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Research Seminar

When: March 25, 2021
Time: 2:30 PM
Location: Microsoft TEAMS

Computational Investigation of B12-Dependent Reactions: Activation of Co-C Bond in MeCbl and AdoCbl-Dependent Systems

Abstract

Vitamin B_{12} derivatives (also known as cobalamins, Cbls) such as adenosylcobalamin (AdoCbl) and methylcobalamin (CH_3Cbl) act as a cofactor in numerous enzymatic reactions[1]. These biologically active cofactors contain a unique organometallic Co-C σ bond. This cleavage of the Co-C bond constitutes the key catalytic step in the AdoCbl-dependent enzymes[2]. The most fascinating, as well as still not fully understood, aspect of AdoCbl-dependent enzymatic reactions is the trillion-fold rate enhancement of $Co\text{-}C_{5'}$ bond homolysis compared to the thermal homolysis in the solution[3]. Although several mechanistic proposals regarding the activation of the $Co\text{-}C_{5'}$ bond have been put forward, precisely what triggers the activation of the $Co\text{-}C_{5'}$ bond remains an open question. In the quest for the underlying mechanism of the trillion-fold rate enhancement of $Co\text{-}C_{5'}$ bond homolysis, we have investigated the activation of the $Co\text{-}C_{5'}$ bond in the Ado-dependent MCM-[ICoA] and substrate-free MCM utilizing the ONIOM-based QM/MM method.[4]

In addition to their roles in thermally driven biological reactions, another important feature of Cbls is that it possesses unique photochemical and photophysical properties[5, 6]. Despite knowing the light-sensitivity of Cbls for the last five decades, the photochemistry of Cbls has recently gained new interest due to its potential application in phototherapeutic and light-activated drug delivery[5]. Furthermore, a molecular-level insight into the photoreaction of Cbls will also be helpful for the effective design of a biomimetic catalyst. Here in this talk, I will be discussing the activation of Co-C bond in the photolysis and native catalysis reactions for Cbl-dependent systems based on DFT, TD-DFT, and QM/MM calculations[7-9].

References

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