Transition Metal Oxo and Hydroxo Complexes

Jessi Wilson
iCID Group Meeting
11/7/2019
Transition Metal Active Sites in Biology

P450 enzymes (Fe), Peroxidases (Fe), Sulfite oxidases (Mo), Xanthine oxidases (Mo), Lipoxygenases (non-heme Fe)

Catalytic cycle of P450 enzyme

Oxygen rebound mechanism proposed by Groves

Transition Metal Active Sites in Biology

P450 enzymes (Fe), Peroxidases (Fe), Sulfite oxidases (Mo), Xanthine oxidases (Mo), Lipoxygenases (non-heme Fe)

Catalytic cycle of P450 enzyme

Oxygen transfer reaction with molybdenum complex

Hydrogen abstraction mechanism for lipoxygenase

**Transition Metal Active Sites in Biology**

P450 enzymes (Fe), Peroxidases (Fe), Sulfite oxidases (Mo), Xanthine oxidases (Mo), Lipoxygenases (non-heme Fe)

Catalytic cycle of P450 enzyme

Oxygen transfer reaction with molybdenum complex

Fe(III)-OH plays a key role in abstracting H from fatty acids

Fe(III)=O not proposed based on lack of π-electrons to stabilized the high valent Fe (not a porphyrin)

Protonation state of intermediates in most peroxidase enzymes unknown

**Synthetic models: oxo and hydroxo complexes**
1) Differences in reactivity while varying protonation state
2) Keep oxidation state and coordination environment the same

**Protonation state affects:**
1) Redox potential
2) pKa
3) Reactivity of active functional group

Early transition metals (V, Cr, Mn, Fe): d(xz) and d(yz) are much higher in energy than px and py

$\pi^*$ Orbitals are metal based

Move to the right: decrease oxo character in $\pi^*$

Early transition metals with high oxidation state: metal oxo $[\text{M}=\text{O}]^{n+} - \text{M}^{n+2}$, dianionic $\text{O}^{2-}$

Late transition metals: metal-oxyl $[\text{M}-\text{O}^*]^{n+}$

Lower valent $\text{M}^+$ and radical $\text{O}^*$

High Valent Oxo and Hydroxo Models

\[ \text{Mn(IV)(OH)}_2 \rightarrow \text{Deprotonate to get Mn(IV)(O)}_2 \]
Dihydroxide more stable, oxo group may be more reactive

\[ \text{H-abstraction:} \]
\[ \text{Mn(O)(OH)} = 84.3 \text{ kcal/mol} \]
\[ \text{Mn(OH)}_2 = 83.0 \text{ kcal/mol} \]

Protonation increases + charge on M center: accounts for change in electronic properties and reactivity (compensation by inc. +)

Thermodynamically similar
Kinetics: the single deprotonated variant reacts >10x faster than fully protonated (fully deprotonated Mn-oxo >40x faster than Mn-OH)

KIE shows H-atom abstraction is RDS in both mechanisms

*Protonation state has a strong influence on H abstraction ability (even with little perturbation of thermodynamic oxidizing ability)*


*Protonation state has a strong influence on H abstraction ability (even with little perturbation of thermodynamic oxidizing ability)*


High Valent Oxo and Hydroxo Models

Mn-O bonds in OH much longer than O=Mn

Mn-OH$_2$ is Mn(III)-phenoxy radical while Mn-OH and Mn=O are phenolate

Only Mn=O can transfer to phosphine or abstract H

*protonation state affects the reactivity of the Mn(IV) center


High Valent Oxo and Hydroxo Models

Proposed mechanism: Fe-O$_2$-Fe formed with O$_2$, O—O bond homolysis yields reactive Fe$^{IV}$-O species

Reaction of Co$^{II}$ to activate O$_2$ is rare, proposed intermediate high valent terminal oxo

With a single H-bond, excess O$_2$ is required, but the Co$^{II}$-O$_2$ species is observable
Without H-bonds, no reaction with O$_2$ is observed

**J.A.C.S. 2010, 132, 12188–12190;**

**J.A.C.S. 2006, 128, 15476-15489**
High Valent Oxo and Hydroxo Models

Employ outer sphere LA (Ca, Sr, Ba) to stabilize M-OH

NMe₄[M₄⁺MST] → [LMB⁺(μ-OH)-MA³⁺MST]OTf

NMe₄[Fe⁺TST(OH₂)] + [1] NMO
DCM or MeCN
N₂, rt

A: 3% (DCM)
B: 22% (MeCN)
C: 27% (MeCN)

High Valent Metal Oxo and Hydroxo Complexes

C-H activation/H-atom abstraction

High Valent Metal Oxo and Hydroxo Complexes

Calculated IBO analysis to help determine concerted nature of reaction

Suggests concerted mechanism, agrees with H/D scrambling experiment (no substrate carbanion product observed)
Summary and Future Work

• When making transition metal oxo complexes – coordination/geometry can be critical!

• Comparison of reactivity between deprotonated and protonated species is important!