



## Alcohols Study Guide

[Link to Series on jOeCHEM](#)

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Hi, gang, and welcome to the Alcohols study guide on jOeCHEM! If this is your **first** study guide (hey, welcome—glad you're here), let me provide some background for what I envision these guides to be and how they are supposed to help you kick organic butt.

For every series on jOeCHEM (aka "Gen Chem Boot Camp", for example), I want these study guides to be a central summary point. If you're starting to study for an exam, and you want to have a general idea of what is contained within a given unit, I hope you can turn to these study guides and get that overview.

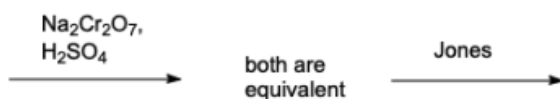
Of course jOeCHEM can't be a perfect substitute for every Organic Chemistry class (each teacher/class is different), but I'll aim to include:

1. Terms you need to know + their definitions
2. An overview of all the key concepts in a given series
3. A summary of all the reactions specific to that series (this will be a thing when we start learning reactions)
4. Tips & Tricks I think could be helpful and may not necessarily fit in the other sections

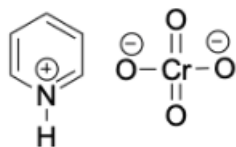
# Terms to Know

Below is a list of terms that you should have a working understanding of. There's a lot of science-y jargon in Organic Chemistry, so to be able to walk-the-walk (do reactions and stuff), we have to have to be able to talk-the-talk (talk and stuff).

- **Oxidation** – a word used to describe when an atom **literally** has more bonds to oxygen. In Gen-Chem you learn about calculating oxidation #'s but in OChem, it's as simple as: an atom having more bonds to oxygen == that atom has been oxidized.
- **Reduction** – the opposite of oxidation! This is a word used to describe when an atom **literally** has less/fewer bonds to oxygen. It's as simple as: an atom having less bonds to oxygen == that atom has been reduced.
- **Jones Reagent** – this is a common phrase you might hear that is equal to the  $\text{Na}_2\text{Cr}_2\text{O}_7$ ,  $\text{H}_2\text{SO}_4$  reagent combination which oxidizes alcohols more aggressively.



- **PCC** – this is a common abbreviation you might hear that stands for **pyridinium chlorochromate**, a reagent that oxidizes alcohols more mildly.



- this is the structure of PCC

- **$\text{LiAlH}_4$**  (aka **LAH**) – lithium aluminum hydride, a very reactive source of hydride, is great at reducing carbonyls. You will see both the chemical formula and the 'LAH' abbreviation.
- **Grignard Reagent** – an organomagnesium halide. That's a fancy phrase for saying a Grignard reagent is a carbanion (carbon with negative charge) will be connected to a magnesium + a halogen:  $\text{RMgX}$ 
  - Grignard's are both excellent bases (they love grabbing  $\text{H}^+$ ) and nucleophiles (they love attacking carbonyls and other electrophiles)
- **Synthesis Problem** – a type of problem in organic chemistry where a target molecule (aka a product) is given and must be created using specific or general starting material
- **Retrosynthetic Analysis** – an approach to synthesis problems where you start at the END of the synthesis problem, working backwards from the product and toward the specified starting material.

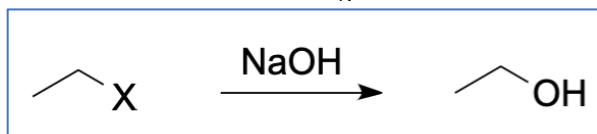
# Overview of Concepts

- Oxidation of Alcohols
  - Creating a carboxylic acid: you'll need a primary alcohol (alcohol attached to a primary carbon) and treat it with  $\text{H}_2\text{SO}_4$ ,  $\text{Na}_2\text{Cr}_2\text{O}_7$  (**Jones Reagent**)
  - Creating an aldehyde: you'll need a primary alcohol (alcohol attached to a primary carbon) and treat it with PCC
  - Remember that you CANNOT oxidize a tertiary alcohol (alcohol attached to a tertiary carbon)
  - If you are oxidizing a chiral carbon, it WILL lose its stereochemistry. You are transforming an  $\text{sp}_3$  (tetrahedral) carbon into an  $\text{sp}_2$  (trigonal planar) one since you are making a carbonyl (either a ketone, aldehyde, or carboxylic acid)
- Reduction of Carbonyls (ketones or aldehydes)
  - At this point in your OChem journey,  **$\text{LiAlH}_4$**  and  **$\text{NaBH}_4$**  *basically* function the same way (this is not true, but you'll learn the finer grained differences in OChem II).
  - Using  $\text{LiAlH}_4$  and  $\text{NaBH}_4$  take carbonyls (ketones or aldehydes) and produce alcohols.
  - If you reduce a carbonyl (which is  $\text{sp}_2$ , trigonal planar) and it is chiral after the fact (attached to four different, unique groups), you will produce a **racemic** result at the carbon that was attacked by hydride.
- Grignard Reagents
  - Grignard Reagents are typically used for attacking carbonyls (ketones & aldehydes). You'll use them in OChem II to attack many other types of carbonyls.
  - While Grignards are amazing at attacking ketones + aldehydes, don't forget that they are:
    - Great bases (they love to pick up  $\text{H}^+$ )—a Grignard will pass up a carbonyl/ $\text{S}_{\text{N}}2$  reaction to pick up an acidic proton
    - Great nucleophiles for general  $\text{S}_{\text{N}}2$  reactions
  - You need to treat an alkyl halide (either an alkyl chloride or bromide) with Magnesium to make a Grignard.
- Retrosynthetic Analysis
  - Count your carbons in the product and in the reactants, and figure out how much of each piece you need
  - Make a "cut" in your product, and assign roles to the reactants—Grignard Reagent and Substrate

- Work backwards. It know it seems wonky, but it really is easier than going forwards
- Make sure your reactions are the most “efficient” way to make all your intermediate molecules. If you need to make a **primary alcohol, use S<sub>N</sub>2** and if you need a **secondary or tertiary alcohol, use S<sub>N</sub>1**. Remember when you should do radical chlorination versus radical bromination when you’re tacking a Leaving Group on. Remember when to use PCC or Na<sub>2</sub>CrO<sub>7</sub>/H<sub>2</sub>SO<sub>4</sub> to make an aldehyde or ketone.

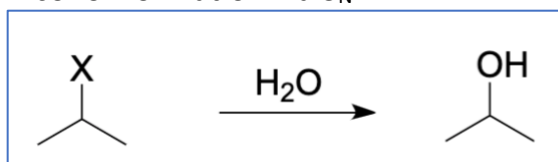
# Summary of Reactions

## Alcohol Formation via $S_N2$



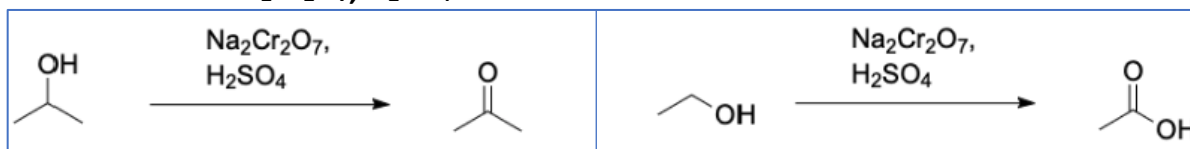
- $S_N2$  alcohol formation works well when attacking a sterically available carbon (primary or methyl)

## Alcohol Formation via $S_N1$



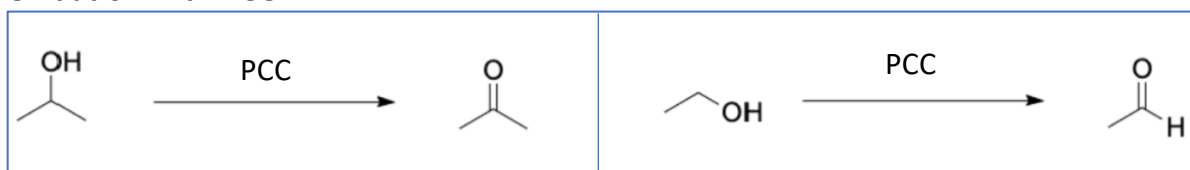
- $S_N1$  alcohol formation works well working with a more substituted carbon (secondary or tertiary), BUT be careful of carbocation shifts

## Oxidation with $\text{Na}_2\text{Cr}_2\text{O}_7, \text{H}_2\text{SO}_4$



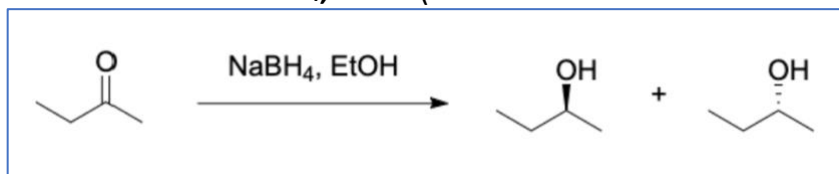
- Also called the 'Jones Reagent'
- The more 'aggressive' oxidation reaction: creates carboxylic acids and ketones
- Cannot oxidize tertiary alcohols

## Oxidation with PCC



- PCC is an abbreviation for pyridinium chlorochromate
- The 'milder' oxidation reaction: creates aldehydes and ketones
- Cannot oxidize tertiary alcohols

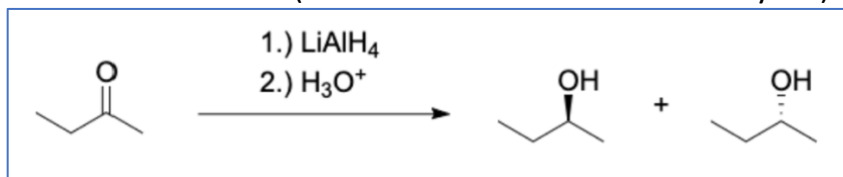
## Reduction with $\text{NaBH}_4, \text{EtOH}$ (reduces both ketones and aldehydes)



- The 'milder' reduction reaction: reduces aldehydes + ketones to alcohols

- A **racemic result** is created if the carbonyl (ketone or aldehyde) that is attacked becomes a stereocenter after the fact

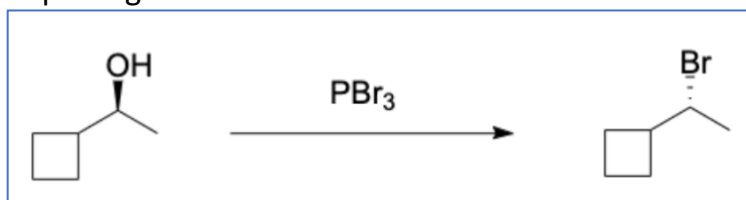
Reduction with **LAH** (reduces both ketones and aldehydes)



- The (crazily) 'aggressive' reduction reaction: reduces aldehydes + ketones to alcohols
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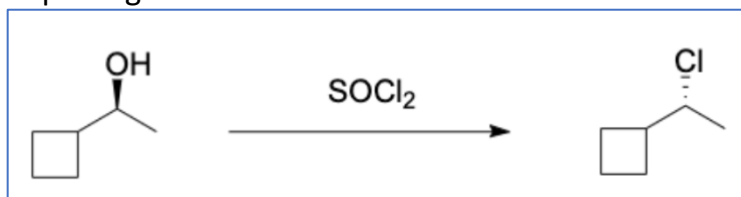
Replacing an alcohol with a chloride

Replacing an alcohol with a bromide



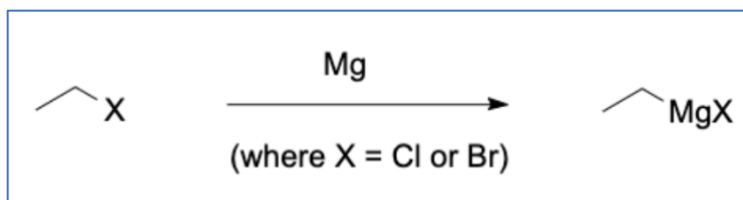
- An  $S_N2$  reaction where an alcohol (during the mechanism) is transformed into a better leaving group and replaced by a bromide
- If the substrate (aka the alcohol) is a stereocenter, the backside attack will invert the stereochem (as shown in the example reaction)

Replacing an alcohol with a chloride



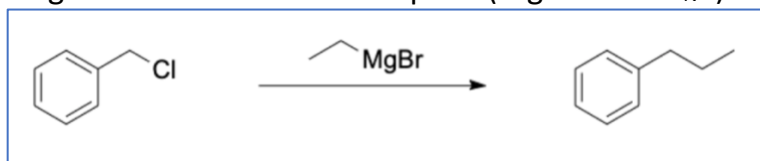
- An  $S_N2$  reaction where an alcohol (during the mechanism) is transformed into a better leaving group and replaced by a chloride
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Grignard preparation (turning an alkyl halide into a Grignard reagent)



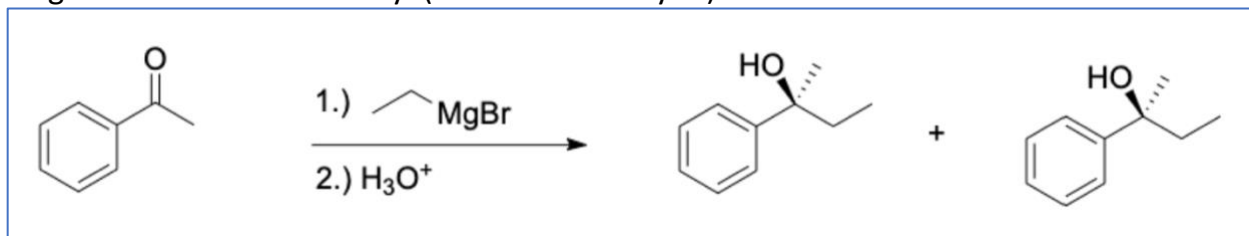
- Sometimes a solvent accompanies the Mg (such as THF)—this *doesn't* make a difference, so if you see it don't be thrown off/confused
- The carbon attached to the -MgX is now a **carbanion**—a very negative, reactive carbon. It controls the 2 electrons in the bond to the MgX
- Grignards are VERY nucleophilic but ALSO very basic—if they see an acidic proton they will go for that first

Grignard attack of an electrophile (regular ole' S<sub>N</sub>2)



- Grignard's, being good nucleophiles, love to and will readily perform S<sub>N</sub>2 on sterically available carbons (nice way to lengthen/combine carbon chains)

Grignard attack of a carbonyl (ketone or aldehyde)



- Grignard's, being good nucleophiles, love to attack carbonyl carbons (since they're partially positive). This is a good way to lengthen carbon chains, producing an alcohol in the product
- A **racemic result** is created if the carbonyl (ketone or aldehyde) that is attacked becomes a stereocenter after the fact

## Tips, Tricks & General Advice

- There is a lot going on in this series, so if it feels like a lot or things are frustrating, don't sweat it. Take a deep breath/a break and keep hammering practice problems. You WILL get it.
- I absolutely sucked at synthesis problems/retrosynthetic analysis when I was first introduced to them. Keep at it—I promise you will be a rock star at them if you keep practicing.