Structure-Function Relationship of Metalloenzymes

Department of Life and Coordination-Complex Molecular Science
Division of Biomolecular Functions

FUJII, Hiroshi
Associate Professor

KURAHASHI, Takuya
Assistant Professor

CONG, Zhiqi Post-Doctoral Fellow
WANG, Chunlan Graduate Student
TANIZAWA, Misako Secretary

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. Comparative Spectroscopic Studies of Iron(III) and Manganese(III) Salen Complexes Having a Weakly-Coordinating Triflate Axial Ligand1)

Salen and porphyrin are among the most versatile synthetic ligands that are widely utilized as catalysts and materials. Both ligands are four-coordinate dianionic ligands that bind a metal ion in a tetradentate fashion, forming a similar square-planar metal complex. Prominently, iron and manganese, which are abundant transition metals in nature, become functional in combination with these ligands. In the case of porphyrin complexes, spectroscopic properties and electronic structures of iron(III) and manganese(III) complexes have been extensively studied, and some unique properties have been found, such as an intermediate spin state of an iron(III) ion in the presence of weak-field anionic axial ligands such as perchlorate (ClO_4^-) and triflate ($CF_3SO_3^-$).

However, relatively less has been investigated for salen complexes bearing these weak-field anionic axial ligands, while spectroscopic and magnetic properties of iron and manganese salen complexes with strongly-coordinating axial ligands such as imidazole are well documented. This is mostly because a monomeric iron(III) salen complex is quite prone to dimerization in the absence of a strongly-coordinating axial ligand. We previously designed a sterically-hindered salen ligand, and successfully synthesized a monomeric iron(III) and manganese(III) complex bearing a weakly-coordinating ClO_4^- ligand. But the sterically-hindered salen ligand is not necessarily suited for electronic tuning by modification of the phenolate rings, which prevented us to obtain in-depth insight into their spectroscopic properties.

We herein prepare mononuclear manganese(III) and iron(III) salen complexes bearing a weakly-coordinating triflate axial ligand, using salen ligands with differing electron-donating properties (Chart 1). We also synthesize nonsymmetrical salen ligands (Chart 1), in order to precisely understand spectroscopic properties. Magnetic susceptibility and dual-mode electron paramagnetic resonance (EPR) data show that iron(III) and manganese(III) salen complexes adopt high-spin d^5 (S = 5/2) and d^4 (S = 2) electronic configurations, respectively, in all the cases in Chart 1. Further insights into electronic structures of central metal are obtained from ^2H NMR spectra of selectively-deuterated complexes, in which Fe^{III}(salen)(OTf) and Mn^{III}(salen)(OTf) exhibit well-resolved paramagnetic NMR signals of quite different shift patterns, due to the presence or absence of the unpaired electron in the $dx^2–y^2$ orbital.

2. Synthesis, Characterization, and Reactivity of Hypochlorito-Iron(III) Porphyrin Complexes2)

Myeloperoxidase (MPO) and chloroperoxidase (CPO) are unique heme peroxidases that catalyze oxidation of chloride ion to hypochlorite ion (OCl^-). MPO is loctaed in azurophil granules of neutrophils and produces OCl^- or hypochlorous acid (HOCl), which works as an antimicrobial agent, from hydrogen peroxide and chloride ion. On the other hand, CPO is an enzyme of *Caldariomyces fumago* and catalyzes chlorination reactions in the biosynthesis of the chlorinated metabolite caldariomycin. It has been proposed that ferric MPO and CPO initially react with hydrogen peroxide to form an oxoiron(IV) porphyrin π-cation radical species known as compound I. Compound I then reacts with chloride ion to form a transient hypochlorito-iron(III) porphyrin intermediate, which finally releases HOCl with the protonation of the heme-bound hypochlorite. In addition, hypochlorito-metal complexes have been proposed as key intermediates in catalytic oxygenation reactions catalyzed by transition-metal complexes. Because of its significant importance, a hypochlorito-iron(III) porphyrin intermediate has been examined to detect in MPO and CPO reactions and to synthesize its model complex. Although previous reports have indicated the possibility of formation of hypochlorito-iron(III) porphyrin intermediates, spectroscopic evidence for the formation of such species has not been reported until now. The reactivity of a hypochlorito-iron(III) porphyrin complex has been also received much attention in relation to those of other terminal oxidant-metal complexes such as hypochlorite, hydroperoxide, and iodosylarene. Herein, we report the preparation, spectroscopic characterization, and reactivity of hypochlorito-iron(III) porphyrin complexes, including a bis-hypochlorite complex, $[(TPFP)Fe^{III}(OCl)_2]^-$ (**1**), and imidazole-hypochlorite complexes, $(TPFP)Fe^{III}(OCl)$ (1-R-Im), where TPFP is 5,10,15,20-tetrakis(pentafluorophenyl) porphyrinate and R is $–CH_3$ (**2**), –H (**3**), or $–CH_2CO_2H$ (**4**). (see Figure 1).

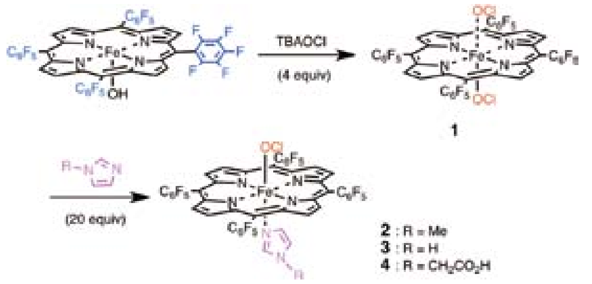

Figure 1. Preparation of hypochlorito-iron(III) porphyrin complexes.

3. Unique Ligand Radical Character of an Activated Cobalt Salen Catalyst that Is Generated by Aerobic Oxidation of a Cobalt(II) Salen Complex[3]

The Co(salen)(X) complex, where salen is chiral *N*,*N*’-bis(3,5-di-*tert*-butylsalicylidene)-1,2-cyclohexanediamine, and X is an external axial ligand, has been widely utilized as a versatile catalyst. The Co(salen)(X) complex is a stable solid that has been conventionally described as a Co^{III}(salen)(X) complex. Recent theoretical calculations raised a new proposal that the $Co(salen)(H_2O)(SbF_6)$ complex contains appreciable contribution from a $Co^{II}(salen^{+\bullet})$ electronic structure (Kochem, A.; Kanso, H.; Baptiste, B.; Arora, H.; Philouze, C.; Jarjayes, O.; Vezin, H.; Luneau, D.; Orio, M.; Thomas, F. *Inorg. Chem.* **51**, 10557–10571 (2012)), while other theoretical calculations for Co(salen)(Cl) indicated a triplet Co^{III}(salen) electronic structure (Kemper, S.; Hrobárik, P.; Kaupp, M.; Schlörer, N. E. *J. Am. Chem. Soc.* **131**, 4172–4173 (2009)). However, there has been no experimental data to evaluate these theoretical proposals. We herein report key experimental data on the electronic structure of the Co(salen)(X) complex ($X = CF_3SO_3^-$, SbF_6^-, and $p\text{-}MeC_6H_4SO_3^-$). The X-ray crystallography shows that Co(salen)(OTf) has a square-planar N_2O_2 equatorial coordination sphere with OTf as an elongated external axial ligand. Magnetic susceptibility data indicate that Co(salen)(OTf) complexes belong to the $S = 1$ spin system. ^1H NMR measurements provide convincing evidence for the $Co^{II}(salen^{+\bullet})$(X) character, which is estimated to be about 40% in addition to 60% Co^{III}(salen)(X) character. The CH_2Cl_2 solution of Co(salen)(X) shows an intense near-infrared absorption, which is assigned as overlapped transitions from a ligand-to-metal charge transfer in Co^{III}(salen)(X) and a ligand-to-ligand charge transfer in $Co^{II}(salen^{+\bullet})$(X). The present experimental study establishes that the electronic structure of Co(salen)(X) contains both $Co^{II}(salen^{+\bullet})$(X) and Co^{III}(salen)(X) character.

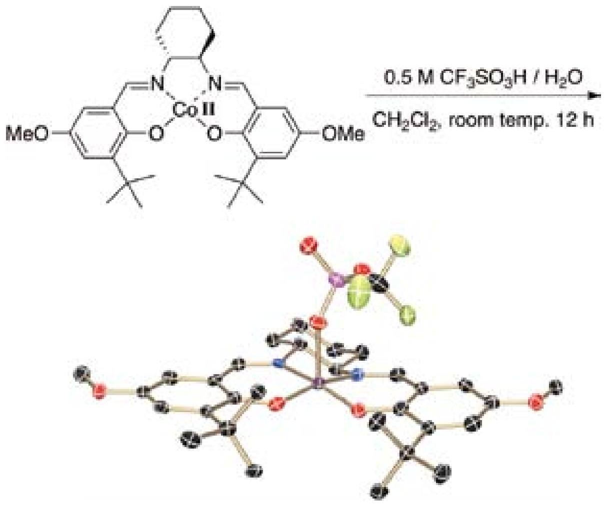

Figure 2. Preparation and Structure of Co(salen)(OTf) complex.

References

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3) T. Kurahashi and H. Fujii, *Inorg. Chem.* **52**, 3908–3919 (2013).

Award

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