LAKE SUPERIOR STATE UNIVERSITY
OFFICE OF THE PROVOST

APPLICATION FOR SABBATICAL LEAVE
(Refer to Section 15.4 of the Faculty Association Agreement)

I. Name R. Adam Mosey Date 11/12/2018

Department Chemistry Ext. No. 2284

Home Address 4800 S. Riverside Dr. SSM, MI Home Phone 517-896-7305

II. Application for leave during the following (*indicate semester and/or year*):

☐ Fall ☐ Spring ✖ Full Year

III. Number of years of faculty service (*minimum of 5 years required*) 6

IV. Year your tenure at LSSU was earned (*tenure required*) 2017

V. Semester or year of last sabbatical (*if applicable*) NA
(*minimum of 5 years since last sabbatical required*)

VI. I agree to return to the University and to provide a complete written report (electronic) to the Provost upon the completion of my sabbatical semester(s) as denoted in section 15.4 of the Faculty Associate Contract.

[redacted] 11-12-18
Signature of Faculty Applicant Date

VII. Signature of your Dean indicating his/her awareness of the application:

[redacted] 12 Nov 18
Signature of Dean Date

VIII. Attachments:
a. Title and Description of Sabbatical Project (Required and described on the next page)
b. Support Documents (Optional but strongly suggested)
c. Curriculum Vitae (Required)

Title and Description of Sabbatical Project.

Provide a document that describes your proposed sabbatical activities. The document should include at a minimum the following components:

- *Project Abstract/Executive Summary:* A summary of the sabbatical project and outcome (150 word maximum).
- *Project Description: A detailed description of the sabbatical project with the following sections:*
  - *Introduction:* Provide an introduction to the topic/field of study.
  - *Background:* Provide information regarding previous work/activities related to the project.
  - *Outcome:* Describe the work to be completed and state the specific outcome(s) of the project. This section must address at least one of the following.
    i. The strength of the relationship between the sabbatical leave proposal involving applied or theoretical research related to professional activities and the advancement of knowledge within disciplinary areas.
    ii. The strength of the relationship between the sabbatical leave proposal involving an external, professionally-related experience/study in a business, industrial, health care, scientific or educational setting and the improvement of instructional/professional activities at the University.
    iii. The strength of the relationship between the sabbatical leave proposal involving travel or advanced study and its yield in improving the quality of instruction at the University.
  - *Timeline:* Provide a timeline for the proposed project activities.

NMR-Guided Reactivity Studies for New Reaction Methodology Development and Structure Activity Relationship Studies for the Development of Potent Proteasome Modulators

Sabbatical Leave Proposal Application for Fall 2019-Spring 2020

Submitted by Dr. R. Adam Mosey

November 15, 2018

Project Abstract

My research interests pertain to the development of new chemical reaction methodologies for the synthesis of unprecedented organic compounds with desired biological properties. The research described herein includes 1) NMR-guided reactivity studies for the development of new reaction methodologies and 2) structure activity relationship studies for the development of potent proteasome modulators. The first part of this project would involve the use of NMR to develop a universal reactivity scale among organic functional groups towards a commonly used chemical reagent and subsequent application of the reactivity scale towards new methodology development. The second part of this project would involve collaborative work with researchers at Michigan State University to engineer molecules capable of modulating proteasomal activity, an area of interest in drug development. The proposed sabbatical leave also involves preparation of grant proposals to enhance LSSU undergraduate research opportunities and dissemination of the work through manuscripts and a national scientific presentation.

Project Description

Introduction

Reaction methodology development and chemical scaffold synthesis are core features of synthetic and medicinal chemistry. Often, new reaction methodologies are developed in order to synthesize target molecules with desired biological activities. Once these methodologies are developed, they are commonly used for the synthesis of structurally diverse compounds with an array of biological properties. This aims of this proposal are to develop chemical tools (i.e. a functional group reactivity scale) for the rapid identification of new reaction methodologies and to use existing reaction methodologies recently developed in my lab for the development of potent proteasome modulators. The proposed studies at LSSU would utilize high-throughput NMR (Nuclear Magnetic Resonance) capabilities as a tool to discover previously unknown reaction methodologies. The NMR would be used to guide the development of a universal reactivity scale among trifluoromethanesulfonic anhydride (Tf_2O)-reactive organic functional groups (a fundamental need in organic chemistry), and the developed reactivity scale

would then be applied towards the development of new chemical reaction methodologies. The proposed collaborative studies with Dr. Jetze Tepe at Michigan State University would involve development of structure activity relationship studies in order to design and construct potent small molecule proteasome modulators, which are of immense interest to the medicinal chemistry community for their potential role in the treatment of numerous diseases, including cancer, Alzheimer's, Parkinson's, and Huntington's diseases. Both portions of this project will involve the synthesis of structurally diverse and potentially biologically active chemical scaffolds, and findings from this project will be utilized both by LSSU student researchers as well as the broader chemical research community. Furthermore, data obtained from both portions of the study will be used for the generation of manuscripts for publication and for the procurement of external grant funding needed to continue and enhance my ongoing research program at LSSU, one which has already funded numerous LSSU student research opportunities and has enabled professional development opportunities for myself, other LSSU faculty, and LSSU students.

Background

A. NMR-Guided Reactivity Studies

Trifluoromethanesulfonic anhydride (Tf_2O) is a widely used dehydrating reagent that has a high affinity for oxygen- and nitrogen-containing functional groups. Compounds bearing these functional groups, including alcohols, amines, amides, carboxylic acids, esters, ketones, and many more, readily react with Tf_2O to generate activated intermediates which can then be captured or attacked by additional functional groups within the same molecule (intramolecular reactions) or in other organic molecules (intermolecular reactions), thereby resulting in the formation of a wide variety of desirable chemical moieties and chemical scaffolds. These reactions may often be performed in tandem in the same reaction vessel, and such "one-pot" reactions lend to rapid construction of compounds by eliminating the need to handle reactive intermediates. Research studies by Movassaghi, Charette, and others have demonstrated that the reagent may be used to transform combinations of simple starting materials into complex products, many of which are valued for their pharmaceutical relevance.[1] My current work with LSSU undergraduate students across two externally funded grants has already resulted in the development of two methodologies involving Tf_2O-mediated amide dehydration for the synthesis of valued heterocycle scaffolds.[2] These studies were primarily carried out by 15 LSSU undergraduate students over the past 5 summers, whose full-time summer work was funded by these grants. While numerous reports of the reagent's use in organic synthesis exist (the reagent appears in more than 7500 publications and patents), there is still no published reactivity trend which ranks functional groups according to their reactivity towards Tf_2O. Due to this dearth of basic fundamental information, each research group working to develop new methodologies involving Tf_2O systematically tests the tolerance of organic substrates bearing different functional groups until they achieve a chemical system that permits their desired transformation. However, even when such an optimal set of substrates and conditions has been established, many Tf_2O reactive organic functional groups are never even tested for compatibility with a given methodology due to the common belief that these functional groups may lead to unwanted side reactions or even failed reactions. As such, a large swath of chemical space remains unexplored, and molecules with potentially exciting biological activities remain unsynthesized.

Incremental mining through organic functional groups to test for reaction condition compatibility hampers the rate at which researchers are able to unearth new chemical methodologies. A more straightforward and broadly beneficial strategy would be to develop a scale of functional group reactivity toward a given reagent (in this case Tf_2O) and then to develop new reactions based off this reactivity scale. This approach has recently been utilized to define a scale of relative nucleophilic and electrophilic properties of organic compounds, such that the respective Lewis base and acid characteristics of organic compounds are readily accessible to researchers working to develop new reactions.[3] Due to the widespread use of Tf_2O, a scale comparing the relative reactivity of functional groups towards this reagent would surely be a boon to the chemical research community.

My proposed work in this area would involve performing competition studies to determine a relative scale of reactivity among common organic functional groups towards Tf_2O for use in reactivity guided reaction methodology development. A straightforward method for determining a reactivity scale would involve performing an array of competition studies, wherein combinations of two compounds bearing different functional groups would be treated with Tf_2O. If equimolar amounts of each compound and Tf_2O were combined (i.e. 1 millimole of each) in the presence of a large excess of a compound capable of quenching Tf_2O-generated reactive intermediates (i.e. anisole), the observed product ratio would provide a measurement of the relative reactivity of the two compounds and their respective functional groups towards Tf_2O. Iterative treatment of combinations of two different compounds at a time with Tf_2O would be used to generate a matrix of reactivity among a large set of reactive compounds (i.e. Compound A vs Compound B, Compound A vs Compound C, Compound B vs Compound C, etc.). As a potentially large data set would need to be generated, this study would be very time and resource intensive when conducted via traditional methodology development, wherein each reaction would undergo workup and product mixture isolation. In this way, perhaps only 1-2 reactions could be completed by a researcher per day. However, these issues would be circumvented by monitoring reaction mixtures via quantitative NMR instead of isolating products. Each competition experiment could be conducted by treating a mixture of two compounds in a suitable solvent in an NMR tube with Tf_2O, and then each reaction would be monitored by 1-dimensional ^{1}H and ^{13}C NMR (in some cases, useful 2-dimensional NMR experiments such as HSQC, HMBC, and NOESY might also be necessary to determine reaction outcomes). As this approach would obviate the need to work up reactions and isolate reaction products, productivity would be greatly increased when compared to traditional synthetic methods, such that a researcher could complete 5-10 reactions per day, being limited primarily by the time required to acquire and interpret spectral data. The high-throughput nature of this approach would permit the generation of a large highly inclusive matrix of functional group reactivity trends, wherein approximately 15-20 nitrogen- and oxygen-containing functional groups could be compared through the monitoring of approximately 200 - 400 reactions. Additional benefits of monitoring competition experiments via NMR include reduced use of reactive substrates and reagents due to the small volume of NMR samples (approximately 0.5 mL each), rapid identification of factors influencing reaction outcomes (i.e. the effect of temperature, solvent, concentration, base additives, etc. on comparative reactivity trends), and establishment of reaction rates using kinetic NMR experiments. While a large volume of NMR data will need to be acquired for this study, routine NMR usage by LSSU faculty and students would not be interrupted due to the auto sampler and remote processing capabilities featured on LSSU's recently acquired 400 MHz NMR. The auto sampler permits recording of NMR data during instrument idle times and off-peak hours (nights and weekends),

which is when these samples would be queued to run in an attempt to minimize disruptions to other users.

Once a comparative scale of reactivity towards Tf_2O has been established, the information will be used to guide the development of new reaction methodologies for the synthesis of desired molecular scaffolds. Instead of using a quenching agent in the reaction mixtures, two compounds with functional groups of differing reactivity towards Tf_2O may be placed together in a reaction vessel, and treatment of the mixture with Tf_2O will initiate a cascade reaction sequence. The compound bearing the more reactive functionality will first consume Tf_2O to form a reactive intermediate, and the second compound will then intercept the reactive intermediate via its functional group to generate a unique chemical arrangement. If these reactions are also screened via NMR, as described above for the development of the reactivity scale, we anticipate the rapid identification of many new potential chemical methodologies for the synthesis of diverse and desirable chemical scaffolds.

B. Development of Proteasome Modulators

The synthesis and degradation of cellular proteins are integral processes involved in maintaining biological homeostasis. Protein degradation, or proteolysis, plays an essential role in many basic biological processes including cell cycle control, cell differentiation, and apoptosis. Proteolysis is also a cellular method used to regulate protein quality control, whereby misfolded, mutant, and damaged proteins can be removed from the cellular environment. The sites of proteolysis are compartmentalized within cells to prevent unregulated protein hydrolysis, and in eukaryotic cells, a major portion of intracellular proteolysis occurs within the proteasome.[4] The 26S proteasome is a large 2.5 MDa complex consisting of a core 20S particle, also known as the 20S proteasome, sandwiched between two 19S regulatory complexes. This important piece of cellular machinery has been investigated as a target in the treatment of diseases, most prominently for the treatment of multiple myeloma. Since 2003, three proteasome inhibitors (bortezomib, carfilzomib, and ixazomib) have been approved by the FDA for the treatment of multiple myeloma.[4] Bortezomib and ixazomib are weakly reversible inhibitors of the 26S proteasome and feature boronic acids that bind to the complex's catalytic site, whereas carfilzomib is an irreversible inhibitor of the 20S proteasome that becomes covalently bound to the complex via its electrophilic epoxide. More recently, the proteasome has received increasing attention for its role in neurodegenerative diseases, such as Alzheimer's, Parkinson's, and Huntington's disease. Under normal conditions, the 20S proteasome routinely degrades intrinsically disordered proteins, including tau and α-synuclein. However, a reduction in proteasomal activity, which is common during aging, leads to an accumulation and aggregation of these nonsoluble proteins, which has been implicated in the pathogenesis of the aforementioned diseases. As such, activation of the 20S proteasome in order to reduce buildup of intrinsically disordered proteins is currently being investigated as a means of treating neurodegenerative diseases.[5]

Both inhibition and activation of proteasomal activity for disease treatment are actively being explored in the Tepe labs at Michigan State University. Research in the Tepe group largely focuses on the synthesis of small molecules and evaluation of the molecules as modulators of the proteasome. In particular, their lab has focused on the synthesis of imidazolines, heterocyclic compounds containing a core amidine moiety (a N-C=N arrangement found within the structure). Many imidazoline compounds

developed in their labs have been shown to potently inhibit proteasomal activity through noncompetitive allosteric inhibition of the proteasome rather than through the aforementioned covalent inhibition.[6] These compounds have proven effective at inhibiting proliferation of numerous cancer cell lines, and one compound is currently moving into clinical trials for the treatment of canine histiocytic sarcomas, aggressive and invasive tumors that occur frequently in Bernese Mountain dogs. Moreover, imidazolines have also recently been identified in their labs which enhance rather than inhibit proteolytic activity, exciting findings which are currently under investigation.

Ongoing studies conducted by undergraduate students in my lab at LSSU have resulted in the development of a multicomponent one-pot method for the synthesis of 3,4-dihydroquinazolines.[2b] The multicomponent nature of this methodology permits the rapid construction of molecules of this compound class with unprecedented structural diversity from simple commercially or readily available starting materials. As dihydroquinazolines are structurally similar to imidazolines, namely both scaffolds feature an amidine moiety positioned within a partially saturated ring system, we initiated a collaboration with the Tepe lab at MSU to determine whether dihydroquinazolines also modulate proteasomal activity. Excitingly, initial evaluation of a limited number of our compounds provided preliminary evidence that indeed dihydroquinazolines do act to modulate the proteasome, and we wish to further investigate the potential of these compounds both as potential inhibitors and activators of the proteasome for use in disease treatment. To progress this study, focused libraries of dihydroquinazolines will need to be synthesized and tested for biological activity as part of structure-activity relationship (SAR) studies. SAR studies are those in which determined biological activities of particular sets of compounds varying in structural features guides the development of molecules which comprise structural features that are observed to lend to biological activity. Often, molecules synthesized to include a combination of these "optimal" structural fragments exhibit enhanced activity relative to the molecules from which they were inspired. We initially plan to broadly screen dihydroquinazolines present in our current compound library for their ability to activate or inhibit the proteasome, and the information gleaned from the screening will be used to guide the synthesis of increasingly potent proteasome modulators. Early SAR studies will focus on determining structural requirements necessary for optimizing biological activity, where increasing activation and inhibition properties of lead structures will be the main focus. Later studies will likely aim to make compounds more druglike by altering structural features to increase water solubility and to decrease potential toxicity arising from compound metabolism. The synthesis portion of the SAR studies will primarily be carried out at LSSU, as the necessary chemicals, equipment, and facilities are currently in place for the rapid construction and structural verification of dihydroquinazoline compounds. Upon synthesis of the target compounds, we will evaluate the ability of the newly synthesized compounds to modulate the proteasome in Dr. Tepe's labs at Michigan State University, which are equipped for high throughput screening activities.

Outcomes

A. The outcomes of the NMR studies at LSSU include development of a comparative reactivity scale among functional groups towards the reagent Tf_2O and use of the reactivity scale for the efficient and rapid design of new Tf_2O-mediated reaction methodologies capable of generating desirable and unprecedented organic compounds. The results of these studies will be disseminated in the form of manuscripts in order

to provide a valuable synthetic chemistry resource for both LSSU undergraduate researchers and the chemical community at large. Additionally, the results of these studies are anticipated to be presented at an American Chemical Society research conference in order to bring attention to the research being conducted at LSSU. Lastly, the data obtained from these studies will be used for the preparation of grant proposals to continue funding excellent scientific student research opportunities at LSSU.

B. The outcomes of the proteasome modulation studies include SAR development of potent proteasome modulators for disease treatment. Results from this work will lay the foundation for future collaborative chemistry studies intended to be carried out by students at both MSU and LSSU. We will use data generated from this study to prepare co-written grants, which if awarded will fund the proposed ongoing collaborative research. The results of this study will also be incorporated into co-written manuscripts, with the intention of involving both LSSU and MSU students as co-authors. Professionally, I will also benefit from this portion of the sabbatical, as I will have the opportunity to give research seminars at MSU while performing research in this exciting field.

Timeline

Fall 2019 Semester:

1. Conduct collaborative SAR studies with the Tepe lab; synthetic work will be completed at LSSU and biological evaluation will be conducted at MSU
2. Initiate NMR-guided reactivity scale studies at LSSU
3. Prepare and submit grant proposal(s) pertaining to proteasome modulation studies

Spring 2020 Semester:

1. Continue collaborative studies with the Tepe Lab
2. Continue NMR-guided reactivity scale studies
3. Develop new Tf_2O-mediated chemical methodologies based off developed reactivity scale
4. Prepare and submit grant proposal(s) pertaining to ongoing and future NMR-guided reactivity studies and new reaction methodology development
5. Prepare and submit manuscript(s) pertaining to NMR studies and/or Tepe collaboration for publication
6. Present findings at a national American Chemical Society Meeting

References

1. For representative examples see: a) Charette, A.; Chua, P. Mild Method for the Synthesis of Thiazolines from Secondary and Tertiary Amides. *J. Org. Chem.* **1998**, *63*, 908-909. b) Movassaghi, M.; Hill, M.; Ahmad, O. Direct Synthesis of Pyridine Derivatives. *J. Am. Chem. Soc.* **2007**, *129*, 10096-10097. c) Regnier, S.; Bechara, W.; Charette, A. Synthesis of 3-Aminoimidazo[1,2-a]pyridines from α-Aminopyridinyl Amides. *J. Org. Chem.* **2016**, *81*, 10348-10356.

2. a) Ellsworth, A.; Magyar, C.; Hubbell, G.; Theisen, C.; Holmes, D.; Mosey, R. One-pot Triflic Anhydride-Mediated Synthesis of 1,2-Disubstituted 2-Imidazolines from *N*-(2-haloethyl)amides and Amines. *Tetrahedron* **2016**, *72*, 6380-6389. b) Magyar, C. L.; Wall, T. J. ; Davies, S. B.; Campbell, M. V.; Smith, S. R.; Barna, H. A.; Savich, C. J.; Mosey, R. A. Triflic Anhydride Mediated Synthesis of 3,4-Dihydroquinazolines: A Three-Component One-Pot Tandem Procedure. *Org. Biomol. Chem*. **2018**, *Submitted*.

3. Mayr, H.; Bug, T.; Gotta, M.; Hering, N.; Irrgang, B.; Janker, B.; Kempf, B.; Loos, R.; Ofial, A.; Remennikov, G.; Schimmel, H. Reference Scales for the Characterization of Cationic Electrophiles and Neutral Nucleophiles. *J. Am. Chem. Soc.* **2001**, *123*, 9500-9512.

4. Manasanch, E. E.; Orlowski, R. Z. Proteasome Inhibitors in Cancer Therapy. *Nat. Rev. Clin. Oncol.* **2017**, 417-433.

5. Jones, C. L.; Njomen, E.; Sjogren, B.; Dexheimer, T. S.; Tepe, J. J. Small Molecule Enhancement of 20S Proteasome Activity Targets Intrinsically Disordered Proteins. *ACS Chem. Biol.* **2017**, *12*, 2240-2247.

6. Azevedo, L. M.; Lansdell, T. A.; Ludwig, J. R.; Mosey, R. A.; Woloch, D. K.; Cogan, D. P.; Patten, G. P.; Kuszpit, M. R.; Fisk, J. S.; Tepe, J. J. Inhibition of the Human Proteasome by Imidazoline Scaffolds. *J. Med. Chem.* **2013**, *56*, 5974-5978.

MICHIGAN STATE UNIVERSITY | Department of Chemistry

Date: October 19, 2018
RE: Prof. Robert A. Mosey

Dear Provost Lynn Gillette:

It is real pleasure for me to invite Prof. R. Mosey as a visiting professor at the Department of Chemistry at Michigan State University.

Prof. Mosey will be working in my research laboratory during the 2019 academic year as part of his sabbatical from Lake Superior State University. Professor Mosey will be working on the synthesis of small heterocyclic scaffolds as proteasome modulators for the treatment of cancer and neurodegenerative disorders.

Under a material transfer agreement, Prof. Mosey provided us with several small molecules synthesized in the Mosey lab for biological evaluation in our laboratory. Recently, we completed our first biological assessment of his new scaffolds and discovered some very exciting biological activity related to regulating the human proteasome. The proteasome is the cells main machinery that regulates the turnover of redundant and misfolded proteins, thereby maintaining a healthy homeostasis. Small molecule regulation of proteasome activity is a clinically validated approach to treat certain cancers, but new research also indicates its potential use in neurodegenerative diseases. As part of his sabbatical work, we plan to collaborate on the exploration of Prof. Mosey's compounds and prepare improved analogues, as possible novel therapeutics. My research lab has all the equipment, infrastructure and material available for Prof. Mosey to conduct his proposed research.

I look forward to a highly productive joint research effort again with Prof. Mosey.

Best wishes,

[redacted]

Jetze Tepe

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EDUCATION

Ph.D. Chemistry (Organic), Michigan State University, East Lansing, Michigan **2010**
Dissertation: Synthesis of Novel Quaternary α-Amino Acids and 2-Imidazolines Derived from Oxazol-5(4*H*)-ones and Evaluation of their Proteasomal Inhibition Activity

B.S. Chemistry (with Honors), *magna cum laude,* Northern Michigan University, Marquette, Michigan **2003**

RESEARCH AND TEACHING POSITIONS

Associate Professor, Lake Superior State University	**2017 - Present**
Assistant Professor, Lake Superior State University	**2012 - 2017**
Postdoctoral Scholar, University of Pittsburgh	**2010 - 2012**
Term Instructor (Sabbatical Replacement), Northern Michigan University	**2008 - 2009**
Lecturer, Michigan State University	**2008**
Graduate Research Assistant, Michigan State University	**2004 - 2010**
Graduate Teaching Assistant, Michigan State University	**2003 - 2008**

AWARDS AND HONORS

45th National Organic Symposium Travel Award, American Chemical Society	**2017**
Excellence in Academic Advising Award, Lake Superior State University	**2016**
Graduate School Dissertation Completion Fellowship, Michigan State University (awarded twice)	**2010**
Graduate Recruitment Fellowship, Michigan State University	**2003**
Lucian S. Hunt Chemistry Award, Northern Michigan University	**2003**
ACS Analytical Chemistry Award, Northern Michigan University	**2002**

TEACHING EXPERIENCE (COURSES TAUGHT)

Assistant/Associate Professor, Lake Superior State University

- Organic Chemistry I and II Lecture and Laboratory
- Advanced Topics in Organic Synthesis Lecture
- Applied Spectroscopy Lecture and Laboratory
- Applied Organic and Biochemistry Lecture and Laboratory
- Introductory Chemistry Laboratory
- Science of Beer Lecture and Laboratory
- Senior Seminar

Instructor, Northern Michigan University

- Introductory Chemistry Discussions
- Organic Chemistry Laboratory

Lecturer, Michigan State University
- Organic Chemistry Lecture

Teaching Assistant, Michigan State University
- Organic Chemistry and Honors Organic Chemistry Recitations

FUNDING

2018 – 2019: Mosey, R. A. (PI) NMR-Guided Methodology Development. LSSU Foundation Enrichment Grant, ***$1,988 Awarded.***

2016 – 2019: Mosey, R. A. (PI); Hutchens, M. A.; Johnson, S. C.; Werner, R. M. MRI: Acquisition of a 400 MHz NMR Spectrometer for Use in Research and Research Training. National Science Foundation, Major Research Instrumentation Award, ***$399,500 Awarded***.

2016 – 2019: Mosey, R. A. (PI) Synthesis and Antimicrobial Evaluation of Diverse 3,4-Dihydroquinazolines. National Institutes of Health, R03 Award, ***$140,266 Awarded***.

2014 – 2017: Mosey, R. A. (PI) Multicyclic Heterocycle Syntheses via Tandem Amidation/Annulation Reactions of N-Containing Heterocycles and Carboxylic Acids. Research Corporation for Science Advancement, Single Investigator Cottrell College Science Award, ***$53,000 Awarded***.

PUBLICATIONS (**LSSU UNDERGRADUATE STUDENT RESEARCHERS)

1. Malcolm, C. I.**; Magyar, C. L.**; Wall, T. J. **; Davies, S. B.**; Campbell, M. V.**; Quevillon, T. J.**; Savich, C. J.**; Hutchens, M.; Mosey, R. A. Inhibition of MRSA Growth and MRSA Biofilm Growth by 3,4-Dihydroquinazolines. *Manuscript in preparation.*
2. Hubbell, G. E.**; Ellsworth, A. A.**; Iretskii, A. V.; Mosey, R. A. Highly Diastereoselective Synthesis of Fused Oxazinone/Imidazolidine Compounds via Annulation Reactions Between Amino Acid Derivatives and 2-Imidazolines. *Manuscript in preparation*.
3. Magyar, C. L.**; Wall, T. J. **; Davies, S. B.**; Campbell, M. V.**; Smith, S. R.**; Barna, H. A.**; Savich, C. J.**; Mosey, R. A. Triflic Anhydride Mediated Synthesis of 3,4-Dihydroquinazolines: A Three-Component One-Pot Tandem Procedure. *Org. Biomol. Chem.* **2018**, *Submitted.*
4. Ellsworth, A. A.**; Magyar, C. L.**; Hubbell, G. E.**; Theisen, C. C.**; Holmes, D.; Mosey, R. A. One-Pot Triflic Anhydride-Mediated Synthesis of 1,2-Disubstituted 2-Imidazolines from N-(2-haloethyl)amides and Amines. *Tetrahedron* **2016**, *72*, 6380-6389.
5. Azevedo, L. M.; Lansdell, T. A.; Ludwig, J. R.; Mosey, R. A.; Woloch, D. K.; Cogan, D. P.; Patten, G. P.; Kuszpit, M. R.; Fisk, J. S.; Tepe, J. J. Inhibition of the Human Proteasome by Imidazoline Scaffolds. *J. Med. Chem.* **2013**, *56*, 5974-5978.
6. Mosey, R. A.; Floreancig, P. E. Isolation, Biological Activity, Synthesis, and Medicinal Chemistry of the Pederin/Mycalamide Family of Natural Products. *Nat. Prod. Rev.* **2012**, *29*, 980-995.
7. Mosey, R. A.; Floreancig, P. E. Versatile Approach to α-Alkoxy Carbamate Synthesis and Stimulus-Responsive Alcohol Release. *Org. Biomol. Chem.* **2012**, *10*, 7980-7985.
8. Mosey, R. A.; Tepe, J. J. New Synthetic Route to Access (+/-) Salinosporamide A via an Oxazolone-mediated Ene-type Reaction. *Tetrahedron Lett.* **2009**, *50,* 295-297.

9. Mosey, R. A.; Fisk, J. S.; Tepe, J. J. Stereoselective Syntheses of Quaternary Substituted α-Amino Acids Using Oxazol-5-(4H)-ones. *Tetrahedron: Asymmetry* **2008**, *19*, 2755-2762.
10. Mosey, R. A.; Fisk, J. S.; Friebe, T. L.; Tepe, J. J. Synthesis of *tert*-Alkyl Amino Hydroxy Carboxylic Esters *via* an Intermolecular Ene-Type Reaction of Oxazolones and Enol Ethers. *Org. Lett.* **2008**, *10*, 825-828.
11. Fisk, J. S.; Mosey, R. A.; Tepe, J. J. The Diverse Chemistry of Oxazol-5-(4*H*)-ones. *Chem. Soc. Rev.* **2007**, *36*, 1432-1440.

PRESENTATIONS (**LSSU UNDERGRADUATE STUDENT RESEARCHERS)

1. Campbell, M.**; Mosey R.A. A One-Pot Reaction Involving a Pictet-Spengler-type Cyclization Step for the Synthesis of Quaternary 3,4-Dihydroquinazolines. Poster Presentation, West Michigan Regional Undergraduate Science Research Conference, Van Andel Institute, Grand Rapids, MI, November 10, **2018**.
2. Campbell, M.**; Mosey R.A. NMR Guided Development and Optimization of a One-Pot Triflic Anhydride Mediated Synthesis of Quaternary 3,4-Dihydroquinazolines. Poster Presentation, LSSU President's Circle Reception, Sault Sainte Marie, MI, September 22, **2018**.
3. Malcolm, C.**; Magyar, C.**; Wall, T.**; Davies, S.**; Campbell, M.**; Quevillon, T.**; Hutchens, M.; Mosey, R.A. Evaluation of 3,4-Dihydraquinazolines as Inhibitors of MRSA Planktonic and Biofilm Growth. Poster Presentation, West Michigan Regional Undergraduate Science Research Conference, Van Andel Institute, Grand Rapids, MI, November 4, **2017**.
4. Davies, S.**; Magyar, C.**; Wall, T.**; Campbell, M.**; Savich, C.**; Quevillon, T.**; Mosey, R.A. A New One-Pot Multicomponent Synthesis Of Diverse 3,4-Dihydroquinazolines: Methodology Development, Reaction Scope Exploration, and Mechanistic Investigation. Poster Presentation, West Michigan Regional Undergraduate Science Research Conference, Van Andel Institute, Grand Rapids, MI, November 4, **2017**.
5. Malcolm, C.**; Magyar, C.**; Wall, T.**; Davies, S.**; Campbell, M.**; Quevillon, T.**; Hutchens, M.; Mosey, R.A. Anti-MRSA and Anti-Biofilm Activity of New 3,4-Dihydroquinazolines. Poster Presentation, LSSU President's Circle Reception, Sault Sainte Marie, MI, September 23, **2017**.
6. Davies, S.**; Magyar, C.**; Wall, T.**; Campbell, M.**; Savich, C.**; Quevillon, T.**; Mosey, R.A. Development of a One-Pot Multicomponent Synthesis of Diverse 3,4-Dihydroquinazolines and Exploration of the Reaction Scope. Poster Presentation, LSSU President's Circle Reception, Sault Sainte Marie, MI, September 23, **2017**.
7. Mosey, R. A.; Magyar, C.**; Wall, T.**; Davies, S.**; Savich, C.**; Malcolm C.**; Hutchens, M. Expanding Diversity About the 3,4-Dihydroquinazoline Scaffold: Gaining Access to an Emerging Class of Antimicrobial Compounds. Poster Presentation, National Organic Symposium, Davis, CA, June 26, **2017**.
8. Mosey, R. A. Truth and Character. Invited Oral Presentation, 2017 LSSU Alpha Chi National College Honor Society Induction Ceremony, Lake Superior State University, Sault Sainte Marie, MI, April 7, **2017**.
9. Wall, T.**; Magyar, C.**; Hutchens, M.; Mosey, R. A. Expanding Diversity About the 3,4-Dihydroquinazoline Scaffold: Gaining Access to an Emerging Class of Antimicrobial Compounds. Poster Presentation, Upper Peninsula American Chemical Society Student Research Symposium, Northern Michigan University, Marquette, MI, March 25, **2017**.
10. Magyar, C.**; Wall, T.**; Mosey, R. A. Development of a Multicomponent Synthesis of Diverse 3,4-Dihydroquinazolines. Poster Presentation, Upper Peninsula American Chemical Society Student Research Symposium, Northern Michigan University, Marquette, MI, March 25, **2017**.
11. Mosey, R. A. Partially Saturated Amidine-Containing Heterocycles: Synthesis and Pharmaceutical Applications. Invited Oral Presentation, Northern Michigan University, Marquette, MI, February 20, **2017**.

12. Hubbell, G. E.**; Ellsworth, A. A.**; Iretskii, A. V.; Mosey, R. A. Diastereoselective Formation of Bicyclic Annulation Products from the Interaction of 2-Imidazolines with Serine Derivatives. Poster Presentation, West Michigan Regional Undergraduate Science Research Conference, Van Andel Institute, Grand Rapids, MI, November 5, **2016**.
13. Korcal, K.**; Wall, T.**; Magyar, C.**; Mosey, R. A.; Hutchens, M. Biofilm Inhibition and Destruction Using Newly Synthesized Compounds. Poster Presentation, Michigan Branch of the American Society for Microbiology, Lake Superior State University, Sault Sainte Marie, MI, October 22, **2016**.
14. Hutchens, M.; Magyar, C.**; Wall, Tyler**; Mosey, R. A. Anti-Staphylococcal Activity of 3,4-Dihydroquinazolines. Poster Presentation, Michigan Branch of the American Society for Microbiology, Lake Superior State University, Sault Sainte Marie, MI, October 22, **2016**.
15. Mosey, R. A. Making it Count. Invited Oral Presentation, 2016 LSSU Student Convocation Ceremony, Lake Superior State University, Sault Sainte Marie, MI, August 26, **2016**.
16. Hubbell, G. E.**; Ellsworth, A. A.**; Iretskii, A. V.; Mosey, R. A. Diastereoselective Formation of Bicyclic Annulation Products from the Interaction of Amino Acid Derivatives and 2-Imidazolines. Poster Presentation, Upper Peninsula American Chemical Society Student Research Symposium, Northern Michigan University, Marquette, MI, April 2, **2016**.
17. Ellsworth, A.**; Theisen, C. C.**; Mosey, R. A. Direct Conversion of Amides to 1,2-Disubstituted 2-Imidazolines. Poster Presentation, Upper Peninsula American Chemical Society Student Research Symposium, Northern Michigan University, Marquette, MI, April 11, **2015**.
18. Ellsworth, A. A.**; Theisen, C. C.**; Mosey, R. A. Multicomponent Reaction to Produce Diversely Substituted 2-Imidazolines. Poster Presentation, 249th ACS National Meeting, Denver, CO, March 23, **2015**.
19. Ellsworth, A. A.**; Mosey, R. A. Multicomponent Reaction to Produce Diversely Substituted 2-Imidazolines. Poster Presentation, Midwestern Symposium on Undergraduate Research in Chemistry, Michigan State University, East Lansing, MI, October 11, **2014**.
20. Gravatt, C. S.**; Mosey, R. A. The Synthesis of a Novel Self-Immolative Lysine-Based Surfactant. Poster Presentation, Upper Peninsula American Chemical Society Student Research Symposium, Northern Michigan University, Marquette, MI, March 29, **2014**.
21. Ellsworth, A. A.**; Mosey, R. A. Imidazoline Synthesis to Investigate the Extent of Heterocycle-Biomolecule Complex Formation. Poster Presentation, Upper Peninsula American Chemical Society Student Research Symposium, Northern Michigan University, Marquette, MI, March 29, **2014**.
22. Gravatt, C. S.**; Mosey, R. A. Mobilization of Petroleum Hydrocarbons in Soil: Progress Towards the Synthesis and Property Characterization of a Novel Self-Immolative Lysine-Based Surfactant. Oral Presentation, 23rd Annual Argonne Symposium, Lemont, IL, November 1, **2013**.
23. Mosey, R. A. Synthesis and Evaluation of Proteasome Inhibitors and Triggered Molecular Release Systems. Invited Oral Presentation, The Lubrizol Corporation, Wickliffe, OH, November 21, **2011**.
24. Mosey, R. A.; Floreancig, P. E. Synthesis and Initial Evaluation of H_2O_2-Sensitive "Smart Drugs" as Antioxidant-Releasing Agents. Poster Presentation, University of Pittsburgh Postdoctoral Association Data and Dine, Pittsburgh, PA, June 9, **2011**.
25. Mosey, R. A. Towards the Synthesis of the Proteasome Inhibitor Salinosporamide A *via* an Ene-Type Alkylation Reaction of Oxazol-5(4H)-ones and Enol Ethers. Invited Oral Presentation, Northern Michigan University, Marquette, MI, April 3, **2009**.
26. Fisk, J. S.; Mosey, R. A.; Tepe, J. J. Intermolecular Ene-type Reactions of Oxazol-5(4H)-ones using Enol Ethers. Poster Presentation, 235th ACS National Meeting, New Orleans, LA, April 8, **2008**.

UNDERGRADUATE RESEARCH STUDENTS ADVISED (LSSU)

1. Anderson, Allie. Current. Increasing Hydrophilicity of 3,4-Dihydroquinazolines through Late Stage Buchwald-Hartwig Amidation Reactions.
2. Burton, Kyle. Current. Structure-Activity Relationship (SAR) Optimization of Antibacterial Properties of 3,4-Dihydroquinazolines.
3. Smith, Sydney. Current. Synthesis of Quinazolines via a DDQ-Mediated Oxidative Debenzylation of 3,4-Dihydroquinazolines.
4. Betty, Meili. Current. Synthesis of 3,4-Dihydroquinazolines for Use as Proteasome Inhibitors.
5. Pazur, Ethan (***Honors***). Current. Development of a Quantitative ^{13}C NMR-Based Method for the Rapid Determination of Ethanol Concentration (ABV) in Alcoholic Beverages.
6. Pulkkinen, Mika. Current. Development of a Synthetic Methodology for the Synthesis of 5-Hydroxyimidazoles and 5-Arylimidazoles from the Tf_2O-Mediated Cyclodehydration of Amides.
7. Moore, Tyler. Current. Synthesis of 4,4-Dialkyl 2-Imidazolinones from the Tf_2O-Mediated Cyclodehydration Reactions of Amides.
8. Malcolm, Celina. Current. Evaluation of Growth Inhibition Properties of 3,4-Dihydroquinazolines Against Multi-strain Resistant Bacteria (Collaborative work with Dr. Martha Hutchens). ***Received LSSU Undergraduate Research Award***
9. Campbell, Molly. Current. NMR-Guided Methodology Development for the Synthesis of 4,4-Disubstituted-3,4-Dihydroquinazolines from a Tf_2O-Mediated Multicomponent Reaction of Amides, Amines, and Ketones. ***Received LSSU Undergraduate Research Award***
10. Quevillon, Travis. 2018. A Suzuki Reaction Approach to the Regioselective Synthesis of 5,7-Disubstituted 3,4-Dihydroquinazolines.
11. Davies, Steven. 2018. Synthesis and Microbial Evaluation of 3,4-Dihydroquinazolines Varying at the N-3 and C-4 Positions.
12. Wall, Tyler. 2018. Synthesis and Antimicrobial Evaluation of 3,4-Dihydroquinazolines Varying About the C-2 Position. ***Awarded 1st Place Poster at 2017 Upper Peninsula American Chemical Society Student Research Symposium***
13. Savich, Christopher. 2018. Synthesis of 6,7-Dialkoxy and 7-Alkyl 3,4-Dihydroquinazolines and Evaluation of their Antimicrobial Properties. ***Received LSSU Foundation's Fund for LSSU Award***
14. Epperson, Kasie. 2017. Purple Loosestrife Capabilities in Bio-fuels.
15. Magyar, Christina. 2017. Development of a One-Pot Multicomponent Synthesis of Diverse 3,4-Dihydroquinazolines. ***Received LSSU Undergraduate Research Award; Awarded 3rd Place Poster at 2017 Upper Peninsula American Chemical Society Student Research Symposium***
16. Hubbell, Grace. 2017. Diastereoselective Formation of Bicyclic Annulation Products from the Interaction of 2-Imidazolines with Serine Derivatives. ***Received LSSU Foundation's Fund for LSSU Award***
17. Emaus, Miranda (***Honors***). 2016. Synthesis and Fluorescence Evaluation of Diversely Substituted 2-Imidazolines.
18. Piche, Lance. 2016. Prodrug Linkers for Selective Drug Delivery in Prostate Cancer.
19. Theisen, Chelsea. 2015. Synthesis of *N*-(2-Haloethyl)amides and 1,2-Disubstituted 2-Imidazolines.
20. Ellsworth, Alyssa (***Honors***). 2015. Direct Conversion of Amides to 1,2-Disubstituted 2-Imidazolines and the Synthesis of Multicyclic Imidazoline Adducts. ***Received LSSU Undergraduate Research Award; Awarded 1st Place Poster at 2015 Upper Peninsula American Chemical Society Student Research Symposium***
21. Gravatt, Chris. 2014. Progress Towards the Synthesis of a Novel Self-Immolative Lysine-Based Biodegradable Surfactant. ***Received LSSU Undergraduate Research Award***

22. Sterrit, Joseph. 2014. Annulation of Various Imidazolines with an Amino Acid.
23. Smrke, Rebecca. 2013. Towards the Synthesis of a Guanidine-like Organocatalyst.
24. Brown, Josh. 2013. Synthesis of Multicyclic Products: Using Annulation Reactions of an Imidazoline and β-Hydroxy Carboxylic Acids.

PROFESSIONAL AFFILIATIONS

American Society of Brewing Chemists	**2014 - 2015**
American Chemical Society	**2003 - Present**

UNIVERSITY SERVICE (LSSU)

LSSU NMR Coordinator	**2018 - Present**
LSSU Curriculum Committee	**2016 - Present**
LSSU Outdoor Adventure Club Faculty Advisor	**2016 - Present**
LSSU Grants & Contracts Work Group	**2015 - Present**
LSSU Chemistry Safety Committee	**2014 - Present**
LSSU Human Subjects Institutional Review Board	**2013 - Present**
LSSU Chemistry Program Assessment Committee	**2013 - Present**
LSSU Chemistry Instrumentation and Facilities Committee	**2013 - Present**