4E11 Stabilization of Substrate Radicals by Cob(II)alamin in Coenzyme B_{12} Dependent Mutases. An Insight from DFT Calculations

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The origin of the enormous catalytic activity of coenzyme B_{12}-dependent enzymes continues to be an outstanding problem in bioinorganic chemistry. During enzymatic catalysis the Co-C bond of coenzyme B_{12} (AdoCbl) is cleaved homolytically, leading to the formation of the 5'-deoxyadenosyl radical and cob(II)alamin. The rate of enzymatically accelerated homolytic cobalt-carbon bond cleavage of AdoCbl exceeds the rate observed in aqueous solution by about 12 orders of magnitude as a consequence of the coenzyme interaction with the substrate in the presence of apoenzyme. Despite the great effort that has been devoted to this problem, the mechanism of the catalytic activation is poorly understood. We applied DFT to investigate the initial step of the Co-C bond cleavage and possible stabilization of substrate radical by cob(II)alamin. Two mechanisms were investigated: concerted and stepwise. It was found that the concerted pathway is energetically lower and leads to substrate radical stabilization by 7 kcal/mol. This effect is due to lowering of transition state energy associated with hydrogen abstraction by presence of the corrin ring (see figure below).