Catechol Dioxygenases: Structure and Mechanism

Aaron K. Justice Inorganic Literature Seminar October 19, 2004

The oxidative cleavage of aromatic compounds is an important reaction in the maintenance of the global carbon cycle. This chemistry is readily catalyzed by biological organisms, but has little precedence in organic chemistry.[1] An example of a class of enzyme that catalyze the cleavage of aromatic compounds with dioxygen is catechol dioxygenases, in which both oxygen atoms are incorporated into the final product.[2]

Catechol dioxygenases are divided into two different classes based upon the position of bond cleavage. If the carbon-carbon bond between the alcohols is oxidized, this is known as intradiol cleavage, and the resulting product is *cis*,*cis*-muconic acid. If the carbon-carbon bond outside of the alcohols is oxidized, this is known as extradiol cleavage, and the resulting product is 2-hydroxymucaldehyde acid.[3] There are many differences between the active sites of the two different classes of the enzyme. These differences have a profound affect on the reaction mechanism, causing the reaction pathways to be very different for each enzyme.[4,5]

The intradiol cleavage active site consists of an iron(III) metal center coordinated by two histidine moieties, two tyrosine moieties and a hydroxide ion in a trigonal bipyramidal geometry (Figure 1).[4] In the presence of catechol substrate one of the tyrosine moieties and the hydroxide ligand are protonated and dissociate away from the iron center.[6] The catechol substrate binds as a bidentate dianion to the iron center. Once bound, the catechol reacts with dioxygen forming a peroxide intermediate.[7,8] The peroxide intermediate undergoes a reaction with iron center, forming a cyclic peroxide, which after rearrangement, results in the desired product of *cis*,*cis*-muconic acid. Typical model complexes implement an iron(III) center chelated by a tetradentate ligand.[9] Modeling efforts have discovered a direct relationship between Lewis acidity and reactivity at the iron center.

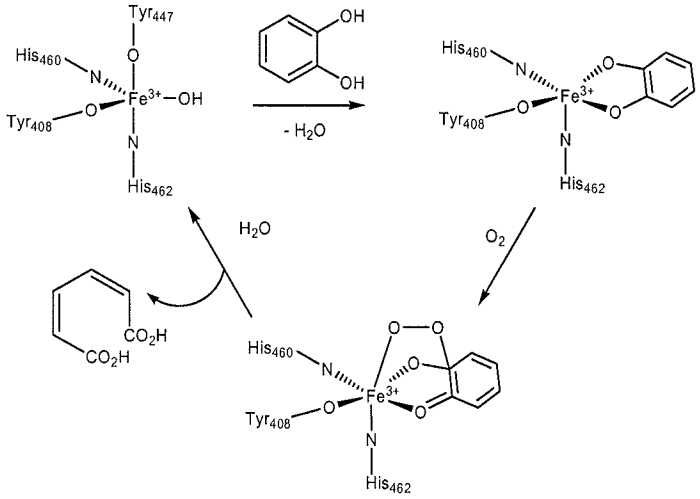

Figure 1. Catalytic cycle for intradiol cleavage.

The extradiol cleavage active site consists of an iron(II) metal center coordinated by two histidine moieties, one glutamate moiety and two water molecules in a square pyramidal geometry.[5] This difference in the oxidation state of the metal and the difference in the ligand environment as compared to the intradiol cleavage active site, causes the catechol to bind in a different mode. In extradiol cleavage mechanism, the catechol is proposed to displace two water molecules, and bind as a bidentate, monoanion.[10] For extradiol cleavage, dioxygen interacts directly with the iron center, resulting in a superoxide intermediate. Evidence to support the mechanism is obtained when the catechol bound complex is reacted with nitric oxide. The nitric oxide binds directly to the iron center forming a catechol bound nitric oxide complex.[11] The superoxide reacts directly with the bound catechcol forming a cyclic peroxide. After rearrangement of the cyclic peroxide, the desired product of 2-hydroxymucaldehyde acid results (**Figure 2**). Modeling efforts are not as numerous for the extradiol cleavage when compared to the intradiol cleavage. The most successful extradiol cleavage model employs tridentate ligands.[12] With a tridentate ligand, the bound catechol complex has an open coordination site on the iron center, allowing direct interaction with dioxygen.

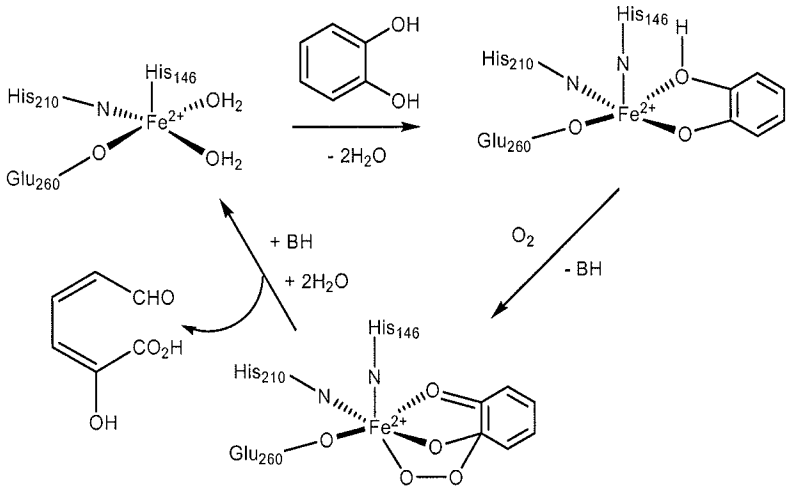

Figure 2: Catalytic cycle for extradiol cleavage.

In conclusion catechol dioxygenase enzymes serve a vital role in the environment by performing the biodegradation of aromatic molecules. The two different classes of the enzyme can perform the biodegradation of aromatic molecules that vary in structure and reaction mechanism.

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