Designing a Model for the Enzyme–Substrate Complex to Investigate the Detailed Catalytic Mechanism of Lactoperoxidase by Quantum Chemical Methods

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Lactoperoxidase (LPO) is a heme enzyme found in exocrine secretions such as milk, saliva and endodermal mucus. LPO catalyzes the formation of oxidizing oxoanions that act as natural antibiotics in those body fluids. LPO is a versatile enzyme that converts thiocyanate ions (SCN^-) to hypothiocyanite ions ($OSCN^-$), as well as halide ions (i.e., Cl^-, Br^- and I^-) to hypohalite ions (i.e., ClO^-, BrO^- and IO^-). By means of quantum-mechanical–molecular-mechanical (QM–MM) calculations, this investigation aims to find the sequence of bond-breaking and bond-forming steps by which LPO converts the anions into the oxoanions in its active-site. In this particular study, we present a molecular model for the LPO active-site, which was generated from a detailed analysis and comparison of the available crystallographic structures of LPO deposited in the Protein Data Bank. We also propose a chemical model for the enzyme–substrate complex, which will be used as the starting structure in the QM–MM computation of the LPO catalytic mechanism.