Incorporating Guided-Inquiry Learning into the Undergraduate Organic Chemistry Laboratory

Dr. Barb Morra
The University of Toronto

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Chemistry
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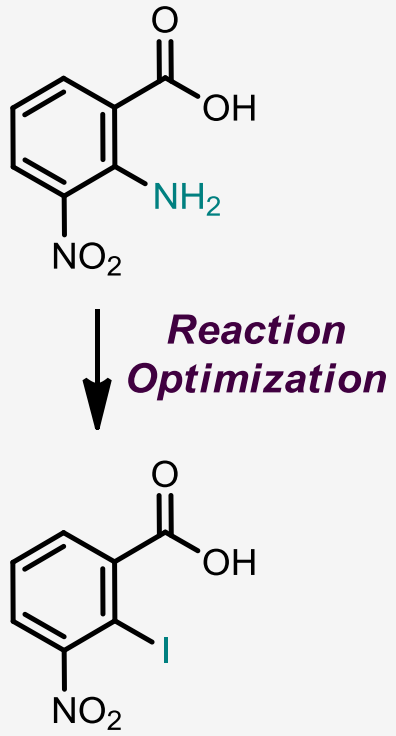


University of Toronto – Undergraduate Chemistry

Organic Chemistry II (CHM249H)

- Second year course designed for students with a passion for chemistry
- 70-80 degree students
- Focus on organic reactions, mechanisms, and synthetic applications
- Emphasis on practical experience (11 experiments in 12 weeks)
- Green chemistry concepts introduced

Introducing Guided-Inquiry Experiments

What are the differences between verification and guided-inquiry experiments?

Verification Laboratory

- "Cookbook" type laboratories
- Students are provided with a detailed procedure
- The outcome of the experiment is typically known and the activity involves a confirmation of anticipated results

Guided-Inquiry Laboratory

- Students are posed with a research question without a complete procedure
- Students must work collaboratively to design a procedure, conduct an investigation and interpret results

Blanchard, M. R.; Southerland, S. A.; Osborne, J. W.; Sampson, V. D.; Annetta, L. A.; Granger, E. M. *Science Education*, **2010**, *94*, 577-616.

The Process of Reaction Optimization

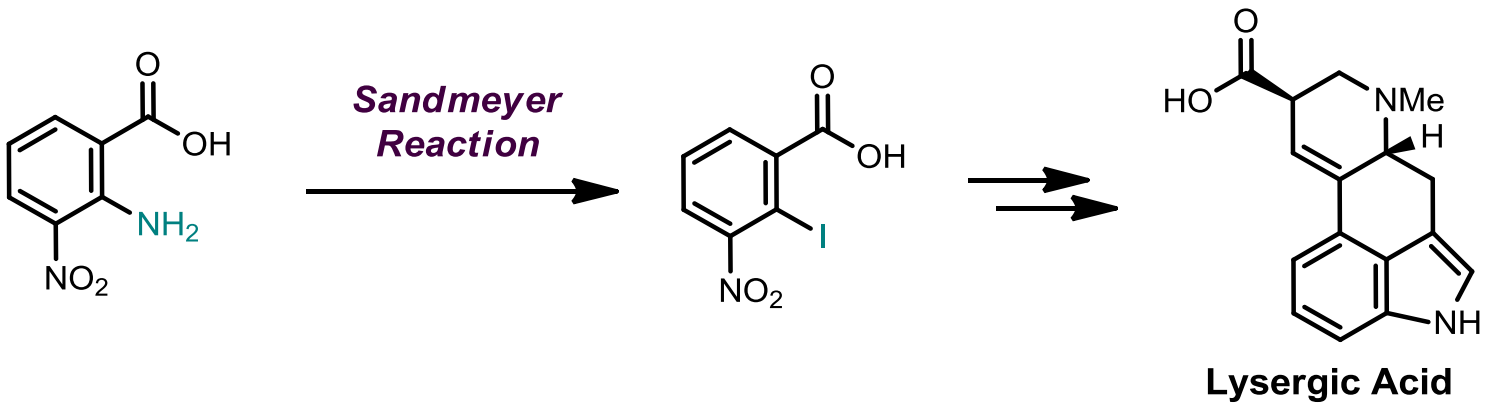
Providing Students with an Industrial Perspective

- Industrial process chemists are responsible for optimizing bench-scale reactions for kilo-scale production
- The final process should:
  - *Maximize* overall product yield, purity, and profitability.
  - *Minimize* the number of steps, reaction time, and waste, while avoiding the use of dangerous, toxic or environmentally hazardous chemicals.
- Industry often utilizes *in-process checks* (IPC) by HPLC analysis

Goals of the New Experiment:

Bridge the gap between the classroom and research laboratory by introducing a research problem with real-world relevance.

Introducing a Research Problem



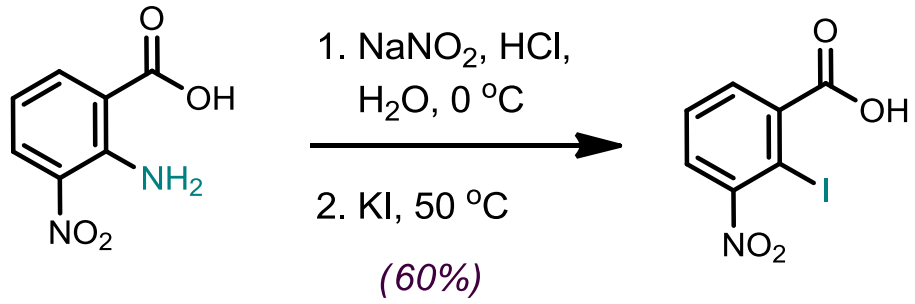
Lysergic Acid

Making Real-World Connections:

- Lysergic acid is a member of a large class of ergoline alkaloids produced by the ergot fungus.
- Derivatives have been identified as potential Active Pharmaceutical Ingredients (API) to alleviate migraines and Parkinson's disease.
- This Sandmeyer reaction originated in the Lautens research laboratory.

Ninomiya, I.; Kiguchi, T. *In The Alkaloids*; Brossi, A., Ed.; Academic Press: San Diego, 1990, Vol. 38, p. 1-156.

Exploring a Novel Sandmeyer Reaction



Goal: Work together with a team of chemists to optimize one of the key steps towards the synthesis of lysergic acid.

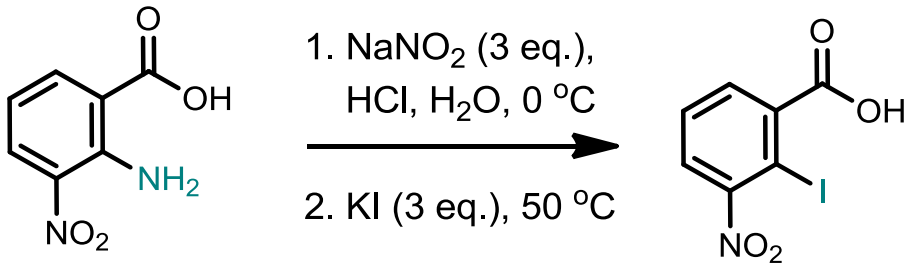
Initial Test Reaction Procedure:

50 mg of 2-amino-3-nitrobenzoic acid, 3 eq **HCl**, and H_2O are stirred at RT for 10 mins. Upon cooling to 0°C, **3 eq of $NaNO_2$** in H_2O are added dropwise, followed by **3 eq of KI**. Reaction is warmed to **50°C** and stirred for 20 mins.

Reaction Variables Explored:

- Type of acid
- Iodide source
- Reagent equivalents
- Reaction temperature

Sandmeyer Reaction Optimization Results



Variable Explored *(Original Condition)*	Reaction Conversion (%)[a]	Reaction Purity (%)[a]
Original Procedure	86	80
TsOH *(HCl)*	90	81
H_2SO_4 *(HCl)*	92	47
CuI *(KI)*	13	1
1 eq. of $NaNO_2$ and KI *(3 eq.)*	0	0
5 eq. of $NaNO_2$ and KI *(3 eq.)*	87	50
70 °C *(50 °C)*	***90***	***87***
90 °C *(50 °C)*	***95***	***88***

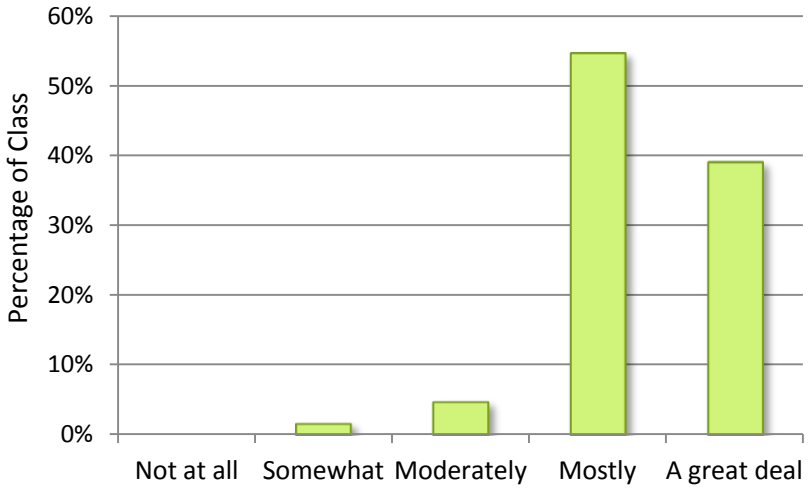
[a] Average value calculated using 7-9 IPCs through HPLC analysis.

Post-Lab Analysis:

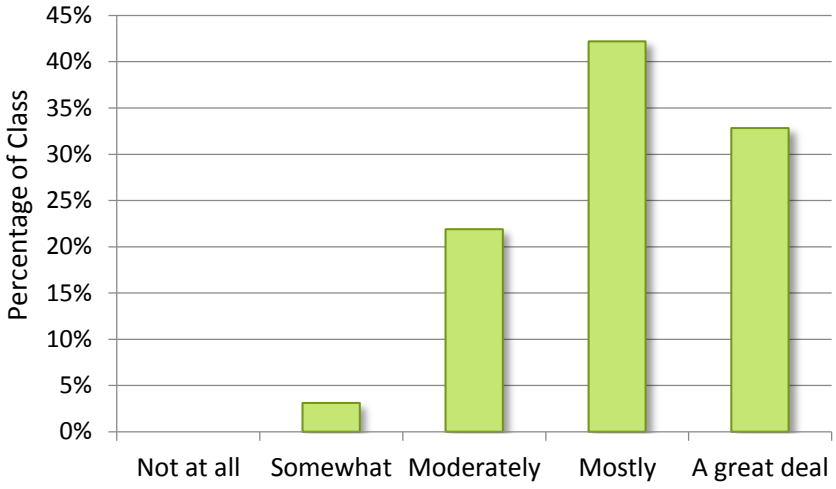
- Students examined their own HPLC spectrum.
- Based on class data, students discussed what the optimal conditions were while taking into consideration reaction conversion, reaction purity and principles of green chemistry.
- Students were evaluated based on their ability to analyze the class results.

Student Feedback

Did you find that the design of the guided-inquiry laboratory helped you understand how reactions are optimized in industry, specifically the process of varying conditions and evaluating the results?



Did you find the design of the guided inquiry laboratory helped you understand the Sandmeyer reaction and the conditions required to achieve optimal results?



Select Student Comments:

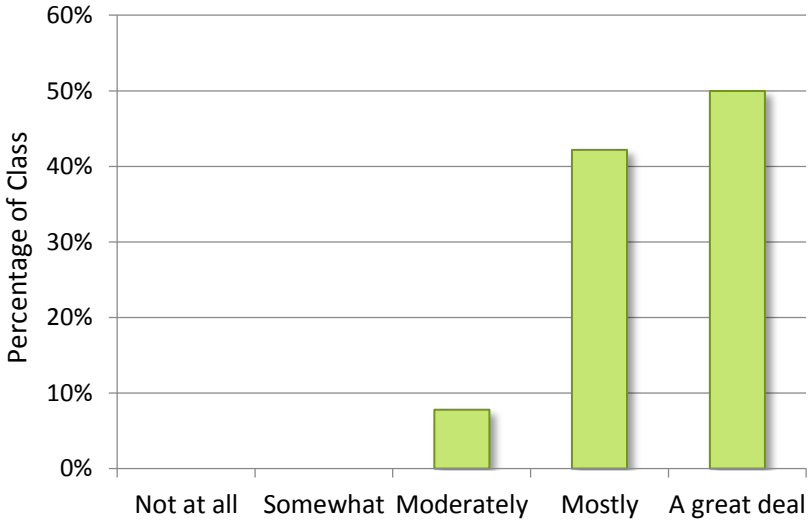
"Very nice contrast to previous synthesis yield based labs…much more practical and relevant to industry."

"It was a very useful experiment for us to learn how chemists work together in industry"

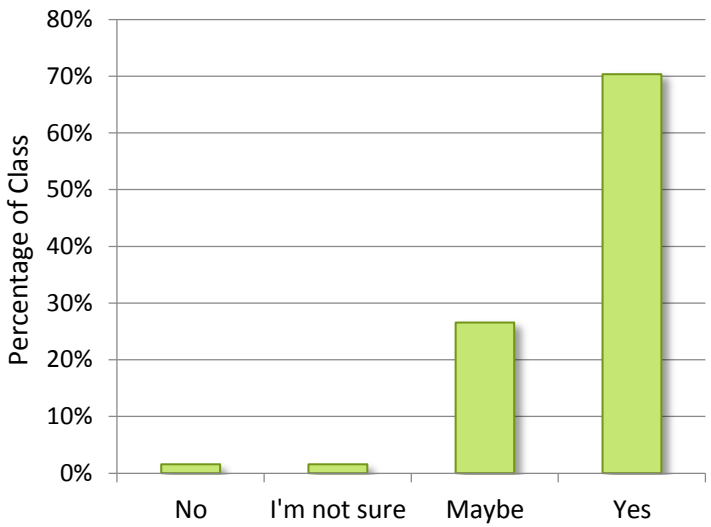
"Very great experience. Would like to see more of this because it adds to the understanding of the nature of the reaction"

Student Feedback

Did you enjoy the structure of the experiment? Specifically, did you enjoy working together with your peers to explore a reaction by evaluating class results?



Would you like to have more guided inquiry laboratories in the course?

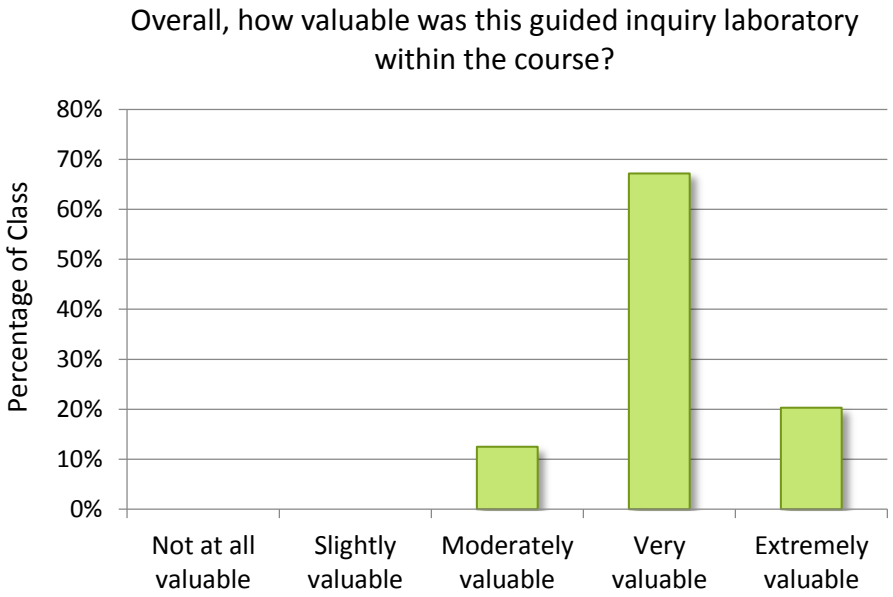


Select Student Comments:

"It was interesting to see different results from my labmates' experiments. I thought it was useful to learn how to analyze data based on different reaction parameters to determine optimized conditions"

"It was my favourite lab! I would be glad to do many more in the future!"

Student Feedback



Select Student Comments:

"Overall, it is a valuable and meaningful experiment!"

"I thought it was really interesting to follow the same process as real life scientists in an everyday lab to optimize reactions in order to get an API. So cool! Loved it! Even learning how to perform reaction purity and conversion calculations was so fun"

Overview of the Reaction Optimization Experiment

This new experiment gave students the opportunity to:

- Bridge the gap between the classroom and research laboratory by conducting a study with an unknown outcome
- Work collaboratively with classmates to tackle a research problem with real-world relevance
- Learn about the process and role of reaction optimization in organic synthesis
- Use HPLC data to evaluate reaction outcomes
- Develop insight into industrial R&D processes

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