【Grant-in-Aid for Specially Promoted Research】
Science and Engineering (Chemistry)

Title of Project : Bioinorganic Chemistry of Oxidoreductases having Unique Active Site Clusters

Kazuyuki Tatsumi
(Nagoya University, Research Center for Materials Science, Professor)

Research Area : Bioinorganic Chemistry, Coordination Chemistry, Organometallic Chemistry
Keyword : Nitrogenase, Hydrogenase, Photosystem II, Transition Metal Cluster

【Purpose and Background of the Research】

An important and pressing mission of chemists has been to synthesize model active-sites of metalloenzymes in vitro and to elucidate the mechanisms of the biological functions, which would eventually lead to artificial enzymes equivalent or even superior to nature's. The investigation of reductases has made a rapid progress in recent years, unfolding novel structures and functions of the active centers consisting of metal sulfide/thiolate clusters, and greatly expanding our established knowledge of chemistry. On the other hand, the structure of photosystem II has been determined, revealing a unique manganese oxide cluster structure at the oxygen-evolving center.

In this project, we challenge the chemical synthesis of these metal sulfide/oxide cluster active sites, where a new method to build clusters in non-polar solvents will be utilized extensively in order to avoid degradation of meta-stable cluster structures. Based upon newly revealed model clusters, we will elucidate the biosynthetic mechanism of the cluster active sites and enzymatic functions.

【Research Methods】

1) Oxygen-evolving center of Photosystem II: We will synthesize [3Mn-Ca-4O-Mn] clusters using various bulky alkoxides in order to control the reactions, and their reactions will be examined.
2) Nitrogenase: Highly improved [8Fe-7S] P-cluster models compared to our early models will be synthesized, and their redox properties studied. Synthesis and reactions of FeMo-co model clusters will also be attempted.
3) Acetyl CoA synthase: [4Fe-4S] cluster will be conjointed to a series of our dinuclear nickel models, and their functions examined.
4) CO dehydrogenase: Synthesis and reactions of [Ni-4Fe-5S] active site model clusters will be examined, where preformed [3Fe-4S] clusters and sulfide-bridged Ni-Fe complexes are utilized.
5) [NiFe] hydrogenase: In addition to our reported oxidized state active site models, reduced state Ni-Fe dinuclear models are to be synthesized, and their reactions with H_2 or H^+ are to be investigated.
6) Unsymmetrical [4Fe-4S] clusters: The 1:3 site-differentiated [4Fe-4S] clusters modeling those found in [NiFe] hydrogenase and DPOR are to be synthesized.

Furthermore, we will expand the scope of bioinorganic chemistry in close cooperation with biochemistry, and will probe the ingenious functions of cluster active sites.

【Expected Research Achievements and Scientific Significance】

This research project is expected not only to bring about new foundations for our understanding the chemistry of enzymes, but also to create new chemistry concepts and environmentally-benign catalysts. For instance, the Haber-Bosch process to make ammonia are very energy-intensive, and 1-2% of the world's total energy output goes to ammonia synthesis. Thus, mimicking the function of nitrogenase would significantly impact the world's energy consumption. The research on the bio-inspired activation of H_2, H_2O, CO, and on bio-inspired synthesis of H_2 and O_2 from water will promote development of advanced science-based innovation and will contribute significantly to realizing a sustainable society.

【Publications Relevant to the Project】

[1]"Synthesis, Structures, and Electronic Properties of [8Fe-7S] Cluster Complexes Modeling the Nitrogenase P-Cluster", Y. Ohki, M. Imada, S. Ohta, and K. Tatsumi, *J. Am. Chem. Soc.*, **131**, 13168-13178 (2009).
[2] A Model for the CO-Inhibited Form of [NiFe] Hydrogenase: Synthesis of $(CO)_3Fe(\mu\text{-}S^tBu)_3Ni\{SC_6H_3\text{-}2,6\text{-}(mesityl)_2\}$ and Reversible CO Addition at the Ni Site. Y. Ohki, K. Yasumura, M. Ando, S. Shimokata, and K. Tatsumi, *Proc. Nat. Acad. Sci. ,USA*, *107*, 3994-3997 (2010).

【Term of Project】 FY2011-2015

【Budget Allocation】 309, 800 Thousand Yen

【 Homepage Address and Other Contact Information】

http://inorg.chem.nagoya-u.ac.jp/e-frame.html