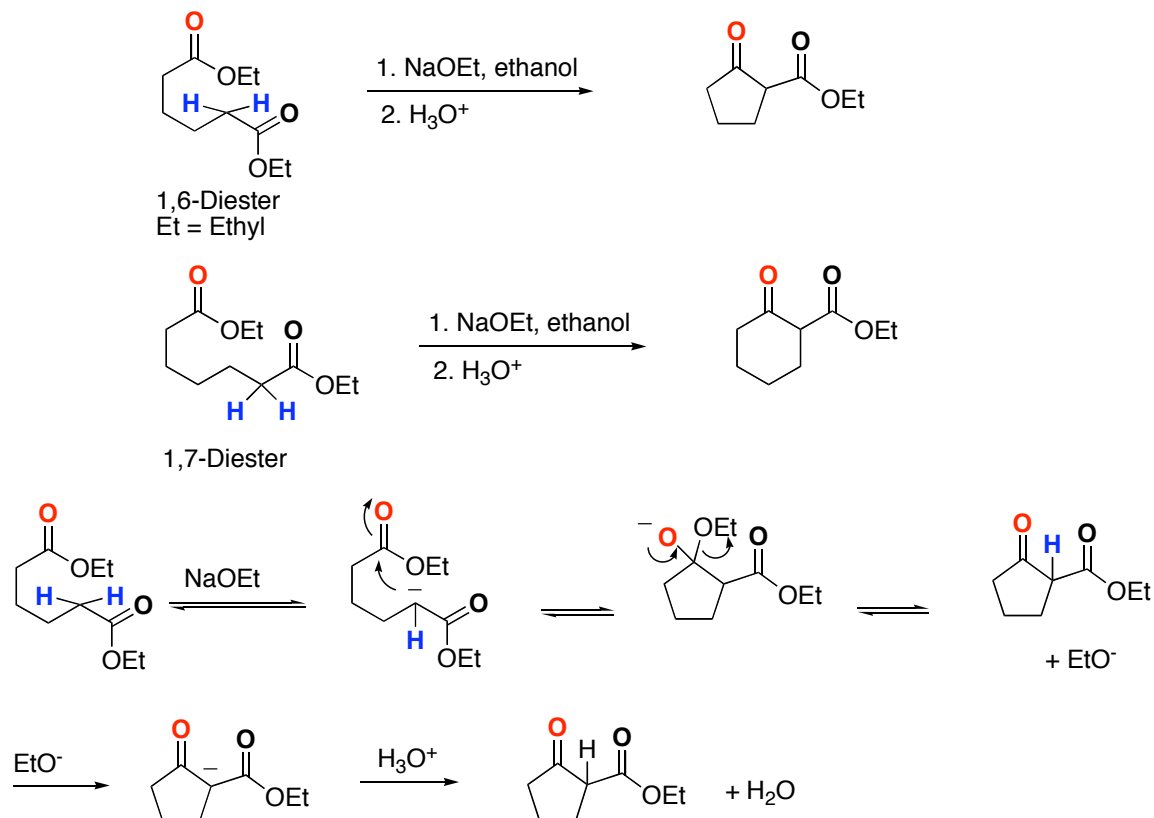


Dieckmann Cyclization

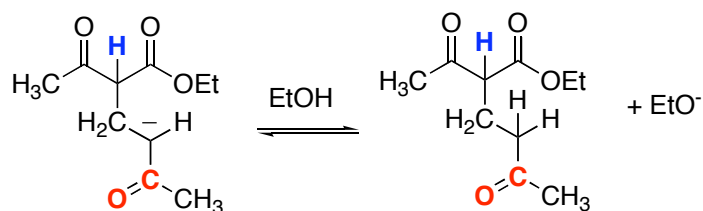
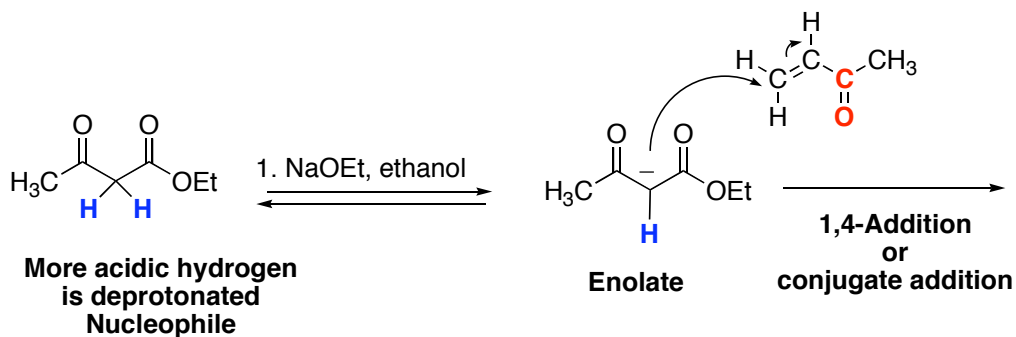
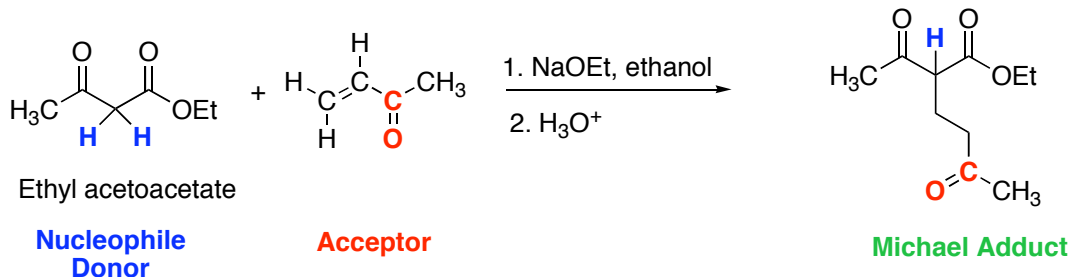
The Dieckmann cyclization is an intramolecular version of the Claisen condensation. As the name implies the reaction provides a cyclic compound. The cyclization works best with 1,6 and 1,7-diester. The cyclic β -keto esters are useful in the preparation of substituted cycloalkanones (see lecture 29).



Michael Reaction

The Michael reaction is a special version of the generic conjugate addition. Enolates can add conjugatively to α,β -unsaturated carbonyl compounds. The reaction results in the formation of a C-C bond. The Michael reaction works best with stable enolates, for example, enolates derived from β -keto esters or 1,3-dicarbonyl compounds.

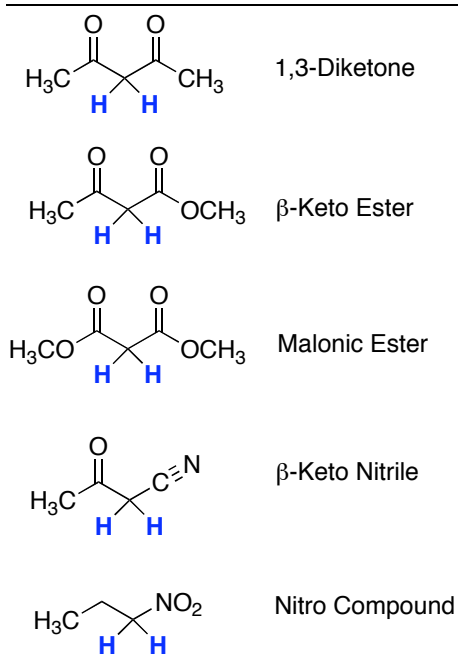
Lecture 34



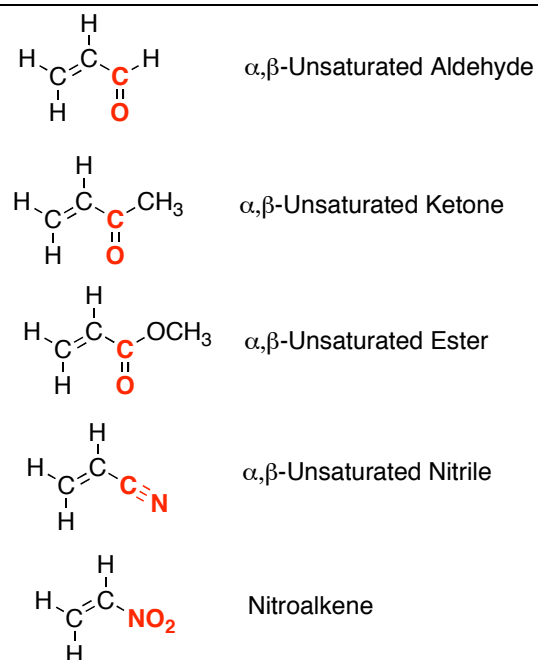
A variety of compounds can be used as donors in the Michael reaction. In general, these compounds have highly acidic protons and thus are capable of forming stabilized enolates. Similarly, a variety of compounds can be used as acceptors. An electron-withdrawing group is required in the acceptor. The soft nucleophile (stabilized enolate) does conjugate addition selectively. These stable nucleophiles will not do 1,2-addition. Thus when properly matched nucleophiles and electrophiles are used, Michael reactions are very efficient.

Lecture 34

Michael Donors (nucleophiles)

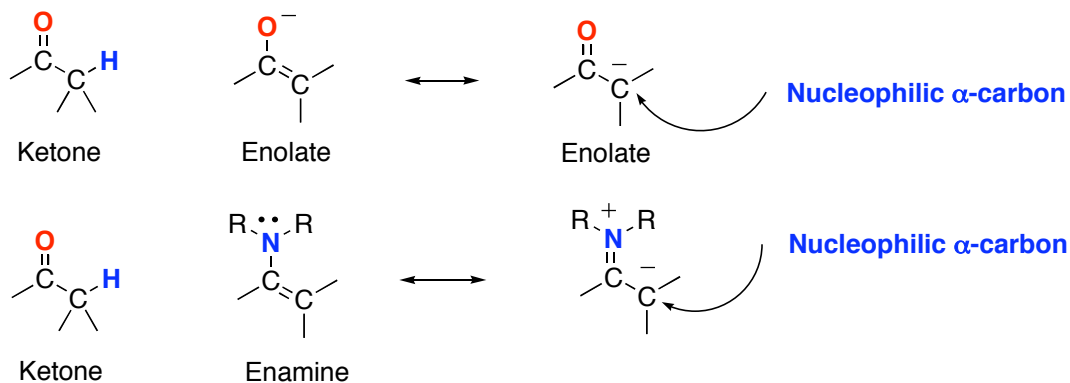
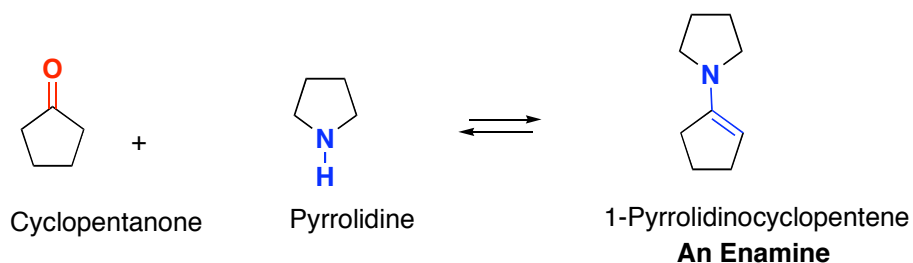


Michael Acceptors (electrophiles)



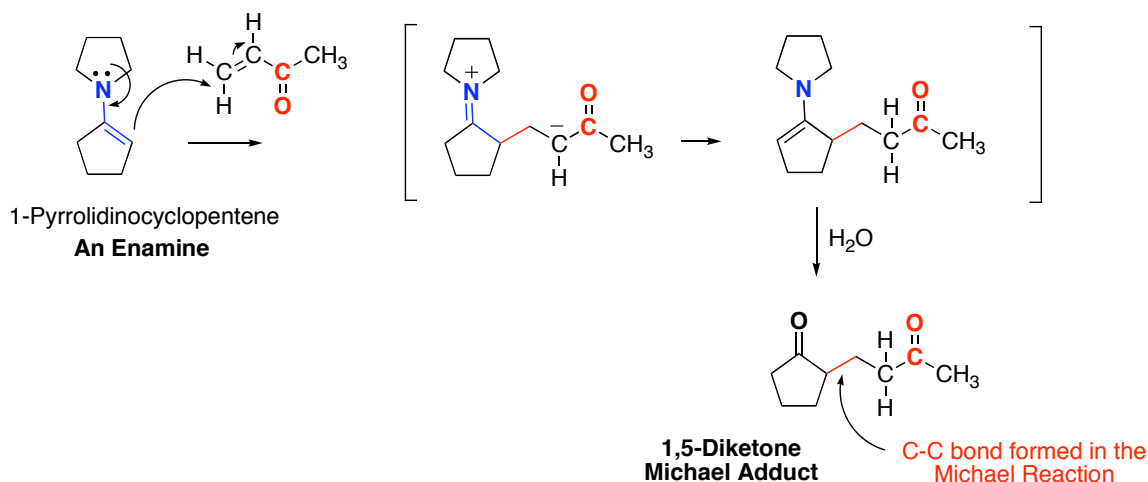
Stork Enamine Reaction

Enamines, readily prepared from carbonyl compounds and secondary amines, are excellent isolable surrogates for enolates. For example, cyclopentanone can be converted to an enamine using pyrrolidine. The enamines are similar to enolates in that the α-carbon is nucleophilic.



Lecture 34

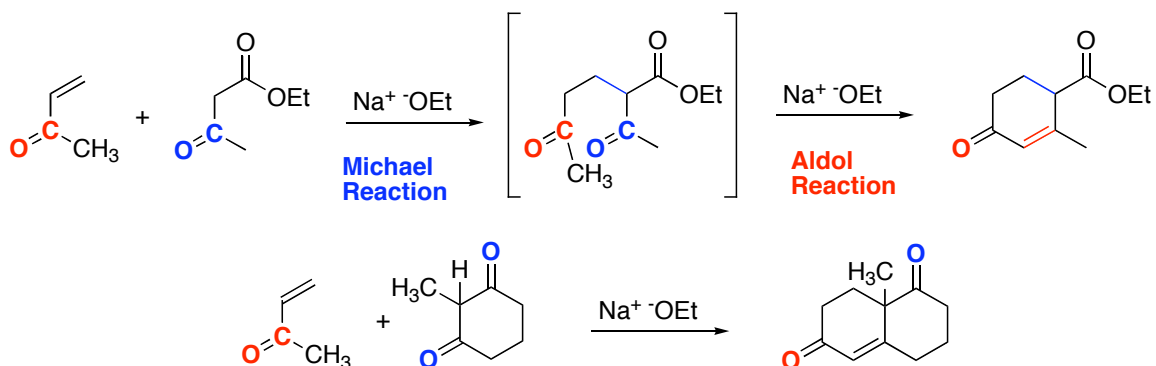
The enamines react with alkylating agents just like enolates to form α -alkylated carbonyl compounds after hydrolysis. Another major use of enamines is in the Michael reaction. The enamines add conjugatively to Michael acceptors in a 1,4-manner. They do not do 1,2-addition. Thus they behave similar to stabilized enolates. The intermediate iminium ion formed can reform an enamine, which undergoes hydrolysis to form the Michael adduct.



Robinson Annulation

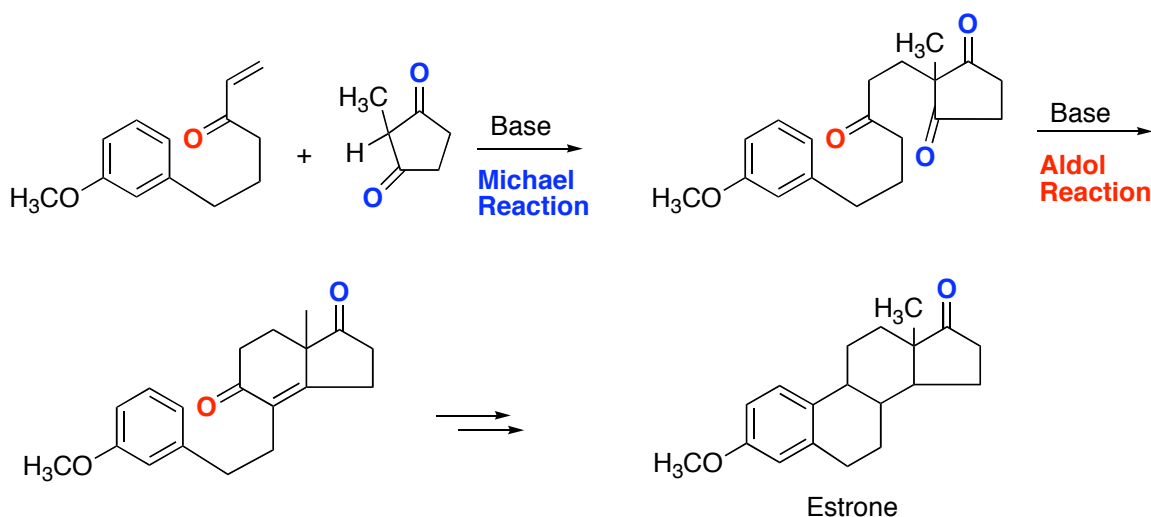
Carbonyl condensation reactions are very useful in organic chemistry. We have discussed the aldol reaction which provides α,β -unsaturated carbonyl compounds. Furthermore, the Michael reaction provides a method for the synthesis of 1,5-dicarbonyl compounds. By a clever combination of these two reactions, one can prepare complex cyclic α,β -unsaturated ketones very efficiently. The process is called the Robinson annulation (annulation = ring formation). The reaction is named after its inventor Sir Robert Robinson (1947 Nobel Laureate).

The first step in the Robinson annulation is a Michael reaction to form a 1,5-dicarbonyl compound. In the second step, the Michael adduct undergoes an intramolecular aldol reaction to give cyclic α,β -unsaturated ketones. Basic conditions are required for the reaction. A variety of acceptors and donors can be used in Robinson annulation.



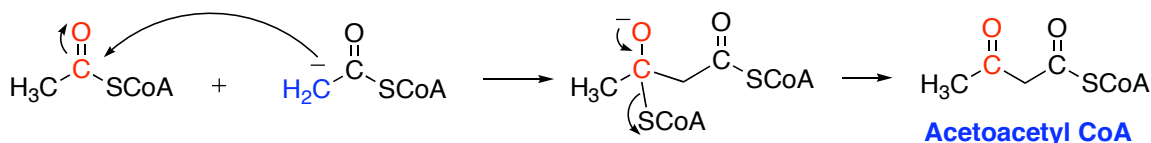
Lecture 34

During the Second World War, synthesis of steroids became very important. One of the many applications of Robinson annulation is in the synthesis of estrone, a steroid hormone.



Biological Carbonyl Condensation Reactions

Nature uses carbonyl condensation reactions for the production of many different molecules including, fats, amino acids, steroids, etc. The principal component in the biosynthesis is the two-carbon acetyl CoA molecule. It can act as both an acceptor as well as a donor. The synthesis of acetoacetyl CoA is shown below.



An example on the use of acetyl CoA in the synthesis of citric acid is shown below.

