Abstract

Project code:	MRG5680143
Title:	Powerful Insight into the Nature of Five- and Six-Membered Ring Carbohydrate Conformation in Catalysis of Glycosidase from Combined Quantum Mechanics/Molecular Mechanics Simulations
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The aim of this research project is to study the hydrolytic mechanism of chito-oligosaccharide substrate and its ring conformation during catalysis of *Serratia marcescens* chitinase B (ChiB) as well as to probe the roles of conserved residues in the ChiB active site by using combined quantum mechanics/molecular mechanics (SCC-DFTB/CHARMM22) simulations and density functional theory. The SCC-DFTB calculations could reproduce the geometries of enzyme-substrate complex determined by X-ray crystallography. Calculated free-energy profiles for the reaction suggested a two-step mechanism in which the first glycosylation step is the rate-determining step with an activation barrier of 20.5 kcal/mol, in a reasonable agreement with the 16.1 kcal/mol barrier derived from the experiment. The pyranosyl substrate (bound in subsite −1) was found to undergo a boat ($^{1,4}B$) ↔ half-chair ($^{4}H_5$) ↔ chair ($^{4}C_1$) conformational change along the reaction path. A variety of conserved residues in the ChiB active site were involved in catalysis and Asp142 and Tyr214 were found to play key roles for catalytic efficiency. In addition, the DFT-based protocol can also be applied to study the conformation of cyclic esters during the ring-opening polymerization.

Keywords : chitinase B; enzyme mechanism ; QM/MM; SCC-DFTB; glycoside hydrolase; ring conformation