

University of Louisville
Department of Chemistry

Megan Joy (Toda) Mackintosh Research Seminar

When: September 24, 2020

Time: 2:30 PM

Location: Microsoft TEAMS

Computational Investigations of the Photochemical Properties of B₁₂-Dependent Systems: From Solution to Enzymes

Abstract

In addition to their roles in biological processes, B₁₂ derivatives (also known as cobalamins, Cbls) have unique photolytic properties.^{1,2} Historically, the light sensitivity of Cbls was viewed as an unwanted and problematic side reaction. However, with the discovery of naturally occurring B₁₂-dependent photoreceptors and the development of synthetic B₁₂ derivatives for phototherapeutics, studies targeting the photolytic properties of Cbls have seen resurgence. In this seminar, the photolytic and photochemical properties of Cbls in solution and in the enzymatic environment will be summarized based on DFT, TD-DFT, and ONIOM calculations. Photoreaction mechanisms will be presented based on ground and excited state potential energy surfaces (PESs). Specifically, antivitamins B₁₂, thiolato-Cbls, and the CarH photoreceptor will be discussed.

(1) Antivitamins B₁₂^{3,4}

Synthetic antivitamins B₁₂ include, 4-ethylphenylcobalamin (EtPhCbl) and phenylethynylcobalamin (PhEtyCbl). EtPhCbl is photolabile albeit with a very low quantum yield of photoproducts, while PhEtyCbl is incredibly photostable. Two possible pathways for photodissociation of EtPhCbl can be identified but only one is energetically feasible. There is not an energetically favorable path for photolysis of PhEtyCbl; rather, internal conversion (IC) is the preferred photophysical event.

(2) Thiolato-cobalamins⁵

The S₁ PES of NACCbl contains three distinct minima in the MLCT and LF regions. Compared to other Cbls, the photodissociation mechanism for NACCbl is neither in line with the alkylCbls nor the non-alkylCbls. The mild photo-responsiveness, observed experimentally, can be attributed to the small gap in energy between the S₁ and S₀ PESs.

(3) Coenzyme-B₁₂ dependent CarH⁶

Adenosylcobalamin (AdoCbl)-dependent photoreceptor, CarH, relies on daylight to perform its catalytic function. In enzymes employing AdoCbl as their cofactor, cleavage of the Co-C_{5'} bond is triggered by substrate binding. In CarH, this bond is instead activated by light. Comparison with other AdoCbl-dependent enzymes indicate that the protein environment in the CarH active center alters the photochemistry of AdoCbl by controlling the stereochemistry of the ribose moiety. Theoretical analysis of experimentally proposed mechanisms will also be presented.

1. Toda, M. J.; Kozłowski, P. M.; Andruinów, T. Chapter 8, **2019**, Springer, 10.1007/978-3-030-11714-6_8.
2. Toda, M. J.; Lodowski, P.; Mamun, A. A.; Jaworska, M.; Kozłowski, P. M. *Coord. Chem. Rev.*, **2019**, 385, 20-43.
3. Lodowski, P.; Ciura, K.; Toda, M. J.; Jaworska, M.; Kozłowski, P. M. *Phys. Chem. Chem. Phys.* **2017**, 19, 30310-30315.
4. Lodowski, P.; Toda, M. J.; Ciura, K.; Jaworska, M.; Kozłowski, P. M. *Inorg. Chem.* **2018**, 57, 7838-7850.
5. Toda, M. J.; Lodowski, P.; Thurman, T. M.; Kozłowski, P. M. *Inorg. Chem.* **2020**, Under Review, Ed. Frank Neese.
6. Toda, M. J.; Mamun, A. A.; Lodowski, P.; Kozłowski, P. M. *J. Photochem. Photobiol. B: Biol.* **2020**, 209, 111919.