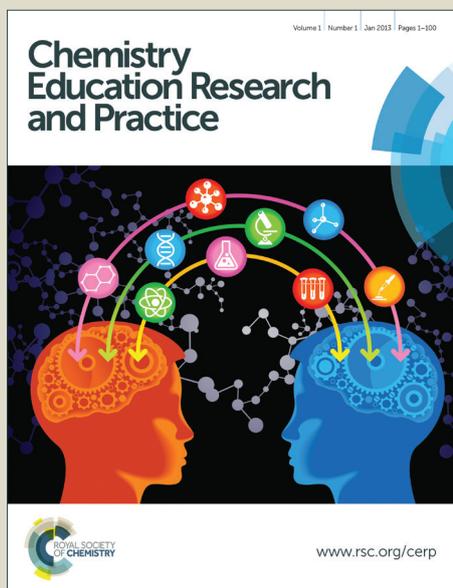


Chemistry Education Research and Practice

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How do students solve organic synthesis learning activities?

Alison B. Flynn

Department of Chemistry

University of Ottawa

10 Marie Curie

Ottawa, ON, Canada

K1N 6N5

alison.flynn@uottawa.ca

Abstract

Organic chemistry has the long-standing reputation as a challenging course, and organic synthesis is an aspect of organic chemistry that requires students to make the most links between concepts and requires the highest order of thinking. One-on-one interviews were conducted with students from a second undergraduate organic chemistry course in which participants solved synthesis problems using a think aloud protocol. Those problems had been previously designed to scaffold students' acquisition of synthesis problem-solving skills. The research question for this study asked whether students worked through the synthesis learning activities as designed, toward the intended learning outcomes. The results show that in some questions students used or tried to use desirable problem solving skills, such as using reaction mechanisms and chemical principles to explore possible solutions. However, with other question types, students (i) relied on familiarity with the reactions in question and lacked a problem-solving strategy when they could not recall the answer or (ii) avoided the purpose of the question and attempted to provide an answer that the professor "wanted." Strategies for promoting desired synthesis skills and addressing other issues are discussed.

Introduction

Organic chemistry has a long-standing reputation as a very difficult subject (Grove & Bretz, 2012). Possibly the most difficult and involved aspect of organic chemistry is designing a synthesis and

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retrosynthesis. To solve a synthesis problem, a student must, on paper, design a series of reactions in which they combine molecules to give a specific, more complex molecule. Student must choose from the dozens of reactions they have learned in current and previous courses, ensuring their strategy accounts for regiochemistry, stereochemistry, and that it maximizes chemoselectivity, safety, and yield, while minimizing cost and waste. Thus, they integrate several aspects of knowledge (J. B. Biggs & Collis, 1982; J. B. Biggs & Tang, 2007), propose one or more solutions to a new problem, and evaluate the solution(s). Some of the skills required to successfully plan a synthesis can be classed at the lower end of the revised Bloom taxonomy (i.e., at the “remember” and “understand” levels) while other skills require higher order thinking skills (e.g., at the “evaluate” and “synthesize” levels) (Krathwohl, 2002).

There is a gap in the teaching of organic synthesis in that students are taught basic reactions and then they are typically expected to propose a full synthesis without having been taught to integrate their knowledge and skills. Previously, synthesis learning activities were designed to scaffold students' acquisition of synthesis skills (Flynn, 2011). The development of the learning activities was based on the author's experience and the existing synthesis education and problem-solving research. The present study asks: How do students solve existing organic synthesis learning activities? Do they do so as intended on their way to achieving the intended learning outcomes (ILOs) and overcoming the barriers to learning? The little research that exists in organic synthesis education is summarized below, followed by a description of the synthesis learning activities that were the focus of the study, then the present study's theoretical framework, methodology, and results.

To begin the discussion on problem-solving, a problem is differentiated from an exercise as follows: “the difference between an exercise and a problem is the result of differences in the level of familiarity with similar tasks the individual brings to a given task” (Bodner & Domin, 2000) Wheatley's problem-solving model (Bodner, 2009) stressed the non-linear nature of the problem-solving process —and it's a messy model!

A key phase in the problem solving process is the very beginning. In those early stages, the relevant information is disembedded from the question and the problem is restructured (Bodner & McMillen, 1986; Larkin, McDermott, Simon, & Simon, 1980). Experts rely on underlying principles and simplify the task at hand (Larkin et al., 1980). Successful chemistry problem-solvers draw preliminary structures to explore solutions (Bodner & Domin, 2000).

A number of commonalities exist between successful problem solvers. Successful problem solvers: switch from one representation to another (Bowen, 1990; Kozma, 2003), move away from

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3 verbal/linguistic representations (Bhattacharyya, 2008; Bodner & Domin, 2000), interpret symbols as
4 having physical representations (not just meaningless letters or numbers on a page as do unsuccessful
5 problem solvers), construct representations that can contain elements of more than one representation
6 system, and use symbolic representations most commonly (rather than writing sentences or phrases)
7 (Bodner & Domin, 2000). Heiser & Tversky (2006) found that experts have expressed mental models
8 that emphasized function rather than form, which is more commonly expressed by novices. Similarly,
9 Kraft, Strickland, and Bhattacharyya (2010) found that the most successful problem-solvers tended to
10 use models-based reasoning.
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18 Kraft, Strickland, and Bhattacharyya (2010) also found that successful problem-solvers broke
19 down the problem into steps (rather than making 'leaps' like unsuccessful problem-solvers) and were
20 more metacognitive, which is becoming a larger focus in chemistry (Urena & Cooper, 2011). Few
21 participants did much 'scratch work' on paper, possibly because the representations would have little to
22 no meaning to students, they didn't recognize the value of writing things down, or they thought it was
23 important to be able to work things out in their heads.
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30 Students' understanding of chemical principles and process also impact their problem-solving
31 abilities. Strickland, Kraft, & Bhattacharyya (2010) investigated organic chemistry graduate students'
32 conceptions of the terms used to describe chemical reactivity (such as functional group, acid, base,
33 nucleophile, and electrophile) and expressed mental models of the images used to depict organic
34 reactions and mechanisms. Participants' conceptualizations contained very few mechanistic, or
35 process-oriented, attributes. Participants' verbalizations revealed a surface-level understanding of the
36 representations used in the diagrams, i.e., they were unable to 'see' beyond the representations. While
37 this work did not focus on synthesis, the tasks students were asked to perform (e.g., define common
38 terms and verbally describe a mechanism and overall transformation) are components of synthesis
39 problem-solving, and so student difficulties in these tasks would inevitably lead to difficulties in more
40 complex, synthesis problem-solving.
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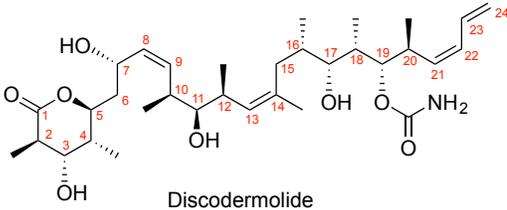
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50 Reaction mechanisms, including the electron-pushing formalism, are integral to experts'
51 problem solving process in organic chemistry; however, Anderson (2009) reported that by undertaking
52 useful problem solving activities, students began to find mechanisms more useful than they did initially
53 and that using mechanisms allowed them to troubleshoot unexpected problems. The electron-pushing
54 formalism is a major focus in the organic chemistry course related to this study and its relevance to
55 synthesis is further discussed later in this manuscript.
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4 The knowledge and skills needed for successful synthetic analysis were identified from the
5 above research and the author's experience. These attributes were used to create the associated specific
6 learning activities that are described below. Understanding students' approaches to these learning
7 activities were the focus of this study.
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10 11 12 **In-class learning activities**

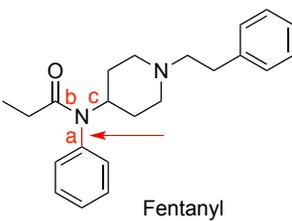
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15 Previously, this author created a number of new types of synthesis questions as in-class learning
16 activities (Flynn, 2011) and modified others to large class settings (Sauers & Morrison, 2007;
17 Straumanis & Ruder, 2009) to help scaffold student learning of organic synthesis (Figure 1).
18 Scaffolding, as defined by Wood, Bruner, and Ross (1976) is a "... process that enables a [...] novice
19 to solve a problem, carry out a task or achieve a goal which would be beyond his unassisted efforts."
20 (p. 90). Scaffolds, or learning supports, are provided to the student to help them solve a problem and
21 then are gradually removed, thus moving the learner from assisted to independent levels of learning.
22 The learning activities are aimed at students' zone of proximal development, the "distance between the
23 actual developmental level as determined by independent problem solving and the level of potential
24 development [through guidance]" (Vygotsky, 1978).
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(A) Identify one site of a given reaction (e.g., aldol)



Discodermolide

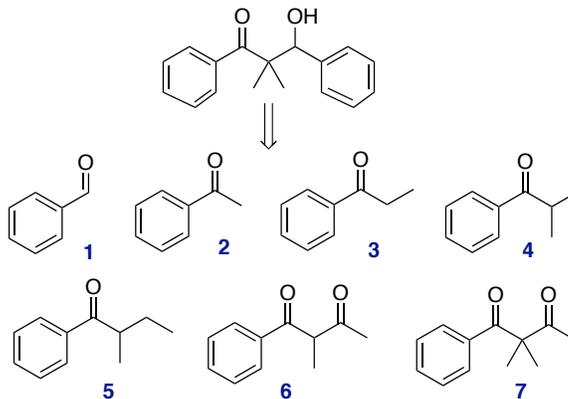
(B) Identify the reaction required to make the indicated bond



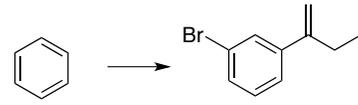
Fentanyl

1. S_N2
2. Friedel-Crafts acylation
3. Nitration
4. Aromatic bromination
5. Oxidation
6. Reduction
7. Acetalization (or related)
8. Wittig
9. Acylation

(C) Identify the starting material(s)



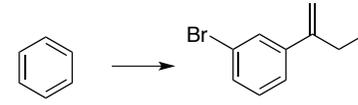
(D) Propose a synthesis (type 1)



Rxn #	Reagents	Product	Reaction name	Reactive electrophile ¹
1	HNO ₃ , H ₂ SO ₄		Nitration	⁺ NO ₂ (nitronium)
2	SO ₃ , H ₂ SO ₄		Sulfonation	SO ₃ H ⁺
3	X ₂ , FeX ₃		Aromatic halogenation	X ₂ FeX ₃
4	RCI, AlCl ₃		Friedel-Crafts Alkylation	RXAlX ₃ or R ⁺
5	RC(O)Cl, AlCl ₃		Friedel-Crafts Acylation	RCO ⁺ (acylium)

Rxn #	Starting material	Reagent(s)	Product	Reaction name
6		Sn, HCl or H ₂ , Pd/C		Reduction
7		H ₂ SO ₄ , H ₂ O		Desulfonation
8		NBS ¹ , peroxides		Benzylic bromination
9		Sn, HCl		Clemmensen reduction

(E) Propose a synthesis (type 2)



1. BH₃
2. H₂O
3. H₃O⁺
4. NaOH
5. H₂O₂
6. PCC
7. FeBr₃
8. AlCl₃
9. Et₃N
10. HCl
11. KOtBu
12. Br₂
13. NaOCH₃
14. Ph₃PCH₂
15. ClC(O)CH₂CH₃
16. ClC(O)CH₂CH₂CH₃

Figure 1. In-class synthesis questions.

Most of the question types used in this study were of the synthetic planning type; most have previously been reported (Flynn, 2011). They do not address project-level problems (such as deciding on a synthetic target) and few addressed day-to-day problems, being the ‘hurdles’ (such as the formation of side products) faced in laboratories while carrying out a synthesis (Raker & Towns, 2012b). The activities, to the extent possible, reflect the experiences of practicing organic chemists (Raker & Towns, 2012a).

In the first question type, students were asked to identify the site of a specific reaction, given a complex final product (Figure 1A) (Flynn, 2011). A numeric question was initiated with the classroom

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3 response system (CRS). Students typed in the numeric response by listing the three numbers of the
4 atoms involved, in order and without punctuation or spaces (e.g., 567). The histogram of results was
5 analyzed, which led to further discussion, in which students compared their answers with those of their
6 classmates. This question type encouraged students to find patterns within a product's structure, such as
7 the 1,3 relationship in the aldol product. They practice finding those patterns in bonds or functional
8 groups that appear "upside down" compared to how students are used to seeing them (e.g., 123) and
9 that have been derivatized after the initial aldol reaction (e.g., 171819).

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12 In the second question type, students were asked to identify the reaction required to make an
13 indicated bond in a complex product, given a list of possibilities (Figure 1B) (Flynn, 2011). Multiple
14 questions could be asked at once by asking students to identify the reaction required to make bonds a,
15 b, and c and listing them in a single answer, or by opening multiple CRS questions simultaneously
16 (preferred). Here, students have to consider all the reactions they have learned in the current course and
17 all previous organic chemistry courses. They are also encouraged to find multiple answers or strategies.

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20 For the complex substrates used in question types A and B, the students were instructed to
21 initially disregard the order of reactions and competing reactions. Follow-up questions were used to
22 further class discussion, such as asking students to compare synthetic routes proposed by their peers or
23 explaining why using one reagent combination might be superior to another.

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26 In the third question type (Figure 1C), developed by Sauers and Morrison (2007) and described
27 by Straumanis and Ruder (2009), students were asked to identify the best starting material(s) needed to
28 generate a specified product. Students had to first identify an appropriate reaction type to generate the
29 product, count atoms to identify which starting material is most appropriate, and use the mechanism in
30 combination with the functional groups in the starting materials and products to determine which
31 pairings are appropriate. They entered their answers using the CRS.

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34 In question types D & E (Figure 1), students were asked to propose a full synthesis of a product;
35 these questions are the culmination of the previous question types. In question type D, students were
36 given tables of reactions and reagents for specific transformations. Question type E was more difficult,
37 in that students were only given the starting material and a list of reagents (Figure 1E). The students
38 typed in the synthetic route on their device of choice (e.g., phone, tablet, computer) using the CRS
39 ("Top Hat," 2014). They could combine multiple reactions or reagents in each step and they typed a
40 period (.) between each step. These full synthesis questions required students to consider the order of
41 the reactions, the roles of the reagents, etc.

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4 All the questions can be asked initially without showing the list of options, to encourage
5 students to generate their own answer first. When first asking questions of this type, the list of options
6 is shown immediately. Later in the course, only the question is shown initially, giving the list of
7 options after students have had a few minutes (3–10 min) to work without cues, thus scaffolding
8 student learning. These questions could be asked in a think-pair-share format (Allen & Tanner, 2002),
9 in which students are first asked to work out the answer individually, then discuss, and finally submit
10 their answer using the CRS; optionally, students could vote after each think-pair-share stage. Using the
11 histogram of responses, class discussion and further questioning could be guided based on the students'
12 answers. This type of follow-up question gave the instructor the opportunity to re-direct common
13 questions and errors back to students for them to work through. For the many questions for which
14 students proposed multiple synthetic routes, an in-class analysis of two to three of those options
15 ensued. For example, students would discuss the options then vote on the best, or would comment on
16 the strengths and flaws of various routes. Doing so in class was meant to demonstrate the validity of
17 multiple synthetic routes. Synthesis questions on exams were marked with a similar philosophy, giving
18 credit for the quality of the proposed route, not for the degree to which it matched the answer key.
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21 The knowledge and skills students will ideally acquire are summarized in Table 1; they were
22 identified by the author's experience and by the existing synthesis research described above. The
23 associated Bloom levels (revised version) (Krathwohl, 2002) were assigned by the author based on her
24 experiences with the specific learning activities; the Bloom level could vary depending on how a given
25 activity is conducted in class. The present study was designed to understand whether students were
26 working through those synthesis questions as desired (i.e., to gain specific skills targeted by the
27 questions).
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Table 1. Requisite synthesis skills and associated revised Bloom levels (Kratwohl, 2002).

Figure 1	Learning activity	Skills targeted (Bloom level)
A	Identify the site of a specified reaction, given a complex molecule	<ul style="list-style-type: none"> Use reaction mechanism to predict product pattern (apply) State or draw patterns of reaction products (analyze) Recognize different oxidation levels and functional group transformations (FGTs) (analyze) Describe features of a reaction (e.g., steric, stereochemical, or electronic consideration) (analyze)
B	Identify the reaction required, given a complex molecule, an indicated bond, and a list of reaction choices (and draw the starting materials)	<ul style="list-style-type: none"> Simplify the structure (understand) Analyze bonds for possible reaction type (apply) Recognize patterns in products (apply) Associate bond type with an appropriate reaction (apply)
C	Identify the starting materials, given the product of a reaction	<ul style="list-style-type: none"> Count carbons (analyze) Identify the site of bond formation (analyze) Consider the mechanism to predict sites of bond formation (apply)
D	Propose a synthesis (type 1), given a table of reactions	<ul style="list-style-type: none"> Decide on sets of reagents to accomplish the transformations (apply) Decide the appropriate order of reactions (evaluate)
E	Propose a synthesis (type 2), given the SMs, products, and a list of reagent choices	<ul style="list-style-type: none"> Interpret the function of each reagent in the list (understand) Analyze synthetic disconnections to identify the best synthetic strategy (evaluate) Draw appropriate reagents to effect the desired transformations (synthesize)

Theoretical framework and research question

The goal of this work was to help students become more successful at complex problem-solving, specifically in the context of organic synthesis. As one step toward this goal, our group has undertaken the evaluation of the synthesis question types (used for in-class learning activities) within Guskey's evaluation framework (Guskey, 2000; 2002). Guskey evaluative model is similar to the Kirkpatrick model (Kirkpatrick, 1996) but also addresses organizational support and change (level 3).

Student satisfaction (level 1) was evaluated using surveys and interviews with students; the results revealed that students were of the opinion that the learning activities were useful, improved their confidence, and should be used again (Syoufi & Flynn, 2012). Their main criticism had been of minor technical difficulties. The second phase of the evaluation, reported here, investigated whether students worked through the learning activities in the intended fashion. The next phase of the evaluation—

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3 which is in progress and will be reported in due course—seeks to determine the impact of the new
4 synthesis questions on students' learning outcomes.
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7 In this phase of the evaluation, the following research question (RQ) was investigated, which
8 evaluated the organic synthesis learning activities at Guskey's level 2: **How do second semester**
9 **organic chemistry students solve the synthesis learning activities described in** Figure 1? Do they
10 do so as intended on their way to achieving the ILOs and overcoming the barriers to learning?
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13 The theoretical framework used for these specific research questions is that of personal
14 constructivism, that is, that the learner constructs his or her own knowledge and understanding. This
15 form of constructivism is tied to the zone of proximal development (Vygotsky, 1978), in that learners
16 link the new information to what they already know (Bodner & McMillen, 1986); in other words:
17 "knowledge is constructed in the mind of the learner" (p. 873). This study was not designed to assess
18 whether students were answering the questions correctly or incorrectly, because they could
19 hypothetically do either with or without using the skills or processes that the learning activities were
20 meant to scaffold. Rather, this study focussed on students' problem-solving process and skill
21 acquisition.
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32 Methodology

33 Students and course

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36 This research was conducted at a large, research-intensive Canadian university with student
37 participants who were enrolled in a second year level organic chemistry course, Organic Chemistry II,
38 in 2013. The course was their second in organic chemistry (Organic Chemistry I is taught in the winter
39 of students' first year). The class enrolment was 398 (~75% Faculty of Science, ~17% Faculty of
40 Health Sciences, ~8% other Faculties).
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46 The course was taught in a flipped format (Flynn, 2014). Students in the course attended two
47 classes (1.5 hours each) and one discussion group session (optional, also called a DGD, tutorial, or
48 recitation) each week, for twelve weeks. Assessment in the course was comprised of pre-class tests
49 (5%), assignments (10%), two midterms (10–20% each), participation in classroom responses system
50 (CRS) questions (5%), and a final exam (40–60%). For components with a range, the weighting that
51 gave the students the best final mark was used. Learning activities related to synthesis and
52 retrosynthesis were conducted at the conclusion of each section, i.e., approx. once every 3 weeks. The
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3 course curriculum had a mechanistic organization rather than a functional group one, in which students
4 learn the electron-pushing formalism before any actual reaction (Flynn & Ogilvie, Submitted & in
5 revision). In the first year organic course, students learn carbonyl addition reactions (simple π bond
6 electrophiles), reactions with π bond nucleophiles, and electrophilic aromatic substitutions (stabilized π
7 bond nucleophiles), in addition to basic structure and bonding concepts. In the second year course,
8 students learned E1, E1, S_N1, S_N2, spectroscopy, and more complex carbonyl reactions (e.g., aldol,
9 Fischer esterification).
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16 17 **Data collection and analysis**

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19 Students from Organic Chemistry II in 2013 (71% class average) were invited to participate in
20 one hour, one-on-one audio-recorded interviews in which they were asked to solve synthesis problems
21 of the types done in classes using a think aloud protocol (Patton, 2002). Thirteen students
22 participated—5 male and 8 female. Their average course grade was 82%.
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26 All phases of the research were reviewed and approved by the University of Ottawa's Office of
27 Research Ethics and Integrity. All research participants were provided with information detailing their
28 rights as human subjects; informed consent was obtained from all of the participants and they could
29 withdraw from the study at any point. Throughout this report, pseudonyms are used in place of the
30 students' real names to protect their identities.
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35 The interviews took place in February 2014, that is, approximately two months after the
36 completion of the course. The participants were provided paper, a pencil and a pen to make any notes.
37 They also had access to the course textbooks (Klein, 2012; Smith, 2011; Wade, 2013) and a summary
38 of the reactions they learned in the course (i.e., a reference page). Participants were asked to elaborate,
39 clarify, and provide more detail about their answers. The recordings were transcribed verbatim, coded,
40 and analyzed for themes using NVivo (QSR International, 2013); the participants' notes were also
41 incorporated into the transcripts. Next, the transcripts were coded and analyzed using constant
42 comparison method (Kolb, 2012; Patton, 2002). First, the data were openly coded and comparisons
43 were made within all the answers for each question type and within one participant's answers, moving
44 back and forth between the data, the codes, the research question, and the intended learning outcomes.
45 Next, axial coding involved making comparisons and connections between the codes and finally,
46 selective coding involved identifying the core categories that related back to the research question and
47 therefore to the intended learning outcomes. Member checking was done to increase the validity of this
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3 study (Creswell, 2011) by asking some of the participants to read the sections that referred to them
4 (e.g., in which they were quoted) and having them comment on the accuracy and completeness of the
5 analysis.
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8 9 10 **Limitations**

11 A fairly small number of students participated, and they had higher grades, on average, than the
12 class average responded to the survey and participated in the interviews. Therefore, a potential
13 limitation of this study was that the results might not have adequately captured the problem solving
14 strategies used by the lower-achieving students. The interviews were conducted two months after the
15 completion of the course, which may have affected their responses. A few of the problems in the first
16 version of the interview guide were not new to the students (i.e., identifying the site of an aldol reaction
17 in discodermolide and identifying the starting materials of an aldol reaction); because of this, the
18 problems might not have been “authentic” ones (Bodner & Domin, 2000) for the student. Because the
19 participants were interviewed by their former professor and they knew the overall goal of the study was
20 to help improve synthesis learning activities, the results of the study could be biased (Rosenthal &
21 Jacobson, 1968). For example, students may have solved problems differently that they might have
22 done in the actual class or exam setting.
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34 35 **Results and discussion**

36 Each type of synthesis question asked in class has its own intended learning outcome. That is,
37 each question is designed to help students acquire and demonstrate specific skills or knowledge. As a
38 first step, we wanted to know if students were working through the problems as designed. For example,
39 a student might use heuristics to obtain the correct answer without using the process skills that each
40 question is designed or “intended” to target. Using heuristics—i.e., simple reasoning processes to
41 reduce the effort in a task (Shah & Oppenheimer, 2008) or rules of thumb—can help students simplify
42 a task and solve a problem, but have been shown to often lead students astray (Maeyer & Talanquer,
43 2010; McClary & Talanquer, 2011; Taber, 2009). If students did not use the intended strategies &
44 skills, they would not be able to achieve the intended learning outcome, even though they might be able
45 to answer a given question. If they were not working through the problems as intended, students’
46 learning and the results of measurement of their learning could be strongly affected.
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Table 1 describes the skills each question type is intended to develop. For most of the synthesis questions, multiple answers were possible and it was the problem-solving strategy and not the answer itself that was emphasized in class and in this study.

Question type: Identify the site of a given reaction (Figure 1A)

The first question type is shown in Figure 1A. Participants were asked to identify the product of 1–2 of the following reaction types: aldol, Baeyer-Villiger, Friedel-Crafts acylation, epoxide opening, or S_N2 ; discodermolide and taxol were the products provided. The ways in which students who were interviewed worked through question type A—identify the site of a specified reaction, given a complex molecule (Figure 1A)—were analyzed.

Students worked through the problems as intended (targeted skills are summarized in Table 1). Some struggled with the question, had to look up answers or be guided, but all the skills identified in Table 1 eventually emerged or was clearly developing.

The five students who answered this question type looking for an aldol product seemed quite familiar with the 1,3-oxygenation pattern indicative of an aldol reaction. It seemed that they had memorized and could easily recall that pattern, likely because it was emphasized in their organic course and was one of the last reactions learned. All the students were able to identify the aldol pattern, with two of them being able to do so immediately, the others did so after looking up the pattern. For example, Louis described how he recognized the aldol product:

I was just looking for 3 carbons and then oxygens, because I remember that's what aldol does. And I remembered you can take off one of the OHs [points to 9], by, uh, I think it's call condensation. Aldol condensation.

Three of the students (Georgia, Avery, and Abigail) drew the aldol pattern of the product (Figure 2). They tended not to use R groups (only one student did so in a single structure) or draw out the mechanisms; all used highly simplified structures to represent the aldol and condensation patterns.

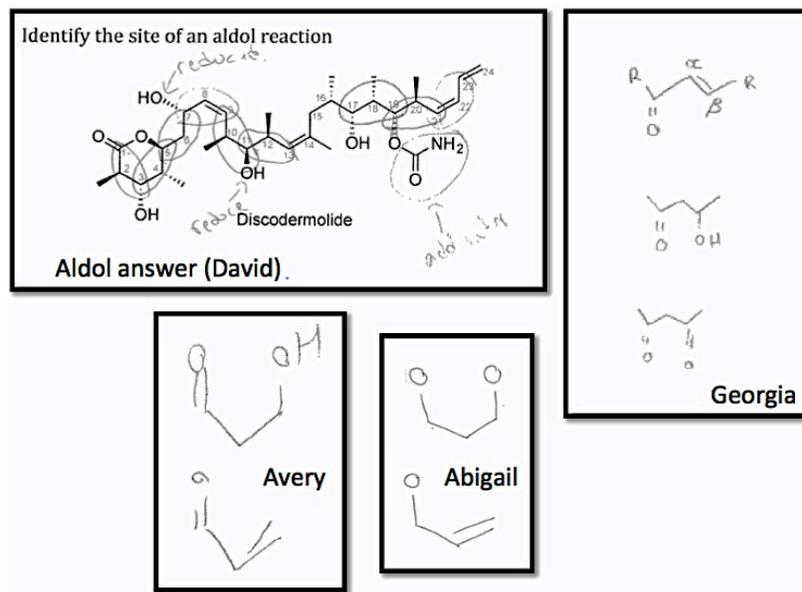


Figure 2. Students' notes to themselves when identifying the site of an aldol reaction in discodermolide.

This tendency to not draw out the mechanism or even structures recurred frequently in other variants of this question type, except in the case of the epoxide opening variant. In that variant, students turned to the mechanism of the reaction. Three of the five students who answered this question drew partial mechanisms as part of their rough work; the other two discussed the mechanism, pointing to bonds in the structure as they did so. It seemed that students relied on the reaction mechanism to solve problems involving less familiar reactions (the epoxide opening had been less-studied in a synthetic context in the course). This outcome seems to reflect the conclusions drawn by (Heiser & Tversky, 2006)—that experts expressed mental models that emphasized function rather than form. While the students who used mechanisms to solve problems in this study could not yet be considered experts, they were certainly demonstrating behaviours consistent with successful problem-solving strategies used by experts.

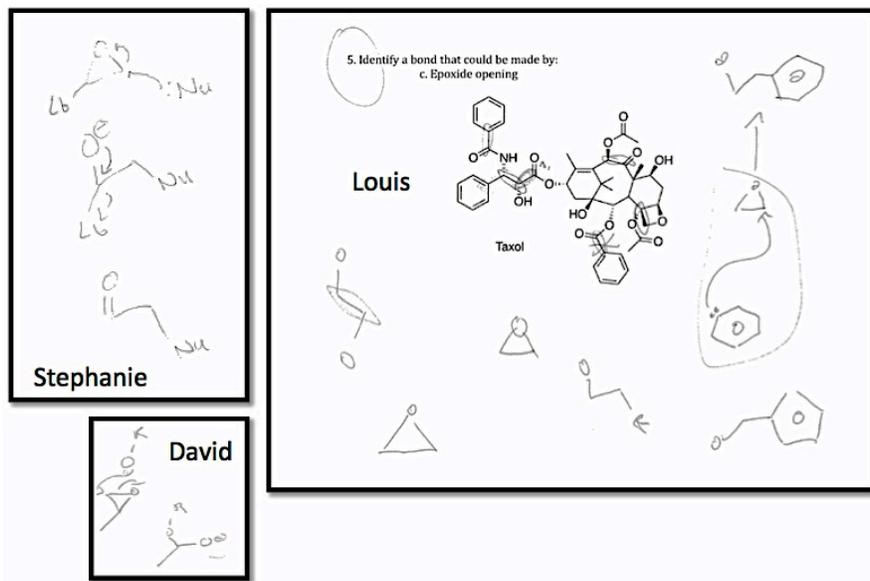


Figure 3. Three of the five students' rough work when answering the "identify the site of an epoxide opening reaction in taxol" included partial mechanisms and structures.

The complexity of the compounds was considered as a factor that could affect how students worked through this type of problem. All students except one—Avery—identified many possible sites of the aldol reaction, including those in which further functional group transformations (FGTs) would have occurred; they worked systematically from one side of the molecule to the other. Avery, on the other hand, pointed out two possible sites of an aldol reaction then seemed to give up, saying: "...that's really bulky and awful to look at." Other students also reported thinking the size of the molecules was daunting. Abigail commented:

Abigail: I always found them like, just such a size, I was like, oh my God, I don't know what to look for. Like I'd always be super overwhelmed by the size of it.

Interviewer: Ok

Abigail: And then like, you know, I'd kind of get over it, but like initially, like, that was super scary for me.

The idea that students can get used to the size and complexity of the molecule and look for patterns is one that recurred throughout the interviews. Avery did not identify many sites of reaction in the aldol question, but later was able to with a different reaction (Friedel-Crafts acylation) in the same question type. He seemed to get used to working with complex molecules in the short time frame of the interview. The importance of working with molecule with some degree of complexity returns later (see below) when questions related to competing reactions are discussed.

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Even when asked to identify many possible sites of reaction (i.e., when the question was extended even farther), students still worked through the question systematically. Some students did not initially recognize that an aldol product could be further derivatized (e.g., the alcohol in the product could be oxidized, alkylated, etc.), but once this was pointed out to them, they began to identify additional reaction sites.

For the same question type but looking for the product of a Baeyer-Villiger reaction, one student (Ryan) who began to identify the possible products immediately did not consult any other aids and did not draw the mechanism or other structures. His familiarity with the reaction and its products seemed to make the use of additional resources of processes unnecessary. In contrast, Madeleine was able to identify many potential products of the Baeyer-Villiger reaction once she had looked up the reaction and drew a partial mechanism. In doing so, she also discussed some of the key features of the reaction mechanism. For example:

And, this one [indicated the benzoate], uh, mm, I feel like the oxygen would of been on this side [the side with the benzene ring] cause the benzene ring is more able, or more capable of stabilizing the positive charge.

When asked about the class atmosphere, a few different ideas recurred. For some, it was “more competition to see who could find more [sites of reaction].” Others described how this question type helped them see patterns they wouldn’t otherwise have recognized. When asked to describe her opinion on this question type, Madelaine said:

Madelaine: I, I like these kinds of questions because it, it like, I like that you did stuff like this in class because it gave me the opportunity to see kinda how other people were thinking too.

Interviewer: Mm. Ok.

Madelaine: And realize like, other points of views but like it just made me, I don’t know, it’s kinda hard to explain. Um. It, it kinda widened my perspective on, yeah.

Interviewer: Ok.

Madelaine: So I, I like doing these kinds of questions in class cause say for example like I would of missed one, like that, that would really stand out to me like, oh ok I missed this one but like everybody else got it so like what am I not doing that their doing and it helped me along...

Two concerns that came up with this question type. First, students were concerned with the parameters or “rules” of the question. For example, were students allowed to imagine that a functional group transformation (FGT) had taken place after the reaction of interest? Louis said: “I don’t know if I

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can do a reaction after the reaction...” They also wondered whether they were allowed to use any reaction conditions. In the epoxide question, for example, Madelaine wondered if only one of acidic or basic conditions could be used, and was greatly reassured when either were “allowed”:

Madelaine: Does like, does it matter, like what we're using for, like for the ring opening, like it's a strong base or a... like a... reaction... conditions?

Interviewer: It can be under any conditions.

Madelaine: Ok. [looked at the reference sheet]

Interviewer: Yeah.

Madelaine: So that one here. [pointed to the oxetane. She continued answering the question giving increasingly advanced answers]

Second, many students reported that when answering this type of question on a midterm or final exam, they did not know exactly how many points were allocated to each identified answer (e.g., was it 1 point for each) and so they felt there was ambiguity knowing when to stop answering. Madelaine stated: “I’m fairly hesitant when it comes to this kind of stuff cause I’m always paranoid that I’m like missing something.” This is in contrast to most other question types, such as “draw the product,” in which students can be more certain when they have completed answering the question.

Eight of the participants answered this type of question. Once it became evident that every student was working through this question type as designed, i.e., that saturation had been reached (Patton, 2002), this question was removed from further interviews. The research question for this type of learning activity had been satisfactorily answered and students demonstrated the skills they were developing.

Summary of this section:

- Students worked through the “identify the site of a given reaction in a complex product” question as intended.
- Students drew all or part of the reaction mechanism when the reaction was less familiar.
- The complex molecules were daunting to some students at first, but they overcame that and all students eventually (within the timeframe of the interview) worked systematically through the questions.
- Students reported working collaboratively in class to find more answers, others competed to find the most answers; both methods reinforce the goals of the question.

- Clarifying the expectations on a final exam would alleviate the ambiguity surrounding the question. For example, students should be told whether FGTs are possible and the number of sites of a given reaction to identify.

Question type: Identify the reaction required to make the indicated bond (Figure 1B)

In this question, students were presented with a complex target molecule and were asked how they would make a specific bond (e.g., Figure 1B). Students were able to identify the reaction required to make the indicated bond only if it was already familiar to them. If they did not recognize the required reaction, they did not have the skills to figure it out or to look it up, either in the reference sheet or in the textbook. For the students who identified the required reaction, they had difficulty drawing the required starting materials, that is, in translating the reaction name into actual starting materials. Hannah gave one example of the search for familiar reactions when she said: “I look at what’s being bonded to what usually and then I go through like the possibilities of like how you can get there, I guess.”

When Hannah could not remember the reaction required for the question or she did not recognize the pattern (e.g., due to the molecule’s complexity), she did not have a strategy to successfully solve the question. When other students, such as Julie (who drew the starting material fragments, unlike many others), could not recognize the reaction required to make a bond, tried to look it up, but none managed to look up a pattern when they did not know the reaction name they were looking for (e.g., none looked for a bond type or functional group as a starting point). That was Julie’s experience when trying to propose the reagents that made bond 2:

Julie: Like...[drew the fragments shown in Figure 4, ~20 sec pause] An oxidation just makes... [mumbling, trailed off, ~15 sec pause] ... I want to say there’s somehow, like a... substitution... onto that one [pointed to B, Figure 4] to make it able to take on the oxygen, er, to make – switch from an alcohol to make the bond? [looked briefly at the reaction reference sheet in the derivatives of CO₂H section, then turned away].

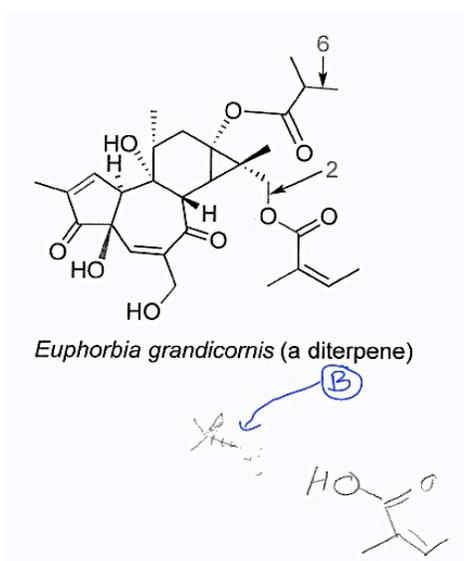


Figure 4. Julie disconnected bond 2, but didn't draw appropriate SMs and could not find a reference reaction (blue arrow and circled "B" were added after the interview by AF).

For two students, the mechanism was an important step in answering the question. Louis drew out the mechanism, then talked it through, then corrected himself in the steps of the mechanism, all even though he had already correctly answered the question. The issue of ambiguity again came up with Louis, who was concerned about how the question would be marked (e.g., whether it was acceptable to ignore possible side reactions).

Ryan's strategy to a solution stood out in particular. He did not resort to naming reaction types, but rather, drew out and analyzed various mechanistic possibilities (Figure 5). His answer was a logical one that was based in chemical principles—closely resembling expert-like thinking. It was Ryan—interviewed 7th—who provided the inspiration to use a synthon approach with later participants (see below).

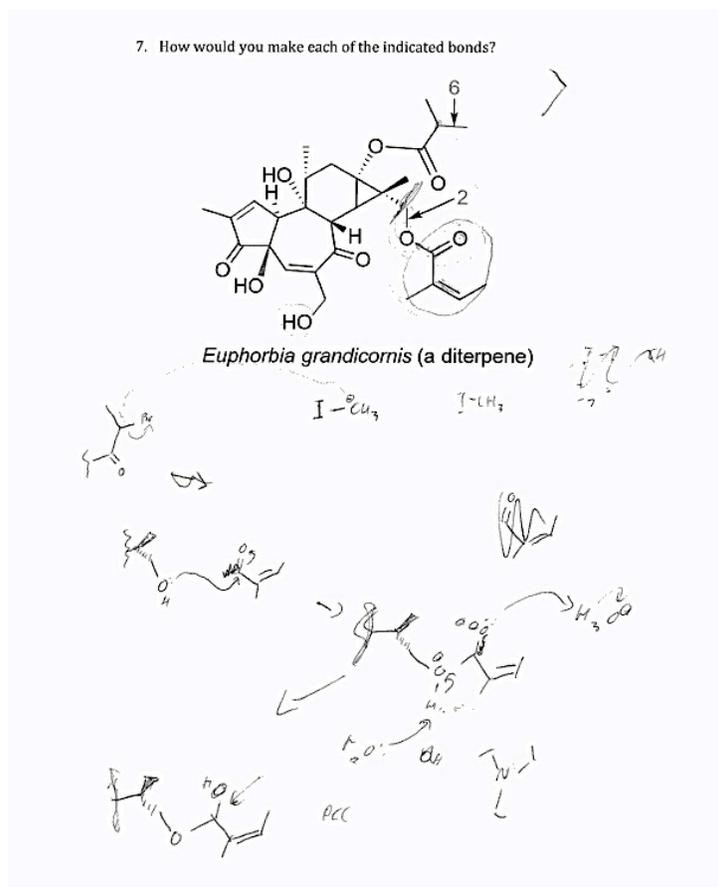


Figure 5. Ryan drew out partial mechanisms while solving the "identify the reaction required to make the bond" question.

Julie struggled with this question type from the start and did not recognize the reaction type that could have made that bond (i.e., it was not familiar to her). Even though she drew the fragments from which bond 2 was formed, those fragments could not have combined in a reaction to make the desired bond 2 (Figure 4). Further, she tried unsuccessfully to look up a suitable reaction type in the reference sheet. At this point, the interviewer described the synthon approach (Corey, 1967; Corey & Cheng, 1989) to her (Figure 6), and she logically and successfully solved both parts of the question using that approach, drawing starting materials for bonds 2 and 6 shown in the diterpene structure in Figure 5.

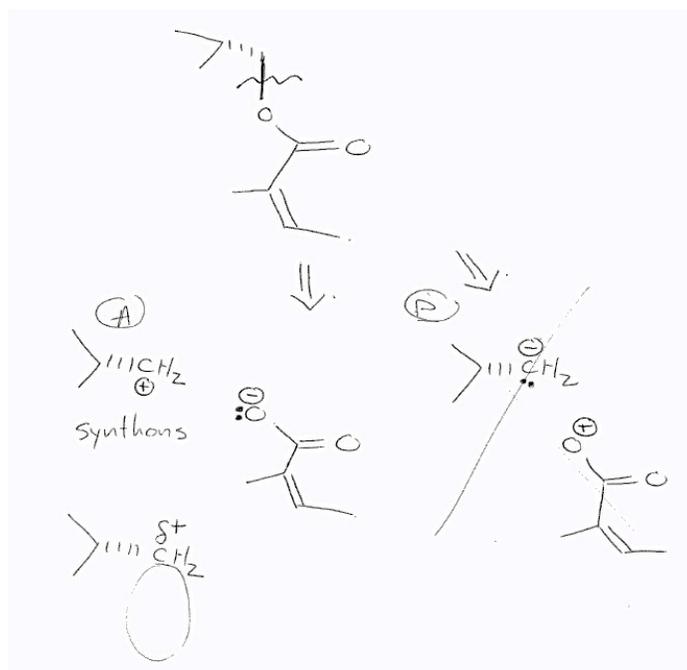


Figure 6. Written portion of the explanation of the synthon approach described to Julie (for bond #2 of the question).

Julie immediately identified pair “A” (Figure 6), in which the oxygen has a negative charge, as being most plausible. When asked to draw the actual reagents, Julie considered two possibilities, but settled on the one that avoided a possible competing reaction:

Julie: Okay. [~70 second pause] So the C-H-2 would have to be attached to something that would have – make the... this one be delta negative I guess?

Interviewer: Yes, exactly.

Julie: Could it be attached to like an alcohol? [5 second pause] But then the H could react with that...

Interviewer: Mhm. [~15 sec pause] What other kind of negative, delta negative groups... have we seen?

Julie: Mm... [~ 10 second pause, looked at cheat sheet] Chlorine... delta negative groups... [mumbling, looked at reference sheet, ~15 second pause] Cause if you, mm... [~15 second pause] Cause if you make the chlorine leave... [drew chloromethane].

Interviewer: Mhm.

Julie: It takes the electrons, so it'd make it uh... positive... and then the C-H-2 could react with the oxygen.

Not only did Julie approach the retrosynthetic analysis while guided through the synthon approach for bond 2 of that question, she also figured out most of a solution for bond 6 without any prompting. She immediately drew a plausible pair of synthons then talked through and dismissed the other possible synthon pair. She readily drew the reagent electrophile although she struggled to draw the reagent required to generate the nucleophile. This difficulty was understandable because metal counterions or use of conjugate acids had not yet been discussed within the context of synthons.

With the next student, Aaron, the synthon approach was explained using an unrelated example before he saw the actual question. He then used the synthon approach to identify the possible synthons, drawing the pair he thought was most probable and explaining why he thought the other pair was less so (Figure 7). From the synthons, he quickly drew the actual reagents. He repeated the approach for second bond. He approached the question in a logical, systematic way, and clearly used chemical principles and reaction mechanisms rather than familiarity with reaction types:

Aaron: C-H-3 plus $[CH_3^+]$ sitting by itself wouldn't happen. So you would have to have something attached to it that was more negative or, uh, delta negative or something [drew bromomethane].

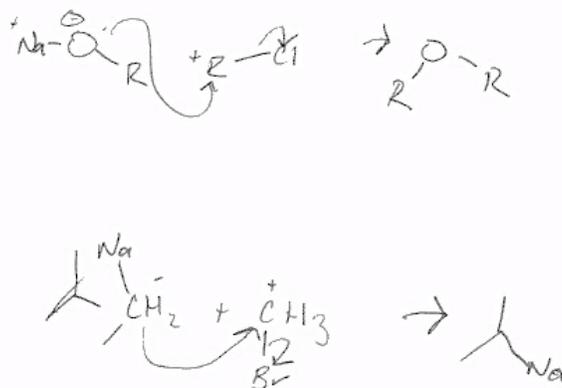


Figure 7. Aaron's drawings when answering the "Draw the SMs" question using the synthon approach (note: he did not erase the + and - signs after adding the Na, Br, and Cl atoms).

Notably, Aaron had written nothing to this point in the interview but quickly and comfortably drew synthons and their related mechanisms, then drew only a partial structure in a later question. Although there were errors in his final reagents because he didn't adjust the formal charges to account for the added bonds/atoms, he took a big step toward solving a difficult question using a chemical strategy and not simply relying on familiarity.

Marta showed an even higher level of mechanistic competence with the clear drawing of the synthons, verbal descriptions of her choices of synthon pairs, and how she determined what reagents to use (e.g., methyl lithium in one situation and the carboxylic acid in the other) synthon pairs in each case (example in Figure 8). Marta went further in her analysis to determine (using acid/base principles) which base would be appropriate to deprotonate the carboxylic acid and generate the requisite nucleophile. Like Aaron, she also started writing for the first time during this question. There seems to be something about the synthon approach that made students think/believe they did not have to solve the question in their heads.

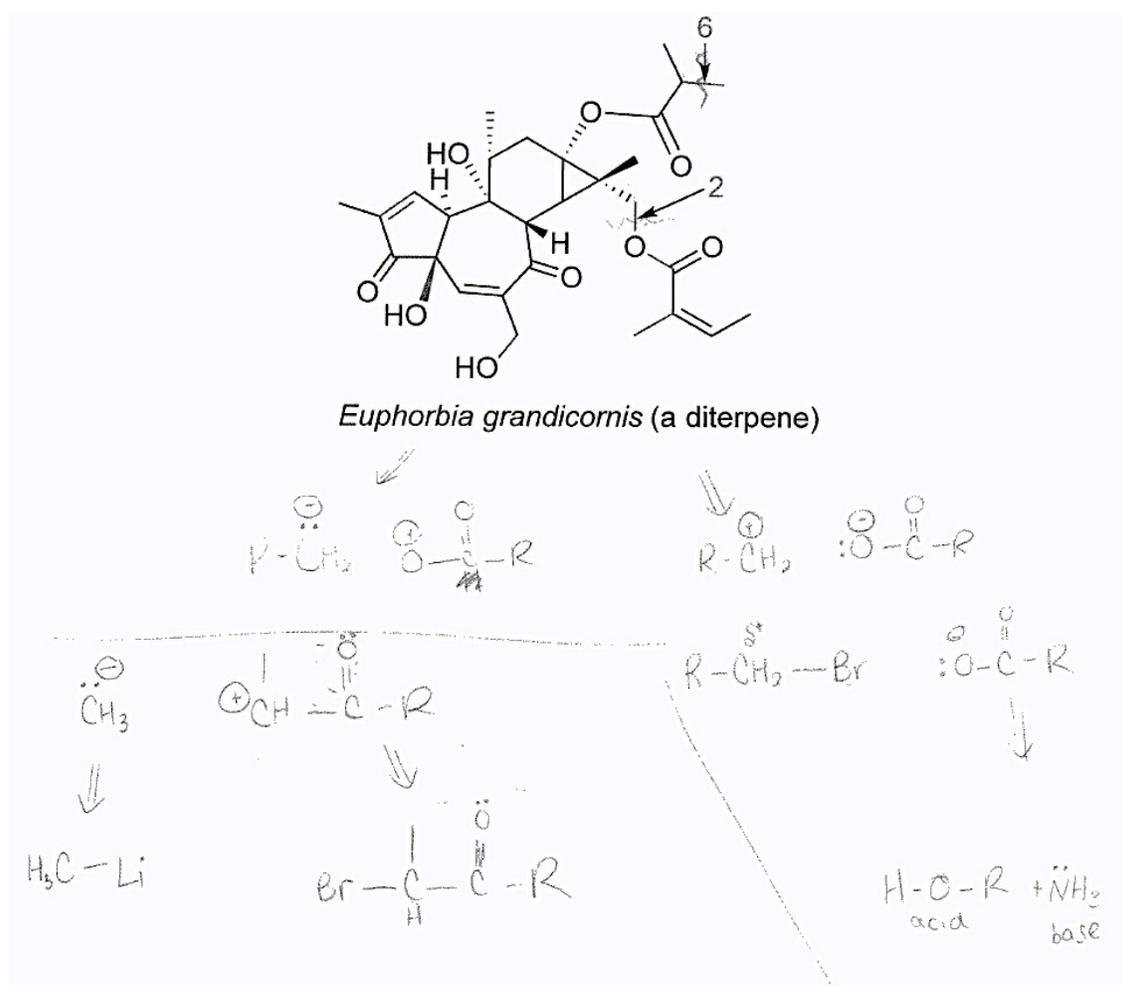


Figure 8. Marta used the synthon approach to determine the starting materials for each of the bonds indicated above.

It was exciting to see that when the synthon approach was explained to the four students, they solved the problem using a mechanistic thought process and relying on chemical principles. They did so even though the synthon approach had not previously been taught in the course. All the students who

worked through the synthon approach starting writing structures and mechanisms without prompting, a habit and skill encouraged for all students in the course. They worked through those question types systematically, even though they involved the complex type of structure that students report finding daunting. Even Marta started her problem solving—before she seamlessly solved the question to the question—with: “Uh oh... it looks so big... Even though, when I think about it, I’m just dealing with individual bonds, so it doesn’t really matter how big it is.” Because of the success with this approach in helping students design a retrosynthetic analysis, the synthon approach will unquestionably form a key synthesis questions in the future.

Summary of this section:

- If students did not already recognize the reaction type, they did not know how to solve the problem.
- Students struggled to look up reaction types; they seemed to lack that basic research skill.
- Students who were able to name the requisite reaction to form a specified bond still often struggled drawing the actual starting materials.
- Introducing a synthon approach (with four students) based in mechanistic considerations and chemical principles provided a strategy for students to systematically and successfully work through the problems.

Question type: Identify the starting material(s) (Figure 1C)

Students were presented with a simpler target molecule and a selection of possible starting materials; they were asked to select the appropriate starting material(s) to generate the desired target (Figure 1). The two students who were given the first version of this question easily eliminated half the options (the alcohols) based on familiarity with the required starting materials. They eliminated the other incorrect options because they looked wrong (i.e., by roughly estimating the number of atoms). For example, Louis described how he arrived at a solution:

Oh, yeah. Well the thing is I counted the carbons after. When I was comparing these two [1 & 6, the correct answer], that’s only when I started counting them. With those other ones [the alcohols], I just started eliminating them. So it could only be one reaction because those couldn’t work that start with OH. Well, they could, but not in this case [i.e., when you don’t have the option to oxidize first]. If I’m doing an aldol then you can’t start with those [alcohols]

so I just eliminated those guys. And I knew that it was either one of these two combinations [1 & 6 or 3 & 8] because the number of carbons... you don't even really have to count them.

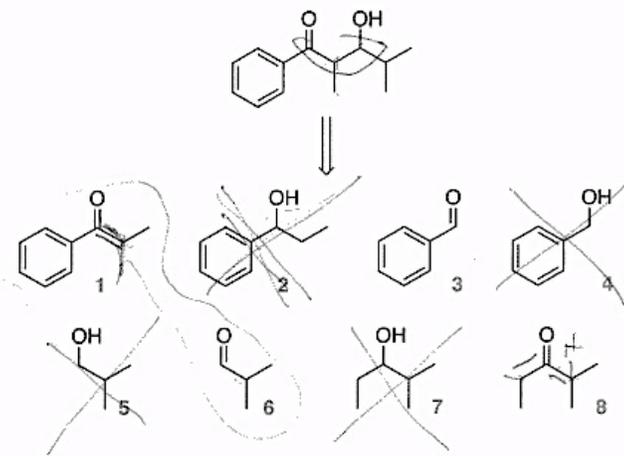


Figure 9. In this first version of the “identify the starting materials” question, students easily eliminated most of the options based on familiarity with reaction type (correct answer 1 & 6).

As with any multiple choice type question, the distracters should be plausible (DiBattista, 2008a; 2008b). Version 2 of the question was created (Figure 10) in which the target and possible answers were changed slightly, so that the molecule seemed to be symmetrical. That apparent symmetry led many students to use #3 twice (once as the nucleophile in enolate form, the other equivalent as electrophile). Ryan, however, drew out the mechanism of the reaction and counted the carbons. He worked through the question systematically, without relying on familiarity.

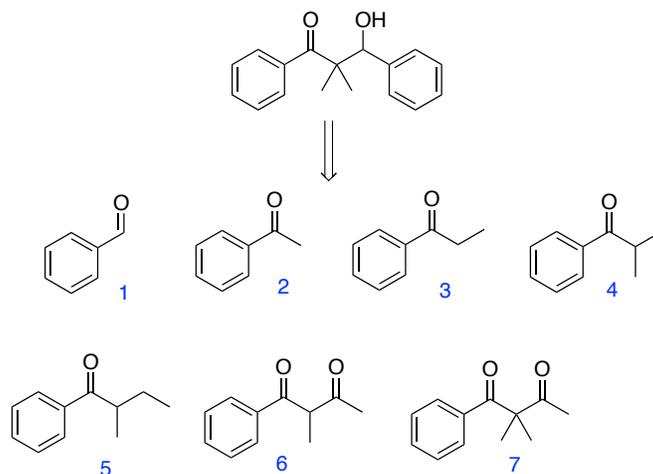


Figure 10. Version two of the “identify the starting materials” question (correct answer 1 & 4).

Ryan initially considered using molecule #3 twice (Figure 10), but eventually settled on 1 and 4 (the correct answers). He explained his reasoning as follows:

Umm... I think it's because I thought that... uh... I could... make an, uh, make an enolate with that [#3]... uh, and then... use that to attack uh, you know, the, the same, same one... But, I dunno just kinda going through it in my head it didn't really make sense because then... cause then this [the α -carbon of 3 that he drew] would be attached to the carbon [indicated the mechanism that he drew]... yeah the carbon wouldn't be the, uh... wouldn't match up.

Julie also drew out mechanisms (Figure 11) and when trying a mechanism between reactants 2 and 4, had to ask herself: "Where did that methyl group [α carbon in 2] go?" She realized by drawing the mechanism that molecules 2 and 4 were not the starting materials. She proceeded to explore mechanisms for other options and count carbons more carefully to eventually arrive at the correct answer.

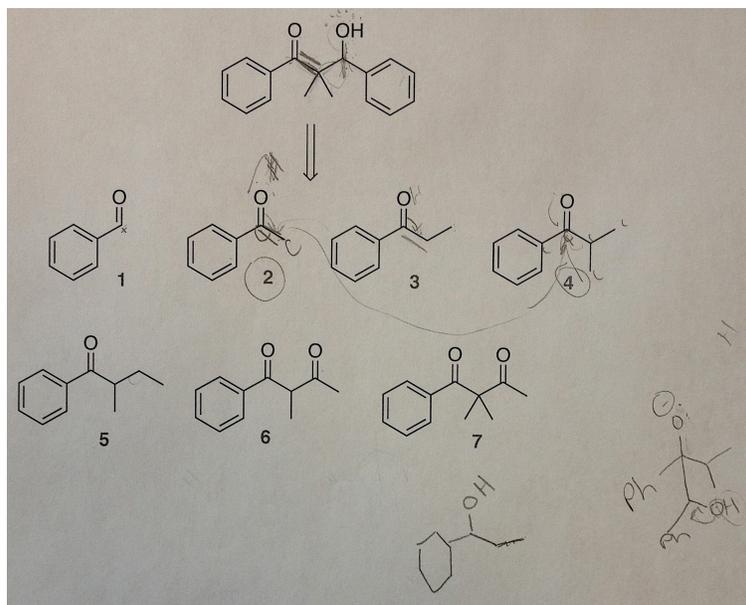


Figure 11. Julie drew out the mechanism between 2 and 4 and in doing so realized that this reaction would not give the desired product (correct answer: 1 & 4).

The clear advantages to this new version of the question were that students could not quickly eliminate options on the basis of functional groups and they had to both consider the mechanism and count carbons. Although the question was presented as a retrosynthesis, students worked through it in the forward direction.

Yet another instance of a student not being able to look up a reaction and recognize a pattern was evident as Marta solved this problem. She found the aldol reaction in the reaction reference sheet,

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3 but did not believe that variation in the carbon structure was possible, as revealed in the following
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5 quote:

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7 *The aldol is looking similar to what this [question] is... But in the product that's drawn on the*
8 *[reference] sheet there's this other methyl group that comes off where the hydroxyl is, and I'm*
9 *not seeing that here, so... I'm trying to remember how...*

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11 These student weaknesses in looking up reactions, which will likely ultimately affect their
12 research abilities and their ability to learn reactions beyond those explicitly taught in the course,
13 suggest a new question type that should be developed (described below). Another issue is suggested by
14 this result: students can probably not take a specific reaction and generalize it—it is not possible to
15 look up a reaction when it is not known what to look for.

16
17 Although not a large sample, all the students who drew mechanisms and counted carbons were
18 successful at solving version 2 of the problem. Only Marta did not draw mechanisms for the reagents in
19 this question (she only did so on the reaction reference sheet), and she did not find a correct answer.

20 21 22 23 24 25 26 27 **Summary of section:**

- 28 • Students considered the mechanism of the reaction and counted carbons—both desirable
29 skills for students to gain—when the question was well designed with plausible distractors.
- 30 • Students struggled to look up the reaction (either in the reference sheet or in the textbook)
31 when it was not familiar to them, suggesting a deficit in research skills.

32 33 34 35 36 37 **Question type: Propose a synthesis (Figure 1 D & E)**

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39 The simplest “propose a synthesis” questions such as the one involving electrophilic aromatic
40 substitution (see Figure 1D) were quite straightforward and asked students to think especially through
41 the order of their reactions (i.e., synthetic strategy). They needed to think less about how to achieve
42 each transformation, because the sets of reagents were provided to them and were fairly standard,
43 particularly for electrophilic aromatic substitution reactions and derivatizations.

44
45 Although aromatic chemistry was covered in first year, this topic seems to have “stuck” with
46 students. They easily recalled the existence of directing groups, although often had to look up the
47 specifics (which most students had difficulty doing). Once they reviewed the directing group
48 principles, solving the problem became straightforward.

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50 The second type of “propose a synthesis” question (see Figure 1E) was more complex because
51 students had to identify which reactions were required to generate various bond types of fragments of
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3 the molecule, decide on the appropriate reagent(s), and then choose appropriate reagents from the list
4 of reagents provide. The list of reagents provided sometimes matched up well with a student's
5 proposed synthesis, but often the student either had to make a minor modification of their synthesis
6 (such as replacing the H₂SO₄ they proposed using with the HCl that was the strong acid available in the
7 reagent list) or had to reconsider their entire synthesis because it was not achievable with the list of
8 reagents provided.
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14 The interviews revealed a key issue with this question type. Students who were able to propose
15 their own synthesis often abandoned their own synthesis when the list of reagents did not fit their
16 proposal. That was Avery's experience:
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19 *I'm kind of stuck in my ways, but the first thing I want to do is I want to find my route to fit*
20 *these new reagents... Cause that's generally the easiest way to do it instead of coming up with a*
21 *new one but mine was totally different from what you... from any option here so I'm just re-*
22 *doing it now... Cause this [not being able to accomplish his synthesis with the list of reagents*
23 *provided] happened a lot. I have a very... um... odd or different way of looking at things. I have*
24 *no idea what it is about it. So the combination or options it [the reagent list] would show was*
25 *90% of the time it was nowhere near what I had.*
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32 Similarly, Madelaine explained the mismatch between her answer and the one provided:
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34 "Especially synthesis questions, I tend to do things like the, the longer way, well like not so much like
35 the longer way but um, I I [*sic*] find I rarely get like the answer that's in the textbook."
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37 During the interviews, seven of the nine students who answered this question type abandoned
38 their own route once provided the list of reagents, even the four students whose routes were completely
39 correct. Of the two students who did not abandon their proposed syntheses, David only needed a hint
40 from the list to complete his own (i.e., his synthesis essentially fit the list) and Louis' synthesis could
41 be accomplished using reagents from the list. When Louis was asked what he would do if his synthesis
42 could not be accomplished using a list of reagents provide, he responded in a way that added evidence
43 that the purpose of this question type was not being achieved: "Ah! I would assume that you wanted a
44 different pathway [laughed] so I would just look for another pathway."
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51 None of the students who successfully proposed a different synthesis than the one in the list
52 made a case for their synthesis being equally valid. This was a concern, because there are usually
53 multiple routes to a given target molecule, and an important value of synthetic analysis (both for
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3 chemistry and in developing transferable skills) is analyzing and testing (in the laboratory) the viability
4 of those different routes.
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7 In addition, the four students who were unsuccessful at proposing their own synthesis, i.e., who
8 got stuck trying to propose their own synthesis and/or could not use the list to generate a proposal, did
9 not have a alternate strategy.
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12 **Summary of this section:**

- 13 • When synthetic strategy (e.g., the order of the reactions needed for regiocontrol) was the focus
14 because the sets of reagents were provided to the students, they worked through the questions as
15 intended (question type in Figure 1D).
16
- 17 • When students proposed their own synthesis first, then tried to match their synthesis to a list of
18 reagents, they tended to completely abandon their own synthetic route if it did not fit the list.
19 This defeated the purpose of synthetic analysis, which should embrace the possibility of
20 different routes and seek to evaluate those alternatives.
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- 22 • This question format seemed to “force” a specific answer rather than allowing for multiple
23 routes to a product, which would enrich the learning experience.
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32 **Research skill: finding analogous reactions and appropriate references**

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34 A theme that emerged across all the question types was the gap in students' abilities to look up
35 answers (e.g., reaction types and reagents) when necessary. This issue emerged initially with the
36 questions intended as warm-up. In these questions, students were presented with a starting material and
37 product and were asked to match the reaction to the one in the reaction reference sheet. This was the
38 first time they were seeing this sheet, which summarized all the reactions from their first and second
39 year organic courses.
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44 If the reaction in question was familiar to the student, then they could usually match it up with a
45 reaction in the sheet. However, if it was not familiar, they were not able to find it. They did not look up
46 reactions on the basis of their functional group or governing mechanism or use the textbook's index
47 efficiently.
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51 For example, Louis and Aaron immediately recognized the required transformation (reduction
52 and acetalization, respectively), then matched the reaction to the appropriate one in the reference sheet:
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54 *Louis: So the first one I see is just a reduction, right? Cause it just changes the carbonyl O to*
55 *an OH... I'm just trying to remember what does that [tentatively started to look at sheet]*
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There, a Grignard... [found the reaction at the right spot in the sheet] I mean, not a Grignard, I mean NaBH_4 [said the letters and number].

Aaron: "So it's making an acetal... Like a ringed acetal. [looked at sheet, found the acetal] ... Or a... so you just have to add... So this is like a diol so you'll add a diol and then, um, you would have to... so you go through all the steps where you hydrolyze all the different things, like the five step [mechanism].

While David recognized the acetal functional group easily (as did the other students), he struggled to find it in the reference sheet:

David: And this one I see that we've um... we've added a protecting group—is that what you call it? And that is just... if I can remember properly [looks at sheet] ... it's adding in basic conditions so you want a base and also um... I think water as well... [still looking at sheet]

Interviewer: What made you recognize a protecting group?

David: Well, it's just, uh, I guess... the two Os and they're bonded by the uh ethane group... I guess and uh it's not really a protecting group unless you're going back and you reconvert it into a.... Well I guess protecting group always makes me think of the two oxygens bonded in that cyclic way.

Interviewer: Ok

David: Alright, so, you need a base first... a strong base... NaOH and then you also need to you should be able to add the ethane in... Ok, perfect, ok... [struggling to look up reactions] ok, so 2 times ... [found the correct reference reaction] ok, sorry, so we'd just use ethanediol [drew it incorrectly] but first I would need to add... um... [looking back and forth between structure and the reference sheet] ... um... water... you're getting water out... base or acid... ok so I would add an acid first because that would protonate that [drew the mechanism of carbonyl protonation] and then that would attack the C of the carbonyl... there.

Aaron also had difficulty finding the alcohol oxidation reaction; he only did so successfully once prompted, and still struggled:

Aaron: So we have to, uh, remove the hydrogen and then we can get a negative charge on that [pointed to the O] which we can bring the electrons down [did not write anything for this question].

Interviewer: Mhm.

Aaron: Um. So you could do that with like a stronger acid. Or yeah.

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3 Interviewer: *Ok. And can you find it? See if you can find the similar reaction in the sheet.*

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5 Aaron: *uh... Ok. It'd be... like an oxidation. So I guess the big thing is you didn't want to go*
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7 *too far with it.*

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9 A weakness in students' abilities to conduct research (e.g., find an appropriate experimental
10 procedure to conduct a specific reaction) was previously noted by this author to be weak in fourth year
11 students (Flynn & Biggs, 2011), but this study revealed an even more fundamental gap in students'
12 skillsets.
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15 16 17 **Summary of this section:**

- 18 • Constructivism is based on ascertaining what the learner knows/can do and teaching
19 accordingly (Ausubel, 1968). The assumption that students could already look up reactions
20 was clearly incorrect and students need to be explicitly taught this skill.
21
- 22 • These results suggest another learning deficit: that students are not able to generalize a
23 specific reaction, which likely lead to difficulties applying their specific learning to new
24 situations.
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30 31 32 **Conclusions:**

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34 The present study gave insight into how students answered many different question types that
35 are designed to help students learn the skills required for synthetic planning. Many themes that were
36 observed were consistent with previous research, such as the important of redrawing structures (Bodner
37 & Domin, 2000), using the reaction mechanism (J. P. Anderson, 2009) and interpreting symbols
38 meaningfully (Kozma, 2003).
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41 As summarized in Table 3, students worked through some question types as intended (i.e.,
42 Figure 1A, C and D), but did not do so with others (i.e., Figure 1B and E). The implication for practice
43 is that question types A, C, and D seem most effective for developing the targeted skills, while types B
44 and E should be redesigned if they are to target the skills described above (Table 1). Students were not
45 using or attempting to use the skills targeted in the latter sections. For example, in question type B,
46 students did not attempt to simplify the structure, analyze bonds for possible reaction type, or associate
47 bond type with an appropriate reaction, unless the bond type immediately linked to a memory of the
48 required reaction (i.e., if they recognized the required reaction).
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While it seems the synthon approach will be a very powerful one for students, more research is needed to understand the strengths and implications of using that approach in the classroom. For synthesis questions—as with any type of question that has multiple possible answers—the existence and value of the multiple answers should be made explicit through the learning activities and intended learning outcomes. This is especially true for students who have been conditioned to believe that science is dichotomous (right/wrong) rather than the highly variable nature of science (Van Dijk, 2014).

Table 3. Summary of results

Question type	Learning activity	Key results
A	Identify the site of a specified reaction, given a complex molecule	<ul style="list-style-type: none"> Students worked through the question as intended (e.g., looked for patterns). Students drew all or part of the reaction mechanism when the reaction was less familiar. The complex molecules were daunting to some students, but only at first. The expectations for the questions must be clearly communicated
B	Identify the reaction required, given a complex molecule, an indicated bond, and a list of reaction choices (and draw the starting materials)	<ul style="list-style-type: none"> If students did not already recognize the reaction type, they did not know how to solve the problem (e.g., they did not simplify the structure or use the mechanism). Students struggled to look up reaction types; that research skill was lacking. Students who were able to name the requisite reaction to form a specified bond still often struggled to draw the starting materials. The synthon approach (with four students)—based in mechanistic considerations and chemical principles—provided a strategy for students to systematically and successfully work through the problems.
C	Identify the starting materials, given the product of a reaction	<ul style="list-style-type: none"> With well-designed questions (bearing plausible distractors), students analyzed the mechanism of the reaction and counted carbons—both desirable skills for students to gain. Students struggled to look up the reaction when it was not familiar to them, again demonstrating the deficit in research skills.
D	Propose a synthesis (type 1), given a table of reactions	<ul style="list-style-type: none"> Students worked through the questions as intended and focused on the synthetic strategy (e.g., regiocontrol).
E	Propose a synthesis (type 2), given the SMs, products, and a list of reagent choices	<ul style="list-style-type: none"> When students proposed their own synthesis first, then tried to find appropriate reagents from the list provided, they tended to completely abandon their own synthetic route if it did not fit the list. This defeated the purpose of synthetic analysis, which should embrace the possibility of different routes and seek to evaluate those alternatives. This question format seemed to “force” a specific answer rather than allowing for multiple routes to a product, which would enrich the learning experience.

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4 For the problematic question types, students resorted to familiarity with reactions, they lacked a
5 defined strategy when their rote memory failed, and they struggled to look up reactions. A major
6 modification of type B—asking some students to adopt a synthon approach—had a notable benefit for
7 those students. They began using mechanistic thinking and drawing out their ideas—components of
8 expert-like thinking. Type E was quite problematic in that students abandoned their own synthetic route
9 if they could not make it match the list of reagents provided. Students did not attempt to evaluate their
10 synthetic designs—a key skill for students to acquire, and one that is applicable across disciplines.
11 Students also relied on familiarity and did not have a problem-solving strategy to fall back on if they
12 came upon an unfamiliar reaction. This tendency of students in organic chemistry to memorize a set of
13 rules and reactions has been previously reported to hinder student learning (T. L. Anderson & Bodner,
14 2008; Grove & Bretz, 2012). Other question types will be designed to replace this question to help
15 students learn to plan syntheses systematically and using mechanistic thinking, as well as evaluate
16 synthetic routes.
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When the synthon approach was explained to four of the students, all of them began to draw molecular structures and reaction mechanisms; all could compare the various synthon pairs to choose the most plausible one and were successful at solving the related synthesis problems.

The gap in research skills will be addressed in part with new learning activities that help students learn to identify general features of reactions and then to research them in a resource such as a textbook. This skill deficit (i.e., the ability to generalize a reaction or make connections between reactions) may be related to students' unawareness that such connections exist; they are not aware that another way of learning organic chemistry exists, i.e., meaningful learning (Grove & Bretz, 2012).

These synthesis questions, in principle, are closing the gap between students' learning of the basic organic chemistry concepts and learning the knowledge and skills to accomplish full retrosynthetic and synthetic analyses. Because only a small number of participants (13) were involved in the study, they were interviewed by their former professor and they knew the overall goal of the study was to help improve synthesis learning activities, the results of the study could be biased (Rosenthal & Jacobson, 1968). In addition, the mechanistic curriculum that we use might be inextricably linked to students' problem-solving process in some questions. For example, in the “draw the starting materials” question, students employed the synthon approach (which required keeping track of electrons) with ease once they were exposed to it.

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4 The next phase in this research project will be to design and evaluate new question types that
5 target the student weaknesses identified in this study. The effect of these types of questions on student
6 learning in the larger course setting and other educational settings (e.g., with teaching assistants in
7 tutorial/recitation settings, at other institutions, other levels of instruction, etc.) will be evaluated, as
8 will the synthon approach. The intent is to promote students' development of higher order thinking
9 skills (Krathwohl, 2002), to encourage students to move their learning from rote to meaningful (Grove
10 & Bretz, 2012), and in doing so, to achieve higher level learning outcomes (J. B. Biggs & Collis,
11 1982).
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