As previously seen, aldehydes and ketones react with $2^\circ$ amines to reversibly form enamines.

Example

\[ \text{2$^\circ$ Amine} + \text{Ketone} \xrightleftharpoons{\text{H}_2\text{O}^+} \xrightarrow{-\text{H}_2\text{O}} \text{Enamine} \]

Reversible

Enamines act as nucleophiles in a fashion similar to enolates. Because of this enamines can be used as synthetic equivalents as enolates in many reactions. This process requires a three steps:

1. Formation of the enamine,
2. Reaction with an electrophile to form an iminium salt,
3. Hydrolysis of the iminium salt to reform the aldehyde or ketone.

Some of the advantages of using an enamine over an enolate are enamines are neutral, easier to prepare, and usually prevent the overreaction problems plagued by enolates. These reactions are generally known as the Stork enamine reaction after Gilbert Stork of Columbia University who originated the work.

Typically we use the following $2^\circ$ amines for enamine reactions
Alkylation of an Enamine

Enamines undergo an $S_N2$ reaction with reactive alkyl halides to give the iminium salt. The iminium salt can be hydrolyzed back into the carbonyl.

Step 1: Formation of an enamine

\[
\text{Pyrrolidine} + \text{Ketone} \xrightleftharpoons{H_2O^+} \xrightarrow{-H_2O} \text{Enamine}
\]

Step 2: $S_N2$ Alkylation

\[
\text{Enamine} + \text{Alkyl Halide} \rightarrow \text{Iminium Salt}
\]

Step 3: Reform the carbonyl by hydrolysis

\[
\text{Iminium Salt} \xrightarrow{HCl, H_2O} \text{Ketone} + \text{Enamine}
\]

All three steps together:
Acylation of Enamines

Enamine can react with acid halides to form β-dicarbonyls

1) Formation of the enamine

2) Nucleophilic attack

3) Leaving group removal

4) Reform the carbonyl by hydrolysis
Michael Addition using Enamines

Enamines, like other weak bases, add 1,4 to enones. The end product is a 1,5 dicarbonyl compound.

Contributors

- Prof. Steven Farmer (Sonoma State University)