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Ab Initio QM/MM Study of the Ester-hydrolysis Reaction Mechanism in Haloalkane Dehalogenase YIMING ZHANG, YU ZHOU, SAROJ NAYAK, ANGEL GARCIA, Department of Physics and Astronomy, Rensselaer Polytechnic Institute, CENTER FOR BIOTECHNOLOGY AND INTERDISCIPLINARY STUDIES COLLABORATION, DEPARTMENT OF PHYSICS COLLABORATION — Ab Initio QM/MM calculations are used to investigate the ester-hydrolysis step of dichloroethane hydrolysis catalyzed by haloalkane dehalogenase. Amino acids around the active site (which includes ASP124, HIS289, ASP260, TRP125, TRP175), dichoroethane and water are treated by QM at a level of HF/6-31G(d,p). The remainder of the protein and solvent are treated classically. Two scenarios of hydrolysis mechanism for the alkyl-enzyme intermediate have been considered. In one, the HIS289-catalyzed water oxygen could be incorporated in the carboxylate group of ASP124, leading the cleavage of one of the original carbonyl bonds on ASP124. In the other, the ASP124 and HIS289 as general base, activate water as the nucleophilic agent, which attacks the alkyl carbon in substrate. The reaction paths and potential energy profiles are compared for both mechanisms.

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