

Development of Bio-Inspired Catalysts for Dechlorination Reactions

Prof. Katherine Van Heuvelen
Department of Chemistry, Harvey Mudd College

Abstract

The nickel-containing cofactor F_{430} found in methyl-coenzyme M reductase (MCR) and the cobalt-containing cobalamin cofactor (Cbl) found in Vitamin B12 carry out the reductive dehalogenation of chlorinated alkenes, which can act as damaging pollutants in the environment. Both F_{430} and Cbl are found in biological systems and carry out this reaction under benign conditions using earth-abundant materials. This work centers on the preparation and investigation of small molecular model compounds that reproduce key geometric and electronic features of cofactors F_{430} and Cbl. In particular, I propose to:

1. Prepare a series of nickel- and cobalt-containing F_{430} model compounds designed to investigate the influence of the supporting ligand on reactivity.
2. Evaluate the reactivity of these complexes towards halogenated substrates.
3. Characterize reaction intermediates using a combination of spectroscopic (UV-visible, infrared, NMR) and computational (density functional theory, DFT) techniques in order to correlate geometric and electronic structure with reactivity.
4. Elucidate the reaction mechanism using insights gained from aims 1–3, ultimately applying a detailed understanding of the fundamental chemistry underlying dehalogenation to the rational design of an improved catalytic system to treat chlorinated pollutants before they enter the water supply.

Start Date, Duration, and Location

This research will be conducted at Harvey Mudd College over a ten-week period in the summer of 2016, which will run from May 23 – July 29. The Chemistry Department is in the process of hiring students for the summer of 2016 and the student working on this project will be identified later in the spring semester.

Proposed Research

The development of inexpensive catalysts for the dehalogenation of chlorinated organic compounds is a topic of great concern for the chemical industry. Trichloroethylene (C_2Cl_3H , TCE) is widely used to degrease metals and clean textiles, but it is also known to accumulate in soil and aquifers.^{1,2} The nickel-containing cofactors F_{430} and cobalt-containing Cbl found in metalloenzymes have been reported to catalyze the dehalogenation of chlorinated organic compounds, including tetrachloroethene (C_2Cl_4 , PCE), TCE, dichloroethene ($C_2Cl_2H_2$, DCE), and chloroform. However, the reaction mechanism is poorly understood. A detailed understanding of the design elements that permit metalloenzymes to catalyze this reaction could

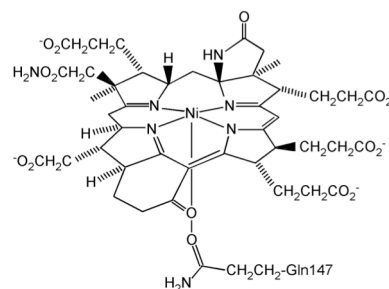


Figure 1. Cofactor F_{430} , found in MCR.

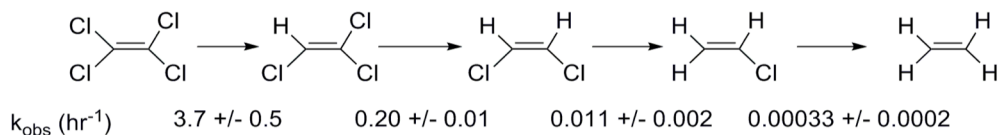


Figure 2. Dehalogenation of PCE as catalyzed by free F_{430} . Rate constants were obtained at 22°C .¹

inform the development and preparation of new, environmentally-friendly catalysts to conduct dehalogenation reactions under benign conditions.

My lab will synthesize chemical models of Cbl and MCR and study their reactivity toward TCE and DCE using a variety of spectroscopic and computational tools. Molecular models will use the cyclam ligand as a base (Figure 3, left). This versatile ligand platform offers many advantages. The parent cyclam ligand is commercially available, which will greatly facilitate the synthesis of model compounds. Metal ions bound by the cyclam ligand reproduce the binding motif observed in cofactor F_{430} and Cbl. Cyclam is also readily functionalized, for example through the addition of an appended chemical tail (Figure 3, right).³ This kind of functionalization is readily accessible to undergraduates, as illustrated by the successful syntheses of multiple cyclam ligands by previous Harvey Mudd students in my laboratory. Varying the “tail” of appended cyclams will allow us to easily modify the steric and electronic properties of our model compounds. In this way, we can tune the reactivity of our model compounds. All ligand and complex syntheses will be based on procedures reported in the chemical literature.⁴⁻⁷ Notably, Ni(cyclam) complexes have been shown to catalyze dehalogenation,⁷ though the reaction mechanism is not well understood. While Co(cyclam) complexes have been reported in the literature,⁸ to my knowledge they have not yet been evaluated as catalysts for dehalogenation reactions.

Reactions consist of reducing our metal compounds to the active oxidation state using chemical and/or electrochemical methods, as appropriate. The active model will then be incubated with organochloride compounds and the reaction monitored by UV-visible spectroscopy. All students will receive appropriate safety training before handling organochloride compounds. The reaction of our molecular models with chlorinated alkenes leads to color changes due to perturbations of the metal oxidation state and coordination number, and these color changes are readily measured by UV-visible spectroscopy. Reactions will be conducted at variable temperatures spanning 22-60°C to allow us to control the reaction rate and obtain kinetic data. We use a variety of standard spectroscopic techniques, including ^{13}C NMR to identify any products resulting from our reactions.

Spectroscopic studies will be complemented by computational investigations. We will use the chemistry software package Gaussian09 to study the electronic structures of our starting materials, reaction products, and probable reaction intermediates. Importantly, we will use computations to predict experimental properties that can be measured in the lab, and only the computations that agree with our experimental data will be used to interpret results. I have a Research Allocation on the XSEDE supercomputer facility, which we will use to conduct our computational studies. This computational aspect of the project will not be affected by this summer’s construction work on the Libra Deck.

Significance of Project for Environmental Quality

The Environmental Protection Agency confirmed that TCE is a human carcinogen in the summer of 2014.⁹ TCE is used in many industrial processes and has been detected in groundwater throughout the United States, so a detailed understanding of the reductive dehalogenation of this compound is of great interest.¹⁰ In addition, organohalides are common pollutants¹¹ and insights

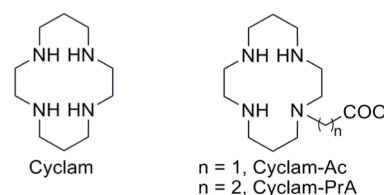


Figure 3. Ligands employed in Ni and Co model compounds.

into the dechlorination of TCE may be applied to other halogenated compounds in the environment. Our ultimate goal is the development of environmentally friendly, inexpensive catalysts made from abundant materials to treat and dechlorinate TCE before it reaches groundwater.

Educational Value

The experimental component of this research reinforces and builds on the laboratory skills introduced in the chemistry curriculum at Harvey Mudd. Students will prepare their model compounds using a variety of standard synthetic techniques, and they will also receive rigorous training in handling air-sensitive chemicals using a Schlenk line and a glove box. DFT studies will complement the use of computational chemistry in courses that include but are not limited to Chem 24, Chem 40, Chem 51, Chem 52, and Chem 110. Dramatic improvements in computer technology over the past decade have greatly facilitated computational studies of chemical compounds ranging from small synthetic complexes to large protein systems. As such studies become increasingly commonplace, it is critical to expose the current generation of undergraduate chemistry students to the advantages as well as the limitations of computational chemistry. Explanation of the theory behind computational chemistry will be determined on a case-by-case basis to complement the individual research student's background and interests. In addition, the student supported by this proposal will cultivate professional skills that include collaborating with other students and faculty members, reading and discussing scientific literature through regular group meetings, and presenting research in a departmental student symposium at the end of the summer.

Feasibility

The chemistry department at Harvey Mudd is well equipped for this project. Laboratory space includes two fume hoods, a glove box, a designated UV-visible spectrophotometer equipped with a temperature control unit, and access to a wide array of departmental spectroscopic equipment. The target model compounds have been reported in the literature, and the synthetic procedures needed to isolate these compounds are accessible for undergraduate students. Computations will be conducted using the XSEDE supercomputer facility. Background reading that is suitable for the student researcher's background and interest will be prepared and will be discussed during regular individual meetings and in the laboratory.

Understanding the mechanism of dehalogenation is a long-term goal, and as such I have broken this project into a series of modular goals suitable for a ten-week summer research period. Over the past three summers, students in my lab have successfully (1) synthesized a variety of appended ligands, (2) prepared and purified nickel- and cobalt-compounds, (3) obtained crystal structures of novel compounds, and (4) run reactivity studies that prove our catalysts can dechlorinate tetrachloroethylene. The summer of 2016 will be devoted to computational investigations of dechlorination (these studies are not affected by the Libra Deck construction) and screening our existing library of Cbl and MCR model compounds.

Budget

Student Stipend:	\$5,000.00 stipend + \$400.00 fringe benefits (8.0%)
Faculty Stipend:	\$1,000.00 stipend + \$329.70 fringe benefits (32.97%)
TOTAL:	\$6,729.70

Materials and supplies will be purchased using start-up funds

References

- (1) Gantzer, C. J.; Wackett, L. P. *Environmental Science and Technology* **1991**, *25*, 715.
- (2) Squaillace, P. J.; Moran, M. J.; Lapham, W. W.; Price, C. V.; Clawges, R. M.; Zogorski, J. S. *Environmental Science and Technology* **1999**, *33*, 4176.
- (3) Studer, M.; Kaden, T. A. *Helvetica Chimica Acta* **1986**, *69*, 2081.
- (4) Kieber-Emmons, M. T.; Schenker, R.; Yap, G. P. A.; Brunold, T. C.; Riordan, C. G. *Angew. Chem. Int. Ed.* **2004**, *43*, 6716.
- (5) Kieber-Emmons, M. T.; Van Heuvelen, K. M.; Brunold, T. C.; Riordan, C. G. *J. Am. Chem. Soc.* **2009**, *131*, 440.
- (6) Ram, M. S.; Riordan, C. G.; Ostrander, R.; Rheingold, A. L. *Inorg. Chem.* **1995**, *34*, 5884.
- (7) Stolzenberg, A. M.; Zhang, Z. *Inorg. Chem.* **1997**, *36*, 593.
- (8) Cho, J.; Sarangi, R.; Kang, H. Y.; Lee, J. Y.; Kubo, M.; Ogura, T.; Solomon, E. I.; Nam, W. *J. Am. Chem. Soc.* **2010**, *132*, 16977.
- (9) Erickson, B. E. *Chem. Eng. News* **2014**, *92*, 24.
- (10) Moran, M. J.; Zogorski, J. S.; Squaillace, P. J. *Environmental Science and Technology* **2007**, *41*, 74.
- (11) Payne, K. A. P.; Quezada, C. P.; Fisher, K.; Dunstan, M. S.; Collins, F. A.; Sjuts, H.; Levy, C.; Hay, S.; Rigby, S. E.; Leys, D. *Nature* **2015**, *517*, 513.