Professional Leave Report Cover Sheet

Name: Hubert Muchalski

Department: Chemistry & Biochemistry

College: Science & Mathematics

Leave taken: (●) Sabbatical ( ) Difference in Pay ( ) Professional Leave without Pay

Time Period: ( ) Fall

(●) Spring 2022

( ) Academic Year

( ) Other

Your report will be sent to your Dean for your PAF and to the Library Archives.

Sabbatical Leave Report

Hubert Muchalski, Department of Chemistry and Biochemistry

October 21, 2022

I would like to acknowledge the College of Science and Mathematics and Fresno State for the opportunity to take sabbatical leave during the AY 21–22 Spring semester. This document describes the activities I engaged in and accomplishments that resulted from those activities.

The overarching goal of my sabbatical leave was to redirect and expand my research program and create an environment that will allow me to collaborate with student researchers on reseasrch problems related to sustainability and control of important chemical processes. I proposed to focus my efforts on the following activities:

1. Development of gold complexes for catalytic reactions in water in collaboration with Dr. Bruce Lipshutz at the University of California, Santa Barbara.
2. Revision of experiment schedule in organic chemistry laboratory courses (CHEM 129) in the context of green chemistry principles.
3. Calibration and validation of peroxidation rate constant for fluorine-containing peroxyl radical clock—collaboration with Dr. Derek Pratt at the University of Ottawa, Canada.

From APM 360:

1. Each faculty member, within ten (10) weeks of the completion of a sabbatical or DIP leave, shall submit to the appropriate dean (or equivalent) a written report of the leave's activities. The report shall be placed in the faculty member's Personnel Action File (PAF). The faculty member will also provide a copy of this report to the Provost, via the Office of Faculty Affairs, to be eventually placed in the University Archives.
2. This written report shall include: a) the accomplishments of the leave in relation to the goals of the original proposal; b) modifications, if any, to the original proposal, and the circumstances that necessitated these modifications; c) the objectives of the original proposal (if any) that were not accomplished; and d) anticipated outcomes for the near future as a consequence of the leave's activities.
3. A copy of the original sabbatical or DIP leave proposal shall be attached to this report.

Accomplishments of the leave in relation to the original proposal

Development of sustainable chemical reactions

Thanks to the support from the CSU Program for Education and Research in Biotechnology (CSUPERB) and the CSMI spent 2 weeks in the lab of prof. Bruce Lipshutz at the University of California, Santa Barbara. Although the visit was relatively short, I learned a lot about synthetic organic chemistry in water. Sabbatical leave allowed my to spend a significant time in the laboratory where my graduate student and I synthesized a new catalyst which I took with me to UCSB to carry out planned experiments. The results showed that the catalyst we prepared is active under micellar conditions, but control experiments in plain water gave similar results. Thus, our hypothesis about more reactive catalyst proved to be correct—we can attribute increased reaction efficiency to the catalyst—but the effect of micelles is not as clear at the moment.

Despite the fact that the results of the experiments were inconclusive, the time I spent at UCSB was a period of intensive intellectual growth which led to a greater command of a subject matter. I learned about aspects of organic synthesis in water that are a common knowledge among its practitioners but are not necessarily disclosed in publications. For example, that certain benign additives can have a big impact on the reaction and the details of preparation of the micelle solution. The comments and suggestions I received from the chemists at UCSB were invaluable and helped me decide on the next direction of the project: study of palladium catalysts, which is likely a significant shift in research focus.

The period of the sabbatical leave also allowed me to better manage students and direct the experiments they do. I think that the reorganization contributed to new discoveries that a team of undergraduate research students is currently exploring. The new chemical reaction we are developing aligns perfectly with the new direction of my research—green and sustainable chemistry. A process which used to take two steps and used a large volume of petroleum-based solvent, can now be accomplished in a single step and in water. Students in my lab used these early findings to apply for Undergraduate Research grants offered by the Division Research and Graduate Studies.

Curriculum development: green and sustainable chemistry in CHEM 129B

My visit at UCSB was also an opportunity to continue my collaboration with prof. Lipshutz on a laboratory manual for sophomore organic chemistry courses. My role in the project is to use my experience as lab instructor and coordinator to adopt the cutting-edge research (organic synthesis in water) to college-level courses. During my visit at UCSB I tested five different experimental protocols and found that all but one can be successfully adopted and brought into the classroom. While at UCSB I also conceived and tested my own idea for a laboratory experiment which will be piloted during the AY 22–23 Fall Semester.

For all tested experiments I wrote comprehensive documentation which was sent as a book proposal to major book publishers. We are currently in discussions with Elsevier about a lab manual, a collection of experiments to be done in undergraduate teaching labs. We believe that such manual will help in the transition of organic chemistry laboratories from petroleum-based solvent-dependent and hazardous waste-generating operation to a sustainable endeavor that safer for students and a better learning environment.

Use of NMR in peroxyl radical clock experiments

As we continue to work in the area of gold catalysis, I remain interested in autoxidation chemistry, an interest I developed during my postdoctoral appointment, especially the idea of using 19F and 31P NMR spectroscopy for analysis. Although my postdoctoral research was also in the general area of autoxidation kinetics, this project is a new research direction. I worked with my graduate student, Karina Bustos, on developing a new method for measuring the rates of reaction of organic molecules with oxygen. We collected a large array of data data using the new Nuclear Magnetic Resonance (NMR) instrument in the department. During the sabbatical leave I could commit a large amount of uninterupted tim to processing and analyzing of the datasets. I am happy to report that the results demonstrated a proof-of-concept we were hoping for. I am very proud and grateful to Karina for her contributions because the preliminary data she collected allowed me to draft two strong grant proposals. The first proposal with a budget of nearly $450,000 was sent to NSF on September 29, 2022. The second proposal was submitted on October 14th to the American Chemical Society Petroleum Research Fund (ACS PRF) requesting $70,000. As most synthetic organic chemists, I have a working knowledge of routine NMR spectroscopy but quantitative heteronuclear NMR is a new area for me that is not reflected by my published record. I strongly believe that the use of NMR spectroscopy in chemistry education is underutilized and the activities outlined in the grant proposals are my attempts to change it.

Grading for growth

The sabbatical leave period was also a time during which I engaged with the latest developments in the area of alternative grading. For some years now I've been following the work of Robert Talbert and David Clark, pioneers of alternative grading in college-level mathematics courses, and have been adopting their ideas and strategies in my own courses. I was invited by Drs. Talbert and Clark to share my experience with specifications grading. They published my case study on their blog and will include it in their upcoming book with a working title "Grading for Growth".[1]

Modifications, if any, to the original proposal, and the circumstances that necessitated these modifications

I requested additional employment for Spring 2022 to continue my involvement with the USAID STESSA project I have been working on in Fall 2021. The aim of the project is to develop STEM degree program for universities in Egypt. This opportunity emerged after I submitted my sabbatical proposal and I agreed to participate in the project because its goals were aligned with the goals of my sabbatical leave. Although my request was approved by the Provost, I just happened that I was not directly involved in the STESSA project during my sabbatical.

[1] https://gradingforgrowth.com/p/case-study-hubert-muchalskis-hybrid

The objectives of the original proposal (if any) that were not accomplished

I had hoped to visit the University of Ottawa, Canada, to work with Dr. Derek Pratt on the peroxyl radical clock project. The objective was to validate our NMR-based results using Dr. Pratt's methodology. Unfortunately, the ongoing pandemic-related travel restrictions and limited funding opportunities made it difficult for me to engage in this collaboration.

Anticipated outcomes for the near future as a consequence of the leave's activities

Gold-catalyzed reactions. I plan to submit the recent results as a journal publication with a graduate student as the lead author and two undergraduate students as co-authors. While we work on the manuscript, we submitted abstracts to present this work at the 2023 CSUPERB Symposium and the Spring National Meeting of ACS in Indianapolis.

Green and sustainable chemistry. We will continue to explore the 2-step 1-pot protocol that utilized palladium catalysts in water as solvent.

Curriculum development. I will continue to incorporate new experiments into CHEM 129 laboratory courses. The results of the pilot are very encouraging I plan to work on a manuscript to be submitted for publication in the *Journal of Chemical Education*. I will continue to expand the portfolio of new experiments and write more protocols to be included in the laboratory manual co-authored with Prof. Lipshutz. I will apply for CSUPERB Curriculum Development grant to further support this work.

Peroxyl radical clock methodology with NMR. We should hear back from the funding agencies in the first quarter of 2023. If the proposals are funded we will engage in experimental work as outlined in the proposals. If the applications are not funded I will revise the proposals based on referees' comments and resubmit during the next cycle. The preliminary results will be presented at the 2023 Spring Meeting of ACS (abstract under review).

Alternative grading. I will explore funding opportunities to help bring Dr. Talbert or Dr. Clark to our campus to share their experiences and expertise in alternative grading.

Seminar

I presented the accomplishments of my sabbatical leave at the department seminar on October 7th, 2022. I also organized a visit of my UCSB host to Fresno State. Prof. Lipshutz gave a seminar talk, met with faculty, and toured the campus. I also organized an informal session where prof. Lipshutz met with students and shared information about the graduate program at UCSB.

Original Proposal

A copy of the sabbatical proposal is attached to this report.

Department of Chemistry & Biochemistry

Sabbatical Report

Hubert Muchalski

Associate Professor

Department of Chemistry and Biochemistry

California State University, Fresno

Friday, October 7, 2022

Noon to 12:50 p.m. @ AgM 102

Abstract

The free radical reaction of molecular oxygen with weak C–H bonds known as autoxidation to chemists and peroxidation to biochemists, is the key reaction that leads to oxidative degradation of hydrocarbon-rich materials. Knowledge of rate constants of autoxidation is key in development of antioxidants, molecules that trap the chain-propagating peroxyl radical and inhibit or terminate autoxidation. Use of peroxyl radical clocks is currently the leading experimental approach used in determination of rate constants of H-atom transfer from substrate to peroxyl radical. The main limitation of peroxyl radical clocks developed to date is that they rely exclusively on chromatography-based analytical tools. Our findings indicate that ^{19}F NMR spectroscopy is a suitable analytical tool for development of a new class of peroxyl radical clock molecules. This talk will also outline the new research direction in the area of green chemistry. Results of a pilot study focused on development of synthetic methodology in aqueous media will be presented.

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Department of Chemistry & Biochemistry Seminar Series

Transitioning Organic Chemistry to Water; It's Our Future!

By Bruce H. Lipshutz

Distinguished Professor
Department of Chemistry and Biochemistry
University of California, Santa Barbara

Friday, October 14, 2022
Noon to 12:50 p.m. @ AgM 102

UCSB Graduate Program Information
3:30 to 4:00 p.m. @ Science 1, 382

Abstract

The facility in which Nature carries out complex organic synthesis is truly astounding, especially from the standpoint of environmental responsibility. Bonds are made in water, under mild conditions, and oftentimes using trace metal-containing catalysts. Indeed, with millions of years of "experience" to its credit, Nature is the perfect model. But since modern organic synthesis continues to be practiced, for the most part, in organic solvents, the "new rules" associated with doing chemistry in water are only recently starting to be uncovered. Processes are accumulating, indicating that real synthetic advances are to be anticipated, in addition to the payoff that such chemistry in water is minimizing waste generation from organic solvents, especially those based on petroleum, minimizing the need for energy to be invested (in the form of heating or cooling), and minimizing our reliance on unsustainable amounts of endangered transition metals. This discussion, therefore, will focus on using "dirty" water (i.e., water that contains a surfactant that forms nanomicelles) that enables recent developments associated with chemistry in water, including new technologies for (1) new heterogeneous nanoparticle-catalyzed Negishi (sp2 -sp3) couplings in recyclable water at the ppm level of Pd; (2) a new, biodegradable designer surfactant ("Savie") enabling synthesis in water; and lastly, (3) opportunities to effect chemoenzymatic catalysis; i.e., both chemocatalysis and biocatalysis, where multiple steps (i.e., ≥2) can be run in 1-pot, all in water.

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Section 1. The Proposal

With this application I am requesting sabbatical leave for the AY 21–22 (Spring 2022). My efforts during the leave will focus on redirecting and expanding my research program so my students and I are better equipped to work on important problems related to sustainability and control of chemical processes. To make progress toward those goals, I plan to work on the following projects:

1. Development of gold complexes for catalytic reactions in water in collaboration with Dr. Bruce Lipshutz at the University of California, Santa Barbara.
2. Revision of experiment schedule in organic chemistry laboratory courses (CHEM 129) in the context of green chemistry principles.
3. Calibration and validation of peroxidation rate constant for fluorine-containing peroxyl radical clock—collaboration with Dr. Derek Pratt at the University of Ottawa, Canada.

Gold catalysis in water

Advances made over the last two decades have put the field gold catalysis at the forefront of contemporary synthetic methods and my research group has been active in this area over last few years. My group recently reported new gold-catalyzed reactions that efficiently syntnesize heterocycles benzothiophenes and benzofurans. Heterocycles are small ring structures that contain at least one non-carbon atom (oxygen, nitrogen, or sulfur), are ubiquitous in natural products and pharmaceuticals, and often are the key molecular motif responsible for the desired therapeutic function. For example, benzothiophenes are the building blocks of drugs such as zileuton (asthma treatment) and sertaconazole (antifungal) as well as compound called BTBT, a leading superconductor material used in organic transistors.

As we continue to investigate gold-catalyzed reactions that produce heterocycles, we want to align our methodology with the ongoing efforts in the synthetic chemistry field, i.e., to reduce the impact of chemical processes on the environment by eliminating the use of organic solvents as reaction medium. It is estimated that solvents account for more than 80% of all organic waste generated by chemical producers, both industrial and academic. An obvious candidate for replacing organic solvents as reaction media is water, but organic reactants typically have poor solubility in water and reactions are too slow to be practical.

Prof. Bruce Lipshutz has offered support for my visit to carry out research in his laboratory at UC Santa Barbara during Spring 2022. The objective of this collaboration is to find a catalyst that will efficiently promote our reactions in water instead of organic solvent. Dr. Lipshutz and his team are world-class experts on micellar catalysis, a technology that uses lipid-based nanoparticles to conduct metal-catalyzed reactions in water. Lipshutz's team has expertise structural modifications that lead to micelle-ready metal complexes. The planned experiments will focus on redesigning and testing of the N-heterocyclic carbene (NHC) reagents used in our reactions to make them compatible with water-based conditions. The planned experiments require a large library of reagents, many not available for purchase, which we don't have available at Fresno State.

The key result that will indicate progress on this project will be identification of a catalyst (or catalysts) that promote our reactions in water–micelle system. The target time window for the project is Spring semester because I want to collect preliminary data to apply for funding from the Chemistry Division of the National Science Foundation (application window is every year in September). With an active catalyst in hand, we will focus on optimizing the reaction conditions and evaluating its scope and limitations. These studies will be carried out at Fresno State.

Collaboration with green chemistry experts will also help me improve organic chemistry laboratory courses. Principles of green chemistry are currently integrated into student learning objectives and students are very interested in this topic. Green chemistry has for long been a goal of chemical enterprise and more attention is being paid to cost- and energy-effectiveness, reuse and recovery of catalysts, abundance of metals, and government regulations. Green chemistry proved to be very powerful pedagogical tool in teaching laboratory courses during the pandemic. In this project I will focus on revision of the curriculum in CHEM 129B, the second semester organic chemistry lab course. The key results that will indicate progress on this project will be identification of 2 projects that students can carry out during the second half of the semester when they work independently on a CURE-type project. This can be accomplished with minimal disruption to the existing schedule and will likely reduce the cost of reagents and waste treatment.

Peroxyl radical clocks with use of fluorine NMR

Peroxyl radical clocks are simple and inexpensive experimental methods of measuring rate constants of hydrogen atom transfer from antioxidant to peroxyl radicals. Peroxyl radicals are reactive intermediates that propagate the free-radical chain oxidation process known as autoxidation or peroxidation. The reactions of peroxyl radicals gather interest from researchers across multiple disciplines because they are involved in degradation of primary petroleum products, fine chemicals, polymers, biomolecules, and foodstuffs. Development of new methods that allow for measuring the rate constants of H-atom transfer is a part of discovery of radical-trapping antioxidants (RTAs), small molecules that slow down peroxidation and have long been a focus of research in the field. A peroxyl radical clock can be viewed as competition kinetics experiment in which the rate constant is determined by measuring the product ratio as a function of antioxidant concentration. Thus, radical clocks are indispensable in structure-activity relationship studies of new antioxidants.

My students are working on a new type of radical clock that uses NMR to measure product distribution in the radical clock experiment. Peroxyl radical clocks developed to date use HPLC or GC for product analysis. However, GC analysis can only be carried out on relatively volatile compounds, HPLC-UV is limited to compounds that absorb in UV-Vis range; and in both methods the resolution of analytes depends the chromatographic column used. In contrast, quantitative 19F NMR spectroscopy (qNMR) is a powerful alternative to chromatographic techniques. It offers resolution of 13C NMR, sensitivity of 1H NMR, and is especially suitable for quantitative assays of mixtures because the analyzed molecule contains only one fluorine atom.

The key result that I seek from this project is to validation the data my students will obtain with NMR spectroscopy. I will carry out GC measurements of samples previously measured with NMR. The experiments will be done in collaboration with Dr. Derek Pratt, who is the co-discoverer of the first peroxyl radical clock and a world-class expert in the field, Dr. Pratt who offered support for my visit in Spring 2022. This visit will be the culmination of research my students and I plan to carry out over the next 12-15 months. Our work in this area was disrupted by the pandemic but we are confident we can synthesize the necessary samples by the time this visit is planned. Dr. Pratt's home department, the Department of Chemistry at the University of Ottawa, is also the home department of Dr. Fabien Gagosz, with whom I share interests in gold catalysis. I am excited by the prospect of interacting with Dr. Gagosz, his students and postdocs to further expand my expertise in organogold chemistry. I hope this visit will establish connections with Canadian colleagues and institutions that will result in joint publications and opportunities to students.

Section 2. Benefits to the faculty member

The long-term objective of the sabbatical leave is to acquire knowledge, skills, and preliminary data that will strengthen my grant proposals and help me support the research program in my lab. I developed a robust research program in the chemistry of gold-catalyzed reactions, but that was not my specialty prior to my appointment at Fresno State. There is still a lot I can learn in this rapidly growing field of science. As I acquire new skills and knowledge, I want to shift the emphasis of my research and teaching activities toward sustainable chemistry and transdisciplinary science that focuses on problems at the interface of food, energy, and water.

Most common responses I receive on grant applications say that I don't have publication record or the expertise in organogold chemistry. Our recently published work in this area address those comments. However, as the direction of my research shifts toward reactions in water, I will likely receive similar feedback unless I show preliminary data that came from a successful collaboration with leading scientists in those fields. Additionally, the long-term success of my research program will depend on how effectively I advise my students. One way to prepare for that is to travel to the location and work together with experts in the field.

Section 3. Benefits to the university

My overarching goal of the requested sabbatical leave is to return from it better equipped to serve university's mission of educating students and advancing knowledge through original research. Through my own professional development during the leave and the collaborations I want to establish, I will build up the research capabilities of the Chemistry Department, College, and University. I hope that this will be a productive period which will result in grant proposals and publications in high impact journals with graduate and undergraduate students as co-authors. The Department will benefit from a revised course offering that is aligned with the contemporary practices in chemical industry, where our students expect to find employment after graduation. I think there is a great opportunity in offering courses in which the student learning objectives originate from the global sustainability goals. Lastly, I hope that my time at UC Santa Barbara and University of Ottawa will strengthen ties between the Fresno State and its partners in California and abroad.

Section 4. Previous leaves

This is my first application for sabbatical leave.