Narongsak Arayalert 2007: The Protein Framework and Solvent Effect on the Energetics of the Acylation step in Butyrylcholinesterase-catalyzed Hydrolysis of Cocaine: An Electronic Embedding Method. Master of Science (Chemistry), Major Field: Physical Chemistry, Department of Chemistry. Thesis Advisor: Professor Jumras Limtrakul, Ph.D. 82 pages.

The geometry parameters of the transition state, intermediate, and prereactive enzyme-substrate complex was optimized at B3LYP/6-31G(d,p) level of theory in the cluster model and the cluster amino model and the corresponding energy barriers have been studied by performing the polarizable continuum model (PCM) and the embedded calculations on the first step of acylation process considered by single point calculation at B3LYP/6-31G(d,p) level of theory 6.71 and 5.07 kcal/mol, respectively and B3LYP/6-31++G(d,p) level of theory 4.51 and 3.75 kcal/mol, respectively. The energy barriers decreased from the cluster amino model by approximately 0.9-2.0 kcal/mol. These calculations allow us to account for the electrostatic interaction of protein environment effects and solvent effects on the pathway and the energy barriers of these enzymatic reactions. This shows the protein environment effect significantly influences the hydrogen bonding between the oxyanion hole and the carbonyl oxygen of cocaine. These computational results provide valuable insights into the future design of BChE mutants with a higher catalytic activity for cocaine.

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