

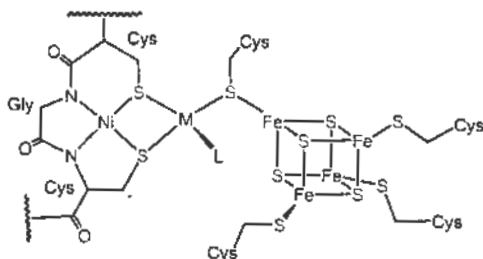
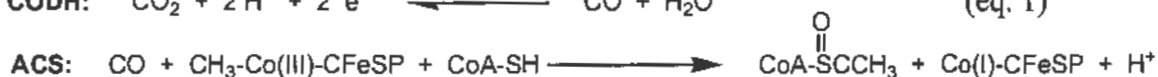
# Active Site Models for the Organometallic Enzyme Acetyl CoA Synthase (ACS): Nickel Carbonyl in Nature?

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Studies on evolutionarily-optimized reaction centers promise to inspire new types of organometallic catalysts. The recent crystallographic characterization of the bifunctional metalloenzyme carbon monoxide dehydrogenase/acetyl coA synthase (CODH/ACS) provides important insights into the bio-processing of carbon monoxide. Annual CO removal from the lower atmosphere by bacteria is  $\sim 1 \times 10^8$  tons.<sup>1</sup> The reactions catalyzed by CODH/ACS are shown in equations 1 and 2.<sup>1</sup>



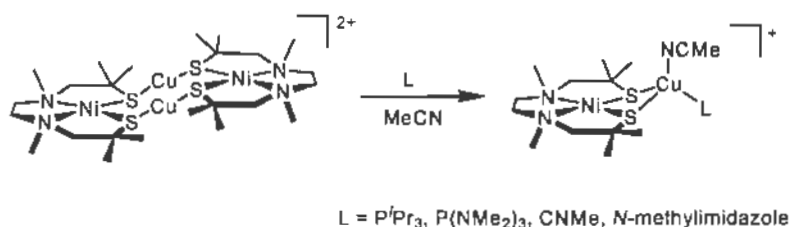
(eq. 2)

**Figure 1:** Active Site Structure of Acetyl CoA Synthase

The active site for ACS, the A-cluster, has an unprecedented three-component system, as shown in Figure 1.<sup>2,3</sup> The distal nickel ion is bound in a diamidodithiolato coordination sphere, provided by the cysteine-glycine-cysteine peptide sequence. The nitrogen donors are deprotonated protein backbone amide ligands, a motif uncovered in only two other metalloenzyme systems.<sup>4,5</sup> The thiolate ligands bridge to a metal in the proximal site. The initial crystallographic characterization of the enzyme determined the metal in the proximal site to be copper.<sup>2</sup> However, in more recent work, both a zinc and nickel have been found in this position.<sup>3</sup> Biochemical experiments have determined that nickel is the metal found in the proximal site in the active form of the enzyme.<sup>6</sup> The proximal metal is further bound to an unidentified non-protein ligand, which has been modeled as a carbonyl or acyl group, and an  $[\text{Fe}_4\text{S}_4(\text{SR})_4]$  cubane via a bridging thiolate. Producing single-molecule bimetallic models of the active site may lead to a better understanding of the mechanism of the enzyme, or perhaps to biologically-inspired catalysts for the removal of CO from the atmosphere.

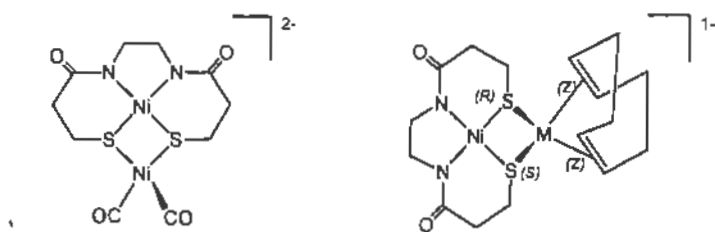
Copper-nickel heterobimetallic species were initially pursued as first generation models of the ACS active site.<sup>7</sup> The 1:1 reaction of  $[\text{Cu}(\text{MeCN})_4]^+$  with a

diaminodithiolato-nickel metalloligand produced a dimeric compound which could be cleaved with a series of donor ligands ( $P^iPr_3$ ,  $P(NMe_2)_3$ , CNMe, N-methylimidazole) (Figure 2).<sup>8,9</sup> Cleavage produced square planar nickel(II)-tetrahedral copper(I) compounds which bore resemblance to the active site. The synthesis of a “biomimetic” dianionic diamidodithiolato-nickel metalloligand,  $(Et_4N)_2[NiN_2S_2O_2C_8H_{12}]$ , led to the isolation of a square planar nickel(II)-trigonal planar copper(I) model,  $(Et_4N)[(NiN_2S_2O_2C_8H_{12})(Cu(P^iPr_3))]$ .<sup>10</sup> None of the nickel-copper models demonstrated reactivity with carbon monoxide, a substrate for ACS which has been postulated to be the unidentified ligand in the ACS crystal structure.



**Figure 2:** Cleavage of Copper-Nickel Dimeric Compound with Donor Ligands

A second crystallographic characterization of the active site of ACS indicated that the identity of the metal in the proximal site is nickel in the active form of the enzyme. The reaction of  $[Ni(cod)_2]$  (cod = 1,5-cyclooctadiene) and  $(Et_4N)_2[NiN_2S_2O_2C_8H_{12}]$  in the presence of carbon monoxide yielded the square planar nickel(II)-tetrahedral nickel(0) model  $(Et_4N)_2[(NiN_2S_2O_2C_8H_{12})(Ni(CO)_2)]$ , shown in Figure 3.<sup>7</sup> This model provides evidence for the  $Ni^{II}$ - $Ni^0$  structure of ACS and demonstrates some of the characteristics of the ACS active site, e.g. lability of the proximal nickel.



**Figure 3:** Structures of the Ni(II)-Ni(0) ACS Model (left) and the Diamidodithiolato-Nickel Rhodium/Iridium-Cyclooctadiene Complex (M = Ir, Rh) (right)

The dianionic diamidodithiolato-nickel metalloligand may also be used to support catalytic metal centers much as a diphosphine does. The geometry of the metalloligand, the dianionic charge, and the presence of another metal close to the catalytic metal center may have effects on catalysis.<sup>11</sup> The reaction of  $[M(cod)Cl]_2$  with two equivalents of  $(Et_4N)_2[NiN_2S_2O_2C_8H_{12}]$  in the presence of  $NaBPh_4$  yielded the compounds  $(Et_4N)_2[(NiN_2S_2O_2C_8H_{12})(M(cod))]$  (M = Ir, Rh) (Figure 3). These compounds react

with CO to liberate 1,5-cyclooctadiene and form the corresponding dicarbonyl species. We will further investigate the ability of these compounds to hydrogenate olefins, in a similar fashion to  $M(\text{cod})\text{P}_2$  systems ( $M = \text{Ir}, \text{Rh}$ ).<sup>12</sup> Complexes incorporating biologically-inspired ligands may lead to new and exciting discoveries in organometallic catalysis.

## References

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