Objectives

After completing this section, you should be able to

1. discuss the reactions of alcohols that have been introduced in previous units. These reactions include
   a. conversion of alcohols into alkyl halides.
   b. conversion of alcohols into tosylates.
   c. dehydration of alcohols to yield alkenes.
   d. conversion of alcohols into esters.

Study Notes

As you read through Section 17.6 you should be prepared to turn back to those earlier sections in which some of the reactions of alcohols were discussed:

• dehydration to alkenes—Section 8.1.
• conversion to alkyl halides—Section 10.5.

You may also wish to review the discussion of acidity constants, which can be found in Section 2.8.

Remember that when an alcohol reacts with tosyl chloride to form a tosylate, it is the O\(-\)H bond of the alcohol that is broken, not the C\(-\)O bond. This means that the absolute configuration of the carbon atom attached to the hydroxyl group remains unchanged throughout the reaction. The reading illustrates how this fact can be exploited to control the stereochemistry in an organic synthesis.

Finally, the reading shows the production of an ester from an alcohol and an acid chloride. In Section 21.3 we will discuss the **Fischer esterification**, a famous reaction that uses an alcohol and a carboxylic acid to form the ester.

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**Conversion of Alcohols into Alkyl Halides**

When alcohols react with a hydrogen halide, a substitution takes place producing an alkyl halide and water:

\[
R\cdot OH + H\cdot X \rightarrow R\cdot X + H_2O
\]

- The order of reactivity of alcohols is 3° > 2° > 1° methyl.
- The order of reactivity of the hydrogen halides is HI > HBr > HCl (HF is generally unreactive).

The reaction is acid catalyzed. Alcohols react with the strongly acidic hydrogen halides HCl, HBr, and HI, but they do not react with nonacidic NaCl, NaBr, or NaI. Primary and secondary alcohols can be converted to alkyl chlorides and bromides by allowing them to react with a mixture of a sodium halide and sulfuric acid:

\[
R\cdot OH + NaX \xrightarrow{H_2SO_4} R\cdot X + NaHSO_4 + H_2O
\]
Mechanisms of the Reactions of Alcohols with HX

Secondary, tertiary, allylic, and benzylic alcohols appear to react by a mechanism that involves the formation of a carbocation, in an \(\text{S}_\text{N1}\) reaction with the protonated alcohol acting as the substrate.

The \(\text{S}_\text{N1}\) mechanism is illustrated by the reaction tert-butyl alcohol and aqueous hydrochloric acid (\(\text{H}_3\text{O}^+, \text{Cl}^-\)). The first two steps in this \(\text{S}_\text{n1}\) substitution mechanism are protonation of the alcohol to form an oxonium ion. Although the oxonium ion is formed by protonation of the alcohol, it can also be viewed as a Lewis acid-base complex between the cation (\(R^+\)) and \(\text{H}_2\text{O}\). Protonation of the alcohol converts a poor leaving group (\(\text{OH}^-\)) to a good leaving group (\(\text{H}_2\text{O}^-\)), which makes the dissociation step of the \(\text{S}_\text{N1}\) mechanism more favorable.

In step 3, the carbocation reacts with a nucleophile (a halide ion) to complete the substitution.

When we convert an alcohol to an alkyl halide, we carry out the reaction in the presence of acid and in the presence of halide ions, and not at elevated temperature. Halide ions are good nucleophiles (they are much stronger nucleophiles than water), and since halide ions are present in high concentration, most of the carbocations react with an electron pair of a halide ion to form a more stable species, the alkyl halide product. The overall result is an \(\text{S}_\text{n1}\) reaction.

Not all acid-catalyzed conversions of alcohols to alkyl halides proceed through the formation of carbocations. Primary alcohols and methanol react to form alkyl halides under acidic conditions by an \(\text{S}_2\) mechanism.

In these reactions the function of the acid is to produce a protonated alcohol. The halide ion then displaces a molecule of water (a good leaving group) from carbon; this produces an alkyl halide:

Again, acid is required. Although halide ions (particularly iodide and bromide ions) are strong nucleophiles, they are not strong enough to carry out substitution reactions with alcohols themselves. Direct displacement of the hydroxyl group does not occur because the leaving group would have to be a strongly basic hydroxide ion:
We can see now why the reactions of alcohols with hydrogen halides are acid-promoted.

Carbocation rearrangements are extremely common in organic chemistry reactions and are defined as the movement of a carbocation from an unstable state to a more stable state through the use of various structural reorganizational "shifts" within the molecule. Once the carbocation has shifted over to a different carbon, we can say that there is a structural isomer of the initial molecule. However, this phenomenon is not as simple as it sounds.

The most common methods for converting 1º- and 2º-alcohols to the corresponding chloro and bromo alkanes (i.e. replacement of the hydroxyl group) are treatments with thionyl chloride and phosphorus tribromide, respectively. These reagents are generally preferred over the use of concentrated HX due to the harsh acidity of these hydrohalic acids and the carbocation rearrangements associated with their use.

Synthetic organic chemists, when they want to convert an alcohol into a better leaving group, have several methods to choose from. One common strategy is to convert the alcohol into an alkyl chloride or bromide, using thionyl chloride or phosphorus tribromide:

### Conversion of Alcohols into Esters

Acid chlorides react with alcohols to form esters

\[
\text{Acid Chloride} + \text{Alcohol} \rightarrow \text{Ester} + \text{HCl}
\]

Example 17.6.3

Exercises
Questions

Q17.6.1

Draw the expected product of the reaction of cyclohexanol with the following reagents.

(a) CrO$_3$, H$_2$SO$_4$, H$_2$O  (b) Dess-Martin Periodinane  (c) SOCl$_2$  (d) NaH and 1-bromoethane  (e) PBr$_3$

Q17.6.2

Given the following reactions oxidize alkenes, use any reaction to prepare 1-butanol from the following.

\[
\begin{array}{ccc}
\text{R} & \xrightarrow{\text{O}_3, (\text{CH}_3)_2\text{S}} & \text{R} \\
\text{OR} & \xrightarrow{\text{KMnO}_4} & \text{R} \\
\text{H}_2\text{O}^+ & \xrightarrow{} & \text{H} \\
\end{array}
\]

(a) Butyric/Butanoic Acid  (b) 1-butanal  (c) 1-butene  (d) 2-butanol  (e) 1-propanol  (f) Propionic/propanoic acid

Q17.6.3

Starting with cyclohexanol, describe how you would prepare the following?

(a) cyclohexyl acetate  (b) 1-allylcyclohexan-1-ol  (c) cyclohexene  (d) ethoxycyclohexane

Q17.6.4

In cyclohexanone, a ketone, indicate the polarity of the bond between oxygen and carbon.

Q17.6.5

In the dehydration of 1-methylcyclohexanol, which product is favored?

Q17.6.6

In the dehydration of this diol the resulting product is a ketone. Draw the mechanism of its formation. (Hint a rearrangement occurs)
Q17.6.7

Draw the mechanism of the reaction of thionylchloride with cyclohexanol, given below.

Q17.6.8

Draw an arrow pushing mechanism for the acid catalyzed dehydration of the following alcohol, make sure to draw both potential mechanisms. Assume no rearrangement for the first two product mechanisms. Which of these two would likely be the major product? If there was a rearrangement, draw the expected major product.

Q17.6.9

The following epoxide can be transformed into an alcohol using a grignard reagent, take for example allylmagnesium chloride. Draw the product of the treatment of this epoxide with this grignard after being worked up with H\textsubscript{2}O. Note the stereochemistry and also remember that benzylic carbons are good Sn2 electrophiles.

Q17.6.10

As seen in the previous example, there are many examples of chiral compounds containing alcohols. One common example of these are sugars, is the given the following sugar, allitol, also chiral?
Solutions

S17.6.1

(a)

(b)

(c)

(d)

(e)

S17.6.2

a. Oxidation with CrO₃, H₂O, and H₂SO₄
b. Oxidation with Dess-Martin Periodinane
c. A condensation with H₂SO₄ and Heat
d. From the previous problem oxidize the double bond on the second carbon with an Oxymercuration using Hg(OAc)$_2$ followed by NaBH$_4$

e. From problem c, perform an oxidative cleavage with KMnO$_4$ and H$_3$O$^+$ or use ozonolysis

f. This can be made by taking the alkene from problem (c), oxidizing it with BH$_3$ followed by H$_2$O$_2$ to get the 1-propanol. This can be oxidized using CrO$_3$, H$_2$O, and H$_2$SO$_4$ to give the carboxylic acid.

S17.6.3

a. This can be seen as a transesterification, acid and some other ester would be needed to form cyclohexylacetate

b. First, oxidize the alcohol to a ketone, take for example Dess-Martin Periodinane, then use an allyl grignard to form 1-allylcyclohexan-1-ol

c. Alcohols can dehydrate to form alkenes under acidic conditions, so using anhydrous acid and heat would yield cyclohexene

d. The alcohol can also be a nucleophile, perform a halogen substitution, using 1-X ethane, to yield ethoxycyclohexane

S17.6.4

Oxygen is more electronegative than carbon creating the polar bond. This is the basis for the carbon’s electrophilicity.

S17.6.5

The more substituted alkene is favored, as more substituted alkenes are relatively lower in energy.

S17.6.6

This is also known as the Pinacol rearrangement.

Note how the carbocation after the rearrangement is resonance stabilized by the oxygen
The major product of this mechanism would be the more highly substituted alkene, or the product formed from the red arrows.

Note the secondary carbocation adjacent a tertiary carbon center, if there were a hydride transfer (rearrangement) to form a tertiary carbocation the following would be the major product. The minor product being the same product as the one formed from the red arrows.
This compound actually has a plane of symmetry, the plane parallel to the carbon chain/backbone. So, it is not chiral, also called a meso compound.

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