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Progress Report

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 "Catalytic Oxidation of Hydrocarbons by Dinuclear Iron Complexes"
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Our efforts during the past eight months were directed towards characterizing synthetic complexes that model the electronic and reactivity properties of the active site of methane monooxygenase (MMO), a metalloenzyme found in methanotrophic bacteria responsible for the biological oxidation of methane to methanol.¹⁻⁵ We have investigated the structural/electronic and reactivity properties of a series of dinuclear model complexes that can function as oxygen atom transfer catalysts.^{1,2} In particular, our studies focused on $[\text{Fe}^{2+}_2(\text{H}_2\text{Hbab})_2(\text{N-MeIm})_2]$, 1, its DMF solvated form, $[\text{Fe}^{2+}_2(\text{H}_2\text{Hbab})_2(\text{DMF})_2(\text{N-MeIm})]$, 2, and the mixed valent species $[\text{Fe}^{2+}\text{Fe}^{3+}(\text{H}_2\text{Hbab})_2(\text{DMF})_4]^+$, 3, (H_4Hbab = 1,2-bis(2-hydroxybenzamido) benzene). We have also examined $[\text{Fe}^{3+}_2(\text{H}_2\text{Hbab})_2(\text{DMF})_4]^{2+}$, 4, $[\text{Fe}^{3+}_2(\text{H}_2\text{Hbab})_2(\text{OMe})_2]$, 5, and μ -oxo- $[\text{Fe}^{3+}_2(\text{H}_2\text{Hbab})_2(\text{DMF})_2]$, 6, which are unable to act as oxygen atom transfer catalysts.

Our spectroscopic analyses indicate that 1 and 2, which are crystallographically characterized, are excellent electronic environment models for the reduced active site of MMO.^{2,3} Results from isothermal distillation studies as well as solid state and frozen solution EXAFS experiments (performed in collaboration with Dr. James Penner-Hahn, Dept. Chemistry, Univ. Michigan) indicate that the integrity of the complex is maintained in solution. This conclusion is consistent with that obtained from the analysis of temperature dependent magnetic susceptibility measurements, performed by my lab at Tufts University Physics Department, and field and temperature dependent Mössbauer spectroscopic studies (performed in collaboration with Dr. Peter Debrunner, Physics Dept. University of Illinois). These solid state and frozen solution studies also indicate that the ferrous centers in our complexes are weakly ferromagnetically coupled, a phenomenon observed in reduced MMO. We are currently simulating the field and temperature dependent SQUID data collected at Tufts using the spin Hamiltonian for dinuclear ferrous systems in order to obtain a more detailed understanding of the electronic characteristics of 1 and 2. Owing to the inherent difficulties analyzing ferrous centers by Mössbauer and magnetic susceptibility studies, we have recently sent samples of 1 and 2 to the Solomon lab at Stanford University for characterization by low temperature magnetic circular dichroism spectroscopy. This multi-technique approach will allow us to obtain unusually deep insight into the electronic characteristics of a crystallographically characterized atom transfer catalyst that when compared to the spectroscopic characterizations of the active sites of methane monooxygenase, ribonucleotide reductase, and hemerythrin should begin to define the basis for the observed differences in reactivity towards molecular oxygen.

The mixed-valence dinuclear species, 3, can be cleanly synthesized in good yield either by electrochemical methods or the addition of a variety of chemical oxidants ($K_{\text{com}} \approx 10^5$).⁴ Cyclic voltammetry experiments indicate that the one-electron oxidation of 2 to 3 is quasi-reversible, ΔE being scan rate dependent. Mössbauer, EPR and magnetic susceptibility measurements are consistent with equal populations of ferrous and ferric sites that exhibit weak through space dipolar coupling. This is unlike all previous mixed valent iron complexes that are characterized by an $S = 1/2$ ground state indicative of antiferromagnetic coupling. The addition of exogenous ligands capable of bridging the iron centers leads to disproportionation of 3 to 2 and 4. These data suggest that 3 lacks any direct atom bridge between the metal centers, a conclusion supported by the absence of an observable Fe-Fe vector in either solid state or frozen solution EXAFS studies (uncorrelated motion of the two iron centers) and the unusual features observed in the electrochemical oxidation of 2 ($[\text{Fe}^{2+}, \text{Fe}^{2+}] / [\text{Fe}^{2+}, \text{Fe}^{3+}]$ and $[\text{Fe}^{2+}, \text{Fe}^{3+}] / [\text{Fe}^{3+}, \text{Fe}^{3+}]$ couples separated by only 250 mV).

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The diferric complex, 4, can be cleanly synthesized in good yield either by electrochemical methods or the addition of a variety of chemical oxidants; the electrochemical oxidation of the mixed valent species to the diferric species is strictly reversible.⁵ Mössbauer, EPR, EXAFS and magnetic susceptibility measurements of this species are consistent with high spin diferric centers. This data also suggests that 4 does not contain any direct bridge between the iron centers. In the presence of methanol and base, however, we can quantitatively isolate the di- μ -methoxy bridged iron dimer, 5, whose crystal structure was solved. This complex can be synthesized by a variety of methods including the air oxidation of the diferrous complex 1 in the presence of methanol. The electronic characteristics of this complex are consistent with other dialkoxy bridged ferric dimers ($J = -12.5 \text{ cm}^{-1}$). Furthermore, the addition of H^+ to solutions of 5 generates complex 4.

The structure of 5 indicates that a ligand rearrangement has occurred at some point during the oxidation of the diferrous complex. We currently hold that the following transformations occur during the oxidation of 1 based on the data presented above:

This is a unique transformation and may be responsible for several of the unusual reactivity properties discussed below. Future studies are designed to test this hypothesis.

We have recently synthesized and structurally characterized a dinuclear Co^{2+} complex, 7, that is isostructural with 1.⁶ Complex 7 appears to form the mixed valent and dinuclear Co^{3+} complexes, although we are still attempting to grow crystals suitable for diffraction studies. Finally, we have isolated a dinuclear Ru^{2+} species, 8, that from IR experiments appears to be isostructural with the dinuclear iron, 1, and cobalt, 7, systems.

The reactivity properties of complexes 1 - 7 are being examined. Our studies demonstrated that the diferrous complex heterolytically decomposed phenylperacetic acid (PPAA) while the diferric complex induced only homolytic cleavage.¹ Furthermore, only complexes containing a ferrous center are capable of catalyzing oxygen atom transfer from PhIO to a variety of organic

substrates; the diferric, μ -oxo- and di- μ -methoxy species are not active oxygen atom transfer catalysts. Complexes 1 and 3 catalyze the oxidation of a variety of olefins such as cyclohexene to cyclohexene epoxide, cyclohexenol and cyclohexenone (≈ 60 turnovers; 1:2:4) and convert alkyl and aryl sulfides to their corresponding sulfoxides and sulfones. It is noteworthy that $\geq 80\%$ of the product distribution observed for the oxidation of cyclohexene by 1 or 3 involves allyl oxidation in contrast to analogous studies using the dicobalt compound, 7, in which the epoxidation reaction dominates ($\geq 85\%$).⁶ These results clearly indicate the influence of d electron count (d^6 , Fe^{2+} ; d^7 , Co^{2+}) on the oxidation process, suggesting a change of mechanism. We have preliminary evidence (low temperature UV/vis) for simple adduct formation between PhIO and 7 and are currently performing experiments designed to identify this species. The observed product distributions are consistent with our working hypothesis that the iron system proceeds through a high valent iron-oxo intermediate (allyl oxidation dominant) while the cobalt system, which is expected to be incapable of forming such a species based on molecular orbital bonding considerations, proceeds through a PhIO adduct. We are continuing our attempts to spectroscopically characterize both the iron and cobalt intermediates to test our current level of understanding of this system. In addition, we hope that our Ru^{2+} complex, 8, will enable us to isolate analogous intermediate species.

Although the diferric complex, 4, is not an atom transfer catalyst in the presence of PhIO, it exhibits remarkable catalytic properties in the presence of peroxides.⁵ Under anhydrous conditions, 4 appears to act as a potent non-heme catalase model, catalyzing the chemical reaction of hydrogen peroxide decomposition into molecular oxygen and water. The oxidizing equivalents produced during this reaction are capable of converting alkanes to alcohols; we have observed the oxidation of isomeric pentanes to a variety of alcohols. We are currently examining the kinetics and structures of any intermediates involved in the reaction. Parallel studies examining substrate specificity are also underway. The observed reactivity property is consistent with our proposed structure for 4, namely a dinuclear complex that contains two iron centers approximately 3.2 Å apart with no direct atom bridges. This suggests that the reaction of O_2 with the diferrous complex 1, superoxide with the mixed valence species 3, and peroxide with the diferric complex 4, ought to give analogous reaction profiles, that is, a potent oxidation catalyst capable of oxidizing alkanes and aromatics. This hypothesis is actively under investigation.

Future studies are designed to continue to probe the nature of the intermediates formed during catalysis, the substrate specificity of these catalysts, the intimate mechanism for substrate epoxidation and oxidation and the development of new complexes that mimic both the electronic and reactivity properties of the unique active site found in methane monooxygenase.

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