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Benefits of Using a Problem-Solving Scaffold for Teaching and Learning Synthesis in Undergraduate Organic Chemistry I

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Abstract

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Keywords

scaffolded learning, synthesis, problem-solving, organic chemistry

Cover Page Footnote

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A problem-solving scaffold approach to synthesis was developed and implemented in two intervention sections of Chemistry 2211K (Organic Chemistry I) at Georgia Gwinnett College (GGC). A third section of Chemistry 2211K at GGC served as the control group for the experiment. Synthesis problems for chapter quizzes and the final examination were designed and administered to all sections participating in the experiment. Student solutions were graded according to a rubric designed to determine student use of the scaffold when solving synthesis problems. Analyses of the quiz results and the synthesis component of the final examination were conducted and intervention section students who employed the Synthesis Scaffold Approach were found to have higher mean scores on related graded events as compared to students who were not exposed to the Synthesis Scaffold Approach.

INTRODUCTION

In the two-semester undergraduate organic chemistry course sequence at Georgia Gwinnett College (GGC), one of the course outcome goals is to “Design multi-step preparative synthesis of organic molecules by applying reaction mechanisms” (Georgia Gwinnett College, 2014). This is one of the most challenging concepts in organic chemistry that students encounter. Creating or synthesizing a chemical compound, by its very name, implies a higher level of learning than most students have engaged in when they first take organic chemistry. As Anderson, Krathwohl, Airasian, Cruikshank, Mayer, Pintrich, Raths and Wittrock (2001) note in their revision of Bloom’s taxonomy, the act of creation is the highest cognitive domain process. Therefore, it is essential that organic chemistry students be provided with the tools necessary that enable them to achieve mastery of synthesis.

Traditionally, students enrolled in undergraduate organic chemistry learn simple reactions as finite pieces of information and often memorize them without consideration of how the reactions take place. Moreover, while some undergraduate organic chemistry texts discuss synthesis strategies, e.g. the “Retrosynthetic or Disconnection approach” (Bruice, 2014), many texts do not provide students with user-friendly, systematic methods that enable the learner to become adept at organic synthesis. This paucity of available methodologies is compounded by the fact that instructors tend not to spend adequate time to help students understand or place those strategies into the proper context. Designing a plan for the synthesis of an organic molecule requires that students move beyond memorization of individual processes and understand the interplay of molecular structure, reagent function and reaction mechanism. Students must be able to visualize the target molecule, grasp how chemical reagents react with the starting material to effect the necessary transformations and sequence them properly to prepare the desired product. A user-friendly methodology that allows students to navigate these requisite steps in a way that helps the student approach a wide range of problems could enhance and ease students’ learning of organic chemistry.

The scaffolded learning process can be brought to bear to address these teaching and learning issues related to organic chemistry synthesis. Scaffolded learning, developed by Wood, Bruner and Ross (1976), is a process whereby students master a skill or concept as the teacher provides feedback and rectifies mistakes. As

the student develops the prerequisite skills to reach the ultimate goal, the teacher “fades” away, or gradually removes assistance to the learner with the final objective of the learner being able to independently work to master the skill. “Scaffolding is actually a bridge used to build upon what students already know to arrive at something they do not know. If scaffolding is properly administered, it will act as an enabler, not as a disabler” (Benson, 1997).

Using scaffolded learning, instructors can intercede to improve student problem-solving ability in the area of synthesis, regardless of the text being used. Framing simple reactions as elementary synthesis problems while emphasizing a systematic approach that incorporates structure and reagent function can provide students with a visual framework or scaffold upon which to “build” their synthetic route from a starting material to the desired product. In other words, the scaffold helps students learn how to “think” about solving organic synthesis problems.

This paper describes the implementation of and benefits derived from an organic chemistry synthesis scaffold methodology that was introduced in a first semester organic chemistry course. This approach, called the “Synthesis Scaffold Approach”, was shown to students as they began to learn elementary organic reactions. For students at our college, the alkene chapter of the course text (Bruice, 2014) is the first exposure to some simple addition reactions; it is here that we introduced the synthesis problem-solving scaffold.

DEVELOPMENT OF THE SYNTHESIS SCAFFOLD APPROACH AND TEACHING METHODOLOGY

Modeling and breaking the task of organic synthesis into smaller parts are two of the key tools that follow the scaffolded learning approach and are germane to our Synthesis Scaffold Approach (SSA). These tools seemed to also help learners maintain motivation and to help decrease unreasonable levels of student stress. The SSA provided options to the organic student in which to approach organic synthesis problems without feeling “lost”. The SSA aided the student in tailoring the synthesis problem to his/her specific learning strengths and weaknesses. By allowing the student to first analyze the chemical reagents and reaction pathways and then to list them in a “menu” format, the SSA forced the student to consider the possible reaction options before creating a chemical synthetic pathway. The approach appeared to help students view

a variety of strategies – even those that they may not have mastered previously – merely by considering the list, or menu, that they just created. As an unexpected result, this methodology assisted students in identifying areas in which they need more practice to become proficient in solving organic synthesis problems.

Synthesis Problem-Solving Scaffold Development. The systematic problem-solving approach to organic chemistry used successfully by Sloop (2010) serves as the basis for designing the synthesis scaffold. The steps for this approach are shown below:

- Given:** What information do we know?
- Find:** What information is sought?
- Plan:** What is the strategy for solving the problem?
- Solve:** Execution of the plan to achieve a solution.
- Check:** Ensure the answer is consistent with known information and the plan.

Application of this approach to the design of the synthesis scaffold was straightforward. We defined the problem solving methodology in the context of information needed by students when solving a synthesis problem. Our expanded approach was as follows:

- Given:** A starting material from which to produce a target molecule (product).
- Find:** Synthetic route to the desired product.
- Plan:** 1. Compare the product to reactant and list transformations.
 2. Determine if the overall number of transformations requires more than a single reaction step.
- Solve:** 1. Use retrosynthetic strategy to “unbuild” the molecule back to the starting material.
 2. Propose structure(s) for any likely intermediate product(s).
 3. Identify and list reagent(s) to be used in the synthetic path that will give the transformations required to prepare the desired product.
 4. If more than one reagent is chosen for a given transformation, select the best reagent based on the required function.
 5. Write the complete synthetic plan.
- Check:** Ensure selected reagents effect the required transformations; ensure intermediate products are correctly drawn and the overall synthetic plan leads to the product.

See Appendix A for a sample scaffold used in the organic chemistry I intervention sections.

Teaching Methodology. The challenge for instructors in the first semester organic chemistry was how best to integrate the teaching of synthesis problem solving using the scaffold with active learning methods in the class and as part of the homework assigned to the students. At GGC, Paredes, Pennington, Pursell, Sloop and Tsoi (2010) have successfully incorporated the Thayer method of teaching and learning in a range of chemistry courses. Other active learning approaches in use by GGC organic chemistry professors include the “flipped” classroom (a recent variation of the Thayer method) (Bergmann and Sams, 2008) and POGIL (Moog and Farrell, 1999). For the sections participating in this study, all instructors used the Thayer method.

Before the course began, example Synthesis Scaffolds were developed and instructors participating in the study discussed how

to employ them in the classroom setting. These scaffolds were uploaded to the College’s learning management system webpage so that all students enrolled in the intervention sections had access to them in advance of the lesson that introduced the concept of organic synthesis. Intervention section instructors informed the students during the preceding lesson that they should download and read the synthesis scaffold example and bring it to the next class.

The Synthesis Scaffolds were designed so as to provide students with a graduated increase in difficulty. When the topic of synthesis was introduced in class, instructors illustrated and reviewed the example scaffold to highlight important points and to demonstrate the potential benefits of employing this methodology to solve organic synthesis problems. Students were then given a simple organic synthesis problem to solve during class. The instructor guided the process and made “on-the-spot” corrections as the students worked. As time permitted, students were assigned additional problems and asked to solve them using the Synthesis Scaffold, but with less guidance and fewer instructions from the instructor.

The students were then given a synthesis homework assignment and asked to apply the SSA when solving the synthesis problem. During the following class session, the instructor and students discussed the solution to this problem as well as any observations or issues arising from the application of the SSA.

Throughout the remainder of the semester, students regularly practiced organic synthesis problems in class to reinforce the process. They were afforded opportunities to work individually as well as in small groups to facilitate peer learning and discussion. Students then “published” their work on the whiteboards mounted in the classroom and were given opportunities to lead the class in a discussion of their problem solutions. Students were also assigned organic synthesis problems as part of their homework for the duration of the course.

As a general practice throughout the semester, intervention section instructors discussed organic synthesis problems in class and employed the SSA to repeatedly model its application for the students. This served to reinforce with the students the systematic nature of the Scaffold’s methodology and inculcate the thought process behind its implementation.

ASSESSMENT TOOL DESIGN – GRADED EVENTS AND SURVEYS

In this study, 43 students in the three Organic Chemistry I course sections were advised that their participation was voluntary; participating students were asked to sign an informed consent form. Of these students, 36 students volunteered to participate in the study – two intervention course sections with a total of 21 students and a non-intervention section with 15 students. The goals of the study were to assess: (1) whether students would chose to implement the Synthesis Scaffold Approach of their own volition when solving organic synthesis problems, and (2) whether the use of this methodology proved advantageous over typical synthesis instructional methods. Assessment of these project goals was accomplished with a combination of selected questions on graded class quizzes and on the course’s final exam. A post-assessment survey was administered to the participating students asking general questions about student impressions and opinions about the SSA and organic synthesis problem solving. A pre-assessment survey

was not administered since the students had no frame of reference on how to approach a synthesis problem at the start of the course.

Graded Event Design. Instructors for both the intervention and non-intervention sections used the same synthesis problems for quizzes on the Alkene chapter, Alkyne chapter and the course final exam. The graded event questions were based on the format of the following example:

Example: Using the systematic problem-solving approach we introduced in class, show all steps to complete the transformation shown below.

Given: 1-pentene, prepare: 1-bromopentane.

Each student's response to the synthesis problems was assessed according to a grading rubric. Based on a 10-point value for the problem, the following grading criteria were used:

1. Evidence that student lists chemical transformations required for the synthesis – 2 points
2. Student applies retrosynthetic strategy – 2 points
3. Student proposes reagent(s) to effect the transformation(s) – 2 points
4. Student selects the correct reagents – 2 points
5. Student proposes the correct synthetic path – 2 points

Quizzes were formatted in a way so that the synthesis problem appeared on a separate page to provide the student ample space for scratch-work; this was in an effort to encourage student application of the Synthesis Scaffold Approach, since it tasks students to list the “menu” of possible synthetic routes and reagents. All student personal information was removed from stored copies. All original quizzes (but not the final exam) were returned to the students after photocopying their responses for data analysis.

Survey Design. The survey used in this study was designed to obtain both semi-quantitative data as well as qualitative impressions from students about using the Synthesis Scaffold Approach on graded events. The survey questions, which had a Likert-scale component as well as open-ended answer opportunities, are shown in Table 1.

ASSESSMENT RESULTS AND DISCUSSION

Graded Event Data Results and Analysis. A statistical analysis

(t-test) of the results from the Alkene and Alkyne chapter quizzes, as well as the Organic Chemistry I final exam was performed. The results are shown below in Tables 2, 3, and 4 for both the intervention sections and the non-intervention section (Sloop, Tsoi, Coppock, 2013).

In addition, an ANOVA analysis of all data collected indicated that there was significant variance between the intervention groups and the non-intervention groups for the Alkene Quiz ($p=0.00149$), Alkyne Quiz ($p<0.0001$), and the Final Exam synthesis questions ($p=0.0521$). Among all students included in this study and who were enrolled in the Organic Chemistry I course ($n = 91$), there was a statistically significant difference between the students that received the SSA, as compared to the students that did not receive instruction that included the SSA (refer to Tables 2, 3, 4). Therefore, we reject the null hypothesis that there was no difference in performance on organic synthesis problems between the intervention students and the non-intervention students. The data indicate that the intervention students scored significantly higher than the non-intervention students on all three graded events ($p = 0.0009, 0.002, \text{ and } 0.006$).

Two interesting observations stand out with respect to the Alkene chapter and Alkyne chapter quiz means. The quiz scores from the intervention sections suggest an improvement in students' synthesis problem-solving ability, even though the synthesis problem on the Alkyne chapter quiz (3 steps) was more difficult than the Alkene chapter quiz (2 steps). For the intervention sections, all students analyzed for this study showed evidence of implementing the SSA when attempting to solve the synthesis problems on these graded events. Second, there is a sizable significant difference ($p<0.006$) in the mean scores of all graded events for students in the intervention sections versus the non-intervention section. This may be an indication of an effect from the introduction and use of the Synthesis Scaffold Approach. However, this statement must be viewed in conjunction with the effect-size, which points to only a moderate effect ($0.3 < r < 0.6$) due to the small sample sizes of the study. Thus, we state our findings with caution and cannot absolutely attribute the significant difference in mean scores of the graded events to the implementation of the SSA in the synthesis problem-solving curriculum. It is interesting to note that in the randomly chosen exit interviews that were conducted with students after the Alkyne chapter quiz, student responses showed that a

TABLE 1. Student Post-Graded Event Synthesis Scaffold Survey

4=strongly agree, 3=agree, 2=disagree, 1=strongly disagree, NA=not applicable

1. I understand the importance of synthesis to organic chemistry.	4	3	2	1	NA
2. I can apply the following problem-solving approach to propose a synthetic strategy for an organic molecule:					
a. Compare product to reactant	4	3	2	1	NA
b. List the differences you see	4	3	2	1	NA
c. Count the number and type of transformations needed	4	3	2	1	NA
d. Devise a retrosynthetic strategy	4	3	2	1	NA
e. List reagents needed	4	3	2	1	NA
f. Propose a synthetic plan	4	3	2	1	NA
3. This problem-solving approach assisted me in developing the ability to apply critical thinking skills to synthesis problems.	4	3	2	1	NA
4. Provide a description of the way(s) in which this problem-solving approach affected your learning, understanding, and/or mastery of solving synthesis problems:					
5. Would you recommend this problem-solving approach to other students? If so, why? If not, why not?					
6. What other techniques, methods, and practices have you found useful for solving synthesis problems? Describe them here and explain why you use them. Which method do you prefer? Why?					
7. Please provide additional comments:					

large majority of the students felt comfortable with the Scaffold Approach and intended to use it for future synthesis problems in subsequent courses. Refer to Appendix B for examples of student quiz solutions.

As well, because the course sections were not randomly assigned (in that students registered for a course section based on factors not analyzed in this study), it cannot be stated with certainty that there would have been insignificant variance in student performance on these three graded events without the implementation of the SSA. In hindsight, a pre-test on prior knowledge and skills in organic synthesis would have lent more power to the suggestion that the SSA may have had a positive effect on students' critical thinking and problem solving in these types of problems.

The final examination for these Organic Chemistry I students included a selection of four synthesis problems; the problems ranged from 3 to 6 steps in the synthesis pathway length. Students were given the opportunity to choose the problems they wished to complete for a grade. In the course, students who did not receive the SSA in their curriculum (n=91) obtained an average score of 48% correct for this part of the exam. However, the intervention groups averaged a 56.8% correct response score, a statistically significant increase (p=0.006) (Sloop, 2013).

Survey Results and Analysis. Students completed the post-assessment survey after the last chapter quiz was administered and before the final examination. The results of the Likert-scaled component of this survey are shown in Table 5.

The survey results suggest that students may possess a high degree of confidence in: understanding the importance of solving organic synthesis problems, comparing chemical reactants to products, and listing the differences between reactant and product. However, challenges seem to remain for students: determining

TABLE 2. Statistical Analysis of Alkene Quiz Student Results

Group	n	Mean	SD	t	df	p	Effect Size (r)
Intervention	21	8	1.673				
Non-Intervention	15	5.4	2.261				
Total				3.775	24	0.000927	0.547

TABLE 3. Statistical Analysis of Alkyne Quiz Student Results

Group	n	Mean	SD	t	df	p	Effect Size (r)
Intervention	21	9.222	1.716				
Non-Intervention	15	6.267	2.404				
Total				3.493	22	0.00205	0.577

TABLE 4. Statistical Analysis of Organic Chemistry I Final Exam Student Results

Group	n	Mean	SD	t	df	p	Effect Size (r)
Intervention	21	40.152	14.491				
Non-Intervention	70	28.778	19.767				
Total				2.888	44	0.00598	0.312

the number and types of transformations needed, devising the retrosynthetic strategy, deciding upon appropriate reagents, and proposing a synthetic plan. These findings are not unusual for students just beginning to learn about organic chemical reactions, reagent functions and reaction sequences that best achieve the proposed organic product.

The free response portion of the survey (questions 4-7) gave students an opportunity to express their thoughts as to whether the Synthesis Scaffold Approach was an effective learning tool for them. Selected student responses to those questions are included after each survey question prompt:

4. Provide a description of the way(s) in which this problem-solving approach affected your learning, understanding, and/or mastery of solving synthesis problems:

"Instead of staring blankly at the paper I was now able to have a starting point and minimize my choices of what I could do to get the product."

"It made it much easier to understand synthesis both backward and forward."

5. Would you recommend this problem-solving approach to other students? If so, why? If not, why not?

"Yes, it's very helpful because you reduce the possibilities of reagents and methods."

"I would recommend making sure that students know how to use specific acids and bases and to repeat the basics that we learned when we started synthesis."

6. What other techniques, methods, and practices have you found useful for solving synthesis problems? Describe them here and explain why you use them. Which method do you prefer? Why?

"Starting at the front of a reaction and it's not easy because there's so many methods to get the product."

"Doing more synthesis problems as a whole group or small group team. I found this useful because it let me hear how other people explained synthesis in their own words."

7. Please provide additional comments: (There were no student entries for this question.)

These response excerpts reflect an increased confidence level in the students' perception of their ability to use the scaffold approach and modify it to suit their needs.

CONCLUSION

The data analyzed from the course graded events indicate that in general, students who used the Synthesis Scaffold Approach to solve organic synthesis problems demonstrated more systematic approaches, provided more detail in their answers, and present-

TABLE 5. Synthesis Scaffold Post-Assessment Survey

	AVG (SD)
1. I understand the importance of synthesis to organic chemistry.	3.71 (0.30)
2. I can apply the following problem-solving approach to propose a synthetic strategy for an organic molecule:	
a. Compare product to reactant	3.62 (0.26)
b. List the differences you see	3.62 (0.26)
c. Count the number and type of transformations needed	2.95 (0.15)
d. Devise a retrosynthetic strategy	2.76 (0.10)
e. List reagents needed	2.81 (0.12)
f. Propose a synthetic plan	2.67 (0.07)
3. This problem-solving approach assisted me in developing the ability to apply critical thinking skills to synthesis problems.	2.90 (0.12)

ed more successful solutions to the problems attempted. Analyzed student graded events show that students who were taught the SSA earned a higher mean score on related graded events than students who were not exposed to the SSA in their course instruction. A modest effect-size limits our conclusions that the SSA had a strong effect on student synthesis problem solving skills and in turn, the mean scores on their graded events. Thus, we can presume that the SSA had only some effect on students' performance on these types of problems. Analyzed student quantitative survey data did indicate that students who used the SSA had a higher level of confidence in their ability to successfully approach organic chemistry synthesis problems. Informal follow-up interviews with students in the subsequent course Organic Chemistry II during the next semester revealed that more than 65% of students previously enrolled in the study continued to use the scaffold, or a modified form of it, when solving synthesis problems.

Since this study's inception, other organic chemistry faculty members were introduced to the Synthesis Scaffold Approach; several of the professors have instituted it in their teaching of organic synthesis problem solving. Faculty members have responded positively to the Approach and have noted that this scaffolded learning framework seems to aid their students in grasping the challenging conceptual nature of organic chemical synthesis and to enhance their students' critical thinking skills.

Future directions include exploring the impact this Synthesis Scaffold Approach may have on other organic chemistry concepts, collecting further data on future students in Organic Chemistry I, and enhancing the approach to include other informational sources that can further assist students in solving organic synthesis problems. As well, introducing it to more students would help add power to our statistical analysis and perhaps provide more indication as to the effect of this approach in teaching students how to effectively solve problems in organic synthesis.

REFERENCES

- Anderson, L.W., Krathwohl, D.R., Airasian, P.W., Cruikshank, K.A., Mayer, R.E., Pintrich, P.R., Raths, J., Wittrock, M.C. (2001). *A Taxonomy for Learning, Teaching, and Assessing: A revision of Bloom's Taxonomy of Educational Objectives*. New York: Pearson, Allyn & Bacon.
- Benson, B. (1997). Scaffolding (Coming to Terms). *English Journal*, 86(7), 126-127.
- Bergmann, J., Sams, A. (2008). Remixing chemistry class. *Learning and Leading with Technology*, 36(4), 24-27.
- Bruice, P. (2014). *Organic Chemistry*, 7th Edition. Upper Saddle

- River, New Jersey: Pearson Education, Inc.
- Georgia Gwinnett College Catalog. (2014). <http://www.ggc.edu/academics/docs/current-catalog/2014-2015-catalog.pdf>
- Moog, R. S., Farrell, J. J. (1999). *Chemistry: A Guided Inquiry*. New York, NY: John Wiley & Sons.
- Paredes, J., Pennington, R., Pursell, D., Sloop, J., Tsoi, M. Y. (2010). Engaging Science Students with Handheld Technology and Applications by Re-Visiting the Thayer Method of Teaching and Learning. *Georgia Journal of Science*, 68(4), 186-195.
- Sloop, J. (2010). *Succeeding in Organic Chemistry: A Systematic Problem-Solving Approach to Mastering Structure, Function and Mechanism*. Bloomington, IN: AuthorHouse Publishing Co.
- Sloop, J., Tsoi, M. Y., Coppock, P. (2013). *A Problem-Solving Scaffold for Teaching Synthesis to Organic Chemistry I Students*. Master Teacher Program Workshop, Center for Teaching Excellence, Georgia Gwinnett College.
- Sloop, J. (2013). Fall 2012 Chemistry 2211K Course Assessment. Submitted to the SS&T, Georgia Gwinnett College Course Assessment Team.
- Wood, D., Bruner, J.S., Ross, G. (1976). The role of tutoring in problem solving. *Journal of Psychology and Psychiatry*. 17.

APPENDIX A. Synthesis Scaffold Student Packet

Organic Chemistry I – Organic Synthesis:
The preparation of organic molecules

As an introductory organic chemistry student, you face many challenges in understanding structure, function and mechanism. During the course of your two-semester organic chemistry experience, you will learn over 100 chemical reagents that introduce functionality to organic starting materials.

Mastering the art of synthesis requires that you bring to bear your critical thinking skills in a way that many of you have not done previously. It is not feasible for you to attempt to memorize the numerous reactions covered in this course. Preparing new organic molecules from organic starting materials and selected reagents requires that you learn and apply a systematic problem-solving approach to this task. You must:

- Understand the function of reagents that you learn → what does a reagent do, e.g. does it oxidize or reduce a carbon atom, does it add a functional group to a multiple bond?
- Think of synthesis as a puzzle → you must put the pieces together (reactants and reagents) in the correct order to achieve the desired product molecule.

A key component of understanding organic synthesis involves a term called “retrosynthetic strategy”. Sounds hard, but all this means is that we “unbuild” the desired target molecule we are preparing in a step-by-step way back to the given starting material. We do this by comparing the product to the starting material and try to identify what transformations are required to arrive at the product given the starting compounds. In other words, we reverse engineer the product to our starting compound. It looks like this:

Target compound → Intermediate product(s) → starting materials

Once you identify this reverse pathway, it is easy to see the number of steps required for your synthesis. What remains is to identify the reagents necessary to will create the transformations at each step.

To assist you in building confidence in your critical thinking and problem-solving abilities so that synthesis can be mastered, this primer has been developed as a sort of “scaffold” around which you can build your synthesis skills. We will look at some simple, single-step synthesis problem examples to help get you started, and gradually progress to more complex cases.

Synthesis Problem Solving Scaffold – Alkene Chapter

Example Problem #1

WORK FLOW (use systematic problem-solving approach):

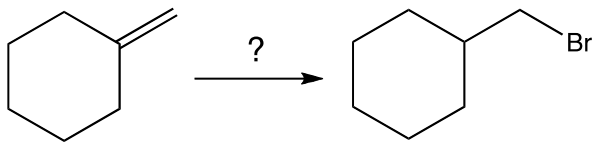
Step 1: Compare product to reactant.

Step 2: List the differences you see.

Step 3: Count the number of transformations needed for each “difference”.

Step 4: Work backwards and match up reagents to your differences.

Given:



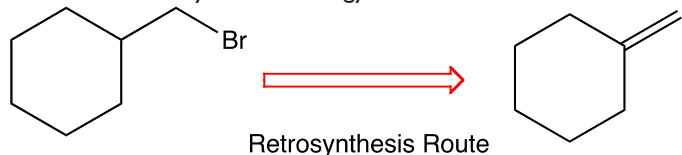
Find: Synthetic route to desired product.

Plan:

1. Compare product to reactant and note transformations.
 - H-Br installed in an anti-Markovnikov fashion on the C=CH₂ alkene unit
2. Determine if the transformations require more than a single reaction step – No

Solve:

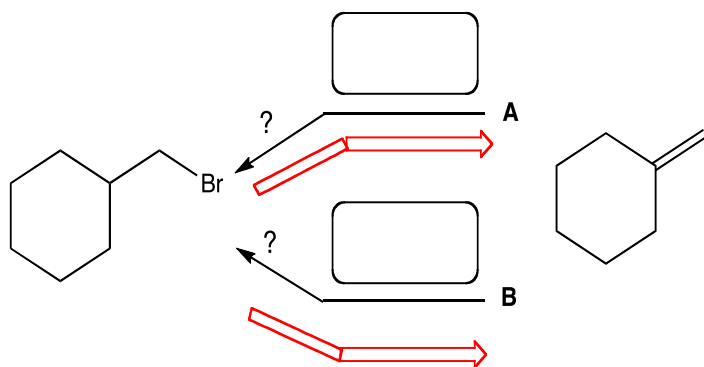
1. Use retrosynthetic strategy to “unbuild” the molecule back to the starting material:



Because there is no intermediate product, we may proceed to identifying the proper reagent set to effect the transformation.

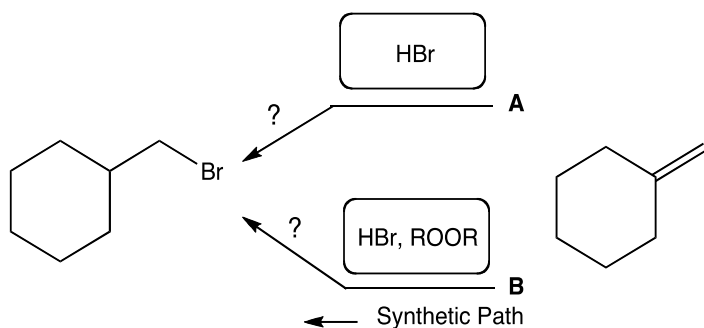
2. Using your Organic Reactions-Interconversion sheet, identify the reagents to be used in our synthetic path that would function to

install a single proton and bromine on a molecule. Fill in the figure below with the reagents.



We find two possible reagent sets.

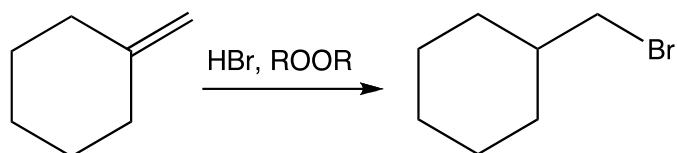
Here is a completed diagram:



3. Now you must choose which of the bromination reagent sets in the figure would lead to the product by recalling their particular function.

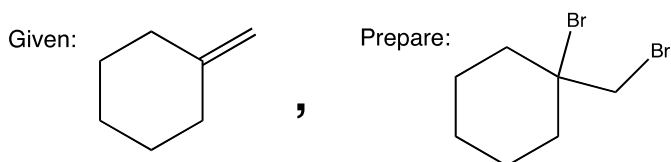
- HBr – adds to the double bond (markovnikov addition) – NO
- HBr, ROOR – adds to the double bond (anti-markovnikov addition) – YES

4. Therefore, path **B** is the correct synthetic route:



Check: Structures drawn correctly, reagent chosen gives the desired transformation.

Example Problem #2 (This time, you try to work through the problem.)



WORK FLOW (use systematic problem-solving approach):

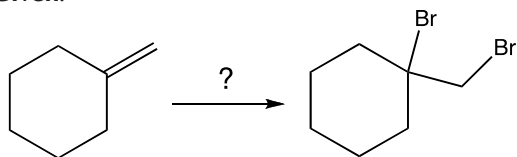
Step 1: Compare product to reactant.

Step 2: List the differences you see.

Step 3: Count the number of transformations needed for each “difference”.

Step 4: Work backwards and match up reagents to your differences.

Given:



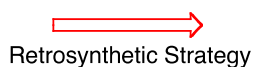
Find: Synthetic route to desired product.

Plan: 1. Compare product to reactant and note transformation(s):

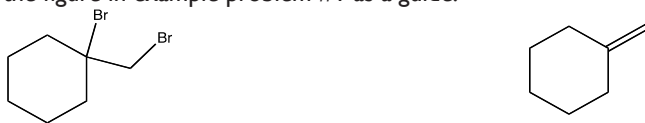
2. Determine if the transformation(s) require more than a single reaction step: YES or NO

Solve:

1. Use retrosynthetic strategy to “unbuild” the molecule back to the starting material:



2. Using your Organic Reactions-Interconversion sheet, identify the reagent(s) to be used in our synthetic path that would function to add one molecule of Br₂ on an organic compound. Complete your figure below with the reagents. If you have multiple reagents, use the figure in example problem #1 as a guide:



3. If you selected more than one bromination reagent set, determine which would lead to the product by recalling and writing their particular function.

- a.
b.

Therefore, path ___ is the correct synthetic route:

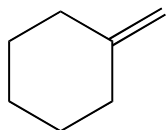
4. Write the completed synthesis:



Check: Structures drawn correctly, reagent chosen gives the desired transformation.

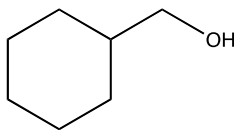
Practice Problem #1 (This time, use what you’ve learned to solve this synthesis problem.)

Given:



,

Prepare:



WORK FLOW (use systematic problem-solving approach):

Step 1: Compare product to reactant.

Step 2: List the differences you see.

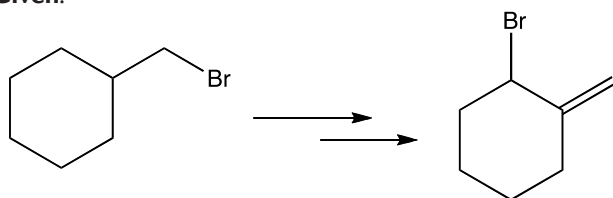
Step 3: Count the number of transformations needed for each “difference”.

Step 4: Work backwards and match up reagents to your differences.**Given:****Find:****Plan:****Solve:**

- 1.
- 2.
- 3.
4. Write the completed synthesis:

Check:

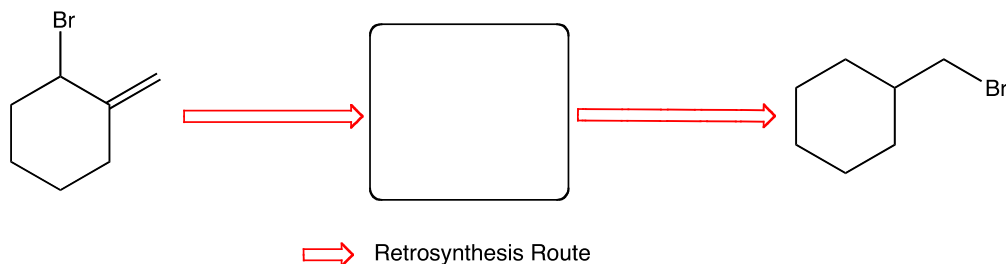
Of course, all synthesis problems are not so simple – many have multiple steps. Here is an example of how to approach and solve a synthesis that involves more than one step.

Example Problem #3**Given:**

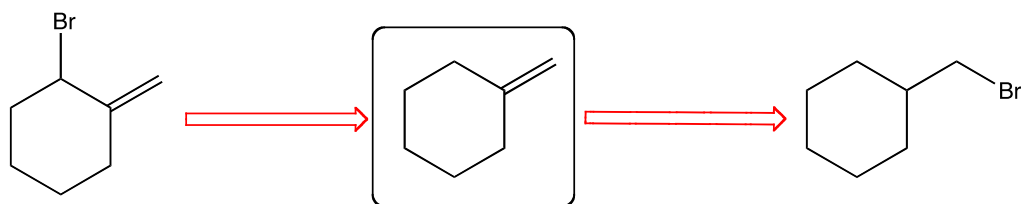
Find: Synthetic route to desired product.

- Plan:**
1. Compare product to reactant and note transformations.
 - a. Bromine installed on the ring
 - b. Double bond formed
 2. Determine if the overall # of transformations require more than a single reaction step – YES, two steps required.

Solve: 1. Use retrosynthetic strategy to “unbuild” the molecule back to the starting material:

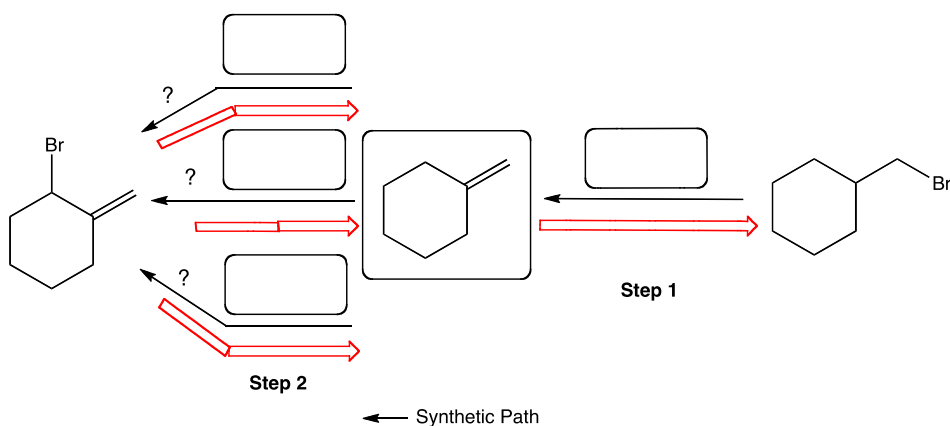


2. Propose the structure for a likely intermediate product:

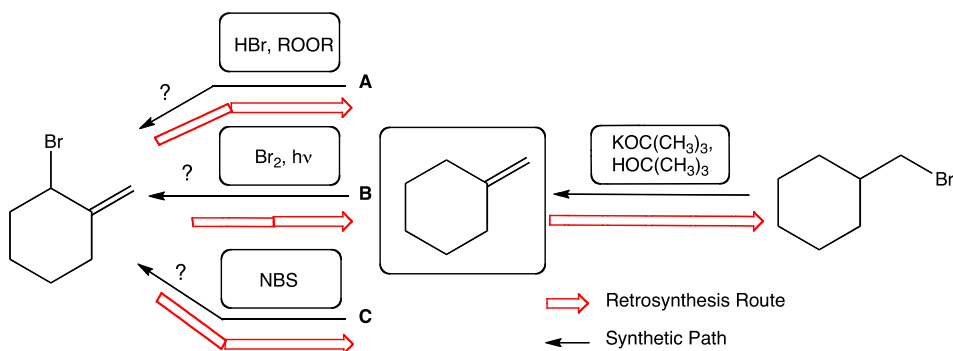


For the intermediate product, we choose a structure that will allow us to arrive at the product with a single reaction. In this instance, a structure with a double bond fused to the cyclohexane ring

3. Using your Organic Reactions-Interconversion sheet, identify the reagents to be used in our synthetic path that would eliminate H-Br to create a double bond (step 1) and those that would install a single bromine atom on a molecule (step 2). Fill in the figure below with the reagents.



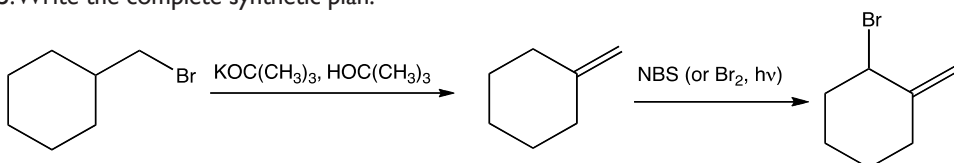
Here is a completed diagram:



4. Now you must choose which of the bromination reagent sets in the figure would lead to the product.

- HBr, ROOR – only adds to the double bond (ant-Markovnikov addition) – NO
- Br₂, hν – provides bromine on an allylic position – YES
- NBS – provides bromine on an allylic position – YES

5. Write the complete synthetic plan:



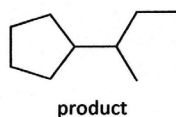
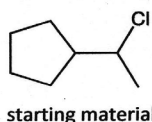
Check: Structures drawn correctly, reagent chosen gives the desired transformation.

Appendix B. Student Quiz Solutions – Alkene and Alkyne Chapters

Name: _____

CH 2211 Quiz Ch 7 continued

(10) 8. Given the starting material provided, propose a synthesis for the product shown. Use the systematic problem-solving approach we have introduced in class.



Differences: ✓
 - Product has ethyl group attached where Cl is on starting material

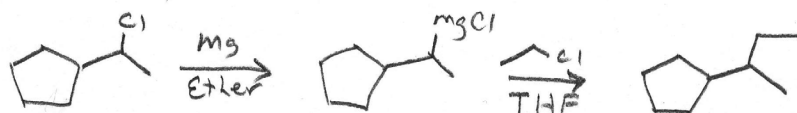
Transformations: ✓
 C-C bond forming rxn

Retro: ✓



Reagents: $-Mg^0$, $\text{CH}_3\text{CH}_2\text{Cl}$ ✓

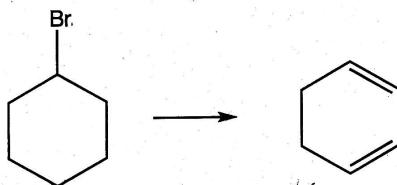
Synthesis: ✓



Name: _____

CH 2211 Quiz Chp. 8 continued

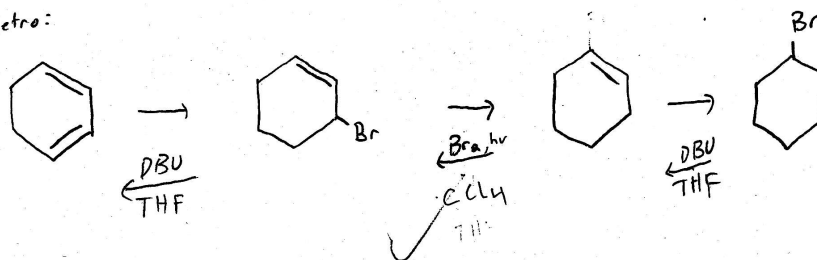
(10) 7. Using the systematic problem-solving approach we introduced in class, show all steps to complete the transformation shown below.



Differences:

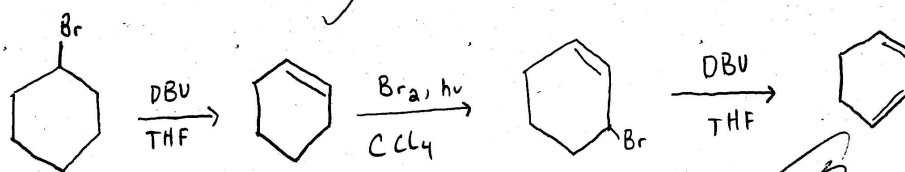
1. no Br. on product
2. 2 double bonds (elimination x2)
3. halogenation (x1)

Retro:



1. DBU
2. Br₂, hν

Synthesis:



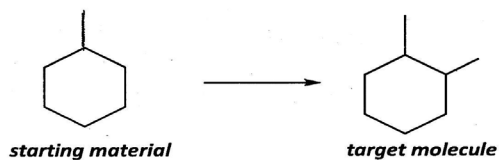
Organic Chemistry I
CHEM 2211, Fall 2012
Version 1

Name: _____
Date: _____

Chapter 10-11 Quiz, Synthesis
20 points

(20) 5. (COG 5) Use the retro-synthesis technique and write the stepwise reactions to make the target product molecules from the given starting material.

a.



differences: - 1 methyl group added

transformations: HBr - add Br to carbon - HBr, ROOR x2

- $\text{CuLi}(\text{CH}_3)_2$ & base (LDA, THF) ✓

- remove Bromine - DBU, THF

- 4 steps

