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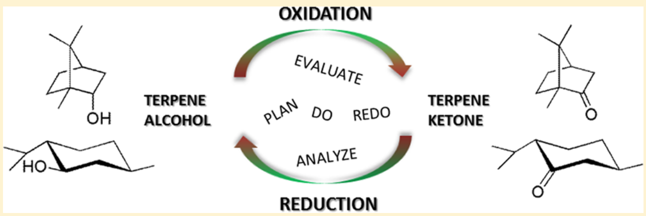
Transforming Undergraduate Students into Junior Researchers: Oxidation−Reduction Sequence as a Problem-Based Case Study

Tiina Saloranta,* Jan-Erik Lönnqvist, and Patrik C. Eklund

Johan Gadolin Process Chemistry Centre, Laboratory of Organic Chemistry, Åbo Akademi University, Turku 20500, Finland

ABSTRACT: In our upper-level undergraduate laboratory course in organic chemistry we focus on a research-oriented task in a context-based and problem-based learning approach. The course starts with a preliminary training period where the students learn how to safely and independently perform synthesis and purification procedures and to operate the most common analysis instruments. In the latter part of the course, the students are asked to perform an oxidation−reduction sequence with a chiral, optically pure terpene alcohol, such as menthol or borneol, as a starting material. This part is presented as a problem scenario and the students, working in small groups, are supposed to plan and execute the experimental work independently. Importantly, the research task presented herein is aimed to promote the undergraduate students' creative thinking as well as the problem solving skills in organic chemistry.



KEYWORDS: *Upper-Division Undergraduate, Organic Chemistry, Inquiry-Based Learning, Oxidation/Reduction, Alcohols, Stereochemistry*

■ INTRODUCTION

The university level education in chemistry is traditionally initiated with a series of lectures and exercises accompanied by practical laboratory courses. The education given on basic level is supposed to give a solid background in general chemistry providing tools for the more advanced level learning characterized by student-centered, research-oriented, and problem-based methods. These learning methods have proven to increase the motivation of students and develop their critical thinking as well as their problem solving and team working skills.

In our current chemistry curriculum within the three year bachelor program in natural sciences,[1] the basic level organic chemistry studies comprise two courses. The lectures cover the fundamentals in organic chemistry, whereas the corresponding laboratory exercises are aimed to introduce the students to most typical laboratory scale synthesis, isolation, purification, and analytical methods. These courses are common for all chemistry (major and minor) students with up to 100 students per year. During the final year of the bachelor program, the chemistry major students will concentrate more on one discipline, that is, analytical, inorganic, organic, or physical chemistry. For this purpose, we have developed a final bachelor level course in organic chemistry, named *Research Project in Organic Chemistry*, where the students will get their first research-oriented challenge. In the current format, the course is feasible with up to 10 students during a relatively intensive two month period.

The course comprises two main periods. During the first period (preliminary training period), the students are involved in ongoing research projects under supervision of the teaching personnel and graduate students. The students are allowed to work in real research laboratories and take part in ongoing research work by performing or assisting the supervisor in various unit operations such as synthesis set up, work up, and purification procedures and analysis. This training period, described in Table 1, lasts for approximately 4 weeks and the aim is to introduce the students to various routine and advanced laboratory techniques including both synthetic and analytical methods. Importantly, the students are trained to work independently in the synthesis laboratory and likewise, they are also allowed to operate independently various analysis instruments such as NMR and IR spectrometers and GC−MS. Some of the techniques included in Table 1 are already covered during the basic level courses, but during this course, the students are trained to apply the techniques for new problems when the cookbook-approach, characteristic for basic level courses, is not anymore valid. The students are supposed to write a short description on each method and collect these in a laboratory portfolio that comprises the final report on this preliminary training period. The portfolio is supposed to be written and submitted individually and is graded with passed/not passed. The aim is that the students will use this portfolio as a reference manual later on during the course.

The second period of this course is characterized by the context-based and problem-based learning approach. The students are given a real research-type problem aiming to introduce them to a process of building on their prior knowledge (partially obtained during the preliminary training period) and to develop their problem solving and critical

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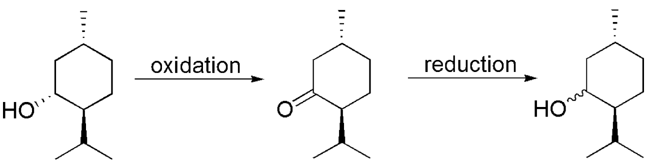
Table 1. Skills and Instrumental Methods Taught during the Preliminary Training Period

Techniques	Didactic Aims	Learning Objectives
Traditional reaction setup	To teach the fundamentals of setting up a synthesis, taking the safety aspects strictly into consideration	The students are able to design a reaction set up and to perform basic synthetic procedures independently
Reaction set up under inert atmosphere	To explain and demonstrate the basic principles of Schlenk techniques	The students are able to work under inert atmosphere under supervision
Glove box techniques	To explain and demonstrate the possibilities and restrictions of glovebox procedures	Students are able to handle chemicals in a glovebox under supervision
Crystallization	To teach the fundamentals of crystallization as a purification method	Students are able to apply crystallization as a purification method
Column chromatography	To teach the fundamentals of column chromatography as a purification method and the theory behind its function	Students are able to independently perform a column chromatographic purification
Flash chromatography instrument	To explain and demonstrate the use of automated flash chromatography instrumentation	Students are able to use the instrument under supervision
Distillation	To teach the distillation procedures (under normal and reduced pressure) and to understand the related safety issues	Students are able to perform distillations independently fulfilling the safety regulations
Freeze-drying	To explain and demonstrate the basic principles of freeze-drying	Students are able to use the freeze-dryer under supervision
Waste management	To teach the principles of chemical waste management	Students are able to independently sort the chemical waste produced in a laboratory
GC and GC−MS	To teach the standard operating procedure for GC and GC−MS instrumentation	Students are able to do routine analyses independently
LC−MS	To explain and demonstrate the principles, possibilities and restrictions of the instrument	Students are able to use the instruments under supervision
NMR spectroscopy	To teach the standard operating procedure for NMR spectrometers used for routine ^{1}H NMR spectroscopic analyses	Students are able to do routine analyses independently
IR spectroscopy	To teach the standard operating procedure for IR spectrometer	Students are able to use the instrument independently
Optical rotation	To teach the standard operating procedure for a polarimeter.	Students are able to use the instrument independently and to interpret the results

thinking skills. This type of context-based and problem-based learning in higher level chemistry education has been discussed thoroughly in the preceding literature.[2−6]

The overall task, described in Scheme 1, consists of an oxidation−reduction sequence with a chiral, optically pure, terpene alcohol as starting material accompanied by structural characterization of the products followed by scientific reporting. Oxidation of secondary alcohols and reduction of corresponding ketones are fundamental transformations included in the organic chemistry curriculum. Likewise, these reactions are traditionally involved in undergraduate laboratory courses as the underlying chemistry is generally well known and the reactions usually proceed representatively in terms of selectivity and yield. Although the overall task may appear trivial, the challenge arises from the fact that the identity, purity, and stereochemistry of the starting material are initially kept unknown to the students and that the spectroscopic characterization of the products is rather demanding. Moreover, the students are not provided with literature procedures but they are supposed to develop their own research skills by designing the synthesis procedures and the required analysis independently. In this article, the idea behind this research-oriented challenge is presented highlighting the pedagogical aims involved. The actual laboratory procedures are not presented in detail as several methods may be employed. However, references to relevant literature are provided. The detailed implementation is left open and can thus to be adjusted for different universities and educational systems.

Scheme 1. Overall Research Project Exemplified with (−)-Menthol as Starting Material



OVERVIEW OF THE RESEARCH-ORIENTED PROJECT

The project is divided into four stages as described in Table 2. The first problem (stage 1) given to students is to analyze and characterize the starting material. In case of multiple student groups, different starting material can be given to each group. The students are asked to choose the proper chromatographic, spectrometric, and spectroscopic methods for the analyses. As a result, the students are also expected to define the stereo-

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Table 2. Four Stages of the Research Project

Stage	Task/Problem	Skills, Methods, and Learning Objectives
1	Complete structural characterization of the starting material	Chromatography and spectroscopy (TLC, GC, IR, NMR) spectrometry (GC–MS), stereochemistry (optical rotation)
2	Oxidation of the secondary alcohol followed by complete structural characterization of the product(s)	Oxidation methods, planning, and execution of a synthesis
3	Reduction of the ketone followed by complete structural characterization of the product(s)	Reduction methods, planning, and execution of a synthesis, selectivity in reduction of cyclic ketones
4	Scientific reporting: written report in journal format and an oral presentation	Report writing, oral presentation skills

chemistry of the unknown starting material and to give the full IUPAC name for the structure with correct *R*/*S* nomenclature. The students are also expected to comment on the purity of the starting material.

After properly analyzing the starting material, the students are asked to plan and execute the oxidation of the alcohol to the corresponding ketone. As these ketones are known and available in the laboratory, the oxidation product is supposed to give the final proof for the structure of the starting material. At this stage (stage 2), the students are first asked to evaluate different oxidation methods taking the overall costs as well as the environmental and safety aspects into consideration. Several methods for similar oxidations are available and many of them have previously been published in this journal. Among these are oxidation-based on chromic acid,[7] oxone,[8] $Ca(ClO)_2$,[9] Dess–Martin periodinane,[10] and PCC.[11] Before starting the experimental work, the students will present the chosen method in detail, and the instructor will ensure that that the students are aware of the safety and practical procedures. The scale of the reaction is not predefined but is typically limited to controllable lab-scale (a few grams). During the experimental work, the students are allowed to work independently in the laboratory but a dedicated instructor is reachable whenever needed. The students are encouraged to evaluate and enhance the literature procedures, thus gradually leaving the cookbook chemistry behind and moving toward research-oriented laboratory work. The second stage is concluded by complete characterization of the purified oxidation product followed by critical evaluation of the chosen oxidation method.

In the third stage, the students are supposed to reduce the obtained ketone back to the corresponding secondary alcohol. The scenario in this stage can be formulated with the question: Was the initial starting material obtained by reduction of the ketone? Again, the students have to search for and choose a solid method and to perform the reaction. Naturally, a complete structural analysis of the products is required. At this stage, the students typically observe that the stereochemistry of the original starting material is not necessarily retained but the product can be obtained as a mixture of diastereomers. Hence, it can be concluded that the starting material was probably not obtained by reduction of the ketone.

In the last stage, the students write a complete scientific report including introduction, results and discussion, experimental part, and conclusions. The report should be written according to instructions following the ACS Style Guide. However, the style guide is not provided to the students; instead, to find and to apply these guidelines comprise the main problem in this stage. In the final report, emphasis lies on the experimental part and logically built results and discussion section. Moreover, the students will also give an oral presentation of their work in a final seminar. Due to the research-oriented character of the course, the students are assessed only with grades passed/not passed. Typically, the final report needs some improvements before it will be accepted following the characteristics of a review process.

■ TIME SCHEDULE

The overall time schedule for the second period of the course is presented in Table 3. Stages 1–3 include also a scheduled discussion/seminar with the instructor at the end of each stage. The time required for each stage is the average active time required. However, if the students are not able to work full time with this course, the time schedule needs to be adjusted accordingly. On the basis of our experience of more than five years, the oxidation–reduction sequence including the proper analytical work and scientific reporting requires approximately four calendar weeks. Typically, the students are simultaneously involved in other courses as well, but because the work is independent by nature, only a few conflicts have occurred. The final seminar is usually booked in advance, hence giving an explicit deadline for the work but the students are still allowed to plan the detailed schedule by themselves. The students usually notice that their original time schedule needs some adjusting during the project. This should not, however, be avoided as the approach teaches organizational skills, group dynamics, and sense of responsibility.

■ PEDAGOGICAL DISCUSSION

The overall research work described herein has been shown to be highly versatile and educating. It can be tuned toward intermediate or advanced levels depending on the level of demand and the questions asked/problems given. To exemplify, if continuous help is provided with the synthesis planning and interpretation of the spectroscopic data, the work will gain more routine-like character. Moreover, the discussions that are scheduled for the midseminars can conveniently be merged with organic chemistry lectures. With these adjustments the project can be fitted into typical organic chemistry course with scheduled weekly laboratory sessions and lectures. In the presented model, the students are introduced to most of the analytical and experimental procedures during the preliminary training period, but a part of this training can be included in the second period as well. The main pedagogical aim of this work is to challenge the students with a real research-oriented problem and to encourage their creative and independent thinking in organic chemistry both as individuals and in a group. This method, hence, is following the context-

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Table 3. Detailed Content and Approximate Time Required for Different Tasks

STAGE	CONTENT	TOTAL TIME RESERVED	ACTIVE TIME IN THE LAB
1	**Introductory lecture** • Presentation of the overall work • Introduction to the problem-based approach	1 – 2 hours	
	Literature search • Planning the required analysis	1 day	
	Complete characterization of the starting material • Chromatography (TLC, GC/LC) • Spectroscopy (IR, NMR) • Mass-spectrometry • Optical rotation	2 days	4 hours
	Mid-seminar 1 (discussion) • Characterization of the starting material	2 – 3 hours	
2	**Literature search** • Critical evaluation of different oxidation methods • Planning the synthesis	2 days	
	Practical synthesis work • Oxidation of the alcohol to the corresponding ketone and purification of the product	1 – 2 days	4 + 4 hours
	Complete characterization of the oxidation product • Same methods as above	2 days	4 hours
	Mid-seminar 2 (discussion) • Presentation of the evaluated oxidation methods • Motivations for the chosen method • Presentation of the oxidation procedure and results	2 – 3 hours	
3	**Literature search** • Critical evaluation of different reduction methods • Planning the synthesis	1 day	
	Practical synthesis work • Reduction of the ketone to the corresponding alcohol • Possible chromatographic separation of the products	1 – 2 days	4 + 4 hours
	Complete characterization of the reduction product(s) • Same methods as above	2 days	4 hours
	Mid-seminar 3 (discussion) • Presentation of the reduction procedure and product(s) • NMR-spectroscopic characterization of cyclic products • Discussion on selectivity in reduction of carbonyl compounds	2 – 3 hours	
4	**Scientific reporting** • ACS format • Main emphasis on the experimental part	4 – 5 days	
	Final seminar • Oral presentation of the overall work with discussion	2 – 3 hours	

based and problem-based learning within the constructivism learning theory.

In stage 1 (analysis of the starting material), the instructor presents the problem without any detailed information. The starting material (typically more than 100 g) in an old chemical bottle with a simple label "menthol" or "borneol" is given to the students at this stage. The students are working in small groups (2 or 3 students per group). Importantly, we have noticed that

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it is beneficial if the instructors steer the formation of the groups. The first task for the students is to find and choose methods for the characterization of the starting material. The group presents the chosen analytical methods including motivations, that is, what knowledge the specific method will provide, to the instructor prior to the actual experimental work. In this way, the students are encouraged to work toward the solution together by gathering and sharing information and by creative thinking. The problem acts as the driving force for the new learning. Before the actual synthesis work, the students should reflect on the characterization process. The possible stereoisomers are discussed, and finally, the students propose a complete name and stereochemical structure for the starting material, including proper nomenclature. At this stage, a more advanced lecture in stereochemistry as well as in some specific nomenclature and natural product chemistry, that is, terpenoid chemistry can be given.

In stage 2, the instructor asks the students to modify their starting material by functional group interconversion, that is, oxidation of a secondary alcohol to the corresponding ketone in order to confirm the structure by comparison with the known ketone, available as a reference compound. No synthetic methods are presented; instead, this is introduced as the second problem. The students should find and evaluate at least three different oxidation methods. Different aspects, such as the sustainability, waste generation, purification methods, toxicity, time schedule, and costs can be included in the synthesis planning. The chosen method is presented to the instructor before the experimental work. During the reaction, the students should monitor the conversion by suitable analytical methods (TLC, GC). After the reaction and possible purification, the students are asked to present a solid proof for the formation of the ketone as well as to comment on the purity of the oxidation product. At this stage, the instructor is encouraged to emphasize the historical perspective regarding structure determination, usually done by chemical derivatizations and comparison with known reference compounds. There are several such examples in terpenoid chemistry; for example, the history of camphor and its structure is highly interesting,[12,13] and the topic can be introduced to the students as a discussion in a seminar, as a home assignment, or as a lecture.

After the second stage is completed, the instructor will introduce the topic of reduction of a ketone to an alcohol. A critical discussion on whether the reduction is stereoselective, which isomers can be formed and which isomer will possibly dominate is required.[14−16] The level of demand depends again on the background of the students. The students are then asked to find a method for reduction (with the same criteria as in stage 2) and to perform this reaction (stage 3). At the end of this stage, the students are asked to study which isomers are formed and in what ratio. The analysis will now be focused on NMR spectroscopy and especially on the spin−spin coupling constants of the proton attached to the carbon bearing the OH-group. The students are encouraged to build molecular models to study the dihedral angles and the coupling constants in order to provide evidence for the structure. Even though NMR spectra of the cyclic secondary alcohols studied herein are rather complicated and the complete assignment of the ^{1}H and ^{13}C NMR spectra would require some computational tools, the crucial coupling constants can be extracted relatively easily. This usually provides enough information to make the required conclusions, especially when combined with the data obtained from other analytical methods. At this stage, the optical rotation can be investigated, even though not necessarily, to be compared with the starting material. It would also be possible to separate the different diastereoisomers by chromatographic methods. However, we have chosen to leave out the purification step and concentrate on the analytical part.

The problem-based approach is applied also in the final stage of the work. The scientific report is supposed to be written in journal format following the ACS style guide. The final report is submitted as a group to further strengthen the importance of team working skills and shared responsibility. The students are supposed to find the guidelines by themselves and build up the report accordingly. The importance of proper reporting is emphasized. Again, the level of demand needs to be adjusted for students on different levels, but we have chosen to put the focus on the experimental part and logical reasoning in the results and discussion part. Finally, the students will give an oral presentation for a larger audience. During the final seminar, the students are given some constructive criticism that further strengthens the learning process. The seminar is usually characterized by dynamic scientific discussions. These discussions show to students the fact that while the given problem seems trivial, there are several aspects that make the overall work surprisingly versatile, resulting in final reports that are always unique.

It is evident that in a course like this, the students cannot be assessed solely by evaluating the final reports but continuous follow-up is required. However, as the number of students has been limited, all of them get practically individual supervision and it is easy to control that the learning objectives are attained. As a main outcome, the course produces enthusiastic junior chemists who are eager to continue with their master's level studies in organic chemistry. At our university, generally more than 80% of the course participants have continued with organic chemistry as their major discipline.

■ SUMMARY AND CONCLUSIONS

Herein, we have described the pedagogical idea behind an upper-level undergraduate laboratory course in organic chemistry consisting of a preliminary training period followed by a research-oriented problem-based period. During the first period, the focus lies on teaching of laboratory safety and practical techniques. In the latter period, the problem-based learning approach is designed to build on the knowledge acquired during the training period, to enhance the scientific skills, and to promote independent and creative thinking and problem solving skills in organic chemistry. Also, transferable skills including communication, working in groups, time management, information technology, and presentation skills are highly emphasized. Our observations have shown that with this approach, the students can achieve versatile knowledge in organic chemistry and enhance their problem solving, scientific writing, and oral presentations skills. After introducing this approach on the bachelor level, we have observed that the students are better prepared for the master's level studies than before. Moreover, the students who have completed the course described herein master a great number of practical tools that are needed in the organic chemistry research. Importantly, the students feel more confident to continue with the more independent research work required at the master's level.

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AUTHOR INFORMATION

Corresponding Author

*E-mail: tiina.saloranta@abo.fi.

Notes

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