Catalysis of Metal Ions in Biological System — Coordination environment of metal center in the active site of non-heme metalloenzymes and their catalyses —

Shiro Hikichi
Department of material and life chemistry, Kanagawa University,
3-27-1, Rokkakubashi, Kanagawa-ku, Yokohama 221-8686, Japan
E-mail; hikichi@kanagawa-u.ac.jp

Non-heme metalloenzymes, which do not contain a porphyrinate ligand, catalyze wide range of chemical reactions ranging from non-redox reaction (e.g., hydrolysis of ester bonds of peptides and nucleic acids) to redox (i.e., reduction and oxidation) reactions.[1] The active metal centers of these enzymes are supported by hetero atom (i.e. N, O, S) donors originated from amino acid residues and peptide bond backbone of the protein. The coordination environment of the metal center may be a key factor for the controlling the catalysis of these enzymes due to the Lewis acidity, oxidation state and spin configuration of metal ions are correlated with the kind of supporting ligands, coordination number, and geometry of metal center.

Oxygenation of organic compounds is catalyzed by oxygenases. The active sites of non-heme oxygenases are composed of Fe or Cu ions: O_2 molecule is activated via electron transfer from the metal center. The reactivity of the resulting reduced oxygen species depends on the properties of the coupled metal centers (kind of element, oxidation and spin states, coordination geometry, *etc.*). In fact, oxide anion (O^{2-}) bound on high-valent iron (Fe(IV) or Fe(V)) center(s) may be the reactive species in the hydroxylation of alkanes (including methane). This oxide anion is formally generated by four-electron reduction of O_2, and therefore, the oxidation process can be disclosed as "reductive oxidation". In contrast to the heme iron oxygenases (e.g., cytochrome P-450; the active site is mononuclear Fe center), the nuclearity of active metal ions is various in the non-heme enzymes. Some enzymes are composed of multi-nuclear Fe and Cu centers: Such active sites may be of advantage to activate oxygen via multi-electronic reduction process. Interestingly, the mononuclear Fe centers of various non-heme oxygenases show common coordination environment; two imidazolyl and one carboxylate are ligated to Fe center, and the remaining coordination sites seem to be O_2 and/or substrates binding sites. The studies on the model compounds contribute to reveal the relationship between the coordination environment (electronic and structural properties) of the metal center and the catalytic reaction mechanism of enzymes (Figure 1).[2]

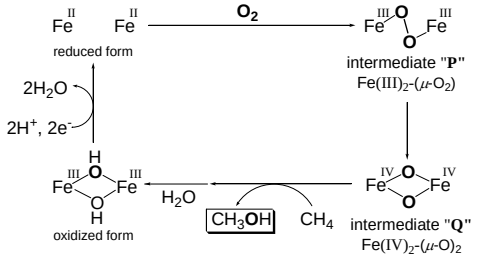

Figure 1. Proposed reaction mechanism for methane monooxygenase (non-heme Fe enzymes) via reductive oxidation process.

[1] (a) Lippard, S. J.; Berg, J. M. *Principles of Bioinorganic Chemistry*, University Science Books: Mill Valley, CA, 1994. (b) Special thematic issue on "*Bioinorganic Enzymology*" (R. H. Holm and E. I. Solomon, eds.), *Chem. Rev.* **96**, 2237–3042 (1996). (c) S. Hikichi, *Catalyst and Catalysis* (*Shokubai*), **46** (2004) 262 (in Japanese).
[2] (a) Special thematic issue on "*Biomimetic Inorganic Chemistry*" (R. H. Holm and E. I. Solomon, eds.), *Chem. Rev.* **104**, 347–1200 (2004). (b) Akita, M.; Hikichi, S. *Bull. Chem. Soc. Jpn.*, **75**, 1657 (2002).