MODELING THE NICKEL-CONTAINING ACTIVE SITE OF ACETYL COA SYNTHASE

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The bifunctional enzyme carbon monoxide dehydrogenase/acetate-CoA synthase (CODH/ACS) catalyzes the reduction of CO2 to CO and the formation of acetyl-CoA from CO and CH3 in methanogenic bacteria. The ACS active site contains a unique Ni-Ni-[Fe4-S4] complex. The chemistry of the enzyme can be explored through inorganic models mimicking the electronic and physical properties of this active site. Our lab has synthesized and studied the reactivity of model complexes toward various substituents to determine the mechanism of acetyl-CoA formation. The presence of two Ni atoms, each with a distinct coordination environment, has led to confusion over the mechanism. My research with various model compounds is consistent with a proposed mechanism where the enzymatic chemistry occurs at the central Ni atom. The role of the second Ni atom remains uncertain and continues to be investigated.