure 1. Changes in the visible spectrum observed in the reaction of $[(N4Py)Fe^{IV}(O)]^{2+}$ (0.50 mM) with *p*-methylthioanisole (5.0 mM) in the (a) absence and (b) presence of Sc^{3+} (10 mM) in CH_3CN at 298 K (left panels). The right panels show time courses monitored at 695 nm.

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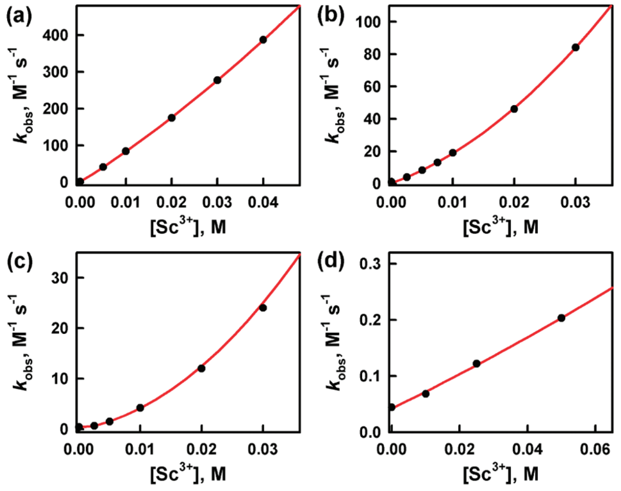

Figure 2. Plots of k_{obs} vs Sc^{3+} concentration in the oxidation of para-X-substituted thioanisoles [X = (a) Me, (b) H, (c) Cl, (d) CN] by $[(N4Py)Fe^{IV}(O)]^{2+}$ in MeCN at 298 K.

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

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

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

where k_0 is the rate constant for the sulfoxidation of a para-substituted thioanisole derivative by $[(N4Py)Fe^{IV}(O)]^{2+}$ (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 $(k_{obs} - k_0)$/$[Sc^{3+}]$ vs $[Sc^{3+}]$ (Figure S3). The k_{obs} value *p*-methylthioanisole in the presence of 10 mM Sc^{3+} was 8.4×10 M^{-1} 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 $[(N4Py)Fe^{IV}(O)]^{2+}$, and this was ascribed to binding of one Sc^{3+} ion and two Sc^{3+} ions to $[(N4Py)Fe^{IV}(O)]^{2+}$, respectively.[11−14]

Similar remarkable acceleration effects of Sc^{3+} were observed in the reactions of $[(N4Py)Fe^{IV}(O)]^{2+}$ 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_{obs} versus the driving force for electron transfer from the thioanisole to $[(N4Py)Fe^{IV}(O)]^{2+}$ ($-\Delta G_{et}$) 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 $[(N4Py)Fe^{IV}(O)]^{2+}$ (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 $[(N4Py)Fe^{IV}(O)]^{2+}$ 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 in the presence of 10 mM Sc^{3+}.[11,15a] In the absence of Sc^{3+}, $-\Delta G_{et}$ is largely negative. This indicates that electron transfer from the thioanisoles to $[(N4Py)Fe^{IV}(O)]^{2+}$ 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 $-\Delta G_{et}$ values.

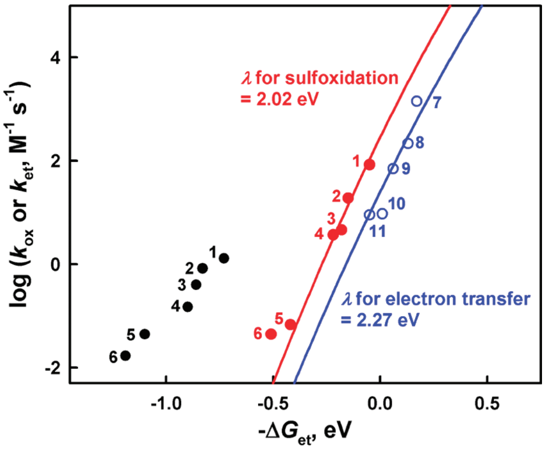

Figure 3. Plot of log k_{obs} for oxidation of para-X-substituted thioanisoles [X = (1) Me, (2) H, (3) Cl, (4) Br, (5) CN, (6) NO_2] by $[(N4Py)Fe^{IV}(O)]^{2+}$ in MeCN at 298 K vs the driving force for electron transfer [$-\Delta G_{et} = e(E_{red} - E_{ox})$] from the thioanisoles to $[(N4Py)Fe^{IV}(O)]^{2+}$ 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_{et}) for electron transfer to $[(N4Py)Fe^{IV}(O)]^{2+}$ from the one-electron reductants (7) $[Fe^{II}(Ph_2\text{-}Phen)_3]^{2+}$, (8) $[Fe^{II}(bpy)_3]^{2+}$, (9) $[Ru^{II}(Me_2\text{-}bpy)_3]^{2+}$, (10) $[Fe^{II}(Cl\text{-}phen)_3]^{2+}$, and (11) $[Ru^{II}(bpy)_3]^{2+}$) in the presence of Sc^{3+} (10 mM) in MeCN at 298 K.

In contrast, the log k_{obs} values obtained in the presence of Sc^{3+} increased remarkably with increasing $-\Delta G_{et}$. 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_{obs} on the driving force for electron transfer ($-\Delta G_{et}$) in the presence of Sc^{3+} (red line in Figure 3) is remarkably parallel to that of log k_{et} for actual electron transfer from one-electron reductants to $[(N4Py)Fe^{IV}(O)]^{2+}$ (blue line in Figure 3). The driving-force dependence of both the rate constants for sulfoxidation of thioanisoles by $[(N4Py)Fe^{IV}(O)]^{2+}$ and electron transfer from one-electron reductants to $[(N4Py)Fe^{IV}(O)]^{2+}$ 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):

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

where Z is the collision frequency (taken as 1×10^{11} M^{-1} 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 $[(N4Py)Fe^{IV}(O)]^{2+}$ in the presence of Sc^{3+} proceeds via Sc^{3+} ion-coupled electron transfer from thioanisoles to $[(N4Py)Fe^{IV}(O)]^{2+}$, which is the rate-determining step, followed

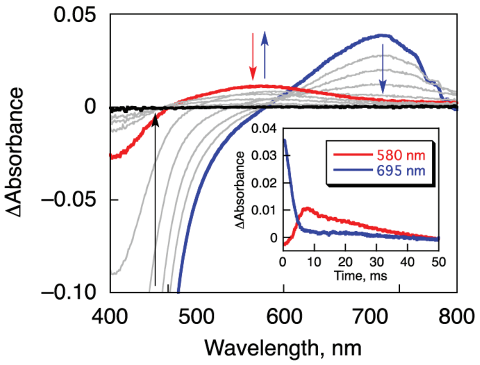

Figure 4. Difference UV−vis spectral changes in the reaction of $[(N4Py)Fe^{IV}(O)]^{2+}$ (1.0×10^{-4} M) with *p*-methoxythioanisole (4.0×10^{-3} M) in the presence of Sc^{3+} (4.0×10^{-3} M) in MeCN at 298 K. The inset shows the time courses monitored at 580 nm for *p*-methoxythioanisole radical cation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

by rapid OAT from $[(N4Py)Fe^{III}(O)]^{+}$ to the radical cation ($ArSR^{\bullet +}$), 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 ($-\Delta G_{et} = 0.01$ 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 $[(N4Py)Fe^{IV}(O)]^{2+}$ (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

Ⓢ 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 $(k_{obs} - k_0)/[Sc^{3+}]$ vs $[Sc^{3+}]$ (Figure S3), the dependence of k_{obs} on $[Sc^{3+}]$ for other substrates (Figure S4), and UV−vis spectra for *p*-MeO-PhSMe$^{\bullet +}$ (Figure S5). This material is available free of charge via the Internet at http://pubs.acs.org.

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