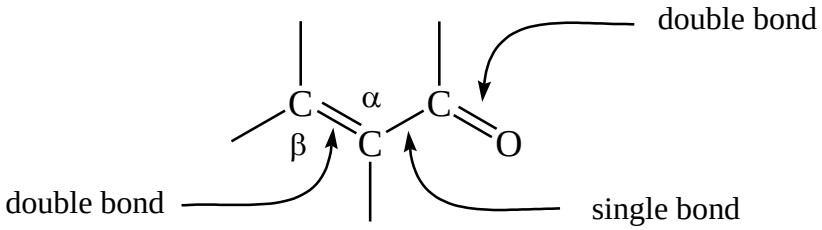
3) α,β-Unsaturated carbonyl compounds:

3:1) Structure and properties:

In general , a compound that contain both of carbon – carbon double bond and carbon – oxygen double bond has properties that characteristic of both functional groups .
At the carbon – carbon double bond an unsaturated ester or ketone undergoes electrophilic addition of acids and halogens, hydrogenation, hydroxylation and cleavage.
At the carbonyl group it undergoes nucleophilic substitution typical of an ester or nucleophilic addition typical of a ketone .
In these compounds, the carbon – carbon double bond and the carbon – oxygen double bond are separated by just one carbon – oxygen single bond; that is the double bonds are conjugated.

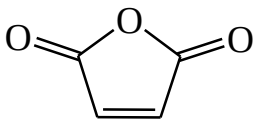


α,β-Unsaturated carbonyl compounds
(conjugated system)

Because of this conjugation, such compounds possess not only the properties of the individual functional groups, but certain properties besides.
So we shall concentrate on the α,β-unsaturated compounds, and on the special reactions characteristic of the conjugated system.

The following table lists some of the most important compounds of this type:

Compound name	**Structure**
Acroline (propenal)	$H_2C{=}CHCHO$
Crotonaldehyde (2- butenal)	$H_3CHC{=}CHCHO$
Cinnamaldehyde	$PhHC{=}CHCHO$
Mesityl oxide	$(H_3C)_2C{=}CHCOCH_3$

Benzalacetone	$PhHC{=}CHCOCH_3$
Dibenzalacetone	$PhHC{=}CHCOCH{=}CHPh$
Bezalacetophenone (chalcone)	$PhHC{=}CHCOPh$
Dypnone	$Ph(H_3C)C{=}CHCOPh$
Acrylic acid (propenoic acid)	$H_2C{=}CHCOOH$
Crotonic acid	trans- $H_3CHC{=}CHCOOH$
Isocrotonic acid	cis- $H_3CHC{=}CHCOOH$
Methacrylic acid	$H_2C{=}\underset{\displaystyle CH_3}{\overset{\displaystyle |}{C}}{-}COOH$
Sorbic acid	$H_3CHC{=}CHCH{=}CHCOOH$
Cinnamic acid	trans- $PhHC{=}CHCOOH$
Maleic acid	cis- $HOOCHC{=}CHCOOH$
Fumaic acid	trans- $HOOCHC{=}CHCOOH$
Maleic anhydride	
Methyl acrylate	$H_2C{=}CHCOOCH_3$
Methyl methacrylate	$H_2C{=}\underset{\displaystyle CH_3}{\overset{\displaystyle |}{C}}{-}COOCH_3$
Ethyl cinnamate	$PhHC{=}CHCOOC_2H_5$
Acrylonitrile	$H_2C{=}CHC{\equiv}N$

3:2) Preparation:

These compounds have been synthesized by different methods like:

1- The aldol condensation to make unsaturated aldehydes or ketones.
2- Dehydrohalogenation of α-halo acids. (α-halo acids prepared by halogenations of unsubstituted acids, which known as Hell-Volhard-Zelinsky).

e.g. for H.V.Z. reaction:

$$RCH_2COOH + X_2 \xrightarrow{P} \underset{\displaystyle X}{\overset{\displaystyle |}{RCH}}COOH + HX$$

X= Cl_2, Br_2

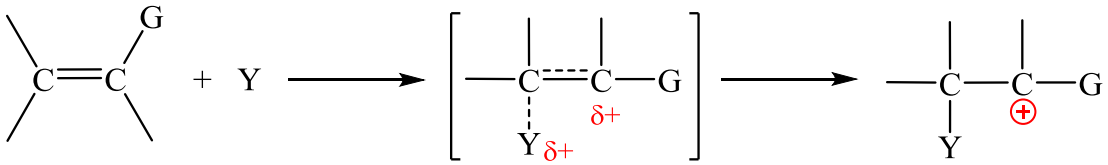
3- Perkin condensation.

Note: *Methods 2 and 3 used to make unsaturated acids. Other methods can be used for making single compounds.*

3:3) Interaction of functional groups:

As we know, electrophilic addition on carbon – carbon double bond is activated by an electron – releasing substituent (EDG) and deactivated by an electron – withdrawing substituent (EWG).

Hint: (the carbon – carbon double bond serve as a source of electrons for electrophilic reagents; the availability of its electrons is determined by the group that attached to it. Moreover EDGs stabilizes the T.S. leading to the initial carbocation by dispersing the +ve charge, this in contrast with EWGs which destabilize the T.S.by intensifying the +ve charge).



If G is an EDG ⟹ activates
If G is an EWG ⟹ deactivates

The C=O, COOH, COOR and CN groups are powerful electron withdrawing groups, and therefore deactivate the C=C toward electrophilic addition, thus α,β-unsaturated ketones, acids, esters or nitriles are in general less reactive than simple alkene toward reagents like bromine and hydrogen halides.

On the other hand this powerful electron withdrawal, which deactivate a carbon – carbon double bond toward reagents seeking electrons, at the same time activates toward reagents that are electron – rich. As a result, the carbon – carbon double bond of an α,β-unsaturated ketones, acids, esters or nitriles is susceptible to nucleophilic attack, and undergoes a set of reactions, nucleophilic addition, that is uncommon for simple alkenes.

3:4) Electrophilic addition:

In general, the addition of an unsymmetrical reagent (E^+) to simple alkenes takes place in such a way that form the most stable intermediate carbocation.

e.g.

2-Chloro propane

The presence of carbonyl group not only lowers the reactivity of the carbon – carbon double bond toward electrophilic addition, but also control the orientation of the addition, thus addition of an electrophile to an α,β-unsaturated carbonyl compound proceed in such a way that hydrogen becomes attached to the α- carbon and the negative group attached to the β- carbon.
e.g.

1) $H_2C{=}CHCHO + HCl\,(g) \xrightarrow{-10°C} CH_2(Cl)CH(H)CHO$

Acroline — β- Chloro propionaldehyde

2) $H_2C{=}CHCO_2H + H_2O \xrightarrow{H_2SO_4,\ 100°C} CH_2(OH)CH(H)CO_2H$

Acrylic acid — β- Hydroxy propionic acid

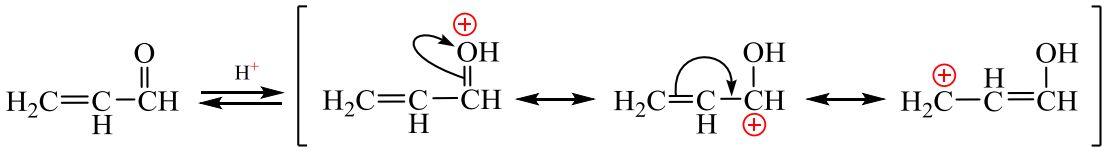
3) $H_3CHC{=}CHCO_2H + HBr \xrightarrow{20°C} CH_3CH(Br)CH(H)CO_2H$

Crotonic acid — β- Bromo butyric acid

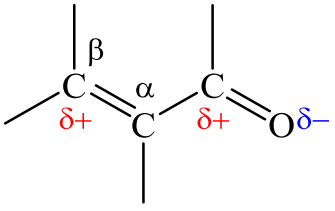
4) $(H_3C)_2C{=}CHCOCH_3 + CH_3OH \xrightarrow{H_2SO_4} H_3C{-}C(CH_3)(OCH_3){-}CH(H)COCH_3$

Mesityl oxide — 4- Methoxy-4-methyl-2-pentanone

The presence of carbonyl group polarize the carbon – carbon double bond, thus addition of an electrophile proceeded as the following:

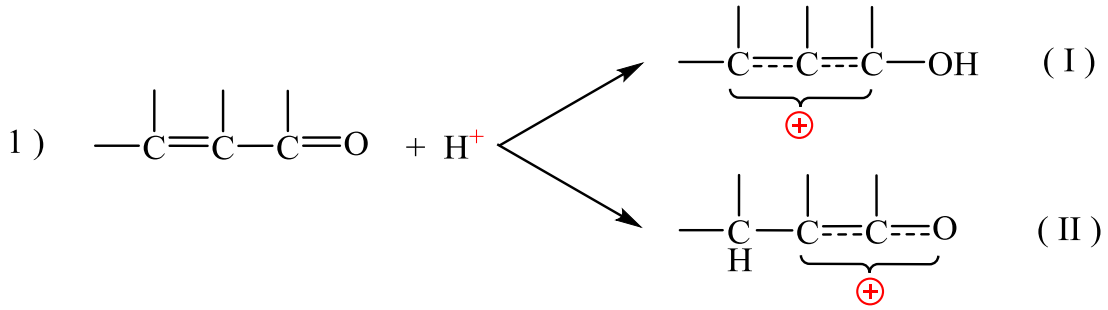


As we can see from the above hybridized structures the β- carbon and the carbonyl carbon bearing a partially positive charge while the carbonyl oxygen bear a partially negative charge:



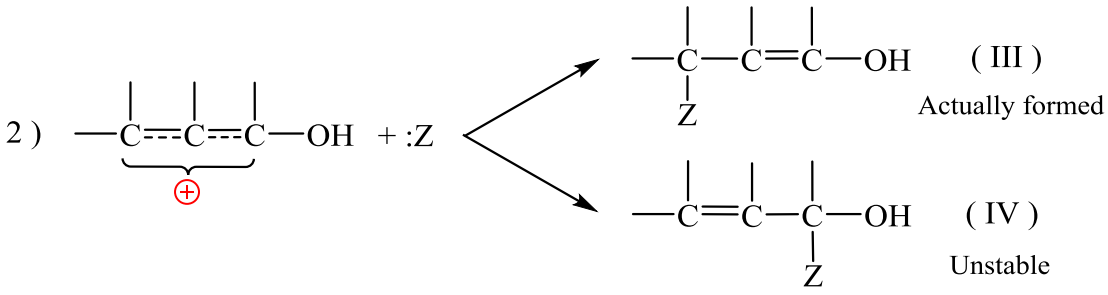
Addition of an electrophile to α,β-unsaturated carbonyl compounds proceed through the formation of more stable carbocation.

Addition can be proceed to either end of the conjugated system taking in our account the stability of the intermediate, thus addition to the carbonyl oxygen end would yield carbocation (I); while addition to the β- carbon end yield carbocation (II).

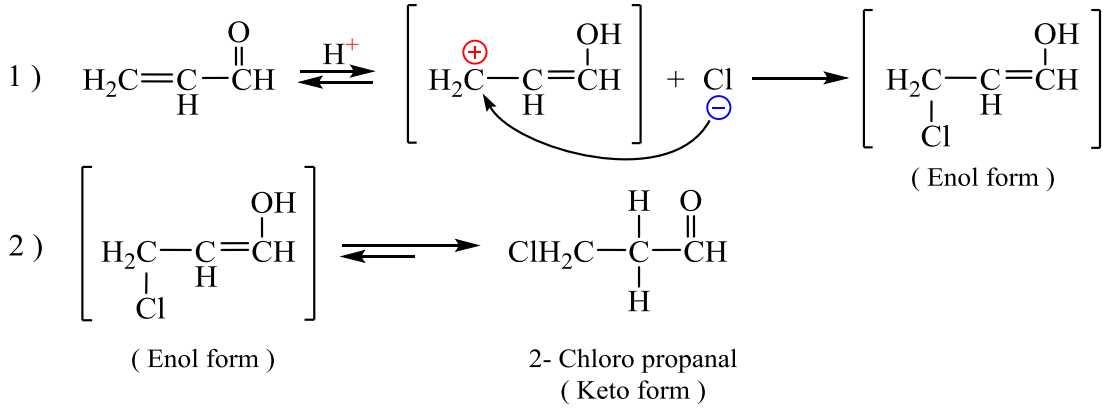


Cation (I) is more stable than cation (II), since the positive charge is carried by carbon atoms alone, rather than partly by the highly electronegative oxygen atom.

In the second step the negative ion or basic molecule attach itself either to the carbonyl carbon or β- carbon of ion (I):

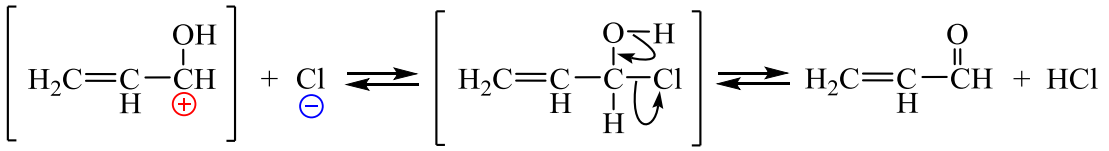


Of the two possibilities, only addition to the β- carbon yields a stable product (III), which is simply the enol form of the saturated carbonyl compound, that undergoes tautomerization to the keto form, as we can see from the following scheme of the addition of HCl gas to acroline:



One can ask why doesn't the nuleophile attack the carbonyl carbon that also bear the positive charge in ion (I) ?

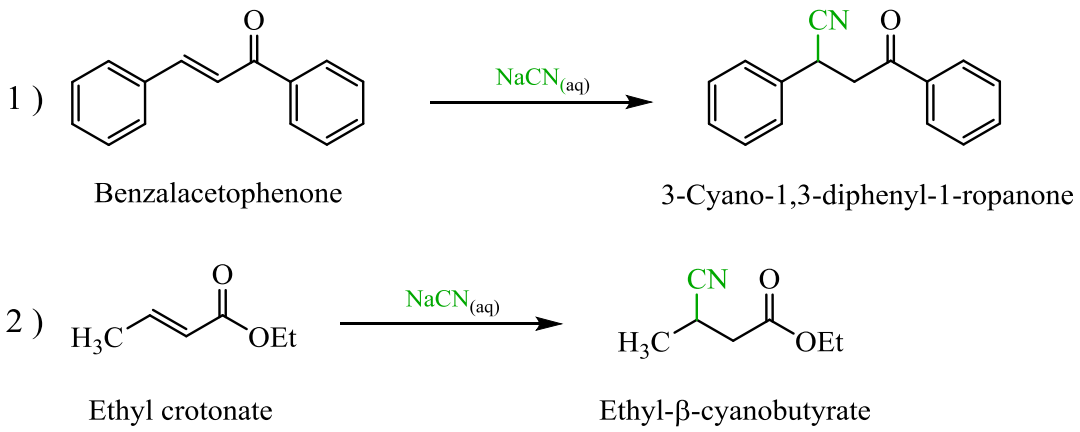
In fact this could be happen, but the product is unstable and convert to the starting material as the following:



3:5) Nucleophilic addition:

Nucleophilic reagents doesn't attack simple alkenes, but in α,β-unsaturated carbonyl compounds the carbon – carbon double bond is polarized, thus nucleophilic reagents could be added to either carbon – carbon double bond or carbon – oxygen double bond.

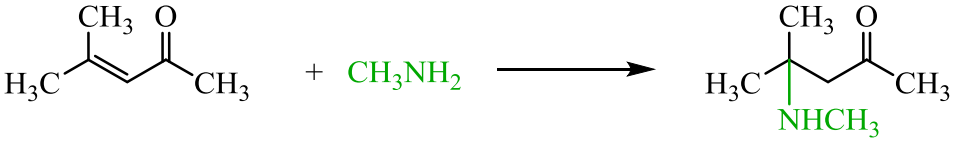
e.g.



Furthermore ammonia or certain derivatives of ammonia (amines, hydroxylamine, phenylhydrazine, --- etc.) added to these compounds to give β-amino carbonyl compounds.

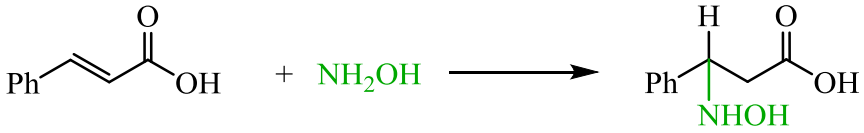
e.g.

1)



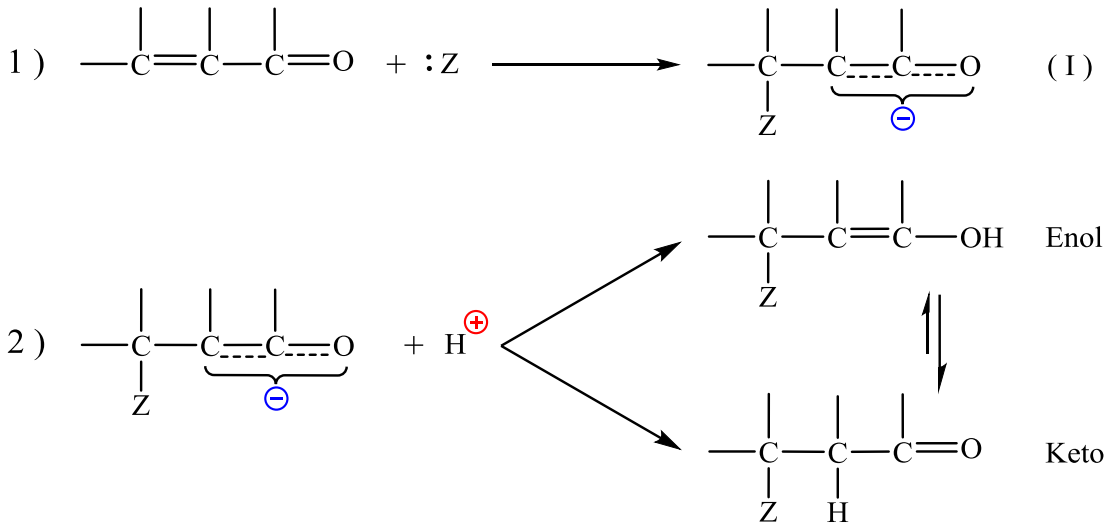
Mesityl oxide Methylamine 4-(N-methylamino)-4-methyl-2-pentanone

2)



Cinnamic acid Hydroxylamine 3-(N-hydroxylamino)-3-phenyl propanoic acid

Mech.: these reactions are believed to take place as the following:

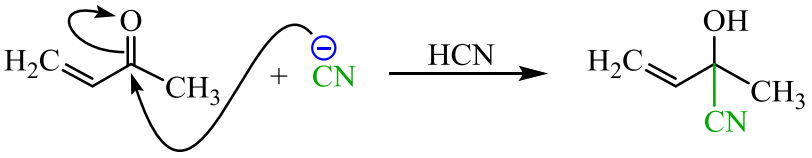


In the first step the nucleophilic reagent adds to the carbon – carbon double bond to give hybrid anion (I), which then accept in step two a hydrogen ion from the solvent to give the final product.
The hydrogen can add either to the α-carbon or to the oxygen, and this will give either the keto or the enol form of the product; in either case the same equilibirium mixture, chiefly keto, is finally obtained.

In the examples that we have just seen, nucleophilic reagent (:Z), is either strongly basic anion, $:CN^-$, or a nuteral base like ammonia and its derivatives, $:NH_2$-G.

These are the same reagents which we have seen, add to the carbonyl group of simple aldehydes and ketones. (Indeed, nucleophilic reagents rearely add to the carbon – carbon double bond of α,β-unsaturated aldehydes, but rather to the highly reactive carbonyl group).

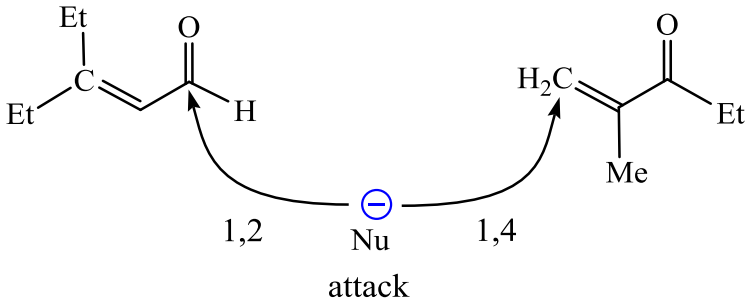
e.g.



Addition of a nucleophile to the carbonyl carbon is known as 1,2-addition, but the addition at the β- carbon is called 1,4- addition.

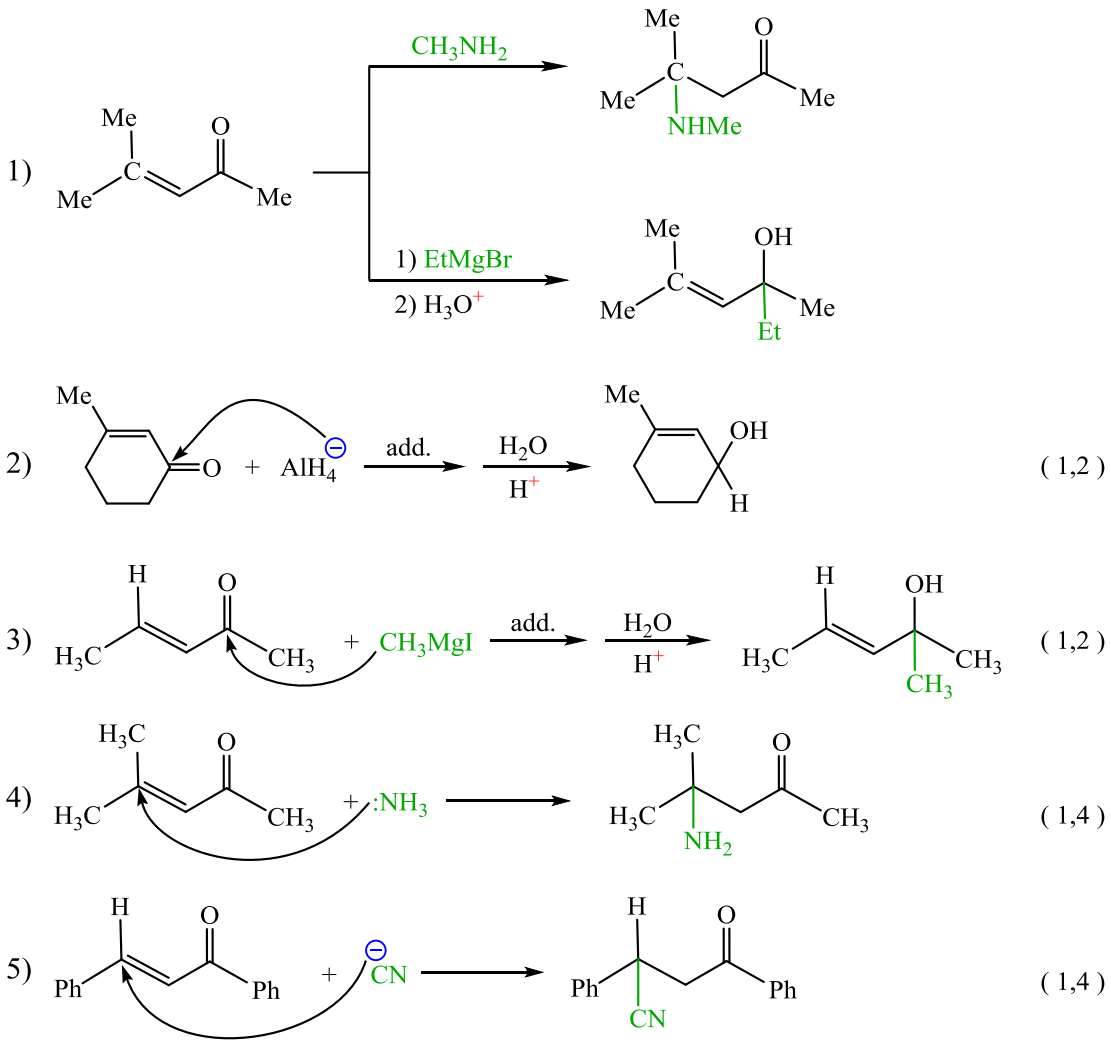
Addition type can be controlled by two factors:

1- Steric hindrance:
Increasing steric hindrance at the carbonyl group will lead to the 1,4- addition product, while increasing steric hindrance at the β-position will lead to the 1,2- addition product.



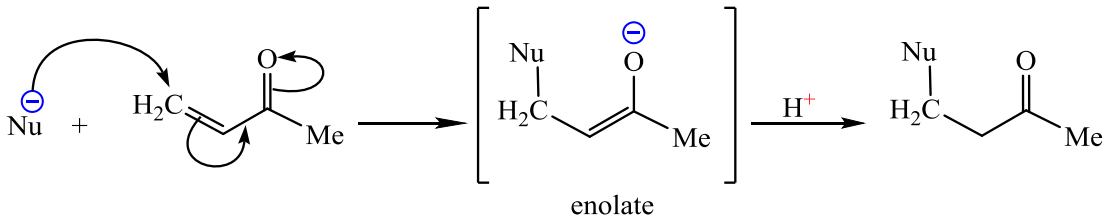
2- Strength of nucleophile:
Strong nucleophiles such as organolithium and Grignard reagents tend to react at the carbonyl group yielding the 1,2-addition products. In contrast weaker nucleophiles such as amines and cyanide ion will react at the β- position yielding the 1,4-addition product.

e.g.



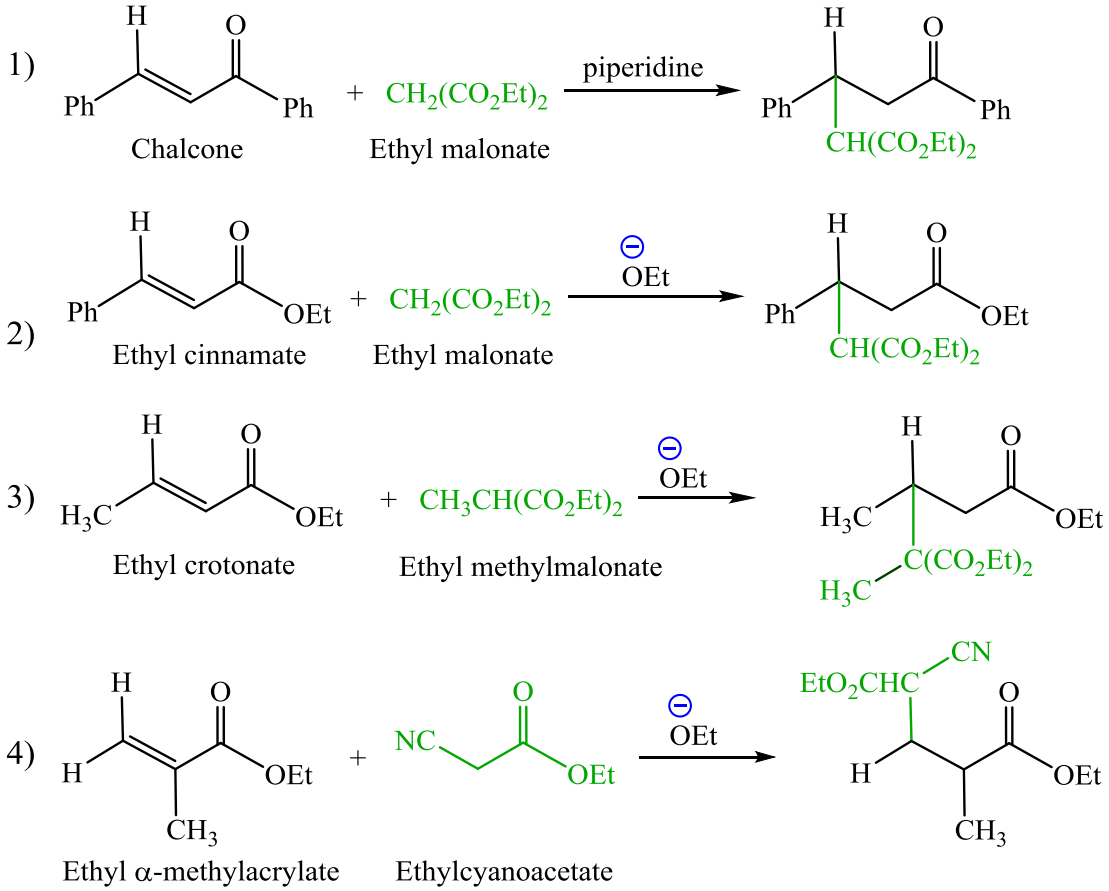
3:6) The Michael addition:

Previously we note that the carbon – carbon double bond that in conjugation with the carbonyl group can be a good reaction center for nucleophilic attack that afford the 1,4-addition reactions as the following:



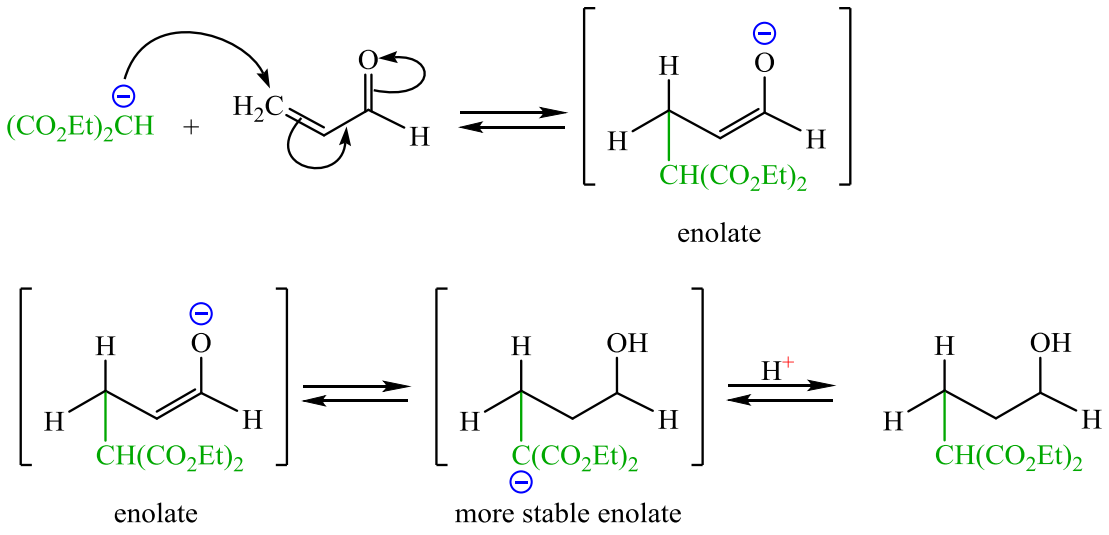
One of special importance in synthesis is the nucleophilic addition of carbanions to α,β-unsaturated carbonyl compounds known as the Michael addition. This reaction results in the formation of carbon – carbon single bond.

e.g.

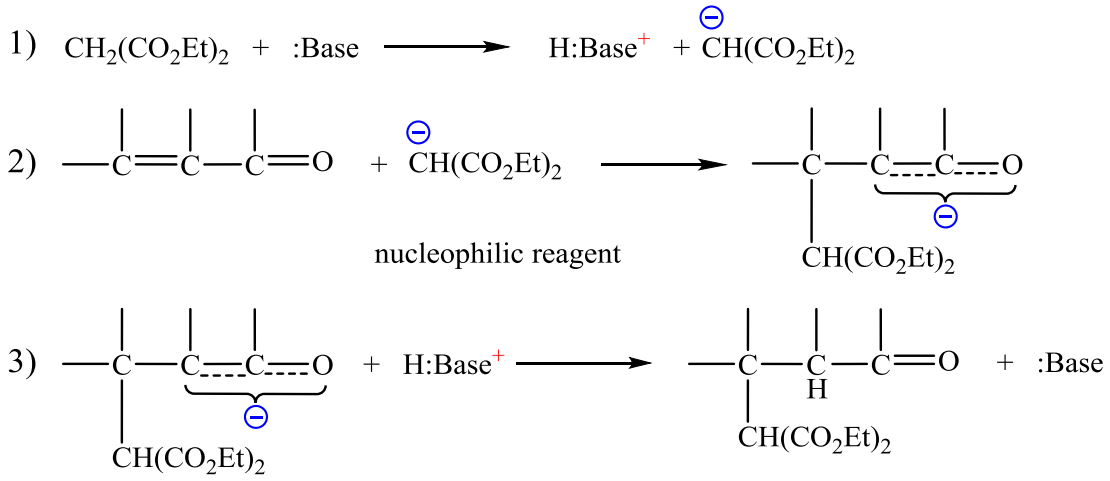


The intermediates are the simply the enolate ion that on protonation give the final 1,4-addition product.

e.g.



The Michael addition is believed to proceed by the following mechanism (shown for malonic ester):

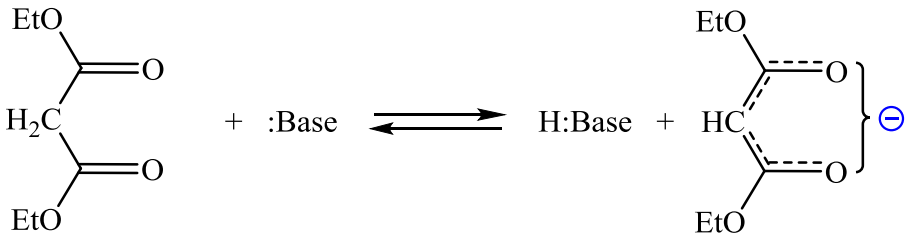


The first step involve abstraction of a hydrogen ion from malonic ester and thus generate a carbanion which act as nucleophilic reagent, then attack the conjugated system in the usual manner (step 2) to give the most stable enolate. The final step involve the addition of a proton to the enolate ion to give the final product.

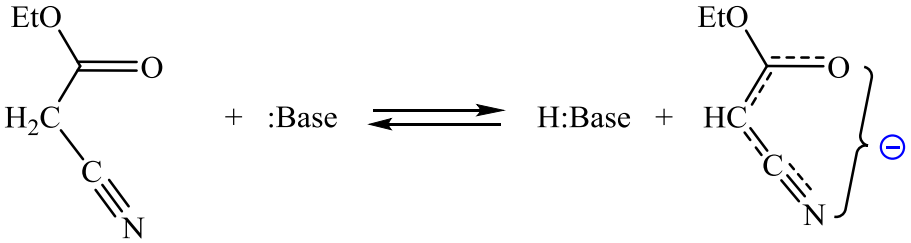
Note:

1- *In place of ethylmalonate, compounds like ethyl cyanoacetate can be used.*

2- *The most stable enolate is due to the presence of two electron-withdrawing groups which can help accommodate the negative charge of the carbanion.*

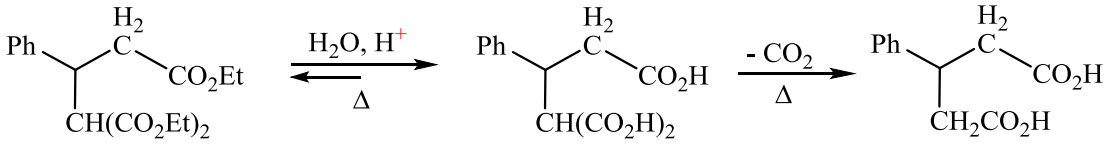


Ethyl malonate



Ethyl cyanoacetate

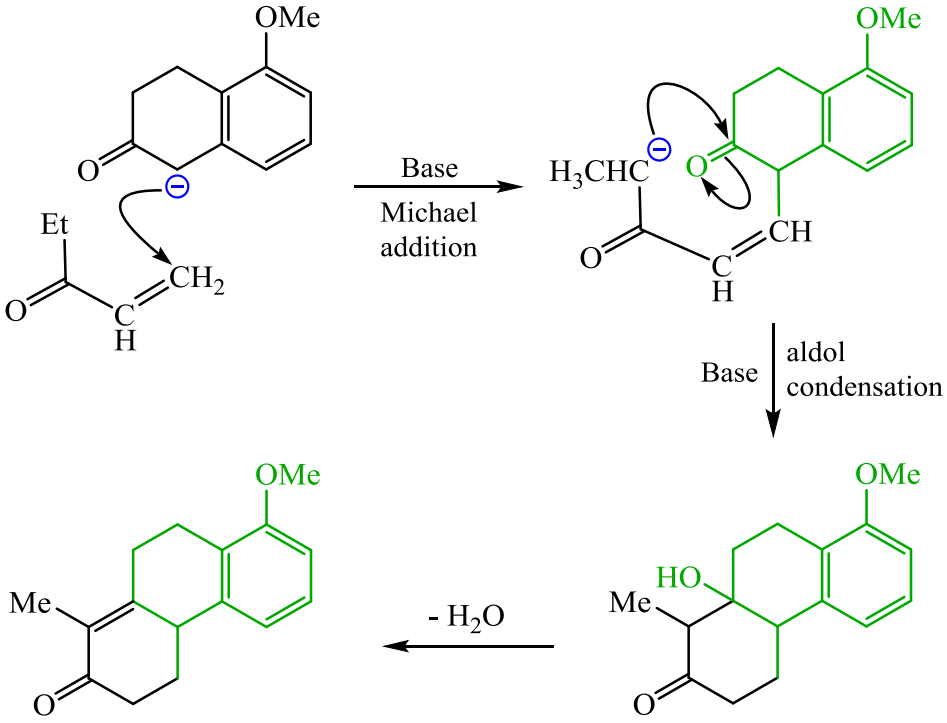
The Michael addition reaction is of great importance in organic synthesis, since if we examine the following reaction:



Tri ester Tri caboxylic acid Di carboxylic acid

Clearly we can see that the starting compound is a tri ester which on saponification and acidification will produce the tri carboxylic acid which can undergoes loss of carbon dioxide molecule to give the di carboxylic acid.

The Michael addition has been used beside other condensation reactions to synthesize important compounds like steroids.



The above reaction is consist of Michael addition and aldol condensation, the overall reaction is called Robinson annulation.

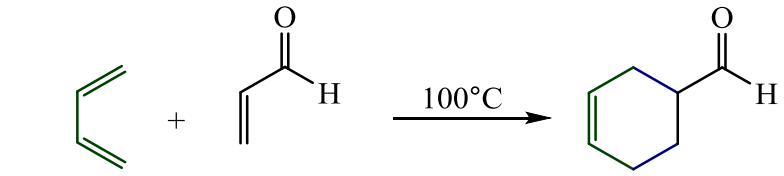
3:7) The Diels – Alder reaction:

α,β-Unsaturated carbonyl compounds undergoes an important and useful reaction with conjugated dienes, known as the Diels – Alder reaction. This is an addition reaction in which C-1 and C-4 of the

conjugated diene system become attached to the doubly – bonded carbons of the unsaturated carbonyl compound to form a six – membered ring.

Note: *Conjugated diene must adopt the s-cis conformation.*

This reaction was discovered by Otto Diels and Kurt Alder which awarded a noble prize in chemistry in 1950 for their discovery.
The reaction takes place by heating a mixture of the conjugated diene and the dienophile to give a six membered ring.
e.g.

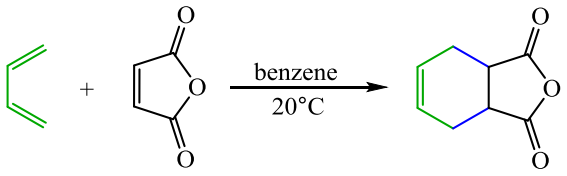


1,3-Butadiene Acroline 3-Cyclohexene-1-carboxaldehyde

This reaction is useful not only because a ring is generated but also because it takes place so readily for a wide variety of reactants. The reaction occurs readily when the dienophile contains a strong electron withdrawing groups, this in contrast with the diene which activated by electron donating groups.
The reaction often takes place with the evolution of heat when reactant simply mixed together.

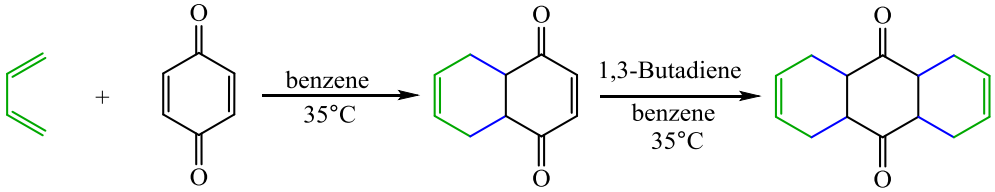
e.g.

1)

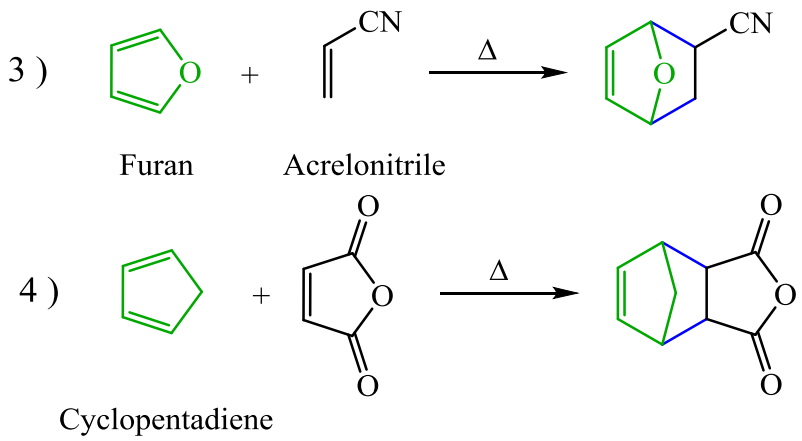


1,3-Butadiene Maleic anhydride Cis-1,2,3,6-tetrahydrophthalic anhydride

2)



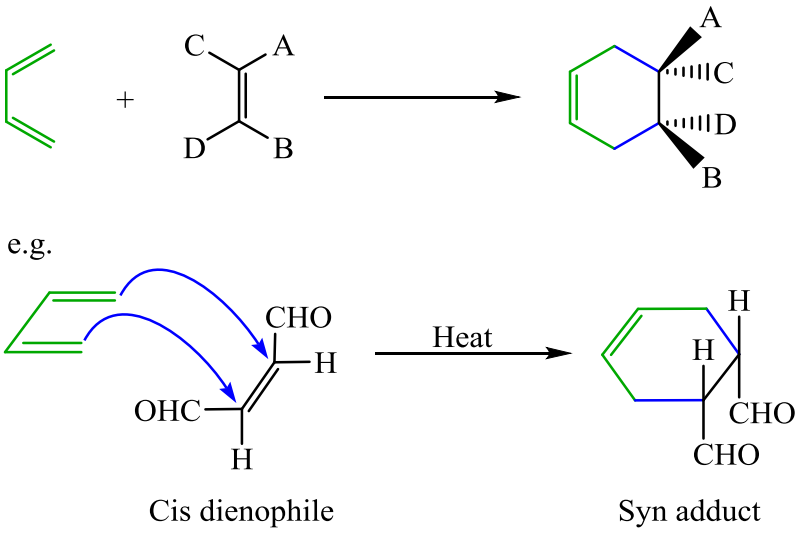
1,3-Butadiene *p*-Benzoquinone 5,8,9,10-Tetrahydro-1,4-naphthoquinone 1,4,5,8,11,12,13,14-Octahydro-9,10-anthraquinone



3.7.1) Stereochemistry of the Diels – Alder reaction:

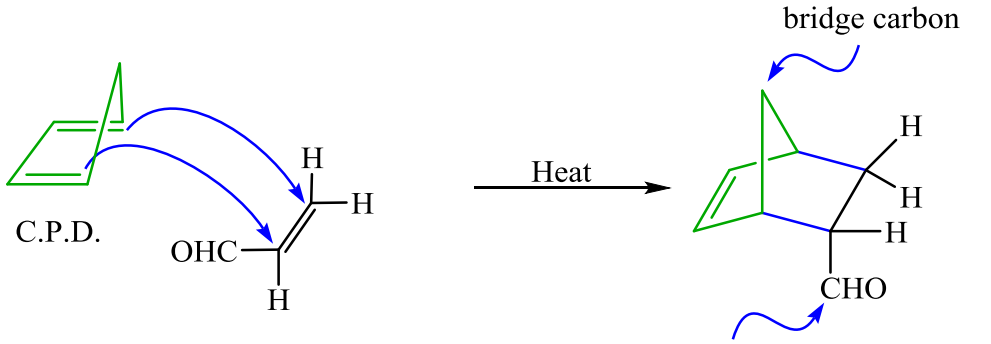
In this reaction, the addition is stereospecifically syn (with respect to the dienophile). This means that groups that are cis in the alkene will be cis in the cyclohexene ring (A – B & C – D), and groups that are trans in the alkene will be trans in the cyclohexene ring (A – D & C – B).

Note: *The reaction is stereospecific and the addition of diene to dienophile occurs from one side (Syn addition).*



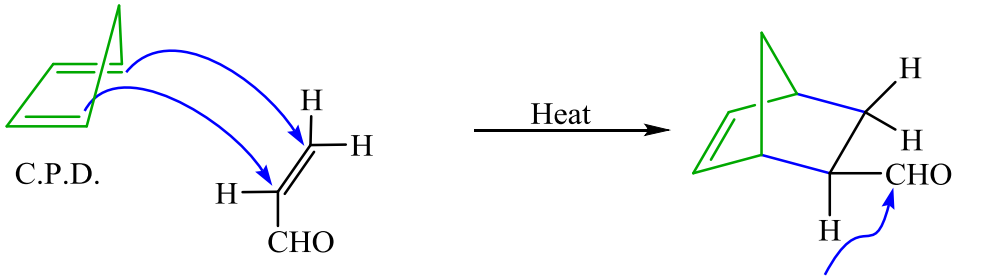
There are two possible ways that the diene approach from the dienophile (i.e. endo addition and exo addition), hence two products may be expected, (endo adduct and exo adduct).

e.g.



Endo addition
The CHO group is under the diene

This group is trans to
the bridge carbon

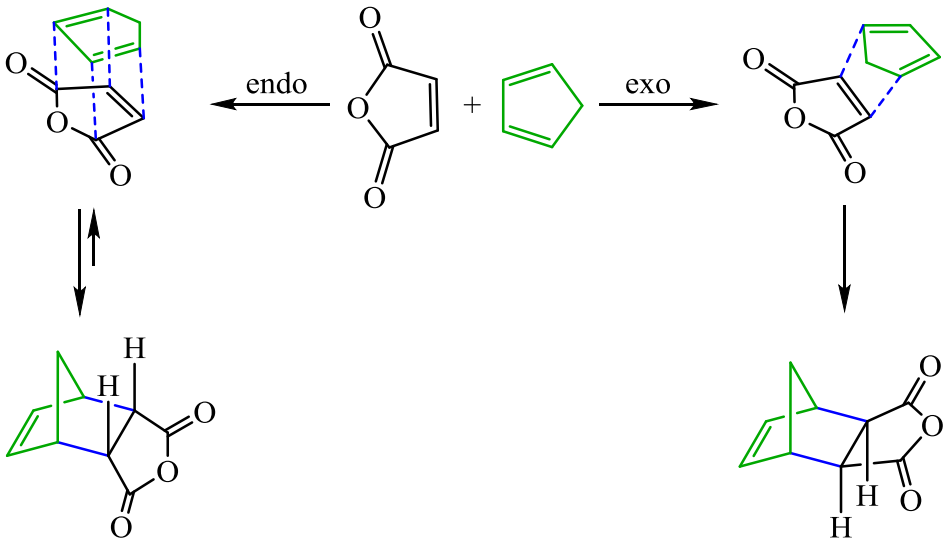


Exo addition
The CHO group lay out relative to
the diene system

This group is cis to
the bridge carbon

Note:

1- *C.P.D. = Cyclopentadiene*
2- *The endo mode of attack is the spatial arrangement of reactants in which the bulkier sides of the diene and dienophile lie one above the other, while in the exo mode of addition the bulkier side of one component is under the small side of the other.*
3- *The endo adduct is usually the major product because of stabilizing secondary orbital interactions in the transition state.*

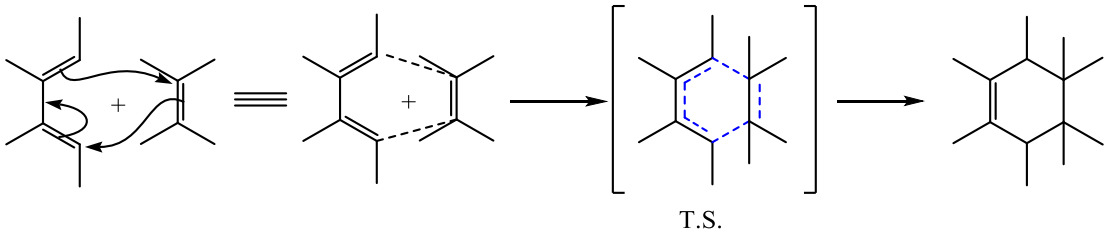


Most of the time, the addition is predominately endo, since most of the addition product adopt the endo stereochemistry due to the overlap between π orbitals of the carbon – carbon bond that formed in the product with those of the dienophile, thus the energy required to reach the transition state will be decreased.

Mechanism of Diels – Alder reaction:

The reaction occurs after the approach of diene and dienophile in a parallel way to each other and in a vertical way to the newly formed bonds.
Broadly speaking, there are three possible mechanisms that have been considered for the Diels – Alder reaction.

In mechanism (a) there is a cyclic six – centered transition state and no intermediate. The formation of the new single bond occurs at the same time (simultaneously) which is known as concerted or pericyclic mechanism.

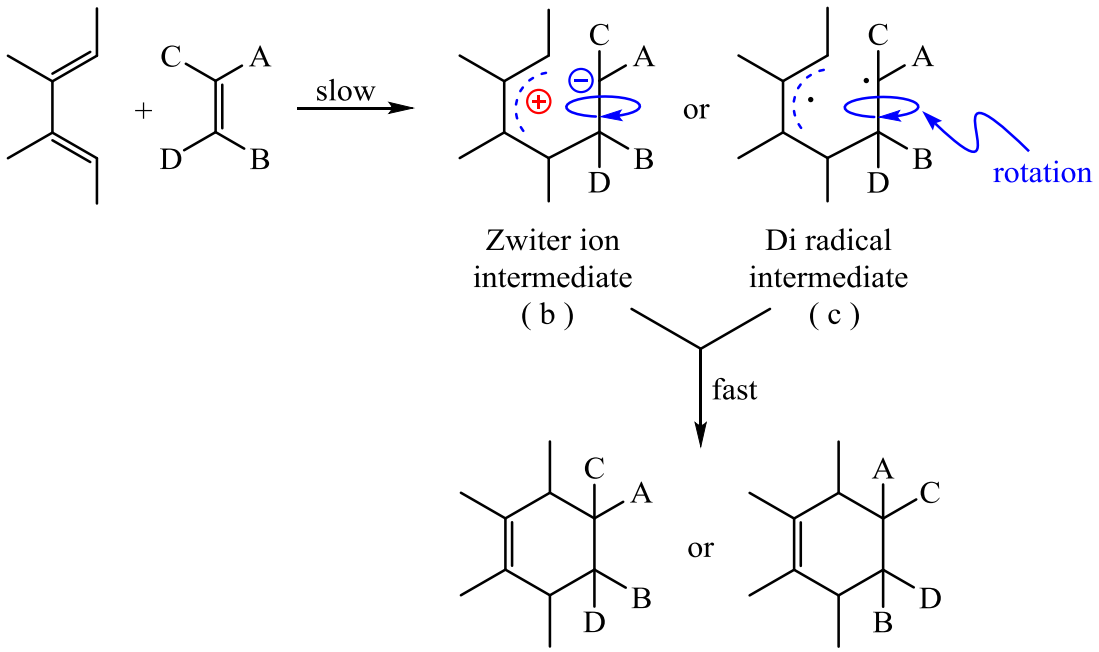


(Concerted or Pericyclic mechanism)

Note: *The reaction occur in one step.*

In mechanism (b), one end of the diene fastens to one end of the dienophile first to give a diradical and then, in the second step, the other end becomes fastened. The first step is the (R.D.S.) i.e. slow step while the second step is fast.

The third mechanism (c) is similar to (b) but the first step involve the formation of intermediate which is a di ion (zwitter ion), this step is also slow (i.e. R.D.S.), while the second step is fast.



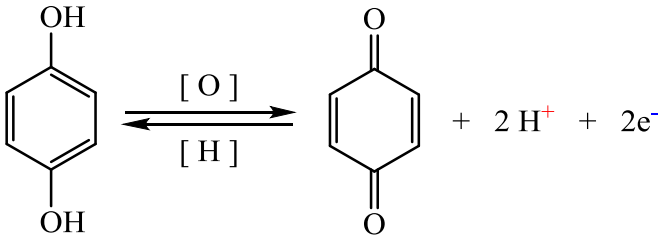
(Mechanisms b & c)

All of the above mechanisms are possible but the main evidence that support mechanism a (one step cyclic mechanism) is the reaction is stereospecific in both of the diene and dienophile.

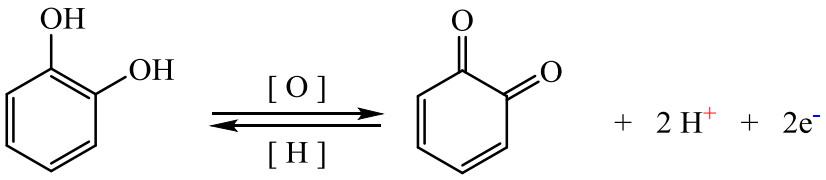
Note: *A completely di radical (b) or di ion (c) probably would not be able to retain its configuration.*

3:8) Quinones:

Quinones are a special type of α,β-unsaturated ketones, these are cyclic di ketones of such a structure that they are converted by reduction into hydroquinones. The simplest quinones are 1,4-benzoquinone and 1,2-benzoquinone which also called *p*-benzoquinone and *o*-benzoquinone respectively. The latter compounds prepared by oxidation of hydroquinone and caticol by the use of mild oxidizing agents like ferric ion (Fe^{+3}) or silver ion.



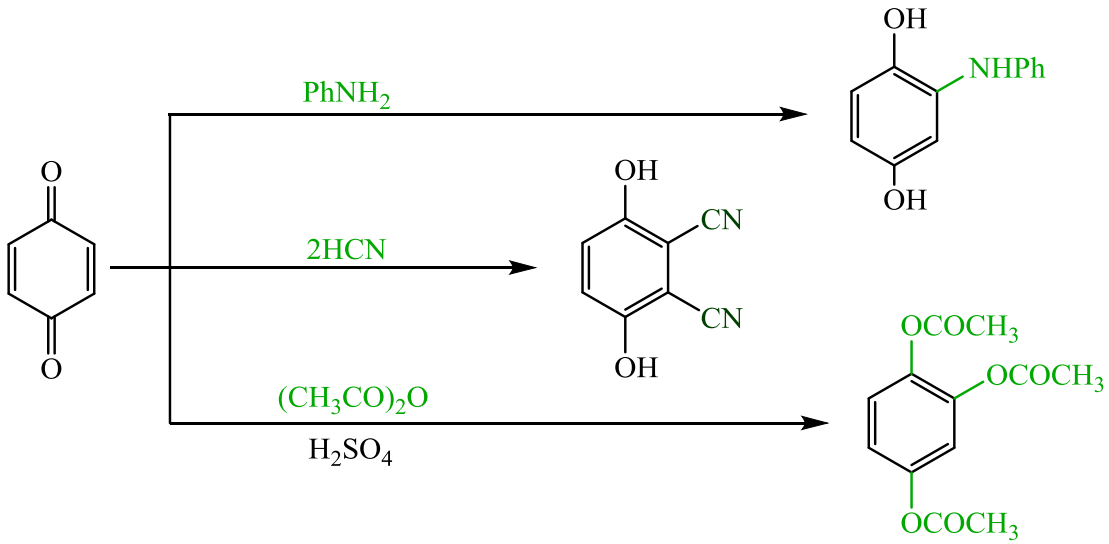
Hydroquinone 1,4-Benzoquinone



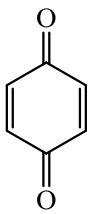
Caticol 1,2-Benzoquinone

Simple hydroquinones are colorless, on the other hand all quinones are colored, due to their highly conjugation.
The capability of hydroquinone to reduce silver ion is the basic feature in the chemistry of photography.
Hydroquinones can be oxidized by either ferric chloride, manganese dioxide – sulfuric acid or by dichromate. The best oxidizing agent is silver oxide in dry ether in the presence of anhydrous sodium sulfate that abstract water from the reaction medium during oxidation.

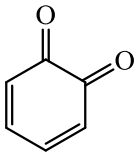
Simple quinones undergoes nucleophilic addition as the following:



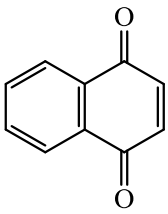
The last reaction is known as Thiele acylation.
Many compounds that contain the quinone system have been used as a dyes such as:



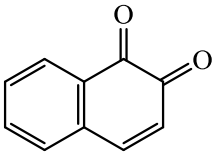
1,4-Benzoquinone
yellow



1,2-Benzoquinone
red



1,4-Naphthoquinone
yellow



1,2-Naphthoquinone
yellow - red