

to transferrin. Other coordination properties and relative iron transfer kinetics of these two proteins will be discussed.

TABLE I. pM Values of Selected Fe(III) Sequestering Agents.

Ligand	pM <sup>a</sup> (-log[Fe <sub>aq</sub> <sup>3+</sup> ])
Enterobactin	35.5
HBED <sup>b</sup>	31.0
MECAM	29.4
MECAMS	29.1
3,4-LICAMS	28.5
Me <sub>3</sub> MECAMS	26.6
Ferrioxamine B	26.6
EHPG <sup>c</sup>	26.4
TRIMCAMS	25.1
NAcMECAMS	25.0
DTPA <sup>d</sup>	24.7
Transferrin	23.6
EDTA <sup>e</sup>	22.2
Tiron <sup>f</sup>	19.5

<sup>a</sup>Calculated for 10 M ligand, 1 M Fe<sup>3+</sup>, pH 7.4. <sup>b</sup>N,N-bis(2-hydroxybenzyl)-ethylenediamine-N,N'-diacetic acid.

<sup>c</sup>Ethylene-1,2-bis(2-hydroxyphenylglycine). <sup>d</sup>Diethylenetriaminepentaacetic acid. <sup>e</sup>Ethylenediaminetetraacetic acid. <sup>f</sup>1,2-Dihydroxy-3,5-disulfobenzene.

#### G4

### Synthetic Models of Metalloenzymes

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Metal ions play an important role in the enzymic catalysis of many metalloproteins. The molecular details of the catalytic cycle are often obscured by the complexity of the biological system. It has been the goal of our research for the past few years to elucidate the mechanisms of metalloenzymes through the synthesis of simple metal complexes that mimic the structure of the active sites. The reactivity of such metal complexes have provided insights into the enzyme mechanism. Further, successful enzyme models have provided a rational basis for the construction of synthetic, biomimetic catalysts. In this lecture, recent advances in the study of active site models of carboxypeptidase A, CPA, a zinc-containing protease, and cytochrome P-450, a heme-containing monooxygenase will be described.

The role of zinc in the peptidase activity of CPA has been ascribed to coordination of the substrate amide carbonyl, coordination of a nucleophilic hydroxide or even to a less specific structural role. To

choose among these possibilities we have synthesized a family of metal-complexing amides which does not allow a metal-carbonyl interaction. Large zinc- and copper-mediated rate enhancements ( $10^4$ – $10^7$ ) for amide hydrolysis are observed with these compounds. Kinetic and titrimetric measurements indicate that the deprotonation of a metal-bound water is a component of this catalysis. A mechanism for amide hydrolysis involving nucleophilic attack of a metal hydroxide is consistent with the observed results.

The catalytic cycle of cytochrome P-450 has been suggested to involve a reactive oxo-iron intermediate which is responsible for oxygen transfer to the substrate. We have prepared the first synthetic example of an iron(IV)-porphyrin cation radical complex (*I*). This species has been shown to be extraordinarily reactive toward hydrocarbons. The physico-chemical characterization of *I* and the elucidation of the mechanism of olefin epoxidation and alkane hydroxylation will be described.

#### G5

### Trisimidazolylphosphine: M(II); Models for the Metal-Binding Site in Carbonic Anhydrase

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The apparently simple processes of CO<sub>2</sub> hydration and HCO<sub>3</sub><sup>-</sup> dehydration (eqn. 1) play a key role in several diverse physiological processes such as gas balance, photosynthesis, shell formation and pH control [1]. So important is this reaction to living systems that Nature has provided virtually all



organisms with an enzyme whose only known physiological role is to facilitate the interconversion of CO<sub>2</sub> and HCO<sub>3</sub><sup>-</sup>. According to X-ray crystallographic determinations [2] the active site of carbonic anhydrase consists of an essential Zn(II) ion held in the protein by three histidine imidazole units in a distorted tetrahedral fashion: the remaining Zn(II) ligand positions are said to be occupied by H<sub>2</sub>O and/or OH<sup>-</sup>, these being important for the catalytic events. Although many studies with the enzymes isolated from human and bovine erythrocytes have been undertaken, the mechanism by which CA catalyses the process in eqn. 1 remains elusive [1].

As an alternative approach to studying the catalysis of CO<sub>2</sub> hydration and HCO<sub>3</sub><sup>-</sup> dehydration, we have initiated a program of synthesizing and evaluating simple *tris*-imidazolyl containing phosphines as approximations for the metal-binding sites in CA. Two