Japan Academy Prize to:

Kazuyuki Tatsumi
Designated Professor, Research Center for Materials Science and Professor Emeritus, Nagoya University

for “Study on Bioinorganic Chemistry of the Active Sites of Metalloreductases”

Outline of the work:

Metalloenzymes are essential for all living organisms on earth, as their metal-incorporating active centers play a major role in regulating highly efficient/selective enzymatic functions. In particular, the research on reductases and related metalloenzymes has progressed rapidly in recent years, unraveling novel structures and functions of the cluster active centers and greatly expanding the established knowledge of chemistry. Newly discovered reductases show remarkable activities, exemplified by nitrogenases catalyzing the reduction of dinitrogen into ammonia, hydrogenases reversibly converting dihydrogen into protons and electrons, and acetyl CoA synthase forming acetyl CoA from carbon monoxide, methyl cobalamin, and coenzyme A (CoA). The brilliant functions of these enzymes stand out as a microcosm of the “the mystery of nature” that modern science should strive to understand, and thus the importance of chemical research on the structure-function relationship of the active sites has been recognized.

Using his theoretical background ingrained from his earlier academic career as a guiding principle, Prof. Kazuyuki Tatsumi has discovered a unique method to synthesize transition metal sulfur clusters based on the highly developed synthetic coordination chemistry in Japan. Prof. Tatsumi has had many successes in the chemical synthesis of cluster compounds modeling the sophisticated and unstable cluster active sites of reductases and elucidating their electronic properties and reactivity. His pioneering work has led the development and stood on the forefront of bioinorganic chemistry of reductases throughout the world. Summarized below are Prof. Tatsumi’s major scientific achievements.

(1) Chemical synthesis of the nitrogenase active sites and their electronic properties

The iron-sulfide clusters in the active centers of nitrogenase have been long-standing targets of synthetic chemists and are extremely challenging due to the instability and complexity of the cluster structures. Prof. Tatsumi has developed a new method for synthesizing transition metal sulfur clusters in non-polar solvents using bulky thiolates, and he synthesized the inorganic core of nitrogenase P-cluster for the first time, which had previously been thought impossible to construct chemically. The model P-cluster was found to exhibit two-step one-electron redox processes, indicating the existence of an intermediate oxidation state. Based on the Mössbauer spectra, two ferric sites in the P-cluster core of the doubly-oxidized 2Fe(III)6Fe(II) state were identified, and correlation between the structure and oxidation state of the P-cluster was elucidated. Furthermore, [1Mo4Fe9S] and [8Fe6S1O] cluster compounds were synthesized and are currently recognized as the optimal structural model for the iron-molybdenum co-factor (FeMo-co) of nitrogenase, which is widely thought to fix dinitrogen. Moreover, a new type of [8Fe7S] cluster compound was synthesized, the structure of which links the P-cluster and FeMo-co cores topologically. This [8Fe7S] cluster may act as a good model for the iron-iron co-factor (FeFe-co) once the structure of FeFe-co in the Fe-nitrogenase is elucidated.
(2) Chemical synthesis of the [NiFe]-hydrogenase active sites and the model reactions

Establishment of a new low-temperature synthetic route pioneered the isolation of a series of dinuclear Ni-Fe complexes as excellent structural models for the active site of [NiFe] hydrogenase in either oxidized or reduced form. As one example, a dinuclear Ni(II)-Fe(II) complex having both carbon monoxide and cyanide at the iron site was synthesized, in which the infrared spectra successfully reproduced the spectra of an oxidized form of hydrogenase. Also successful were the syntheses of Ni(0)-Fe(II) complexes modeling the reduced form of hydrogenase, and a model complex for CO-inhibited form. Additionally, sulfido-bridged W-Ru and Ge-Ru complexes as well as an Ir thiolate complex were synthesized, and these complexes have been found to induce heterolytic cleavage of molecular hydrogen under mild conditions corresponding to the function of hydrogenase.

(3) Chemical synthesis of the active site of acetyl CoA synthase and the functional model

Making use of S2N2 macrocyclic ligands, which mimic the coordination of amino acids in acetyl CoA synthase at the Ni site, a series of unprecedented dinuclear nickel models was constructed. As an example, the dinuclear nickel complex Ni(S2N2)-Ni derived as a result was treated with a methyl-cobalamin model complex and 2,6-dimethylphenyl thiolate, and the starting reaction intermediate model complex was regenerated, completing a reaction cycle modeling the enzymatic function of acetyl CoA synthase.

As summarized above, Prof. Tatsumi has revealed new facets of bioinorganic chemistry and has dedicated himself to expanding the scope of the discipline based on the successful chemical synthesis of the cluster active sites of reductases, previously thought to have been very difficult. His research has provided a scientific foundation for further elucidation of enzymatic functions and has contributed greatly to the development of biochemistry of reductases, for which Prof. Tatsumi received the Inoue Prize for Science (1998), the Humboldt Award (2004), the Chemical Society of Japan Award (2006), and the Seibold Prize (2011). He was also awarded an honorary doctorate from the University of Münster in Germany in 2011 and is currently serving as President of the International Union of Pure and Applied Chemistry, the international organization acting as the preeminent representative for chemical communities throughout the world.

Selected Publications

4. “Synthesis of Bis{(2-dimethylphosphino)ethane-1-thiolato} bis(t-butylthiolato) Molybdenum (IV) and
13


15. “Cooperative Catalytic Activation of Si-H Bonds by a Polar Ru-S Bond: Regioselective Low