Hey guys! My name is Sebastian Alberti, and I am a senior Chemistry Major on the pre-dental track here at Baylor. I will be the Master Tutor in OChem 2 this fall, helping you all to conquer this class. Each week I will be providing a resource just like this one that will cover the relevant topics that you all will talk about for the week. Additionally, once a week I will hold a group tutoring session, where we can go over difficult topics, practice problems, and any questions you may have. **In-person group tutoring sessions will take place every Wednesday from 5:15 to 6:15 PM in Sid Rich Room 74.** To reserve a spot, go to [https://baylor.edu/tutoring](https://baylor.edu/tutoring). I hope to see you there!

**TOPIC OF THE WEEK:** Alcohols and Their Reactions (Chapter 12)

**Keywords:** Alcohols, Ethers, Epoxides, Reduction, Oxidation

What are Alcohols? They are molecules with:

- A hydroxyl (-OH) attached to the carbon chain
- A higher pKa compared to a standard carbon chain, because of the hydroxyl
- Higher boiling points because of their ability to hydrogen bond

**Reactions of Alcohols:** Many reactions involving alcohols can be summed up easily in a table. They are all reactions that you actually touched upon in OChem 1, so its a great idea to be familiar with the material.

<table>
<thead>
<tr>
<th>Mechanism</th>
<th>Reactant</th>
<th>Reagents</th>
<th>Product</th>
</tr>
</thead>
<tbody>
<tr>
<td>SN2</td>
<td>Primary Halide</td>
<td>NaOH (any strong -OH base)</td>
<td>Primary Alcohol</td>
</tr>
<tr>
<td>SN1</td>
<td>Tertiary Halide</td>
<td>Water</td>
<td>Tertiary Alcohol</td>
</tr>
<tr>
<td>Addition (Acid Catalyzed)</td>
<td>Alkene</td>
<td>Dilute H$_2$SO$_4$</td>
<td>-OH is placed on the more substituted carbon</td>
</tr>
<tr>
<td>Addition (Oxymercuration Demercuration)</td>
<td>Alkene</td>
<td>1. Hg(OAc)$_2$, H$_2$O</td>
<td>-OH is placed on the more substituted carbon, added anti to the hydrogen</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2. NaBH$_4$</td>
<td></td>
</tr>
<tr>
<td>Addition (Hydroboration-Oxidation)</td>
<td>Alkene</td>
<td>1. BH$_3$, THF</td>
<td>-OH is placed on the less substituted carbon, added syn to the hydrogen</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2. H$_2$O$_2$, NaOH</td>
<td></td>
</tr>
</tbody>
</table>
Reduction
| Carbonyl (Ketone or Aldehyde) | 1. NaBH₄  
2. MeOH  
Or  
1. LiAlH₄  
2. H₂O | Can give any type of alcohol, depending on the starting reactant (primary, secondary, etc.) |

Grignard Reaction
| Carbonyl (Ketone or Aldehyde) | 1. RMgX  
2. H₂O | Either a secondary or tertiary alcohol |

**Important Note!** Not all reducing agents are equal in strength. Specifically, NaBH₄ cannot reduce molecules such as carboxylic acids, while LiAlH₄ can easily do so.

Alcohol Eliminations:
Two new reactions that you will learn about are in regards to the elimination of alcohols. The first one is quite simple, using concentrated acid to eliminate the hydroxyl group.

![Alcohol elimination with concentrated H₂SO₄](image)

The second reaction uses a new reagent, tosyl chloride, to transform our hydroxyl into a tosylate (OTs). While hydroxyls are poor leaving groups, tosylates are great at being pulled off a molecule, and will easily be eliminated using a strong base.

![Alcohol elimination with tosyl chloride](image)
**HIGHLIGHT #1: Ethers and Epoxides**

Ethers are compounds which contain an oxygen molecule within the carbon chain (NOT on the terminal ends). They can be cyclic, or in a straight chain.

**Naming Ethers:** Ethers are special in that they can be named in two different ways, using either the IUPAC name or the common naming convention.

**Common Name:**
1. Identify the two R groups attached to the oxygen atom
2. Arrange both groups alphabetically, and add ether at the end

**IUPAC Name:**
1. Find the longer of the two R groups, this will be the parent chain
2. The shorter R group, will then be an alkoxy substituent, for example, a methyl bonded to an oxygen would be a methoxy substituent

![Ethyl Methyl Ether and 1-methoxypropane](image)

**Reactions with Ethers:**

<table>
<thead>
<tr>
<th>Mechanism</th>
<th>Reactant</th>
<th>Reagent</th>
<th>Product</th>
</tr>
</thead>
<tbody>
<tr>
<td>Williamson Ether Synthesis</td>
<td>1°, 2°, or 3° alcohols</td>
<td>1. NaH 2. Primary or secondary halide</td>
<td>Either symmetrical or asymmetrical ether</td>
</tr>
<tr>
<td>Alkoxymercuration-demercuration</td>
<td>Alkene</td>
<td>1. Hg(OAc)$_2$, ROH 2. NaBH$_4$</td>
<td>-OR group is added to the more substituted carbon, and is anti to the hydrogen</td>
</tr>
<tr>
<td>Acidic Cleavage</td>
<td>Ether</td>
<td>1. Excess HX 2. Heat</td>
<td>Two alkyl halides, and water</td>
</tr>
<tr>
<td>Alcohol Dehydration</td>
<td>2 of the same primary alcohol</td>
<td>1. H$_2$SO$_4$ 2. Heat</td>
<td>A symmetrical ether</td>
</tr>
</tbody>
</table>
Not only do these conventions and reactions work best with straight chain ethers, but we can also work with cyclic ethers. These molecules are so important, that they actually have their own classification, epoxides.

**Naming epoxides:**
1. Find the longest carbon chain, including those in the epoxide
2. Using this chain as the parent chain, each branching point will be its own substituent.
   The oxygen portion of the epoxide will be an epoxy substituent.

Or
1. The oxirane is the parent portion, and will be the namesake of the molecule
2. Every carbon chain branching off the epoxide will be named as its own substituent.

![2,3-epoxy-4-methylpentane](image1)

![2-chloro-3-methyl-oxirane](image2)

**Reactions with Epoxides:**

<table>
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<th>Mechanism</th>
<th>Reactant</th>
<th>Reagent</th>
<th>Product</th>
</tr>
</thead>
<tbody>
<tr>
<td>Addition using Peroxy Acids</td>
<td>Alkene</td>
<td>1. mCPBA</td>
<td>Epoxide ring, retaining cis/ trans stereochemistry of the original molecule</td>
</tr>
<tr>
<td>Conversion of Halohydrins</td>
<td>Alkene</td>
<td>1. X₂, H₂O, 2. NaOH</td>
<td>Epoxide ring, retaining cis/ trans stereochemistry of the original molecule</td>
</tr>
<tr>
<td>Ring Opening (Acid Catalyzed)</td>
<td>Epoxide</td>
<td>1. HX</td>
<td>The nucleophile prefers attacking at a 3° carbon, but favors 1° carbons over 2°, with inverted stereochemistry</td>
</tr>
<tr>
<td>Ring Opening (Base Catalyzed)</td>
<td>Epoxide</td>
<td>1. Strong base / nucleophile, 2. H₂O</td>
<td>The nucleophile attacks at the least substituted carbon,</td>
</tr>
</tbody>
</table>
and inverting stereochemistry.

| Ring Opening (Grignard Reagent) | Epoxide | 1. RMgBr 2. H₂O⁺ | The nucleophile attacks at the least substituted carbon, inverting stereochemistry. |

Sharpless Asymmetric Epoxidation (SAE):

\[
\text{Ti(OPr) - (+) - DET} \rightarrow \frac{\text{tBuOOH}}{} \rightarrow \text{Epoxide}
\]

This is a very difficult type of reaction involving 3D space that you will need to know. It is good to understand how to accurately do this reaction each time.

1. Orient the alkene so that the hydroxyl substituent is facing towards the bottom right corner, by flipping and rotating the molecule.
2. Next determine which way the epoxide will face. If the reagent is (+)-DET, then the epoxide will face downwards, and when using (-)-DET, the epoxide will face upwards.
3. Now that the epoxide is created, re-orient the molecule to be in its original position. If it was flipped, this will change which direction the epoxide is facing. (If you flipped your molecule over, then a downward-facing epoxide would become an upward facing one).

THINGS YOU MAY STRUGGLE WITH:

- As mentioned above, SAE can be difficult because of the in & out of the page aspect. Having a model kit can be very helpful to visualize what is going on
- Memorize and **UNDERSTAND** what certain reagents will open epoxides the way they do. Also, make sure to keep track of whether or not the reaction is acid or base-catalyzed and the substituents present, this can get **TRICKY**!
- **OChem 2** is focused a lot on reactions, mechanisms, and knowledge from **OChem 1**. Just because you finished **OChem 1** doesn’t mean you should forget it, instead you should be focused on keeping up with older material.
- For extra support, a good YouTube resource is the Organic Chemistry Tutor [https://www.youtube.com/watch?v=B_ketdzJtY8&list=PL0o_zxa4K1BXP7TUO7656wg](https://www.youtube.com/watch?v=B_ketdzJtY8&list=PL0o_zxa4K1BXP7TUO7656wg)
Not only does he have videos about the important topics, he also has some on the more obscure reactions, which can be super helpful.

**PRACTICE PROBLEMS!**

Provide an efficient synthesis for this reaction:

\[
\begin{array}{c}
\text{OH} \\
\text{CH}_3 \\
\text{CH}_3 \\
\end{array}
\xrightarrow{?}
\begin{array}{c}
\text{CO} \\
\text{CH}_3 \\
\end{array}
\]

Predict the product for each reaction:

\[
\text{H}_2\text{C}=\text{C} \xrightarrow{1. \text{NaBH}_4} \text{CH}_3\text{C}\text{H}_2\text{C}_5\text{H}_11
\]

\[
\text{H}_2\text{C}=\text{C} \xrightarrow{2. \text{MeOH}} \text{CH}_3\text{C}\text{H}_2\text{C}_5\text{H}_11
\]

\[
\text{H}_2\text{C}=\text{C} \xrightarrow{\text{HCl}} \text{CH}_3\text{C}\text{H}_2\text{C}_5\text{H}_11
\]

**ANSWERS TO PRACTICE PROBLEMS:**

**Problem 1:**

1. **Step 1.**
   \[
   \text{OH} \xrightarrow{\text{Na}_2\text{Cr}_2\text{O}_7, \text{H}_2\text{SO}_4} \text{CO}
   \]

2. **Step 2.**
   \[
   \text{CO} \xrightarrow{\text{CH}_3\text{MgBr, H}_2\text{O}} \text{OH}
   \]

3. **Step 3.**
   \[
   \text{OH} \xrightarrow{\text{Conc. H}_2\text{SO}_4} \text{CH}_3\text{C}\text{H}_2\text{C}_5\text{H}_11
   \]

**Problem 2:**

1. **Step 1.**
   \[
   \text{OH} \xrightarrow{\text{Na}^+, \text{(complex)}} \text{CH}_3\text{C}\text{H}_2\text{C}_5\text{H}_11
   \]

2. **Step 2.**
   \[
   \text{HO} \xrightarrow{\text{MeOH}} \text{CH}_3\text{C}\text{H}_2\text{C}_5\text{H}_11
   \]

**Product:**

\[
\text{HO} \xrightarrow{\text{H}} \text{CH}_3\text{C}\text{H}_2\text{C}_5\text{H}_11
\]
Problem 3:

Step 1.

\[
\begin{align*}
\text{Step 2.} & \\
\text{Product:} & \\
\end{align*}
\]

Anyways that’s a wrap guys! Thank you for checking out this resource, I hope that you will find it to be useful for your studies. Later on if you want to review you can always access this online (https://www.baylor.edu/case/index.php?id=978656).

_All tables are property of Organic Chemistry by David Klein. All diagrams and molecules were made by me._