

Structure-Function Relationship of Metalloproteins

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Metalloproteins are a class of biologically important macromolecules, which have various functions such as oxygen transport, electron transfer, oxidation, and oxygenation. These diverse functions of metalloproteins have been thought to depend on the ligands from amino acid, coordination structures, and protein structures in immediate vicinity of metal ions. In this project, we are studying the relationship between the electronic structures of the metal active sites and reactivity of metalloproteins.

1. One-Electron Oxidation of Electronically-Diverse Manganese(III) and Nickel(II) Salen Complexes: Transition from Localized to Delocalized Mixed-Valence Ligand Radicals¹⁾

Ligand radicals from salen complexes are unique mixed-valence compounds, in which a phenoxyl radical is electronically linked to a remote phenolate via a neighboring redox-active metal ion, providing an opportunity to study electron transfer from a phenolate to a phenoxyl radical mediated by a redox-active metal ion as a bridge. We herein synthesize one-electron oxidized products from electronically-diverse manganese(III) salen complexes, in which the locus of oxidation is shown to be ligand-centered, not metal-centered, affording manganese(III)–phenoxyl radical species. The key point in the present study is an unambiguous assignment of IVCT (intervalence charge transfer) bands by using non-symmetrical salen complexes, which enables us to obtain otherwise inaccessible insight into the mixed-valence property.

A d^4 high-spin manganese(III) ion forms a Robin-Day Class II mixed-valence system, in which electron transfer is occurring between the *localized* phenoxyl radical and the phenolate. This is in clear contrast to a d^8 low-spin nickel(II) ion with the same salen ligand, which induces a *delocalized* radical (Robin-Day Class III) over the two phenolate rings, as previously reported by others. The present findings point to a fascinating possibility that electron transfer could be drastically modulated by exchanging the metal ion that bridges the two redox centers.

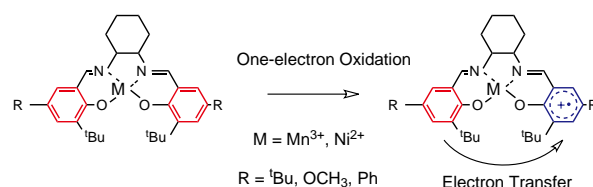


Figure 1. Mixed-Valence Ligand Radicals formed from manganese (III) and nickel(II) salen Complexes.

2. Redox Potentials of Oxoiron(IV) Porphyrin π -Cation Radical Complexes: Participation of Electron Transfer Process in Oxygenation Reactions²⁾

The oxoiron(IV) porphyrin π -cation radical complex (compound I) has been identified as the key reactive intermediate of several heme enzymes and synthetic heme complexes. The redox properties of this reactive species are not yet well understood. Here, we report the results of a systematic study

of the electrochemistry of oxoiron(IV) porphyrin π -cation radical complexes with various porphyrin structures and axial ligands in organic solvents at low temperatures. The cyclic voltammogram of (TMP)Fe^{IV}O, (TMP = 5,10,15,20-tetramesitylporphyrinate), exhibits two quasi-reversible redox waves at $E_{1/2} = 0.88$ and 1.18 V vs. SCE in dichloromethane at -60 °C (Figure 2). Absorption spectral measurements for electrochemical oxidation at controlled potential clearly indicated that the first redox wave results from the (TMP)Fe^{IV}O/[(TMP⁺)Fe^{IV}O]⁺ couple. The redox potential for the (TMP)Fe^{IV}O/[(TMP⁺)Fe^{IV}O]⁺ couple undergoes a positive shift upon coordination of an anionic axial ligand, but a negative shift upon coordination of a neutral axial ligand (imidazole). The negative shifts of the redox potential for the imidazole complexes are contrary to their high oxygenation activity. On the other hand, the electron-withdrawing effect of the meso-substituent shifts the redox potential in a positive direction. Comparison of the measured redox potentials and reaction rate constants for epoxidation of cyclooctene and demethylation of *N,N*-dimethylanilines enable us to discuss the details of the electron transfer process from substrates to the oxoiron(IV) porphyrin π -cation radical complex in the oxygenation mechanisms.

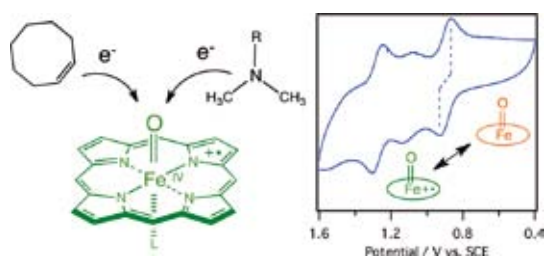


Figure 2. Cyclic Voltammogram of Oxoiron(IV) Porphyrin π -Cation Radical Complex.

3. Oxidation of Chloride Ion and Subsequent Chlorination of Organic Compounds by Oxoiron(IV) Porphyrin π -Cation Radical Complexes³⁾

Chloroperoxidase (CPO) and myeloperoxidase (MPO) are the only heme peroxidases that catalyze oxidation of chloride ion with hydrogen peroxide. CPO is an enzyme of *Caldariomyces fumago* and catalyzes chlorination reactions in the biosynthesis of chlorine-containing compounds. CPO is also known to exhibit peroxidase, catalase, and cytochrome P450-like activities. CPO has a thiolate heme axial ligand like cytochrome P450. This makes CPO distinct from other heme

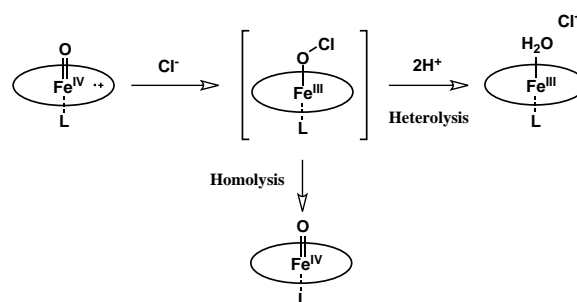


Figure 3. Cyclic Voltammogram of Oxoiron(IV) Porphyrin π -Cation Radical Complex.

peroxidases which have a histidine imidazole as the heme axial ligand. On the other hand, MPO is found in the granules of myelocytes (precursors of neutrophils), and works as a major component of the antimicrobial system of neutrophils. MPO belongs to the animal peroxidase superfamily and has an imidazole heme axial ligand. Numerous biological studies have suggested that an oxoiron(IV) porphyrin π -cation radical species known as compound I, is responsible for oxidation of chloride ion and for addition of a chloride ion to the ferryl oxygen atom of compound I to produce a transient ferric hypochlorite complex, Fe(III)-OCl. The ferric hypochlorite complex is believed to act as a key compound in the reactions leading to chlorination of organic substrates by CPO and antimicrobial activity in MPO. Although the oxidation process has been studied by multi-mixing stopped-flow experiments in which transiently formed compound I were reacted with chloride ion, spectroscopic evidence for the formation of the ferric hypochlorite complex has not been obtained and it remains unclear how compound I oxidizes chloride ion. Furthermore, the identity of the true chlorinating agent in the subsequent chlorination of organic substrates is not known and more information is needed about the exact roles of the hypochlorite adduct, free hypochlorous acid, and Cl₂. Here, we report the direct observation of oxidation of chloride ion with synthetic compound I model complexes and subsequent reactions leading to chlorination of organic compounds (Figure 3).

References

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