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Reactivities of Mononuclear Non-Heme Iron Intermediates Including Evidence that Iron(III)−Hydroperoxo Species Is a Sluggish Oxidant

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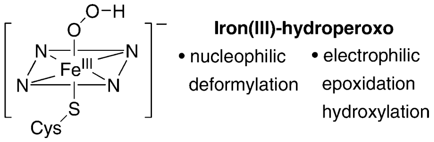
Abstract: There is an intriguing, current controversy on the involvement of iron(III)−hydroperoxo species as a "second electrophilic oxidant" in oxygenation reactions by heme and non-heme iron enzymes and their model compounds. In the present work, we have performed reactivity studies of the iron−hydroperoxo species in nucleophilic and electrophilic reactions, with in situ-generated mononuclear non-heme iron(III)−hydroperoxo complexes that have been well characterized with various spectroscopic techniques. The intermediates did not show any reactivities in the nucleophilic (e.g., aldehyde deformylation) and electrophilic (e.g., oxidation of sulfide and olefin) reactions. These results demonstrate that non-heme iron(III)−hydroperoxo species are sluggish oxidants and that the oxidizing power of the intermediates cannot compete with that of high-valent iron(IV)−oxo complexes. We have also reported reactivities of mononuclear non-heme iron(III)−peroxo and iron(IV)−oxo complexes in the aldehyde deformylation and the oxidation of sulfides, respectively.

Introduction

Elucidation of the nature of reactive intermediates in the catalytic oxygenation of hydrocarbons by heme and non-heme iron enzymes has remained of continuing interest to the bioinorganic chemistry community.[1,2] In heme iron enzymes and iron porphyrin models, high-valent iron(IV)−oxo porphyrin π-cation radicals, the so-called Compound I, have been proposed as active oxidants that effect the oxygenation reactions. However, recent studies have provided experimental evidence that multiple oxidants are involved in the catalytic oxygenation reactions and that the mechanism of oxygen atom transfer is much more complex than initially believed.[3] Especially, an iron(III)−hydroperoxo species, Fe^{III}−OOH, has been proposed as a "second electrophilic oxidant" in a variety of oxygenation reactions including alkane hydroxylation and olefin epoxidation (Scheme 1),[3,4] but direct evidence for such reactions has yet to be obtained.

Scheme 1. Iron(III)−Hydroperoxo Porphyrin Intermediate in Cytochrome P450-Catalyzed Reactions[4b]



The multiple oxidants hypothesis has also been invoked in non-heme iron complex-catalyzed oxidation reactions.[5] For example, the formation of different products in olefin oxidation by non-heme iron complexes and H_2O_2 has been interpreted with the involvement of two distinct oxidants (i.e., a predominant epoxide formation by Fe^{III}−OOH and a mixture of epoxide and *cis*-diol formation by HO−Fe^{V}═O).[6] In addition, a low-spin Fe^{III}−OOH species has been characterized for "activated bleomycin", which is the last detectable intermediate in the reaction cycle of bleomycin and a plausible oxidant responsible for DNA cleavage.[7] The iron−hydroperoxo species have also been often proposed as reactive intermediates in the oxygenation of olefins and alkanes by non-heme iron catalysts and H_2O_2.[8]

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Table 1. Mononuclear Non-Heme Iron Intermediates Used in Reactivity Studies[a]

L	$[(\mathrm{L})\mathrm{Fe^{III}}{-}\mathrm{O_2}]^{+}$	$[(\mathrm{L})\mathrm{Fe^{III}}{-}\mathrm{OOH}]^{2+}$	$[(\mathrm{L})\mathrm{Fe^{IV}}{=}\mathrm{O}]^{2+}$
N4Py	O (**1**)	O (**4**)	O (**7**)
Bn-TPEN	O (**2**)	O (**5**)	O (**8**)
TMC	O (**3**)	X	O (**9**)
TPA	X	O (**6**)	O (**10**)

[a] The circled (O) intermediates that have been spectroscopically characterized previously were used in the present reactivity studies, whereas the crossed (X) intermediates have not been identified yet.

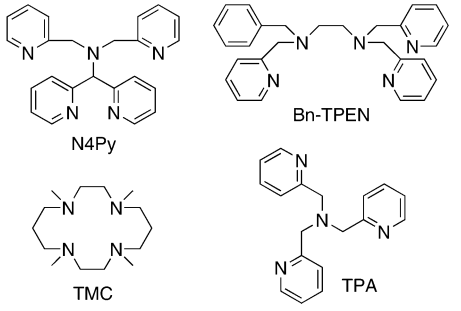


Figure 1. Ligand structures of iron(II) complexes used in generating mononuclear non-heme iron intermediates.

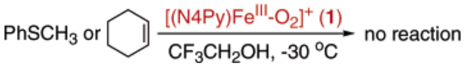
However, there is no direct evidence that such $\mathrm{Fe^{III}}{-}\mathrm{OOH}$ species are indeed involved in the oxidative DNA cleavage reaction and the oxygenation of hydrocarbons. Since the participation of iron(III)−hydroperoxo intermediates in oxygen-atom transfer reactions has been proposed mainly on the basis of product analyses of catalytic reactions, we have investigated reactivities of in situ-generated non-heme iron(III)−hydroperoxo complexes in nucleophilic (e.g., deformylation of aldehydes) and electrophilic (e.g., the oxidation of sulfides and olefins) reactions under stoichiometric conditions. Other non-heme iron intermediates such as iron(III)−peroxo and iron(IV)−oxo species have also been studied in the aldehyde deformylation and the oxidation of sulfides, respectively.

Results and Discussion

Mononuclear non-heme iron intermediates, such as iron(III)−peroxo $\{[(\mathrm{L})\mathrm{Fe^{III}}{-}\mathrm{O_2}]^{+}\}$, iron(III)−hydroperoxo $\{[(\mathrm{L})\mathrm{Fe^{III}}{-}\mathrm{OOH}]^{2+}\}$, and iron(IV)−oxo $\{[(\mathrm{L})\mathrm{Fe^{IV}}{=}\mathrm{O}]^{2+}\}$ (Table 1), that have been well characterized previously with various spectroscopic techniques were used in the present reactivity studies. The ligand structures such as N4Py, Bn-TPEN, TMC, and TPA are depicted in Figure 1,[9] and the preparation of the intermediates has been described in detail in Experimental Section.

Iron(III)−Peroxo Complexes. We have shown very recently that non-heme iron(III)−peroxo complexes such as $[(\mathrm{N4Py})\mathrm{Fe^{III}}{-}\mathrm{O_2}]^{+}$ (**1**) and $[(\mathrm{TMC})\mathrm{Fe^{III}}{-}\mathrm{O_2}]^{+}$ (**3**) are capable of deformylating aldehydes via an oxidative nucleophilic reaction.[10] For example, the reaction of **1** with 2-phenylpropionaldehyde (2-PPA) afforded acetophenone as a major product within 1 min at −30 °C (eq 1).[10] In the present study, we have tested the reactivity of $[(\mathrm{Bn\text{-}TPEN})\mathrm{Fe^{III}}{-}\mathrm{O_2}]^{+}$ (**2**) in the deformylation of 2-PPA in $\mathrm{CH_3OH}$ at −15 °C and obtained the same result that acetophenone was produced as a major product (see Experimental Section for detailed reaction procedures).

$$\mathrm{PhCH(CH_3)CHO} \xrightarrow[\mathrm{CF_3CH_2OH,\ -30\ ^{o}C}]{[(\mathrm{N4Py})\mathrm{Fe^{III}\text{-}O_2}]^{+}\ (\mathbf{1})} \begin{array}{c}\mathrm{PhC(O)CH_3}\\ + \\ \mathrm{HCO_2H}\end{array} \qquad (1)$$



(2)

We then investigated the reactivity of iron(III)−peroxo complexes in electrophilic reactions such as the oxidation of sulfide and olefin. When **1**, **2**, and **3** were reacted with thioanisole and cyclohexene under the conditions of the aldehyde deformylation, there were virtually no absorption spectral changes of the reaction solutions. Also, product analysis of the reaction solutions revealed that no oxygenated products were formed in the oxidation of thioanisole and cyclohexene by the iron(III)−peroxo complexes. These results demonstrate that non-heme iron(III)−peroxo species do not react with nucleophiles (eq 2). On the basis of the results presented above, we conclude that as it has been well established in iron(III)−peroxo porphyrin reactions,[11] non-heme iron(III)−peroxo complexes are capable of deformylating aldehydes via a nucleophilic reaction but not capable of oxygenating substrates via an electrophilic reaction.

Iron(III)−Hydroperoxo Complexes. It has been proposed that iron(III)−hydroperoxo porphyrins can behave as a nucleophile and attack a carbonyl group of an aldehyde in cytochrome P450-catalyzed deformylation of aldehydes (Scheme 1).[12] We therefore generated non-heme iron(III)−hydroperoxo complexes such as $[(\mathrm{N4Py})\mathrm{Fe^{III}}{-}\mathrm{OOH}]^{2+}$ (**4**), $[(\mathrm{Bn\text{-}TPEN})\mathrm{Fe^{III}}{-}\mathrm{OOH}]^{2+}$ (**5**), and $[(\mathrm{TPA})\mathrm{Fe^{III}}{-}\mathrm{OOH}]^{2+}$ (**6**) and examined their reactivity in the deformylation of aldehydes. Upon addition of 2-PPA to the solutions of **4**, **5**, and **6** (eqs 3−5) (see Experimental Section for reaction conditions), the reaction solutions did not show any absorption spectral changes. Moreover, product analysis revealed that the acetophenone product was not formed. These results indicate that non-heme iron(III)−hydroperoxo species are not capable of deformylating aldehydes via a nucleophilic reaction (eqs 3−5).

$$\mathrm{PhCH(CH_3)CHO} \xrightarrow[\mathrm{CF_3CH_2OH,\ -30\ ^{o}C}]{[(\mathrm{N4Py})\mathrm{Fe^{III}\text{-}OOH}]^{2+}\ (\mathbf{4})} \text{no reaction} \qquad (3)$$

$$\mathrm{PhCH(CH_3)CHO} \xrightarrow[\mathrm{CH_3OH,\ 0\ ^{o}C}]{[(\mathrm{Bn\text{-}TPEN})\mathrm{Fe^{III}\text{-}OOH}]^{2+}\ (\mathbf{5})} \text{no reaction} \qquad (4)$$

$$\mathrm{PhCH(CH_3)CHO} \xrightarrow[\mathrm{CH_3CN,\ -45\ ^{o}C}]{[(\mathrm{TPA})\mathrm{Fe^{III}\text{-}OOH}]^{2+}\ (\mathbf{6})} \text{no reaction} \qquad (5)$$

We then investigated the electrophilic character of the non-heme iron−hydroperoxo complexes by carrying out the oxidation of sulfide and olefin by **4**, **5**, and **6**. Upon addition of thioanisole and cyclohexene to the solutions of **4**, **5**, and **6** (eqs 6−8) (see Experimental Section for reaction conditions), the intermediates remained intact without showing any absorption spectral changes, and no oxygenated products were formed in

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(9) Abbreviation used: 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; TMC, 1,4,8,11-tetramethyl-1,4,8,11-tetraazacyclotetradecane; TPA, tris(2-pyridylmethyl)amine.

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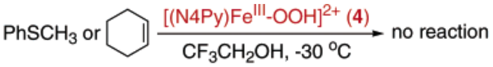
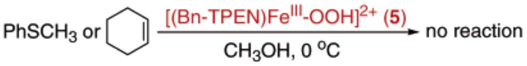
the reactions. These results demonstrate that non-heme iron(III)−hydroperoxo complexes are not capable of oxidizing sulfide and olefin, supporting the computational proposal that iron(III)−hydroperoxo species cannot be an active oxidant for the sulfoxidation and epoxidation reactions (eqs 6−8).[13,14]



(6)



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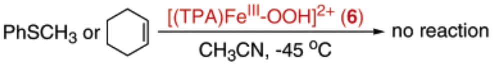

(8)

However, upon warming the reaction solutions to room temperature, we have observed the disappearance of the intermediates and the formation of oxygenated products (e.g., methyl phenyl sulfoxide in the oxidation of thioanisole). We interpret these results that the O−O bond cleavage of $[(L)Fe^{III}{-}OOH]^{2+}$ species at room temperature generates high-valent iron−oxo intermediates that are responsible for the formation of oxygenated products. Indeed, the product formation in the catalytic oxygenation of organic substrates by non-heme iron complexes and H_2O_2 at room temperature has been well demonstrated by Que and co-workers.[15,16]

In the oxidation of PPh_3, **4** and **5** disappeared immediately upon addition of PPh_3, whereas **6** disappeared slowly with a rate comparable to the natural decay (Supporting Information, Figure S1). The latter result is astonishing to us, since PPh_3 is an easily oxidized substrate and can be oxidized by H_2O_2 even in the absence of metal catalysts. The hydroxylation of cyclohexane by $[(N4Py)Fe^{III}{-}OOH]^{2+}$ (**4**) was also investigated, since it has been reported previously that **4** is involved as an active oxidant in the catalytic hydroxylation of cyclohexane by $[Fe(N4Py)]^{2+}$ and H_2O_2.[8b] Upon addition of cyclohexane to the solution of **4**, neither the disappearance of **4** nor the formation of oxygenated products were observed. These results clearly indicate that **4** is not a hydroxylating intermediate and that an intermediate different from **4** is generated as an active oxidant in the reaction of $[Fe(N4Py)]^{2+}$ and H_2O_2 that is responsible for the cyclohexane hydroxylation (e.g., $Fe^{V}{=}O$ species).[16]

In this section, we have demonstrated that iron(III)−hydroperoxo species are sluggish oxidants in both oxidative nucleophilic and electrophilic reactions and the oxidizing power of the intermediates cannot compete with that of iron(IV)−oxo complexes (vide infra).[13,17] Further, the observation that non-heme iron(III)−hydroperoxo species are not able to oxygenate substrates leads us to suggest that porphyrin analogues, (Porp)$Fe^{III}{-}OOH$, cannot be a “second electrophilic oxidant” in electrophilic reactions,[4,13,14] since the latter species bearing a negatively charged porphyrin ligand is presumed to be less reactive than the former bearing a neutral non-heme ligand toward nucleophiles {e.g., (Porp)$Fe^{III}{-}OOH$ vs $[(L)Fe^{III}{-}OOH]^{2+}$}.[18] Finally, it is worth noting that other metal−hydroperoxo complexes (e.g., $Cu^{II}{-}OOH$) have shown low reactivities with exogenous substrates[19] and that, to the best of our knowledge, there is no direct evidence for the involvement of metal−hydroperoxo species in the oxygenation of hydrocarbons such as olefin epoxidation and alkane hydroxylation.

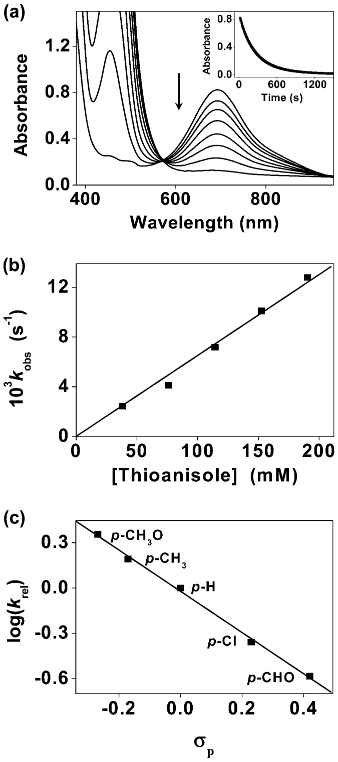

Figure 2. Reactions of **7** with thioanisoles in CH_3CN at 0 °C: (A) UV−vis spectral changes of **7** (2 mM) upon addition of 20 equiv of thioanisole (40 mM). (Inset) Time course of the reaction monitored at 695 nm. (B) Determination of second-order rate constant by plotting k_{obs} against thioanisole concentration. (C) Plot of log k_{rel} against σ_p of *p*-X-thioanisoles to determine Hammett ρ value for the oxidation of para-substituted thioanisoles.

Iron(IV)−Oxo Complexes. It has been shown recently that mononuclear non-heme iron(IV)−oxo species are capable of oxygenating various organic substrates such as PPh_3, sulfides, olefins, alcohols, and alkanes.[20] In the present study, we have compared relative reactivities of non-heme iron(IV)−oxo complexes such as $[(N4Py)Fe^{IV}{=}O]^{2+}$ (**7**), $[(Bn\text{-}TPEN)Fe^{IV}{=}O]^{2+}$ (**8**), $[(TMC)Fe^{IV}{=}O]^{2+}$ (**9**), and $[(TPA)Fe^{IV}{=}O]^{2+}$ (**10**) in the oxidation of thioanisoles (eq 9). Upon addition of

$$PhSCH_3 \xrightarrow[CH_3CN]{[(L)Fe^{IV}{=}O]^{2+}\ (\mathbf{7, 8, 9, 10})} PhS(O)CH_3 \qquad (9)$$

thioanisole to the solutions of **7**, **8**, **9**, and **10**, the intermediates

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Table 2. Comparative Reactivities of Non-Heme Iron(IV)−Oxo Complexes in Sulfide Oxidation

	$[(N4Py)Fe^{IV}{=}O]^{2+}$ (**7**)	$[(Bn\text{-}TPEN)Fe^{IV}{=}O]^{2+}$ (**8**)	$[(TMC)Fe^{IV}{=}O]^{2+}$ (**9**)	$[(TPA)Fe^{IV}{=}O]^{2+}$ (**10**)
reaction temperature	0 °C	−20 °C	35 °C	−45 °C
k_2 ($M^{-1}\,s^{-1}$)	$6.5(5) \times 10^{-2}$	$7.5(5) \times 10^{-2}$	$2.9(3) \times 10^{-2}$	$4.4(3) \times 10^{-1}$
Hammett ρ value	−1.4	−1.5	−2.5	−1.6

reverted back to the starting iron(II) complexes, yielding methyl phenyl sulfoxide quantitatively (eq 9) (see Experimental Section for detailed reaction procedures). Pseudo-first-order fitting of the kinetic data allowed us to determine k_{obs} values (Figure 2a for the reaction of **7**; Supporting Information, Figure S2 for the reactions of **8**, **9**, and **10**). The pseudo-first-order rate constants increased proportionally with thioanisole concentration, allowing us to determine the second-order rate constants for the reactions of **7**, **8**, **9**, and **10** (Table 2) (Figure 2b for the reaction of **7**; Supporting Information, Figure S3 for the reactions of **8**, **9**, and **10**). Taking into consideration the second-order rate constants and the different reaction temperatures, the relative reactivities of the iron−oxo complexes are in the order of **10** > **8** > **7** > **9**. The different reactivities have been rationalized previously with the accessibility of substrates toward the iron−oxo group of the intermediates.[21] In addition to the steric effect, other factors such as the electronic nature of iron(IV)−oxo complexes may also influence the relative reactivities. Indeed, it has been demonstrated that the reactivities of high-valent iron(IV)−oxo porphyrin π-cation radicals are significantly affected by the electronic nature of iron porphyrins.[22] Further, when pseudo-first-order rate constants were determined with various *para*-substituted thioanisoles and plotted against σ_p, we were able to determine Hammett ρ values for the reactions of **7**, **8**, **9**, and **10** (Table 2) (Figure 2c for the reaction of **7**; Supporting Information, Figure S4 for the reactions of **8**, **9**, and **10**). The negative ρ values indicate the electrophilic character of the oxo group of the non-heme iron(IV)−oxo complexes and a positive charge buildup on sulfur in sulfoxidation reactions.[20d,23] As a conclusion, we have shown that non-heme iron(IV)−oxo species oxidize sulfides to the corresponding sulfoxides via an electrophilic reaction and that reactivities of the iron(IV)−oxo complexes are markedly influenced by the ligand structures.

Conclusions

The reactivities of mononuclear non-heme iron(III)−peroxo, iron(III)−hydroperoxo, and iron(IV)−oxo complexes have been investigated in nucleophilic and electrophilic reactions under stoichiometric conditions. As the results are summarized in Scheme 2, iron(III)−peroxo complexes are capable of deformylating aldehydes via a nucleophilic reaction but not capable of oxygenating substrates via an electrophilic reaction. We have provided the first strong experimental evidence that non-heme iron(III)−hydroperoxo complexes are sluggish oxidants in nucleophilic and electrophilic reactions, indicating that the oxidizing power of the intermediates cannot compete with that of high-valent iron(IV)−oxo complexes in oxygen atom transfer reactions. It should be noted here that the previous suggestions for the involvement of iron(III)−hydroperoxo species in the oxygenation of organic substrates such as olefins and alkanes were mainly based on results obtained under catalytic conditions in heme and non-heme iron enzymes and their model compounds.[4a] Therefore, the evidence that has been used to propose the iron(III)−hydroperoxo species as a second electrophilic oxidant should be carefully reevaluated with isolated intermediates. In the reactivity studies of non-heme iron(IV)−oxo complexes, the electrophilic character and the relative reactivities of the intermediates have been discussed with the results of sulfide oxidation that has been performed with in situ-generated iron(IV)−oxo complexes bearing different non-heme ligands.

Scheme 2. Reactions of Mononuclear Non-Heme Iron Intermediates

Experimental Section

Materials. All chemicals obtained from Aldrich Chemical Co. were the best available purity and were used without further purification unless otherwise indicated. Solvents were dried according to published procedures and distilled under Ar prior to use.[24] Iodosylbenzene was prepared by a literature method.[25] *m*-Chloroperbenzoic acid (*m*-CPBA) purchased from Aldrich was purified by washing with phosphate buffer (pH 7.4) followed by water and then dried under reduced pressure. Peracetic acid (CH_3CO_3H, 32 wt % solution containing <6% H_2O_2) and H_2O_2 (30 wt % solution in water) were obtained from Aldrich. Iron(II) complexes such as $Fe(N4Py)(ClO_4)_2$,[8b] $Fe(Bn\text{-}TPEN)(CF_3SO_3)_2$,[20c,26] $Fe(TMC)(CF_3SO_3)_2$,[20a] and $Fe(TPA)(ClO_4)_2$[20b] were prepared in a glovebox by literature methods.

Caution: Perchlorate salts are potentially explosive and should be handled with great care!

Instrumentation. UV−vis spectra were recorded on a Hewlett-Packard 8453 spectrophotometer equipped with an Optostat*DN* variable-temperature liquid-nitrogen cryostat (Oxford instruments) or a circulating water bath. Product analyses for the deformylation of 2-phenylpropionaldehyde and the oxidation of thioanisole were performed with

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DIONEX Pump series P580 equipped with a variable wavelength UV-200 detector (HPLC), Agilent Technologies 6890N gas chromatograph (GC), and a Hewlett-Packard 5890 II Plus gas chromatograph interfaced with Hewlett-Packard model 5989B mass spectrometer (GC−MS). Product analysis for cyclohexene epoxidation was performed with Agilent Technologies 6890N gas chromatograph (GC) and a Hewlett-Packard 5890 II Plus gas chromatograph interfaced with Hewlett-Packard model 5989B mass spectrometer (GC−MS).

Reactions of Iron(III)−Peroxo Complexes. Iron(III)−peroxo complexes, $[(\mathrm{N4Py})\mathrm{Fe}^{\mathrm{III}}{-}\mathrm{O}_2]^+$ (**1**),[27] $[(\mathrm{Bn\text{-}TPEN})\mathrm{Fe}^{\mathrm{III}}{-}\mathrm{O}_2]^+$ (**2**),[28,29] and $[(\mathrm{TMC})\mathrm{Fe}^{\mathrm{III}}{-}\mathrm{O}_2]^+$ (**3**),[10] were prepared by adding 10 equiv of H_2O_2 to the solutions of $\mathrm{Fe(N4Py)(ClO_4)_2}$ (2 mM) in CF_3CH_2OH (2 mL) at −30 °C, $\mathrm{Fe(Bn\text{-}TPEN)(CF_3SO_3)_2}$ (2 mM) in CH_3OH (2 mL) at −15 °C, and $\mathrm{Fe(TMC)(CF_3SO_3)_2}$ (2 mM) in CF_3CH_2OH (2 mL) at 0 °C, respectively, in the presence of triethylamine (10 mM). Then, 40 equiv of substrates (2-phenylpropionaldehyde, thioanisole, and cyclohexene) were added to the reaction solutions. All reactions were followed by monitoring UV−vis spectral changes of the reaction solutions at 650, 745, and 750 nm for the reactions of **1**, **2**, and **3**, respectively. In the case of 2-phenylpropionaldehyde (2-PPA), the intermediates, **1**, **2**, and **3**, disappeared within 1, 50, and 80 min, respectively. In contrast, the intermediates remained intact for several hours in the cases of thioanisole and cyclohexene under the identical conditions of aldehyde deformylation reactions. Product analysis was performed by injecting the resulting solutions directly into HPLC, GC, and GC−MS, and products were identified by comparing retention times and mass patterns of the products to those of known authentic samples. Product yields were determined by comparison against standard curves prepared with authentic samples. Decane was used as an internal standard for the GC analysis. Product analysis of the 2-PPA reactions revealed that acetophenone was produced as a major product,[10] and the yields of acetophenone were 15(3), 18(3), and 25(3)% (based on H_2O_2 used) for the reactions of **1**, **2**, and **3**, respectively.

Reactions of Iron(III)−Hydroperoxo Complexes. Iron(III)−hydroperoxo complexes, $[(\mathrm{N4Py})\mathrm{Fe}^{\mathrm{III}}{-}\mathrm{OOH}]^{2+}$ (**4**),[28] $[(\mathrm{Bn\text{-}TPEN})\mathrm{Fe}^{\mathrm{III}}{-}\mathrm{OOH}]^{2+}$ (**5**),[28,29] and $[(\mathrm{TPA})\mathrm{Fe}^{\mathrm{III}}{-}\mathrm{OOH}]^{2+}$ (**6**),[30] were prepared by adding 10 equiv of H_2O_2 to the solutions of $\mathrm{Fe(N4Py)(ClO_4)_2}$ (1 mM) in CF_3CH_2OH (2 mL) at −30 °C, $\mathrm{Fe(Bn\text{-}TPEN)(CF_3SO_3)_2}$ (1 mM) in CH_3OH (2 mL) at 0 °C, and $\mathrm{Fe(TPA)(ClO_4)_2}$ (1 mM) in CH_3CN (2 mL) at −45 °C, respectively. Then, 40 equiv of the respective substrate (2-phenylpropionaldehyde, thioanisole, and cyclohexene) was added to each reaction solution. All reactions were followed by monitoring UV−vis spectral changes of the reaction solutions at 548, 537, and 538 nm for the reactions of **4**, **5**, and **6**, respectively. The reaction solutions did not show any absorption spectral changes at least for 1 h, and product analysis of the reaction solutions, performed with HPLC, GC, and GC−MS and compared with authentic samples, did not show the formation of oxygenated products. PPh_3 (20 equiv, diluted in 50 μL of CH_3CN) was added to the reaction solutions prior to the product analysis.

In the oxidation of PPh_3, the reaction conditions were the same as described above except that **6** was prepared by reacting $\mathrm{Fe(TPA)(ClO_4)_2}$ (1 mM) with 5 equiv of H_2O_2 at −35 °C in CH_3CN (2 mL). Upon addition of 20 equiv of PPh_3 (diluted in a solvent mixture (100 μL) of CH_3CN and CH_2Cl_2 (1:1)), the intermediates, **4** and **5**, disappeared immediately, whereas the disappearance of **6** was slow. The rate of the natural decay ($k_{\mathrm{obs}} = 3.8(6) \times 10^{-3}\ \mathrm{s}^{-1}$) and the reaction rate with PPh_3 ($k_{\mathrm{obs}} = 5.2(8) \times 10^{-3}\ \mathrm{s}^{-1}$) in the reactions of using 5 equiv of H_2O_2 were determined by fitting the changes in absorbance at 538 nm (Supporting Information, Figure S1).

Reactions of Iron(IV)−Oxo Complexes. Non-heme iron(IV)−oxo complexes, $[(\mathrm{N4Py})\mathrm{Fe}^{\mathrm{IV}}{=}\mathrm{O}]^{2+}$ (**7**),[20c] $[(\mathrm{Bn\text{-}TPEN})\mathrm{Fe}^{\mathrm{IV}}{=}\mathrm{O}]^{2+}$ (**8**),[20c] $[(\mathrm{TMC})\mathrm{Fe}^{\mathrm{IV}}{=}\mathrm{O}]^{2+}$ (**9**),[20a] and $[(\mathrm{TPA})\mathrm{Fe}^{\mathrm{IV}}{=}\mathrm{O}]^{2+}$ (**10**),[20b] were prepared from the reactions of $\mathrm{Fe(N4Py)(ClO_4)_2}$ (2 mM) and excess solid PhIO or *m*-CPBA (2.4 mM) at 0 °C, $\mathrm{Fe(Bn\text{-}TPEN)(CF_3SO_3)_2}$ (2 mM) and excess solid PhIO at −20 °C, $\mathrm{Fe(TMC)(CF_3SO_3)_2}$ (2 mM) and PhIO (2 mM, diluted in 50 μL of CH_3OH) at 35 °C, and $\mathrm{Fe(TPA)(ClO_4)_2}$ (2 mM) and CH_3CO_3H (2.4 mM) at −45 °C, respectively, in CH_3CN (2 mL). Then, appropriate amounts of thioanisole were added to the reaction solution at the given temperature. All reactions were followed by monitoring UV−vis spectral changes of the reaction solutions. Pseudo-first-order rate constants were determined by fitting the changes in absorbance at 695, 735, 820, and 720 nm for the reactions of **7**, **8**, **9**, and **10**, respectively (Figure 2 and Supporting Information Figures S2−S4). Product analysis was performed by injecting the reaction solution directly into GC and HPLC, and product yields were determined by comparison with standard curves of known authentic samples. In the oxidation of thioanisole by **7**, **8**, **9**, and **10**, methyl phenyl sulfoxide was produced quantitatively.

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Supporting Information Available: Figures S1−S4. This material is available free of charge via the Internet at http://pubs.acs.org.

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