Learning Guide for Chapter 15 - Alcohols (II)

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III. Reactions of alcohols with electrophiles
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   Tosyl chloride
IV. Reactions of alkoxides
V. Reactions of alcohols and diols with oxidizing agents

I. Introduction to alcohol reactivity

In which of the following ways can an alcohol react?

As a base: yes no if the acid has a pKa less than -2.4

As a nucleophile: yes no if the electrophile is fairly reactive

As an acid: yes no if the conjugate acid pKa is greater than 18

As an electrophile: yes no even though C is partially +, OH is not a good LG

Can they be oxidized? yes no can gain bonds to O - become aldehyde, ketone, COOH
Can they be reduced? yes no

II. Reactions of Alcohols with Acids

What is the first intermediate formed when an alcohol reacts with an acid?

What happens when a protonated alcohol dissociates?

Which of the following alcohols can form a protonated alcohol that can dissociate?
What happens to the ones that can't?

What are the three things that can happen to a carbocation?

Rearrange whenever a more stable C+ can be formed

React w/ a Nu S_N1 - rxn

React w/ a base E1 rxn
What else do we need to know to determine if the carbocation will react as an electrophile or acid?

if the conjugate base of the acid is a nucleophile or not

What will happen when H₂SO₄ or H₃PO₄ is used as the acid?

Could this reaction give constitutional isomers and/or stereoisomers?

yes - if there are different H's, or cis/trans

Why is the acid catalytic?  because H₃O⁺ is formed

Why is heat usually required in this reaction?  a C⁺ is formed

Could this reaction go backward?  yes - acid-catalyzed hydration of an alkene

The equilibrium constant is near 1.0 - how can we get a good yield?

high conc of alcohol - use as solvent
remove water - absorb
remove alkene - distill off

What will happen if HBr or HCl is used as the acid?

In order to make this reaction work well with HCl, what else needs to be added?

HCl, ZnCl₂ - Lucas reagent
How could you use the Lucas test to determine whether the following alcohols were $1^o$, $2^o$, or $3^o$?

\[
\begin{align*}
&\text{HCl} \\ &\text{ZnCl}_2
\end{align*}
\]

- no reaction (at room temp) nothing happens
- slow reaction cloudy, then 2nd layer insoluble
- fast reaction 2nd layer almost immediately insoluble

Predict the products of the following reactions.

\[
\begin{align*}
&\text{H}_2\text{SO}_4 \\ &\text{HBr} \\ &\text{H}_3\text{PO}_4 \\ &\text{HCl} \\ &\text{ZnCl}_2
\end{align*}
\]

- \(\text{H}_2\text{SO}_4\)
- \(\text{HBr}\)
- \(\text{H}_3\text{PO}_4\)
- \(\text{HCl}\)
III. Reactions of Alcohols with Electrophiles

What electrophile have we previously encountered that can react with an alcohol?

\[
\text{carbocation} \quad \text{Nu}
\]

\[
\text{SN1} \quad \text{Br} : \quad \text{cyclohexane} + \text{CH}_3\text{OH} \rightarrow \text{CH}_3\text{O} : \quad \text{Br} :: \quad \text{CH}_3\text{O} : \quad \text{CH}_3
\]

Halogenated phosphorus and sulfur compounds

What are the two most common phosphorus and sulfur reagents used as electrophiles with alcohols?

- phosphorus tribromide \( \text{PBr}_3 \)
- thionyl chloride \( \text{SOCl}_2 \)

What type of compound results when they react with alcohols? \( \text{alkyl halide} \)

\[
\text{OH} \quad \text{PBr}_3 \rightarrow \quad \text{Br} : \quad + \text{H}_3\text{PO}_3 \quad \text{water soluble - wash w/ H}_2\text{O}
\]

\[
\text{OH} \quad \text{SOCl}_2 \rightarrow \quad \text{Cl} : \quad + \text{SO}_2 + \text{pyr-H}^+ \text{Cl}^- \quad \text{solid - filter off}
\]

What advantages do these reactions have when isolating the product?

\[
\text{pyr} = \text{pyridine} \quad \text{N} \rightarrow \quad \text{N}^+ \quad \text{Cl} :: \quad \text{good for absorbing HCl}
\]

What is the mechanism of the \( \text{PBr}_3 \) reaction?

- attack-push off
- attack-push off

What type of alcohols work best in these reactions? Why?

\( 1^\circ \text{ best, } 2^\circ \text{ OK} \quad \text{steric hindrance} \)
What products will the following reactions give?

\[
\begin{align*}
\text{OH} & \quad \text{PCl}_3 & \quad \text{Cl}^+ : & \quad + \text{H}_3\text{PO}_3 \\
\text{OH} & \quad \text{PCl}_5 \quad \text{pyr} & \quad \text{Cl}^+ : & \quad + \text{POCl}_3 + \text{HCl} \\
\text{OH} & \quad \text{P} \quad \text{I}_2 & \quad \text{Cl}^+ : & \quad + \text{H}_3\text{PO}_3
\end{align*}
\]

If you want to convert an alcohol to an alkyl halide, which is the best way to do it?

<table>
<thead>
<tr>
<th>R-Cl</th>
<th>R-Br</th>
<th>R-I</th>
</tr>
</thead>
<tbody>
<tr>
<td>SOCl₂</td>
<td>PBr₃</td>
<td>P, I₂</td>
</tr>
<tr>
<td>HCl or SOCl₂</td>
<td>HBr or PBr₃</td>
<td>HI or P, I₂</td>
</tr>
<tr>
<td>HCl</td>
<td>HBr</td>
<td>HI</td>
</tr>
</tbody>
</table>

Convert the following alcohols to the products shown.

\[
\begin{align*}
\text{OH} & \quad \text{PBr}_3 & \quad \text{Br}^- : \\
\text{P} \quad \text{I}_2 & \quad \text{I}^- : \\
\text{OH} & \quad \text{SOCl}_2 \quad \text{pyr} & \quad \text{Cl}^- : \\
\text{OH} & \quad \text{I}_2 & \quad \text{Cl}^- :
\end{align*}
\]
Tosyl chloride

What product results when an alcohol reacts with tosyl chloride in pyridine?

\[
\text{TsCl} \quad \text{pyr} \quad \text{OTs}
\]

How does this reaction occur?

How do tosylates react? OTs is a leaving group - like Br

Give the products of the following reactions:

\[
\text{OTs} \quad \text{NaOCH}_3 \quad \text{OTs}^+ \quad \text{OTs}^{-}
\]

\[
\text{OTs} \quad \text{NaCN} \quad \text{cyclopropane} \quad \text{cyanide}
\]

\[
\text{OTs} \quad \text{KOC(CH}_3\text{)}_3 \quad \text{cyclopentene}
\]
IV. Formation and reactions of alkoxides

What reagents would be appropriate to form an alkoxide from the following alcohols?

Give the products of the following reactions:
From what alkoxide and tosylate could each of the following ethers be formed?

V. Oxidation of Alcohols and Diols

What type of reaction is represented by all of the transformations below? Give a reagent that would be effective for each.

What products can the following compounds be oxidized to?
Which reagents are commonly used for the following transformations?

1\textdegree\ alcohol \rightarrow \text{aldehyde}

\text{CrO}_3, \text{pyridine} = \text{Collin's reagent}

\text{CrO}_3, \text{pyridine}, \text{HCl} = \text{PCC}

1\textdegree\ alcohol \rightarrow \text{carboxylic acid}

\text{Na}_2\text{CrO}_4 \text{H}_2\text{O}, \text{H}_2\text{SO}_4

\text{Na}_2\text{Cr}_2\text{O}_7 \text{H}_2\text{O}, \text{H}_2\text{SO}_4

\text{CrO}_3 \text{H}_2\text{O}, \text{H}_2\text{SO}_4 \ = \text{Jones reagent}

2\textdegree\ alcohol \rightarrow \text{ketone}

\text{all of the above}

Give the products of the following reactions:

\begin{align*}
\text{Ph-OH} & \xrightleftharpoons[\text{CrO}_3, \text{H}_2\text{O}, \text{H}_2\text{SO}_4]{\text{CrO}_3} \text{Ph-COOH} \\
\text{Cyclo-C-OH} & \xrightleftharpoons[\text{Na}_2\text{Cr}_2\text{O}_7, \text{H}_2\text{O}, \text{H}_2\text{SO}_4]{\text{Na}_2\text{Cr}_2\text{O}_7} \text{Cyclo-COOH} \\
\text{Me-C-OH} & \xrightleftharpoons[\text{PCC}]{\text{PCC}} \text{Me-COOH} \\
\text{C-C-OH} & \xrightleftharpoons[\text{Jones reagent}]{\text{Jones reagent}} \text{C-COOH}
\end{align*}
What would you observe when doing a Jones test on the following alcohols?

- orange → blue-green positive test
- stays orange negative test

What reagent is needed to cleave vicinal diols? periodic acid - HIO₄ or H₃IO₆

What products will result from the following reactions?

- What reaction of alkenes gives the same result? ozonolysis
Summary of Alcohol Reactions

1\textsuperscript{o} alcohol \xrightarrow{\text{Collins or PCC}} \text{aldehyde}

1\textsuperscript{o} alcohol \xrightarrow{\text{Jones, etc}} \text{carboxylic acid}

1\textsuperscript{o} alcohol \xrightarrow{\text{TsCl, pyr}} \text{tosylate} \xrightarrow{\text{Nu}} \text{ether, alkyne, nitrile, etc}

1\textsuperscript{o}, 2\textsuperscript{o} alcohol \xrightarrow{\text{PBr}_3, \text{SOCl}_2 \text{ etc}} \text{alkyl halide}

2\textsuperscript{o} alcohol \xrightarrow{\text{Jones, Collins etc}} \text{ketone}

2\textsuperscript{o}, 3\textsuperscript{o} alcohol \xrightarrow{\text{H}_2\text{SO}_4} \text{alkene}

2\textsuperscript{o}, 3\textsuperscript{o} alcohol \xrightarrow{\text{HI, HBr, HCl/ZnCl}_2} \text{alkyl halide}

alcohol, phenol \xrightarrow{\text{NaH, Na, K NaOH}} \text{alkoxide} \xrightarrow{\text{RX or ROTs}} \text{ether}