Enhancing Research Skills and Attitudes in Undergraduate Organic Chemistry via Organic Synthesis

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Georgia Gwinnett College
School of Science and Technology
First new public 4-year college of the 21st century - charter to ‘do things differently’
First new public 4-year college created in GA in more than one hundred years
Admitted first class of juniors in August 2006
Admitted first class of freshmen in August 2007 (~750 students)
Earned full SACS accreditation in 2009
Fall 2011 enrollment was 8500; 10,000 projected for Fall 2012
Georgia Gwinnett College

GGC Vision

- learning takes place continuously in and beyond the classroom
- innovative use of educational technology
- integrated educational experience that develops the whole person
- dynamic learning community
- faculty engagement in teaching and mentoring students
- innovative approaches to education

SST Mission

... provides an innovative, engaging, outcomes-based learning experience for students in science courses ... (charge from Dean Thomas G. Mundie)

1Georgia Gwinnett College Web page, http://www.ggc.usg.edu/about-ggc
2School of Science and Technology Mission, http://www.ggc.usg.edu/academics/school-of-science-and-technology
"The infamous, dreaded 'orgo', a marathon of memorization."

Unfortunately, that's how all too many college students view their first exposure to organic chemistry. Their trepidation is justified: one-quarter to one-half of beginning organic students don't do well enough to continue on to the next course.


- Many students take organic chemistry as preparation for careers in the health professions (medical, dental, veterinary, pharmacy, graduate studies)
- Some students take organic to be chemists
- Avoid the “dreaded orgo” by enhancing student understanding and appreciation of one of the more challenging aspects of the course, organic synthesis
Organic Synthesis

- ‘Higher Order’ skill in organic chemistry - requires knowledge of a large range of organic chemistry reactions, and the ability to piece together a select few of these in a cohesive fashion to form the desired products from designated starting materials.

- At GGC, synthesis skills are assessed by a paper-based synthesis exam (open-book, open note).

- Due to the complex and applied nature of organic synthesis, average exam score in Fall 2011 was 39/70 (55.7%).

- Thus, we sought ways to improve student performance in organic synthesis.
Our proposed solution

- Traditionally, students are only exposed to organic synthesis in the classroom, with a solely paper-based approach.

- Our hypothesis was that if students were to be exposed to organic synthesis in the laboratory as well as the classroom, the greater overlap and exposure would enhance their understanding and appreciation.

- 2nd semester organic chemistry lab completely redesigned, from a set of separate, disconnected experiments to a semester-long synthetic project.

- In 1st semester lab, students learn a variety of experimental techniques, and then these are applied in the 2nd semester.

- Students have increased ownership in the experiments they perform - the work is truly all theirs, and their product at the end of the semester depends on how they work all the way through.
## Project Objectives

**Goal:** Enhance students’ exposure to, and understanding of, paper-based and lab-based synthesis practices, by synthesizing a novel class of *sulfa drugs* on the mini and/or micro scale. This goal will be measured by use of the following learning objectives. Students will:

<table>
<thead>
<tr>
<th>Objective</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Objective 1:</strong></td>
<td>Read primary literature and extract needed information - IEE 1 and IEE 3</td>
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<td><strong>Objective 2:</strong></td>
<td>Verbally report results and findings to peers, faculty members and the larger community (oral presentation and poster presentation) - IEE 1</td>
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<tr>
<td><strong>Objective 3:</strong></td>
<td>Design and troubleshoot a logical, step by step synthetic pathway for a target compound - IEE 2</td>
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<tr>
<td><strong>Objective 4:</strong></td>
<td>Keep and maintain an orderly notebook containing enough detail to replicate experiments - IEE 2</td>
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<tr>
<td><strong>Objective 5:</strong></td>
<td>Communicate and collaborate with peers in a research group setting - IEE 4 and IEE 7</td>
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<tr>
<td><strong>Objective 6:</strong></td>
<td>Collect and analyze qualitative and quantitative data - IEE 8</td>
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</table>
• Students will have more interest in a project if it involves something that they can relate to.

• Sulfa drugs - attractive synthetic target molecules because:

(a) well-known; as some of the earliest examples of widely-used antibiotics (variants of which are still used today), many students recognize the term ‘sulfa drug’

(b) relatively simple chemical structure, thus could in theory be prepared in the undergraduate organic chemistry lab in a relatively small number of steps, without the need for elaborate, specialized equipment
Synthetic Targets

(A) $\text{H}_2\text{N-N=O-S=O-N=S-NH}_2$  
4-amino-$N$-$p$-tolylbenzenesulfonamide

(B) $\text{H}_2\text{N-N=O-S=O-N=S-NH}_2\text{Br}$  
4-amino-$N$-(4-bromophenyl)benzenesulfonamide

(C) $\text{H}_2\text{N-N=O-S=O-N=S-NH}_2\text{CO}_2\text{H}$  
$N$-(4-acetylphenyl)-4-aminobenzenesulfonamide

(D) $\text{H}_2\text{N-N=O-S=O-N=S-NH}_2\text{CO}_2\text{H}$  
ethyl 4-(4-aminophenylsulfonamido)benzoate

(E) $\text{H}_2\text{N-N=O-S=O-N=S-NH}_2\text{CH}_2\text{CO}_2\text{H}$  
4-amino-$N$-benzylbenzenesulfonamide
Synthetic Pathway

Amines used in step 3:

- Br-\(\text{NH}_2\)
- \(\text{O} \text{C} \text{C} \text{S} \text{O} \text{C} \text{N} \text{H}_2\)
- \(\text{H} \text{C} \text{C} \text{C} \text{N} \text{H}_2\)
- \(\text{H} \text{C} \text{C} \text{N} \text{H}_2\)
- \(\text{O} \text{C} \text{C} \text{S} \text{O} \text{C} \text{N} \text{H}_2\)
- \(\text{S} \text{O} \text{C} \text{N} \text{H}_2\)
# Project Timeline

<table>
<thead>
<tr>
<th>Week</th>
<th>Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Week 1</td>
<td>Synthesis Project Intro Day - Group memberships / Synthetic targets decided</td>
</tr>
<tr>
<td>Week 2</td>
<td>Library / Online Research for sulfonamide synthesis</td>
</tr>
<tr>
<td>Week 3</td>
<td>Library / Online Research for sulfonamide synthesis</td>
</tr>
<tr>
<td>Week 4</td>
<td>Lab work - day 1</td>
</tr>
<tr>
<td>Week 5</td>
<td>Lab work - day 2</td>
</tr>
<tr>
<td>Week 6</td>
<td>Lab work - day 3</td>
</tr>
<tr>
<td>Week 7</td>
<td>Lab work - day 4</td>
</tr>
<tr>
<td>Week 8</td>
<td>Lab work - day 5</td>
</tr>
<tr>
<td>Week 9</td>
<td>Lab work - day 6</td>
</tr>
<tr>
<td>Week 10</td>
<td>Spring Break - No Lab</td>
</tr>
<tr>
<td>Week 11</td>
<td>Lab work - day 7</td>
</tr>
<tr>
<td>Week 12</td>
<td>Synthesis Exam</td>
</tr>
<tr>
<td>Week 13</td>
<td>Lab work - day 8</td>
</tr>
<tr>
<td>Week 14</td>
<td>Lab work - day 9</td>
</tr>
<tr>
<td>Week 15</td>
<td>Lab work - day 10</td>
</tr>
<tr>
<td>Week 16</td>
<td>Final Group Presentations</td>
</tr>
</tbody>
</table>
• Push students out of their ‘comfort zone’ of using traditional ‘cookbook’ procedures for experiments.
• Students wrote their own experimental procedure for each reaction step, using a bare-bones procedure as a guide.

Step 1: Acetylation of aniline (synthesis of acetanilide)

• Chemicals used: aniline, acetic anhydride, distilled water.
• Equipment used: stir/hotplate, Erlenmeyer flask (size depends on scale that you wish to run the reaction), magnetic stir bar.
• Mole table: Use a 1:1.2 molar ratio of aniline to acetic anhydride. Note that both aniline and acetic anhydride are liquid reagents.
• Procedure: Aniline placed into Erlenmeyer flask. Distilled water added, at about 7.5 times the volume of aniline used. With stirring, acetic anhydride carefully added into mixture. Second volume of distilled water added into mixture (volume is 2.5 times that of original volume of distilled water used). Resultant mixture stirred with heating, until all solids and residual oils are dissolved.
Current Progress

- Spring 2012 is the first semester that this project has run, so our current students are the guinea pigs.

- 6 sections of Organic II offered by 5 different instructors

- Only a few weeks to go before the end of the semester - some student groups have successfully isolated their sulfa drug product already, some are very close to completion, other groups not so close…

- Students have not yet taken the synthesis exam, and success of the project (in terms of improving student synthesis skills) cannot yet be determined.
## Midsemester Feedback

Respond to the statements using the scale below:

<table>
<thead>
<tr>
<th>Strongly Agree</th>
<th>Agree</th>
<th>Neutral</th>
<th>Disagree</th>
<th>Strongly Disagree</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Overall</th>
<th>AVE</th>
<th>STDev</th>
</tr>
</thead>
</table>

1. I am satisfied with the progress that my group is making.  
   Overall: 4.0  
   AVE: 4.0  
   STDev: 1.0

2. I feel like I have been pushed out of my comfort zone in preparation for the experimental work for this synthetic project.  
   Overall: 3.0  
   AVE: 3.0  
   STDev: 1.2

3. I like the fact that my group gets to decide the scale of each reaction run so far, rather than simply following a given procedure.  
   Overall: 3.8  
   AVE: 3.8  
   STDev: 1.2

4. I feel that I have had to use my critical thinking and decision making skills in this project so far, more so than if I was following a given procedure.  
   Overall: 4.0  
   AVE: 4.0  
   STDev: 0.9

5. Based on my experiences so far, I would like to see more chemistry labs organized into projects like this.  
   Overall: 3.9  
   AVE: 3.9  
   STDev: 1.1
# Midsemester Feedback

Respond to the statements using the scale below:

<table>
<thead>
<tr>
<th>Scale</th>
<th>5</th>
<th>4</th>
<th>3</th>
<th>2</th>
<th>1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Strongly Agree</td>
<td>Agree</td>
<td>Neutral</td>
<td>Disagree</td>
<td>Strongly Disagree</td>
<td></td>
</tr>
</tbody>
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<table>
<thead>
<tr>
<th>Statement</th>
<th>Per Organic II Instructor</th>
<th>AVE</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. I am satisfied with the progress that my group is making.</td>
<td>4.2 3.6 4.4 3.6 4.0</td>
<td>4.0</td>
</tr>
<tr>
<td>2. I feel like I have been pushed out of my comfort zone in preparation for the experimental work for this synthetic project.</td>
<td>3.1 3.8 3.0 3.2 2.4</td>
<td>3.0</td>
</tr>
<tr>
<td>3. I like the fact that my group gets to decide the scale of each reaction run so far, rather than simply following a given procedure.</td>
<td>4.4 2.3 4.2 3.4 3.5</td>
<td>3.8</td>
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<td>4. I feel that I have had to use my critical thinking and decision making skills in this project so far, more so than if I was following a given procedure.</td>
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<td>4.0</td>
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<td>5. Based on my experiences so far, I would like to see more chemistry labs organized into projects like this.</td>
<td>4.2 2.6 4.3 3.6 3.8</td>
<td>3.9</td>
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Things I like about the project so far:

- I like the critical thinking and decision-making aspect of the labs. Having to figure out how much product I want to make & working with a partner gets me to think more about the procedure than just following directions.

- The independence to work at my own pace & develop the procedure.

- The feeling that I am actually applying concepts in a more practical manner.

- Freedom given to us. We get to decide what happens in our experiment. Makes it feel like it is more my experiment than just another required lab.

- That it is a group project and not individual. It helps when one person is confused about something, the other person can help out.

- I’m able to critically think and analyze how to perform a synthetic procedure on my own. It has also taught me partner skills and how to cooperate with a colleague who I am not familiar with.

- Love the practical, hands-on application of designing my own procedure, and it’s based on medicinal chemistry!
Things I dislike about the project so far:

- There is always a level of uncertainty as to whether or not the reactions we are doing are going well.
- I dislike some of the freedom given to students, only for the reason that it allows for some students to slack and not fully live up to their responsibilities.
- It is hard to know if your product will keep its integrity from week to week, especially with breaks between (e.g., midterm, spring break). It’s hard to know a good stopping point.
- You can expect certain results, but sometimes we feel unsure, which is / could be the case in a work setting.
- It’s less structured than the orgo I lab.
- Too much pressure in case you make a mistake, not enough time to go back and start over.
- The way the instructions were presented. I would rather have the instructions posted on blackboard one step at a time.
Students and faculty responded positively to new approach to organic chemistry II lab.

Depending on the instructor, students felt varying degrees of being pushed out of their comfort zone in this semester-long synthetic project.

Need data on synthesis exam performance to gauge if this project has improved student synthesis skills.

Conclusion

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Results so far

- Students and faculty responded positively to new approach to organic chemistry II lab.
- Depending on the instructor, students felt varying degrees of being pushed out of their comfort zone in this semester-long synthetic project.
- Need data on synthesis exam performance to gauge if this project has improved student synthesis skills.

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