Enzyme Models

Oxygen-Atom Transfer between Mononuclear Nonheme Iron(IV)–Oxo and Iron(II) Complexes**

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High-valent iron(IV)–oxo species have been implicated as the key reactive intermediates in the catalytic oxidation of organic substrates by mononuclear nonheme iron enzymes and their model compounds.[1] Recently, such nonheme iron(IV)–oxo species were observed directly in enzymatic and biomimetic reactions.[2–5] For example, an intermediate with a high-spin iron(IV)–oxo unit was identified and proposed as an active oxidant in the catalytic cycle of

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E. coli taurine, namely in α-ketoglutarate dioxygenase (TauD).[2,3] In biomimetic studies, mononuclear nonheme iron(IV)–oxo complexes bearing tetradentate N4 and pentadentate N5 ligands were synthesized and characterized by various spectroscopic techniques including X-ray crystallography.[4,5] The iron(IV)–oxo species have shown reactivities in a variety of oxidation reactions such as alkane hydroxylation,[4c,5b,c] olefin epoxidation,[4b,5b,c] alcohol oxidation,[4h] and the oxidation of sulfides,[4e,i] dihydroanthracene,[4f,k] and PPh3.[4a,e,j,5c]
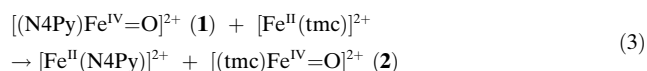
Very recently, Golubkov and Gross reported the transfer of a nitrogen atom between manganese complexes of salen (*N*,*N*′-bis(salicylidene)ethylenediamine dianion), porphyrin, and corrole ligands.[6] Prior to this work, intermetal transfer of a nitrogen atom was well documented in metalloporphyrin (M = Mn and Cr) reactions.[7] In addition to the transfer of nitrogen atoms, the transfer of oxygen atoms between high-valent metal-oxo and metal complexes has also been demonstrated.[7,8] In the case of iron porphyrins, the reaction of iron(IV)–oxo and iron(II) porphyrins resulted in the generation of μ-oxo-bridged iron(III) porphyrin dimers (that is, incomplete intermetal transfer of an oxygen atom) [Eq. (1),

$$[(Porp)Fe^{IV}=O] + [Fe^{II}(Porp)] \rightarrow [(Porp)Fe^{III}\text{-}O\text{-}Fe^{III}(Porp)] \quad (1)$$
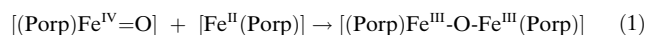
Porp = porphyrin].[7a,9] Although the oxidation of organic substrates by nonheme iron(IV)–oxo complexes has been demonstrated recently, the intermetal transfer of oxygen atoms between nonheme iron complexes has never been explored previously. Herein, we report that in contrast to iron porphyrins,[9] nonheme iron(IV)–oxo complexes transfer their oxygen atom to iron(II) complexes, thus affording the corresponding iron(II) and iron(IV)–oxo complexes (that is, complete intermetal transfer of an oxygen atom occurs)[7a] [Eq. (2)].

$$[(L_1)Fe^{IV}=O]^{2+} + [Fe^{II}(L_2)]^{2+}$$
$$\rightarrow [Fe^{II}(L_1)]^{2+} + [(L_2)Fe^{IV}=O]^{2+} \quad (2)$$
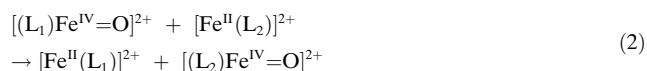
The oxygen-atom transfer reactions were carried out by adding nonheme iron(II) complexes to in situ generated nonheme iron(IV)–oxo complexes in CH3CN at 25°C. The addition of [Fe^II(tmc)]^{2+} to the solution of [(N4Py)Fe^IV=O]^{2+} (**1**) afforded changes in the absorption spectra which are consistent with the transfer of an oxygen atom from **1** (λ_{max} at 695 nm) to [Fe^II(tmc)]^{2+} [Eq. (3)], thereby producing

$$[(N4Py)Fe^{IV}=O]^{2+} (\mathbf{1}) + [Fe^{II}(tmc)]^{2+}$$
$$\rightarrow [Fe^{II}(N4Py)]^{2+} + [(tmc)Fe^{IV}=O]^{2+} (\mathbf{2}) \quad (3)$$

[(tmc)Fe^IV=O]^{2+} (**2**; λ_{max} at 820 nm) and [Fe^II(N4Py)]^{2+} (λ_{max} at 450 nm; Figure 1; see the Supporting Information for nonheme ligand structures).[10] Well-defined isosbestic points were observed at 570 and 790 nm. The reaction was complete within 20 minutes, and an increase in the concentration of the reactants diminished the reaction time (data not shown). The latter results indicate the reaction to be first order in each of the reactants. In contrast, the intermediate **2** remained intact upon addition of [Fe(N4Py)]^{2+}, thus indicating that the
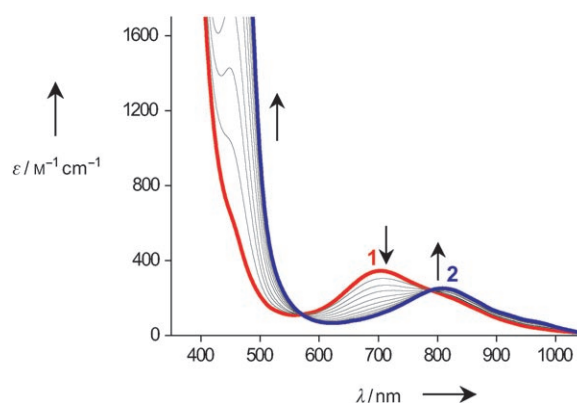
Figure 1. UV/Vis spectral changes showing the formation of **2** (blue) upon addition of 4 equiv [Fe(tmc)(CF3SO3)2] (2 mM, diluted in 50 μL CH3CN) to the solution of [(N4Py)Fe^IV=O]^{2+} (**1**, 0.5 mM; red) in CH3CN (2 mL) at 25°C.

transfer of an oxygen atom from **2** to [Fe(N4Py)]^{2+} does not occur [namely, the reverse reaction of Eq. (3) does not occur].

The transfer of an oxygen atom between nonheme iron complexes was also evidenced by changes in the electrospray ionization mass spectra of the reaction solution recorded at different times (Figure 2). Mixing equimolar amounts of [Fe(tmc)]^{2+} and **1**-^{18}O resulted in a decrease in the signals corresponding to [Fe(tmc)]^{2+} (m/z 461) and **1**-^{18}O (m/z 590) with a concomitant increase in the signals corresponding to **2**-^{18}O (m/z 479) and [Fe(N4Py)]^{2+} (m/z 572). Such mass spectral
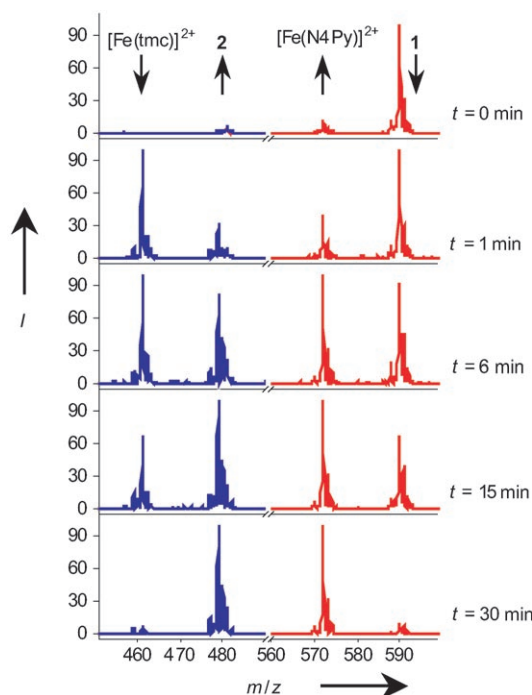
Figure 2. Changes in the electrospray ionization mass spectra in the reactants [Fe^II(tmc)(CF3SO3)]^+ (m/z 461) and [Fe^IV(N4Py)(^{18}O)-(CF3SO3)]^+ (**1**-^{18}O; m/z 590) as well as the products [Fe^IV(tmc)(^{18}O)-(CF3SO3)]^+ (**2**-^{18}O; m/z 479) and [Fe^II(N4Py)(CF3SO3)]^+ (m/z 572) in the reaction of equimolar amounts of [Fe^II(tmc)]^{2+} (0.5 mM) and [(N4Py)Fe^IV=O]^{2+} (**1**; 0.5 mM) in CH3CN at 25°C.
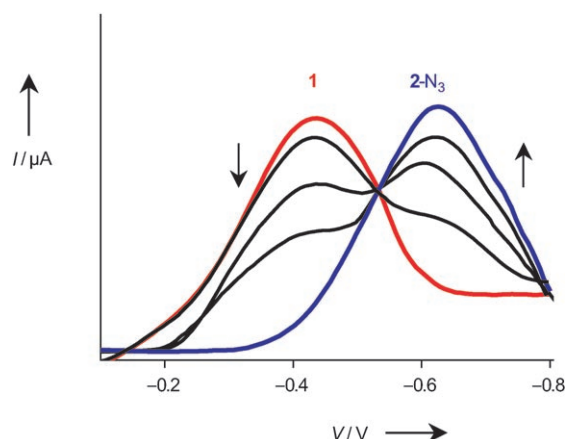
changes strongly demonstrate the transfer of an oxygen atom from **1** to $[Fe(tmc)]^{2+}$ which results in the formation of $[Fe(N4Py)]^{2+}$ and **2** [Eq. (3)]. Furthermore, the observation of the ^{18}O transfer from **1** to **2** indicates that molecular oxygen was not involved in the oxygen atom transfer reaction.

Further evidence for the transfer of an oxygen atom was obtained by electrochemical methods. First, cyclic and differential pulse voltammograms (CV and DPV) of nonheme iron(II) complexes $[Fe(N4Py)]^{2+}$ and $[Fe^{II}(tmc)(N_3)]^+$ as well as their iron(IV)–oxo complexes **1** and $[Fe^{IV}(tmc)(O)(N_3)]^+$ (**2**-N_3) were recorded. The $[Fe(N4Py)]^{2+}$ and $[Fe^{II}(tmc)(N_3)]^+$ complexes exhibit reversible and quasireversible redox waves for the Fe^{III}/Fe^{II} couple at $+0.64$ and $+0.35$ V, respectively (see the Supporting Information). We then attempted to identify voltammetric responses corresponding to the iron(IV)–oxo species, by carrying out titration experiments by adding different amounts of PhIO to solutions of the iron(II) complexes. Incremental addition of PhIO to the solution of $[Fe^{II}(tmc)(N_3)]^+$ resulted in a decrease in an oxidation peak at $+0.35$ V for the $[Fe^{III}(tmc)(N_3)]^{2+}/[Fe^{II}(tmc)(N_3)]^+$ couple with a proportionate increase in a new reduction peak at -0.63 V (Figure 3a). The new reduction peak is irreversible in nature, and the increase in the peak current was proportional to the amount of **2**-N_3 formed in the reaction of $[Fe^{II}(tmc)(N_3)]^+$ and PhIO (see UV/Vis spectral data in Figure 3b).[4j] Furthermore, the addition of PPh_3 to the solution of **2**-N_3 resulted in the reduction peak at -0.63 V

disappearing and the regeneration of the redox wave at $+0.35$ V which corresponds to the $[Fe^{III}(tmc)(N_3)]^{2+}/[Fe^{II}(tmc)(N_3)]^+$ couple (data not shown); the disappearance of **2**-N_3 is the result of the oxygenation of PPh_3.[4j] On the basis of the results described above, we conclude that the irreversible wave at -0.63 V results from the reduction of **2**-N_3.[11–13] Similarly, we found that the reduction peak of **1** appears at -0.44 V (see the Supporting Information for the CV and DPV traces of **1** and **2**-N_3).[13] The transfer of an oxygen atom from **1** to $[Fe^{II}(tmc)(N_3)]^+$ was followed by monitoring the changes in the DPV trace of the reactant (**1**) and the product (**2**-N_3) in the reaction solution [Eq. (3)]. Addition of $[Fe^{II}(tmc)(N_3)]^+$ to the solution of **1** resulted in the peak current at -0.44 V corresponding to **1** disappearing gradually, whereas the reduction peak current at -0.63 V corresponding to **2**-N_3 increased (Figure 4). The decrease and increase in the peak
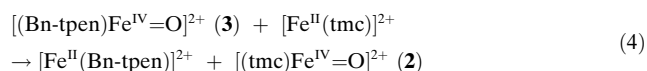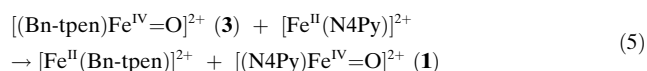
Figure 4. Differential pulse voltammograms of **1** (red) and **2**-N_3 (blue) upon addition of $[Fe^{II}(tmc)(N_3)]^+$ (1 mM) to a reaction solution containing **1** (1 mM) and nBu_4NPF_6 (0.1 M) in CH_3CN at 25°C.

currents of **1** and **2**-N_3, respectively, demonstrate again that the oxo group of **1** was transferred to $[Fe^{II}(tmc)(N_3)]^+$, thus giving rise to the formation of **2**-N_3.

The transfer of an oxygen atom was also examined between $[(Bn\text{-}tpen)Fe^{IV}=O]^{2+}$ (**3**)[10] and $[Fe^{II}(tmc)]^{2+}$ as well as between **3** and $[Fe^{II}(N4Py)]^{2+}$. Addition of $[Fe^{II}(tmc)]^{2+}$ (2.0 mM) to the solution of **3** (0.5 mM) in CH_3CN at 25°C resulted in changes in the electronic absorption spectra, namely the disappearance of **3** and the formation of **2** [Eq. (4)] (data not shown). Addition of $[Fe^{II}(N4Py)]^{2+}$ to the

$$[(Bn\text{-}tpen)Fe^{IV}=O]^{2+} \text{ (3)} + [Fe^{II}(tmc)]^{2+}$$
$$\rightarrow [Fe^{II}(Bn\text{-}tpen)]^{2+} + [(tmc)Fe^{IV}=O]^{2+} \text{ (2)} \qquad (4)$$

solution of **3** resulted in the disappearance of **3** and the concomitant formation of **1** in the electronic absorption and ESI mass spectra [Eq. (5); see the Supporting Information].

$$[(Bn\text{-}tpen)Fe^{IV}=O]^{2+} \text{ (3)} + [Fe^{II}(N4Py)]^{2+}$$
$$\rightarrow [Fe^{II}(Bn\text{-}tpen)]^{2+} + [(N4Py)Fe^{IV}=O]^{2+} \text{ (1)} \qquad (5)$$

In contrast, the reverse reactions such as the transfer of an oxygen atom from **2** to $[Fe^{II}(Bn\text{-}tpen)]^{2+}$ and from **1** to

Figure 3. a) Cyclic voltammograms and b) UV/Vis spectral changes for the conversion of $[Fe^{II}(tmc)(N_3)]^+$ into $[Fe^{IV}(tmc)(N_3)(O)]^+$ (**2**-N_3) upon addition of different amounts of PhIO. Reaction conditions: PhIO (black, 0 equiv; red, 0.4 equiv; green, 0.8 equiv; blue, 1.2 equiv) was added to a reaction solution containing $[Fe^{II}(tmc)(N_3)]^+$ (1 mM) and tetrabutylammonium hexafluorophosphate (nBu_4NPF_6, 0.1 M) in CH_3CN at 25°C.

[Fe^{II}(Bn-tpen)]$^{2+}$ did not take place [that is, the reverse reactions of Eqs. (4) and (5)]. The transfer of an oxygen atom was not observed between **2**-X (X = CH$_3$CN and N$_3^-$) and [Fe^{II}(tmc)(X)]. The latter results may be ascribed to the fact that the accessibility of an iron(II) ion toward an iron(IV)–oxo group is not favorable because of a steric interaction between the tmc ligands of the iron complexes.[4a,g]

In conclusion, we have reported the first example of the transfer of an oxygen atom between mononuclear nonheme iron complexes. The transfer of an oxygen atom from iron(IV)–oxo to iron(II) complexes was clearly evidenced by spectrophotometric, ESI mass spectrometric, and voltammetric techniques. The results (summarized in Scheme 1)
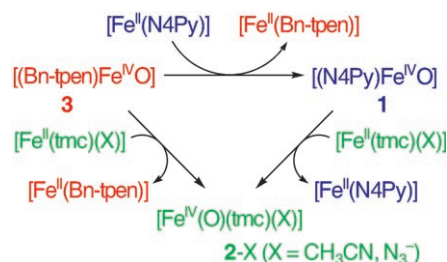
Scheme 1. Summary of the transfer of an oxygen atom between nonheme iron(IV)–oxo and iron(II) complexes.

show that the transfer of the oxygen atom was dependent on the oxidizing power of the iron(IV)–oxo complexes; the oxidizing power of iron(IV)–oxo complexes was determined to be in the order **3** > **1** > **2** in the oxidation of organic substrates.[4c,h,j] Detailed investigations of mechanistic aspects (e.g., complete transfer of an oxygen atom in nonheme iron models versus incomplete transfer in iron porphyrins)[8,9] and kinetic parameters of the transfer from nonheme iron(IV)–oxo to iron(II) complexes are currently underway.

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[10] Abbreviations used: tmc 1,4,8,11-tetramethyl-1,4,8,11-tetraazacyclotetradecane; N4Py *N,N*-bis(2-pyridylmethyl)-*N*-bis(2-pyridyl)methylamine; Bn-tpen *N*-benzyl-*N,N′,N′*-tris(2-pyridylmethyl)ethane-1,2-diamine.

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[13] We only observed the reduction of the iron(IV)–oxo complexes and did not identify the products and reaction pathways during the electrochemical reduction. Detailed electrochemical studies of mononuclear nonheme iron(IV)–oxo species are underway and will be presented elsewhere.