Chapter 19 - Aldehydes and Ketones: Nucleophilic Addition Reactions

Addition of Amines - Imine and Enamaine Formation

Primary amines (RNH\textsubscript{2}) will react with aldehydes and ketones to form imines. If the amine is a secondary amine (R\textsubscript{2}NH) then enamines are formed. This is an acid-catalyzed reaction very similar to acid catalyzed hydration.

\[
\begin{align*}
\text{Imine formation} & : \\
\text{O} & + \text{R-NH}_2 + \text{H}^+ & \rightarrow & \text{H} & \text{N} & \text{R} & \rightarrow & \text{R} & \text{N} & \text{H} & + \text{H}_2\text{O}
\end{align*}
\]

Imine formation begins just like the hydration of ketones. The acid protonates the carbonyl making it more electrophilic. The amine attacks the carbonyl carbon and the conjugate base takes the proton off of the nitrogen. This generates a hemiaminal. This is not very stable. If the acid protonates the OH group, it can leave, facilitated by the lone pair on nitrogen. The conjugate base then deprotonates the nitrogen to form the imine.

**NEED TO KNOW MECHANISM**

**Mechanism for Imine Formation**

Up to here this is identical to a hydration with amine as nucleophile instead of water.
The mechanism for the formation of an enamine from a secondary amine is exactly the same up to the last deprotonation step. As there is no hydrogen on the nitrogen, the conjugate base deprotonates the alpha carbon instead, neutralizing the intermediate and forming the carbon-carbon double bond.

**NEED TO KNOW MECHANISM**

**Mechanism for Enamine Formation**

![Diagram of mechanism for enamine formation](image)

The only difference is this last step. There is no proton on the nitrogen to come off, so a proton is taken off of the alpha carbon.

As practice, try writing out each step of these mechanisms for the reverse reaction. The hydrolysis of imines and enamines follows the same path but in reverse. Start by protonating the nitrogen of the imine or enamine.

**Oximes and Hydrazines**

Many kinds of amines participate in imine formation reactions including hydroxyl amine and hydrazine.

![Diagram of oxime and hydrazone formation](image)

**Oxime**

\[
\text{O} \quad \xrightarrow{\text{H}_2\text{N}-\text{OH}} \quad \text{N}^{\text{OH}}
\]

**Hydrazone**

\[
\text{O} \quad \xrightarrow{\text{H}_2\text{N}-\text{NH}_2} \quad \left[ \begin{array}{c}
\text{N}^{\text{NH}_2} \\
\end{array} \right]
\]

**Wolff-Kishner Reduction**

\[
\left[ \begin{array}{c}
\text{N}^{\text{NH}_2} \\
\end{array} \right] \xrightarrow{\text{KOH}} \text{H}_2\text{H}
\]