Recent Advances in Biomimetic Models of Methane Monooxygenase Hydroxylase

Kristin Kay Smith Literature Seminar September 25, 2001

Current industrial processes that convert alkanes to alcohols require extreme heat, pressure, or both.[1,2] Nature, however, has developed several enzymes that can catalyze this conversion easily under mild conditions. Certain microorganisms, called methanotrophs, contain methane monooxygenase hydroxylase (MMOH) (Figure 1), an enzyme that converts methane to methanol.[3] Model studies of the enzyme aim to elucidate mechanistic intermediates. Another goal of modeling is to be able to carry out the reaction on a practical scale.[2] Models of MMOH may be structural, functional, or both. This discussion will describe three representative models, each with its own advantages and disadvantages.

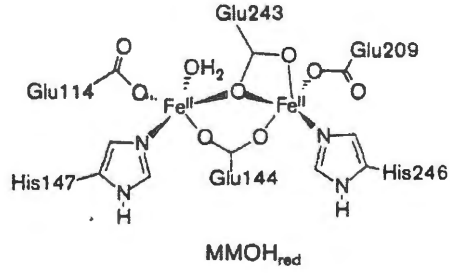

Figure 1. The active site of one form of MMOH in its reduced state.

The first model, Model I, involves the complex $[Fe(TPA)(CH_3CN)_2](ClO_4)_2$ (TPA = tris(2-pyridylmethyl)amine) in the presence of H_2O_2.[4] Although this complex is mononuclear[5] and MMOH is binuclear,[6] the system mimics the function of MMOH in that it is capable of stereospecific oxidation of saturated hydrocarbons. Because the oxidation reaction is stereospecific, a mechanism involving radicals is unlikely. The mechanism may be like that of heme alkane hydroxylation, in which an Fe^{V}=O species abstracts a hydrogen atom from the substrate.[7] Alternatively, the mechanism could involve an (η^2-peroxo)metal intermediate.[8]

Model II involves the binuclear complex $[Fe_2O(L)_2(OAc)]^+$ in which L is *N,N'*-bis(3,4,5-trimethoxybenzyl)ethylenediamine *N,N'*-diacetic acid dihydrochloride.[9] Addition of O_2 in the presence of ascorbate yields a complex in which one of the benzyl groups on the ligand has been oxidized and the resulting phenolate coordinates to the iron center of the complex, which is now mononuclear. The importance of this model lies in the fact that the reaction takes place in aqueous solution and the oxidant is molecular oxygen; these conditions exactly match the reaction conditions of MMOH. Mechanistic studies suggest a concerted mechanism, with no free radical intermediates.

Model III is based on the complex $Fe_2(\mu\text{-}O_2CAr^{Tol})_2(O_2CAr^{Tol})_2(N,N\text{-}Bn_2en)_2$ where O_2CAr^{Tol} = 2,6-bis(para-tolyl)benzoate and *N,N*-Bn_2en = *N,N*-dibenzylethylenediamine.[10] This model entails the use of very bulky ligands to simulate

the steric environment of the protein around the active site of MMOH. When the dinuclear complex is treated with molecular oxygen, a benzyl group from one of the ligands reacts and PhCHO is released. The resulting metal complex contains two iron atoms joined by two μ-OH groups and one μ-O_2CR group; this product closely resembles the structure of the core of oxidized MMOH. The mechanism and intermediates of this reaction are currently under study.

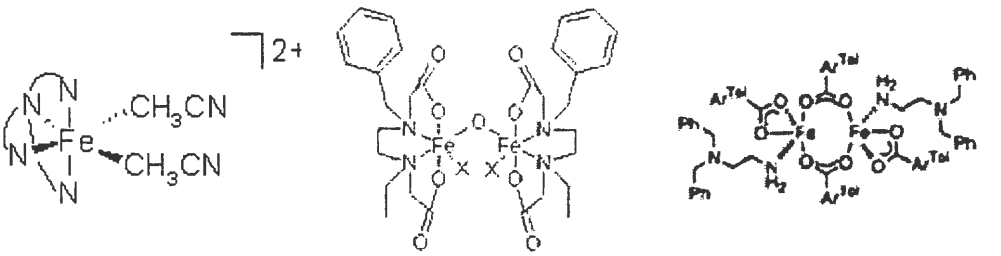

Figure 2. Structures of the complexes of Models I, II, and III.

These three models represent recent advances in the study of MMOH. Future work involves further study to better understand the catalytic mechanism.[10] Synthesizing models with efficiencies rivaling that of the enzyme, improving selectivity, and applying the enzyme to other reactions such as the hydrolysis of DNA.[11]

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