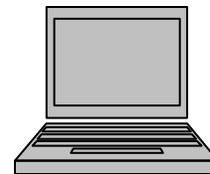




FACULTY FORUM

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Learning Organic Chemistry Reactions as a Nursing Student

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Abstract: This paper delineates a clear way to learn the fundamentals of organic chemistry and biochemistry for students ranging from those preparing for careers in the health field to non-science majors. It looks in depth at the reactions relevant to the biochemical processes of the human body, such as the reactions involving alcohols, carboxylic acids, esters, amines, amides, and disulfides. The object is to present the subject matter in such a way that students clearly can relate it to things relevant to their particular fields of study. This can be done using mnemonic assists such as acronyms, or by using real-life examples of how these chemical reactions occur in the human body or even in the processing of various pharmaceuticals. These methods provide students with concrete and practical examples of how chemistry is used in the field, enabling them to have a firmer grasp on the concepts necessary to succeed in a fundamental chemistry course.

Introduction

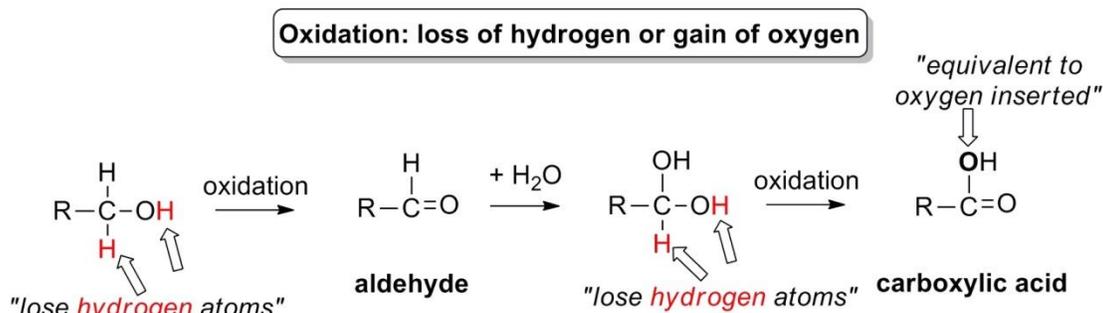
Many students (including the author) take a one-semester fundamental chemistry lecture-and-laboratory course that surveys the fundamentals of organic chemistry and biochemistry (Van Lanen *et al.*, 2000). It is organized around topics of organic chemistry, but with some biological perspective (Miner, 1948; Isom, 2006). This course is often required for students in health-oriented programs, especially the nursing program (at the University of South Carolina, Chemistry 102 is required in the nursing curriculum, as shown at <http://uscsalkehatchie.sc.edu/home/academics/academic-programs/bachelors-degree-programs/nursing/nursing-curriculum/>), and it may also serve as a laboratory science for students in other fields of study (Price, 1976; Mamantov and Wyatt, 1978). This course often emphasizes selected principles important to the understanding of human biological functions and related medical concerns. However, this course is often seen by students as a difficult and professionally irrelevant barrier in pursuing a career in medicine or nursing. Moreover, even though knowing detailed chemical properties of organic molecules is not a main objective for this course, students are required to comprehend some basic organic reactions, especially those closely

related to biochemical processes in the human body. Some typical examples are the oxidation of an alcohol, the formation of a disulfide bond, carboxylic acid and amine dissociation, esterification, amide formation, etc. However, learning organic reactions for non-science-major students has often been unpleasant (Rowe, 1983; Burgess and Bino, 1988). This article describes how to help students understand and utilize some important organic reactions without being overwhelmed by the reaction mechanisms.

1. Oxidation and Reduction Reactions

1.1 Oxidation of a primary alcohol to give an aldehyde, further oxidation to give a carboxylic acid.

Alcohol oxidation is an important organic reaction because more than 90% of the ethyl alcohol that enters the body is metabolized by oxidation to acetic acid (Peters and Preedy, 1998). In terms of oxygen and hydrogen transfer, oxidation is a process of gaining oxygen or losing hydrogen atoms, while reduction is a process of losing oxygen or gaining hydrogen atoms. We find this easy to remember using the acronym "OIL RIG": Oxidation Is a Loss (of hydrogen atoms); Reduction Is a Gain (of hydrogen atoms). Although these are old definitions that are not used very much in current texts, we often will come across them in organic chemistry. As Scheme 1 shows of primary alcohols, removal of two hydrogen atoms (one from the hydroxyl group and another from the hydroxyl-bearing carbon atom) results in an aldehyde. In the presence of water, the aldehyde will then form aldehyde hydrate, from which two hydrogen atoms are removed (one from the hydroxyl group and another from the hydroxyl-bearing carbon atom) to result a carboxylic acid. The net effect for the second oxidation from the aldehyde to the carboxylic acid is the insertion of an oxygen atom. In the human body, this process happens in the liver and is mainly catalyzed by alcohol dehydrogenase (ADH) and acetaldehyde dehydrogenase (ALDH), respectively (Xiao *et al.*, 1996).

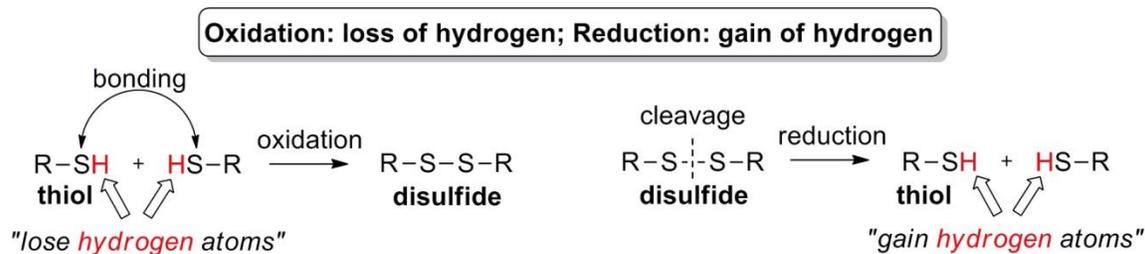


Scheme 1. Oxidation of primary alcohols to carboxylic acids via aldehydes.

1.2 Oxidation of a thiol and reduction of a disulfide.

Thiols are the sulfur analogue of alcohols (sulfur replaces oxygen in the hydroxyl group of an alcohol). Thiols differ dramatically from alcohols in their oxidation chemistry. Following the aforementioned oxidation/reduction definitions and manipulations, mild oxidation (e.g. using O_2) converts two thiols to a disulfide by taking one hydrogen atom from each thiol molecule (Scheme 2, left). These two removed hydrogen atoms may join with the oxidizing agent to form a water molecule. The reverse reaction occurs via reduction, in which two hydrogen atoms are

added on each sulfur atom after cleavage of the sulfur-sulfur bond (Scheme 2, right). These two reactions are very important in the chemistry of proteins, as the thiol functional group is present in the amino acid cysteine. When the thiol groups of two cysteine residues are brought near each other in the course of protein folding, an oxidation reaction can generate a disulfide bond (-S-S-, called cystine). This disulfide bond can contribute to a protein's tertiary structure if the cysteines are part of the same peptide chain. It can also contribute to the quaternary structure of multimeric proteins by forming fairly strong covalent bonds between different peptide chains.



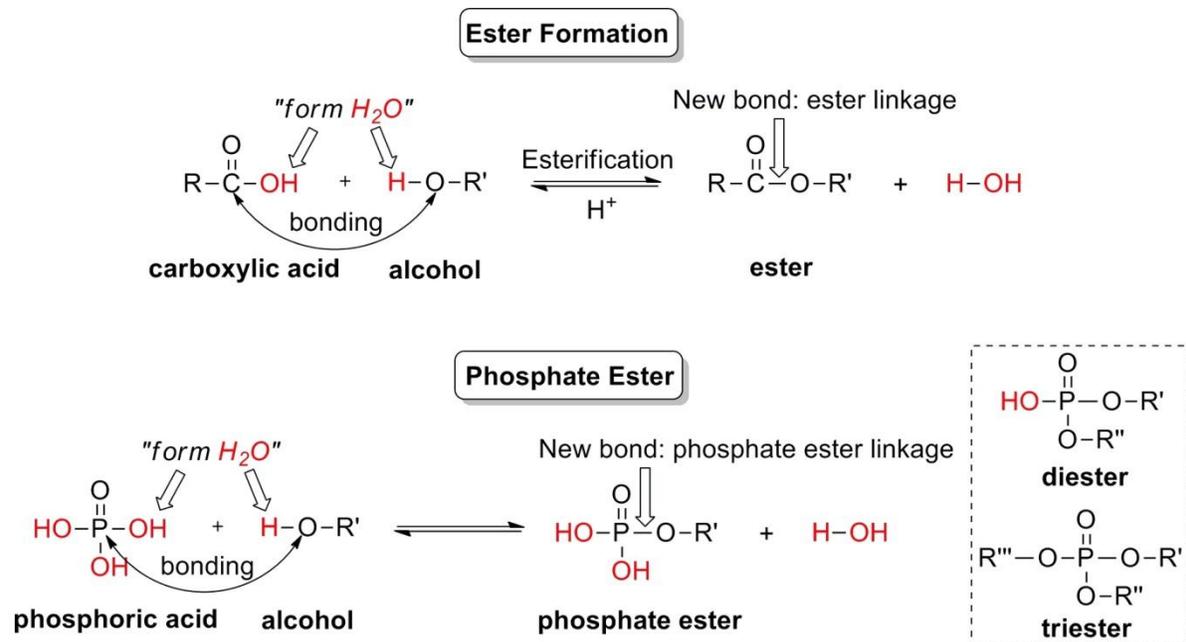
Scheme 2. Oxidation of a thiol and reduction of a disulfide.

2. Esterification and Ester Hydrolysis

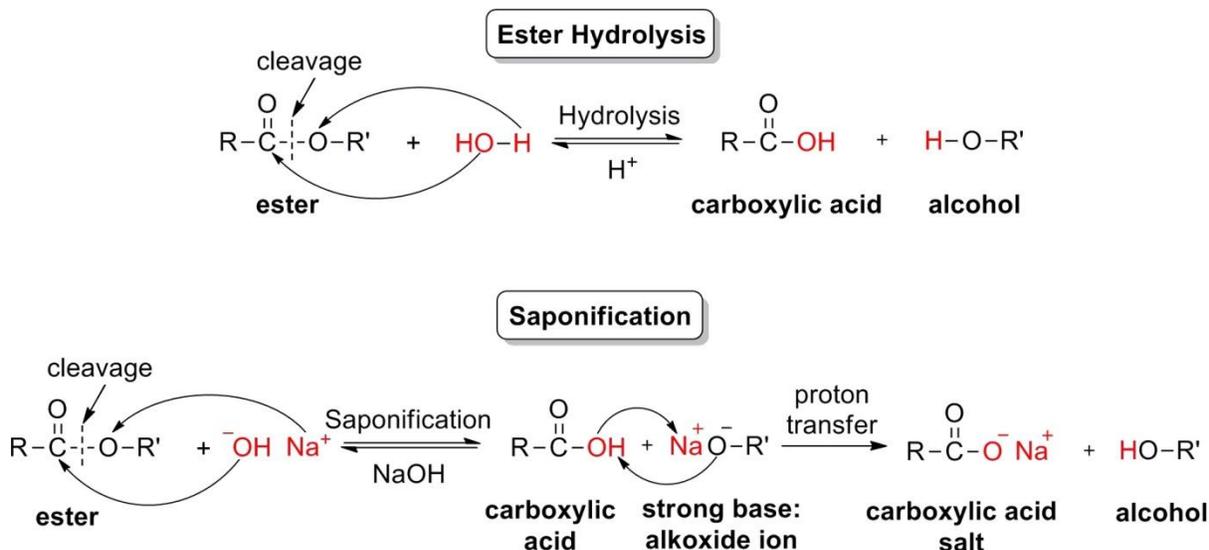
A very important reaction occurs when carboxylic acids are heated with alcohols in the presence of an acid catalyst. In this reaction, the hydroxyl group is removed from the carboxylic acid and a hydrogen is removed from the alcohol: the hydroxyl group and the hydrogen then join to form a molecule of water. The carbonyl carbon bonds with the oxygen molecule on the alcohol to form a new bond: the ester linkage (Scheme 3). Esters are ubiquitous. Most naturally occurring fats and oils are the fatty acid esters of glycerol. Phosphoesters (phosphoric acid esters) form the backbone of DNA molecules. In addition, many esters are very fragrant and represent some of nature's more pleasant aromas. It is necessary to remember that the water comes from the carboxylic acid -OH and the alcohol -H. Hence, one can say, *"It is like the -OH from the carboxylic acid and the -OR' from the alcohol swap places."* Students often find this statement helpful in simplifying the reaction mechanism of esterification.

In a similar way, the -OH groups in phosphoric acid can also be condensed with alcohols to form phosphate esters. The oxygen from the alcohol molecule bonds with the phosphorus to generate the phosphate ester linkage (Scheme 3). Since phosphoric acid has three -OH groups, it can form a mono-, di-, or triester with one, two, or three alcohol molecules (regardless of whether the alcohols' structures are the same or different). Different types of phosphate esters play important roles in cell metabolism (e.g. adenosine triphosphate [ATP] and nucleic acid structures [e.g. RNA and DNA]).

Interestingly, when catalyzed by acid, the esterification reaction establishes equilibrium where the reverse reaction (ester hydrolysis) also takes place. During hydrolysis, the ester linkage (represented by the carbonyl-oxygen single bond) is broken. The elements of water contribute to this reaction as the -OH is attached to the carbonyl carbon to form a carboxylic acid, and the -H is attached to the alcohol oxygen to form an alcohol (Scheme 4). In study groups and tutoring sessions, students often say, *"During ester hydrolysis, the -OH from the water and the -OR' from the ester swap places."*



Scheme 3. Ester and phosphate ester formation.



Scheme 4. Ester hydrolysis under acid and basic conditions.

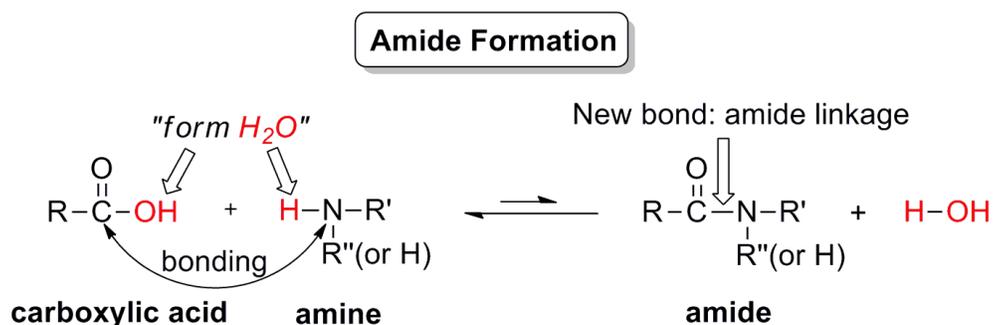
In contrast, there is an irreversible ester hydrolysis, called saponification, which is a process involving a base (i.e. NaOH) (Scheme 4). In a manner similar to the ester hydrolysis reaction previously discussed, the ester bond is cleaved and the hydroxide anion (OH^-) is attached to the carbonyl carbon. This manipulation momentarily results in a carboxylic acid and a strong base (the alkoxide ion with a negatively charged oxygen atom that is associated with the positive sodium ion). The formed carboxylic acid is quickly deprotonated (its proton is taken) by the strong base alkoxide ion to give the final products of saponification, which are the carboxylic

acid salt and the alcohol. It is worth noting that saponification is the process of producing soap—fatty acid salts, if triglycerides (vegetable oils and animal fats) are used as the starting material (Phanstiel *et al.*, 1998).

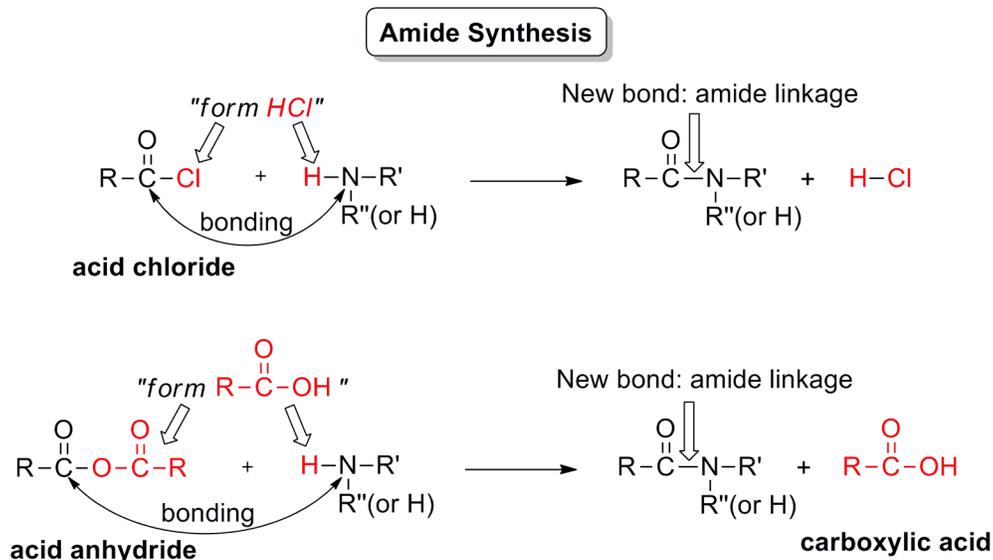
3. Amide Formation

Amide linkages are the key chemical connections of peptides and proteins in living systems. Most amide bonds are formed by complex biological “factories” in the cells called ribosomes. Amides are also the basis for some of the most widely used synthetic polymers, such as nylon and related polyamide products, over three billion pounds of which are produced annually. These products are used in furnishing, clothing, automobile manufacturing, etc.

Amides are formed by the condensation reaction between a carboxylic acid and an amine (primary or secondary amines, or ammonia). Water is formed as a byproduct from the carboxylic acid $-OH$ and the amine $-H$ (Scheme 5). It could be very easy to understand amide formation if you recall the ester formation reaction (Scheme 3). However, unlike ester formation, the amide reaction equilibrium is highly unfavorable for the manufacturing of products because a competing acid-base reaction occurs between a carboxylic acid and amine. Many methods are thus used to drive the reaction to the right. For example, either acid chloride or acid anhydride is used as a more reactive carboxylic acid derivative to prepare amides. In a similar way, the amide bond is formed between the carbonyl carbon and the amine nitrogen while the $-Cl$ joins $-H$ to form HCl (when using acid chloride) or the $RCOO-$ joins $-H$ to form a carboxylic acid (when using acid anhydride) (Scheme 6). In addition to learning these concepts in lecture, students engage in laboratory experiments such as the synthesis of nylon from adipoyl chloride and hexamethylenediamine that serve as good strategies to reinforce the concept of amide formation and solidify student understanding of this reaction.



Scheme 5. Amide formation.



Scheme 6. Amide synthesis using acid chloride or acid anhydride.

4. Student Learning Results

In a survey, 19 students who are currently enrolled in fundamental chemistry were asked to rate their understanding of the specific reactions discussed above (on a scale of 1–5, with 1 being very low understanding and 5 being very high understanding) before and after studying our suggested methods in a study session. The majority of students indicated that they had a more clear understanding after the study session. Results are summarized in Table 1, with the average ratings illustrated in Figure 1; they convincingly demonstrate the effectiveness of the teaching and learning methods.

Table 1. Summary of student ratings of their understanding of the specific reactions discussed in this manuscript before and after studying the manuscript methods (on a scale of 1–5, with 1 being very low understanding and 5 being very high understanding).

Reaction	Before studying the methods							After studying the methods							Change
	1	2	3	4	5	Avg.	N	1	2	3	4	5	Avg.	N	
Oxidation of a primary alcohol	4	5	7	3		2.5	19	2		2	4	11	4.2	19	↑1.7
Oxidation of a thiol and reduction of a disulfide	11	6	1	1		1.6	19	2	3	4	5	5	3.4	19	↑1.8
Ester and phosphate ester formation	9	6	4			1.7	19	2	1	2	10	4	3.7	19	↑2.0
Ester hydrolysis	6	6	4		1	2.1	17	2	1	2	3	9	3.9	17	↑1.8
Amide formation and synthesis	8	8	1	1	1	1.9	19	3	1	4	7	4	3.4	19	↑1.5

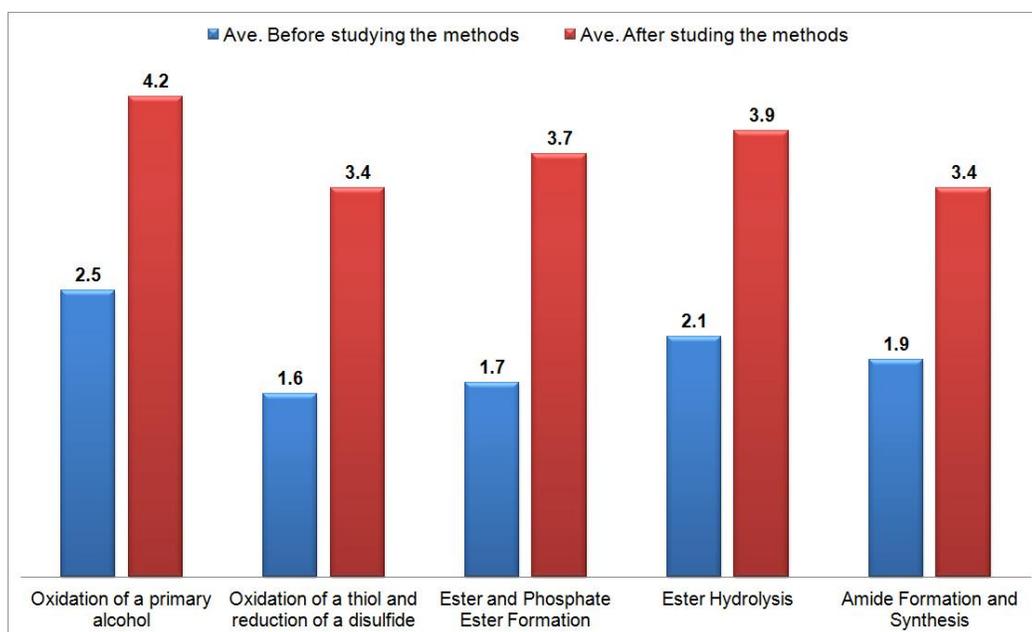


Figure 1. Average student ratings of their understanding of the specific reactions discussed in this manuscript (data from Table 1).

Some students chose to provide comments on the suggested methods. While the sample is unlikely to be statistically representative, it does provide information beyond that contained in the quantitative scores.

- “It was a good help with the diagram.”
- “Very helpful! I find it helpful to hear about it from other people after the lecture.”
- “The paper was pretty thorough and was simply put, so we could understand. The illustrations of the different reactions were easy to read and it broke down the reaction to show the different formations. It was put together nicely. It was easier to follow.”

Summary

For nursing students, learning organic reactions can be challenging, especially since understanding the details of all reaction mechanisms is not generally listed as a learning outcome in fundamental chemistry courses. As such, nursing students must lower the level of complexity and study to meet their specialized needs. Instead of being overwhelmed by the need to memorize completely each individual reaction, students should be encouraged to draw comparisons and recognize similarities between the reactions and the functional groups involved, making these reactions easier to understand as a whole. We describe here several examples of how to comprehend basic organic reactions, especially those closely related to biochemistry, health sciences, and various other aspects of our daily lives. Without knowing the complete story, we are focused on the key transformation itself and the potential use of the reaction in future studies. We hope that this paper will enhance learning efficiency and provide a method for nursing students further to interpret and understand the fundamental principles of chemistry.

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