ACCOUNTS
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Understanding the Oxidative Relationships of the Metal Oxo, Hydroxo, and Hydroperoxide Intermediates with Manganese(IV) Complexes Having Bridged Cyclams: Correlation of the Physicochemical Properties with Reactivity

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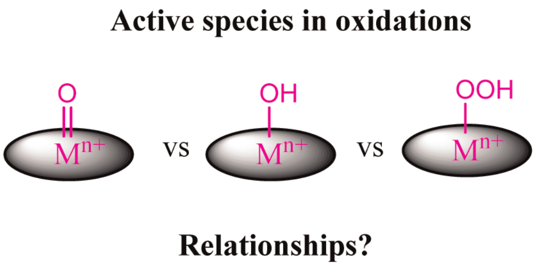
RECEIVED ON JULY 15, 2012

CONSPECTUS



Multiple transition metal functional groups including metal oxo, hydroxo, and hydroperoxide groups play significant roles in various biological and chemical oxidations such as electron transfer, oxygen transfer, and hydrogen abstraction. Further studies that clarify their oxidative relationships and the relationship between their reactivity and their physicochemical properties will expand our ability to predict the reactivity of the intermediate in different oxidative events. As a result researchers will be able to provide rational explanations of poorly understood oxidative phenomena and design selective oxidation catalysts. This Account summarizes results from recent studies of oxidative relationships among manganese(IV) molecules that include pairs of hydroxo/oxo ligands.

Changes in the protonation state may simultaneously affect the net charge, the redox potential, the metal–oxygen bond order ($M-O$ vs $M=O$), and the reactivity of the metal ion. In the manganese(IV) model system, $[Mn^{IV}(Me_2EBC)(OH)_2](PF_6)_2$, the $Mn^{IV}-OH$ and $Mn^{IV}=O$ moieties have similar hydrogen abstraction capabilities, but $Mn^{IV}=O$ abstracts hydrogen at a more than 40-fold faster rate than the corresponding $Mn^{IV}-OH$. However, after the first hydrogen abstraction, the reduction product, $Mn^{III}-OH_2$ from the $Mn^{IV}-OH$ moiety, cannot transfer a subsequent OH group to the substrate radical. Instead the $Mn^{III}-OH$ from the $Mn^{IV}=O$ moiety reforms the OH group, generating the hydroxylated product. In the oxygenation of substrates such as triarylphosphines, the reaction with the $Mn^{IV}=O$ moiety proceeds by concerted oxygen atom transfer, but the reaction with the $Mn^{IV}-OH$ functional group proceeds by electron transfer. In addition, the manganese(IV) species with a $Mn^{IV}-OH$ group has a higher redox potential and demonstrates much more facile electron transfer than the one that has the $Mn^{IV}=O$ group. Furthermore, an increase in the net charge of the $Mn^{IV}-OH$ further accelerates its electron transfer rate. But its influence on hydrogen abstraction is minor because charge-promoted electron transfer does not enhance hydrogen abstraction remarkably. The $Mn^{IV}-OOH$ moiety with an identical coordination environment is a more powerful oxidant than the corresponding $Mn^{IV}-OH$ and $Mn^{IV}=O$ moieties in both hydrogen abstraction and oxygen atom transfer. With this full understanding of the oxidative reactivity of the $Mn^{IV}-OH$ and $Mn^{IV}=O$ moieties, we have clarified the correlation between the physicochemical properties of these active intermediates, including net charge, redox potential, and metal–oxygen bond order, and their reactivities.

The reactivity differences between the metal oxo and hydroxo moieties on these manganese(IV) functional groups after the first hydrogen abstraction have provided clues for understanding their occurrence and functions in metalloenzymes. The P450 enzymes require an iron(IV) oxo form rather than an iron(IV) hydroxo form to perform substrate hydroxylation. However, the lipoxygenases use an iron(III) hydroxo group to dioxygenate unsaturated fatty acids rather than an iron(III) oxo species, a moiety that could facilitate hydroxylation reactions. These distinctly different physicochemical properties and reactivities of the metal oxo and hydroxo moieties could provide clues to understand these elusive oxidation phenomena and provide the foundation for the rational design of novel oxidation catalysts.

10.1021/ar300208z

Introduction

Transition metal ions play the critical roles in a series of electron transfer, oxygen transfer, and hydrogen abstraction events. In addition to the well-known metal oxo moieties,[1−3] that is, $M^{n+}{=}O$, recent developments have disclosed many exceptions. In chloroperoxidases, compound II has been assigned to an $Fe^{IV}{-}OH$ moiety rather than the long-believed $Fe^{IV}{=}O$. In lipoxygenases, an $Fe^{III}{-}OH$ rather than $Fe^{III}{=}O$ has been proposed to perform hydrogen abstraction from an unsaturated fatty acid to generate the corresponding alkyl hydroperoxide product.[4] In addition to the $Fe^{IV}{=}O$ and $Fe^{IV}{-}OH$ moieties, the $Fe^{III}{-}OOH$ group is also proposed as a third oxidant in a variety of oxygenation processes.[5−8] The immediate issue is "what are the reactivities of these metal oxo, hydroxo and hydroperoxide intermediates in oxidations and what are the relationships between these three moieties?" Clarifying this issue would substantially enhance the understanding of the redox metalloenzymes and their highly selective roles in biological processes and benefit rational design and reactivity control of the oxidation catalysts.[9]

Having the identical oxidation state and coordination environment, the viable difference between a $M^{n+}{=}O$ moiety and its corresponding $M^{n+}{-}OH$ is their protonation state (Figure 1), which is responsible for their differences in net charge, metal−oxygen bond order, redox potential, and metal ion reactivity. To compare the oxidative relationships of the metal oxo, hydroxo, and hydroperoxide moieties, several requirements need to be satisfied: (1) they should occur in one general molecular form having the same central metal ion with identical coordination environments, (2) they should be redox active, (3) the metal ion should be in the same oxidation state, and (4) the pK_a between the $M^{n+}{=}O$ and $M^{n+}{-}OH$ derivative would be preferably controllable in the pH range of 1−14. However, due to the dominant dimerization or oligomerization of metal oxo and hydroxo species, available monomeric high oxidation state transition metal complexes having the oxo or hydroxo group are very limited, which slows the progress in this field. This Account mainly describes our studies on the oxidative relationships of the $Mn^{IV}{=}O$, $Mn^{IV}{-}OH$, and $Mn^{IV}{-}OOH$ moieties in a family of manganese(IV) complexes with bridged cyclam. With the sound understanding of the $Mn^{IV}{=}O$ and $Mn^{IV}{-}OH$ moieties, the correlations of the reactivity of an active intermediate with its physicochemical properties, including net charge, redox potential, and metal−oxygen bond order, have also been considered.

FIGURE 1. The metal oxo and its corresponding metal hydroxo form.

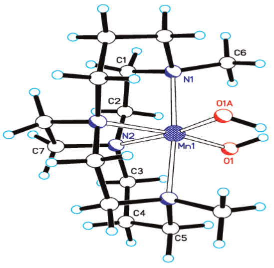


FIGURE 2. The structure of $Mn^{IV}(Me_2EBC)(OH)_2{}^{2+}$.

Nature of the Manganese(IV) Model with Two Hydroxide Ligands

To avoid the formation of dimers or oligomers involving monomeric metal oxo or hydroxo moieties, the ligand surrounding the central metal ion needs to present effective steric hindrance. Borovik designed a tris[(*N*′-*tert*-butylureayl)-*N*-ethylene]amine (H_3buea) ligand and synthesized a series of monomeric iron(III) and manganese(III) complexes having oxo or hydroxo groups.[10] Dimerization was prohibited by the ligand through the protection of the three bulky *tert*-butyl groups and a rigid H-bonding cavity around the coordination sites. The Busch group demonstrated another pattern that stabilizes the monomeric metal hydroxo groups and does not interfere with the reactivity of the manganese. As shown in Figure 2, the synthesized manganese(IV) complex, $[Mn^{IV}(Me_2EBC)(OH)_2](PF_6)_2$, has two hydroxide ligands (Me_2EBC: 4,11-dimethyl-1,4,8,11-tetraazabicyclo[6.6.2]hexadecane).

The dimerization is prohibited by the steric hindrance from the two *N*-methyl groups, which project above and below the plane containing two hydroxide ligands.[11]

This manganese(IV) complex has a redox potential of +0.756 V (vs SHE) for the Mn^{IV}/Mn^{III} couple and is stable for days in neutral to acidic solution but gradually degrades to the corresponding manganese(III) complex in basic media. Potentiometric titrations revealed three pK_a values for this manganese(IV) complex. One accurate pK_a at 6.86 represents the deprotonation of the first hydroxide from $Mn^{IV}(Me_2EBC)(OH)_2{}^{2+}$ to generate the $Mn^{IV}(Me_2EBC)(O)(OH)^{+}$ having 1+ net charge. Two approximate pK_a values at ∼2 and 10 represent adding one proton to form $Mn^{IV}(Me_2EBC)(OH)(OH_2)^{3+}$ having 3+ net charge and losing the last proton to form neutral $Mn^{IV}(Me_2EBC)(O)_2$. Therefore, the $Mn^{IV}(Me_2EBC)(OH)(OH_2)^{3+}$ species with one $Mn^{IV}{-}OH$ functional

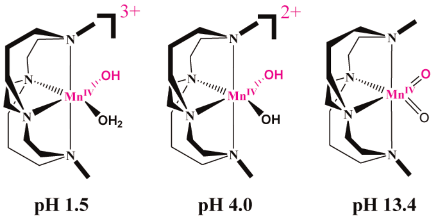


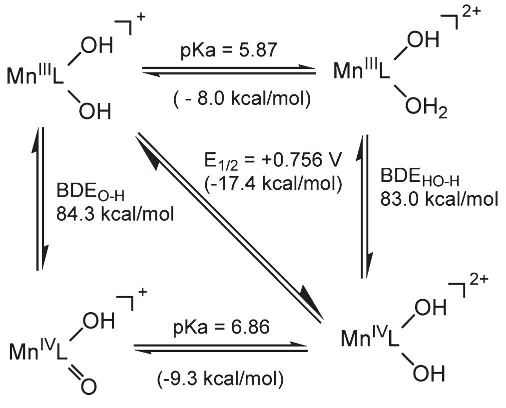
FIGURE 3. The net charge and form of the manganese(IV) species under different pH conditions.

group dominates at pH 1.5, the Mn^{IV}(Me$_2$EBC)(OH)$_2{}^{2+}$ with two Mn^{IV}−OH groups dominates at pH 4.0, and the Mn^{IV}(Me$_2$EBC)(O)$_2$ having two Mn^{IV}=O groups dominates at pH 13.4 (Figure 3). Consequently, the reasonable stability, the feasibly controllable pK_a values and the moderate oxidizing power have positioned this manganese(IV) complex to serve as a rare platform for investigation of the oxidative relationships of the M^{n+}=O and M^{n+}−OH functional groups. In addition, ligand exchange with hydrogen peroxide generates the Mn^{IV}−OOH intermediate, providing the opportunity to compare the reactivity of the M^{n+}=O, M^{n+}−OH, and M^{n+}−OOH in one model.

The Hydrogen Abstraction Capability of the Mn^{IV}−OH and Mn^{IV}=O Moieties

The hydrogen abstraction capabilities of the Mn^{IV}−OH and Mn^{IV}=O functions for this manganese(IV) complex were first evaluated using the method developed by Mayer.[12] The calculated thermodynamic driving force of the Mn^{IV}−OH in hydrogen abstraction is limited to 83.0 kcal/mol, while it is 84.3 kcal/mol for the Mn^{IV}=O, revealing a surprisingly comparable oxidizing power on the part of the Mn^{IV}−OH (Scheme 1). According to the Marcus cross relation,[13] a 1.3 kcal/mol difference in the hydrogen atom affinities could predict a factor of 3 difference in rate, other things being equal. Experimentally both Mn^{IV}−OH and Mn^{IV}=O extract hydrogen atoms from substrates having bond energies of approximately 80 kcal/mol or less.[14,15] The limited capability of the Mn^{IV}−OH and Mn^{IV}=O in hydrogen abstraction indicates that, through ligation to the manganese(IV) cation, the water molecule has been activated. That is, the first bond dissociation energy of the O−H bond (BDE$_{OH}$) in the ligated water is 83.0 kcal/mol, and the second BDE$_{OH}$ is also limited to 84.3 kcal/mol, far less than those in bulk water (119 kcal/mol). Thus, it provides rare evidence to support that, in the oxygen evolution center of photosytem II, the water in the tetramanganese core may have been fully activated to facilitate the hydrogen abstraction by the tyrosine radical with BDE$_{OH}$ of 86 kcal/mol.[16] Similar thermodynamic driving forces of the M^{n+}=O and M^{n+}−OH moieties in hydrogen abstraction have also been disclosed from different models including 84 kcal/mol of the Ru^{IV}=O in [(bpy)$_2$(py)Ru^{IV}O]$^{2+}$,[17] 82 kcal/mol of the Mn^{III}−OH in [Mn^{III}(PY5)(OH)]$^{2+}$ (PY5 = 2,6-bis-(bis(2-pyridyl)methoxymethane)pyridine), 80 kcal/mol of the Fe^{III}−OH in [Fe^{III}(PY5)(OH)]$^{2+}$,[18,19] and 89 kcal/mol of the Mn^{IV}=O, 77 kcal/mol of the Mn^{III}=O, 66 kcal/mol of the Fe^{III}=O in Borovik's complexes with buea ligand.[20]

SCHEME 1



Although the Mn^{IV}−OH and Mn^{IV}=O demonstrate comparable hydrogen abstraction capabilities, their reaction rates are significantly different.[14,15] In hydrogen abstraction from 9,10-dihydroanthracene, the second-order rate constant (k_2) is 3.52 × 10^{-4} M^{-1} s^{-1} for the Mn^{IV}−OH in Mn^{IV}(Me$_2$EBC)(OH)$_2{}^{2+}$, while it is 0.01496 M^{-1} s^{-1} for the Mn^{IV}=O in Mn^{IV}(Me$_2$EBC)(O)$_2$, demonstrating a greater than 40-fold faster rate for Mn^{IV}=O than the corresponding Mn^{IV}−OH. The substantial rate differences were also observed in other models. In Fe^{IV}(β-BPMCN) complex (BPMCN = *N,N*′-bis(2-pyridylmethyl)-*N,N*$_0$-dimethyl-*trans*-1,2-diaminocyclohexane), Que observed that the rate difference between Fe^{IV}=O and Fe^{IV}−OH could reach up to 200-fold with 1,4-cyclohexadiene substrate at −70 °C, where the Fe^{IV}=O and Fe^{IV}−OH moieties were identified by Mössbauer, XAS, EXAFS, Raman, NMR, and MS.[21] In the Mn^{IV}(Salen) model, Fujii also observed that the Mn^{IV}=O demonstrates much faster rate than Mn^{IV}−OH in hydrogen abstraction from the OH group of substituted phenols. Particularly, their driving forces are also limited to 83.1 and 84.2 kcal/mol, almost identical to those in the Mn^{IV}(Me$_2$EBC) model.[22] Obviously, these results have revealed that protonation of an active M^{n+}=O moiety to generate the corresponding M^{n+}−OH does not affect its hydrogen abstraction capability seriously but it does make important changes in the reaction rate.

TABLE 1. The Kinetic Parameters for Hydrogen Abstraction from DHA-h_4 and DHA-d_4 by $Mn^{IV}-OH$ at pH 4.0 and by $Mn^{IV}=O$ at pH 13.4 in the $Mn^{IV}(Me_2EBC)$ Model

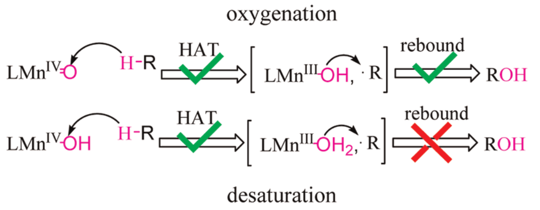
Mn(IV) moiety	$Mn^{IV}-OH$	$Mn^{IV}=O$
E_H (kcal/mol)	15.6 ± 0.5	14.3 ± 0.6
E_D (kcal/mol)	21.7 ± 0.6	20.3 ± 0.5
A_H (s^{-1})	9.3×10^6	7.6×10^7
A_D (s^{-1})	6.5×10^{10}	7.3×10^{11}
$\Delta H_H^\ddagger$ (kcal/mol)	15.2 ± 0.6	13.7 ± 0.6
$\Delta H_D^\ddagger$ (kcal/mol)	21.1 ± 0.6	19.7 ± 0.7
$\Delta S_H^\ddagger$ ($cal \cdot mol^{-1} \cdot K^{-1}$)	-27.9 ± 2.0	-24.5 ± 2.2
$\Delta S_D^\ddagger$ ($cal \cdot mol^{-1} \cdot K^{-1}$)	-11.1 ± 1.9	-6.3 ± 2.3
$E_D - E_H$	6.1	6.0
A_H/A_D	1.43×10^{-4}	1.1×10^{-4}
$\Delta\Delta H^\ddagger_{H/D}$	5.9	6.0
$\Delta\Delta S^\ddagger_{H/D}$	-16.8	-18.2
a (Å)	0.60	0.58
Q_t	4.50	4.36

In the case of $Mn^{IV}(Me_2EBC)$, the kinetic isotope effects (KIEs) for hydrogen abstraction from 9,10-dihydroanthracene are very similar for the $Mn^{IV}-OH$ and $Mn^{IV}=O$ moieties, that is, 3.27 vs 3.78, and they are 2.4 for the $Mn^{III}-OH$ in $[Mn^{III}(PY5)(OH)]^{2+}$, and 3 for the $Fe^{IV}-OH$ in $[Fe^{IV}(\beta\text{-BPMCN})(OH)]^{2+}$, supporting the view that hydrogen atom abstraction is the rate-determining step for both $M^{n+}-OH$ and $M^{n+}=O$ functional groups.[15,19,21] The detailed kinetic studies of $Mn^{IV}(Me_2EBC)$ oxidation using 9,10-dihydroanthracene (DHA-h_4) and the deuterated 9,10-dihydroanthracene (DHA-d_4) substrates further revealed that $Mn^{IV}-OH$ and $Mn^{IV}=O$ have unexpectedly similar kinetic characteristics at the transition state. Their parameter differences for the pre-exponential terms (A) and activation energy (E) in the Arrhenius equation, activation enthalpy ($\Delta H^\ddagger$) and activation entropy ($\Delta S^\ddagger$) in the Eyring equation, barrier half-width (a), and the tunneling correction (Q_t) are almost identical (Table 1).[23]

Product Distributions Revealing Different Reactivity Properties of $Mn^{IV}-OH$ and $Mn^{IV}=O$ after First Hydrogen Abstraction

For some substrates, after hydrogen abstraction by $M^{n+}=O$ or $M^{n+}-OH$ to generate the substrate radical, there exists two possible subsequent reaction pathways, desaturation and oxygenation. In the case of 9,10-dihydroanthracene, desaturation produces anthracene, while oxygenation yields 9-hydroxy-9,10-dihydroanthracene, which can, in principle, be oxidized to anthraquinone. Thus, the ratio of the desaturation and oxygenation products is a source of additional clues to distinguish the reactivity differences between the $M^{n+}=O$ and $M^{n+}-OH$. In investigating the product distributions of hydrogen abstraction from 9,10-dihydroanthracene, it was found that, at pH 4.0, hydrogen abstraction by the $Mn^{IV}-OH$ in $Mn^{IV}(Me_2EBC)(OH)_2^{2+}$ yields solely the desaturation product, whereas at pH 13.4, $Mn^{IV}=O$ in $Mn^{IV}(Me_2EBC)(O)_2$ gives both desaturation and oxygenation products.[24] In fact, the desaturation and oxygenation properties of the $M^{n+}=O$ moieties are widely known in hydroxylases, desaturases, and related chemical systems.[25−28] Formation of anthraquinone at pH 13.4 can be rationalized by the well-known oxygen rebound mechanism in which a $M^{n+}=O$ abstracts a hydrogen atom from substrate to generate the reduced $M^{(n-1)+}-OH$ moiety; then the $M^{(n-1)+}-OH$ replaces the OH group back to the substrate radical to generate the hydroxylated product.[29] In the case of 9,10-dihydroanthracene, the hydroxylated product, 9-hydroxy-9,10-dihydroanthracene, can be oxidized to anthraquinone. Clearly, the reactivity properties of the $Mn^{IV}-OH$ and $Mn^{IV}=O$ moieties are different after the first hydrogen abstraction. For $Mn^{IV}-OH$, after hydrogen abstraction, the reduced $Mn^{III}-OH_2$ cannot rebind the OH group over to the substrate radical to generate the hydroxylated product. In contrast, the reduced $Mn^{III}-OH$ from $Mn^{IV}=O$ is capable of rebounding the OH group to the substrate radical to form the oxygenation product (Scheme 2).[24] It is worth noting that with synthetic complexes, rebound may occur in an intermolecular fashion, that is, the $Mn^{IV}-OH$ can react with a freely diffusing $R^\bullet$ radical generated by another $Mn^{IV}-OH$ center. Apparently, in this $Mn^{IV}-OH$ mediated hydrogen abstraction, the $R^\bullet$ radical does not diffuse out of the solvent cage.

SCHEME 2



The reactivity differences revealed by the $Mn^{IV}-OH$ and $Mn^{IV}=O$ functional groups in $Mn^{IV}(Me_2EBC)$ are significant for understanding the redox metalloenzyme's *choice* between the $M^{n+}-OH$ and $M^{n+}=O$ groups in a specific oxidation event. In P450 enzymes, the $Fe^{IV}=O$ cation radical form of compound I is critical for substrate hydroxylation through the oxygen rebound mechanism. If an $Fe^{IV}-OH$ functional group served as compound I, after hydrogen abstraction to form the $Fe^{IV}-OH_2$ species, replacement of the OH group could not occur as observed for the $Mn^{IV}-OH$ moiety here (Figure 4).[24] On the other hand, the $Fe^{III}-OH$ or $Mn^{III}-OH$ form of the key intermediate is the same critical step as in the lipoxygenases. If an $M^{n+}=O$ moiety served in hydrogen

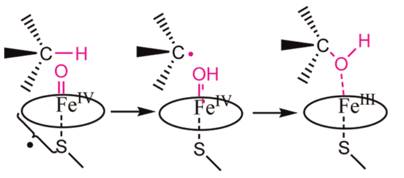


FIGURE 4. Hydroxylation of substrate by $Fe^{IV}=O$ with oxygen rebound mechanism.

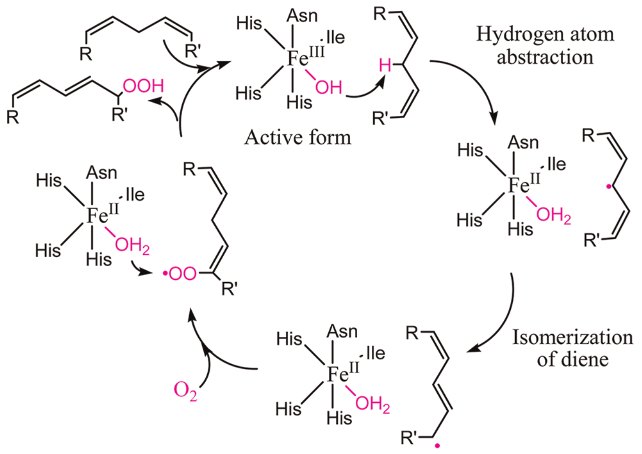


FIGURE 5. Dioxygenation mechanism of the $Fe^{III}-OH$ moiety in lipoxygenases.

abstraction from unsaturated fatty acid, subsequent rebounding of the OH group from the reduced $M^{(n-1)+}-OH$ may occur to form the hydroxylation product, which would block the rearrangement of the substrate radical, thus blocking the next trapping of dioxygen to generate the alkyl hydroperoxide product (Figure 5).[30] Certainly, the high oxidizing power of compound I in P450 enzymes, which is two oxidation levels above iron(III), is crucial for its capability to play key roles in versatile biological metabolism events.

The Oxygenation Properties of the $Mn^{IV}-OH$ and $Mn^{IV}=O$ Moieties

Although versatile $Mn^{IV}=O$ and $Mn^{V}=O$ moieties have been proposed to serve as the active intermediates in olefin epoxidation,[31,32] neither $Mn^{IV}-OH$ nor $Mn^{IV}=O$ in the $Mn^{IV}(Me_2EBC)$ complex is capable of transferring oxygen to olefins.[33,34] However, they are capable of oxygenating easily oxidized substrates like triphenylphosphine to form triphenylphosphine oxide.[35] Oxygenation of triphenylphosphine by the $Mn^{IV}(Me_2EBC)$ complex revealed an inverse solvent kinetic isotope effect (sKIE). In acetone/water, for example, a sKIE value of 0.611 was obtained at 298 K. The inverse sKIE implies that protonation of one $Mn^{IV}-OH$ in $Mn^{IV}(Me_2EBC)(OH)_2^{2+}$ to generate $Mn^{IV}(Me_2EBC)(OH)(OH_2)^{3+}$ is happening prior to PPh_3 oxygenation. Next, the Hammett plots reveal that oxygenation by the $Mn^{IV}-OH$ in $Mn^{IV}(Me_2EBC)(OH)(OH_2)^{3+}$ proceeds by electron transfer with a sensitive substituent effect ($\rho = -0.697$), whereas it proceeds by concerted oxygen transfer for the $Mn^{IV}=O$ in $Mn^{IV}(Me_2EBC)(O)_2$, showing an insensitive substituent effect ($\rho = -0.08$) (Figure 6). Thus, two distinct mechanisms occur in the $Mn^{IV}-OH$ and $Mn^{IV}=O$ mediated oxygenations.

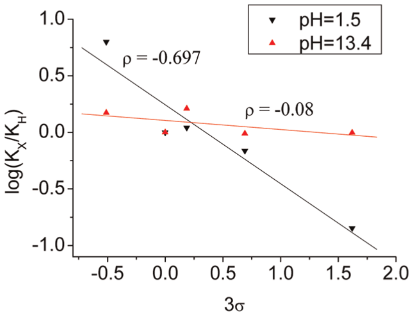


FIGURE 6. Hammett plot for the oxygenation of triarylphosphines by $Mn^{IV}-OH$ and $Mn^{IV}=O$ moieties in acetone/water (4:1) at 293 K.

The Influence of the Net Charge on the Oxidative Properties of the $Mn^{IV}-OH$ and $Mn^{IV}=O$ Moieties

The oxidative properties of the redox active metal ions have been extensively investigated through ligand modifications, but attention is rarely paid to the net charges of the reacting complexes. In natural enzymes, the proton could be frequently added and removed from the reaction center through the hydrogen bond network of proteins; thus the reactivity of the active metal ion could be modulated as needed.[36] Three easily controllable pK_a values of the $Mn^{IV}(Me_2EBC)$ complex, including ~2, 6.86, and 10, provide in this manganese(IV) model a rare chance to investigate the influence of the net charge on its oxidation properties. At pH 1.5 and 4.0, the manganese(IV) species has the identical functional group, that is, $Mn^{IV}-OH$, with different net charges, 3+ vs 2+ (see also Figure 2). Significantly, the different ligands in $Mn^{IV}(Me_2EBC)(OH)(OH_2)^{3+}$ and $Mn^{IV}(Me_2EBC)(OH)_2^{2+}$, H_2O and OH^-, are perpendicular to the $Mn^{IV}-OH$ functional group; thus, there is no axial ligand change for the $Mn^{IV}-OH$ moiety (the axial ligand change would significantly impact the reactivity of the active metal functional group[37]). Thus, their reactivity differences would undoubtedly reflect the influence of the net charge.

The electron transfer and hydrogen abstraction reactivities were independently investigated for the manganese(IV) species having the $Mn^{IV}-OH$ group at pH 1.5 and 4.0,

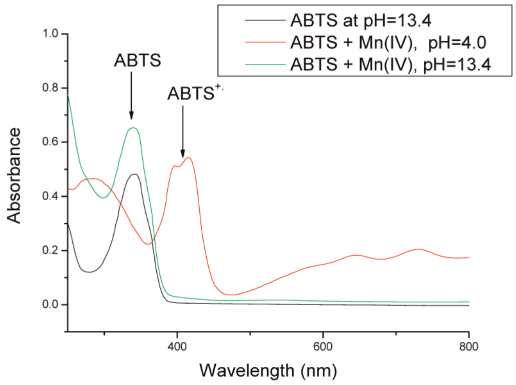


FIGURE 7. The UV–vis spectra of electron transfer tests from ABTS by $Mn^{IV}-OH$ at pH 4.0 and $Mn^{IV}=O$ at pH 13.4 in aqueous solution.

respectively.[38] In oxygenation of tris(4-methoxyphenyl)-phosphine through electron transfer, the $Mn^{IV}-OH$ having a 3+ net charge at pH 1.5 reacts at a 10–20-fold faster rate than the corresponding $Mn^{IV}-OH$ having a 2+ net charge at pH 4.0. This is a charge-promoted electron transfer phenomenon. For example, at 283 K, the k_2 at pH 1.5 is 0.806 $M^{-1}\ s^{-1}$, while it is 0.045 $M^{-1}\ s^{-1}$ at pH 4.0, representing a 17.9-fold rate difference. According to the Marcus cross relation,[13] with other things being equal, a 10–20-fold constant difference in electron transfer would correspond to a difference of 120 to 150 mV in potential. The distinct electron transfer abilities between the $Mn^{IV}-OH$ and $Mn^{IV}=O$ derivatives were identified with 2,2′-azino-di-(3-ethylbenzthiazoline-6-sulfonic acid) (ABTS), a reactive electron transfer agent. In aqueous solution at pH 13.4, the $Mn^{IV}=O$ in $Mn^{IV}(Me_2EBC)(O)_2$ is incapable of electron transfer from ABTS, whereas at pH 4.0, the electron transfer from ABTS to the $Mn^{IV}-OH$ moiety in $Mn^{IV}(Me_2EBC)(OH)_2{}^{2+}$ can be completed in minutes (Figure 7).[24] The redox potentials of the Mn^{IV}/Mn^{III} couple at pH 1.5, 4.0, and 13.4 are 0.54, 0.46, and 0.10 V (vs SCE), respectively. Similarly, a 360 mV potential difference would predict a 10^3-fold rate difference in electron transfer between $Mn^{IV}-OH$ and $Mn^{IV}=O$, well consistent with their distinctly different activity in electron transfer from ABTS. In another case, Goldberg also found that the $[(Cz)^{+\bullet}Mn^V(O)]^+$ demonstrates >100-fold faster oxygenation rate in sulfoxidation than does the corresponding $(Cz)Mn^V(O)$, which differs by only one unit of charge, and the rate acceleration was also attributed to the enhanced eletrophilicity of the $[(Cz)^{+\bullet}Mn^V(O)]^+$.[39] In investigating the oxidative properties of $(N4py)Fe^{IV}=O$ (N4Py = *N*,*N*-bis(2-pyridylmethyl)-*N*-bis(2-pyridyl)methylamine), Nam and Fukuzumi found that the external non-redox metal ion, for example, Sc^{3+}, could greatly accelerate the electron transfer rate of the $Fe^{IV}=O$ moiety up to 10^8-fold, and the redox potential of the Fe^{IV}/Fe^{III} couple also increases from +0.51 to +1.35 V (vs SCE).[40] Furthermore, adding Sc^{3+} could shift the oxygenation mechanism of sulfide by $(N4py)Fe^{IV}=O$ from concerted oxygen transfer to electron transfer.[41] This oxygenation mechanism shift resembles the $Mn^{IV}-OH$ and $Mn^{IV}=O$ mediated oxygenations in our $Mn^{IV}(Me_2EBC)$ system in which the $Mn^{IV}-OH$ oxygenates triphenylphosphine by electron transfer whereas the reaction with $Mn^{IV}=O$ proceeds by concerted oxygen transfer.[35] Also, Goldberg found that the redox-inactive Zn^{2+} can enhance the oxidizing capability of the $(TPB_8Cz)Mn^V(O)$ in electron transfer and the presence of the proton may drive the $(TPB_8Cz)Mn^V(O)$ mediated electron transfer (TBP_8Cz = octakis(*p-tert*-butylphenyl)corrolazinato(3−)).[42,43]

However, the influence of the net charge is insignificant in $Mn^{IV}-OH$ mediated hydrogen abstraction in the $Mn^{IV}(Me_2EBC)$ system. For example, at 293 K, the k_2 for hydrogen abstraction from 1,4-cyclohexadiene is $9.09 \times 10^{-4}\ M^{-1}\ s^{-1}$ for the $Mn^{IV}-OH$ having a net charge of 3+ at pH 1.5, while it is $8.68 \times 10^{-4}\ M^{-1}\ s^{-1}$ for the same $Mn^{IV}-OH$ having a net charge of 2+ at pH 4.0. As described by Mayer in eq 1, where C is a constant (57.6 kcal/mol),[12] the thermodynamic driving force of an active metal ion in hydrogen abstraction can be inferred from the bond dissociation free energy of the generated O–H bond ($BDFE_{OH}$), which is determined from the redox potential of the active metal ion and the pK_a value of its reduced form. Here, the insensitivity of hydrogen abstraction to the net charge change can be rationalized as follows. In determining the hydrogen abstraction capability of the $Mn^{IV}-OH$, the increased redox potential (0.54 V at pH 1.5 vs 0.46 V at pH 4.0 (vs SCE)) has been compensated by the decreased pK_a value of the corresponding reduced manganese(III) complexes (~1.6 vs 5.87[44]). Similarly, the comparable hydrogen abstraction capability of the $M^{n+}=O$ with its protonated counterpart, $M^{n+}-OH$, could also be attributed to this *compensation effect*.

$$BDEF_{OH} = 23.06E_{1/2} + 1.37pK_a + C \qquad (1)$$

Oxidative Reactivity of the $Mn^{IV}-OOH$ Moiety

In investigating the $Mn(Me_2EBC)Cl_2$ mediated olefin epoxidations by H_2O_2, it was eventually found that the key active intermediate for epoxidation is a manganese(IV) hydroperoxide moiety, $Mn^{IV}-OOH$, and the reaction proceeds by the Lewis acid pathway.[33,34] Isotopic labeling experiments using $H_2{}^{18}O$, $H_2{}^{18}O_2$ and ${}^{18}O_2$ and the existence of the $Mn^{IV}-OOH$ intermediate, as shown by an ESI-MS study

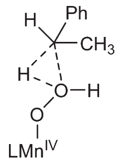


FIGURE 8. The plausible transition state of oxygen insertion by the $Mn^{IV}-OOH$ moiety.

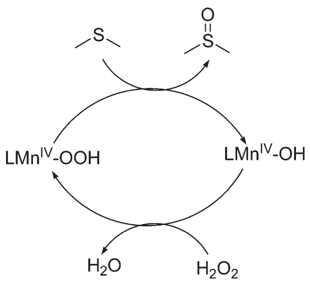


FIGURE 9. Concerted oxygen transfer by the $Mn^{IV}-OOH$ moiety.

and supported by later independent DFT calculations,[45] provided strong evidence for this mechanism. Importantly, in $Mn(Me_2EBC)Cl_2$ mediated pollutant degradation, the proposed key species responsible for degradation has been established as a $Mn^{IV}-OOH$ moiety rather than the common hydroxyl radical, which implies that the $Mn^{IV}-OOH$ may perform many other oxidations in addition to epoxidation.[46] The apparent variety of oxidative capabilities of the $Mn^{IV}-OOH$ moiety have led us to specifically investigate its oxidative reactivity.[47] It was found that the $Mn^{IV}-OOH$ functional group is capable of hydrogen abstraction from diphenylmethane ($BDE_{CH} = 82$ kcal/mol) and ethylbenzene ($BDE_{CH} = 85$ kcal/mol), demonstrating more powerful oxidizing power than the corresponding $Mn^{IV}-OH$ and $Mn^{IV}=O$ derivatives. Experimentally, the driving forces of the hydrogen abstraction by $Mn^{IV}-OH$ and $Mn^{IV}=O$ are limited to 80 kcal/mol. The $Mn^{IV}-OOH$ can also oxygenate various sulfides such as diphenyl sulfide, which is not oxidized by either $Mn^{IV}-OH$ or $Mn^{IV}=O$. Notably, its oxygenating efficiency is much higher than that in hydrogen abstraction. For example, the TOF of hydrogen abstraction from diphenylmethane is only $1.2\ h^{-1}$ when H_2O_2 is used as oxidant in *t*-butyl alcohol at 50 °C, whereas it is $13.8\ h^{-1}$ for diphenyl sulfide oxygenation. The ^{18}O-labeling experiments using $H_2{}^{18}O$ and $H_2{}^{18}O_2$ reveal that the $Mn^{IV}-OOH$ mediated hydrogen abstraction proceeds by a concerted oxygen insertion mechanism, while the oxygenation proceeds by a concerted oxygen transfer mechanism (Figures 8 and 9). Also, a parallel electron transfer mechanism may have been involved in both hydrogen abstraction and sulfoxidation.[47] This issue is not fully understood yet. A powerful hydrogen abstraction capability of the metal hydroperoxide intermediates has also been reported for $Fe^{III}-OOH$ mediated oxidations.[7,8]

The Correlation of the Physicochemical Properties of an Active Intermediate with Its Reactivity

As represented in Figure 1, having the identical oxidation state and coordination environment, the viable difference in the central metal ions having oxo or hydroxo groups is their protonation state. Protonation of a $M^{n+}=O$ moiety to form the corresponding $M^{n+}-OH$ group changes the metal–oxygen bond order from a double bond to a single bond with one unit of positive charge increase, and its reactivities in oxidations change as well. In the case of the $Mn^{IV}(Me_2EBC)$ compounds, the correlations of the reactivity with these physicochemical properties, including net charge, redox potential, pK_a, and the manganese–oxygen bond order, of the manganese(IV) species have been summarized in Table 2. Although the pK_a of the reduced $Mn^{III}(Me_2EBC)(O)(OH)$ is unknown, it should be highly basic to provide the driving force for its enhanced hydrogen abstraction rate for the $Mn^{IV}=O$ in $Mn^{IV}(Me_2EBC)(O)_2$.

Thus, a sound understanding of the oxidative properties of the $Mn^{IV}-OH$ and $Mn^{IV}=O$ moieties in the $Mn^{IV}(Me_2EBC)$ example has revealed the relationships of the reactivity with the physicochemical properties of an active intermediate including the net charge, redox potential, and metal–oxygen bond order, which are as follows. (1) Increasing the net charge of the redox metal ion increases its redox potential, and its electron transfer ability increases as well; however, the influence on hydrogen abstraction is negligible due to the *compensation effect* in which the increased potential of the oxidant has been compensated by the decreased pK_a in the reduced metal form as described in eq 1. (2) The greatest difference exists between the $M^{n+}=O$ and $M^{n+}-OH$ moieties in which the metal–oxygen bond order decreases from a double bond to a single bond, due to protonation, upon converting $M^{n+}=O$ into $M^{n+}-OH$: (i) the redox potential increases greatly; (ii) the $M^{n+}-OH$ moiety demonstrates a much more powerful electron transfer ability than the corresponding $M^{n+}=O$ group; (iii) the hydrogen abstraction rate decreases substantially; however, the hydrogen abstraction capability remains relatively unchanged as a result of the *compensation effect* described above; (iv) the $M^{n+}=O$ moiety can perform electron transfer, hydrogen

TABLE 2. The Thermodynamic Parameters and Oxidative Activity of the $\mathrm{Mn^{IV}(Me_2EBC)}$ Species

$\mathrm{Mn^{IV}}$ moiety	$\mathrm{[LMn^{IV}{-}OH]^{3+}}$	$\mathrm{[LMn^{IV}{-}OH]^{2+}}$	$\mathrm{[LMn^{IV}{=}O]}$
net charge	3+	2+	0
$E_{1/2}$ (V) vs SCE	+0.54	+0.46	+0.10
pK_a of the corresponding $\mathrm{Mn^{III}}$ complex[a]	~1.6	5.87	
$\mathrm{BDFE_{O-H}}$ kcal/mol	77.8	81.9	
electron transfer rate	$\mathrm{[LMn^{IV}{-}OH]^{3+} > [LMn^{IV}{-}OH]^{2+} \gg [LMn^{IV}{=}O]}$		
hydrogen abstraction rate	$\mathrm{[LMn^{IV}{-}OH]^{3+} \approx [LMn^{IV}{-}OH]^{2+} \ll [LMn^{IV}{=}O]}$		

[a] The pK_a values were obtained from ref 43.

abstraction, hydroxylation by the oxygen rebound mechanism, and oxygenation by concerted oxygen transfer, whereas the $\mathrm{M}^{n+}{-}\mathrm{OH}$ only performs hydrogen abstraction and electron trasnfer.

Concluding Remarks

Up to now, it has been found that three categories of the active intermediates, the functional group including $\mathrm{M}^{n+}{=}\mathrm{O}$, $\mathrm{M}^{n+}{-}\mathrm{OH}$, and $\mathrm{M}^{n+}{-}\mathrm{OOH}$ moieties, may play critical roles in versatile oxidation processes. The available data reveal that, with the identical coordination environment, the $\mathrm{M}^{n+}{-}\mathrm{OH}$ and $\mathrm{M}^{n+}{=}\mathrm{O}$ moieties have comparable hydrogen abstraction capabilities but different rates. Particularly, they demonstrate similar kinetic characteristics in the hydrogen abstraction transition state. However, they also display distinct differences in the hydrogen abstraction event. After first hydrogen abstraction, the reduced $\mathrm{M}^{(n-1)+}{-}\mathrm{OH_2}$, derived from $\mathrm{M}^{n+}{-}\mathrm{OH}$, is incapable of capturing the OH group to form a hydroxylation product. In contrast, the reduced $\mathrm{M}^{(n-1)+}{-}\mathrm{OH}$ derived from $\mathrm{M}^{n+}{=}\mathrm{O}$ does bind the OH group to the substrate radical in what has long been called the rebound mechanism. Their comparable capability and similar reactive nature is the basis for their occurrence as key intermediates in hydrogen abstraction processes, while their different behavior after hydrogen abstraction is the determining factor in facilitating substrate hydroxylation by P450 enzymes, which seem to select the $\mathrm{Fe^{IV}{=}O}$ intermediate form, and the very different behavior of the lipoxygenases, which require the $\mathrm{Fe^{III}{-}OH}$ or $\mathrm{Mn^{III}{-}OH}$ intermediate to cause the dioxygenation of unsaturated fatty acids.

Besides their differences in hydrogen abstraction processes, the metal ion containing the $\mathrm{M}^{n+}{-}\mathrm{OH}$ moiety demonstrates a much more powerful electron transfer ability than the $\mathrm{M}^{n+}{=}\mathrm{O}$ moiety. Certainly, the protonation of the $\mathrm{M}^{n+}{=}\mathrm{O}$ moiety to generate $\mathrm{M}^{n+}{-}\mathrm{OH}$ changes the metal−oxygen bond order from double to single bond with a net charge increase, and an increase in redox potential as well. Continuously increasing the net charge of the $\mathrm{M}^{n+}{-}\mathrm{OH}$ may further accelerate its electron transfer rate; however, its influence on hydrogen abstraction is minimal because of the *compensation effect*. In peroxidases, which perform electron transfer rather than oxygenation,[48] the evidence available to researchers to support an $\mathrm{Fe^{IV}{=}O}$ or $\mathrm{Fe^{IV}{-}OH}$ form of compound II has previously remained controversial. The electron transfer ability difference discussed here between $\mathrm{M}^{n+}{-}\mathrm{OH}$ and $\mathrm{M}^{n+}{=}\mathrm{O}$ may help to clarify the peroxidases' choice between the two. For oxidations occurring on the surface of metal oxide catalysts, the key active species have generally been assigned to the metal or bridged metal oxo species, that is, $\mathrm{M}^{n+}{=}\mathrm{O}$ or $\mathrm{M}^{n+}{-}\mathrm{O}{-}\mathrm{M}^{n+}$. Recent discoveries have shown that minor amounts of moisture in the gas feed may substantially enhance the catalytic activity of the heterogeneous catalysts like supported gold nanoparticles.[49,50] Although different explanations have been provided to rationalize those acceleration phenomena, solid evidence is still scarce. Generally, a small increase in moisture may significantly affect the protonation state of the $\mathrm{M}^{n+}{=}\mathrm{O}$ or $\mathrm{M}^{n+}{-}\mathrm{O}{-}\mathrm{M}^{n+}$ moieties, for example, to form certain hydroxo moieties like $\mathrm{M}^{n+}{-}\mathrm{OH}$ or $\mathrm{M}^{n+}{-}\mathrm{O(H)}{-}\mathrm{M}^{n+}$. As disclosed in these studies, the distinctly different redox potential, electron transfer ability, and other oxidative properties of the $\mathrm{M}^{n+}{=}\mathrm{O}$ and $\mathrm{M}^{n+}{-}\mathrm{OH}$ moieties may lead to improved understanding of the role of moisture in those heterogeneous oxidations. Specifically, the sound understanding of the reactivity of the $\mathrm{Mn^{IV}{-}OH}$ and $\mathrm{Mn^{IV}{=}O}$ moieties from the $\mathrm{Mn^{IV}(Me_2EBC)}$ complex provide the chance to correlate the physicochemical properties of an active intermediate with its reactivity and to understand the oxidative relationships of the $\mathrm{M}^{n+}{=}\mathrm{O}$, $\mathrm{M}^{n+}{-}\mathrm{OH}$, and $\mathrm{M}^{n+}{-}\mathrm{OOH}$ intermediates. Since these three categories of active intermediates may simultaneously exist under oxidative conditions, their different reactivities apparently indicate the occurrence of competing mechanisms. Thus, it seems wiser to focus on the parallel pathways and seek to optimize and exploit each for its own advantage in oxidations. However, how the knowledge of the redox chemistry discussed in this Account benefits the understanding of the enzymatic and chemical oxidations remains an open area, which appeals for continuous and extensive investigations involving a variety of different families of examples.

The author is deeply grateful to Professor Daryle Busch of the University of Kansas for many discussions on this topic, and Prof. Busch has had a profound influence on the author. The author is also indebted to students, postdoctoral associates, colleagues, and collaborators who have been a great part of this work. The financial support from the National Natural Science Foundation of China (Grants 20973069 and 21273086), and versatile analysis performed in the Analytical and Testing Center of Huazhong University of Science and Technology are also gratefully acknowledged.

BIOGRAPHICAL INFORMATION

Guochuan Yin was born in the suburb of Chengdu, China, and went to Zhejiang University for his undergraduate studies, graduating in 1990. In 1998, he received his Ph.D. in Chemistry with Prof. Zuwei Xi from Dalian Institute of Chemical Physics, Chinese Academy of Sciences. Then, he was appointed as a faculty member in Nanjing University. In 1999, he went to Kyushu University as a JSPS fellow with Prof. Yuzo Fujiwara. After that, he joined Prof. Daryle Busch's laboratory at University of Kansas as a postdoctoral associate. In 2008, he returned to China to take up a faculty position in Huazhong University of Science and Technology where he is currently a full professor. His interests include homogeneous oxidation, biomass conversion, and pollutant degradation, and he has special interests in mechanistic studies in redox chemistry which he started in Busch's laboratory.

FOOTNOTES

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The author declares no competing financial interest.
Dedicated to Daryle H Busch on the occasion of his 85th birthday.

REFERENCES

1 Valentine, J. S.; Foote, C. S.; Greenberg, A.; Liebman, J. F. *Active Oxygen in Biochemistry*; Chapman & Hall: New York, 1995.

2 Gunay, A.; Theopold, K. H. C−H Bond Activations by Metal Oxo Compounds. *Chem. Rev.* **2010**, *110*, 1060–1081.

3 Nam, W. High-Valent Iron(IV)-Oxo Complexes of Heme and Non-heme Ligands in Oxygenation Reactions. *Acc. Chem. Res.* **2007**, *40*, 522–531.

4 Neidig, M. L.; Wecksler, A. T.; Schenk, G.; Holman, T. R.; Solomon, E. I. Kinetic and Spectroscopic Studies of N694C Lipoxygenase: A Probe of the Substrate Activation Mechanism of a Nonheme Ferric Enzyme. *J. Am. Chem. Soc.* **2007**, *129*, 7531–7537.

5 Nam, W.; Ho, R.; Valentine, J. S. Iron-Cyclam Complexes as Catalysts for the Epoxidation of Olefins by 30% Aqueous Hydrogen Peroxide in Acetonitrile and Methanol. *J. Am. Chem. Soc.* **1991**, *113*, 7052–7054.

6 Kerber, W. D.; Ramdhanie, B.; Goldberg, D. P. H_2O_2 Oxidations Catalyzed by an Iron(III) Corrolazine: Avoiding High-Valent Iron-Oxido Species? *Angew. Chem., Int. Ed.* **2007**, *46*, 3718–3721.

7 Neese, F.; Zaleski, J. M.; Zaleski, K. L.; Solomon, E. I. Electronic Structure of Activated Bleomycin: Oxygen Intermediates in Heme versus Non-Heme Iron. *J. Am. Chem. Soc.* **2000**, *122*, 11703–11724.

8 Cho, J.; Jeon, S.; Wilson, S. A.; Liu, L. V.; Kang, E. A.; Braymer, J. J.; Lim, M. H.; Hedman, B.; Hodgson, K. O.; Valentine, J. S.; Solomon, E. I.; Nam, W. Structure, Interconversion, and Reactivity of Active Oxygen Ligands Bound to Nonheme Iron. *Nature* **2011**, *478*, 502–505.

9 Yin, G. Active Transition Metal Oxo and Hydroxo Moieties in Nature's Redox Enzymes and Their Synthetic Models: Structure and Reactivity Relationships. *Coord. Chem. Rev.* **2010**, *254*, 1826–1842.

10 Borovik, A. S. Bioinspired Hydrogen Bond Motifs in Ligand Design: The Role of Noncovalent Interactions in Metal Ion Mediated Activation of Dioxyge. *Acc. Chem. Res.* **2005**, *38*, 54–61.

11 Yin, G.; McCormick, J. M.; Buchalova, M.; Danby, A. M.; Rodgers, K.; Day, V. W.; Smith, K.; Perkins, C. M.; Kitko, D.; Carter, J. D.; Scheper, W. M.; Busch, D. H. Synthesis, Characterization and Solution Properties of a Novel Cross-bridged Cyclam Manganese(IV) Complex Having Terminal Dihydroxo Ligand. *Inorg. Chem.* **2006**, *45*, 8052–8061.

12 Mayer, J. M. Hydrogen Atom Abstraction by Metal-Oxo Complexes: Understanding the Analogy with Organic Radical Reactions. *Acc. Chem. Res.* **1998**, *31*, 441–450.

13 Mayer, J. M. Understanding Hydrogen Atom Transfer: From Bond Strengths to Marcus Theory. *Acc. Chem. Res.* **2011**, *44*, 36–46.

14 Yin, G.; Danby, A. M.; Kitko, D.; Carter, J.; Scheper, W. M.; Busch, D. H. Understanding the Selectivity of a Moderate Oxidation Catalyst: Hydrogen Abstraction by a Fully Characterized, Activated Catalyst, the Robust Dihydroxo Manganese(IV) Complex of a Bridged Cyclam. *J. Am. Chem. Soc.* **2007**, *129*, 1512–1513.

15 Yin, G.; Danby, A. M.; Kitko, D.; Carter, J. D.; Scheper, W. M.; Busch, D. H. Oxidative Reactivity Difference between the Metal Oxo and Metal Hydroxo Moieties: pH Dependent Hydrogen Abstraction by a Manganese(IV) Complex Having Two Hydroxide Ligands. *J. Am. Chem. Soc.* **2008**, *130*, 16245–16253.

16 Pecoraro, V. L.; Baldwin, M. J.; Caudle, M. T.; Hsieh, W.; Law, N. A. A Proposal for Water Oxidation in Photosystem II. *Pure Appl. Chem.* **1998**, *70*, 925–929.

17 Bryant, J. R.; Mayer, J. M. Oxidation of C−H Bonds by $[(bpy)_2(py)Ru^{IV}O]^{2+}$ Occurs by Hydrogen Atom Abstraction. *J. Am. Chem. Soc.* **2003**, *125*, 10351–10361.

18 Goldsmith, C. R.; Cole, A. P.; Stack, T. D. P. C−H Activation by a Mononuclear Manganese(III) Hydroxide Complex: Synthesis and Characterization of a Manganese-Lipoxygenase Mimic? *J. Am. Chem. Soc.* **2005**, *127*, 9904–9912.

19 Goldsmith, C. R.; Stack, T. D. P. Hydrogen Atom Abstraction by a Mononuclear Ferric Hydroxide Complex: Insights into the Reactivity of Lipoxygenase. *Inorg. Chem.* **2006**, *45*, 6048–6055.

20 Gupta, R.; Borovik, A. S. Monomeric MnIII/II and FeIII/II Complexes with Terminal Hydroxo and Oxo Ligands: Probing Reactivity via O−H Bond Dissociation Energies. *J. Am. Chem. Soc.* **2003**, *125*, 13234–13242.

21 Fiedler, T.; Que, L., Jr. Reactivities of Fe(IV) Complexes with Oxo, Hydroxo, and Alkylperoxo Ligands: An Experimental and Computational Study. *Inorg. Chem.* **2009**, *48*, 11038–11047.

22 Kurahashi, T.; Kikuchi, A.; Shiro, Y.; Hada, M.; Fujii, H. Unique Properties and Reactivity of High-Valent Manganese-Oxo versus Manganese-Hydroxo in the Salen Platform. *Inorg. Chem.* **2010**, *49*, 6664–6672.

23 Wang, Y.; Shi, S.; Wang, H.; Zhu, D.; Yin, G. Kinetics of Hydrogen Abstraction by the Active Metal Hydroxo and Oxo Intermediates: Revealing Their Unexpected Similarities in the Transition State. *Chem. Commun.* **2012**, *48*, 7832–7834.

24 Shi, S.; Wang, Y.; Xu, A.; Wang, H.; Zhu, D.; Roy, S. B.; Jackson, T. A.; Busch, D. H.; Yin, G. Distinct Reactivity Differences of Metal Oxo and Its Corresponding Hydroxo Moieties in Oxidations: Implications from a Manganese(IV) Complex Having Dihydroxide Ligand. *Angew. Chem. Intl. Ed.* **2011**, *50*, 7321–7324.

25 Sono, M.; Roach, M. P.; Coulter, E. D.; Dawson, J. H. Heme-Containing Oxygenases. *Chem. Rev.* **1996**, *96*, 2841–2888.

26 Hull, J. F.; Balcells, D.; Sauer, E. L. O.; Raynaud, C.; Brudvig, G. W.; Crabtree, R. H.; Eisenstein, O. Manganese Catalysts for C−H Activation: An Experimental/Theoretical Study Identifies the Stereoelectronic Factor That Controls the Switch between Hydroxylation and Desaturation Pathways. *J. Am. Chem. Soc.* **2010**, *132*, 7605–7616.

27 Sawant, S. C.; Wu, X.; Cho, J.; Cho, K.; Kim, S. H.; Seo, M. S.; Lee, Y.; Kubo, M.; Ogura, T.; Shaik, S.; Nam, W. Water as an Oxygen Source: Synthesis, Characterization, and Reactivity Studies of a Mononuclear Nonheme Manganese(IV) Oxo Complex. *Angew. Chem., Int. Ed.* **2010**, *49*, 8190–8194.

28 Wu, X.; Seo, M. S.; Davis, K. M.; Lee, Y.; Chen, J.; Cho, K.; Pushkar, Y. N.; Nam, W. A Highly Reactive Mononuclear Non-Heme Manganese(IV)-Oxo Complex That Can Activate the Strong C−H Bonds of Alkanes. *J. Am. Chem. Soc.* **2011**, *133*, 20088–20091.

29 Groves, J. T. Key Elements of the Chemistry of Cytochrome P-450: The Oxygen Rebound Mechanism. *J. Chem. Educ.* **1985**, *62*, 928–931.

30 Schneider, C.; Pratt, D. A; Porter, N. A; Brash, A. R. Control of Oxygenation in Lipoxygenase and Cyclooxygenase Catalysis. *Chem. Biol.* **2007**, *14*, 473–488.

31 Goldberg, D. P. Corrolazines: New Frontiers in High-Valent Metalloporphyrinoid Stability and Reactivity. *Acc. Chem. Res.* **2007**, *40*, 626–634.

32 Arasasingham, R.; He, G.; Bruice, T. C. Mechanism of Manganese Porphyrin-Catalyzed Oxidation of Alkenes. Role of Manganese(IV)-oxo Species. *J. Am. Chem. Soc.* **1993**, *115*, 7985–7991.

33 Yin, G.; Buchalova, M.; Danby, A. M.; Perkins, C. M.; Kitko, D.; Carter, J. D.; Scheper, W. M.; Busch, D. H. Olefin Oxygenation by the Hydroperoxide Adduct of a Nonheme Manganese(IV) Complex: Epoxidations by a Metallo-Peracid Produces Gentle Selective Oxidations. *J. Am. Chem. Soc.* **2005**, *127*, 17170–17171.

34 Yin, G.; Buchalova, M.; Danby, A. M.; Perkins, C. M.; Kitko, D.; Carter, J. D.; Scheper, W. M.; Busch, D. H. Olefin Epoxidation by the Hydrogen Peroxide Adduct of a Novel Non-heme Mangangese(IV) Complex: Demonstration of Oxygen Transfer by Multiple Mechanisms. *Inorg. Chem.* **2006**, *45*, 3467–3474.

35 Xu, A.; Xiong, H.; Yin, G. Distinct Oxygenation Difference Between Manganese(IV) Hydroxo and Oxo Moieties: Electron Transfer vs Concerted Oxygen Transfer. *Chem.—Eur. J.* **2009**, *15*, 11478–11481.

36 Denisov, I. G.; Makris, T. M.; Sligar, S. G.; Schlichting, I. Structure and Chemistry of Cytochrome P450. *Chem. Rev.* **2005**, *105*, 2253–2278.

37 Prokop, K. A.; de Visser, S. P.; Goldberg, D. P. Unprecedented Rate Enhancements of Hydrogen-Atom Transfer to a Manganese(V)−Oxo Corrolazine Complex. *Angew. Chem., Int. Ed.* **2010**, *49*, 5091–5095.

38 Wang, Y.; Sheng, J.; Shi, S.; Zhu, D.; Yin, G. The Influence of the Net Charge on the Oxidative Properties of a Manganese(IV) Species: Revealing the Charge Promoted Electron Transfer But Not Hydrogen Abstraction. *J. Phys. Chem. C* **2012**, *116*, 13231–13239.

39 Prokop, K. A.; Neu, H. M.; de Visser, S. P.; Goldberg, D. P. A Manganese(V)-Oxo π-Cation Radical Complex: Influence of One-Electron Oxidation on Oxygen-Atom Transfer. *J. Am. Chem. Soc.* **2011**, *133*, 15874–15877.

40 Morimoto, Y.; Kotani, H.; Park, J.; Lee, Y.; Nam, W.; Fukuzumi, S. Metal Ion-Coupled Electron Transfer of a Nonheme Oxoiron(IV) Complex: Remarkable Enhancement of Electron-Transfer Rates by Sc^3. *J. Am. Chem. Soc.* **2011**, *133*, 403–405.

41 Park, J.; Morimoto, Y.; Lee, Y.; Nam, W.; Fukuzumi, S. 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. *J. Am. Chem. Soc.* **2011**, *133*, 5236–5239.

42 Leeladee, P.; Baglia, R. A.; Prokop, K. A.; Latifi, R.; de Visser, S. P.; Goldberg, D. P. Valence Tautomerism in a High-Valent Manganese−Oxo Porphyrinoid Complex Induced by a Lewis Acid. *J. Am. Chem. Soc.* **2012**, *134*, 10397–10400.

43 Fukuzumi, S.; Kotani, H.; Prokop, K. A.; Goldberg, D. P. Electron- and Hydride-Transfer Reactivity of an Isolable Manganese(V)-Oxo Complex. *J. Am. Chem. Soc.* **2011**, *133*, 1859–1869.

44 Hubin, T. J.; McCormick, J. M.; Alcock, N. W.; Busch, D. H. Topologically Constrained Manganese(III) and Iron(III) Complexes of Two Cross-Bridged Tetraazamacrocycles. *Inorg. Chem.* **2001**, *40*, 435–444.

45 Haras, A.; Ziegler, T. DFT Mechanistic Studies on the Epoxidation of Cyclohexene by Non-heme Tetraaza Manganese Complexes. *Can. J. Chem.* **2009**, *87*, 33–38.

46 Xu, A.; Xiong, H.; Yin, G. Decolorization of Dye Pollutions by Manganese Complexes with Rigid Cross-Bridged Cyclam Ligands and Its Mechanistic Investigations. *J. Phys. Chem. A* **2009**, *113*, 12243–12248.

47 Wang, Y.; Shi, S.; Zhu, D.; Yin, G. The Oxidative Properties of a Manganese(IV) Hydroperoxide Moiety and Its Relationships with the Corresponding Manganese(IV) Oxo and Hydroxo Moieties. *Dalton Trans.* **2012**, *41*, 2612–2619.

48 Nocek, J. M.; Zhou, J. S.; Forest, S. D.; Priyadarshy, S.; Beratan, D. N.; Onuchic, J. N.; Hoffman, B. M. Theory and Practice of Electron Transfer within Protein−Protein Complexes: Application to the Multidomain Binding of Cytochrome c by Cytochrome c Peroxidase. *Chem. Rev.* **1996**, *96*, 2459–2489.

49 Dat, M.; Okumura, M.; Tsubota, S.; Haruta, M. Vital Role of Moisture in the Catalytic Activity of Supported Gold Nanoparticles. *Angew. Chem., Int. Ed.* **2004**, *43*, 2129–2132.

50 Wallace, W. T.; Wyrwas, R. B.; Whetten, R. L.; Mitrić, R.; Bonačić-Koutecký, V. Oxygen Adsorption on Hydrated Gold Cluster Anions: Experiment and Theory. *J. Am. Chem. Soc.* **2003**, *125*, 8408–8414.