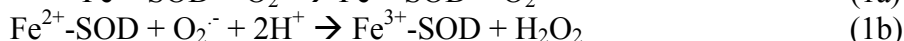
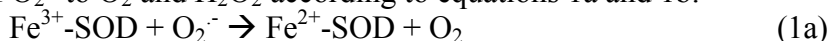


# Spectroscopic and Computational Studies of Substrate Analog Adducts of Iron-Dependent Superoxide Dismutase

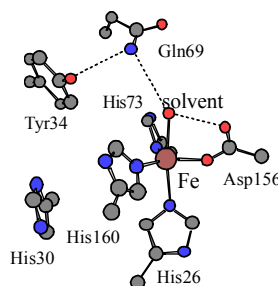
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Iron-dependent superoxide dismutase (Fe-SOD) is a metalloenzyme that defends biological systems against oxidative damage caused by the superoxide radical,  $\text{O}_2^{\cdot-}$ . This is accomplished through disproportionation of  $\text{O}_2^{\cdot-}$  to  $\text{O}_2$  and  $\text{H}_2\text{O}_2$  according to equations 1a and 1b.



The Fe in the active site of Fe-SOD is in an approximately trigonal bipyramidal coordination environment consisting of three histidine residues and one aspartate residue from the enzyme, as well as a solvent molecule (see figure). Substrate analogs such as NO,  $\text{F}^-$ , and  $\text{N}_3^-$  have been used to model active site/substrate interactions. The resulting analog-metal adducts have been studied in our laboratory using density functional theory (DFT) calculations in conjunction with absorption, resonance Raman (rR), circular dichroism (CD), magnetic CD (MCD), and electron paramagnetic resonance (EPR) spectroscopies. These studies reveal the existence of two different substrate binding sites, demonstrate a difference in binding of substrate analogs to  $\text{Fe}^{3+}$ - and  $\text{Fe}^{2+}$ -SOD, and provide insight into the role of outer-sphere amino acid residues in the reaction mechanism. We will also present preliminary spectroscopic and computational data for the HS-FeSOD adduct.



Active Site of Fe-SOD