Chem. 218 Problem Set 10


a. 
\[ \text{CH}_3\text{CH}_2\text{OH} \xrightarrow{\text{SOCl}_2} \text{CH}_3\text{CH}_2\text{Cl} \]

b. 
\[ \text{CH}_3\text{CH}_2\text{OH} \xrightarrow{\text{H}^+} \text{CH}_3\text{CH}_2\text{O} \text{CH}_3 \]

c. 
\[ \text{CH}_3\text{CH}_2\text{OH} \xrightarrow{1. \text{SOCl}_2} \text{CH}_3\text{CH}_2\text{O} \text{CH}_3 \xrightarrow{2. \text{H}^+} \text{CH}_3\text{CH}_2\text{O} \text{CH}_3 \]

d. Here are two possibilities:

1. \( \text{H}_2\text{O} \xrightarrow{1. \text{LiAIH}_4} \text{CH}_3\text{CH}_2\text{OH} \)
2. \( \text{CH}_3\text{CH}_2\text{OH} \xrightarrow{2. \text{LiCu}_2} \text{CH}_3\text{CH}_2\text{O} \text{CH}_3 \)
3. \( \text{CH}_3\text{CH}_2\text{OH} \xrightarrow{3. \text{PCC}} \text{CH}_3\text{CH}_2\text{O} \text{CH}_3 \)
4. \( \text{CH}_3\text{CH}_2\text{OH} \xrightarrow{4. \text{PCC}} \text{CH}_3\text{CH}_2\text{O} \text{CH}_3 \)

or

1. \( \text{LiAIH}_4 \)
2. \( \text{PCC} \)
3. \( \text{MeMgBr} \)
4. \( \text{MeMgBr} \)
5. \( \text{PCC} \)

e. 
\[ \text{CH}_3\text{CH}_2\text{OH} \xrightarrow{\text{MeOH, H}^+} \text{CH}_3\text{CH}_2\text{O} \text{Me} \xrightarrow{\text{MeMgBr (excess)}} \text{CH}_3\text{CH}_2\text{OH} \]

or

1. \( \text{LiAIH}_4 \)
2. \( \text{PCC} \)
3. \( \text{MeMgBr} \)
4. \( \text{PCC} \)
5. \( \text{MeMgBr} \)
2. Predict the products:

a. 
\[ \text{H}_2\text{N}^+\text{Cl}\overset{\text{CH}_3\text{O}^-}{\longrightarrow}\text{H}_2\text{N}^-\text{OCH}_3 \]

b. 
\[ \text{H}_3\text{CO}^+\text{Cl}\overset{\text{NH}_2^-}{\longrightarrow}\text{H}_3\text{CO}^-\text{NH}_2 \]

3. When a carboxylic acid is dissolved in isotopically labeled water, the label rapidly becomes incorporated into both oxygens of the carboxylic acid. Explain why.

After attack by water, the intermediate is:

\[ \text{R}^+\text{OH} \]

This compound can undergo proton transfer to give:

\[ \text{R}^-\text{OH}^+ \]

At this point in the mechanism, one of the hydroxyl groups becomes protonated to make it into a good leaving group. If one of the non-labeled oxygens becomes protonated, it will become the leaving group:

\[ \text{R}^-\text{OH}^- \]

The next step is to bring the electrons from one of the hydroxyl groups down to reform the carbonyl and kick out water. Either hydroxyl group can donate its electrons, so the product will either have the label on the carbonyl carbon or the hydroxyl carbon:

\[ \text{R}^+\text{OH}^- \quad \text{or} \quad \text{R}^-\text{OH}^- \]

The whole process is repeated until both oxygens are labeled. Because the labeled water is present in a large excess, the final product has both oxygens labeled.
4. One frequently used method for preparing methyl esters is by reaction of carboxylic acids with diazomethane, \( \text{CH}_2\text{N}_2 \):

\[
\text{R-OH} + \text{CH}_2\text{N}_2 \rightarrow \text{R-OCH}_3
\]

The reaction occurs in two steps: (1) protonation of diazomethane by the carboxylic acid to give the diazonium ion \( \text{CH}_3\text{N}_2^+ \) plus a carboxylate anion, and (2), reaction of the carboxylate with the diazonium ion.

(a) Draw two resonance structures of diazomethane to account for step 1.

(b) What kind of reaction occurs in step 2?

\( \text{S}_\text{N}2 \):

5. Acetate groups are commonly used as protecting groups for alcohols. The following methods have all been used to install an acetate protecting group on an alcohol. Draw all of the products that are formed in addition to the acetate, and draw the mechanism for each reaction.

(a)

(b)
6. The following methods have been used to remove acetate protecting groups. Draw all of the products and mechanism for each reaction.

(a)
7. It is possible to remove an acetate protecting group from an alcohol in the presence of an amine. Explain why.

Amides are much more stable than esters, so they are much less reactive to nucleophiles such as methoxide.

8. When lactic acid (2-hydroxypropanoic acid) is heated with one equivalent of thionyl chloride, a product with MF C_6H_8O_4 is formed. Draw the product and the mechanism for its formation. Hint: it is cyclic.
9. Propose a synthesis of the following molecule using the starting materials given:

(a) Retrosynthesis:

Forward:

(b)