Diverse reactivity from a few simple ligands: the case of non-heme iron dioxygenases and their biomimetic analogs

Jon Askim Literature Seminar September 8, 2009

Understanding the relationship between molecular structure and reactivity is one of the most fundamental questions of chemistry. Such relationships are particularly subtle in enzymes, where the protein matrix often profoundly affects the chemistry of simple coordination cores. Non-heme iron dioxygenases uniquely illustrate such subtleties. The first coordination spheres are simple and similar, yet the reactivity of these enzymes is remarkably diverse.[1]

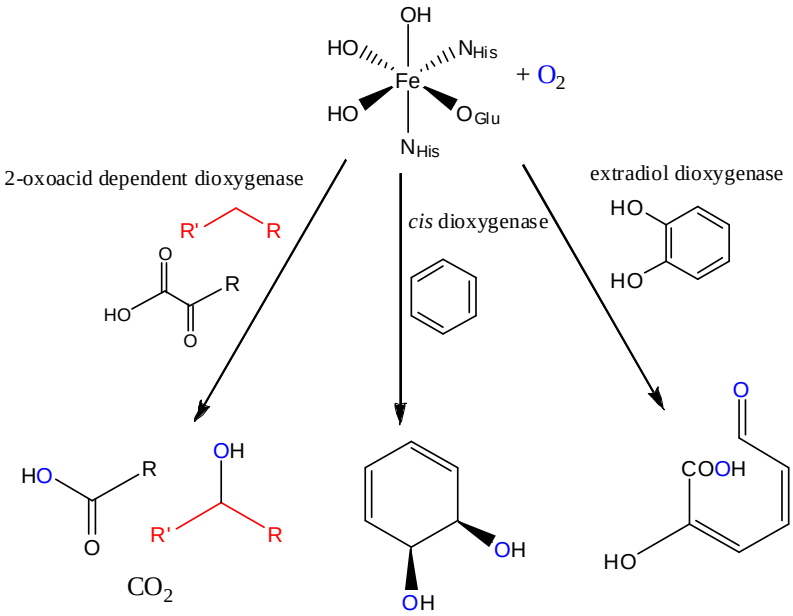

Figure 1. Summary of reactivity of dioxygenases containing the 2-His-1-Carboxylate facial triad. 2-oxoacid dependent dioxygenases (left), *cis* dioxygenases (middle), extradiol dioxygenases (right).

Three of the main classes of non-heme iron dioxygenases share a common ligand set and similar geometries, described by Que et al. as the 2-His-1-Carboxylate facial triad.[2] The first of these, the 2-oxoacid dependant dioxygenase family, is a large class that catalyzes the hydroxylation of a wide array of substrates including both aliphatic and aromatic compounds.[1,3] The second, the *cis* dioxygenase family, catalyzes the dihydroxylation of aromatic substrates.[1,4] The third class is the extradiol dioxygenase family, which catalyzes the cleavage of catechols adjacent to the enediol moiety.[1,9] The diverse reactivity of these enzymes (Figure 1) makes dioxygenase enzymes an attractive catalyst for fields ranging from drug synthesis[1] to bioremediation of persistent pollutants, such as polychlorinated biphenyls (PCBs).[4]

The ability of this simple ligand set to catalyze a disparate set of reactions, which includes both C-H and C-C bond activation, raises the question of the origin of this

behavior. An approach that has generated a testable hypothesis is the systematic analysis of functional biomimetic complexes.

Functional biomimetic complexes offer straightforward tunability over a range of parameters *via* modification of ligands. An approximately homologous series of polydentate nitrogen-containing ligands was synthesized while maintaining core electronic structure. The number of adjacent open coordination sites correlated with the reactivity of native non-heme iron dioxygenases,[4-9] offering a hypothesis as to the nature of the predominant factor influencing the functions of both non-heme iron dioxygenases and their biomimetic analogs.

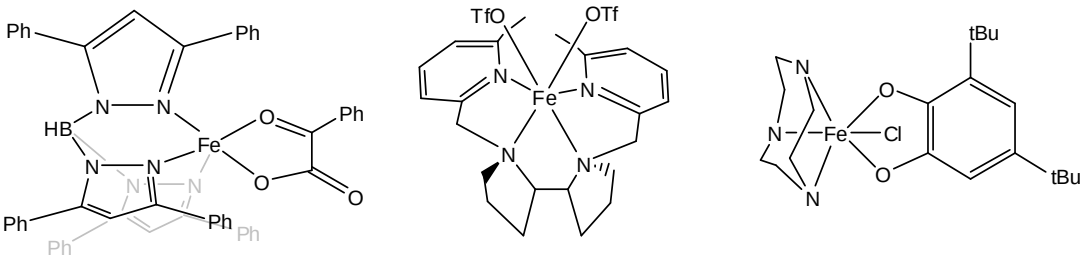

Figure 2. Representative functional biomimetic complexes of dioxygenases containing the 2-His-1-Carboxylate facial triad. Complexes mimic the reactivity of 2-oxoacid dependent dioxygenases[8] (left), *cis* dioxygenases[6] (middle), and extradiol dioxygenases[9] (right).

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