

Alcohols

3 - Reactions

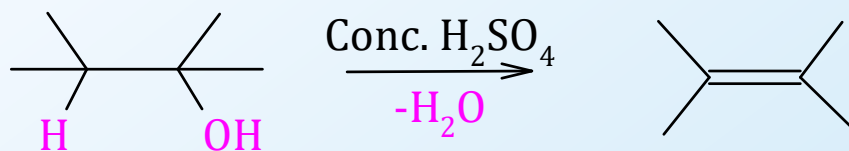
Dr. Sapna Gupta

Types of Alcohol Reactions

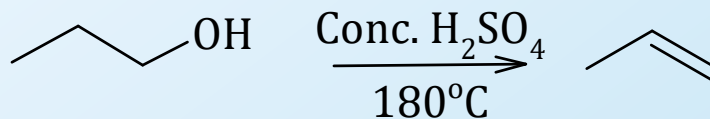
- Elimination - Dehydration to alkene
- Substitution to form alkyl halide
- Tosylation
- Oxidation

Dehydration Reactions

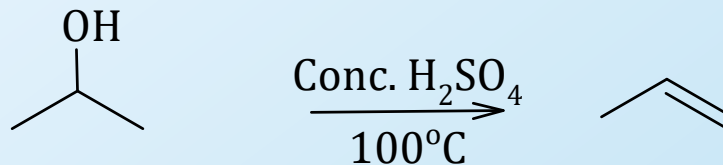
Treatment of alcohols with conc. H_2SO_4 produces alkene via E1. Mechanism is via carbocation. Because of carbocation mechanism, rearrangement can also occur, and the major product is Zaitsev product.



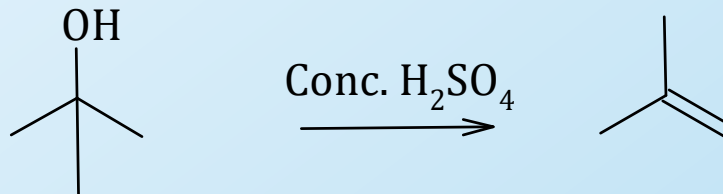
- Primary Alcohols



- Secondary Alcohols



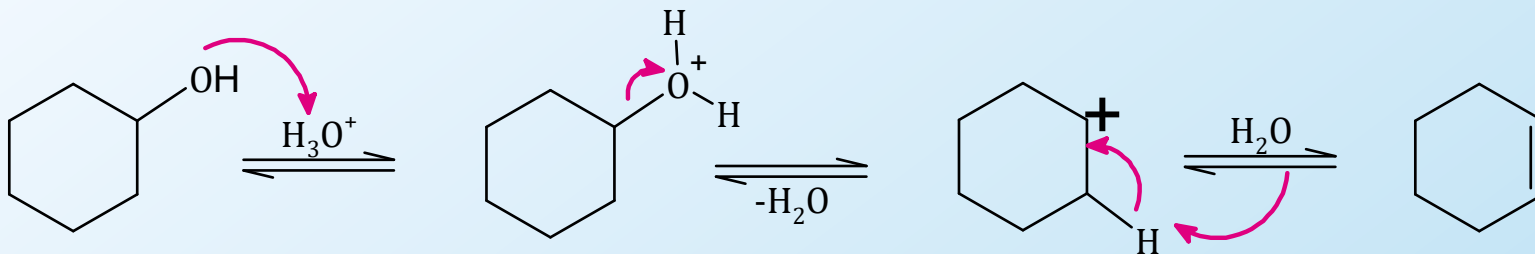
- Tertiary Alcohols



Dehydration Mechanism

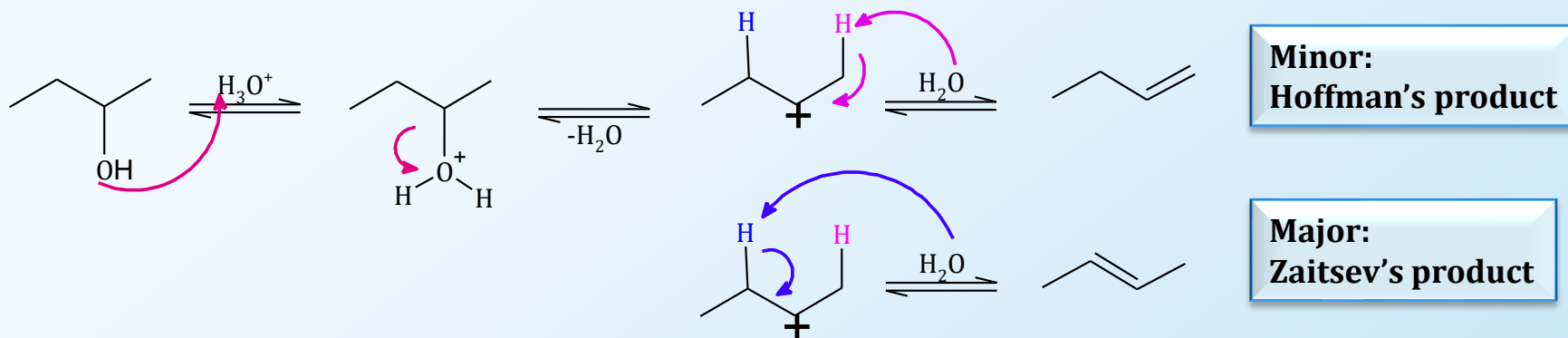
The acidic conditions of the reaction indicate that the reaction is a carbocation mechanism. Primary alcohols are the hardest to dehydrate because primary carbocations are not stable. The reaction is generally in equilibrium, in presence of concentrated acid will shift equilibrium forward to give alkene and more water will shift it reverse to form the alcohol.

Ease of dehydration ($3^\circ > 2^\circ > 1^\circ$)

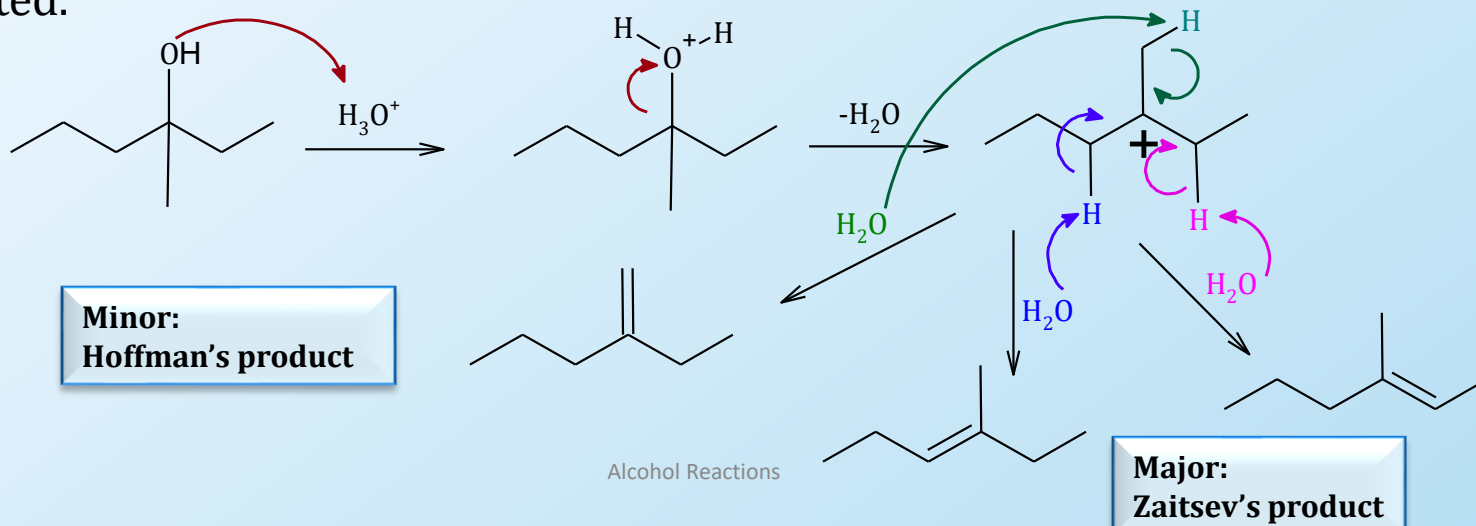


Dehydration Regioselectivity

- Where possible, the alkene having the greater number of substituents on the double bond (the more stable alkene) is the major product (Zaitsev's rule).

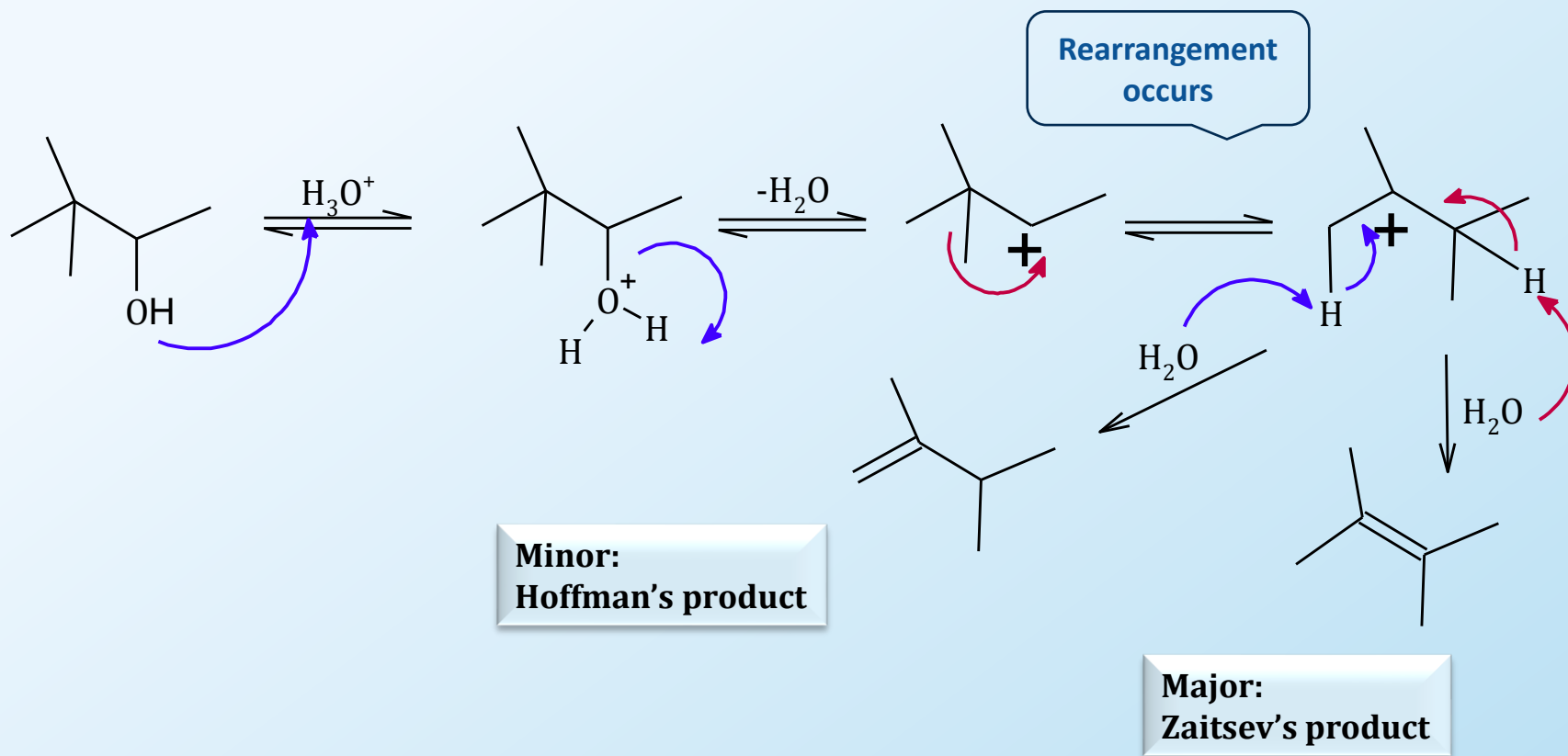


- Here is another example. The color of arrow and H shows you which H is getting eliminated.



Dehydration - Rearrangement

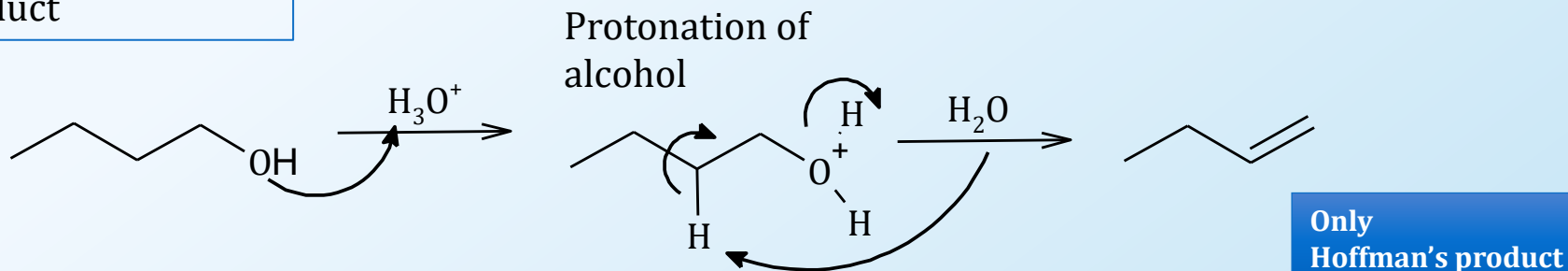
Protonation of alcohol followed by formation of carbocation (*this is where rearrangement can occur*) and finally elimination step (*this is where Zaitsev's product is formed*) gives the alkene.



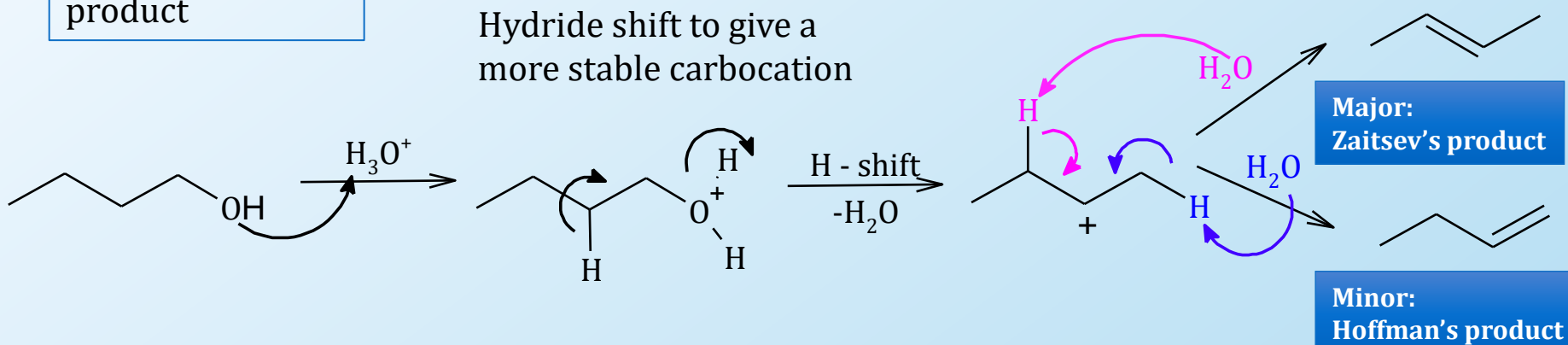
Dehydration – Primary Alcohols

Primary alcohols give Hoffman's product by regular E2 mechanism, and Zaitsev's product after hydride shift.

E2 elimination to give Hoffman's product

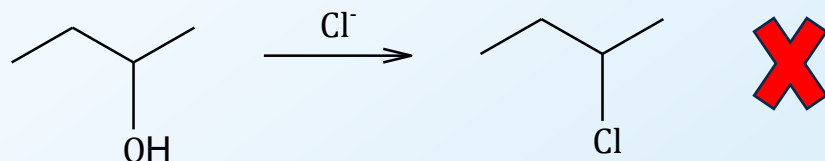


E1 elimination to give Zaitsev's product

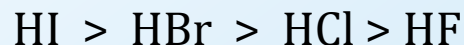


Substitution with Hydrogen Halide

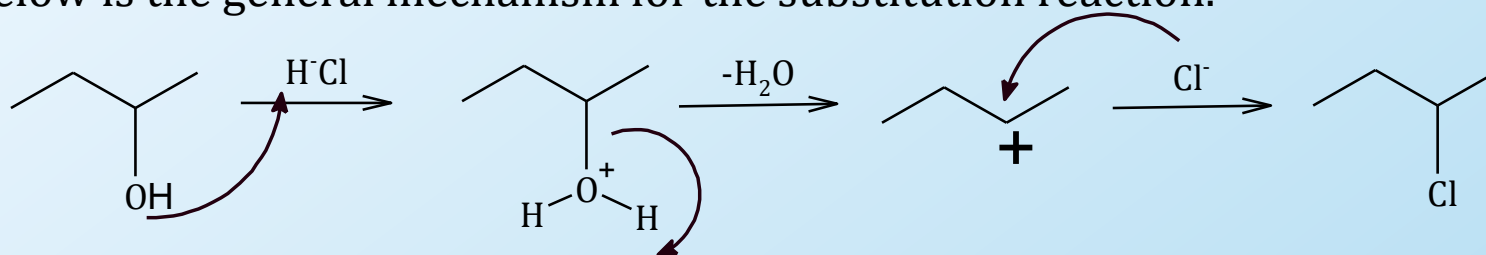
Alcohol groups are poor leaving groups so the reaction below cannot occur since chloride is not a strong nucleophile to displace alcohol group.



The best way to make alkyl halide from alcohol is to use a halide in an acidic medium. A haloacid will also work. The order of reactivity is:

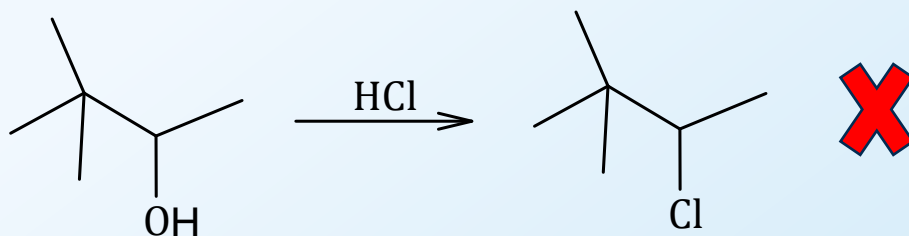


- Tertiary alcohols will react fastest, indicating that the mechanism is $\text{S}_{\text{N}}1$ via carbocation formation. $\text{S}_{\text{N}}1$ mechanism for 3° , 2° , allylic alcohol.
- These reactions are prone to carbocation rearrangements.
- Below is the general mechanism for the substitution reaction.

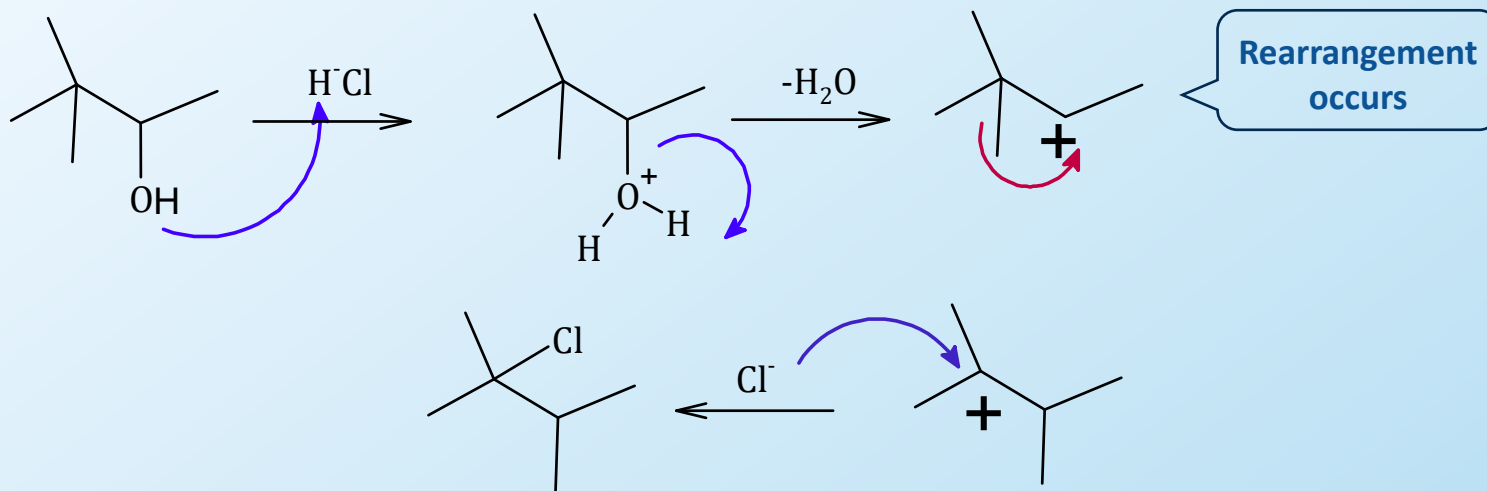


Alkyl Halides Rearrangement

In a carbocation mechanism there is always the possibility of rearrangement. The reaction below will not occur as written.



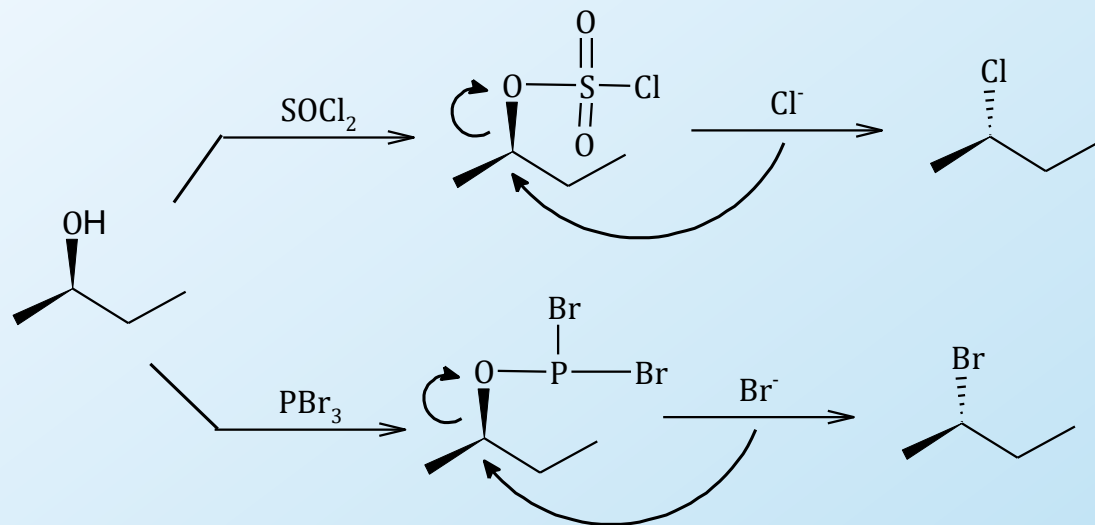
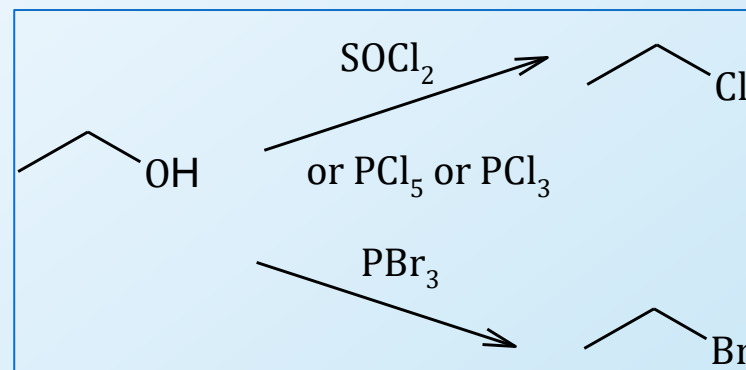
Since the reaction is S_N1 , the carbocation can rearrange to form a more stable carbocation. In this case, a methyl shift will occur.



Reaction with PCl_5 and SOCl_2

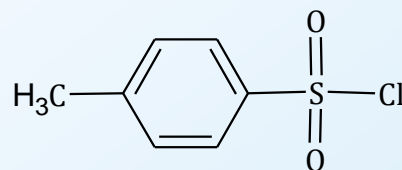
The common methods for making 1° and 2° alkyl halides from alcohols, are given below. Both work via $\text{S}_\text{N}2$, so no rearrangement occurs. Note that to make alkyl iodides the best way is 3° alcohol and HI.

- PCl_3 and PCl_5 and SOCl_2 for alkyl chlorides.
- PBr_3 for alkyl bromide

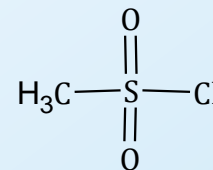


Tosylates and Mesylates

The hydroxyl group of an alcohol can be converted to a good leaving group by conversion to a sulfonate ester.



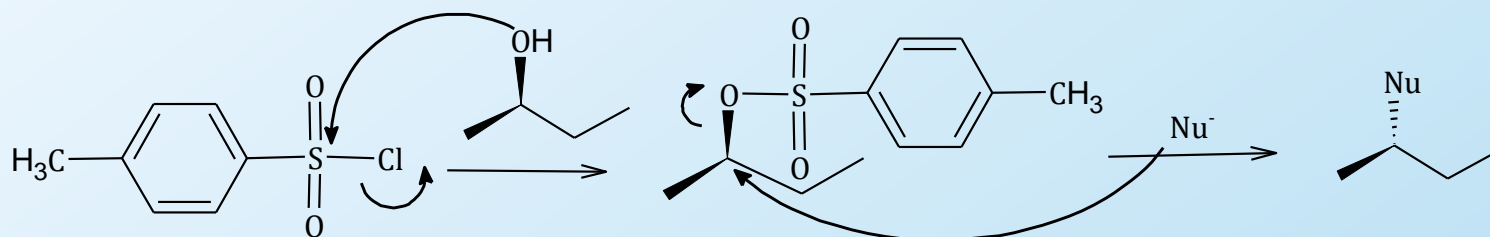
p-Toluene Sulfonyl Chloride
Tosyl chloride (TsCl)



Methyl Sulfonyl Chloride
Mesyl chloride (MeCl)

Sulfonyl chlorides are used to convert alcohols to sulfonate esters which makes the resulting tosylate a good leaving group. At this point even a weak nucleophile can displace the tosylate via S_N^2 mechanism to give substituted products.

- If the alcohol hydroxyl group is a stereo center, then the overall reaction with the nucleophile proceeds with inversion of configuration (S_N^2). The second step to form a sulfonate ester proceeds with retention of configuration.

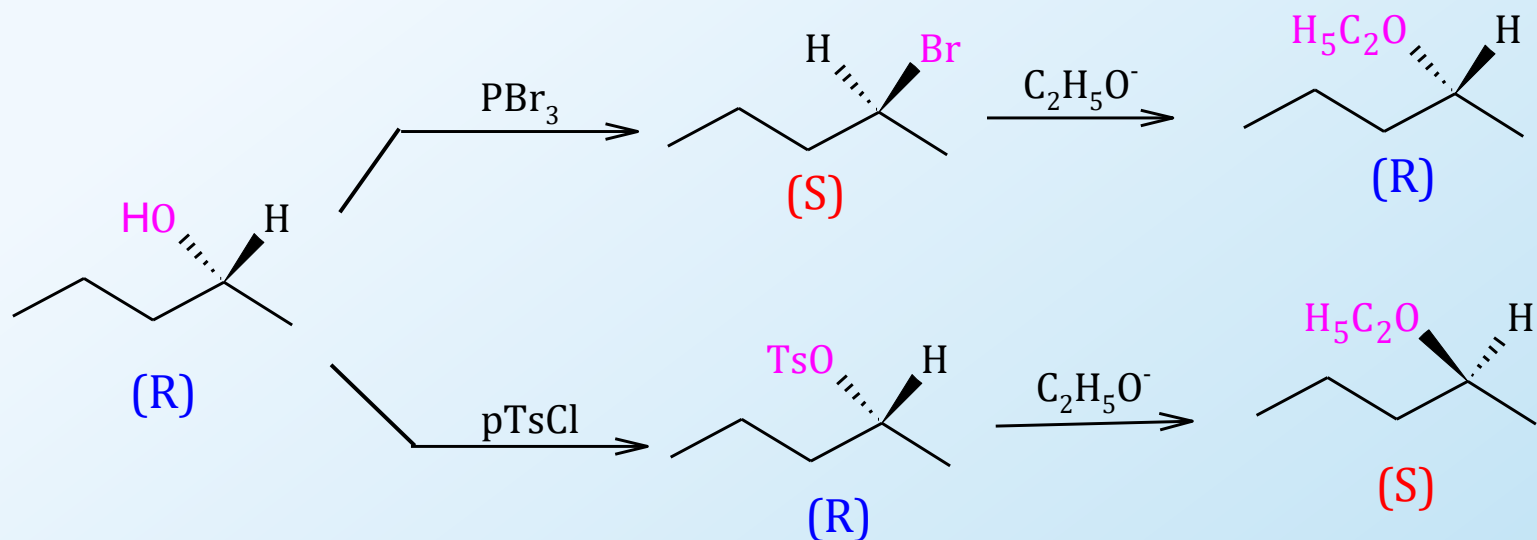


Retention of
stereochemistry

Inversion of
stereochemistry

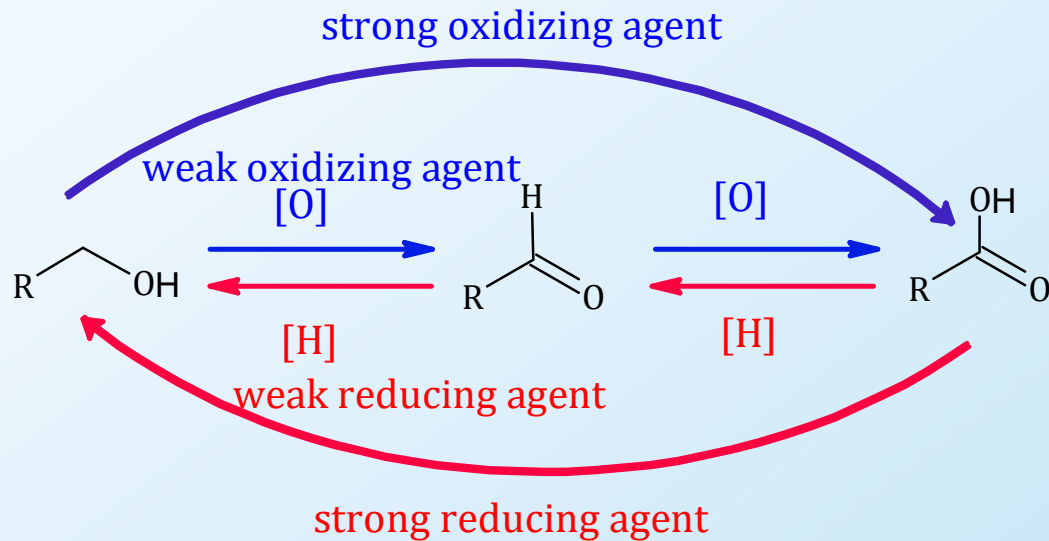
Stereochemistry of Tosylates

- The S_N2 reaction of an alcohol via an alkyl halide proceeds with *two* inversions, giving product with same arrangement as starting alcohol
- The S_N2 reaction of an alcohol via a tosylate, produces inversion at the chirality center

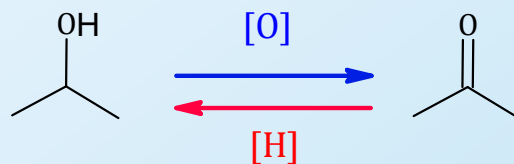


Oxidation of Alcohols

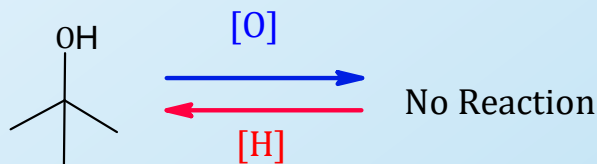
Primary alcohols can be oxidized to aldehydes and further to carboxylic acids.



Secondary alcohols can be oxidized to ketones.



Tertiary alcohols cannot be oxidized.

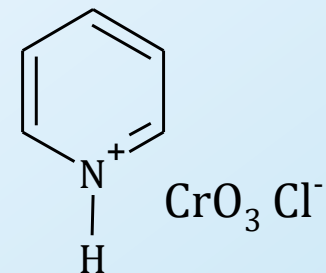


The [O] indicates an oxidizing agent and [H] indicates a reducing agent. These reactions can undergo oxidation reduction reactions by using the appropriate reagents.

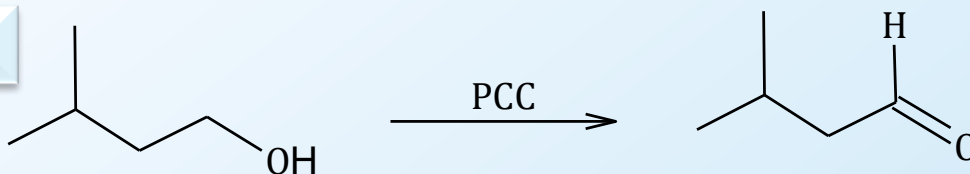
Oxidation of Alcohols contd..

Oxidation of Primary and Secondary Alcohols

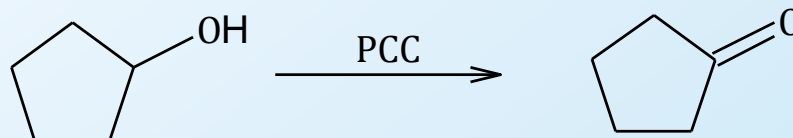
- A reagent which stops the oxidation at the aldehyde stage is pyridinium chlorochromate (PCC).
- Oxidation of a secondary alcohol stops at the ketone (e.g. chromic acid (H_2CrO_4) and Jones reagent (CrO_3 in H_2SO_4).



1° alcohol



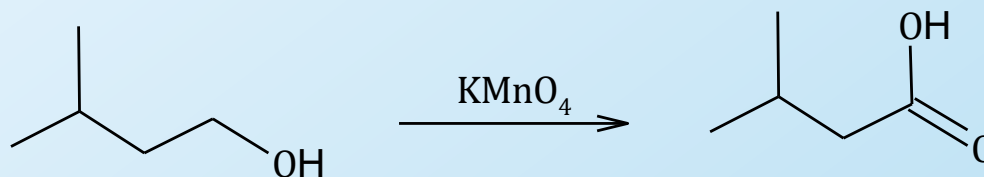
2° alcohol



Oxidation of Primary Alcohols to Carboxylic Acids

Potassium permanganate (KMnO_4) is a typical reagent used for oxidation of a primary alcohol to a carboxylic acid.

1° alcohol



Oxidation of Alcohols Summary

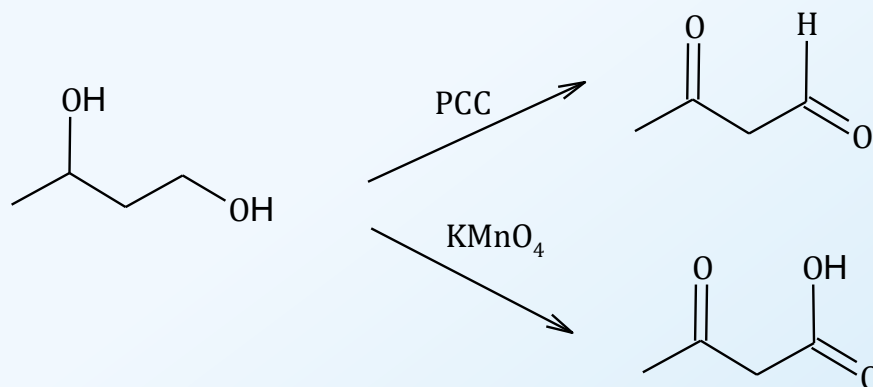
It is important to use the appropriate oxidizing agent to carry out the oxidations. The table below gives all the reagents we have learned so far.

Summary of Oxidation of Alcohols		
Substrate	Product	[O]
1° Alcohol	Aldehyde	Weak
1° Alcohol	Acid	Strong
2° Alcohol	Ketone	Weak or strong
3° Alcohol	Don't get oxidized	NR

Strength of Oxidizing Agents	
Weak	Strong
PCC	Chromic acid (H_2CrO_4) KMnO_4 $\text{Na}_2\text{Cr}_2\text{O}_7$ Jones reagent: $\text{CrO}_3/\text{H}_2\text{SO}_4$

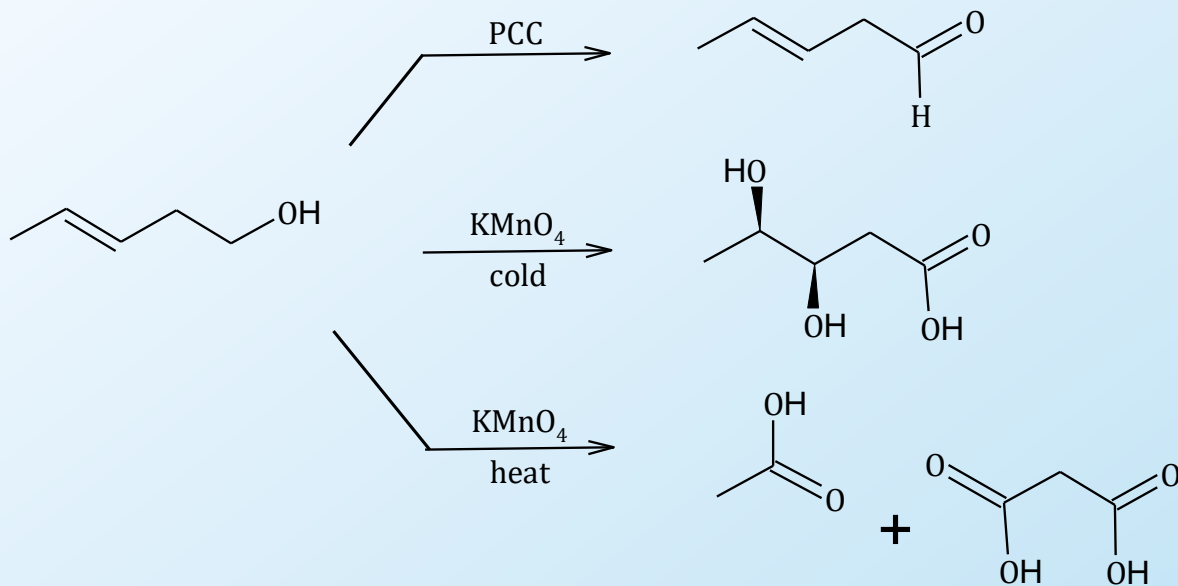
Oxidation of Alcohols contd...

Some more examples of oxidations.



Both 1° and 2° alcohols oxidize with weak oxidizing agent.

2° alcohol gives a ketone and 1° oxidizes to give acid with a strong oxidizing agent like KMnO_4 .



1° oxidizes to give aldehyde with a weak oxidizing agent, alkene does not react.

1° oxidizes to give acid with a strong oxidizing agent KMnO_4 and alkene gives a diol with cold KMnO_4 .

1° oxidizes to give acid with hot KMnO_4 , and the alkene will also cleave to give acids.

Alcohol Qualitative Analysis

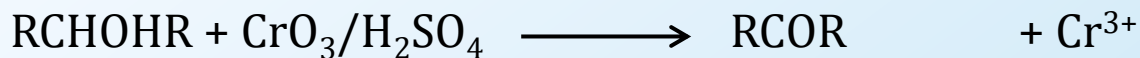
Oxidation of Primary and Secondary Alcohols

- **Chromium oxide** in acid has a clear orange color (from Cr^{6+} ion) which changes to greenish opaque (from Cr^{3+} ion) if an oxidizable alcohol is present

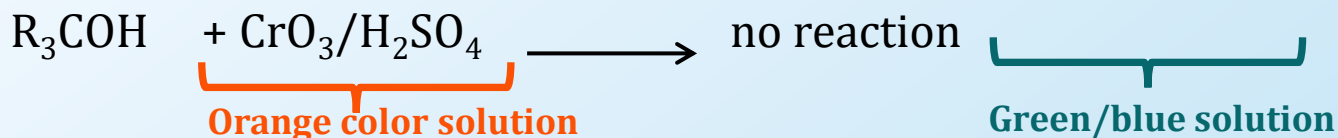
1° alcohol



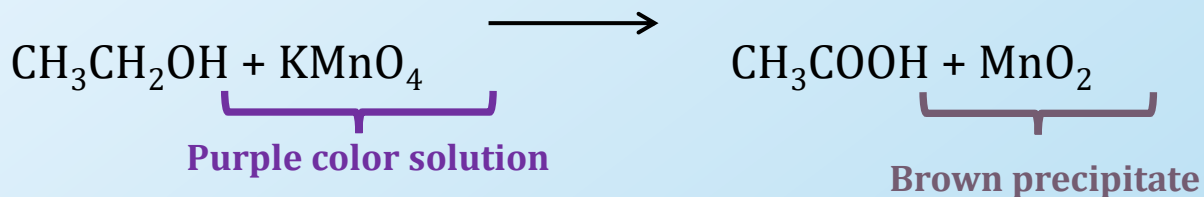
2° alcohol



3° alcohol

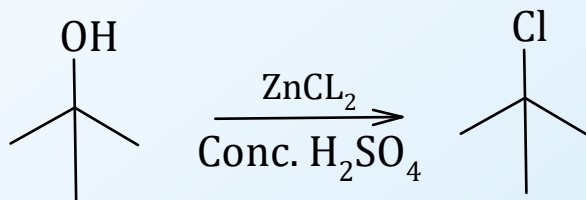
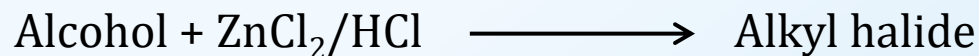


- **Potassium permanganate** KMnO_4 can also give a color change with primary and secondary alcohols. KMnO_4 is purple color solution which when oxidizes alcohol, it itself gets reduced to MnO_2 , which is a brown precipitate.



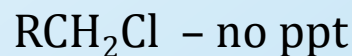
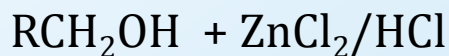
Alcohol Qualitative Analysis

Lucas test

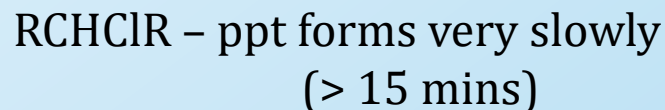
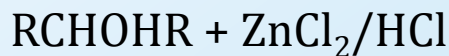


The alkyl halide gives a white precipitate (ppt)/cloudiness with alcohols. This reaction occurs by S_N^1 mechanism and is favored by tertiary alcohols.

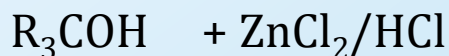
1° alcohol



2° alcohol



3° alcohol



Key Concepts

- Dehydration of alcohols (Zaitsev's product and rearrangement)
- Synthesis of alkyl halides from alcohols (stereochemistry)
- Mesylates and tosylates (stereochemistry)
- Oxidation of alcohols
- Qualitative Analysis of alcohols