An Organic II Course-Based Research Experience: Synthesis of Neurolenin Analogs

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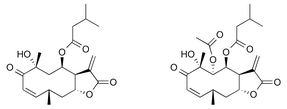
Evolution of the Project

Kristine Trotta '14

- 2013-2014
- Smith biology lab thesis student
- Focus on lymphatic filariasis (tropical disease, infects over 100 million people)
- Isolated neurolenins from *Neurolaena lobata* (*J. Org. Chem.* **1978**, *43*, 4352)
- Active against worm assay for lymphatic filariasis



Neurolenin A Neurolenin B

2014 Organic II – Lab Section #6

- All 8 groups isolated neurolenins
- Each group ran their own reaction
- 5 reactions did not produce products
- 3 reactions yielded products

Katie McGeough '16

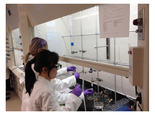
- 2014-2015
- Shea lab summer and thesis student
- Separate and identify neurolenins
- Detailed NMR analysis
- Reproduce preliminary results from Organic II lab
- Synthesize neurolenin analogs for analysis by biology collaborators
- Results – see poster #32

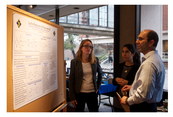
Course Details and Student Quotes

"I know this is mostly because the lab section is experimental, but I would love if the expectations of what we are to do in preparation for and in follow up to lab were more clear. We are given the huge topic of synthesizing molecules, and I am not sure if the expectation is for us to spend one hour outside of class preparing, or ten hours."

"Today is the big day! Our first day of performing our reactions! I am extremely nervous and worried that we will do something wrong and lose all of our product."

"It was really fun and rewarding to have the poster session today. We received feedback that was really encouraging and has given us a few ideas/directions to pursue in the next week or so. We were also able to look at and hear about the ideas of our classmates, which was a lot of fun, especially because I feel like I understand some of the reactions better now than I did earlier in the semester, when we presented our proposals. Everyone I talked to wanted to repeat their reaction again, using the knowledge and experience in the lab that we now have, and that is how I feel too. This was my first poster session that I took part in and it was a great experience!"





Week # 1 2 3 4 5 6 7 8 9 10 11 12 13

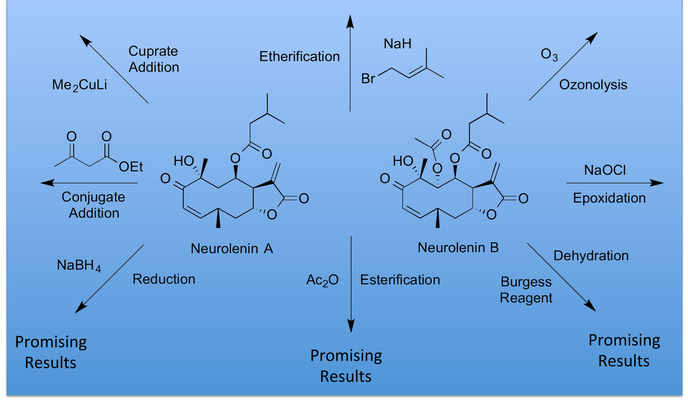
Soxhlet Extraction | Charcoal Purification | Flash Column | NMR Analysis | Project Proposal Presentations | ← Independent Projects → | Poster Session

"It was really cool to hear about everyone else's projects. I realized that even proposals that seemed straightforward at first can easily become tricky because it is difficult or impossible to control where the reactant reacts when there are multiple sites for the same functional group. It was also really interesting to think about which new functional groups may add more biological function to the compound."

"I'm a little bit disappointed that we didn't make the ether product, but I'm still really glad that we did the individual projects. I feel like I've gained more confidence in lab. I have learned several different lab techniques, like column chromatography, rotovapping, cannulation, and working under nitrogen. I think that the experimental lab was a really good idea."

"Well, December sure was a whirlwind! This was a very scary, but very impactful course. Definitely worth the worry! The poster session was so fun, it was great to get to feel knowledgeable and hear other people's feedback. I only wish we had more time to purify our potential Neurolenin A product and redo Neurolenin B!"

Reactions Attempted



Course Design

Overview

This lab will focus on applying your base of chemical knowledge to actual transformations from the literature. Working with a partner, you will isolate and purify the natural products neurolenin A and neurolenin B. You will then propose and carry out reactions on one of these molecules in hopes of preparing a previously unknown molecule that the Williams Lab can test for biological activity. Professional presentation of your results, both in written and oral formats, will be a major component of the course.

Grading

- Project Proposal
- Lab Report
- Poster
- Journal
- Preparation/Technique
- Notebook

Learning Goals

Beyond the specific chemistry-related goals mentioned above, there are numerous broader goals that I hope each of your will achieve. If successful, you should be able to utilize these skills long after you have forgotten the specific details of the reactions and techniques we will study.

- Think like a chemist
- Work productively as a member of a team
- Learn how to efficiently perform database and literature searches
- Evaluate hazards of chemicals and techniques
- Work safely with hazardous materials
- Repeat experiments described in the literature
- Write clear and concise scientific papers
- Learn something new from books and papers
- Learn how a new instrument works
- Clearly present results obtained in lab

General Goals

The general goal for this lab is to develop an understanding of how chemists plan, run, purify, analyze, and report reactions with a focus on practical applications in the laboratory. We will apply our knowledge from Organic I and II to help address a real world problem, namely the development of new molecules to fight the tropical disease lymphatic filariasis.

Formal Course Evaluations

1) How would you describe your own efforts to learn in this course?

- WOW!!!!! WOW, I think I did too much work for this, but it all paid off!!!

2) In what ways could specific features of this course be improved?

- More structure, more help for students, it's really hard to do research for the first time with no experience and therefore students should be supported more throughout the process.

3) What features of this course made the most valuable contributions to your learning?

- One of the greatest features of this course was that it was an independent lab project. Students had the opportunity to conduct their own projects.

4) Numbers

- Course contributed significantly to my education - 3.85
- Average for other 6 sections - 3.39

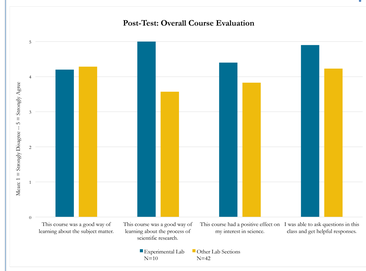
Conclusions

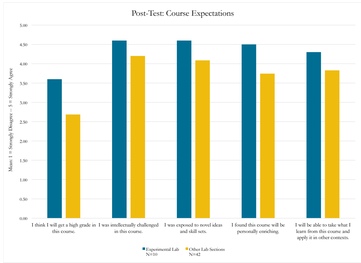
- Very successful
- Rewarding teaching experience
- Sustainable model
- Dreyfus Foundation funding for 4 total lab sections 2016-2018

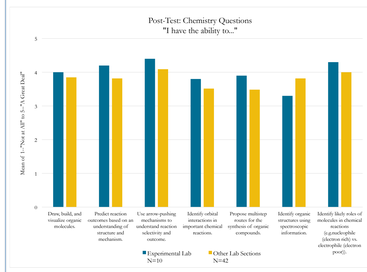
Funding

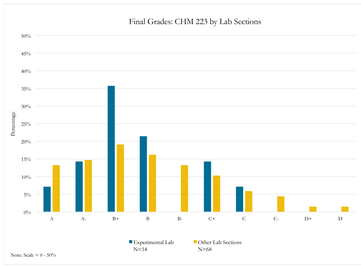
- Clark Science Center
- Chemistry Department
- HHMI
- Dreyfus Foundation

Traditional Labs vs. Experimental Lab Surveys and Grades



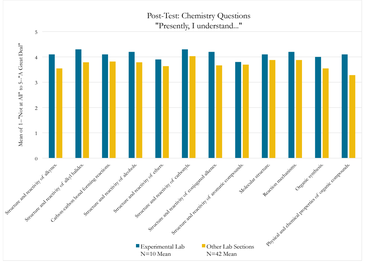






Organic II mean course grades by lab section

	Section #	Mean Grades
All Other Labs	1	2.93
	2	3.15
	3	2.69
	4	2.86
	5	3.36
	7	2.95
All other labs combined (n=69)		3.02
Experimental Lab Section (n=14)	6	**3.11**
Grand Total		3.03



Informal Course Evaluations

Looking back, would you choose to be in this lab section if you were starting Organic III over again?

- All students said yes.

What will you take from this experience as you move forward at Smith?

- Hoping it will help me stand out as a candidate for a lab internship over the summer.
- Failure is fun.
- It has taught me how to be resilient - as a researcher and as a student - and how to move forward when something doesn't go well initially.
- I can do research with less fear.
- I learned a lot about how to work with someone that I didn't necessarily jive with. I think that will be really helpful moving on in life in general.

Pros

- Having the opportunity to do actual experimental research and learn chemistry in the context of real life applications
- No weekly lab reports
- It was really exciting to be doing reactions that weren't fully spelled out for us in a lab manual. We were able to explore reactions that were interesting to us, and I felt really invested in my group's project.
- This lab section was a lot more interesting than any other general lab section that I've been in. I really liked not having mindless busywork; it felt like we actually had a personal stake in what was happening.

Cons

- Being almost completely oblivious to the work done in the regular lab sections, and this may have helped understand concepts in lecture
- This lab definitely took more time than a normal class lab.
- This lab was a bit overwhelming/demoralizing at times, but not excessively so.
- Stressing over having no idea what the heck I'm doing.
- Less practice writing lab reports

Comments on the impact of investigating a novel problem versus your lab experience in Organic I

- This lab experience for me was something I found extremely rewarding. I was much more independent with my approach, problem solving strategies, critical thinking, etc. since we had to do all the research for our experiment on our own. I definitely took charge of this lab experience (with the help of my partner) rather than simply "going with the flow" as I have done in the past.
- This lab helped me realize what it takes to be a chemist rather than mindlessly running reactions.
- Lab was less stressful because it was self-guided.
- Because we were responsible for designing the experiment ourselves, I felt like I understood much more about why we were doing each step, instead of just following instructions like in Organic I.
- I definitely felt more invested in and involved with what we were doing in lab. It didn't feel like just a class.
- In normal lab, if you are having a hard time, there's no real motivation to understand the problem - a million people already did the same thing, so why am I struggling just to do it again?