

Hydrocarbon Dissociation Pathways in MerB Catalysis: A Molecular Dynamics Study
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The bacterial organomercurial lyase, MerB, catalyzes the protonolysis of organomercurial compounds. MerB cleaves Hg-C bonds of various substrates ranging from the methylmercury cation (MeHg) to merbromin. Upon Hg-C bond cleavage, Hg^{2+} and an organic molecule are produced. For example, methane is the product resulting from the protonolysis of MeHg. The release pathway and mechanism of the organic product are unclear. Here, we have applied molecular dynamics and free energy simulations to study the dissociation of a series of organic molecules. The x-ray crystallographic structure of MerB with a bound Hg^{2+} cation was used as the starting model, and the organic products were manually placed in the active site. The umbrella sampling method was used to obtain free energy profiles for the dissociation pathways. Several hydrophobic sidechains of MerB were found to interact with the organic molecules and may have important roles in the dissociation process. The relatively low free energy barriers of dissociation suggest that organic product dissociation is not rate limiting.