Simulated ^{18}O Kinetic Isotope Effects in Enzymatic Hydrolysis of Guanosine Triphosphate

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Abstract—We compare the computed on the base of quantum mechanical–molecular mechanical (QM/MM) modeling kinetic isotope effects (KIEs) for a series of the ^{18}O-labeled substrates in enzymatic hydrolysis of guanosine triphosphate (GTP) with those measured experimentally. Following the quantitative structure–activity relationship concept, we introduce the correlation between KIEs and structure of substrates with the help of a labeling index, which also aids better imaging of presentation of both experimental and theoretical data. An evident correlation of the computed and measured KIEs provides support to the predominantly dissociative-type reaction mechanism of enzymatic GTP hydrolysis predicted in QM/MM simulations.

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