THEORETICAL MECHANISTIC STUDIES OF THE GUT MICROBIAL CHOLINE-TMA LYASE ENZYME CUTC

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Endogenous choline-derived trimethyl amine (TMA) production in humans through gut microbial enzyme action of choline trimethylamine-lyase (CutC) can be detrimental when abnormal levels are achieved. Abnormal levels of TMA in humans can lead to a multitude of diseases such as renal disorders, cancer, obesity, diabetes, cardiovascular diseases, and neuropsychiatric disorders. Experimental data and X-ray crystallographic results indicate that a direct elimination of TMA may occur through a radical enzyme catalysis mechanism. To further explore the polar active site and hydrogen bonding observed experimentally by Drennan and Balskus, quantum mechanical (QM) calculations of small and larger cluster intermediates and transition states were performed with the Gaussian16 suite in all calculations using unrestricted Hartree-Fock level of theory and the double-zeta 6-31G (d) basis set. Potential energy surfaces (PES) were constructed to observe how well the computational mechanism correlated with the experimentally proposed reaction pathway.