Synthetic Modeling of the Heme-Copper Active Site O_2-Reactivity

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Heme-copper oxidases, including cytochrome c oxidases, are terminal respiratory membrane proteins which catalyze the four-electron four-proton reduction of dioxygen to water, coupling this chemistry to membrane protein translocation. The active site where dioxygen binds is a binuclear center with heme and proximate copper ion moiety. To contribute to a fundamental understanding of O_2-reactivity at heme/Cu centers, we have studied reactions with a series of $(P)Fe^{II}/Cu^{I}$ (P = porphyrinate) complexes or components employing a tetrakis(2,6-difluorophenyl)porphyrinate or close analogue, and copper species with tri- or tetradentate chelate.

Low-temperature oxygenation of these reduced Fe^{II}/Cu^{I} complexes leads to adducts, formulated as μ-peroxo Fe^{III}-(O_2^{2-})-Cu^{II} species. Stopped-flow kinetic studies show that in solvents containing EtCN, initial dioxygen binding to the heme occurs, giving a $(EtCN)Fe^{III}$-O_2^{-} intermediate (akin to oxymyoglobin). Attack by the cuprous ion moiety follows to give the Fe^{III}-(O_2^{2-})-Cu^{II} product. The systems are all S = 2 spin systems with strong magnetic coupling between the iron and copper centers. Ligand influences manifest themselves as striking differences in the nature of bridging-peroxo moiety; compared to complexes with a tetradentate Cu-chelate, a tridentate moiety leads to dramatically lowered ν(O-O) values suggested these possess a μ-η^2:η^2 side-on/side-on peroxo bridging structure.

With a series of heme-copper dioxygen adducts in hand, chemistry aimed at effecting O-O bond reductive cleavage is being carried out. This includes comparisons of high-spin systems (above) and low-spin analogs formed by addition of a heme axial "base" ligand such as dicyclohexylimidazole. The results of studies where heme-peroxo-copper complexes are subjected to proton and electron sources will be described.