Structure-Function Relationship of Metalloenzymes

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Professional Employment
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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.

Selected Publications

- H. Fujii, "Effects of the Electron-Withdrawing Power of Substituents on the Electronic Structure and Reactivity in Oxoiron(IV) Porphyrin π-Cation Radical Complexes," *J. Am. Chem. Soc.* **115**, 4641–4648 (1993).
- H. Fujii, X. Zhang, T. Tomita, M. Ikeda-Saito and T. Yoshida, "A Role for Highly Conserved Carboxylate, Aspartate-140, in Oxygen Activation and Heme Degradation by Heme Oxygenase-1," *J. Am. Chem. Soc.* **123**, 6475–6485 (2001).
- H. Fujii, "^{13}C-NMR Signal Detection of Iron Bound Cyanide Ions in Ferric Cyanide Complexes of Heme Proteins," *J. Am. Chem. Soc.* **124**, 5936–5937 (2002).
- H. Fujii, X. Zhang and T. Yoshida, "Essential Amino Acid Residues Controlling the Unique Regioselectivity of Heme Oxygenase in *Psudomonas aeruginosa*," *J. Am. Chem. Soc.* **126**, 4466–4467 (2004).
- M. Kujime and H. Fujii, "Spectroscopic Characterization of Reaction Intermediates in Nitrite Reduction of Copper(I) Nitrite Complex as a Reaction Model for Copper Nitrite Reductase," *Angew. Chem., Int. Ed.* **45**, 1089–1092 (2006).
- C. Wang, T. Kurahashi and H. Fujii, "Structure and Reactivity of Iodosylarene Adduct of Manganese(IV) Salen Complex," *Angew. Chem., Int. Ed.* **51**, 7809–7811 (2012).
- A. Takahashi, D. Yamaki, K. Ikemura, T. Kurahashi, T. Ogura, M. Hada and H. Fujii, "The Effect of the Axial Ligand on the Reactivity of the Oxoiron(IV) Porphyrin π-Cation Radical Complex: Higher Stabilization of the Product State Relative to the Reactant State," *Inorg. Chem.* **51**, 7296–7305 (2012).
- Z. Cong, S. Yanagisawa, T. Kurahashi, T. Ogura, S. Nakashima and H. Fujii, "Synthesis, Characterization, and Reactivity of Hypochlorito-Iron(III) Porphyrin Complexes," *J. Am. Chem. Soc.* **134**, 20617–20620 (2012).

1. Oxygen-Atom Transfer from Iodosylarene Adducts of a Manganese(IV) Salen Complex: Effect of Arenes and Anions on I(III) of the Coordinated Iodosylarene[1)]

This paper reports preparation, characterization, and reactivity of iodosylarene adducts of a manganese-(IV) salen complex. In order to systematically investigate steric and electronic factors that control reactivity and selectivity, we prepared iodosylarene adducts from iodosylbenzene, iodosylmesitylene, 2,4,6-triethyliodosylbenzene, and pentafluoroiodosylbenzene. We also investigated the effect of anions on I(III) by using chloride, benzoate, and *p*-toluenesulfonate. Spectroscopic studies using ^{1}H NMR, electron paramagnetic resonance, infrared spectroscopy, and electrospray ionization mass spectrometry show that these iodosylarene adducts are manganese(IV) complexes bearing two iodosylarenes as external axial ligands. Reactions with thioanisole under the pseudo-first-order conditions show that the electron-withdrawing pentafluorophenyl group and the *p*-toluenesulfonate anion on I(III) significantly accelerate the oxygen-atom transfer. The high reactivity is correlated with a weakened I–OMn bond, as indicated by IR spectroscopy and mass spectrometry. Stoichiometric reactions with styrenes show that both enantioselectivity and diastereoselectivity are dependent on the arenes and anions on I(III) of the coordinate iodosylarenes. Notably, the pentafluorophenyl group and the *p*-toluenesulfonate anion suppress the *cis*-to-*trans* isomerization in the epoxidation of *cis*-β-methylstyrene. The present results show that iodosylarene adducts of manganese(IV) salen complexes are indeed active oxygen-atom-transfer reagents and that their reactivity and selectivity are regulated by steric and electronic properties of the arenes and anions on I(III) of the coordinated iodosylarenes.

2. Di-μ-oxo Dimetal Core of Mn^{IV} and Ti^{IV} as a Linker Between Two Chiral Salen Complexes Leading to the Stereoselective Formation of Different *M*- and *P*-Helical Structures[2)]

Because of restricted rotational freedom along the metal–metal axis, a di-μ-oxo dimetal core could be an excellent building block to create dinuclear compounds with well-defined stereochemistry, but their stereoselective synthesis remains a challenge. We herein report the formation of di-μ-oxo dimanganese(IV) complexes with tetradentate salen ligands bearing different degrees of steric bulk, in order to study stereochemical aspects of the dimerization reaction that potentially generates multiple stereoisomers. X-ray crystallography shows that the di-μ-oxo dimanganese(IV) complex with salen, where salen is (*R*,*R*)-*N*,*N*'-bis(3,5-di-*tert*-butylsalicylidene)-1,2-cyclohexanediamine, adopts a unique structure in which two salen complexes are arranged in an *M*-helical fashion. According to the solution study using ^{1}H, ^{2}H NMR, and circular dichroism spectroscopies, the dimerization reaction is highly diastereoselective in the presence of the *tert*-butyl group at the 3/3' position as a determinant steric factor. In contrast, the di-μ-oxo dititanium(IV) complex with the same salen ligand was previously reported to afford an opposite *P*-helical dimer. The present DFT study clarifies that a less-covalent Ti–O bonding causes a distortion of the di-μ-oxo dititanium(IV) core structure, generating a completely different framework for interligand interaction. The present study provides a solid basis to understand the stereochemistry for the formation of the di-μ-oxo dimetal core.

References

1) C. Wang, T. Kurahashi, K. Inomata, M. Hada and H. Fujii, *Inorg. Chem.* **52**, 9557–9566 (2013).

2) T. Kurahashi, M. Hada and H. Fujii, *Inorg. Chem.* **53**, 1070–1079 (2014).