

Model Complexes for the A-Cluster of CODH/ACS; Incorporation of Thiolate Donation Using 2,2'-Dithiodibenzaldehyde

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1. Introduction

Carbon Monoxide Dehydrogenase / Acetyl CoA Synthase (CODH/ACS) is a bifunctional enzyme that catalyzes the reduction of CO₂ to CO and the assembly of Acetyl CoA [1]. There are four metal-containing domains in this enzyme, the A, B, C, and D-clusters. The A and C-clusters catalyze the previously mentioned reactions, with the A-cluster catalyzing the assembly reaction and the C-cluster catalyzing the reduction reaction, while the B and D-clusters are present for electron transfer. The A-cluster has a number of features which distinguish it from other naturally-occurring metalloenzymes: it is one of few enzymes which contain an active-site nickel atom, some of the donors to the metal are amide nitrogens from the protein backbone, and the catalytic cycle involves an organometallic intermediate with a coordinated methyl group.

The A-cluster active site of CODH/ACS, as seen in Figure 1, contains a Fe-S cubane bridged by a cysteine thiolate to a dinuclear M(μ-S)M' cluster where both M and M' are nickel in the active enzyme [2,3]. This project focuses on the synthesis of model complexes for the dinuclear metal center. Model complexes are useful in gaining a more complete understanding of the catalytic mechanisms. The goal is to synthesize a compound with two central nickel atoms: one, Ni_p, having both a nitrogen and sulfur bound, (NS coordination), the other, Ni_d, with two nitrogen atoms, (NN coordination), and for these two nickel atoms to be bridged by an additional two sulfur atoms, as shown in Figure 2.

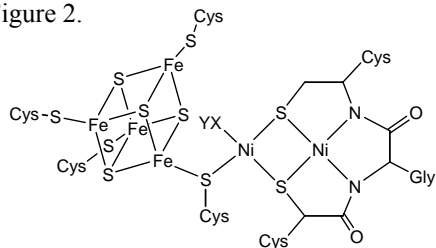


Figure 1: Expansion of the A-cluster of CODH/ACS

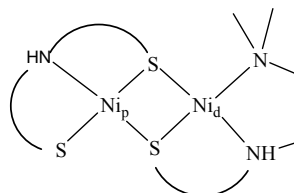


Figure 2: Desired dinuclear nickel model complex of A-cluster

2. Experimental

We are using 2,2'-dithiodibenzaldehyde (DTDB, Figure 3), an air-stable disulfide, to introduce thiolate coordination to a transition metal by allowing it to react with a transition metal complex that contains a coordinated primary amine [4]. Preliminary metal complexes (Ni(NN)₂⁺ and Ni(NS)₂) are formed by reacting 2 equivalents of a diamine or amine/thiol ligand with a nickel (II) salt. These are then combined with DTDB in CH₃OH/CH₂Cl₂, which are isolated by differential precipitation.

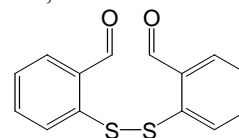
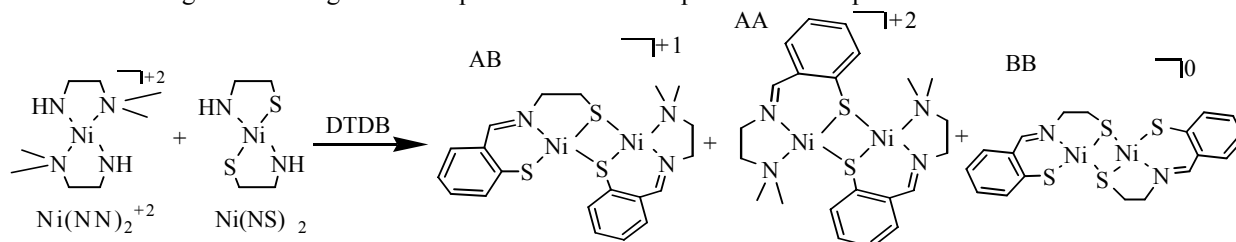


Figure 3. Dithiodibenzaldehyde (DTDB)

3. Results and Discussion

Reaction of Ni(NN)₂ with DTDB is expected to form a N₂S coordinated nickel complex which will be further noted as fragment A. The other two reactant complexes, Ni(NS)₂, with DTDB have been shown to form a NS₂ coordinated nickel complex [5], which will be noted as fragment B. As illustrated in Figure 2, our desired model

complex has one component each of fragment A and fragment B. This is model complex AB. Using equivalent molar ratios of ligand A and ligand B is expected to form three products in this procedure as illustrated:



Scheme 1: Reaction procedure for synthesis of the three metal complexes

These three metal complexes labeled, AA, AB, and BB, have different charges due to the number of thiolate sulfur atoms present. This should lead to different solubilities based on solvent polarity. Neutral BB is insoluble in polar solvents, and can be isolated by washing the product mixture with a very non-polar solvent such as toluene. Separating the other two charged species is done through the use of solvents of differing polarities since AA is expected to be much more soluble in more polar solvents than AB due to its +2 charge.

The BB nickel dimer has been synthesized and fully characterized by our group [5]. Reaction of N,N-dimethylethylenediamine, **DTDB**, and NiCl₂ or Ni(NO₃)₂ results in the isolation of NiA-Cl or NiA-NO₃, in which Ni is coordinated by the desired tridentate N₂S ligand, but the fourth coordination site is occupied by the anion. These have been characterized by X-ray crystallography (Fig. 4). ESI-Mass spectrometry of the reaction mixture which yielded NiA-Cl (Fig. 5) shows a peak corresponding to the AA dimer (*m/z*=566), providing evidence that fragment A is capable of forming a dimeric species. In order to avoid coordination of the anion, we carried out the reaction in Scheme 1 using the BF₄⁻ salt of Ni(NN)₂⁺. After washing with toluene to remove any BB dimer and extracting the precipitate with acetonitrile, ESI-MS characterization of this reaction (Fig. 6) shows a peak corresponding to the AB dimer at *m/z* = 518.

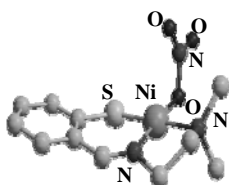


Figure 4. Crystal structure of NiA-NO₃

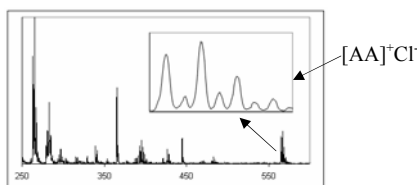


Figure 5. ESI-MS spectra for [AA]⁺Cl⁻

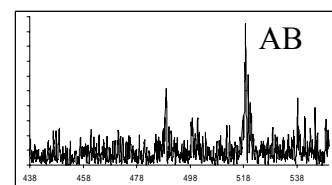


Figure 6. ESI-MS of AB

4. Conclusions

Isolation and characterization of NiA-NO₃ and NiA-Cl demonstrates that DTDB will combine with N,N-dimethylethylenediamine to form an N₂S ligand. Identification of the AA dimer by mass spectrometry demonstrates the ability of this ligand to bridge two Ni atoms. The desired AB complex, which serves as a first-generation model for the dinuclear portion of the CODH/ACS A-cluster, has been identified by mass spectrometry.

5. Acknowledgements

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