

REACTIONS OF ALCOHOLS

Created by: Mohammad Heidarian

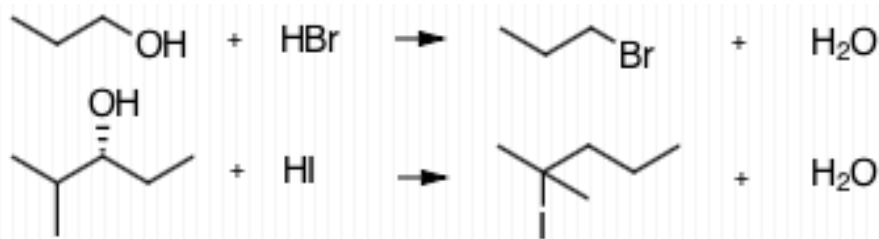
Nucleophilic Substitution, β -Elimination, and Oxidation reactions are the main type of reactions associated with alcohols.

Nucleophilic Substitution: A reaction in which a nucleophile replaces a leaving group in either one-step mechanism- SN2- or two-step mechanism- SN1. Following reactions convert -OH of alcohols into a better leaving group and a halide -acting as a nucleophile- replaces the leaving group.

Reaction with HI, HBr, HCl: These reactions result in production of **haloalkanes**.

- Type of alcohol $\left\{ \begin{array}{l} \text{Methyl and primary alcohols react by SN2 mechanism} \\ \text{Secondary and tertiary alcohols react by SN1 mechanism} \end{array} \right.$
- Rearrangements are possible for reactions with SN1 mechanism.
- Since the conditions are protic, reactions with SN1 mechanism and the most stable carbocation proceed the fastest.

Example)

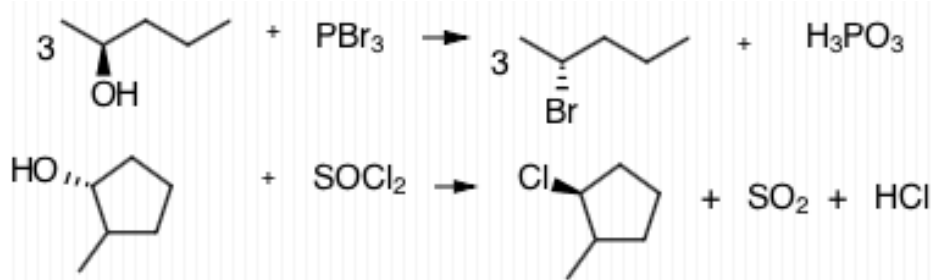


Note: Rearrangement occurred in the second reaction.

1) Reaction with PBr₃, SOCl₂: These reactions also result in production of bromoalkanes and chloroalkanes; however:

- Since this reaction follows **SN2** mechanism, only methyl, primary and secondary alcohols can be used.
- Rearrangements do **NOT** occur.

Example)



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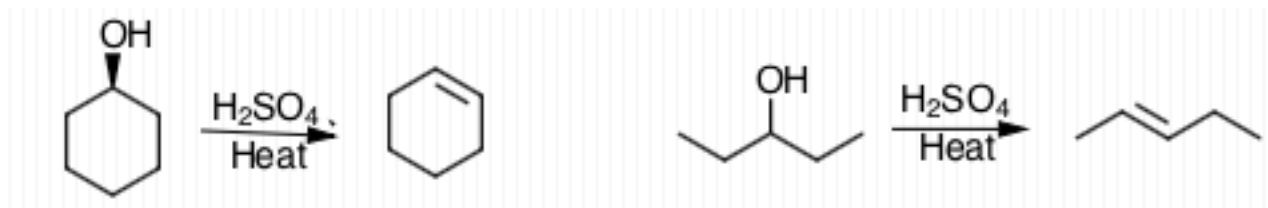
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β -Elimination: A reaction in which two substituents are removed from adjacent carbon atoms in either one or two-step mechanism known as E2 and E1 respectively.

1) **Acid-Catalyzed Dehydration of Alcohols:** Water is eliminated upon reaction of alcohols with strong acids such as H_2SO_4 to produce **alkenes**.

- Type of Alcohol $\left\{ \begin{array}{l} \text{Primary alcohols react by E2 mechanism} \\ \text{Secondary and tertiary react by E1 mechanism} \end{array} \right.$
- If more than one product is possible, **Zaitsev's rule** is applied: The major product is the most highly substituted alkene.
- Rearrangements are possible for reactions with E1 mechanism.
- Since the conditions are protic, reactions with SN_1 mechanism and the most stable carbocation proceed the fastest.

Example)



2) **The Pinacol Reaggrement:** Special case of acid-catalyzed dehydration of vicinal diols- compounds with two $-OH$ groups attached to adjacent carbons- to give a ketone or aldehyde.

- One of the $-OH$ group is protonated and leaves the molecule which is followed by hydride or alkyl migration from adjacent carbon that is attached to remaining $-OH$. Finally, the resulting cation intermediate gives rise to a ketone or an aldehyde.
- In unsymmetrical vicinal diols, the $-OH$ group that is protonated and leaves is the one which results in more stable carbocation.

Example)



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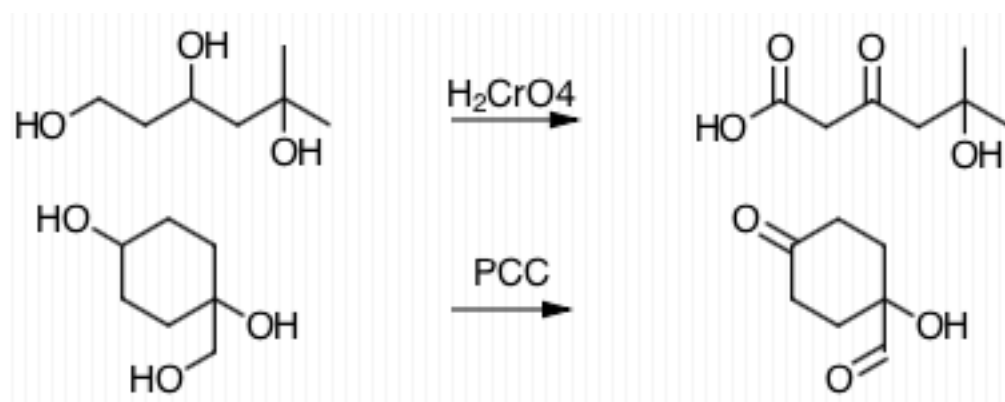
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Oxidation: Different oxidizing reagents can oxidize primary and secondary alcohols into different compounds.

- 1) **Oxidation by Chromic acid (H_2CrO_4):** $\left\{ \begin{array}{l} \text{primary} \rightarrow \text{carboxylic acid} \\ \text{secondary} \rightarrow \text{ketone} \end{array} \right.$
- 2) **Oxidation by PCC:** $\left\{ \begin{array}{l} \text{primary} \rightarrow \text{aldehyde} \\ \text{secondary} \rightarrow \text{ketone} \end{array} \right.$
- 3) **Oxidation by 1) $(\text{COCl})_2$, DMSO 2) Et_3N a.k.a Swern Oxidation:** $\left\{ \begin{array}{l} \text{primary} \rightarrow \text{aldehyde} \\ \text{secondary} \rightarrow \text{ketone} \end{array} \right.$
- 4) **Oxidation by DMP a.k.a Dess- Martin oxidation:** $\left\{ \begin{array}{l} \text{primary} \rightarrow \text{aldehyde} \\ \text{secondary} \rightarrow \text{ketone} \end{array} \right.$

Note: Tertiary alcohols do **NOT** oxidize.

Example)



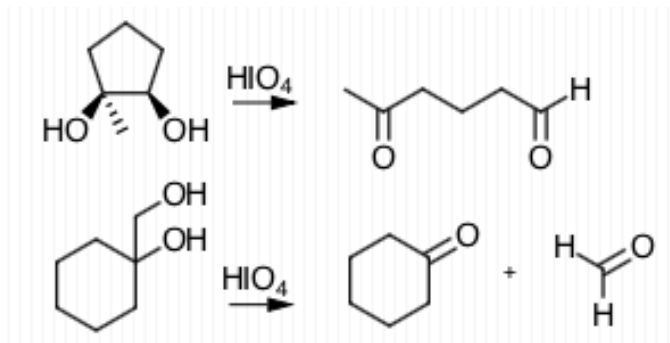
Note: In the second reaction, Swern oxidation and Dess- Martin oxidation would have given the same product as oxidation by PCC.

- 5) **Oxidation cleavage of vicinal diols by HIO_4 :** This reaction cleaves the bond between carbons with $-\text{OH}$ groups and convert $-\text{OH}$ groups to carbonyl groups.
 - $-\text{OH}$ groups have to be in syn position otherwise there is no reaction.

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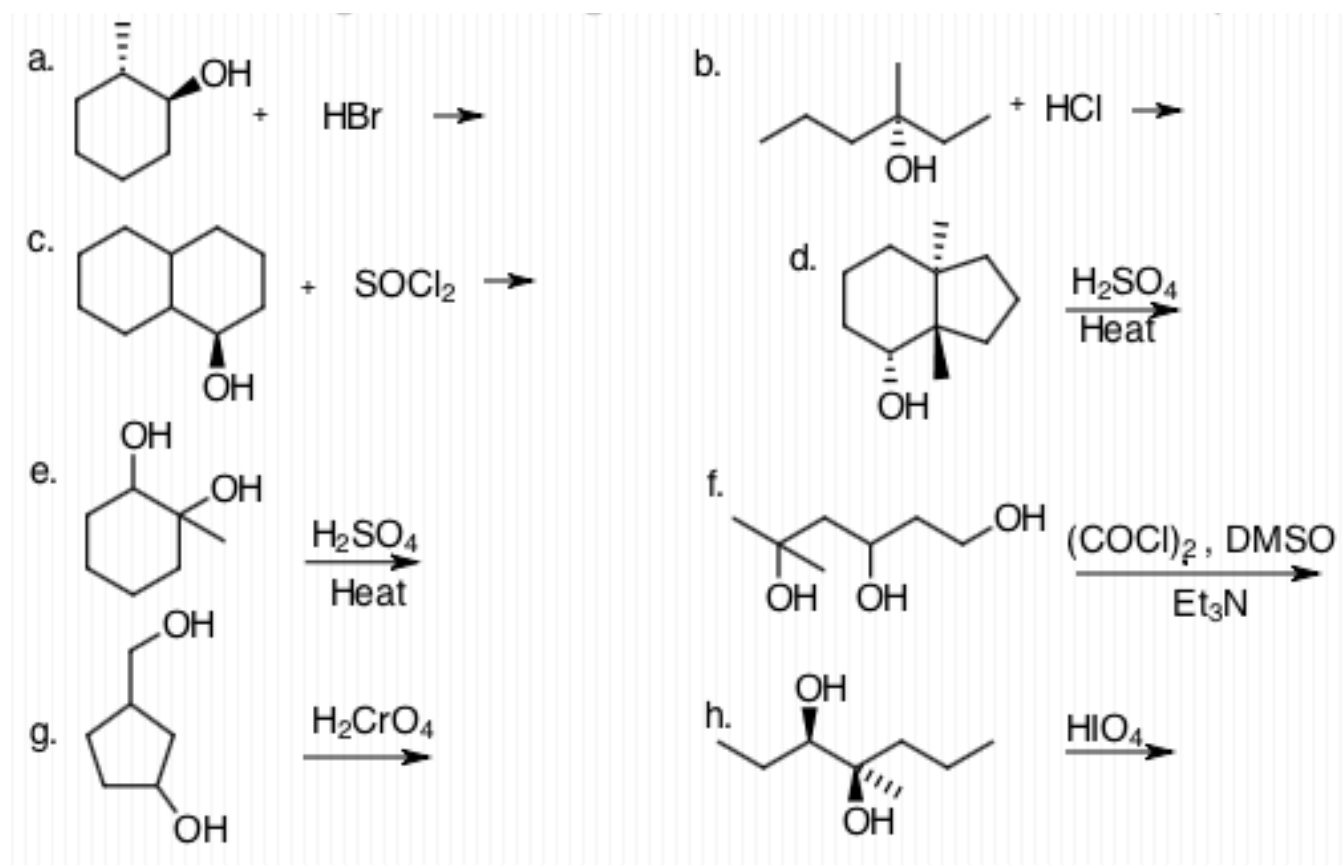
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Example)



Problems:

Draw the structural formula for the **major organic compound** of following reactions.

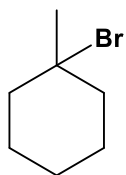


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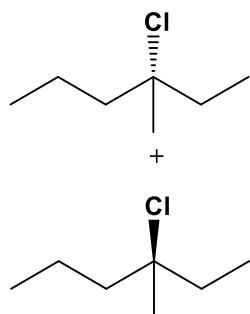
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Solution:

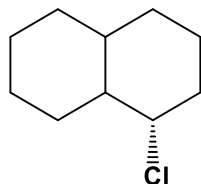
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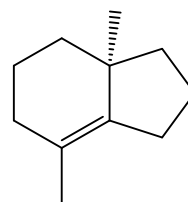
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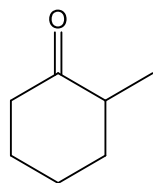
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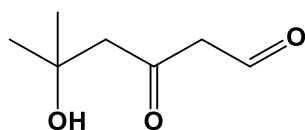
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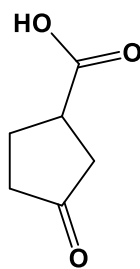
e.



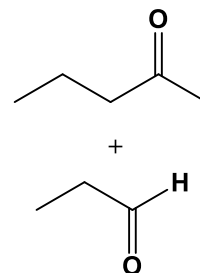
f.



g.



h.



References:

The following resources were referenced during the creation of this handout: Ann Kotechvar's Lecture Notes and *Organic Chemistry* by Brown, Iverson, Anslyn, and Foote.