Chemical Approaches to Complex Heterometal Sites in Biology

R. H. Holm*, C. Berlinguette, S. Bhaduri, D. Hong, J. Jiang, R. Panda, and P. V. Rao

Department of Chemistry and Chemical Biology, Harvard University, Cambridge, MA 02138

Bridged metal-sulfur assemblies, consisting of two recognizable entities juxtaposed by one or more covalent bridges, are among the most complex metal sites in biology. Examples include the catalytic centers of sulfite oxidase, [Fe]-hydrogenases, [NiFe]-hydrogenases, nitrogenase, and carbon monoxide dehydrogenase (CODH). The synthesis of structural and functional analogues of these sites provides a major challenge in biomimetic inorganic chemistry. Synthetic approaches to bridged assemblies will be summarized, with emphasis on the P^N $\{Fe_8S_7(S_{Cys})_2\}$ and FeMo-cofactor $\{MoFe_7S_9\}$ clusters of nitrogenase, and the A-cluster ($\{Fe_4S_4\}$-(μ_2-S_{Cys})-Ni[(μ_2-S_{Cys})$_2$Gly]Ni}, acetylcoenzyme A synthase site) and C-cluster ($\{NiFe_4S_5\}$, CO/CO_2 interconversion site) of CODH will be emphasized. New reactions and structures will be discussed, including realization of the P^N topology in Mo/V-Fe-S clusters, thiolate bridging interactions between an Fe_4S_4 and Ni^{II} and two Fe_4S_4 clusters, and the synthesis and properties of cubanoid MFe_3S_4 clusters (M = Ni, Pd, Pt) containing planar M^{II} sites as in the C-cluster of CODH. The feasibility of attaining these bridged assemblies without the stabilizing influence of protein structure will be considered.