

Organic Chemistry-I

CHEM 373

Ex-PPP Lyp-FSD

6th Semester

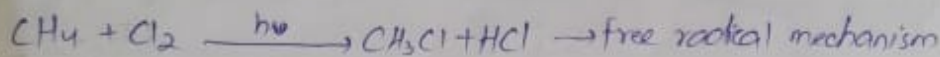
Lecture 1:-

Reaction Mechanism

It is defined as step by step description of a chemical reaction. Mostly, there are two steps

- 1- Elementary step
- 2- Rate determining step (RDS)
 - ↳ overall reaction is elementary step
 - ↳ slowest step is rate determining step.

e.g. $A \longrightarrow D \rightarrow \text{elementary/overall}$

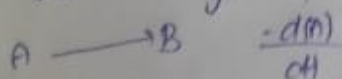


Rate determining step can be determined by the knowledge of chemical kinetics.

A reaction mechanism must satisfy the following requirements

- The elementary step should be present in balanced eqn.
- The rate law for the rate determining step must agree with the experimentally determined rate law.

rate law \rightarrow change of conc. per unit time]



There are many types of reactions. (2)

1. Substitution reaction, addition reaction, oxidation, reduction reaction, elimination reaction.

In substitution reaction, there are two types

- Nucleophilic substitution
- Electrophilic substitution

Nucleophilic Substitution Reaction S_N

S_N2

Bimolecular nucleophilic substitution reaction

Primary alkyl halide \rightarrow Three hydrogens are attached to Carbon

Tertiary alkyl halide \rightarrow No hydrogen is attached to Carbon

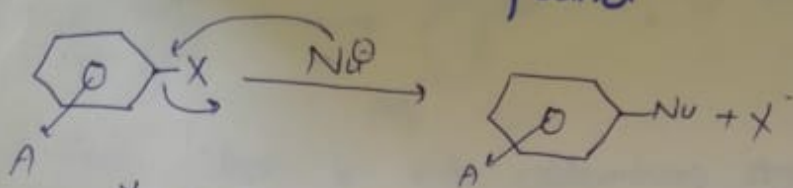
S_N1

Unimolecular substitution reaction

NSR

Lecture 2:-

Nucleophilic Substitution Reaction in aromatic compound (3)



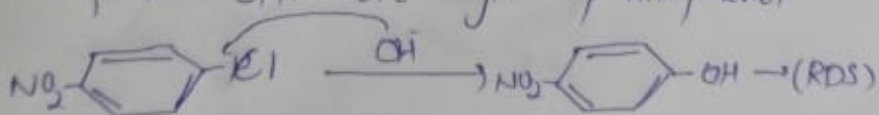
X are good leaving groups.

There are two types

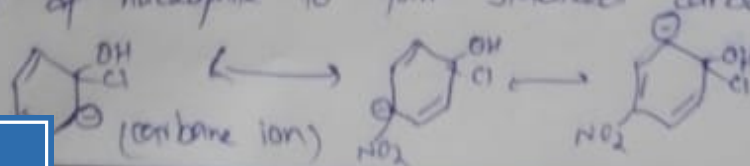
1. addition-elimination mechanism
2. elimination-addition.

Addition-Elimination Reaction

In this reaction, aromatic compounds are used in which strong electron withdrawing groups like nitro are present on the ring on the ortho or para position. When nucleophile attack, it will give substituted product. For example, *p*-nitro *p*-chloronitrobenzene react with strong nucleophile OH⁻ and give *p*-nitrophenol.



The mechanism of this reaction has two steps
1- addition of nucleophile to form stabilized carbanion ion



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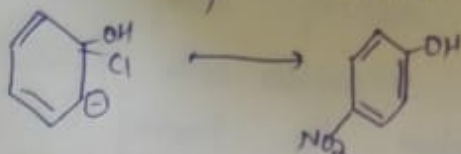
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anism of reactions

$\left[\begin{array}{l} \text{-ve charge on carbene} \rightarrow \text{carbene ion} \\ \text{+ve charge on carbon} \rightarrow \text{carbonium ion} \end{array} \right]$

(4)

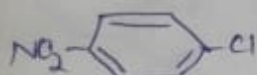
2 in Second step, elimination of leaving group takes place



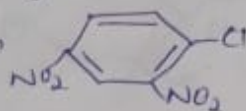
First step is rate determining step because in this step aromatic benzene ring lost their aromaticity.

In second step, leaving group leaves and benzene ring again restore its aromaticity. This is fast step.

Such types of reaction, reactivity may be increased by increasing the number of electron withdrawing groups on the ring.

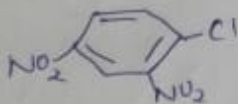


A

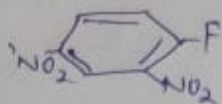


B

B is more reactive than A because it contains two electron withdrawing groups.



B



C

C is more reactive than B because C contains more electronegative atom than B.



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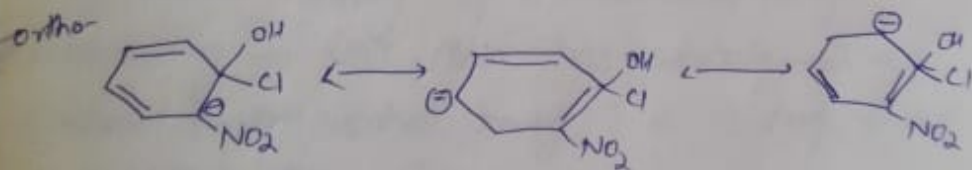
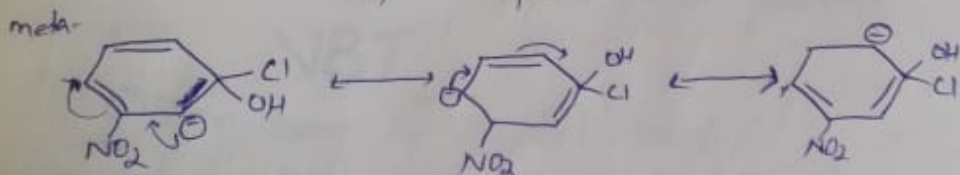


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NO_2 group should be present at ortho or para ⁽⁵⁾ positions because when NO_2 group is present at ortho or para position then $-ve$ charge of carbocation will also delocalize on NO_2 group but when it is present at meta position then $-ve$ charge will not delocalize on NO_2 group. So it is important that NO_2 group should be present at ortho or para position.

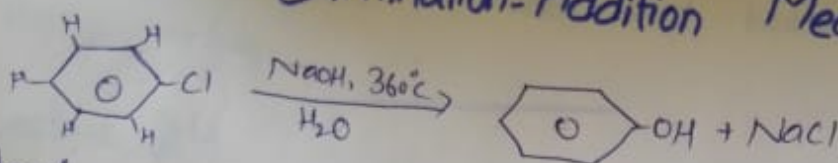


Organic Chemistry

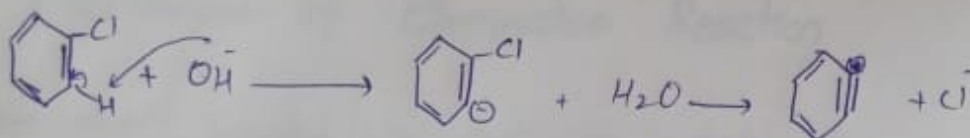
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Elimination-Addition Mechanism

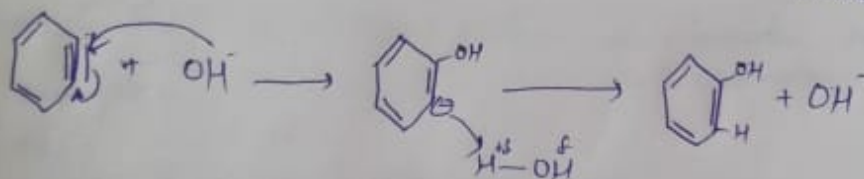


step 1:-



benzyne
intermediate

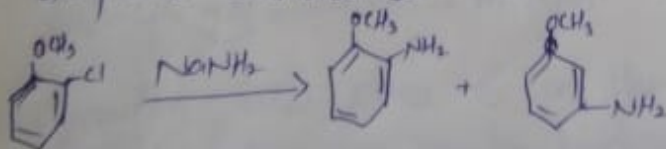
step 2:-



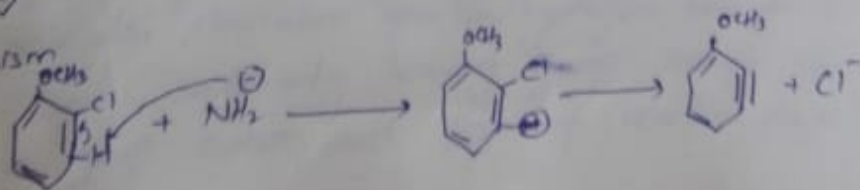
1- Elimination of H and X from 2 adjacent carbons and form a reactive benzyne intermediate.

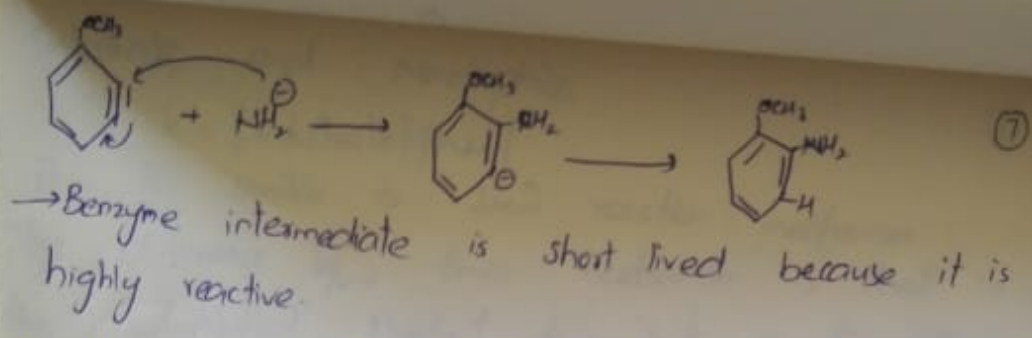
step 2:- In this step, addition of Nucleophile takes place and form a final product.

For example, ortho-chloroanisole react with NaNH_2



mechanism

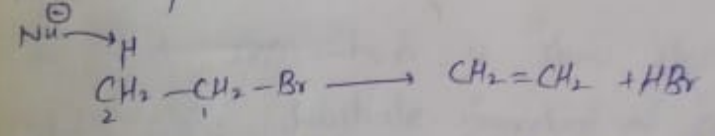




Mechanism of Elimination Reaction

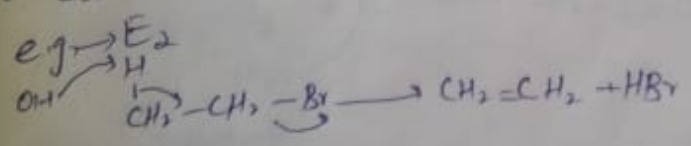
Elimination reaction is that in which atom or group of atoms are removed from adjacent carbons. This is also called α -elimination reaction. 1,2 elimination

For example:



Elimination reactions are of two types:-

1. E_1
2. E_2



This reaction takes place in one step. In Bimolecular elimination reaction, hydrogen remove from β -carbon and simultaneously leaving group leaves from functional group carbon. And Rate of reaction depends on

Substrate and Nucleophile

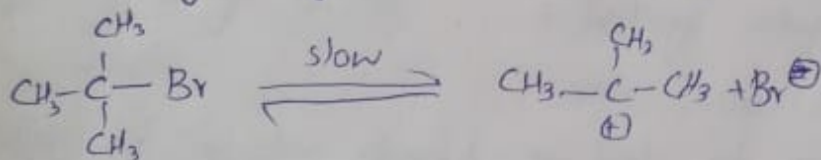
$$k = [\text{Substrate}][\text{Nu}^-] \quad (8)$$

It is similar to S_N2 reaction mechanism.
The difference b/w two mechanism is that in S_N2 the substituted product form but in E_2 alkene is formed.

E_1 :- Unimolecular elimination.

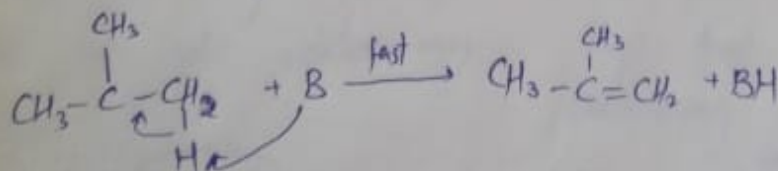
↳ It takes place in two steps

↳ Tertiary alkyl halide is used.



In first step, which is slow step, leaving group leaves the substrate. formation of carbonium ion.

In second step,



$$\text{Rate} = [\text{substrate}]$$

ter. carbonium > Sec carbonium > Pri. Carbonium
stability order

Difference b/w

⑨

SN2

1- It is bimolecular ~~sub~~ Nucleophilic substitution reaction

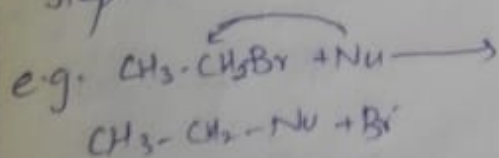
2- It takes place in one step.

3- Primary alkyl halides are used.

4- Rate of reaction depends on the substrate and nucleophile.

$$\text{Rate} = [\text{Substrate}][\text{Nu}]$$

5- There is only one step that is rate determining step.



SN1

1- It is unimolecular nucleophilic ~~sub~~ substitution reaction.

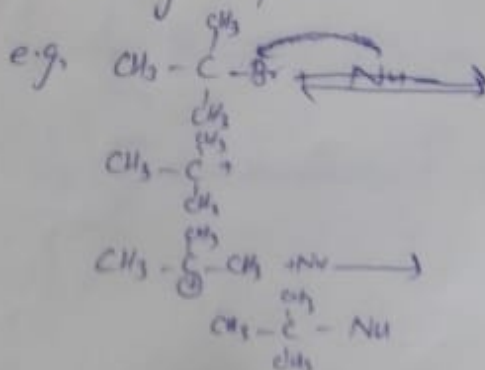
2- It takes place in two steps.

3- Tertiary alkyl halides are used.

4- Rate of reaction depends only on the substrate

$$\text{Rate} = [\text{Substrate}]$$

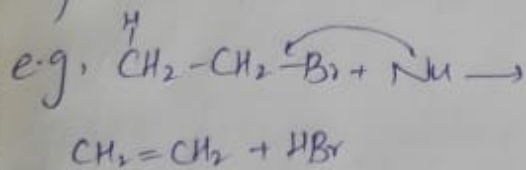
5- The first step is slowest step that is rate determining step.



Difference b/w

E₂

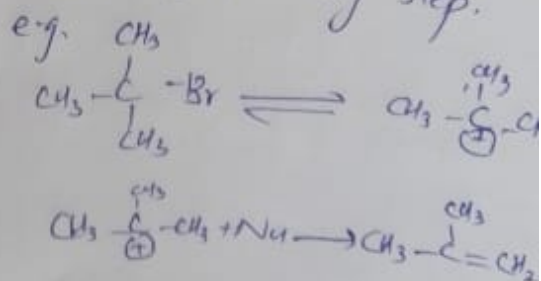
- 1- It is bimolecular elimination reaction.
- 2- It takes place in one step.
- 3- Primary alkyl halides undergo E₂ reaction.
- 4- Rate of reaction depends on the substrate and Nucleophile.
- 5- There is only one step that is rate determining step.



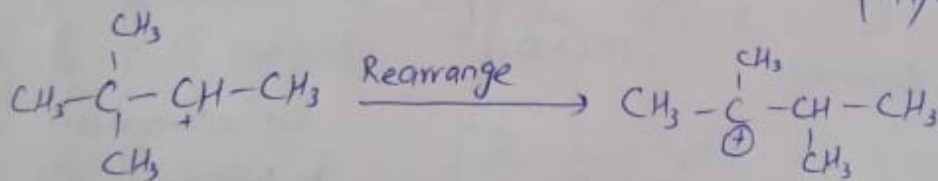
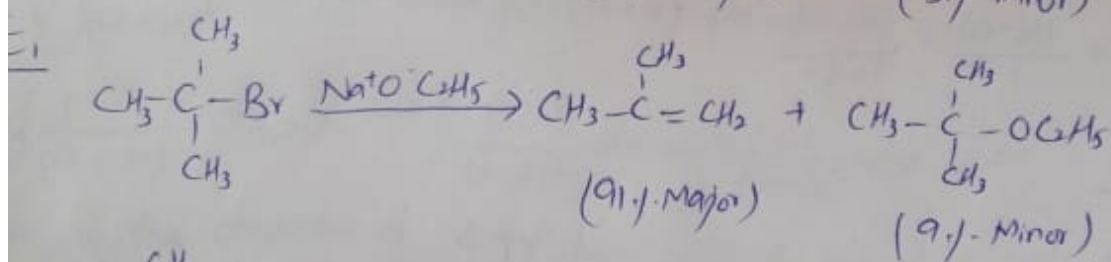
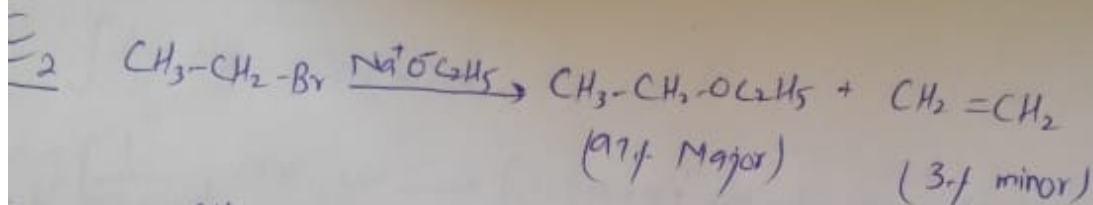
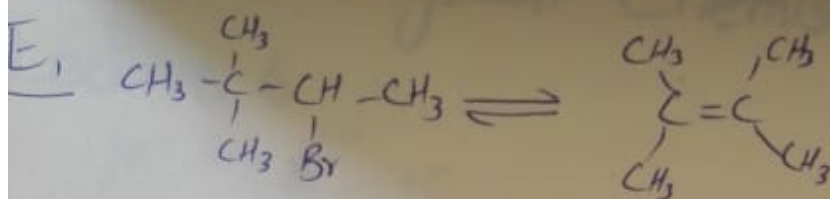
(Markovnikov's Rule)

E₁

- 1- It is unimolecular elimination reaction.
- 2- It takes place in two steps.
- 3- Tertiary alkyl halides undergo E₁ reaction.
- 4- Rate of reaction depends only on the amount of substrate.
- 5- There are two steps and first step takes place is slow that is rate determining step.



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Organic Chemistry

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Factors affecting the Elimination Reaction

Substrate

In E_1 mechanism tertiary alkyl halide substrate and in E_2 primary secondary is used in the E_1 and depending upon the reaction condition.

Effect of temperature

Elimination reaction is favoured by increasing temp. Whether the mechanism of E_1 and E_2 because the activation energy of elimination reaction is higher.

Effect of attacking base

In elimination reaction solvent is used as base there is no need of external base. Strong base favours the E_2 mechanism while for E_1 mechanism moderate weak base is used.

Effect of solvent

E_1 mechanism mostly proceed by polar solvents because it involved ionization step and E_2 mostly favoured by non-polar solvents.

Effect of leaving group

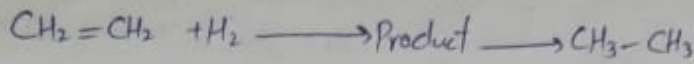
Better leaving group favour the reaction because the ionization step is more easier and good leaving groups favour E_2 mechanism. Halogens are good leaving groups.

1-What is good leaving group and bad leaving group? (13)

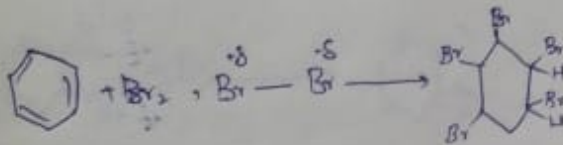
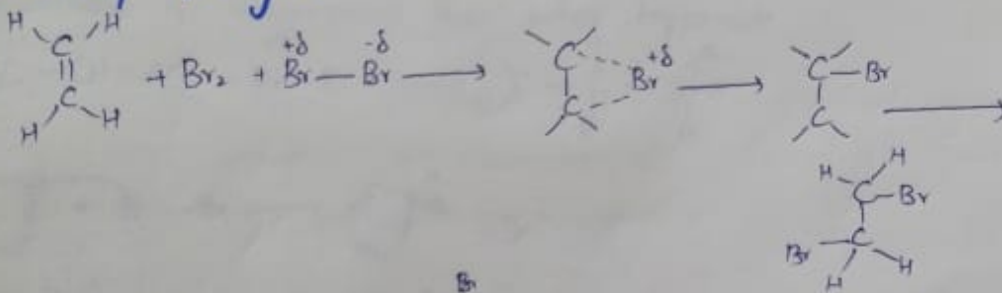
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Addition Reaction

Alkene

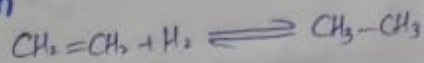


Addition of Halogens

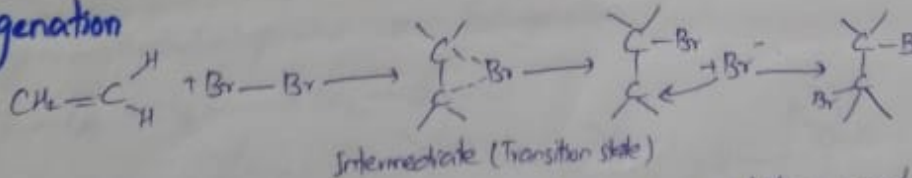


Lecture 7

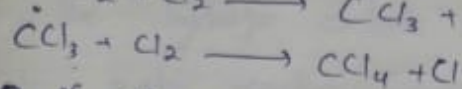
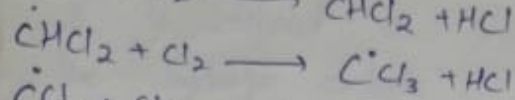
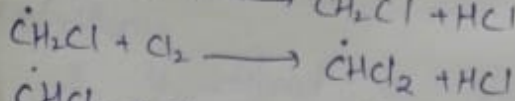
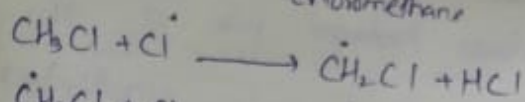
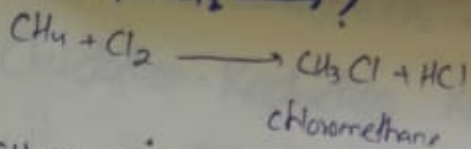
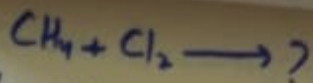
Hydrogenation



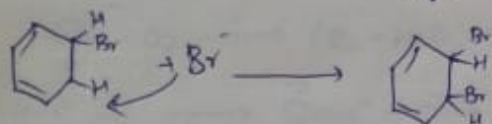
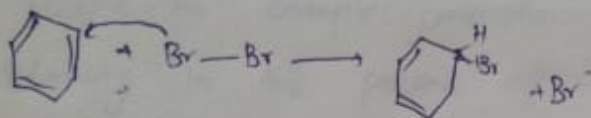
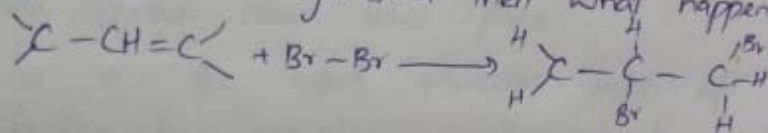
Halogenation



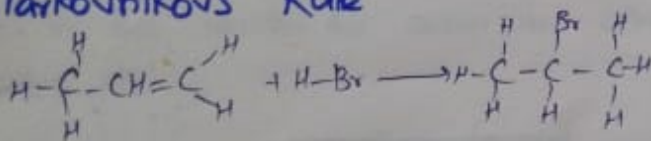
The addition of Halogen like bromination gives addition product and this addition is called trans-addition. Similarly HBr may also be added in alkene by this mechanism.



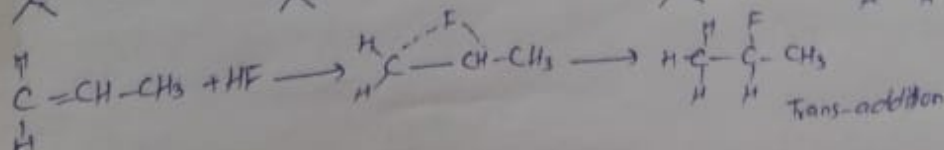
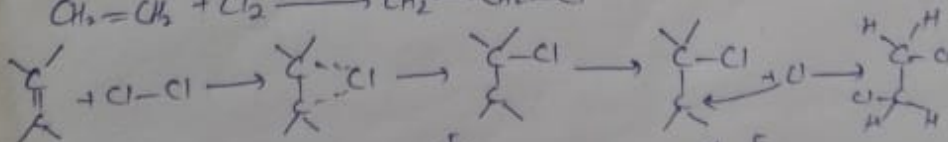
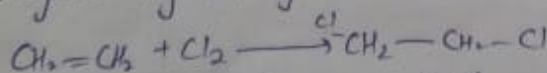
Q. If alkene is unsymmetrical then what happens?

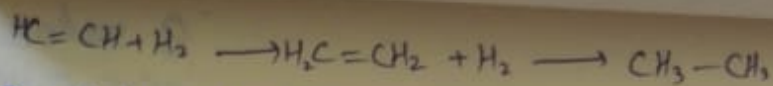


Markovnikov's Rule



Negative part will go to that carbon that has less no. of Hydrogens \rightarrow Hydrohalogenation or halogenation.





Oxidation-Reduction Reaction

It is very important reaction in chemistry.

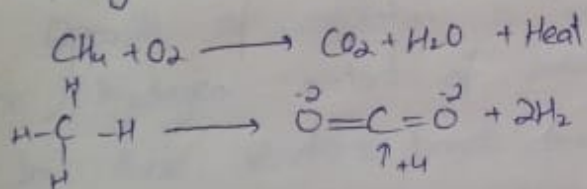
Definition:-

It is defined as increasing the oxygen contents, decreasing the hydrogen contents.

In such reaction, formation of bond to more electronegative atom than carbon atom takes place.

So in the result oxidation state of carbon becomes more positive. for example, combustion reaction.

Burning in the presence of oxygen is called combustion.

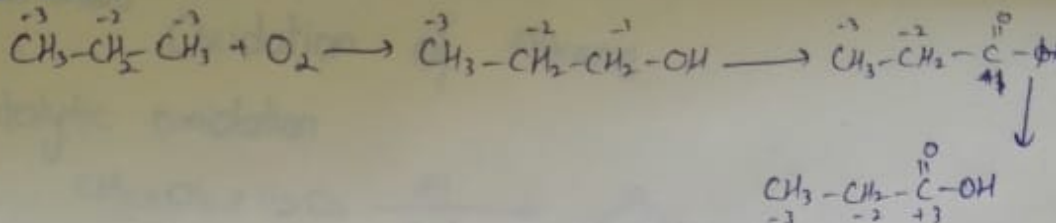


So, in this reaction, the carbon has attain maximum oxidation state +4.



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24-2-2020



This is oxidation reaction but back of this reaction is reduction
 Oxidizing agents: - $\text{K}_2\text{Cr}_2\text{O}_7$, KMnO_4

Reducing agents: - H_2 , Pt

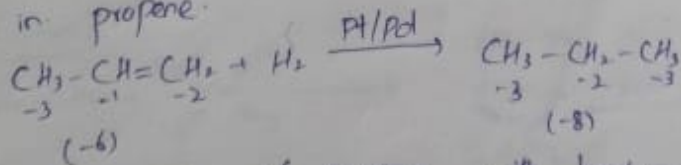
In oxidation reaction, conversion of functional group to higher category take place and increasing of oxidation number of particular carbon of functional group takes place.

Opposite of oxidation is reduction in which, increasing the hydrogen content of organic molecule takes place.

In these reactions, bond formation to more electropositive atom than carbon atom taking place and shifting oxidation state of carbon to more electronegative number.

e.g. addition of hydrogen across carbon-carbon double bond in the presence of catalyst

e.g. in propene.

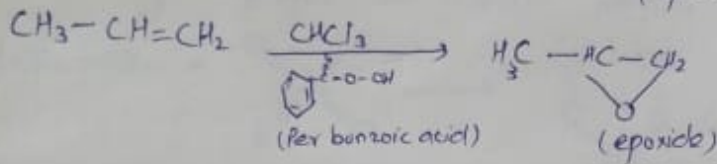
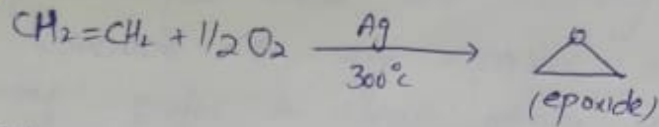


In this reaction of propene with hydrogen in the presence of catalyst, hydrogen content is increasing but the negative oxidation state has also increased.

25-2-2020

Oxidation of Alkene

- Catalytic oxidation

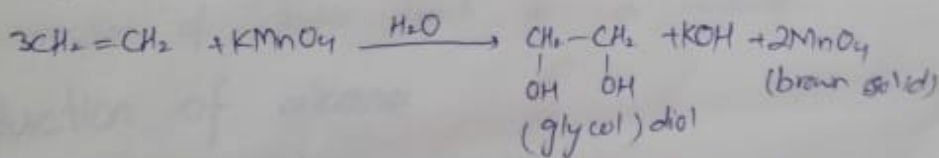


There are many oxidizing agents used for this purpose.
 1- KMnO_4 , H_2O_2 (hydrogen peroxide), $\text{K}_2\text{Cr}_2\text{O}_7$.

Oxidizing agents are basically electron deficient species but alkene double bond is rich in electrons.

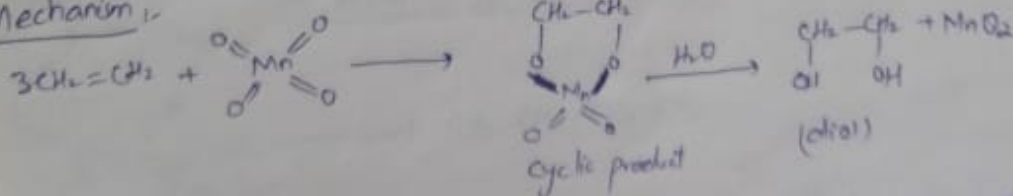
2- Hydroxylation

In this reaction, KMnO_4 oxidizing agent is used to convert alkene into alcohol.



Brown solid is the confirmation of this reaction.

Mechanism 1-

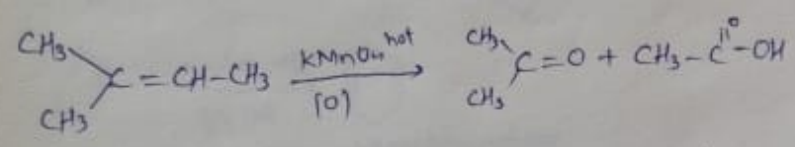
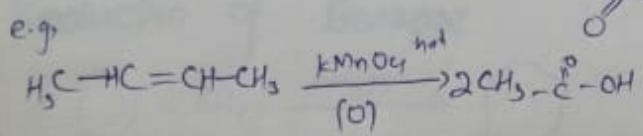
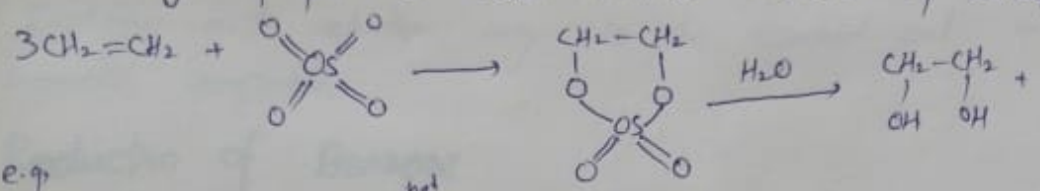


This reaction is called Baeyer test. In this reaction cis-addition of OH is formed through a cyclic transition state (Manganate ester).

22-3-2020 Oxidation of alkenes
 18/11/20

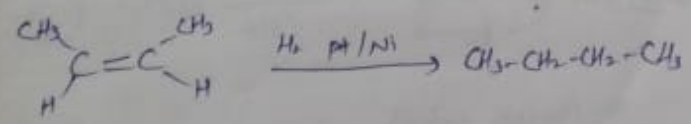
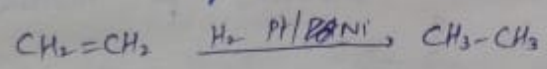
which convert after hydrolysis into diol.
 (OsO₄) is also used for this reaction
 osmium tetroxide

The difference b/w these two oxidizing agent is that osmium tetroxide is very expensive and highly toxic we may prefer to use KMnO₄ instead of OsO₄.



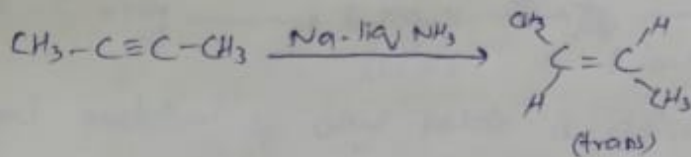
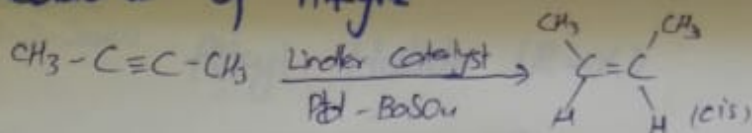
These two reactions are called oxidative cleavage of alkenes. In oxidative cleavage of alkene may be used to locate the position of double bond in a molecule.

Reduction of alkene



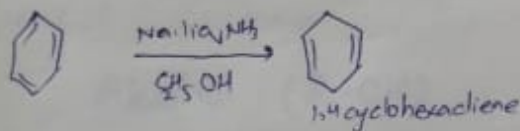
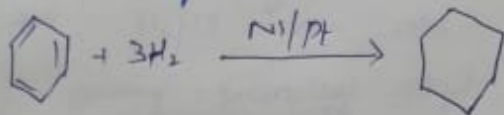
In this reaction, Pt instead of Pt we can use Ni-Al alloy. It is also called Raney-Nickel.

Reduction of Alkyne



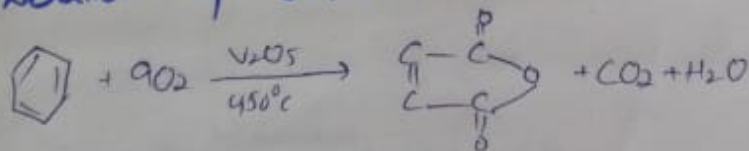
Oxidation and reduction may also be carried out in aromatic compounds.

Reduction of Benzene



This reaction is called Birch reduction. In this reduction Na-metal in liquid NH_3 in the presence of CH_3OH is used and get controlled reduction of benzene to 1,4-cyclohexadiene.

Oxidation of Benzene



Maleic anhydride

Benzene is very resistant to oxidation reaction. No reaction with $\text{K}_2\text{Cr}_2\text{O}_7$, MnO_2 . But it can be oxidized under different condition to anhydride in presence of V_2O_5 at 450°C .

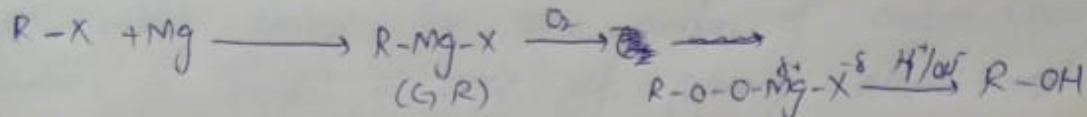


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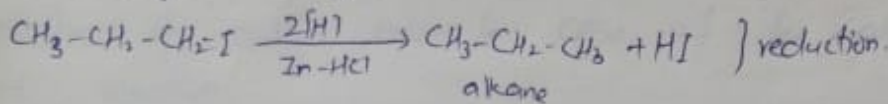
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Alkyl Halide (R-X)



Direct oxidation of alkyl halide is difficult. So we first convert into Grignard reagent and then to alcohol.

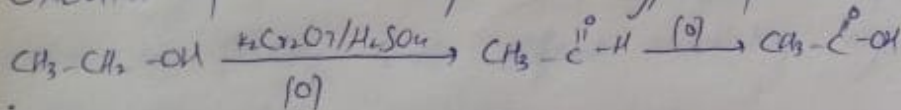


Similarly, $LiAlH_4$ may also be used as reducing agent. Ni/Pd , H_2/Pt can also be used.

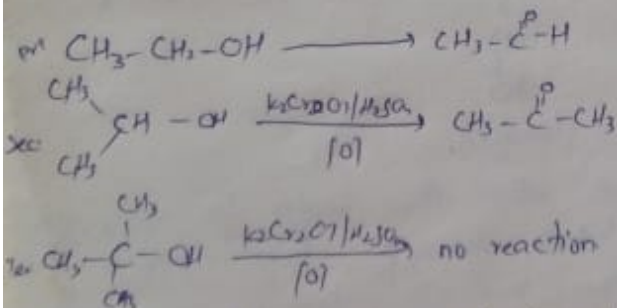
If primary, secondary alkyl halide is used in reduction product is same.

Alcohol (R-OH)

Oxidation of alcohol depend on type of alcohol.



There are number of oxidizing agents used $KMnO_4$, $K_2Cr_2O_7$, H_2/A .



These reactions are used to distinguish alcohol. Oxidation of alcohol gives aldehydes or ketones.

Primary alcohol is heated with oxidizing agent $K_2Cr_2O_7/H_2SO_4$ (21) instead of all it convert into aldehyde and then to carboxylic acid, which contain the same number of carbon. Orange solution is formed in case of primary alcohol and secondary alcohol reaction react with oxidizing agent then ketone will be formed of green solution, and give ketone of same number of carbon atom. In case of tertiary alcohol there is no reaction.

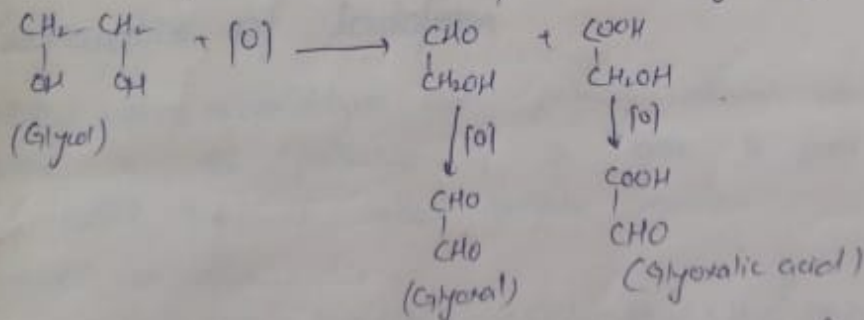
→ In order to limit the oxidation of alcohol to aldehyde Jones's reagent is used.

Jones's reagent $\rightarrow Cr_2O_3 + \text{dil. } H_2SO_4$
chromic acid

Oxidation of polyhydric alcohol

Oxidation of polyhydric

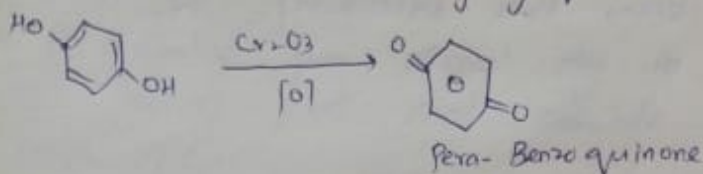
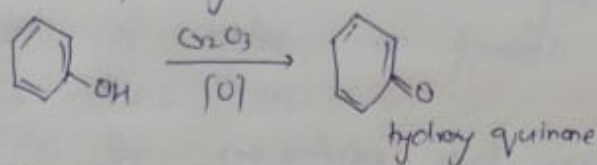
alcohol is possible with different oxidising agent.



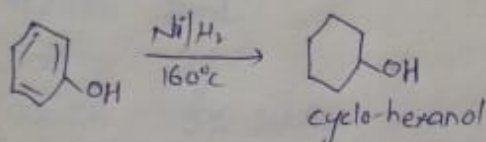
Oxidation of glycol with nitric acid give no. of substance eg. glyoxal and glyoxylic acid this reaction is controlled reaction in which as we want, we make.

Aromatic Alcohol

Aromatic alcohol may also be oxidized into corresponding ketone. (2)



If we want to reduce the aromatic alcohol then we used Ni/H₂

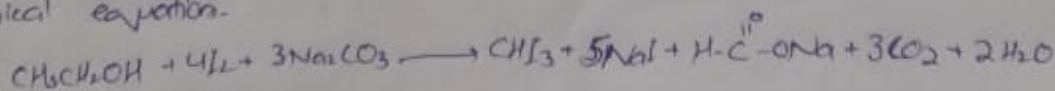


Practical

Preparation of Iodoform

Methyl ketone, acetaldehyde and primary alcohol react with iodine in the presence of a base to form yellow crystals of iodoform. This is called iodoform reaction.

Chemical equation-



Procedure

1- Dissolve 10g of Na₂CO₃ in 50ml of distilled water in a round bottom flask and warm up to 60°C on a water bath.

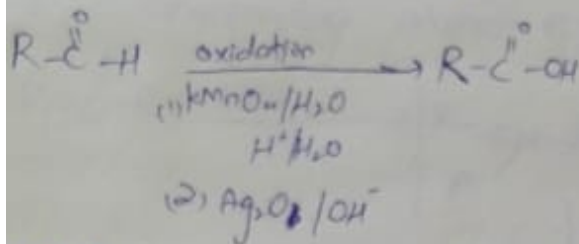


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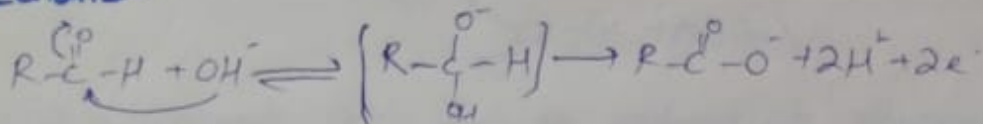
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Oxidation of aldehyde and ketones



Mechanism



Oxidation of aldehyde and ketone can be carried in the presence of oxidising agent in basic media. in nucleophile attack on carbonyl carbon.

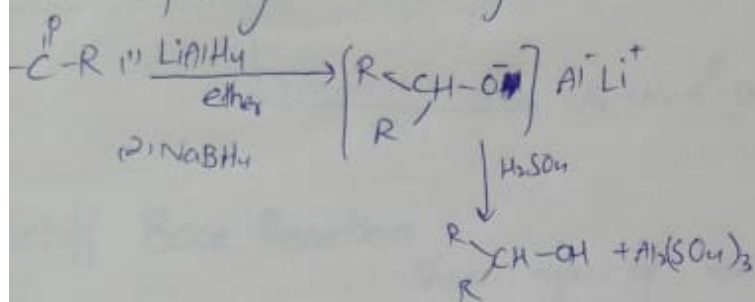
Oxidation of ketone is difficult as compared to aldehyde into carboxylic acid. for ketone, strong oxidising agent may be used. eg, Ag_2O

Lab Test to distinguish aldehyde and ketone

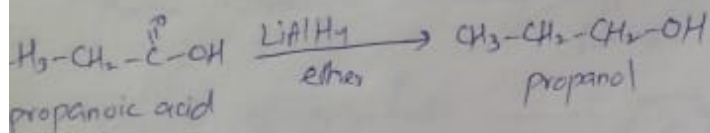
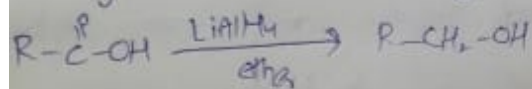
- 1- Silver mirror test / Tollen's reagent test
- 2- Fehling's solution test
- 3- Benedict's test

Reduction of Aldehyde and ketone (24)

Aldehyde and ketone may be reduced with different catalyst corresponding alcohol. e.g.



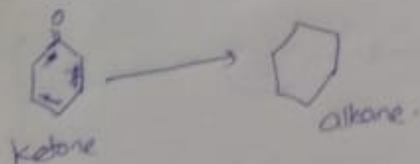
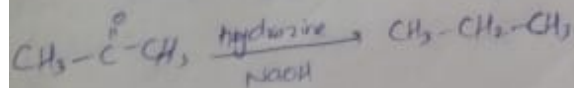
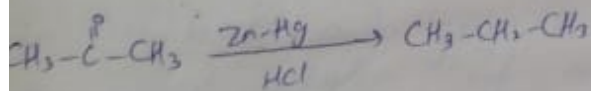
Similarly, Carboxylic acid may be reduced into corresponding alcohol



Difference b/w Clemmenson and Wolf-kishner reduction

Wolf-kishner Reduction \rightarrow hydrazine

Clemmenson reduction \rightarrow Zn-Amalgam

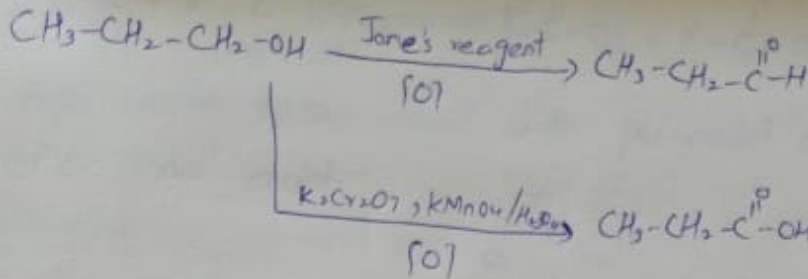




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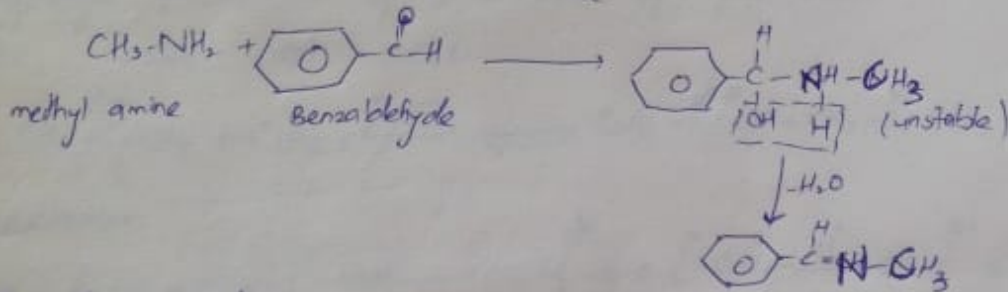
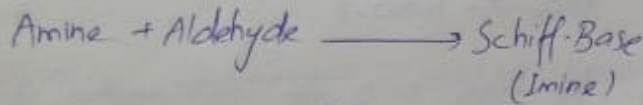
3-2020

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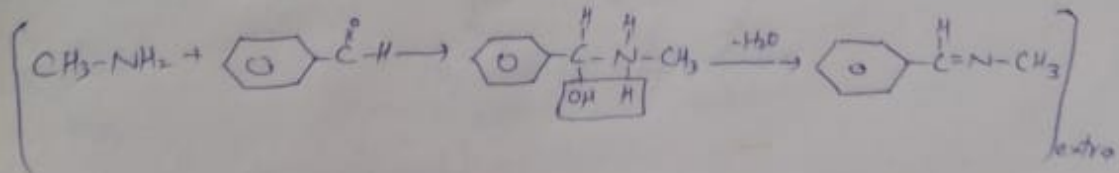
Schiff Base Reaction

These types of reactions are given by aldehyde but not ketone. In this reaction, amine react with aldehyde and form schiff base/imine. e.g,



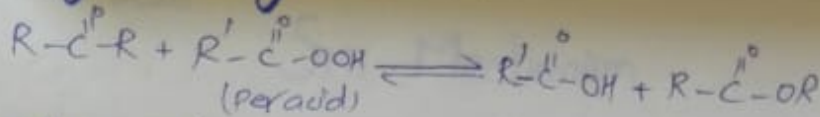
In this reaction, amino group is reduced into imine. This is so called reduction of amine.

(Advantage is that if we hydrolyze the imine it gives amine)



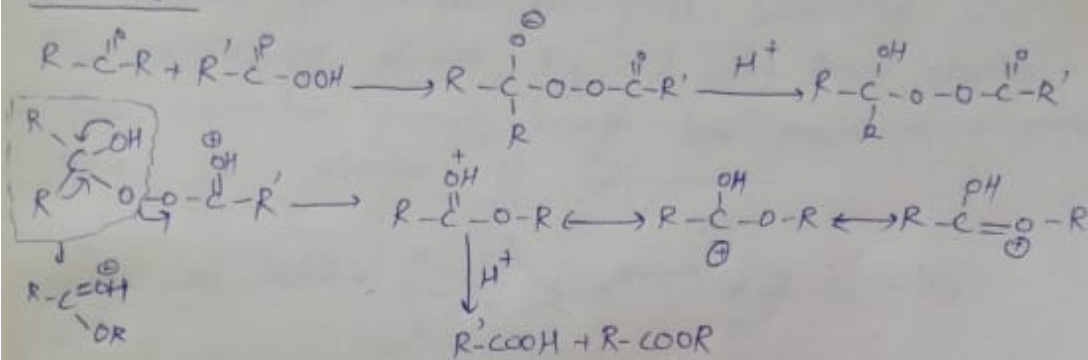
Baeyer's villiger oxidation

(26)



In this reaction ketone react with per-acid and convert into ester and acid.

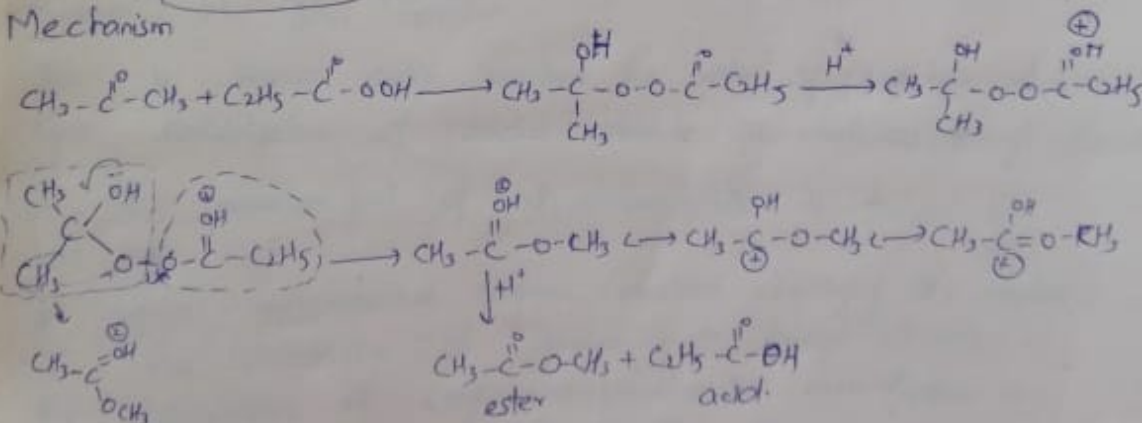
Mechanism



Hydrolytic dissociation of O-O bond of per acid, which convert into ester and acid.



Mechanism



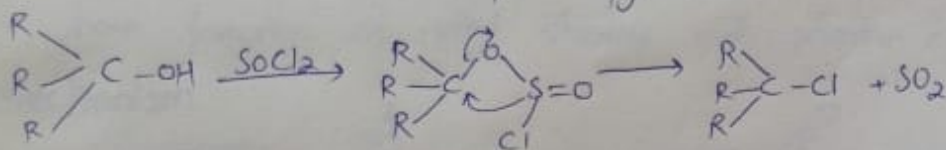
(Per acid converts \longrightarrow acid)
 (Acetone converts \longrightarrow ester)

Online Lecture
25-3-2020

(27)

S_Ni Mechanism

- Aliphatic Nucleophilic substitution reaction leading to retention of configuration
- S_Ni stands for internal nucleophilic substitution
- The displacement of $-OH$ by $-Cl$ using thionyl chloride.
- This substitution proceeds through S_Ni mechanism, in which there is retention of configuration.



The reaction follows second order kinetics.

$$\text{Rate} \propto [R_3C-OH][SOCl_2]$$

Internal or intermolecular nucleophilic substitution reaction is known as S_Ni reaction.

This is second order reaction as rate of reaction depends upon concentration of alcohol molecule as well as thionyl chloride.

→ In this reaction, first of all, chlorosulphite is formed by loss of HCl .

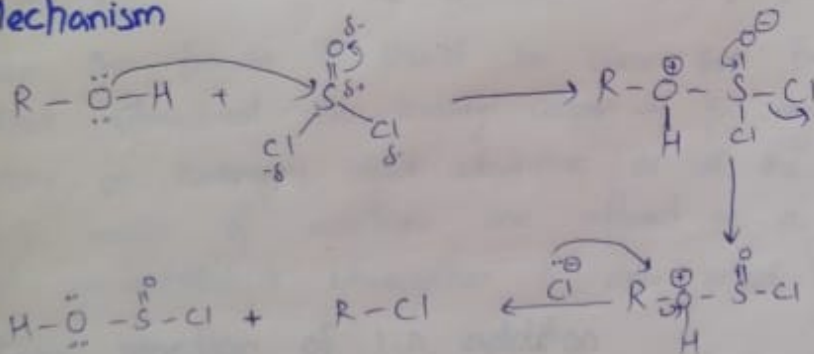
A typical representative organic reaction displaying this mechanism is the chlorination of alcohol with thionyl chloride, or the decomposition of alkyl chloroformates, the main feature is "retention of stereochemical configuration".

What happens here?

(28)

SOCl_2 coordinates to the alcohol, with loss of HCl and formation of a good leaving group (chlorosulfite). The chlorosulfite leaving group can spontaneously depart, forming a carbocation and when it does so, an **intimate ion pair** is formed where the carbocation and negatively charged leaving group are held tightly together in space. From here, the chlorine can act as nucleophile - attacking the carbocation on the same face from which it is expelled - and after expulsion of SO_2 we have formation of alkyl chloride with retention of configuration.

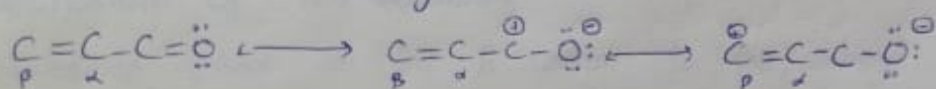
Mechanism



Conjugate Addition Reactions

(29)

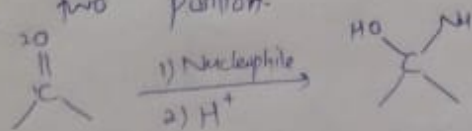
One of the largest and most diverse classes of reactions is composed of additions to a carbonyl group. Conjugation of a double bond to a carbonyl group transmits the electrophilic character of a carbonyl carbon to the beta-carbon of the double bond. These conjugated carbonyls are called enones or α,β unsaturated carbonyls. A resonance description of this transmission is given below:-



From this formula it should be clear that nucleophiles may attack either at the carbonyl carbon, as for any aldehyde, ketone or carboxylic acid derivatives or at the beta carbon. These two modes of reactions are referred to as 1,2-addition and 1,4-addition. A 1,4-addition is also called "conjugate addition".

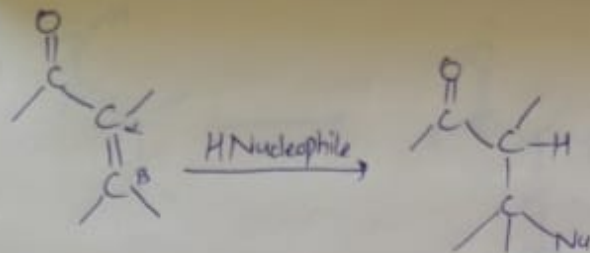
Basic reaction of 1,2 addition

Here the nucleophile adds to the carbon which is in the one position. The hydrogen adds to the oxygen which is in the two position.



Basic reaction of 1,4 addition

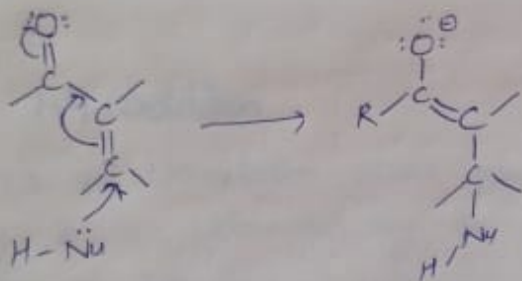
(30)



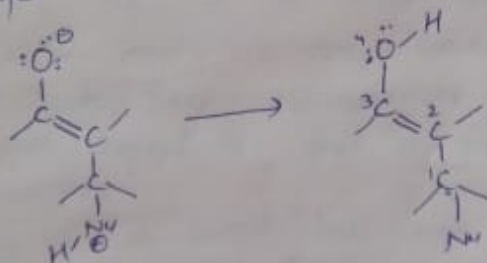
In 1,4 addition the Nucleophile is added to the β carbons of the carbonyl while the hydrogen is added to the α -carbon to the carbonyl

Mechanism of 1,4 addition

1- Nucleophile attack on the β carbon to the carbonyl



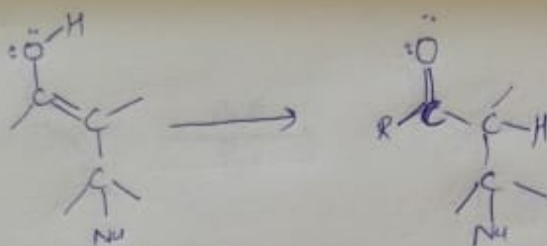
2- Proton Transfer



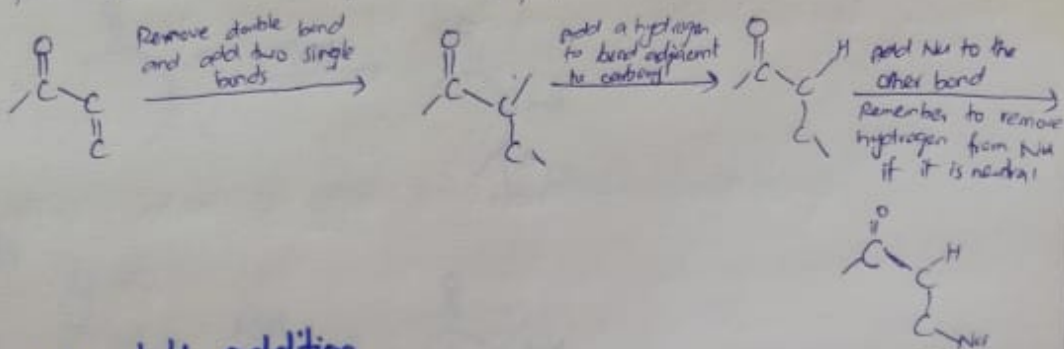
Here we can see why this addition is called 1,4. The nucleophile adds to the carbon in the one position and the hydrogen adds to the oxygen in four position.

Tautomerization

(3)



going from reactant to product simplified

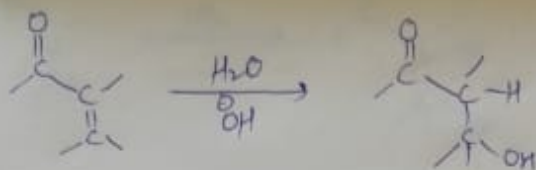


1,2 vs. 1,4 addition

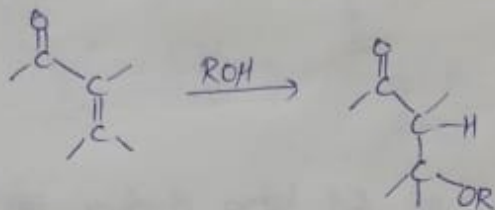
Whether 1,2 or 1,4-addition occurs depends on multiple variables but mostly it is determined by the nature of nucleophile. During the addition of Nu there is competition b/w 1,2 and 1,4 addition products. If the Nu is a strong base, such as Grignard reagent, both 1,2 and 1,4 are irreversible and therefore are under kinetic control. Since 1,2-additions to carbonyl group are fast, we would expect to find a predominance of 1,2-products from these reactions.

If the Nu is a weak base, such as alcohol or amine, then 1,2 addition is reversible. This means the competition b/w 1,2 and 1,4 addition is under thermodynamic control. In this case, 1,4 addition dominates because stable carbonyl group is retained.

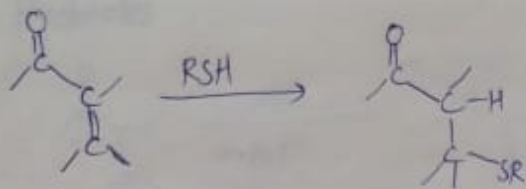
Nucleophiles which add 1,4 to α,β unsaturated carbonyl⁽³⁾
water



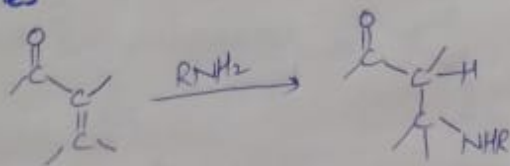
Alcohols



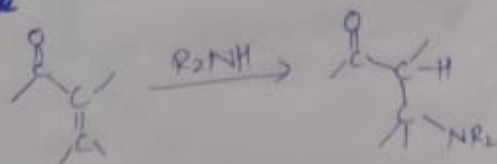
Thiols



1° Amines

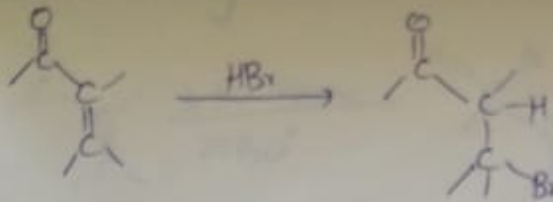


2° Amine

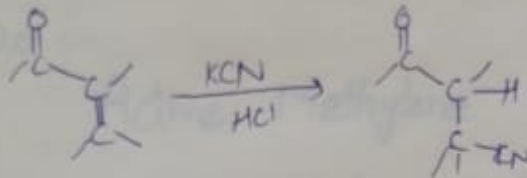


Hydroboration

(31)

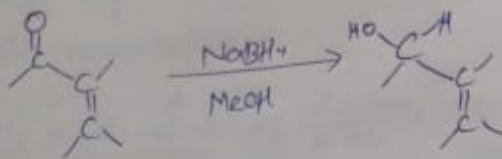
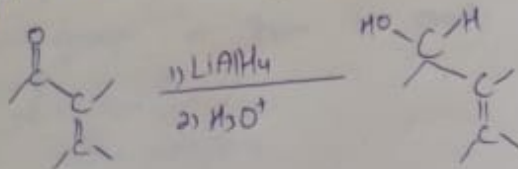


Cyanides

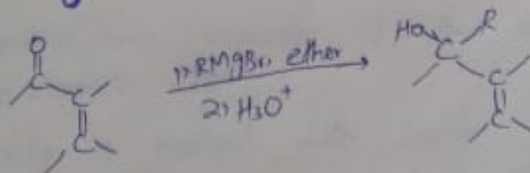


Nucleophiles which add 1,2 to α,β unsaturated carbonyl

Metal Hydrides

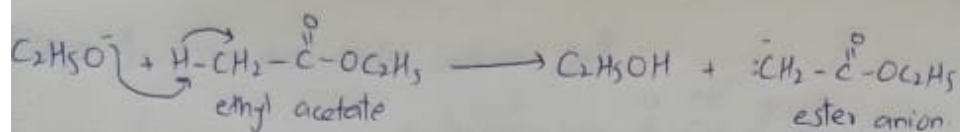


Grignard Reagents

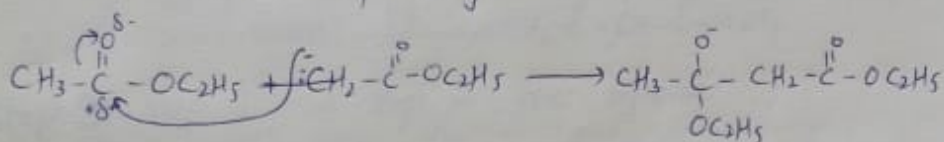


Mechanism

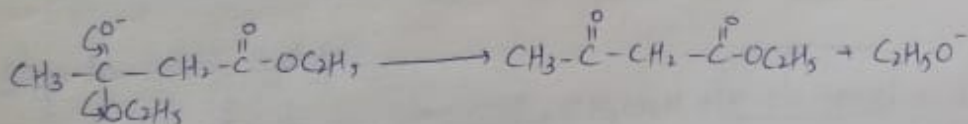
Step 1:- Ethoxide ion (from C_2H_5ONa) attacks ethyl acetate to give ethyl alcohol and the ester anion. (35)



Step 2:- ester anion attacks the carbonyl group of a second molecule of ethyl acetate.



Step 3:- Ethoxide ion is eliminated



Note:- The reaction b/w ethyl acetate and sodium ethoxide is followed by acidification because the α -hydrolysis of ethylacetoacetate are acidic of very reactive

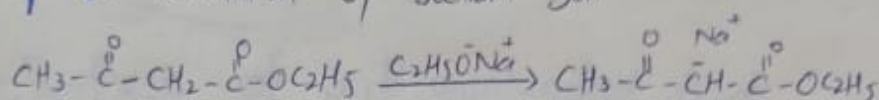
So, the α -hydrolysis react with sodium ethoxide to form a salt. The acidification of salt gives back ethyl acetoacetate.

Lecture
2-4-2020

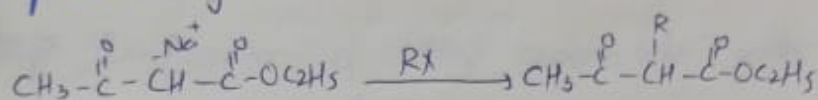
(36)

2-Synthesis of dialkyl acetic acid (carboxylic acid)

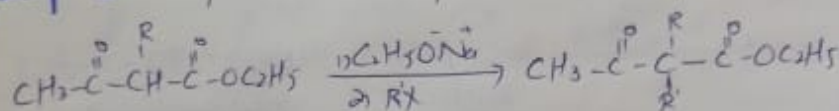
Step 1:- Formation of sodium salt



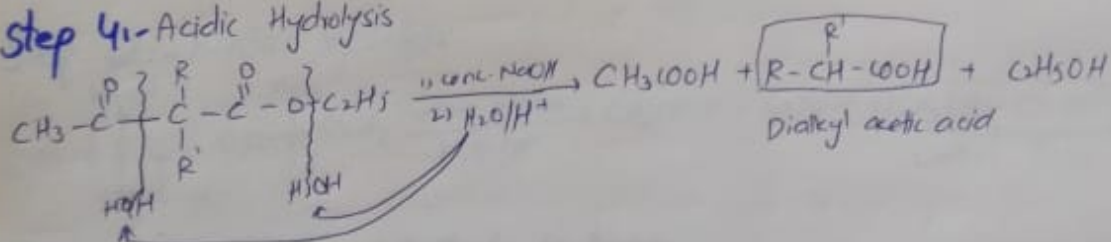
Step 2:- Alkylation



Step 3:- Step 1 and step 2 are repeated

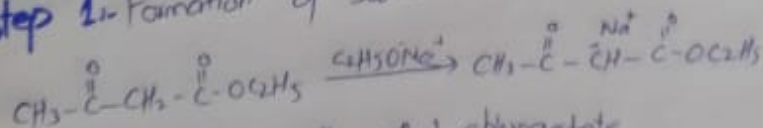


Step 4:- Acidic Hydrolysis

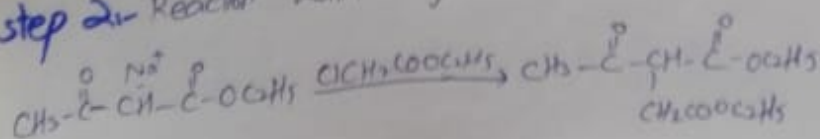


3-Synthesis of Succinic Acids (carboxylic acid)

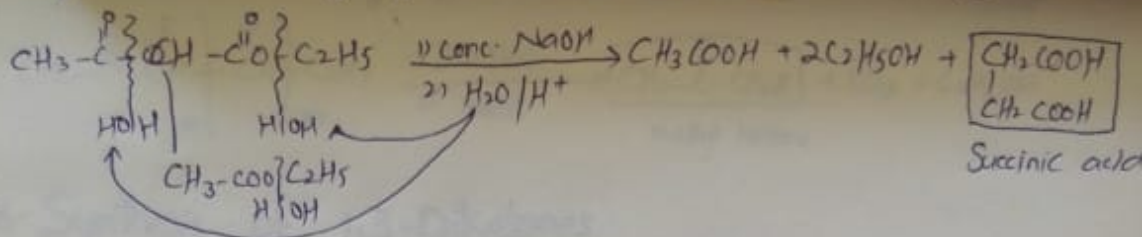
Step 1:- Formation of sodium salt



Step 2:- Reaction with ethyl chloroacetate



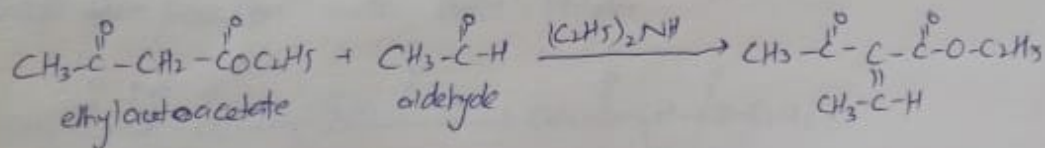
Step 3:- Acidic hydrolysis



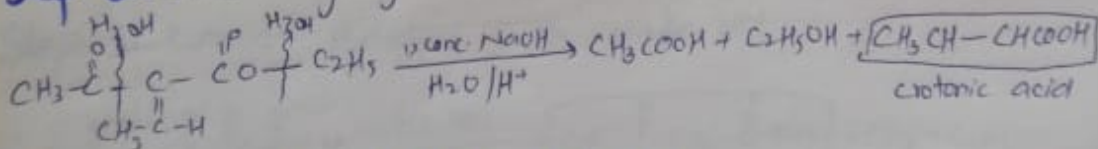
4. Synthesis of α, β -unsaturated Acids

(crotonic acid) (carboxylic acid)

Step 1:- Reaction of ethyl acetoacetate with aldehyde, catalysed by a base.



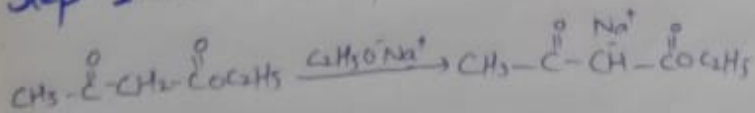
Step 2:- Acidic hydrolysis



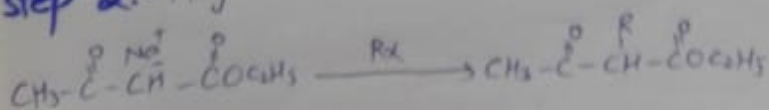
5. Synthesis of Methyl Ketones

(e.g. 2-Butanone)

Step 1:- Formation of sodium salt

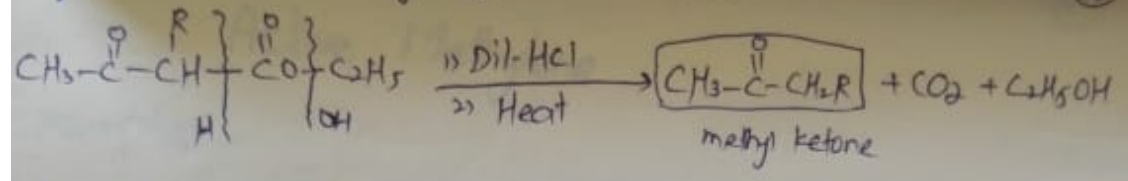


Step 2:- Alkylation



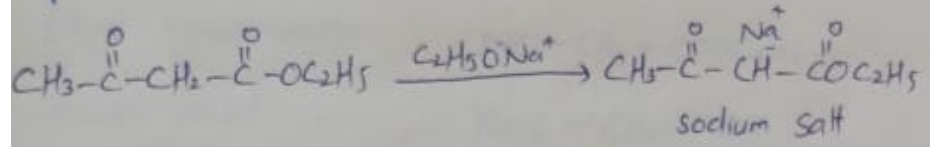
Step 3:- Ketonic Hydrolysis with HCl

(38)

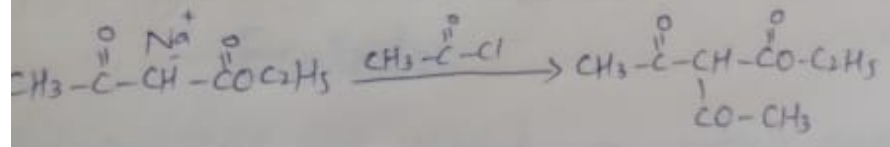


- Synthesis of 1,3-Diketones

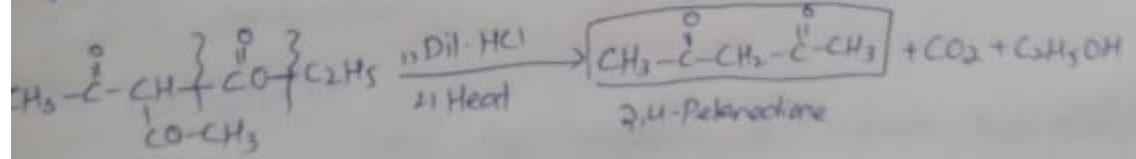
Step 1:- Formation of sodium salt



Step 2:- Reaction with Acid Halides



Step 3:- Ketonic Hydrolysis with dilute HCl

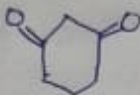


Lecture
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Active Methylene

Examples:-

- 1- Ethyl acetoacetate $\text{CH}_3\text{CO}-\text{CH}_2-\text{COOC}_2\text{H}_5$
- 2- Diethyl malonate $\text{H}_5\text{C}_2\text{COOC}-\text{CH}_2-\text{COOC}_2\text{H}_5$
- 3- Ethyl cyanoacetate $\text{NC}-\text{CH}_2-\text{COOC}_2\text{H}_5$
- 4- Oxalic acid $\text{HOOC}-\text{CH}_2-\text{COOH}$
- 5- 1,3-cyclohexadione 

Enolization

Formation of that product in which double bond and alcohol is present.
e.g. aldol condensation

Aldol Condensation

These are reactions in which two same molecules of aldehyde or ketone combine together in the presence of acid and base and form a new product aldol.

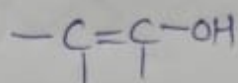
→ Aldol reaction is confined to that aldehyde or ketone molecules that contain α -hydrogen.

→ The reaction in which H_2O is removed is called condensation.

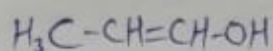
Enolization

Enols

Compounds containing hydroxy group directly attached to a C=C bond.

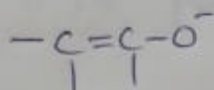


e.g,



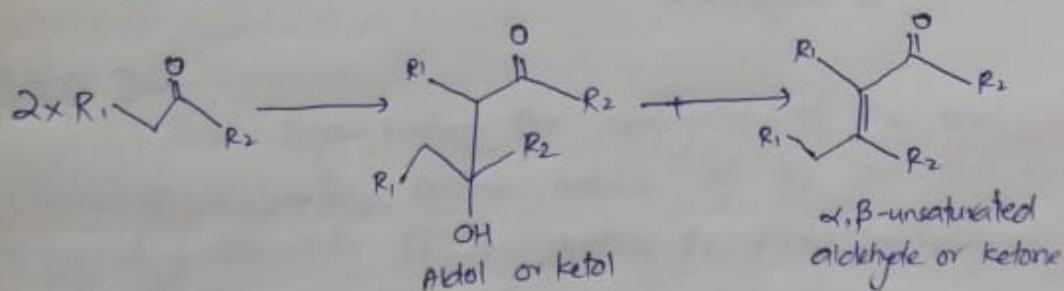
Enolate ions

Anions of enols are called enolate ions



e.g, $\text{H}_3\text{C}-\text{CH}=\text{CH}-\text{O}^-$

Aldol Condensation



DRAFT

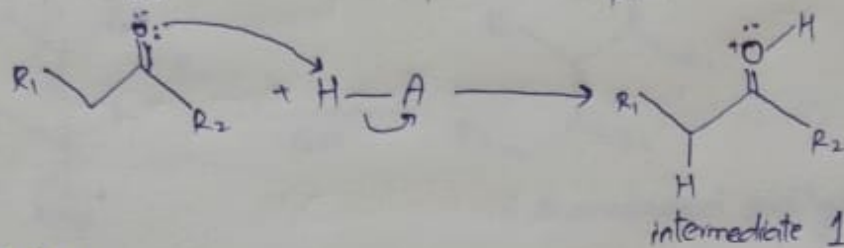


DRAFT

Mechanism of Acid Catalyzed Aldol Condensation (4)

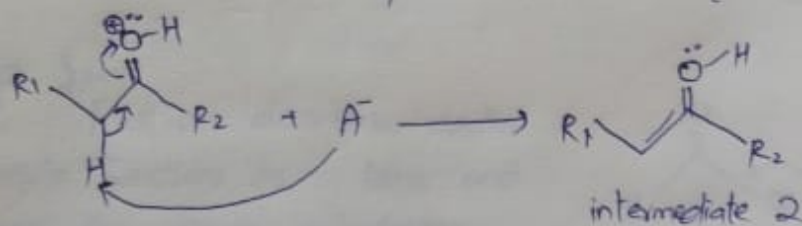
Step 1:-

The acid acts as a proton donor and activates carbonyl oxygen into a protonated form.



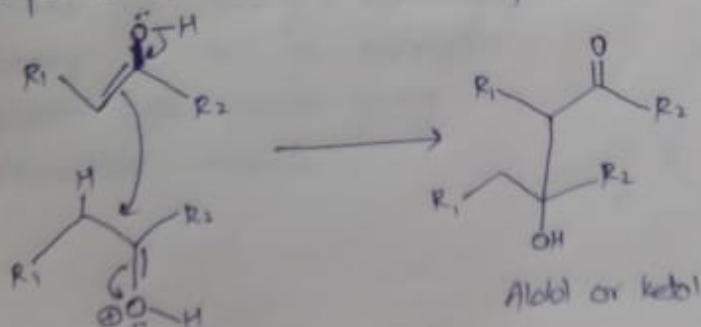
Step 2:-

The intermediate 1 reacts with the conjugate base of the acid (i.e. A⁻) to produce the enol (intermediate 2).



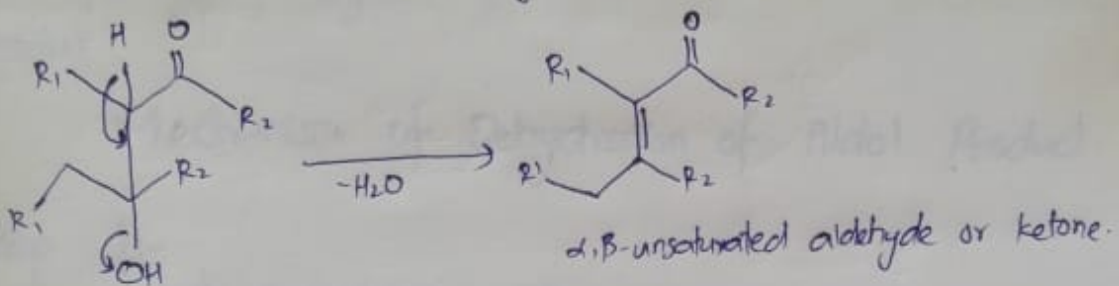
Step 3:-

This step involves the conjugation of the enol (intermediate 2) with another molecule of the activated carbonyl compound (intermediate 1) to produce the aldol (or ketol).



Step 4:-

The aldol (or ketol) undergoes spontaneous dehydration due to base catalyzed dehydration to yield the α,β -unsaturated aldehyde or ketone.



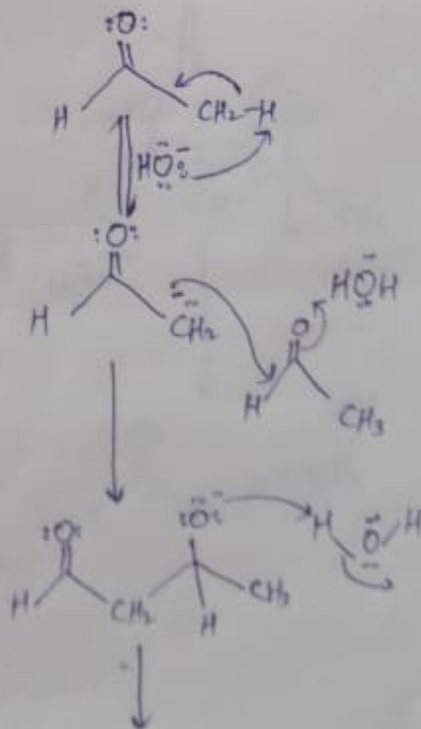
Mechanism of the Base-Catalyzed aldol Condensation

Step 1:-

First, an acid-base reaction. Hydroxide functions as a base and removes the acidic α -hydrogen giving the reactive enolate.

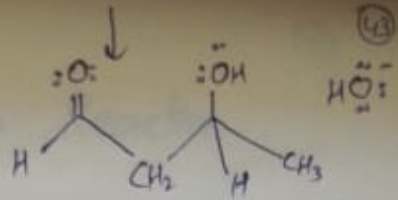
Step 2:-

The nucleophilic enolate attacks the aldehyde at electrophilic carbonyl C in a nucleophilic addition type process giving an intermediate alkoxide.



Step 3:-

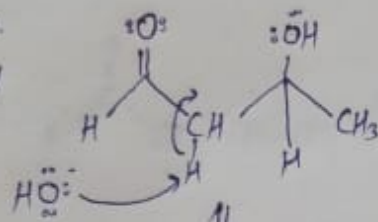
The alkoxide deprotonates a water molecule creating hydroxide and β -hydroxyaldehydes or aldol product.



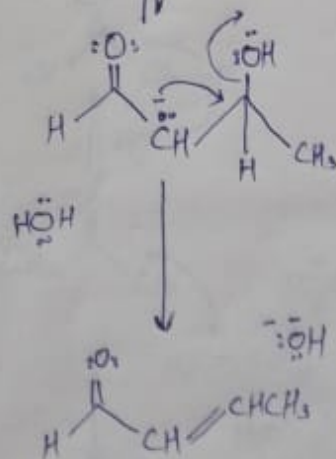
Mechanism of Dehydration of Aldol Product

Step 1:-

Firstly, an acid base reaction. Hydroxide functions as a base and removes an acidic α -hydrogen giving the reactive enolate.



Step 2:- The electrons associated with the negative charge of enolate are used to form C=C bond and displace the leaving group regenerating hydroxide giving the conjugated aldehyde.



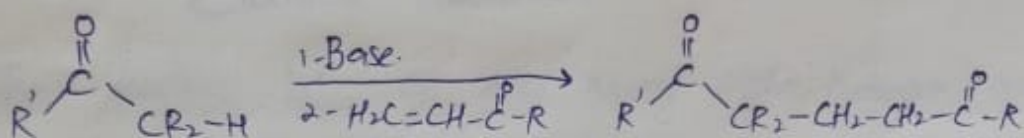
Lecture
3-4-2020

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The Michael Addition Reaction

A conjugate addition with a carbonium nucleophile is as Michael addition or reaction.

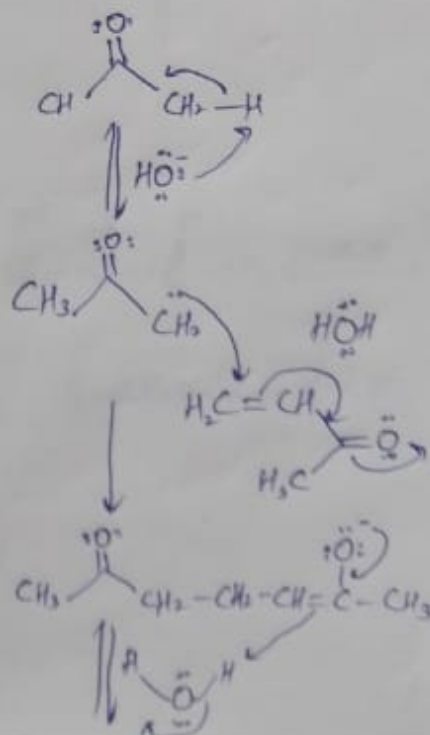
- The first step is the formation of enolate.
- Enolates tend to react with α,β -unsaturated ketones via conjugate addition.



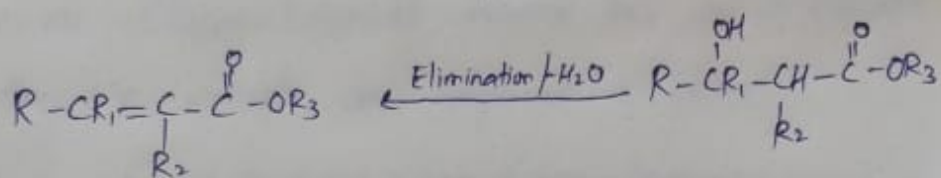
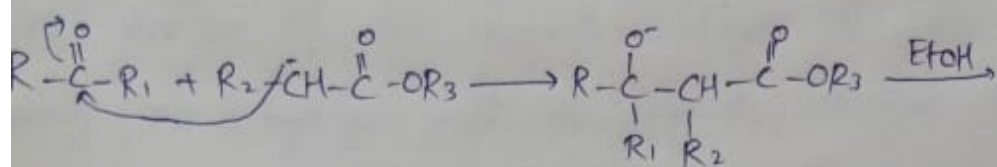
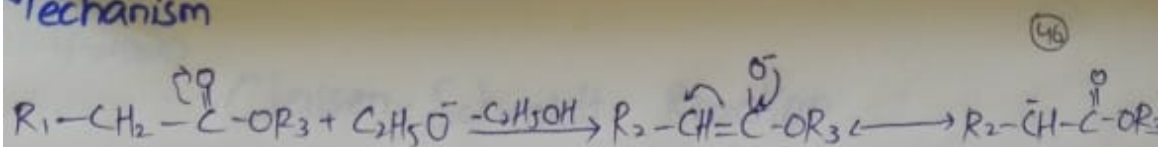
Mechanism

Step 1:- First, an acid-base reaction. Hydroxide functions as a base and removes acidic α -hydrogen giving the reactive enolate.

Step 2:- The nucleophilic enolate attacks the conjugated ketone at the electrophilic alkene C in a nucleophilic addition type process with the electrons being pushed to electronegative O, giving intermediate enolate.



Mechanism

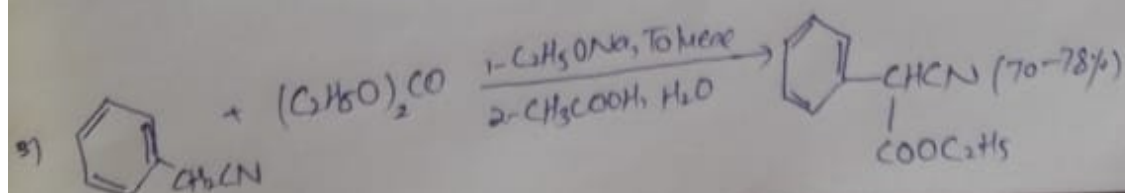
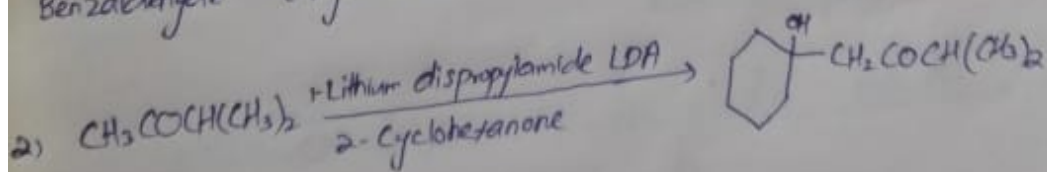
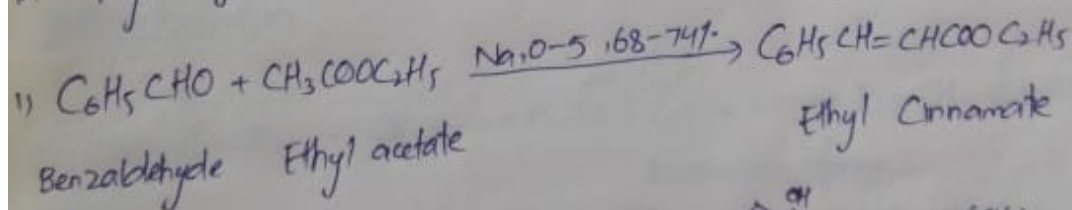


(Condensation Product)

(Addition Product)

Examples

The Claisen reaction is a useful method to get β -hydroxy ester or α,β -unsaturated esters and corresponding esters in high yield.



Lecture

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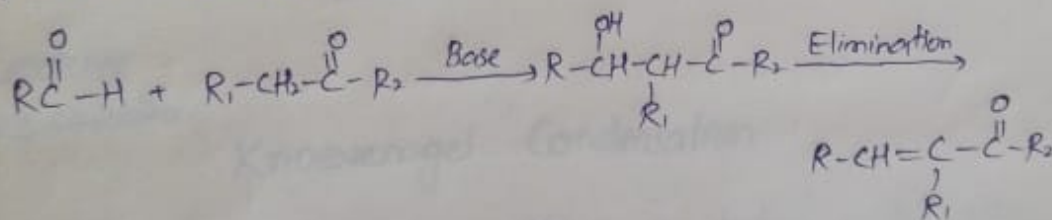
(47)

Claisen-Schmidt Reaction

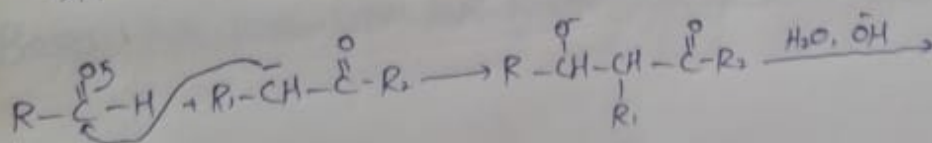
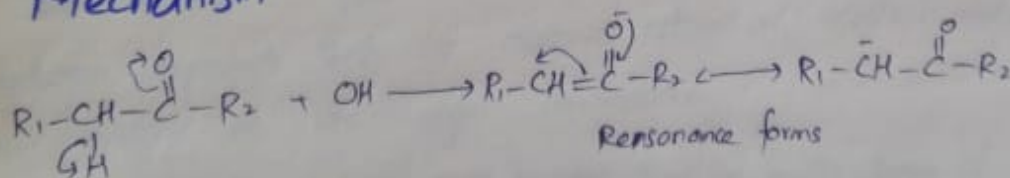
The reaction of an aromatic aldehyde or other aldehyde having no α -hydrogen with an aliphatic aldehyde or ketone is known as Claisen-Schmidt reaction. This is a crossed aldol reaction in which one compound is ketone.

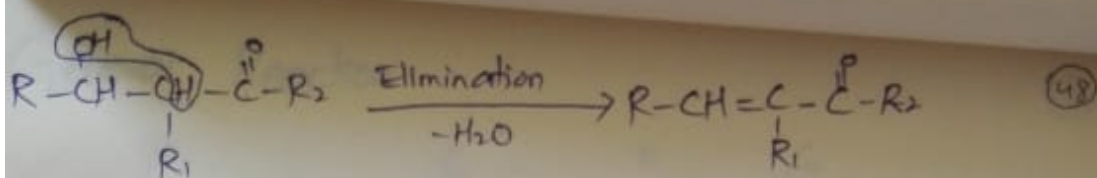
Bases:- Aqueous NaOH, Alcoholic NaOH, $\text{C}_2\text{H}_5\text{ONa}/\text{C}_2\text{H}_5\text{OH}$

General Reaction:-

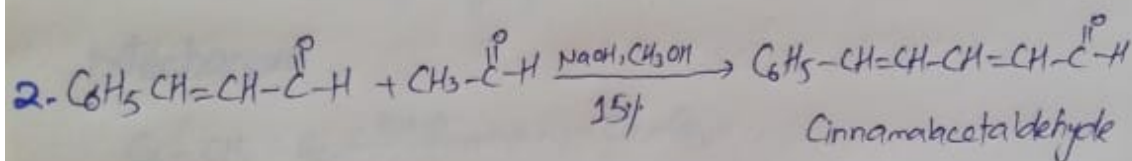
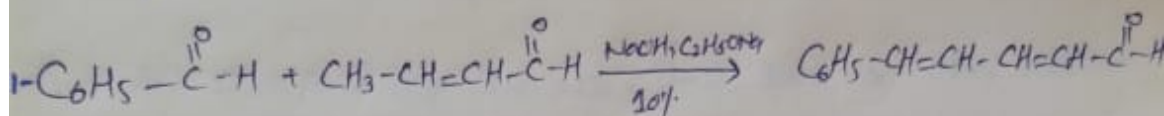


Mechanism





Example:-



Lecture

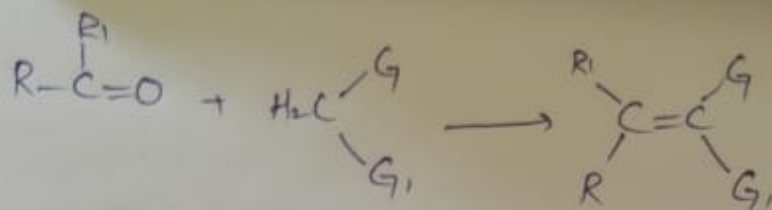
23-4-2020

Knoevenagel Condensation

The condensation b/w an aldehyde or ketone, with active hydrogen compounds such as malonic esters or related compounds is known as Knoevenagel condensation.

Bases:- NH_3 , RNH_2 , R_2NH , R_3N , Pyridine, Pyrrolidine with trace of piperidine

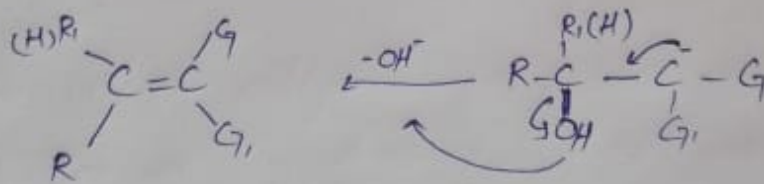
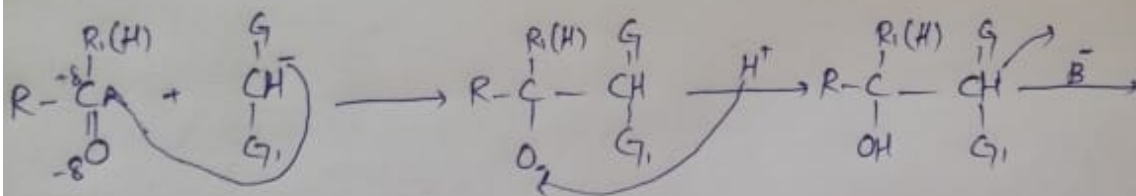
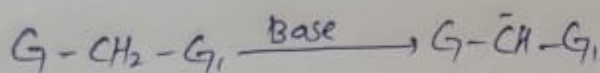
General Reaction



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G or G₁ = CHO, COOR, COR, CN, NO₂, $\overset{O}{\parallel}S-R$, SOOR or other electron-withdrawing groups.

Mechanism



Example

