

UNIT - 1

# Organic Reaction Mechanism & Introduction of drugs

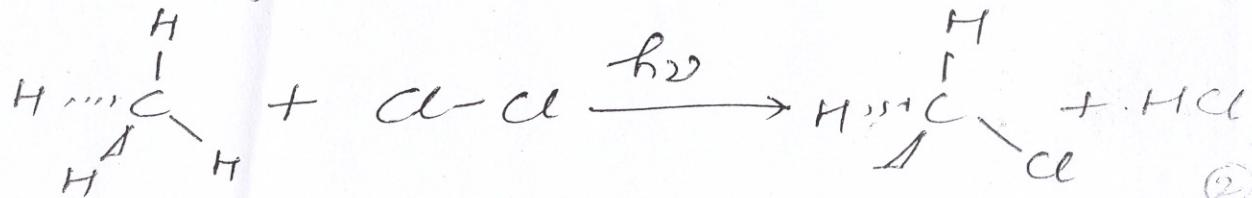
Organic reactions are those reactions in which organic compounds are involved. These are of following types -

1. Substitution 2. Elimination
3. Addition 4. Rearrangement
5. Pericyclic 6. Photochemical
7. Redox

1. Substitution Rea<sup>n</sup> — In these Rea<sup>n</sup> one functional gr. in a organic compound is replaced by other.

These are of two types -

- (i) Nucleophilic substitution Rea<sup>n</sup>  
(Attacking reagent is nucleophile)
  - (ii) Electrophilic  
(Attacking reagent is "electrophile")
- e.g. Halogenation of alkanes.



Difference bet<sup>n</sup> intermediate and transition state -

(2A)  
②

Intermediate :- Stable & can be isolated  
e.g. carbocation, free radicals, carbanion

Transition State :- An imaginary state.

Nature of attacking group :-

1. Nucleophilic Reagent :- These are electron rich species & have a tendency to donate pair of electrons. Generally these are negatively charged.

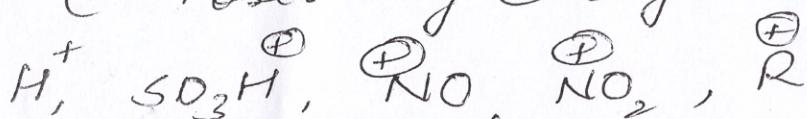
e.g.  $\text{OH}^-$ ,  $\text{OR}^-$ ,  $\text{Cl}^-$ ,  $\text{Br}^-$ ,  $\text{F}^-$ ,  $\text{NH}_3^-$ .

(ii) All Lewis base having lone pair of  $\text{e}^-$   $\text{H}_2\ddot{\text{O}}$ ,  $\text{R}-\ddot{\text{O}}-\text{H}$ ,  $\ddot{\text{N}}\text{H}_3$ ,  $\text{R}-\ddot{\text{N}}\text{H}_2$ ,  $\text{R}_3\ddot{\text{N}}$

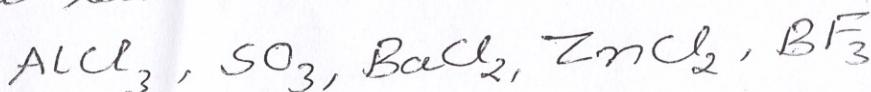
2. Electrophiles / Electrophilic Reagents :-

~~Cation~~ These are electron-deficient species and have a tendency to accept electron pair so these are Lewis acids. These may be positively charged or neutral species

e.g. (i) Positively Charged species -



(ii) Neutral electrophiles -  
all Lewis acid -



(3)

## Nucleophilic Substitution Rea<sup>n</sup>-

③ ④

These reactions are of two types-

(i) unimolecular nucleophilic sub. ( $S_N^1$ ) -

## (ii) Bimolecular

SN' →

九

( $S_N^2$ )

(CZ) -

Where  $s$  = substitution

N = Nucleophile

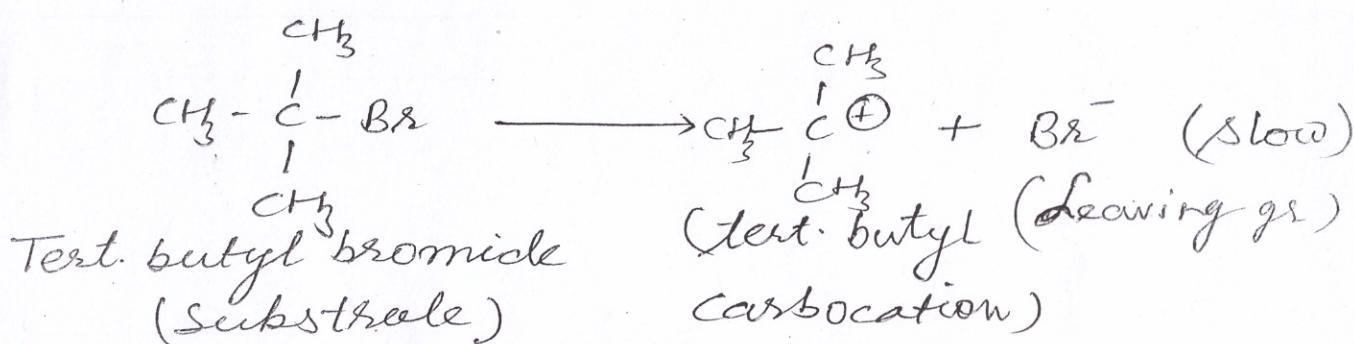
I = unimolecular

In these type of reactions the rate of reactions depends on only on alkyl halide. It shows I order kinetics.

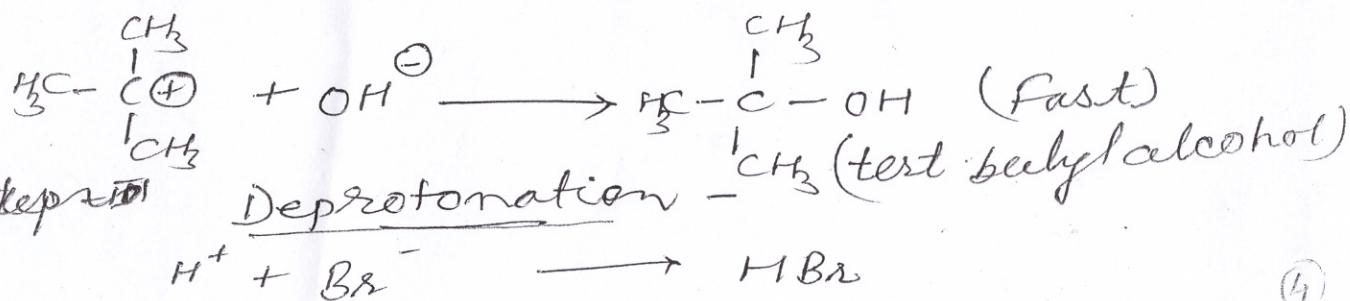
e.g. Hydrolysis of tert-butyl bromide

## Mechanism

## Step - I Formation of carbocation



## Step-II Nucleophilic attack



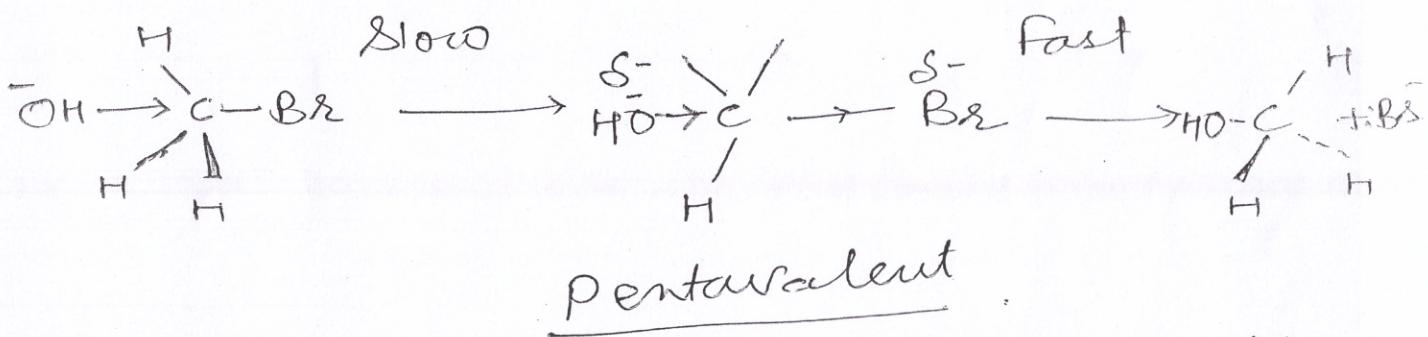
The  $S_N^1$  mechanism has two steps. In 1st step, the leaving gr. departs, forming carbocation. In II step the Nucleophile ( $:Nu^-$ ) attacks to the carbocation and forms covalent bond.

Stability of carbocation -



$S_N^2$  → Rate of reactions depends upon concentration of reactant (substrate) and nucleophile both

Mechanism -



The breaking of bond and formation of bond takes place simultaneously.

Reactivity of substrate -

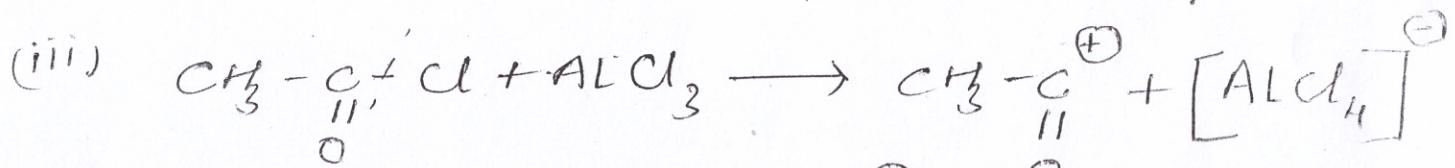
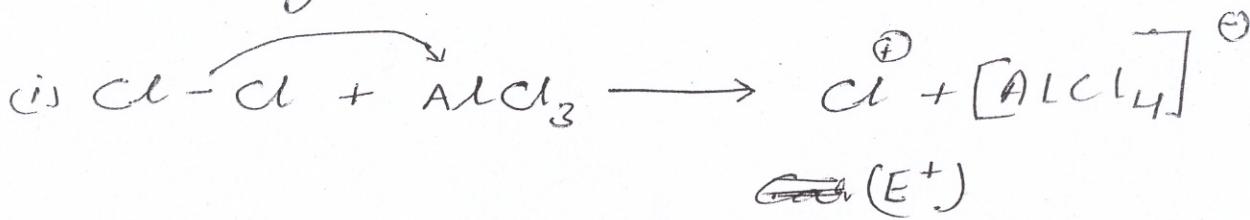


## Mechanisms of Electrophilic Sub. Reac (S<sub>E</sub>)

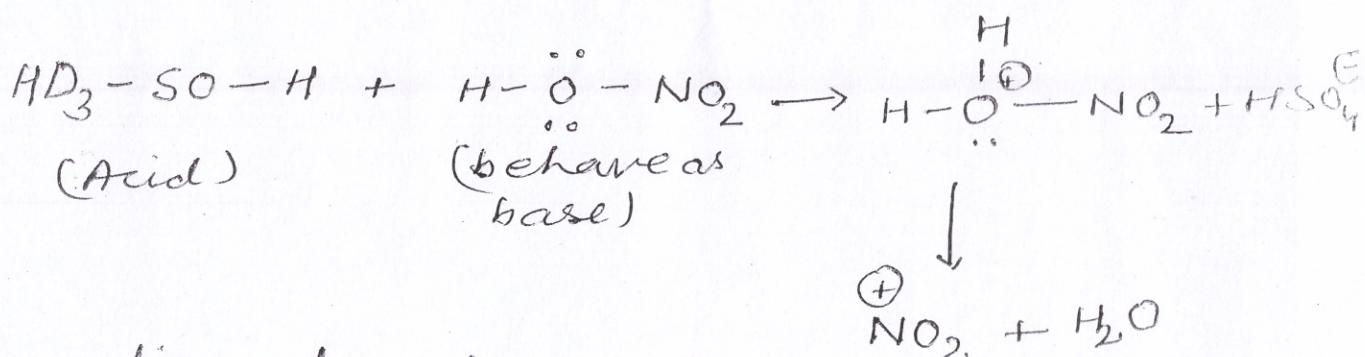
(i) Generation of electrophile - (E<sup>+</sup>) :-

It is generated from reagent.

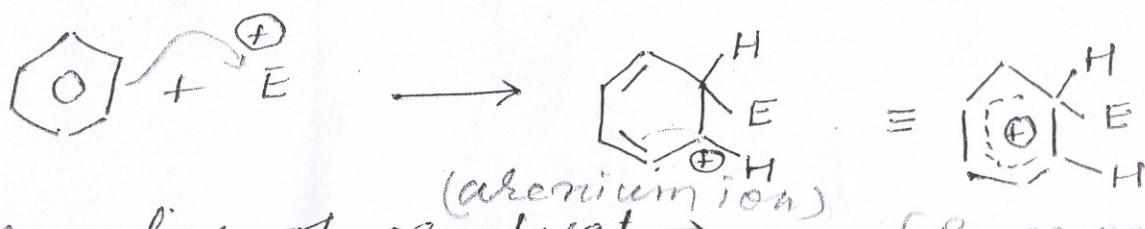
For e.g. during chlorination, alkylation and acylation of benzene.



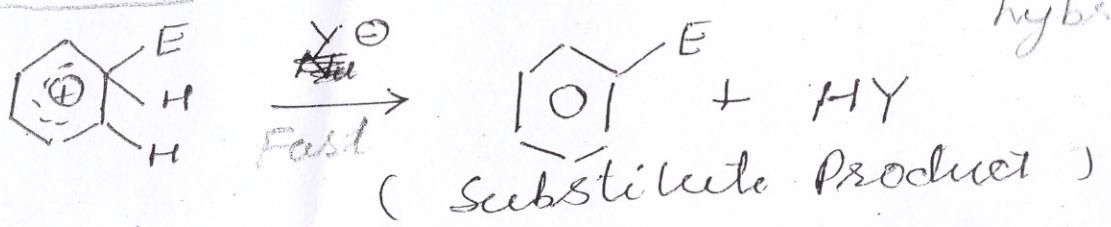
In case of nitration  $\text{NO}_2^+$  is produced by transfer of a proton from  $\text{H}_2\text{SO}_4$ .



(ii) Formation of intermediate carbocation →



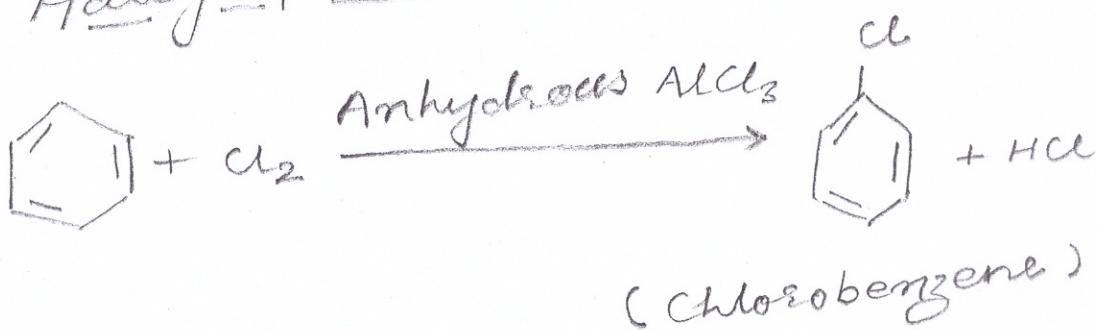
(iii) Formation of product →



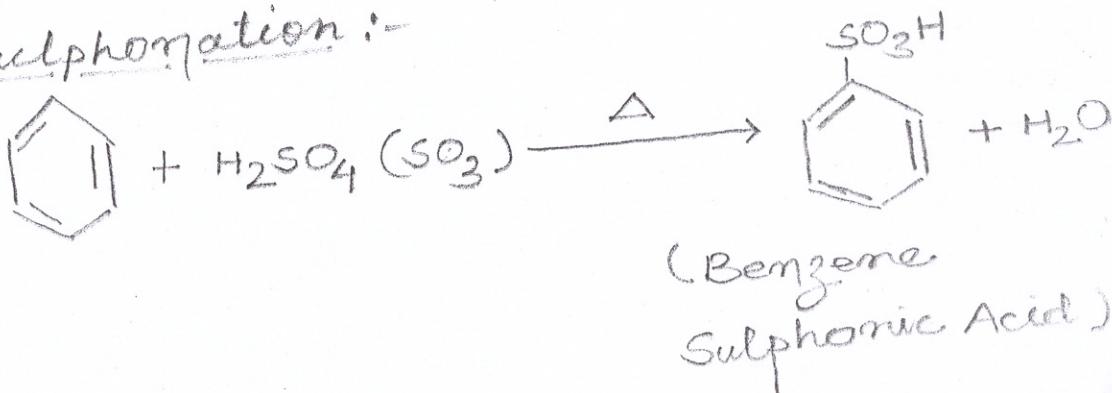
Q. 6

Examples of electrophilic substitution reactions (6)

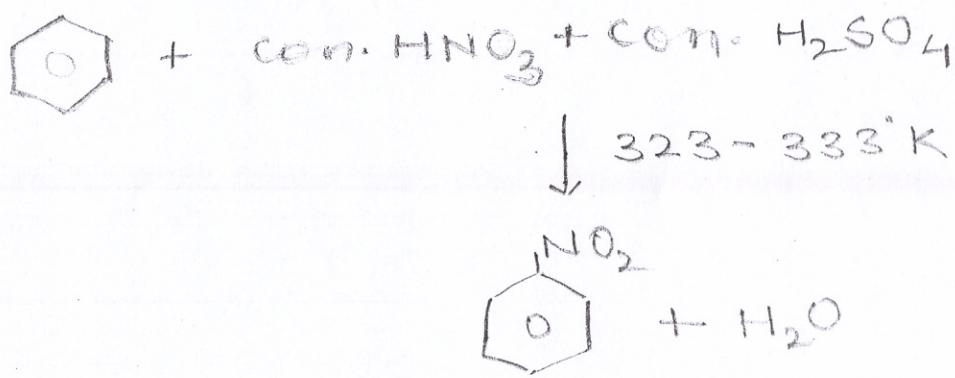
(i) Halogenation



(ii) Sulphonation:

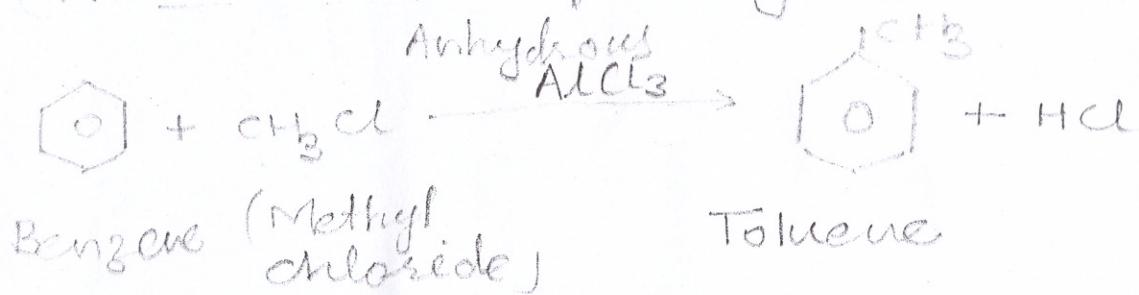


(iii) Nitration:



(Nitrobenzene)

(iv) Friedel-Crafts alkylation:



(6.1) 6

## Free Radical Substitution Reactions

### of alkanes -

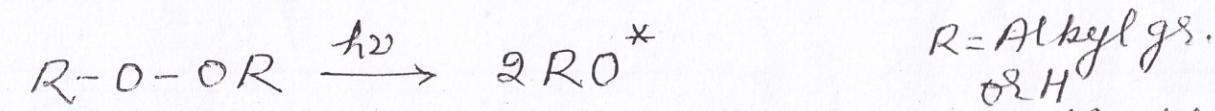
Replacement of hydrogen atom of alkane by halogen atom (halogenation)

In this type of mechanism the substitution is take place by free radical in following steps-

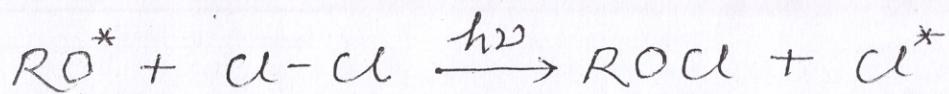
#### Step - I Initiation

(Formation of free radical)

Formation of free radical in presence of sun light or heat or peroxide.



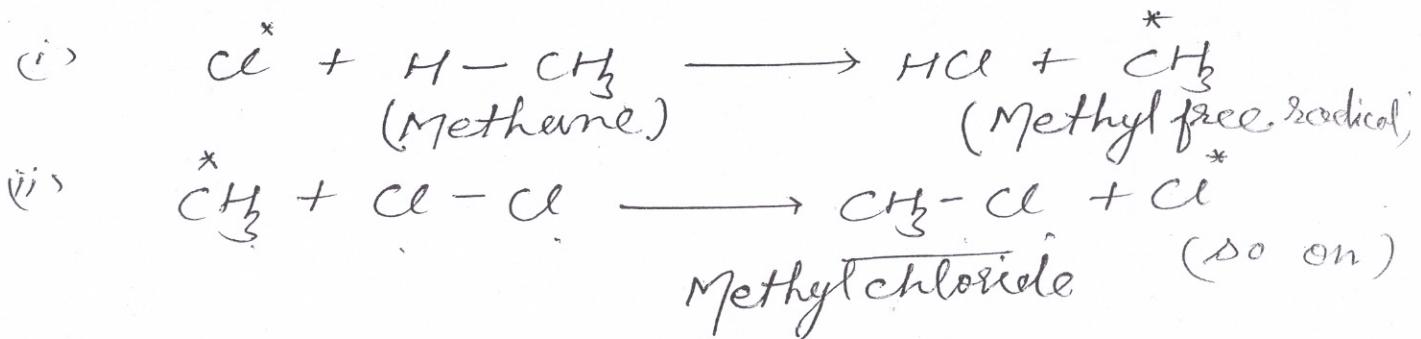
Peroxide (Peroxide free radical)



(Chlorine)

(Chlorine free radical)

## Step - II - Propagation of free radical (8)



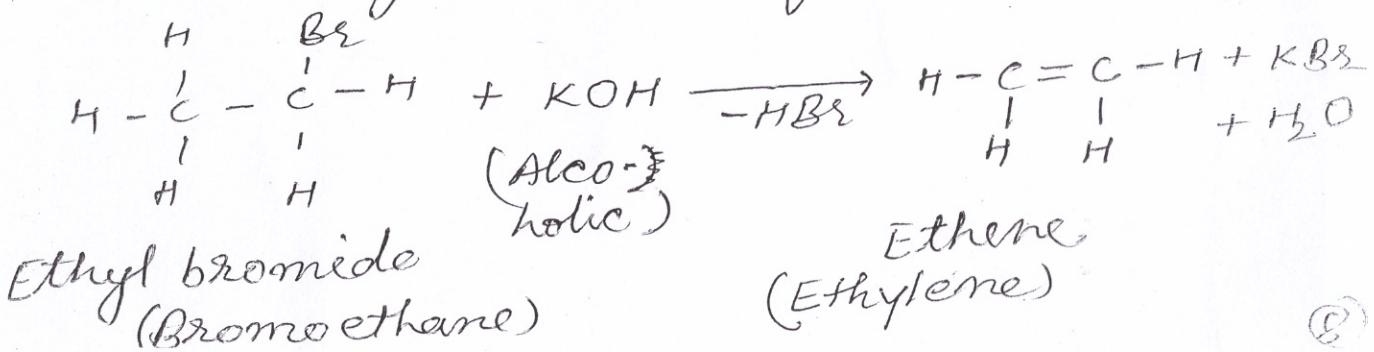
Step - III Chain Termination -  
 Possible steps are -

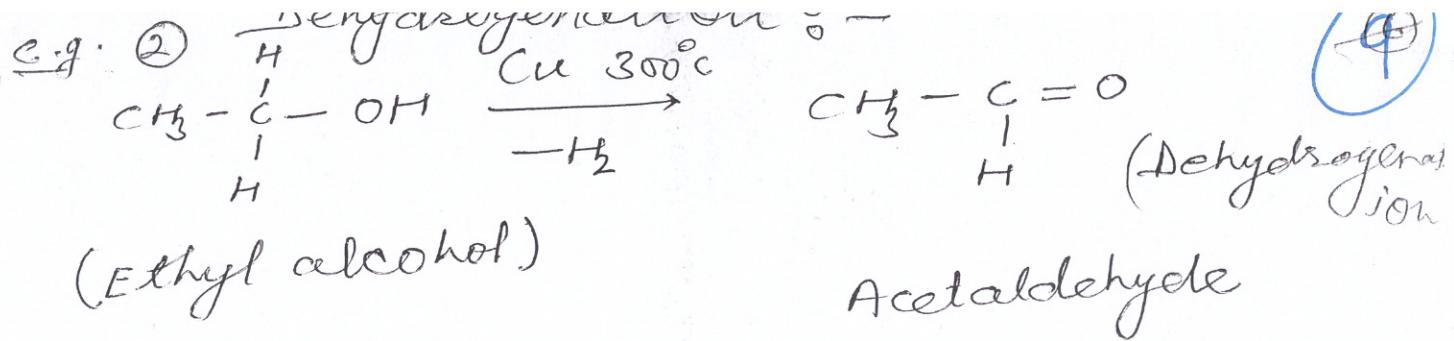


Eg. Chlorination & Bromination of alkanes (methyl chloride).

Elimination Rea<sup>n</sup> - These rea<sup>n</sup> involves the loss of atoms / group from the organic compound to generate double / triple bond. The state of hybridization changes from  $sp^3$  to  $sp^2$  &  $sp$ .

E.g. ① dehydrohalogenation of alkyl halide and dehydration of alcohols.





It may be  $\alpha$ -elimination ( $\text{1},\text{1}$ -elimination) or  $\beta$ -elimination ( $\text{1},\text{2}$ -elimination)

Elimination reac<sup>n</sup> mechanism are of two types -

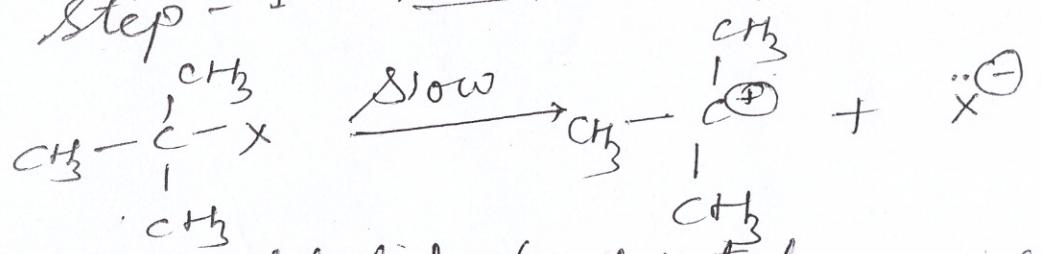
i)  $E^1$  (unimolecular) ) ii)  $E^2$  (Bimolecular)

•  $E^1$  reactions →  $E^1$  elimination  
 • Starts with same unimolecular dissociation and follows the loss of  $\text{H}^+$  from the intermediate carbocation rather than by substitution.

e.g. Dehydrohalogenation of alkyl halide -

Mechanism -

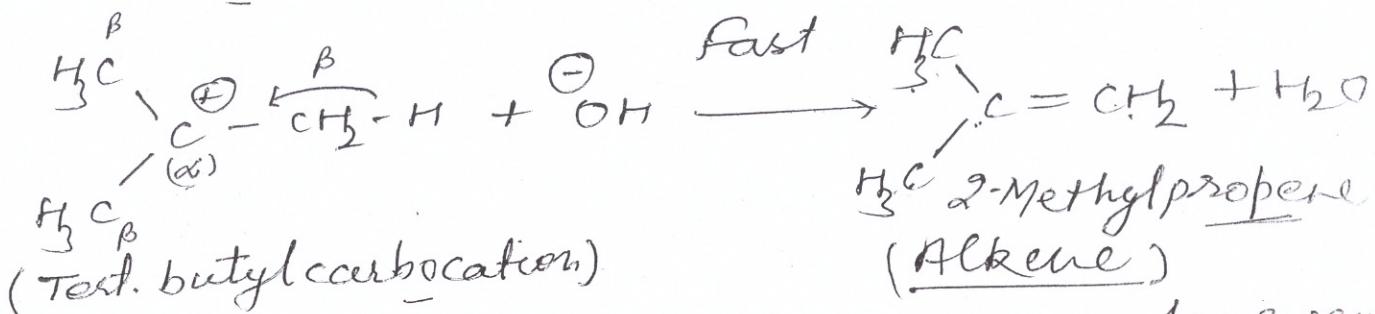
Step - I Formation of carbocation



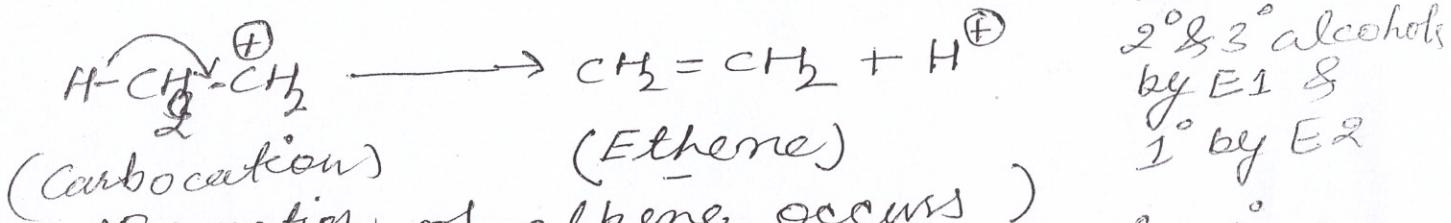
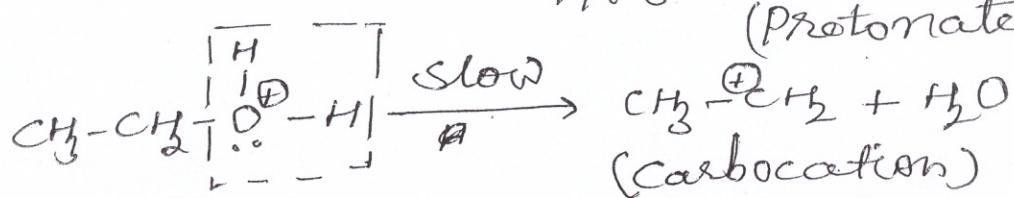
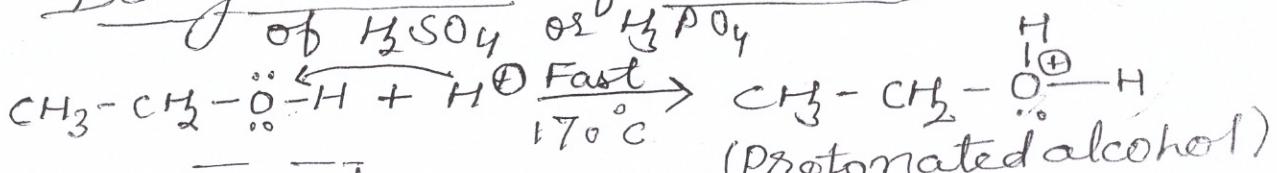
Tert. butyl halide (Tert. butyl carbocation)  $\text{X} = \text{Cl, Br etc.}$  (9)

The Saytzeff Rule: - If alkyl halide (10) have two/more different  $\beta$ -carbons, more than one alken is formed. The product is determine by Saytzeff rule according to which ~~or~~ the most mightly substituted alkene will the major product. and stable.

Step II:- Carbocation loses a proton II  
from the  $\beta$ -carbon atom by the base (nucleophile) to form alkene



(ii) Dehydration of alcohols :- In presence of  $\text{H}_2\text{SO}_4$  or  $\text{H}_3\text{PO}_4$

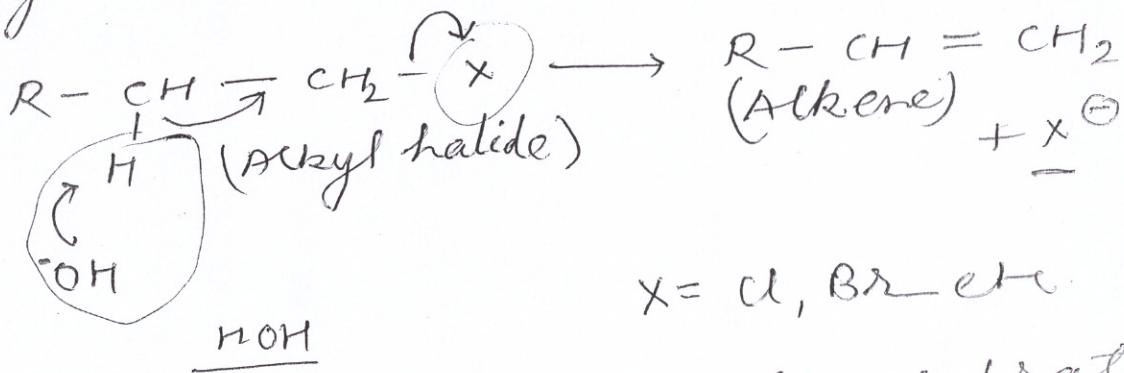


(Formation of alkene occurs)

Order of dehydration of alcohol  $3^\circ > 2^\circ > 1^\circ$

E-2 (Elimination Bimolecular Mech.)

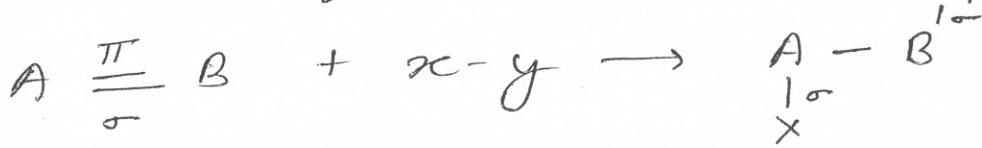
e.g. Dehydrohalogenation of primary alkyl halide to form alkenes



Rate of Reac<sup>n</sup> depends on both substrate.  
II order kinetics. It is also one step process.

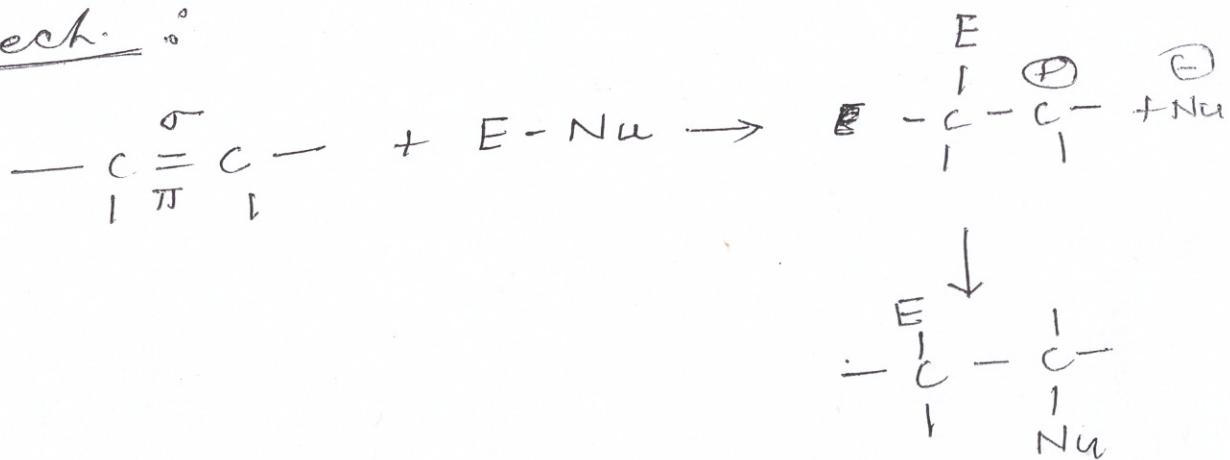
Addition  $\text{Rea}^3 \rightarrow \pi$ -bond is broken to form  $2\sigma$  bonds.

(P2)

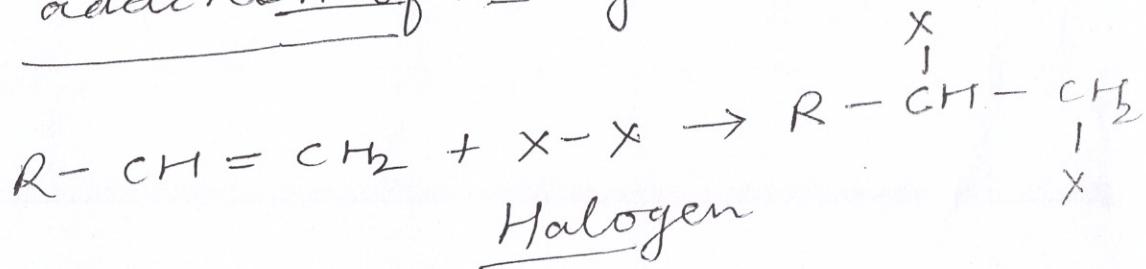


Electrophilic addition in alkene -

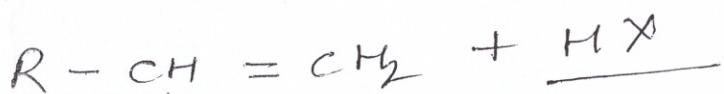
Mech.:



e.g. addition of halogen



Markownikoff Rule  $\Rightarrow$



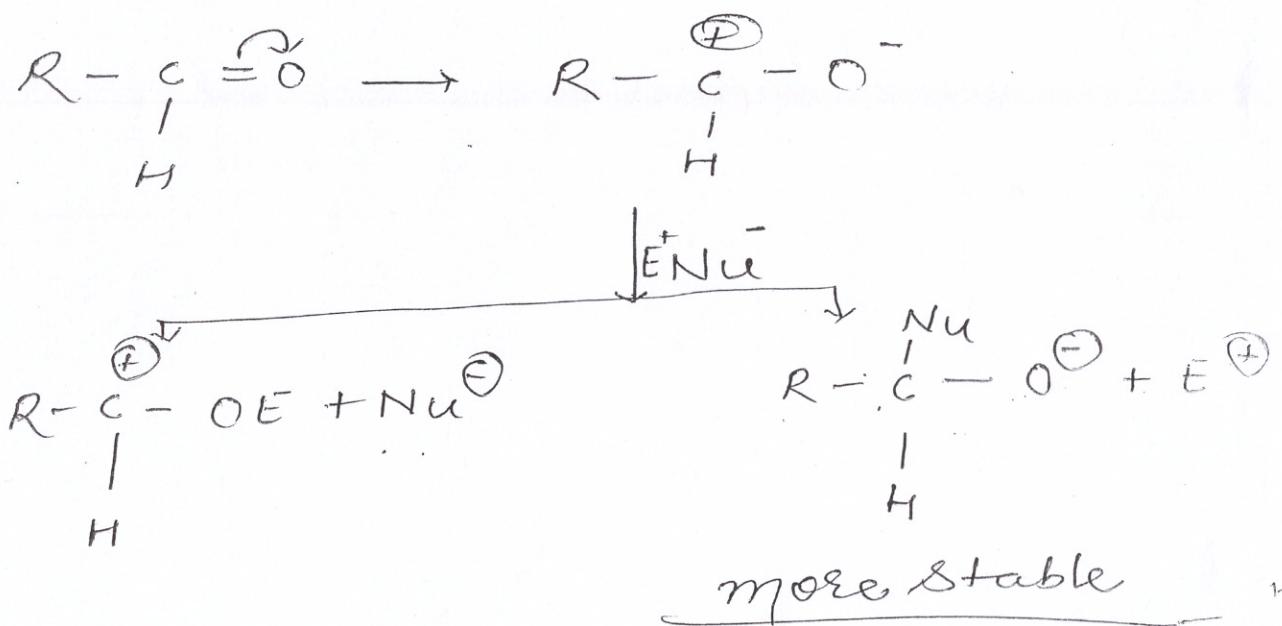
(unsaturated compound)      hydrogen halide

halogen atom goes to that c atom which bearing lesser no. of hydrogens or on atom where X is already attached.

Nucleophilic addition in aldehydes and Ketones :-

(13)

In carbonyl gr ( $\text{C}=\text{O}$ ) oxygen is more electronegative than C and therefore the oxygen atom with a negative charge is more stable than the positively charged C atom. Therefore an nucleophile will attack on carbonium ion much readily than the electron-deficient reagent (an electrophile) attacks the negative oxygen atom.



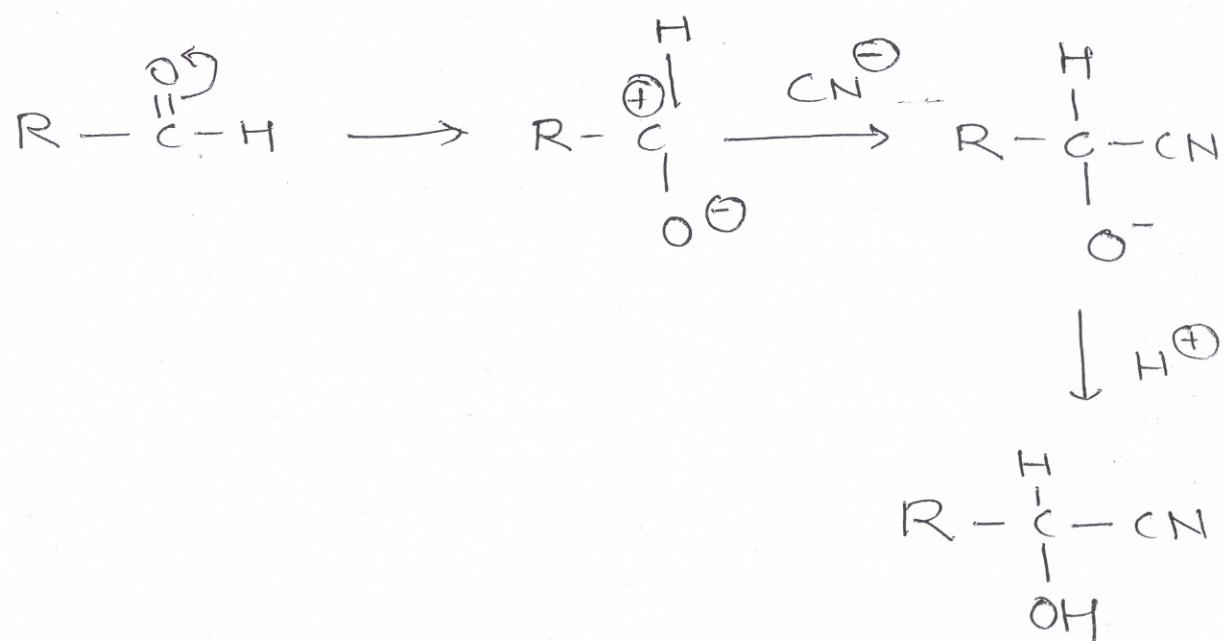
(as the  $\ominus$  charge on the more electronegative oxygen atom hence formed)

(12)

# Hydrogen cyanide

(14)

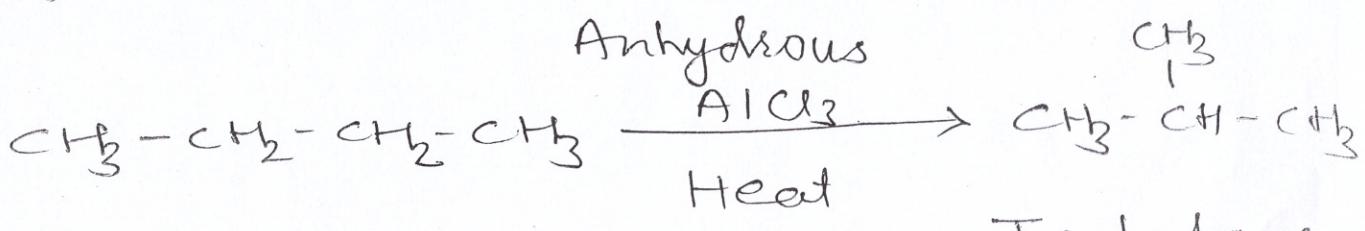
e.g. addition of  $\text{HCN}$   $\rightarrow$



Aldehyde cyanohydrin

Rearrangement Rea<sup>n</sup>  $\rightarrow$  Shift of an atom/group from one position to another within the molecule.

e.g.



Isobutane

(2-methylpropane)

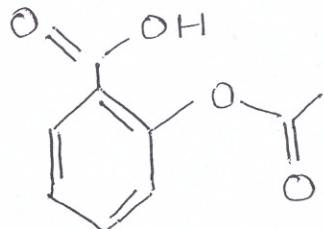
These are

(13)

(15)

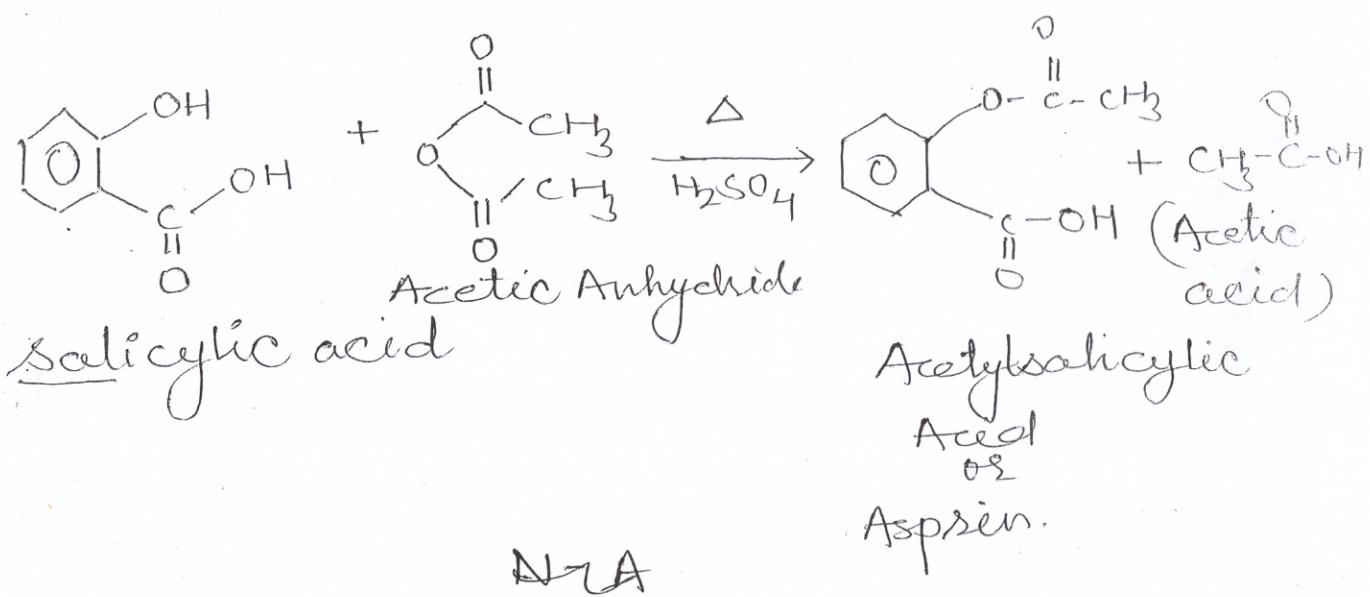
Aspirin - It is also known as acetylsalicylic acid (ASA).

Structure :-



Synthesis :- It is synthesized by an esterification reaction. In this process (heated) salicylic acid is treated or reacted with excess amount of acetic anhydride in presence of small amount of sulfuric acid/phosphoric acid. The product is then treated with water to remove the excess acetic anhydride and cause the aspirin to crystallize.

Chemical reaction :-



(15)

(46)

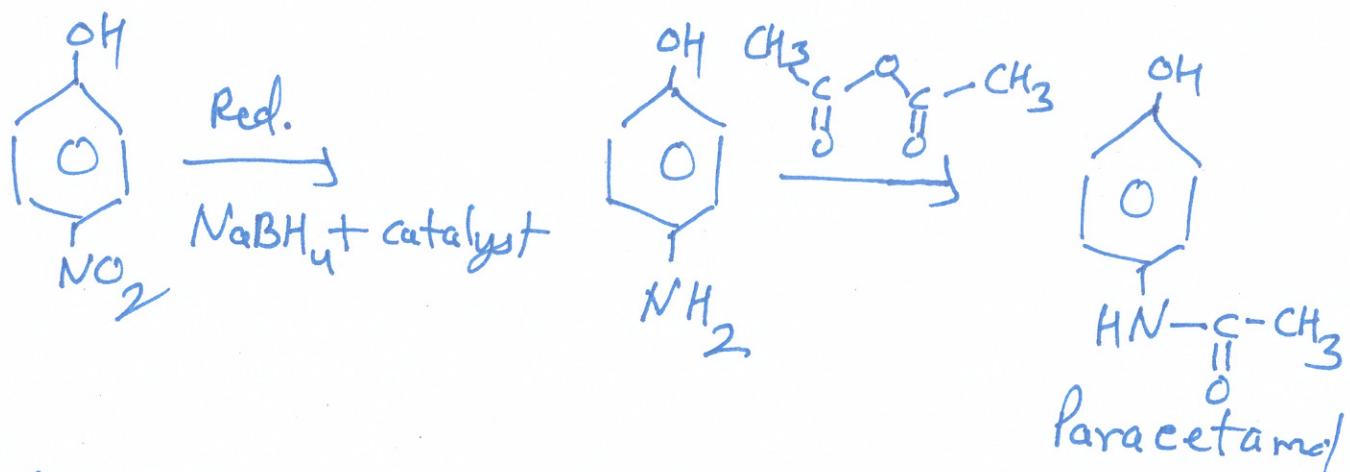
Properties of Aspirin : Aspirin is a non-steroidal anti-inflammatory drug (NSAID). It is not steroids but have similar benefits. It is one of the most widely used drug in the world.

Uses :-

1. It is used for treating mild to moderate pain & fever.
2. It can reduce - (High doses)
  - (i) Rheumatic fever
  - (ii) Rheumatic arthritis
  - (iii) inflammatory joint conditions.
3. In low doses it is used-
  - (i) To prevent blood clots and reduce the risk of a transient ischaemic attack (TIA).
  - (ii) To prevent a stroke
  - (iii) To prevent myocardial infarction With cardiovascular disease
  - (iv) To prevent colorectal cancer.

# (17)

Paracetamol (Acetaminophen)  
or P-acetamido-phenol



Uses:- It is used as analgesic which acts as painkiller in mild to moderate pain. It is antipyretic (to reduce fever).

## Assignment - 5

- (1) Why do substitution reaction occur in benzene?
- (2) what are electrophile & nucleophiles give examples also ?
- (3) Describe synthesis & properties of Aspirin & Paracetamol.
- (4) Explain mechanism of electrophilic and free radical addition in alkene.
- (5) Define elimination reaction with example?
- (6) What is Markonikov & Anti markonikov rule, Explain Saytzeff rule.