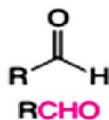




Aldehydes & Ketones

Structure

Aldehydes are compounds of the general formula RCHO; ketones are compounds of the general formula RR'CO. The groups R and R' may be aliphatic or aromatic.

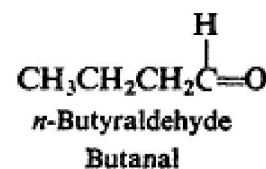
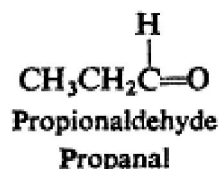
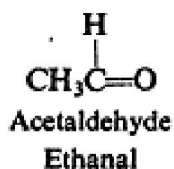
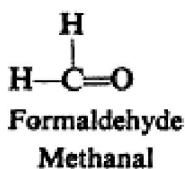


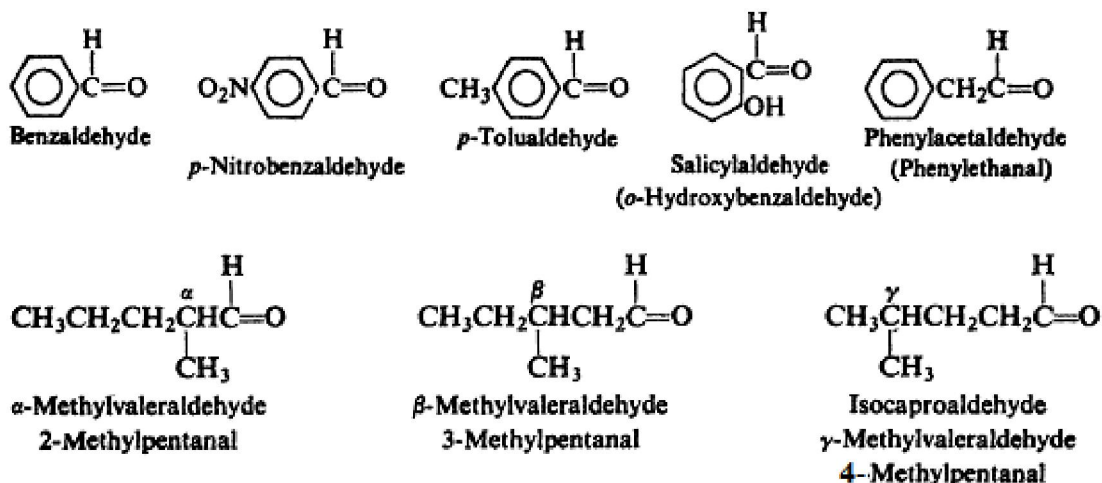
Both aldehydes and ketones contain the carbonyl group, C=O, and are often referred to collectively as carbonyl compounds. It is the carbonyl group that largely determines the chemistry of aldehydes and ketones. Aldehydes and ketones resemble each other closely in most of their properties. However, there is a hydrogen atom attached to the carbonyl group of aldehydes, and there are two organic groups attached to the carbonyl group of ketones. This difference in structure affects their properties in two ways: (a) aldehydes are quite easily oxidized, whereas ketones are oxidized only with difficulty; (b) aldehydes are usually more reactive than ketones toward nucleophilic addition, the characteristic reaction of carbonyl compounds.

Nomenclature

The common names of aldehydes are derived from the names of the corresponding carboxylic acids by replacing -ic add by -aldehyde .

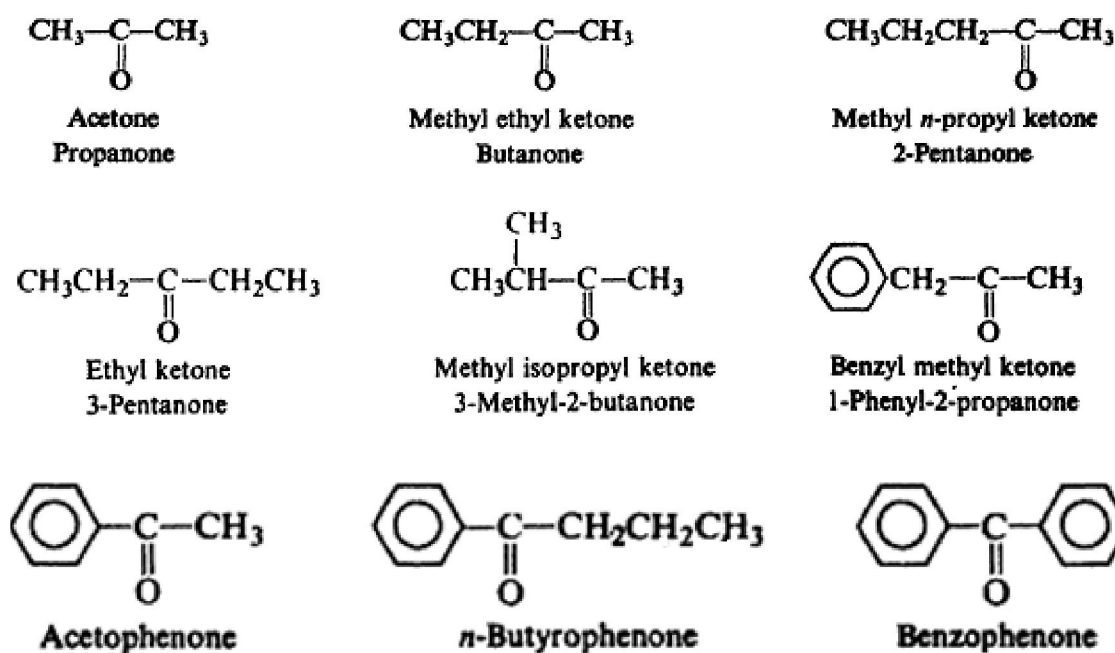
The IUPAC names of aldehydes follow the usual pattern. The longest chain carrying the CHO group is considered the parent structure and is named by replacing the -e of the corresponding alkane by -al. The position of a substituent is indicated by a number, the carbonyl carbon always being considered as C-1 . Here, as with the carboxylic acids, we notice that C-2 of the IUPAC name corresponds to alpha of the common name.

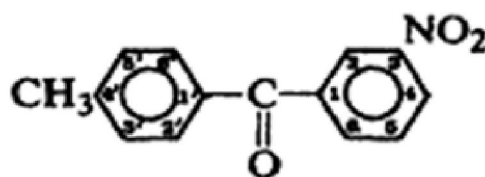




The simplest aliphatic ketone has the common name of acetone. For most other aliphatic ketones we name the two groups that are attached to carbonyl carbon, and follow these names by the word ketone. A ketone in which the carbonyl group is attached to a benzene ring is named as a -phenone, as illustrated below .

According to the IUPAC system, the longest chain carrying the carbonyl group is considered the parent structure, and is named by replacing the -e of the corresponding alkane with -one. The positions of various groups are indicated by numbers, the carbonyl carbon being given the lowest possible number.





3-Nitro-4'-methylbiphenyl-4-one

Physical properties

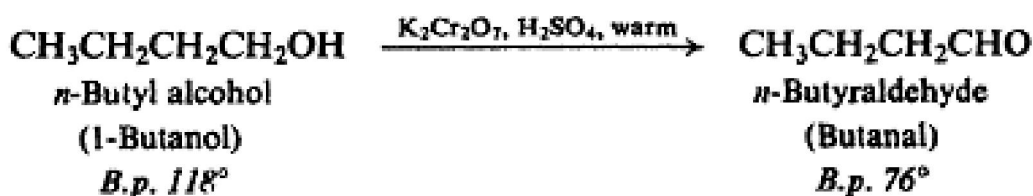
The polar carbonyl group makes aldehydes and ketones polar compounds, and hence they have higher Boiling points than non-polar compounds of comparable molecular weight. By themselves, they are not capable of intermolecular hydrogen bonding since they contain hydrogen bonded only to carbon; as a result they have lower boiling points than comparable alcohols or carboxylic acids. .

The lower aldehydes and ketones are appreciably soluble in water, presumably because of hydrogen bonding between solute and solvent molecules; borderline solubility is reached at about five carbons. Aldehydes and ketones are soluble in the usual organic solvents.

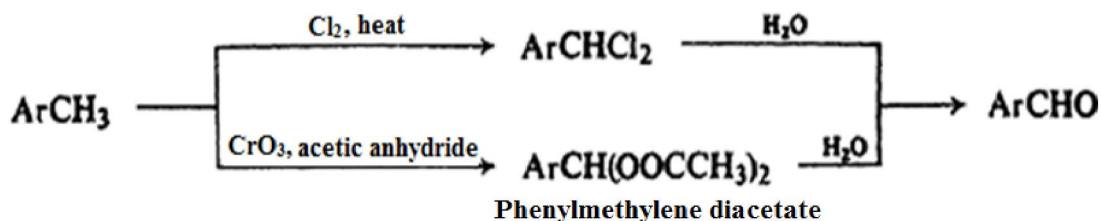
Preparation

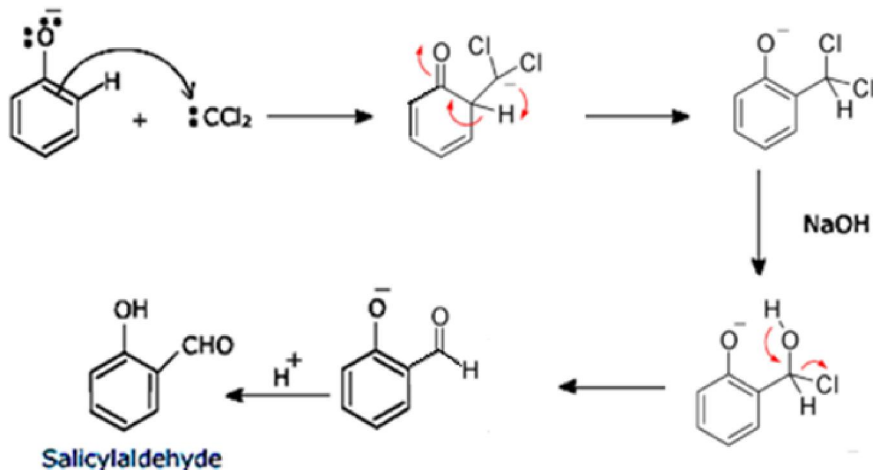
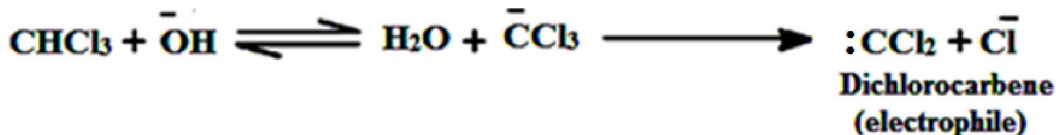
a-Preparation of aldehydes by oxidation methods

1. Oxidation of primary alcohols.



2. Oxidation of methylbenzenes.

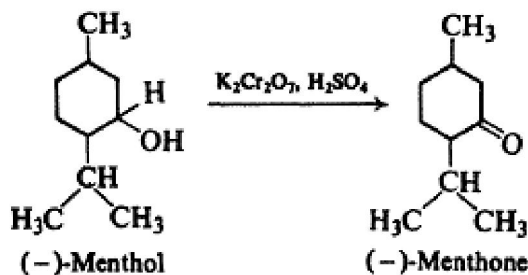




b- Preparation of ketones

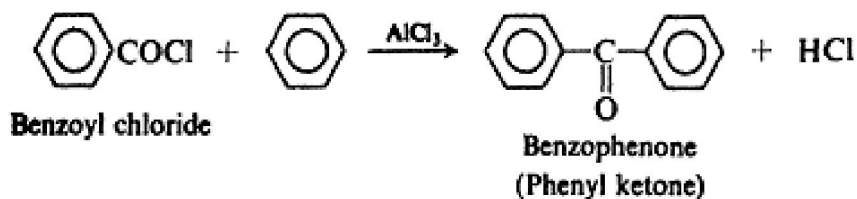
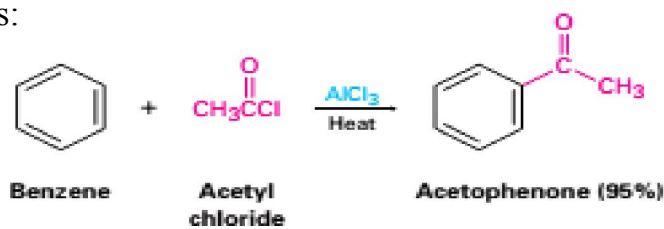
1. Oxidation of secondary alcohols.

Example:

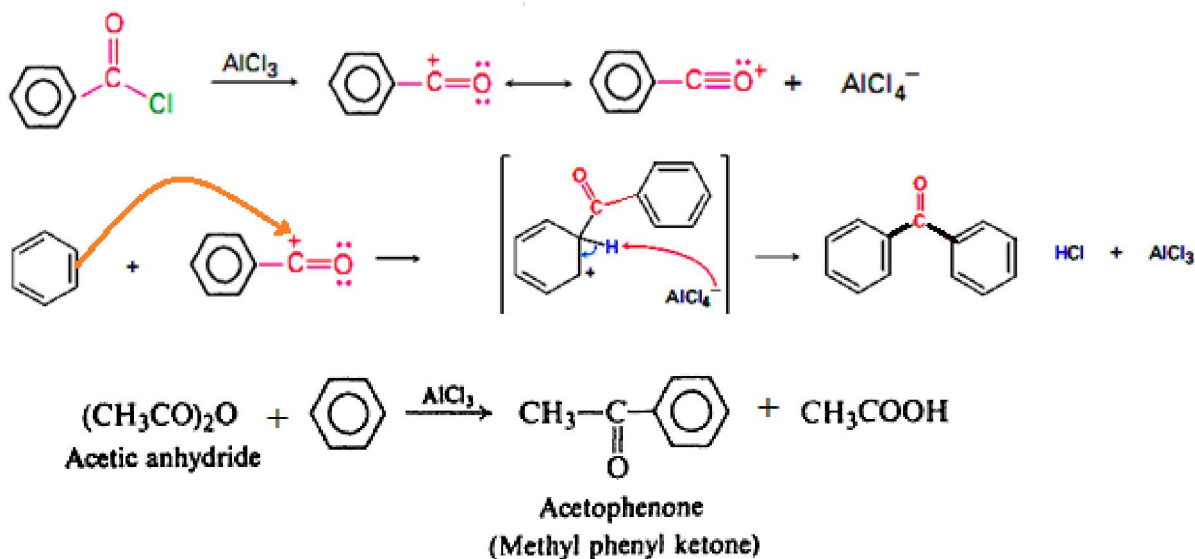


2. Friedel-Crafts acylation.

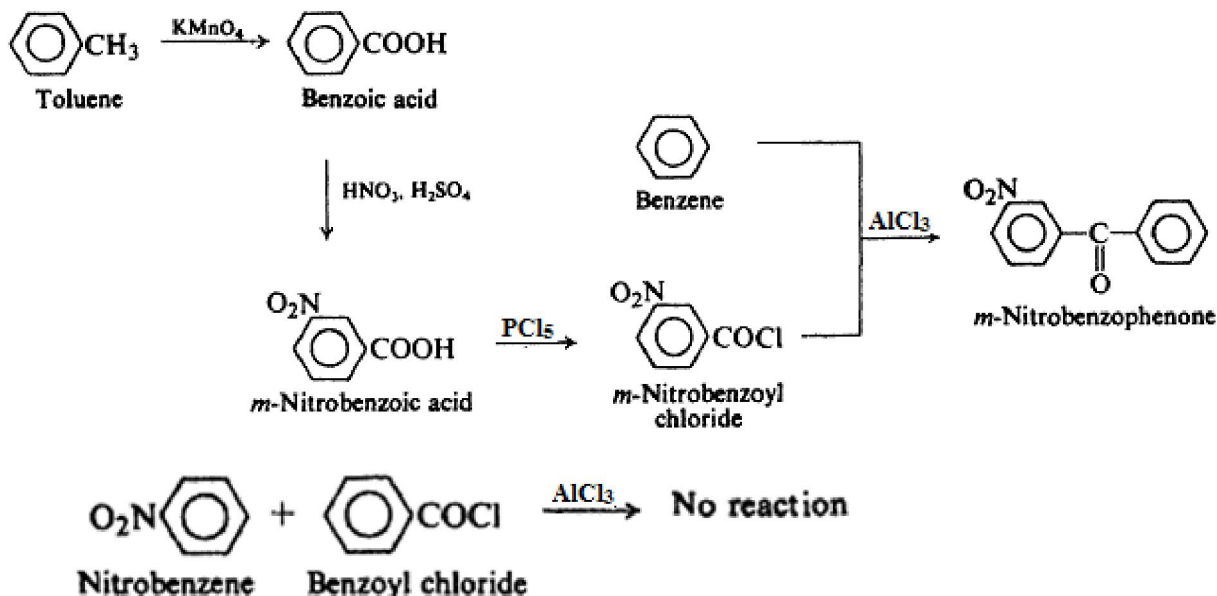
Examples:



Mechanism:



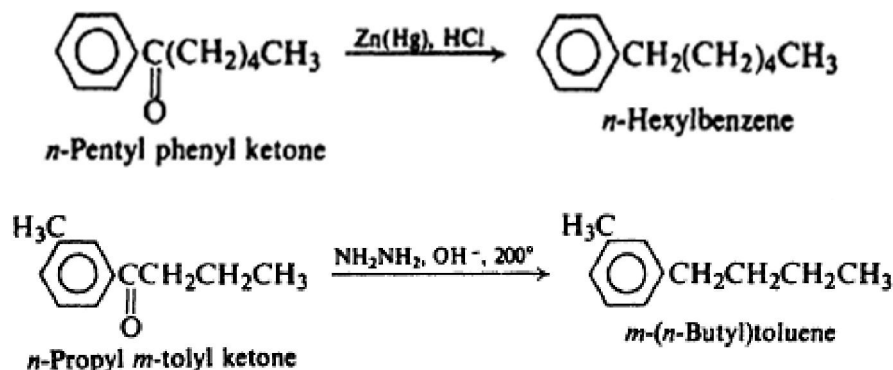
In planning the synthesis of diaryl ketones, ArCOAr , it is particularly to select the right combination of ArCOCl and ArH . In the important preparation of *m*-nitrobenzophenone, for example, the nitro group can be present in the acid chloride but not in the ring undergoing substitution, since as a strongly deactivating group it prevents the Friedel-Crafts reaction.



Of particular importance is the conversion of the acyl group into an alkyl group. This can be accomplished by the **Clemmensen reduction** (amalgamated zinc and



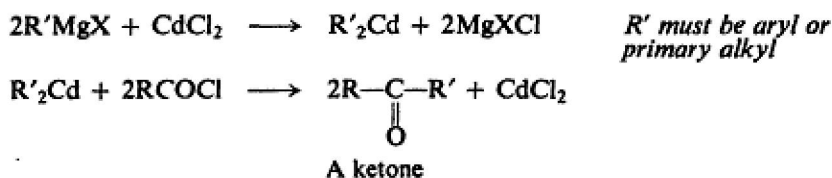
concentrated hydrochloric acid), or the **Wolff-Kishner reduction** (hydrazine and base). For example:



A straight-chain alkyl group longer than ethyl generally cannot be attached in good yield to an aromatic ring by Friedel-Crafts alkylation because of rearrangement.

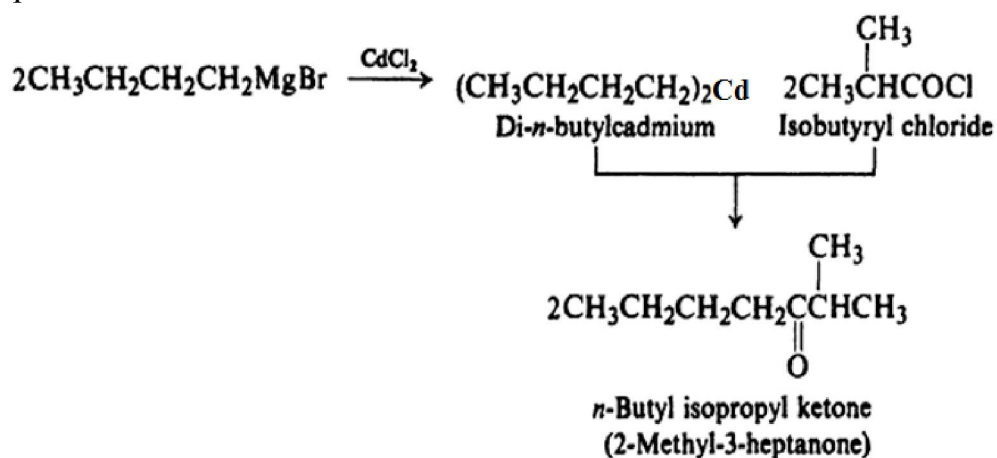
3. Reaction of acid chlorides with organocadmium compounds.

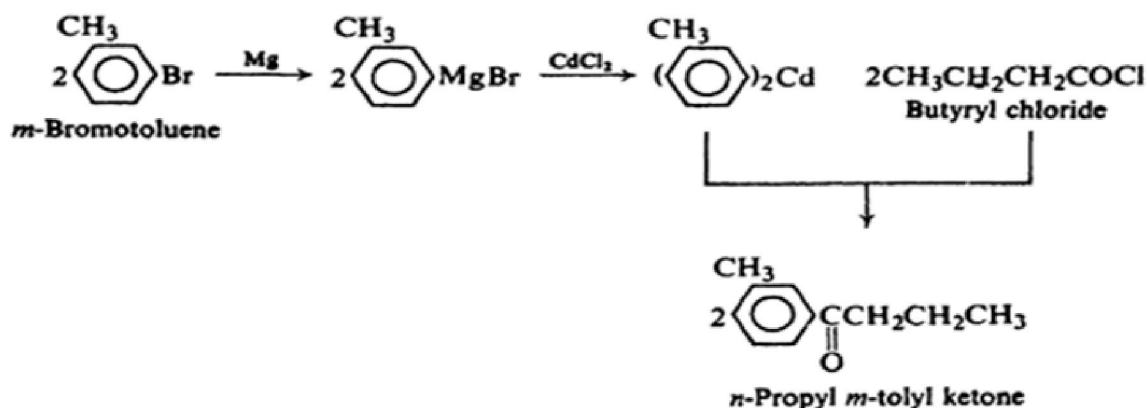
Grignard reagents react with dry cadmium chloride to yield the corresponding organocadmium compounds, which react with acid chlorides to yield ketones :



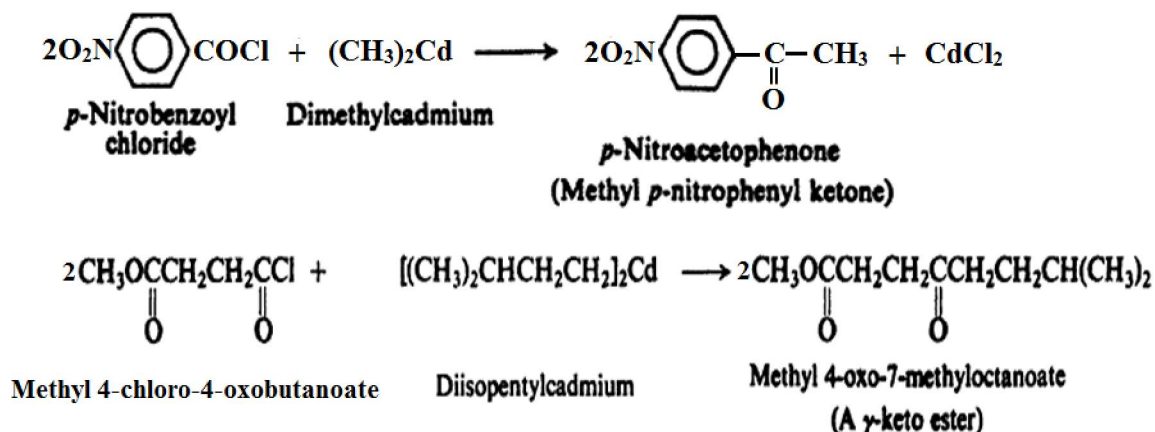
The acid chloride is undergoing nucleophilic substitution, the nucleophile being the basic alkyl or aryl group of the organometallic compound.

Examples:





The comparatively low reactivity of organocadmium compounds not only makes the synthesis of ketones possible, but in addition widens the applicability of the method. Organocadmium compounds do not react with many of the functional groups with which the Grignard reagent does react: $-\text{NO}_2$, $-\text{CN}$, $-\text{CO}$, $-\text{COOR}$, for example. Consequently, the presence of one of these groups in the acid chloride molecule does not interfere with the synthesis of a ketone. For example:

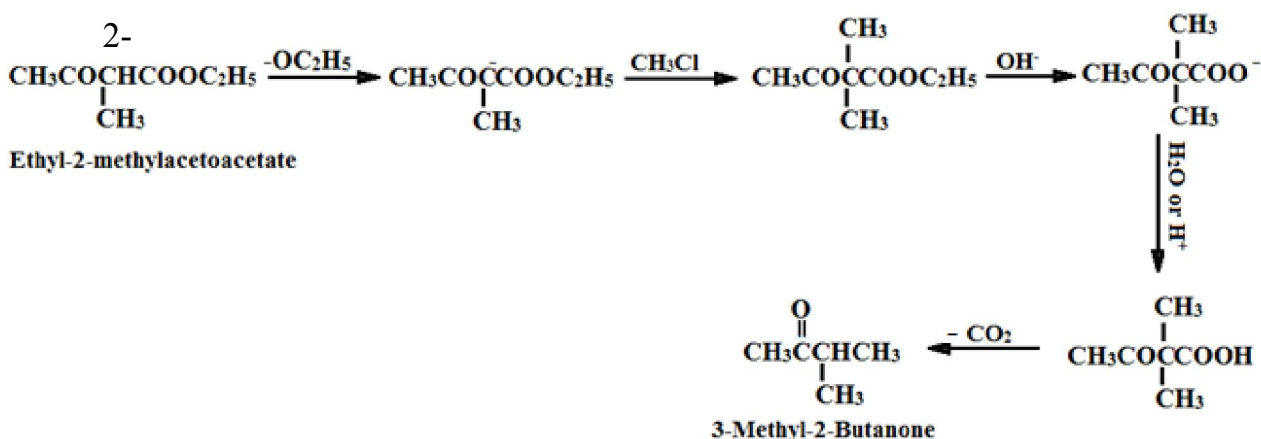
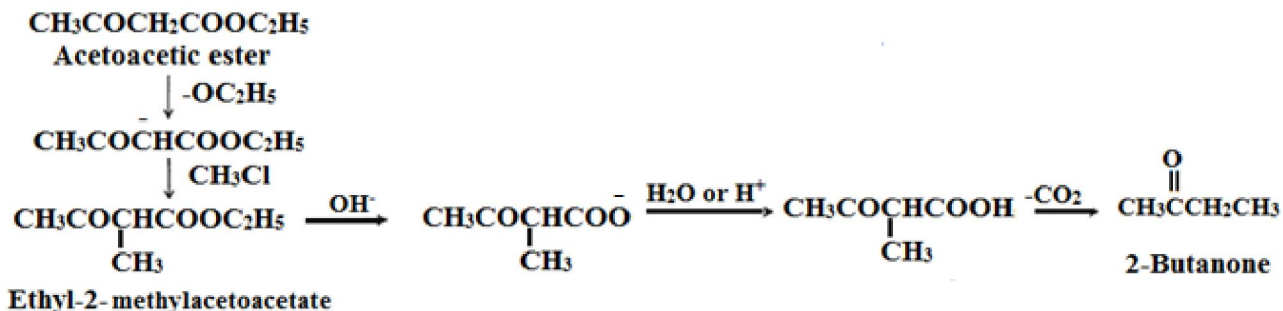


4. Acetoacetic ester synthesis.

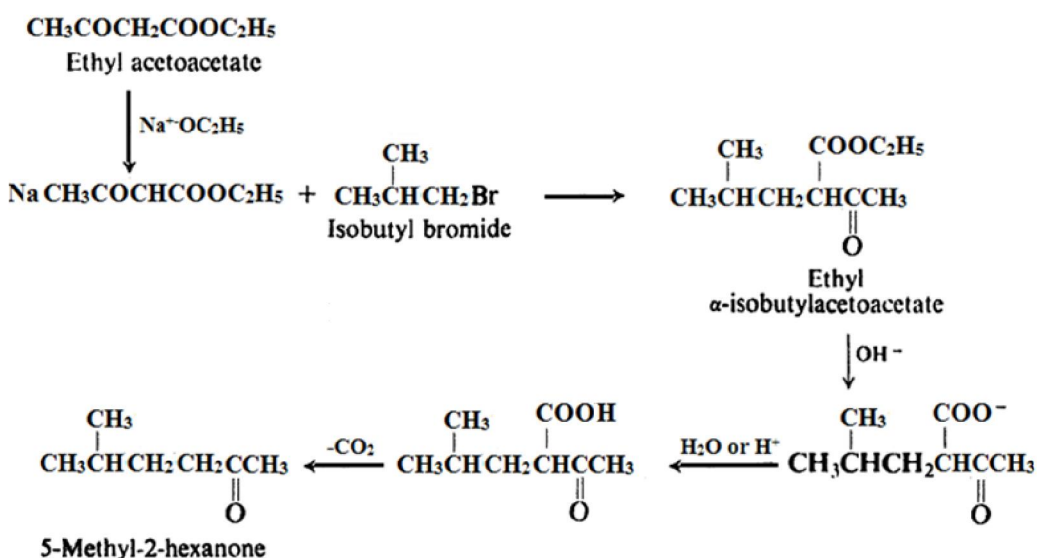
One of the most valuable methods of preparing ketones makes use of ethylacetoacetate (acetoacetic ester), $\text{CH}_3\text{COCH}_2\text{COOC}_2\text{H}_5$, and is called the acetoacetic ester synthesis of ketones. Acetoacetic ester is converted by sodium ethoxide into the sodioacetoacetic ester, which is then allowed to react with an alkyl halide to form an alkylacetoacetic ester (an ethyl alkylacetoacetate), $\text{CH}_3\text{COCHRCOOC}_2\text{H}_5$ if desired, the alkylation can be repeated to yield a dialkylacetoacetic ester, $\text{CH}_3\text{COCRR}'\text{COOC}_2\text{H}_5$. All are conducted in absolute alcohol.



Examples: 1-



The acetoacetic ester synthesis of ketones yields an acetone molecule in which one or two hydrogens have been replaced by alkyl groups. For example - 5-methyl-2-hexanone can be considered as acetone in which one hydrogen has been replaced by an isobutyl group.

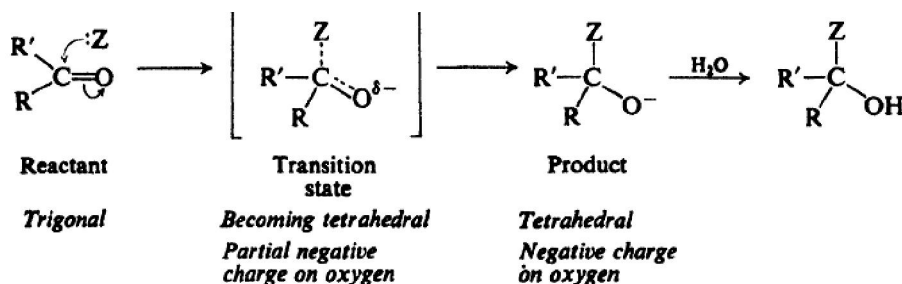




Reactions

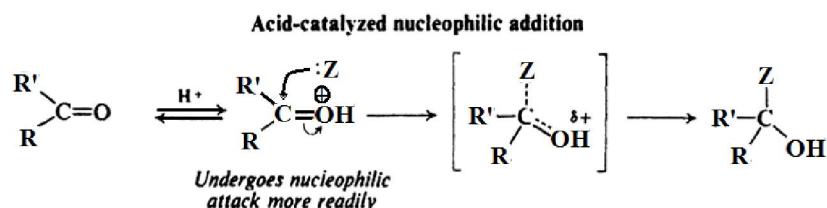
Nucleophilic addition

The carbonyl group, C=O, governs the chemistry of aldehydes and ketones. It does this in two ways: (a) by providing a site for nucleophilic addition and (b) by increasing the acidity of the hydrogen atoms attached to the alpha carbon. The important step in these reactions is the formation of a bond to the electron-deficient (acidic) carbonyl carbon.



Aldehydes generally undergo nucleophilic addition more readily than ketones. This difference in reactivity is consistent with the transition states involved, and seems to be due to a combination of electronic and steric factors. A second alkyl or aryl group of a ketone is larger than the hydrogen of an aldehyde, and resists more strongly the crowding together in the transition state. An alkyl group releases electrons, and thus destabilizes the transition state by intensifying the negative charge developing on oxygen.

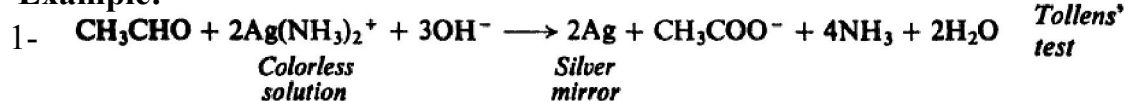
If acid is present, hydrogen ion becomes attached to carbonyl oxygen. This prior protonation lowers the E_{act} for nucleophilic attack, since it permits oxygen to acquire the π electrons without having to accept a negative charge. Thus nucleophilic addition to aldehydes and ketones can be catalyzed by acids (sometimes, by Lewis acids).



1. Oxidation.

(a) Aldehydes

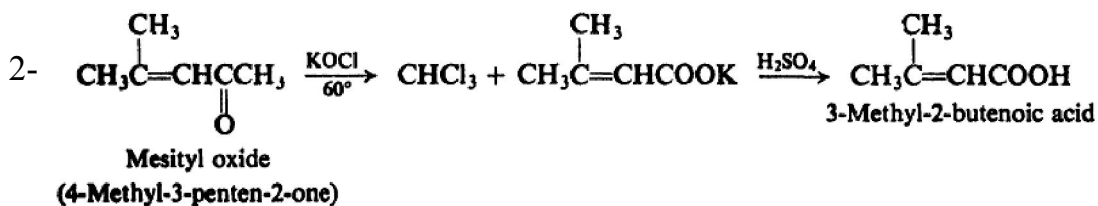
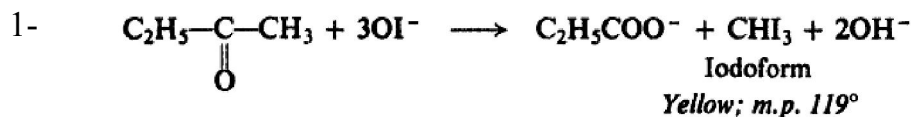
Example:





(b) Methyl ketones

Examples:

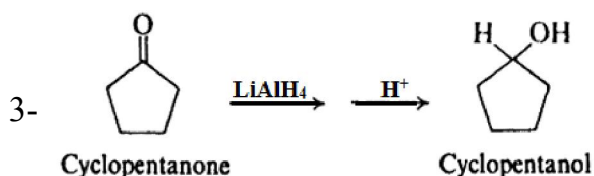
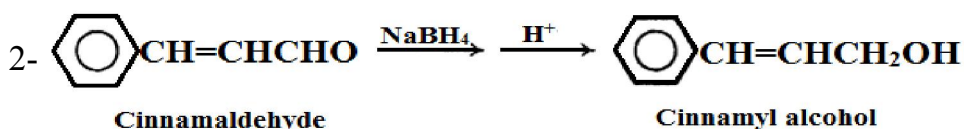
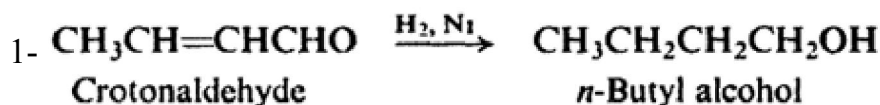


2-Reduction:

a) Reduction to alcohol

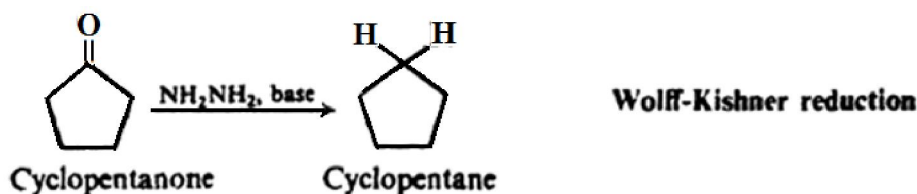
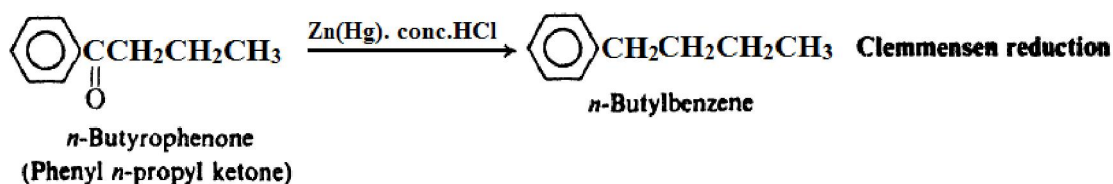
Aldehydes can be reduced to primary alcohols, and ketones to secondary alcohols, either by catalytic hydrogenation or by use of chemical reducing agents like lithium aluminum hydride, LiAlH_4 .

Examples:



b) Reduction to hydrocarbons.

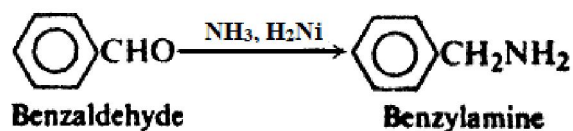
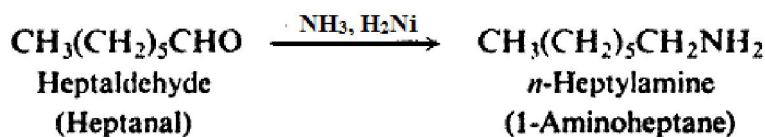
Aldehydes and ketones can be reduced to hydrocarbons by the action of (a) amalgamated zinc and concentrated hydrochloric acid, **the Clemmensen reduction**; or (b) of hydrazine NH_2NH_2 and a strong base like KOH or potassium *tert*-butoxide, **the Wolff-Kishner reduction**.



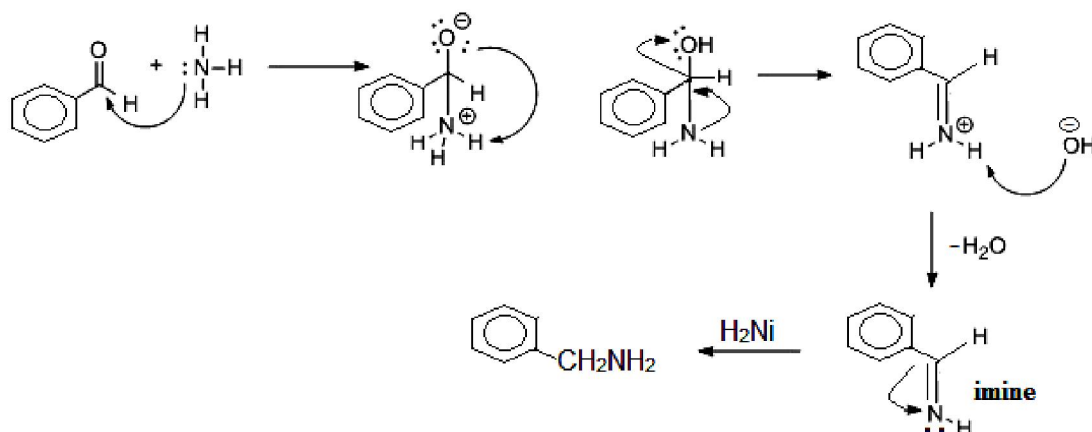
c) Reductive amination

Many aldehydes and ketones are converted into amines by reductive amination. Reduction can be accomplished catalytically or by use of sodium cyanohydridoborate, NaBH₃CN. Reaction involves reduction of an intermediate compound (an imine, RCH=NH) or (R₂C=NH) that contains a carbon -nitrogen double bond.

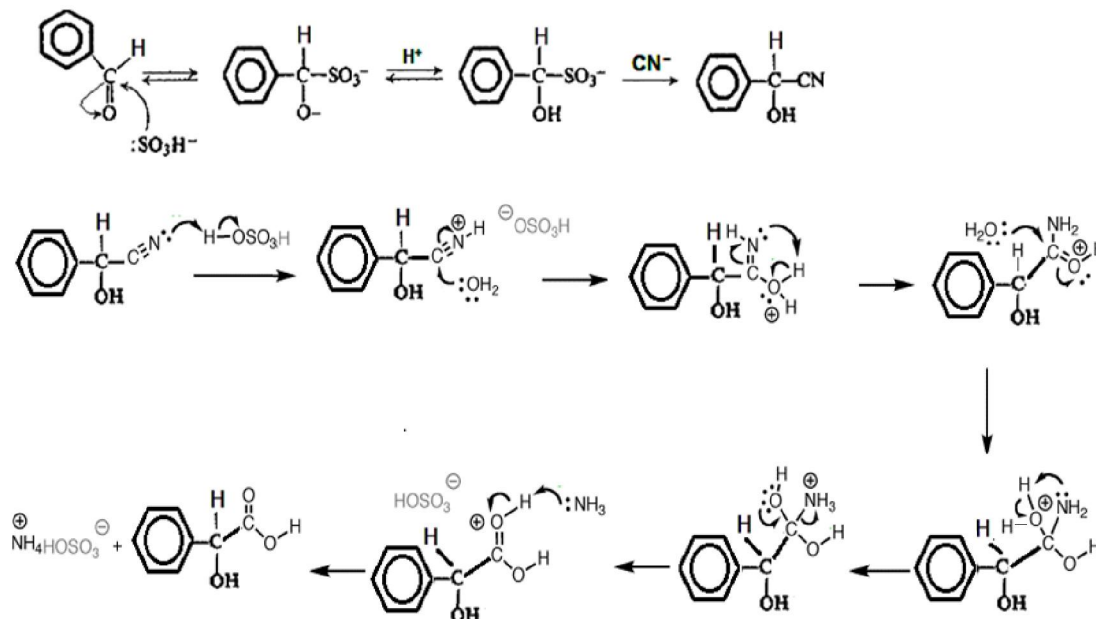
Examples:



The Mechanism of the reaction

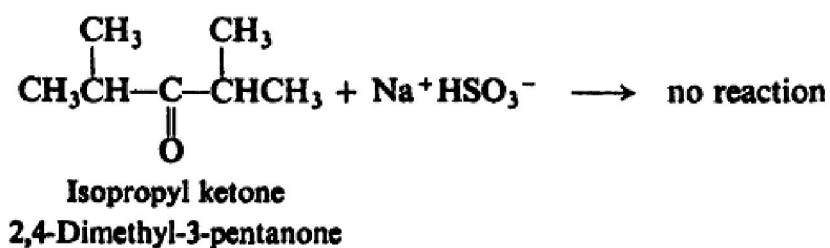
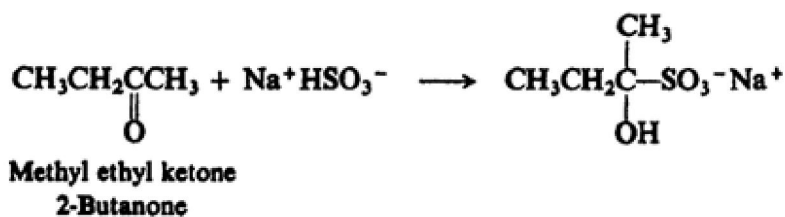


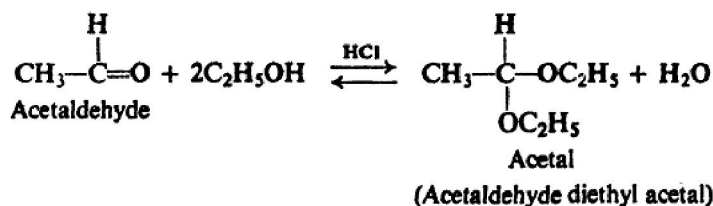
The mechanism of the reaction



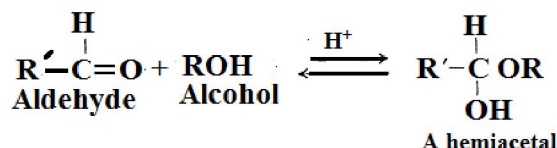
5-Addition of bisulfite

The reaction is carried out by mixing the aldehyde or ketone with a concentrated aqueous solution of sodium bisulfite. Ketones containing bulky groups usually fail to react with bisulfite, presumably for steric reasons.

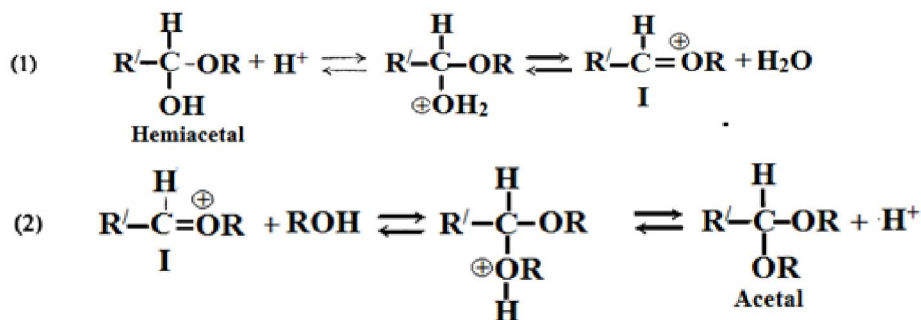




There is good evidence that in alcoholic solution an aldehyde exists in equilibrium with a compound called a hemiacetal:

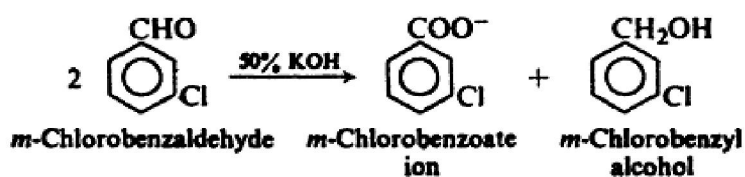
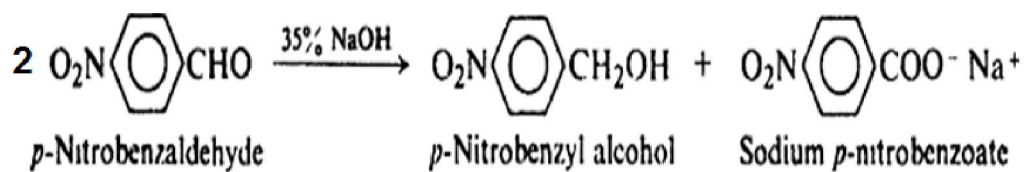
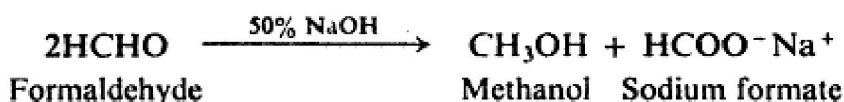


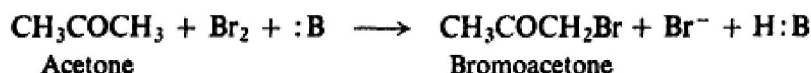
In the presence of acid the hemiacetal, acting as an alcohol, reacts with more of the solvent alcohol to form the acetal. an ether. The reaction involves two steps.



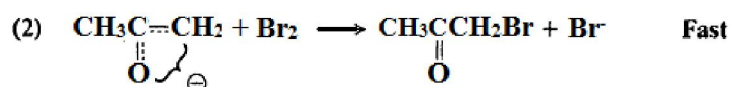
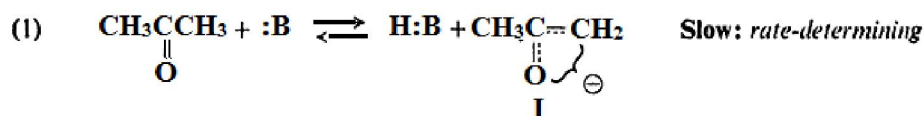
8-Cannizzaro reaction

In the presence of concentrated alkali, aldehydes containing no α -hydrogens undergo self-oxidation-and-reduction to yield a mixture of an alcohol and a salt of a carboxylic acid, this reaction known as the **Cannizzaro reaction**.



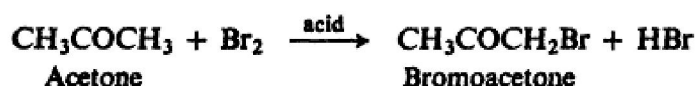


The kinetics is quite consistent with the following mechanism. The base slowly abstracts a proton (step 1) from acetone to form carbanion.I, which then reacts rapidly with bromine (step 2) to yield bromoacetone .

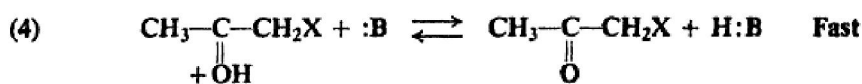
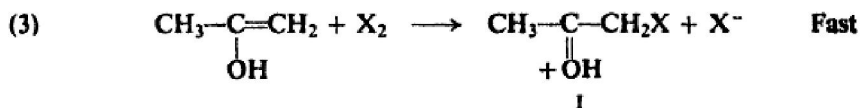
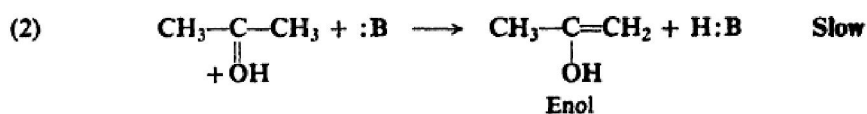
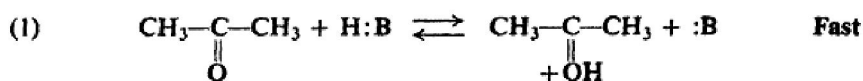


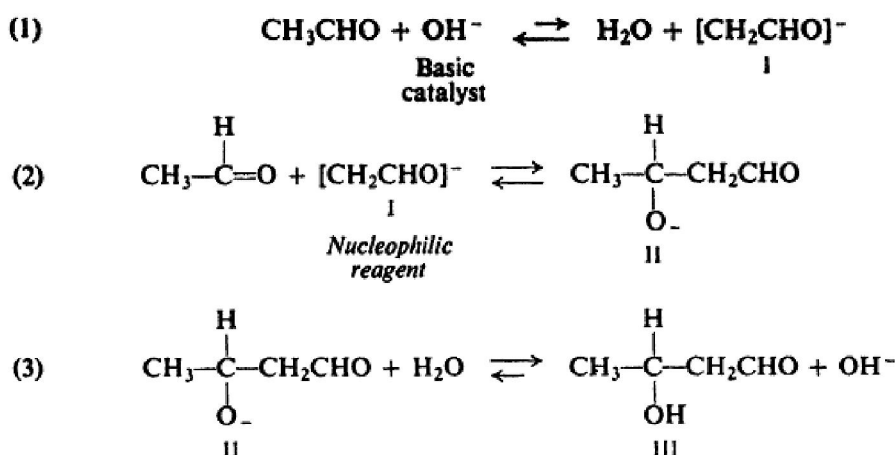
b) Acid-catalyzed halogenation of ketones. Enolization

Acids, like bases, speed up the halogenation of ketones.



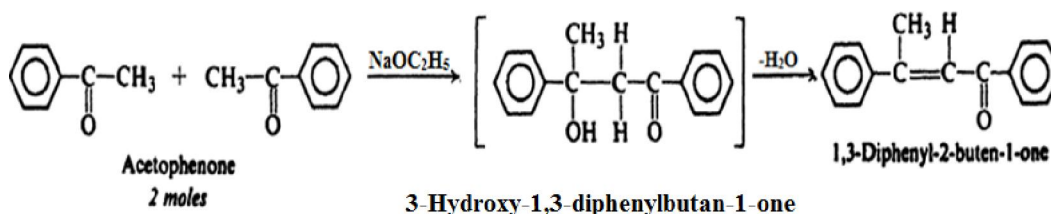
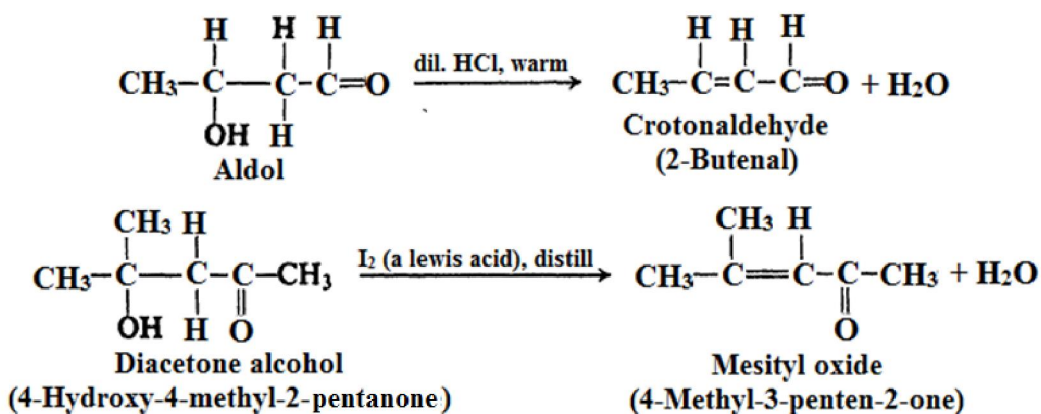
The rate-determining reaction here is the formation of the enol, which involves two steps: rapid, reversible protonation (step 1) of the carbonyl oxygen, followed by the slow loss of an α -hydrogen (step 2). Once formed, the enol reacts rapidly with halogen (step 3). We might have expected the unsaturated enol to undergo addition and, indeed, the reaction starts out exactly as though this were going to happen: positive halogen attaches itself to form a cation.





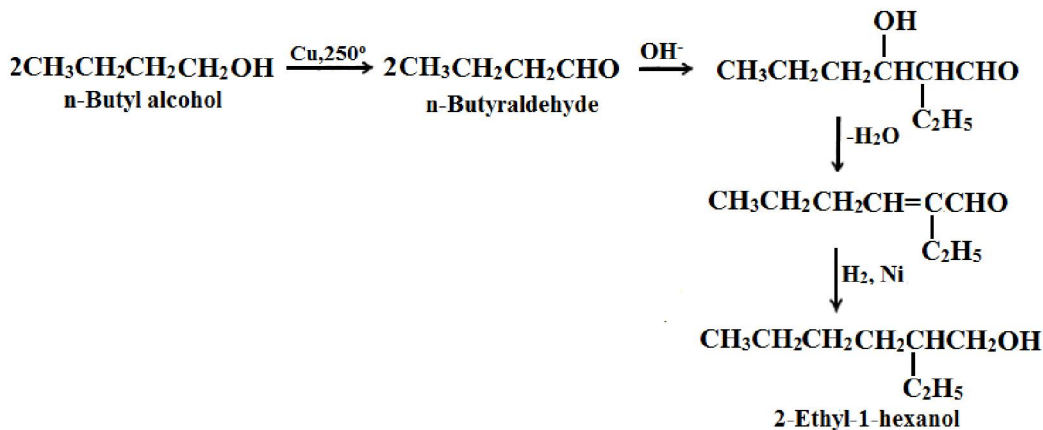
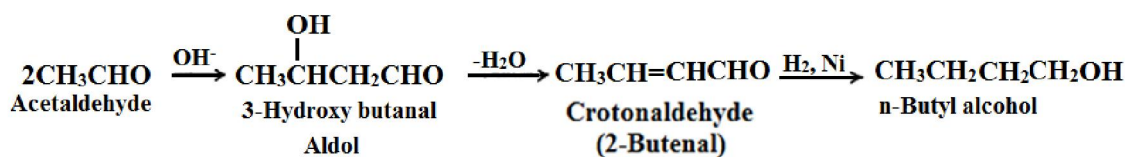
2) Dehydration of aldol products

The β -hydroxyaldehydes and β -hydroxyketones obtained from aldol condensations are very easily dehydrated; the major products have the carbon-carbon double bond between the α - and β -carbon atoms. For example:



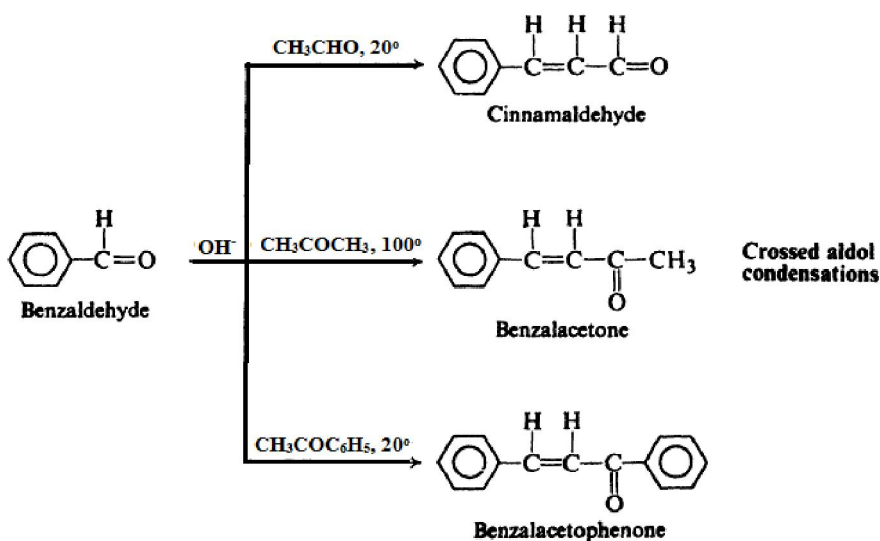
3) Use of aldol condensation in synthesis

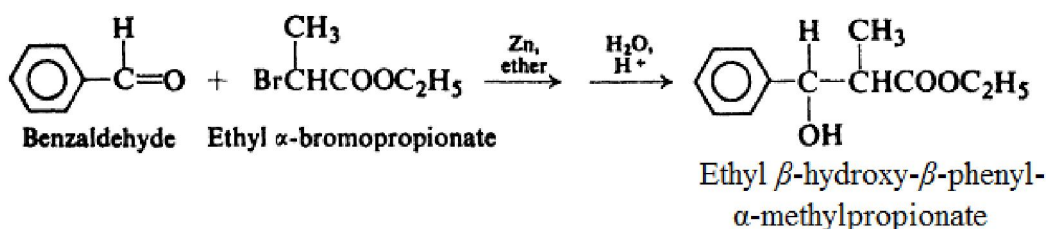
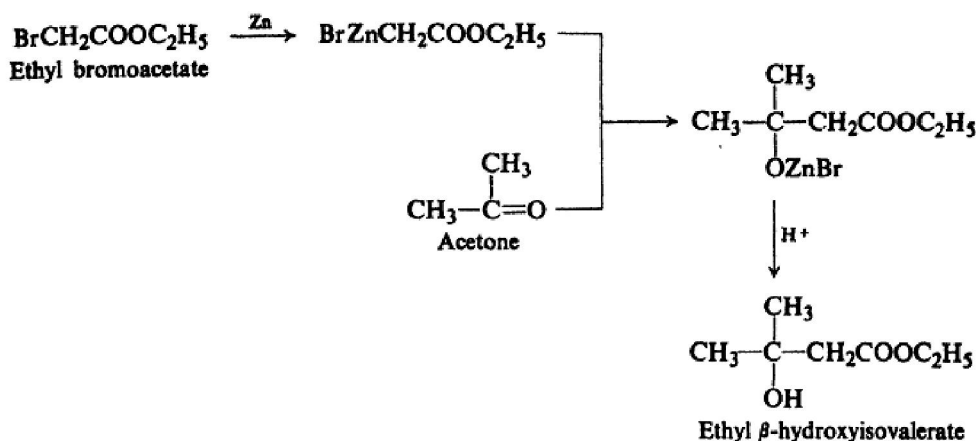
Catalytic hydrogenation of α , β -unsaturated aldehydes and ketones yields saturated alcohols, addition of hydrogen occurring both at carbon-carbon and at carbon-oxygen double bonds.



4) Crossed aldol condensation

An aldol condensation between two different carbonyl compounds also called crossed aldol condensation is not always feasible in the laboratory, since a mixture of the four possible products may be obtained. Under certain conditions, a good yield of a single product can be obtained from a crossed aldol condensation: (a) one reactant contains no α -hydrogens and therefore is incapable of condensing with itself (e.g., aromatic aldehydes or formaldehyde); (b) this reactant is mixed with the catalyst; and then (c) a carbonyl compound that contains α -hydrogens is added slowly to this mixture. There is thus present at any time only a very low concentration of the ionizable carbonyl compound, and the carbanion it forms reacts almost exclusively with the other carbonyl compound which is present in large excess.





The Reformatsky reaction takes place only with esters containing bromine in the alpha position, and hence necessarily yields beta-hydroxy esters. By the proper selection of ester and carbonyl compound, a wide variety of rather complicated β -hydroxy carboxylic acids can be prepared.

