SEM II STUDY MATERIAL

Substitution and Elimination Reactions

Nucleophilic Substitution in aliphatic Compounds:

Generally represented as

$$R-X + \overset{(-)}{Nu} \longrightarrow R-Nu + \overset{(-)}{X}$$

Aliphatic nucleophilic substitution reaction may be further classified into the following three types.

i) SN^2 reaction. iv) $SN^{2'}$ reaction.
ii) SN^1 reaction. v) $SN^{i'}$ reaction.
iii) SN_i reaction.

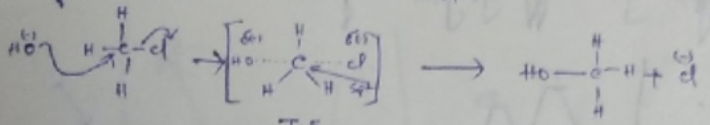
S = Substitution
N = Nucleophile } SN
2 ⇒ order / molecularity
i ⇒ intramolecular

SN_2 reaction:

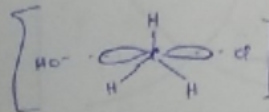
main features of SN_2 reaction may be noted as follows:

i) Single step process.
ii) bimolecular
iii) Here nucleophile approaches to the carbon bearing leaving group from very backside with respect to leaving group.
iv) If the leaving group bearing carbon is chiral, inversion of configuration occurs at this chiral carbon.

e.g., $CH_3Cl + \overset{(-)}{OH} \longrightarrow CH_3OH + \overset{(-)}{Cl}$

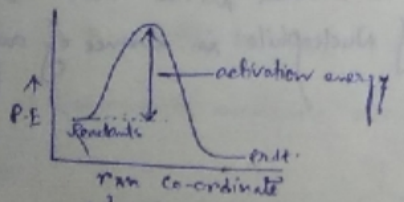


T.S



v) This reaction passes through five membered T.S. as shown above.

If we represent the SN_2 reaction graphically, we shall get the following type of energy profile diagram



Here reaction rate ~~proportional to Concentration~~ $\propto [\text{Substrate}][Nu]$

$= K \cdot [\text{Substrate}][Nu]$ [K = Rate const]

There are two concentration variables here. Any change either in the Concentration of Substrate or in the Concentration of nucleophile will alter the rate of reaction

Evidence in favour of S_N2 reaction :→

1) Kinetic Study :

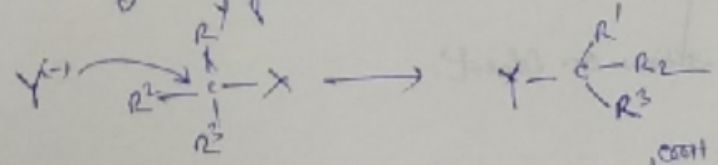
Rate = K [Substrate] [Nucleophile]

2 ⇒ Molecularity.

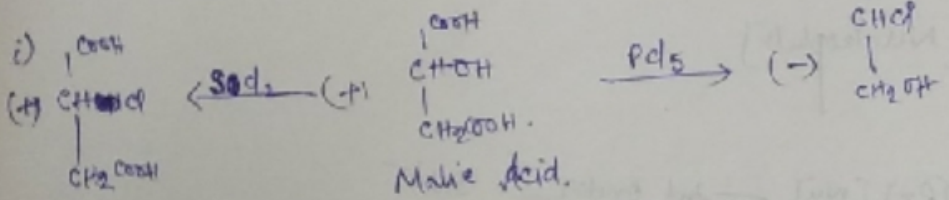
Rate = K [Substrate]

Pseudo 1st Order reaction

2) Inversion of Configuration :→ Walden Inversion.



i)

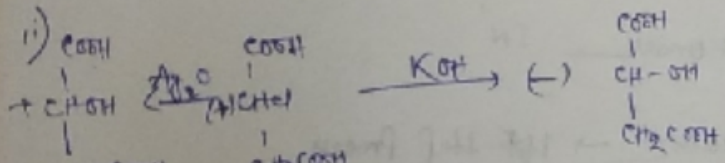


Malic Acid.

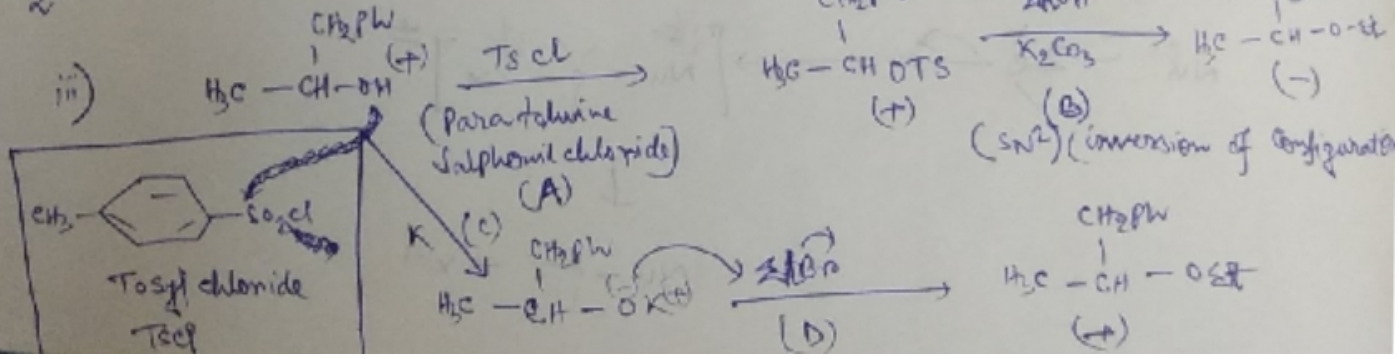
One retension and other inversion.

Which is which ?

ii)



iii)



S_N1 reactions: Main features of S_N1 reaction may be noted as follows

i) This is two step process

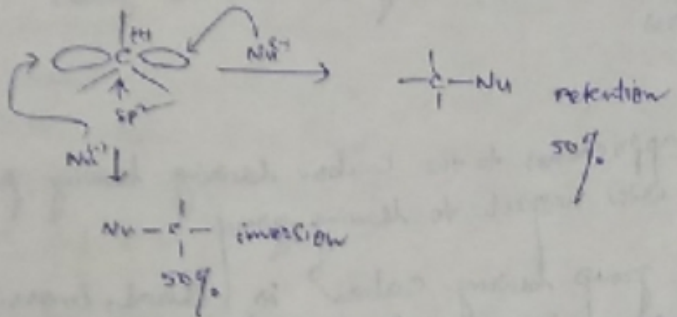
ii) Unimolecular

iii) In the first step of this reaction the substrate undergoes slow reversible dissociation to form carbocation. In the next step nucleophile adds to this carbocation to form product molecule.

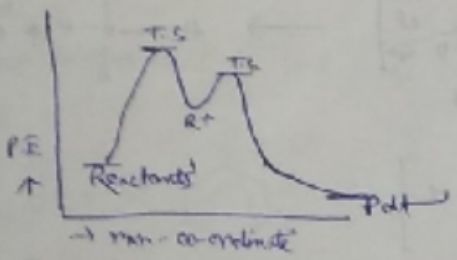
iv) Here racemisation occurs. (If the substrate is chiral)

$$R\text{-}X \underset{\text{fast}}{\overset{\text{slow}}{\rightleftharpoons}} R^{(+)} + X^{(-)}$$

$$R^{(+)} \xrightarrow{Nu^{(-)}} R\text{-}Nu \text{ or } Nu\text{-}R$$



If we represent this reaction graphically, we shall get the following type of energy profile diagram



$$\text{Reaction rate} \propto [\text{Substrate}]$$

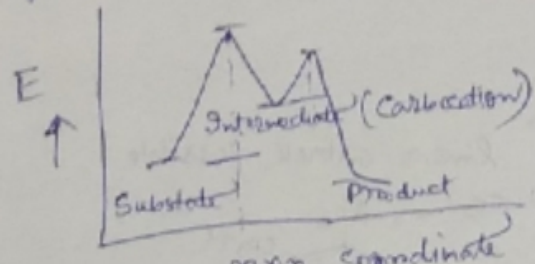
$$= K \cdot [\text{Substrate}]$$

Only substrate concentration is involved in the rate equation. In fact, solvent may play the role of Nucleophile in absence of any external nucleophile.

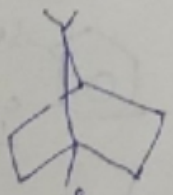
Evidence in favour of SN1 mechanism:

1) Rate = k[Substrate] — 1st order

Energy profile diagram

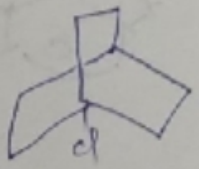


2) Isolation of carbocation.



(I) [2,2,1]

80% NaOH in ethanol → no reaction, No SN1



[2,2,2] (II)

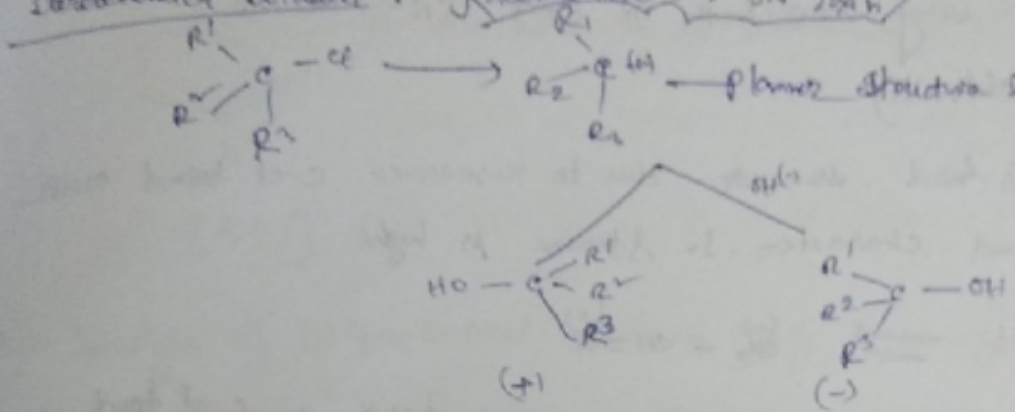
SN1 reagent → Slow rate SN1

[3,1,1] (III)

SN1 reagent → Slow rate SN1

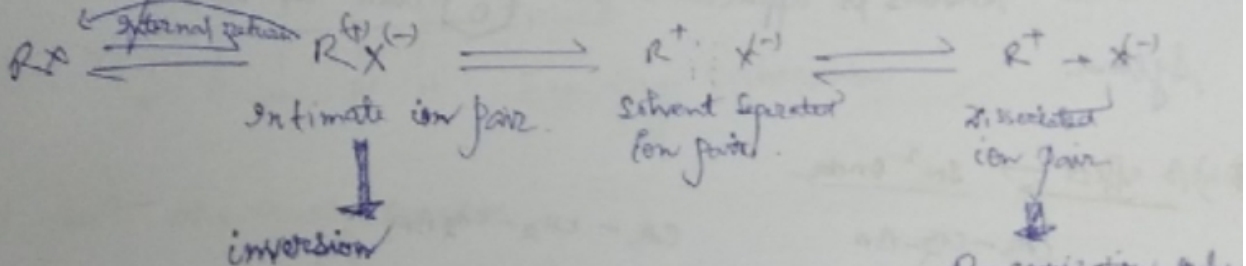
Two methyl group in (I) hinder the formation of carbocation, thus it does not take part in reaction; Formation of carbocation is easy for II to III. Thus SN1 reaction occurs through carbocation formation.

Stereochemical evidence :- Racemization in S_N1 reaction



Racemic mixture

⇒ Net 5-20% inversion and rest is racemisation in case of S_N1 reaction



[As in case of S_N1 ~90% racemisation observed. Thus it must go through carbocation formation.]

S_Ni → inversion
S_N1 → Racemisation
S_Ni → retention

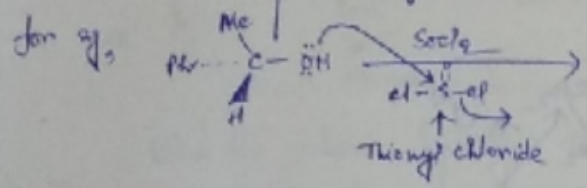
S_Ni rxn :- Internal nucleophilic substitution

↓

Here no external nucleophile is required.

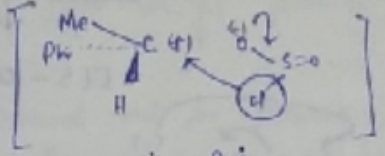
Here nucleophile is generated internally

for eg:-

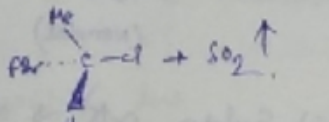


Alkyl chloro sulfite intermediate

↓



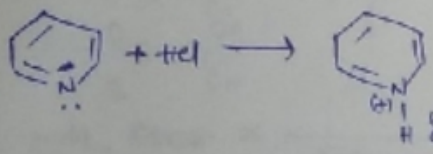
ion pair
(intimate)

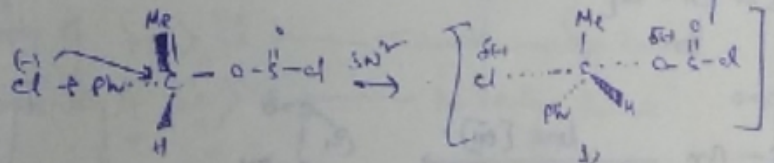


Alkyl chloride with retention of configuration.

S_Ni rxn involves the formation of alkyl chlorosulphite intermediate. This intermediate breaks down into the intimate ion pair as shown above, then attack by Cl^- occurs on the same side of carbocation from which $OSOCl$ departs. Thus here retention of configuration occurs.

When the above reaction is carried out in presence of Pyridine, Pyridine hydrochloride is generated by the rxn with HCl. Here Cl^- is an effective nucleophile. So rxn follows S_N2 mode and it will give product with inversion of configuration.





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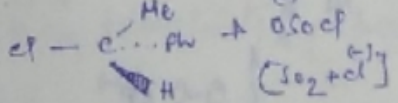


Nucleophilic Substitution at allylic Carbon —

S_N2' :→

$$R-CH=CH-CH_2-X \xrightarrow{Y^{(-)}} R-CH=CH-CH_2 + R-CH-CH=CH_2$$
$$\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\quad Y \qquad\qquad\qquad\quad Y$$

$CH_2=CH-CH_2Cl$
Allyl chloride

$$R-CH=CH-CH_2X \rightleftharpoons [R-CH=CH-CH_2]^{(+)} \longleftrightarrow [R-\overset{(+)}{C}H-CH=CH_2]$$
$$\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\quad \downarrow Y^-$$
$$\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\quad R-CH-CH=CH_2$$
$$\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\quad\ \ Y$$
$$\downarrow Y^-$$
$$R-CH=CH-CH_2$$
$$\qquad\quad Y$$

$$H_3C-CH=CH-CH_2Cl \xrightarrow{NaOH} H_3C-CH=CH-CH_2OH + H_3C-CH(OH)-CH=CH_2$$
$$\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\quad 60\% \qquad\qquad\qquad\qquad 40\%$$

$$H_3C-CH(Cl)-CH=CH_2$$

$$H_3C-CH(Cl)-CH=CH_2 \xrightarrow{NaOH} H_3C-CH=CH-CH_2OH + CH_3-CH(OH)-CH=CH_2$$
$$\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\quad 42\% \qquad\qquad\qquad\qquad 58\%$$

Product Spread.

$$CH_3-CH=CH-\overset{(+)}{C}H_2\ \overset{(-)}{Cl}$$
$$\downarrow$$

From Intimate ion pair we get some Substrate in percentage vary

S_N2' :

$$R-CH=CH-CH_2Cl \xrightarrow[S_N2']{Y^{(-)}} R-CH-CH=CH_2$$
$$\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\quad Y$$

$$R-CH=CH-CH_2-Cl \xrightarrow[S_N2]{Y^{(-)}} R-CH=CH-CH_2$$
$$\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\quad Y$$

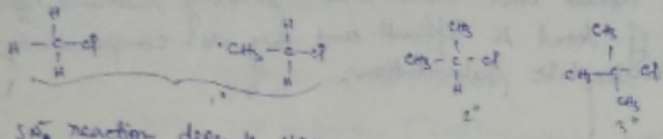
Larger the size of nucleophile and leaving group larger will be the chance of S_N2'.

$$Ph-CH=CH-CH_2-X$$
$$X=Br, Cl \longrightarrow 100\%\ S_N2$$
$$X=\overset{(+)}{P}Ph_4\ Br^- \longrightarrow 100\%\ S_N2'$$

Comparative study of SN^2 and SN^1 reaction:

1) Nature of substrate.

2) Nature of the alkyl group:

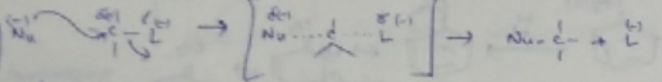


Rate of SN^2 reaction depends upon

i) Electrophilicity of the carbon bearing leaving group

ii) Steric repulsion in the five membered TS

+I effect of alkyl group decreases electrophilicity of carbon bearing leaving group.
Presence of alkyl group around the carbon increases steric repulsion in the TS



Rate of SN^1 reaction depends upon the stability of the carbocation

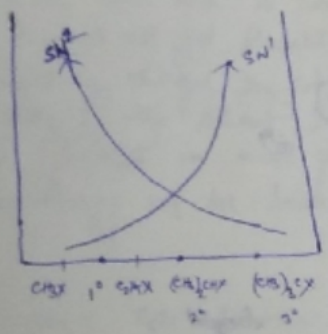
From L to R in the above alkyl halides rate of SN^2 reaction decreases though SN^1 reaction rate increases with increasing stability of the formed carbocation.

From the above discussion we can conclude that,

Generally, 1° alkyl halide ⇒ SN^2 rxn rate high

2° alkyl halide ⇒ mixed SN^1 and SN^2

3° alkyl halide ⇒ SN^1 rxn rate high



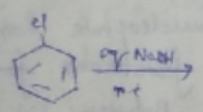
Some Examples:

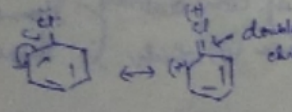
1) $CH_2=CH-CH_2-Cl$ ⟶ $CH_2=CH-\overset{(+)}{C}H_2$ ↕ $\overset{(+)}{C}H_2-CH=CH_2$ SN^1 possible

Allyl chloride
$C_{sp^2}-Cl$

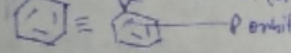
$CH_2=CH-Cl$ → Resistance to nucleophilic attack

$C_{sp^2}-Cl$
Vinyl chloride





$C_{sp^2}-Cl$

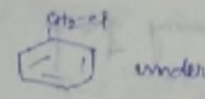


↕

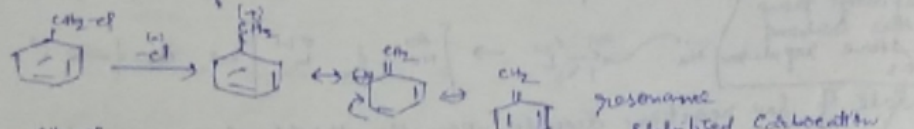
(now aromatic)

Allyl chloride can undergo nucleophilic substitution because it contains $C_{sp^2}-Cl$ bond and it can form resonance stabilized carbocation. But vinyl cation and phenyl cation are unstable. They contain $C_{sp^2}-Cl$ bond and this bond may get double bond character involving resonance effect. So here breaking of bond is difficult and they are comparatively inert towards nucleophilic substitution.

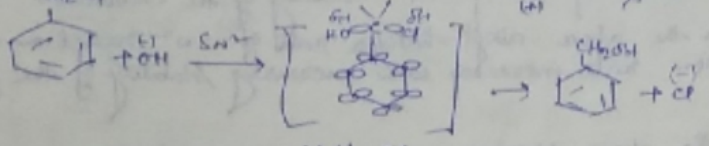
(ii) Benzyl Chloride:



undergoes fast S_N2 and S_N1 reaction.



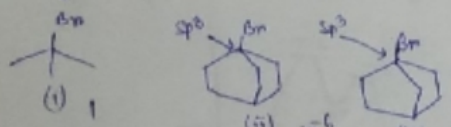
resonance stabilised carbocation



Stable T.S

In case of benzyl chloride S_N1 reaction rate is high for stable carbocation formation in case of S_N2 reaction. The p orbital of the central carbon atom is parallel with the p-orbital of benzene ring and the T.S becomes very stable. So S_N2 rxn rate becomes high.

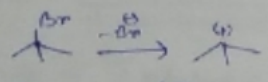
(iii)

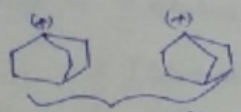


(i) 1 (ii) 10^{-6} (iii) 10^{-14}

Relative rxn rate

S_N1



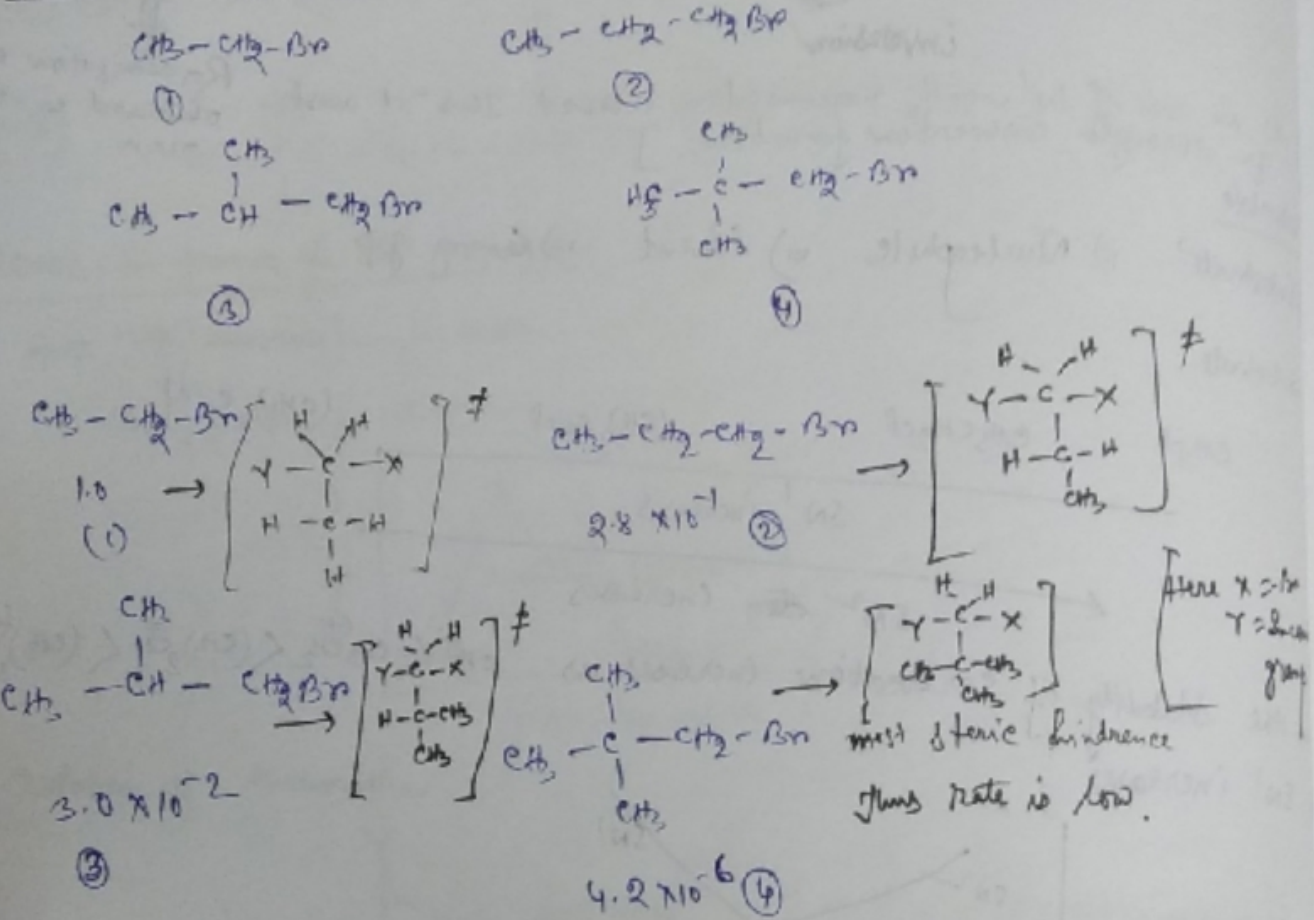


unstable

bicyclic rigid cage like.

In the above three compounds, S_N1 rxn rate is high for tertiary-butyl bromide molecule because it can form stable tertiary-butyl carbocation. Substrates (ii) and (iii) are rigid, bicyclic and cage like. They cannot undergo carbocation formation for their rigidity. Again in case of S_N2 rxn the nucleophile has to undergo enter from cage like structure, this is not favourable for high steric repulsion. So, they will not undergo S_N2 rxn. Between (ii) and (iii), (ii) is comparatively symmetrical and flexible, so its rxn rate higher than (iii) which is more rigid.

(iv) β effect :→ S_N2 order



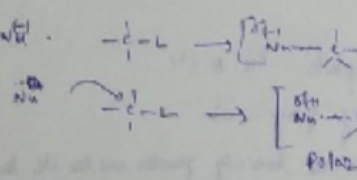
The reaction rate is expressed in EtOH with $-EtO^{(-)}$ in 55°C.

2) Nature of Solvent :-

Solvent → Protic
Solvent → Aprotic
Amphoteric

Polar - hydroxylic - (H_2O, CH_3OH)

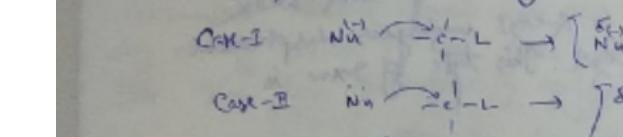
Polar - non hydroxylic [DMF ($HCONMe_2$), DMSO ($(CH_3)_2SO$)]



Polar — Polar decreases polar

S_N1 → As S_N1 rxn occurs through the formation of Carbocation, any Solvent that will increase ionisation and stability of Carbocation, will make S_N1 rxn faster. So generally polar solvent assists ionisation and increases stability of Carbocation, so S_N1 rxn will be very favourable in more polar solvent like CH_3OH, MeOH, H_2O etc.

The effect of solvent on S_N2 rxn depends upon the nature of transition state.



In case of (I) the rxn rate is retarded with increasing solvent polarity. Because this type of T.S will not get stability from polar solvent - where both ends are partially negatively charged. In case of (II) the rate of the S_N2 rxn is increased as the polarity of the solvent increases as this T.S is polar, this type of T.S is more solvated in more polar solvent. So this T.S will be more stable, activation energy will be lower and S_N2 rxn will be faster.

3) Nature of nucleophile :

S_N1 rxn : Rate $\propto$ [Substrate]

S_N2 rxn : Rate $\propto$ [Substrate] [Nucleophile]

Thus we can say change of concentration or on nature of nucleophile in case of S_N1 rxn has no important role. But concentration and nature of nucleophile may play important role on a S_N2 rxn. In case of S_N1 rxn, in absence of nucleophile solvent may play the role of nucleophile.

Now the nucleophilicity of different ions like halide ions depends upon the nature of solvent also. In protic solvent nucleophilicity of $I^{(-)} > Cl^{(-)} > Cl^{(-)} > F^{(-)}$. But in aprotic solvent (DMF, DMSO etc) nucleophilicity of $F^{(-)} > Cl^{(-)} > Br^{(-)} > I^{(-)}$. In aprotic solvent only charge density factor is considered as there solvation plays no role. Higher the charge on the ions, higher will be nucleophilicity. So in aprotic solvent nucleophilicity of $F^{(-)} > Cl^{(-)} > OH^{(-)} > I^{(-)}$. This is also the basicity order.

[P.T.O]

Nucleophilicity & Basicity :→

① electron pair donates to C — Nucleophilicity
electron pair donates to H — basicity.

② Basicity ⟶ Thermodynamically controlled.
Nucleophilicity ⟶ Kinetically controlled.

③ Nucleophilicity depends on Steric crowdicity.
⇒ Steric effect increases → Nucleophilicity decreases.
⇒ Basicity does not depend on Steric crowding.

HSAB Principle: Hard acid tends to bind with hard base and soft acid tends to bind with soft base.

Hard base : $R\ddot{O}^{(-)}$ ← more electronegative electron donating atom (Hard to oxidised).

Soft base : $R\ddot{S}^{(-)}$ ← less electronegative electron donating atom (easy to oxidised)

Polarisibility :

- More polarisable ⇒ Soft base
- Less polarisable ⇒ Hard base.

Hard Acid → $H^{(+)}$

Soft acid → $Nu^{(-)}$ + CH_3-Cl (Soft)

$H^{(+)}$ — Hard acid

- Nucleophilicity and Basicity order :

~~[illegible]~~

i) $OH^{(-)} > H_2O$ more nucleophilic than its conjugate acid.

ii) $\ddot{N}H_2^{(-)} > NH_3$

ii) Attacking atom is same, basicity and nucleophilicity Parallel

$MeO^{(-)} > PhO^{(-)} > MeCO_2^{(-)}$

③ Attacking atom are in the same period. ([illegible])
Basicity order and nucleophilicity are same

$\overset{(-)}{N}H_2 > RO^{(-)} > \overset{(-)}{O}H > R_2\ddot{N}H > ArO^{(-)} > NH_3 >$ Pyridine $> F^{(-)} > H_2O$

④ Attacking atom are in the same group then nucleophilicity and basicity are opposite in protic polar solvent.

$I^{(-)} > Br^{(-)} > Cl^{(-)}$ - Nucleophilicity order
$Cl^{(-)} > Br^{(-)} > I^{(-)}$ - Basicity order
$RS^{(-)} > RO^{(-)}$ Nucleophilicity; $RO^{(-)} > RS^{(-)}$ basicity

} In protic polar solvent — MeOH, H_2O (H bonding)

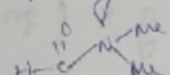
i) Polarisibility of $I^{(-)}$ is high so better bond formation.

~~Hard acids tend to bind with hard bases and soft acids tend to bind with soft bases.~~
ie $I^{(-)} \longrightarrow CH_3-Cl$

⑤ Freer the nucleophile better the nucleophilicity.

DMF → Aprotic polar solvent

$Cl^{(-)} > Br^{(-)} > I^{(-)}$ → Nucleophilicity order



(No H-bonding)

| Non polar solvent − CCl_4 |

[illegible]

⑥ α-effect : Nucleophilicity increases if there is a nucleophilic group beside a nucleophile. eg) NH_2-NH_2 highly nucleophile.
2. ⇒ $HO_2^{(-)}$ $H-O-O^{(-)}$ highly Nucleophile. (α-effect)

⑦ LiX → $Cl^{(-)}$ → 1 [Nucleophilicity of X^-]
$Br^{(-)}$ − 5.7
$I^{(-)}$ − 6.2

$Bu_4\overset{(+)}{N}\overset{(-)}{X}$ → $Cl^{(-)}$ → 68
free nucleophile — $Br^{(-)}$ → 18
I^- → 3.7

In case of LiX, X^- is not free enough. But in case of $Bu_4\overset{(+)}{N}X^-$, X^- is a free nucleophile hence the nucleophilicity order.

~~[illegible]~~

3) **Ambident Nucleophile**

$\overset{(-)}{C} \equiv N$ [when nucleophilic attack can take place from both side of the nucleophile]

1. $R-Cl + KCN \longrightarrow R-CN \longleftarrow S_N2$

$R-Cl + AgCN \longrightarrow R-NC - S_N1$

[$\overset{(-)}{C} \equiv N$ — hard; C — soft] ⇒ Ambident nucleophile

$R-Cl + AgCN \longrightarrow AgCl\downarrow + R^{(+)}$ ↖ Hard centre

$\overset{(-)}{CN}$ (soft) → $\overset{\delta+}{CH_3} - Cl$ (soft) $\longrightarrow CH_3CN + KCl$

$CH_3^{(+)} + \overset{(-)}{NC} \longrightarrow CH_3NC + AgCl$
(hard) (hard)

[Product formation can be predicted using HSAB principle.]

2. $H_3C - \overset{O}{\overset{\|}{C}} - CH_2 - CO_2Et$

↓ $OH^{(-)}$

[$H_3C - \overset{O}{\overset{\|}{C}} \leftrightarrows \overset{(-)}{CH} - CO_2Et$]

Ambident nucleophile

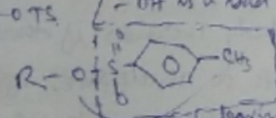
4) **Nature of leaving group** ⇒

1) Strength of C – X bond.
2) Polarisability of X (good entering group also a good leaving group.)
3) Stability of $X^{(-)}$

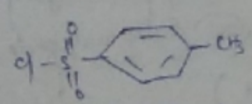
$R-OH \xrightarrow{OH^{(-)}}$ bad leaving group

Strong base → bad leaving group.

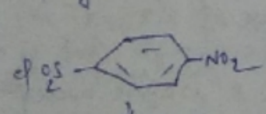
$R-OH \longrightarrow R-OTs$ [– OH is a bad leaving group but – OTs is a good leaving group.]



good leaving group



Para-toluenesulfonyl chloride
Tosyl chloride



(Nosyl chloride)

These compounds are used to prepare a compound having good leaving group from a compound having bad leaving group.

In protic solvent, solvation factor is more important than charge density factor. Lower the size of the ion, solvation will be higher and nucleophilic attack for it will be difficult. So in protic solvent nucleophilicity of $I^{(-)} > Br^{(-)} > Cl^{(-)} > F^{(-)}$.

Catalysed S_N2 rxn:

$$RCH_2Cl \xrightarrow[S_N2 \text{ slow}]{\text{aq NaOH}} RCH_2OH + NaCl$$

$$\text{fast } S_N2 \downarrow \text{cat KI}$$

$$R\text{-}CH_2\text{-}I + \overset{(-)}{Cl} + \overset{(+)}{K}$$

$$S_N2 \downarrow \text{aq NaOH}$$

$$R\text{-}CH_2OH + NaI$$

Nucleophile - $\overset{(-)}{O}H$ & $I^{(-)}$

Leaving group - $\overset{(-)}{Cl}$

Lower the basicity greater will be its leaving group ability

When the above reaction is carried out in absence of $I^{(-)}$, reaction rate become slow because $I^{(-)}$ is stronger nucleophile than $\overset{(-)}{O}H$ and $I^{(-)}$ can attack C of C-Cl bond very fast. This is not possible in absence of KI and then reaction rate become slow. When this reaction is carried out in presence of KI, very fast displacement of $Cl^{(-)}$ by $I^{(-)}$ occurs and we get alkyl iodide. Now C-I bond is longer and weak. Again $I^{(-)}$ is better leaving group than $Cl^{(-)}$. So $R\text{-}CH_2I$ undergoes displacement by $\overset{(-)}{O}H$ at a much faster rate than RCH_2Cl. This type of rxn is called catalysed S_N2 rxn.

Explain the following observation:

$$R\text{-}CH_2\text{-}Cl \xrightarrow{NaCN/KCN} R\text{-}CH_2\text{-}CN \text{ — cyanide}$$

$$R\text{-}CH_2\text{-}Cl \xrightarrow{AgCN} RCH_2\text{-}NC \longrightarrow \text{isocyanide}$$

Ambident nucleophile and HSAB principle

Ambident nucleophile $\overset{(-)}{C} \equiv N$ ← hard donor; ↑ soft donor (C)

$-\overset{|}{\underset{|}{C}}^{(+)}$ hard $-\overset{|}{\underset{|}{C}}^{\delta+} \longrightarrow X^{\delta-}$ soft

$$(S_N1)\ R\text{-}CH_2\text{-}Cl \xrightarrow{AgCN} AgCl\downarrow + R\text{-}\overset{(+)}{C}H_2 \text{ [Hard]}$$

$$\downarrow \overset{(-)}{C} = \ddot{N} \text{ (hard)}$$

$$R\text{-}CH_2NC \text{ (Major pdt)}$$

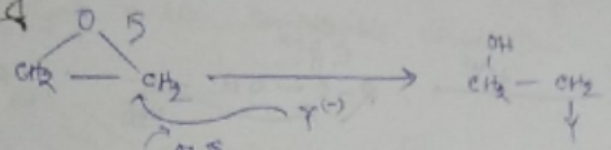
$$R\text{-}CH_2\text{-}Cl \xrightarrow[KCN]{NaCN} \overset{(-)}{C}\equiv N\ (S_N2) \left[N\equiv \overset{\delta-}{C} \cdots \underset{R}{C} \cdots \overset{\delta-}{Cl} \right] \xrightarrow[\text{Combination}]{\text{soft-soft}} N\equiv C\text{-}CH_2R + \overset{(-)}{Cl}$$

When the above reaction is carried out in presence of AgCN, rxn follows S_N1 type path through the precipitation of AgCl and formation of carbocation. Again $\overset{(-)}{C}N$ is ambident nucleophile. So hard-hard combination occurs and it will give alkyl isocyanide.

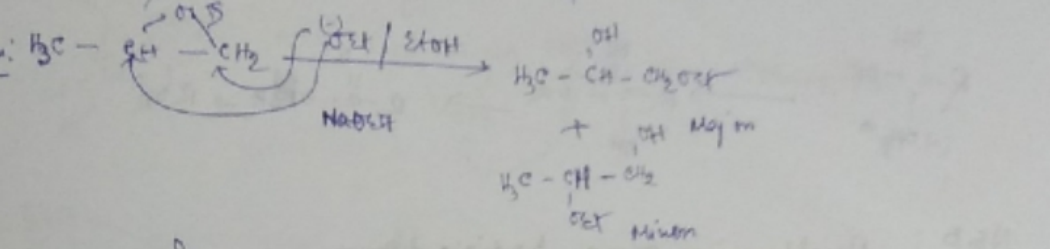
When this rxn is carried out in presence of NaCN, rxn follows S_N2 path, soft-soft combination occurs and it will give alkyl cyanide.

Nucleophilic Substitution at epoxide :

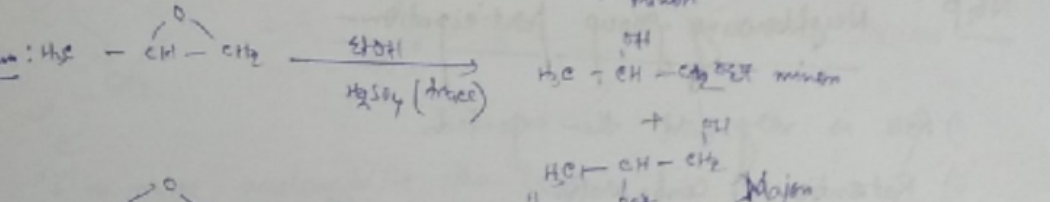
Ring opening –

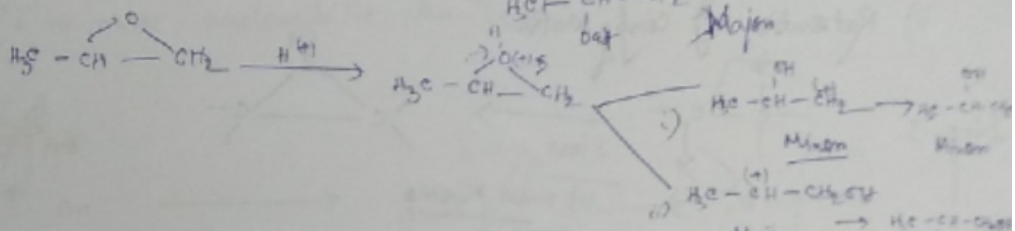


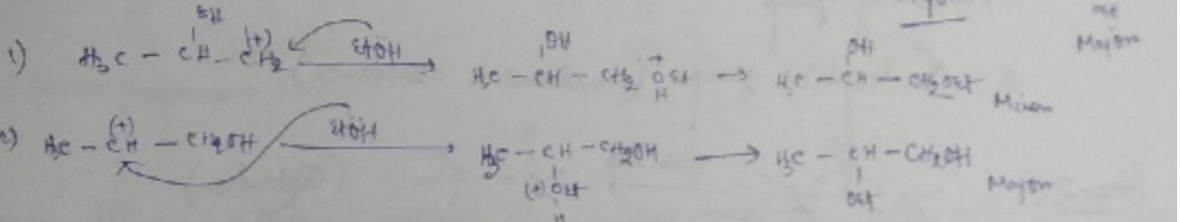
1. Basic medium:



2. Acidic medium:





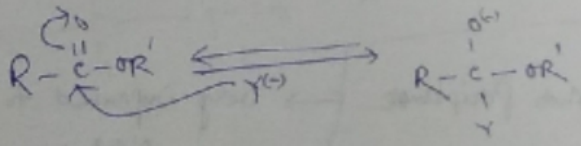


Nucleophilic Substitution at tri-gonal carbon :→

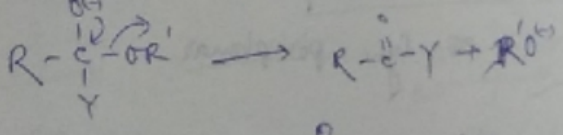
Tetrahedral Mechanism.

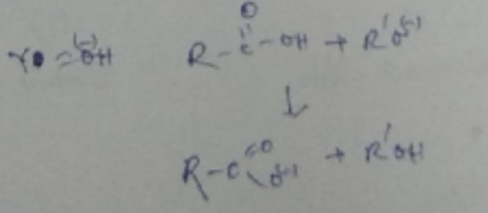
1. Basic Medium :

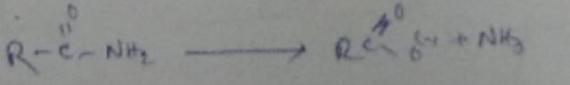
Step-I →



Step II →

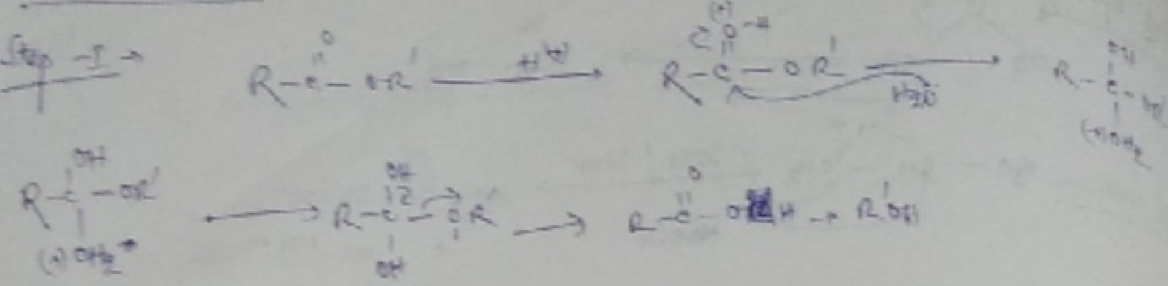






2. Acidic Medium :-

Step - I →

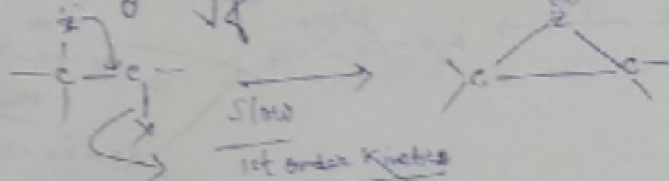


NGP : Neighbouring group participation —

i) Rate is very fast than expected.

ii) Retention of configuration.

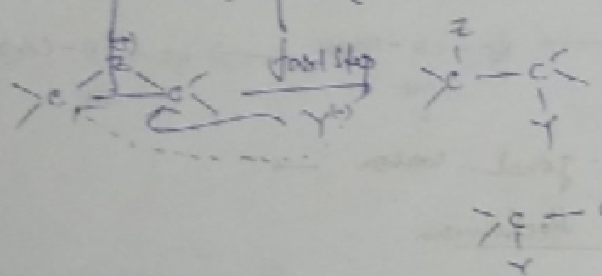
Step-I



X - leaving group

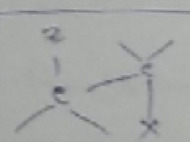
Z = Nucleophilic group (Anchimeric assistance)

Step-2 -

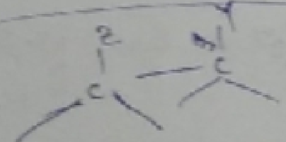


(Retention)

With rearrangement



→ Anti Periplanar ⟷ very important to take place NGP



or Syn-periplanar

Z = $CO_2^{(-)}$, COOR,

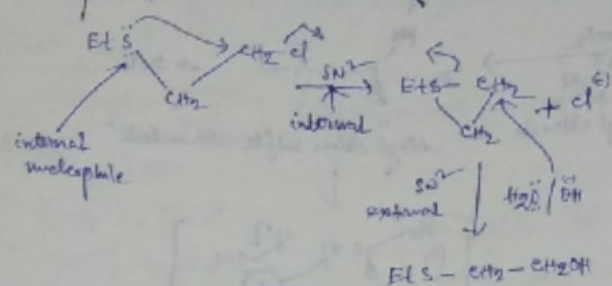
$-NH_2$, $-OH$, $-SH$,

$-Cl$, $-Br$, $-I$

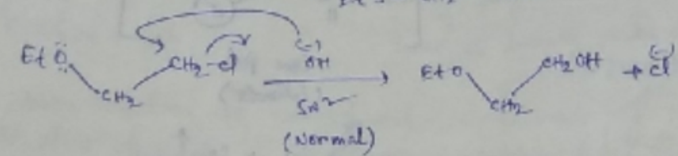
Neighbouring Group Participation : (NGP)

Ex: $EtS-CH_2-CH_2-Cl$ undergoes solvolysis 10^4 times faster than $EtO\text{-}CH_2CH_2Cl$.
— Explain.

Case-I

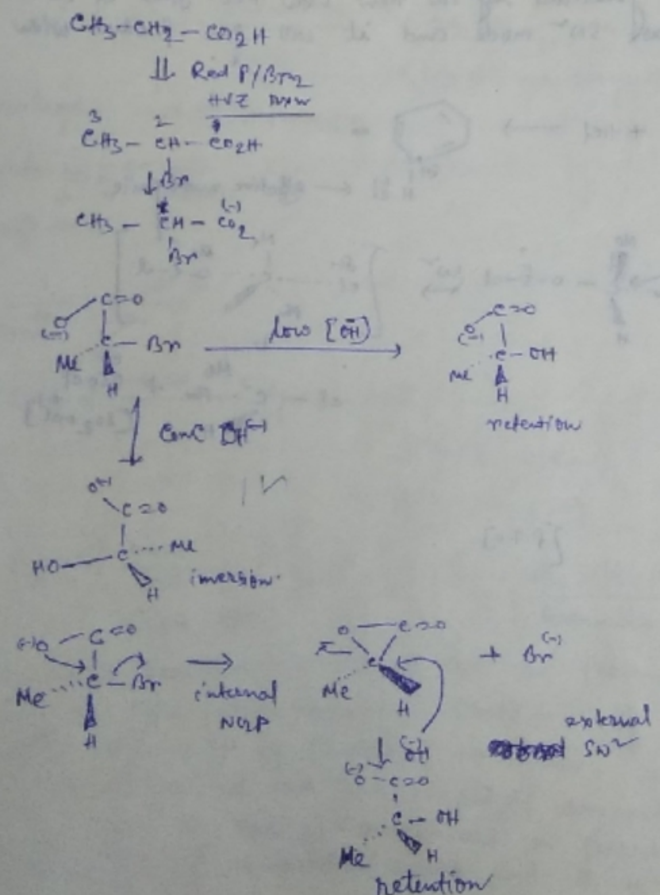


Case-II

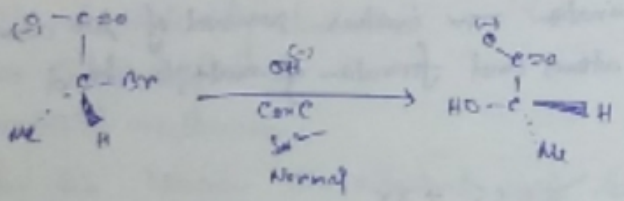


In case of (I) Sulphur acts as a neighbouring group. Here two consecutive S_N2 attack occurs. First S_N2 is internal and the second S_N2 is external. Thus the rxn rate becomes faster. In case of (II) NGP by oxygen is difficult is as, oxygen is sufficiently electronegative. So this rxn follows normal S_N2 path and become slow.

Another example of oxygen as a neighbouring group occurs in the hydrolysis of 2-bromo propanoate anion at low concentration of $\overset{(-)}{O}H$.



Nucleophilicity $-\overset{\overset{O}{\|}}{C}-H < \overset{(-)}{-}OH$



When the above hydrolysis raw is carried out in presence of low conc of $\overset{(-)}{O}H$. Then internal nucleophilic group $-CO_2^{(-)}$ can compete with $\overset{(-)}{O}H$ and then NGP by oxygen becomes possible. Thus we get product with retention of configuration.

When the above raw is carried out in presence of conc $\overset{(-)}{O}H$, then $-CO_2^{(-)}$ cannot compete with $\overset{(-)}{O}H$ and reaction follows normal in path. Thus solvolysis raw becomes slower and we get pdt with inversion of configuration.

****

Phase transfer Catalysis :-

$C_8H_{17}Cl \xrightarrow{KCN} C_8H_{17}CN + K^{(+)}Cl^{(-)}$

$C_8H_{17}Cl$ → Soluble in $CHCl_3$ or CH_2Cl_2

KCN ($CN^{(-)}$) → Soluble in water.

i) Tetra butyl ammonium chloride/ Bromide

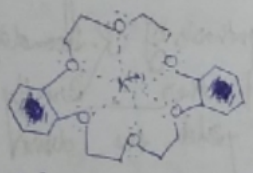
$R_4N^{(+)}Cl^{(-)}$

$R_4P^{(+)}Cl^{(-)}$

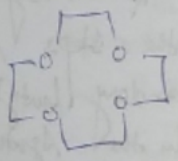
Organic phase - $R_4N^{(+)}CN^{(-)} + R\text{-}Br \rightleftharpoons R\text{-}CN + R_4N^{(+)}Br^{(-)}$

Aqueous phase - $R_4N^{(+)}Cl^{(-)} + X^{(+)}Br^{(-)} \rightleftharpoons KCN + R_4N^{(+)}Br^{(-)}$

ii) Crown ether → Large cyclic ether compound.



dicyclohexano [18]-Crown-6 for K^+ ion



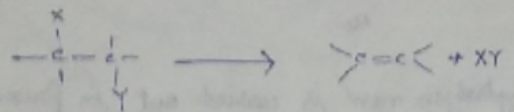
[12]-Crown-4 for Li^+ ion

From the above mention reaction we can see that, the substrate is soluble in Chloroform or Dichloromethane. But the reagent is soluble in aqueous medium. In order to occur the reaction substrate and reagent must be in the same phase. Hence phase transfer catalyst is introduced to bring the substrate and reagent in the same phase.

- In case of (i), tetra butyl ammonium chloride/bromide is soluble in aqueous solvent. When we add KCN in aqueous solution. Then it reacts with $R_4N^+Cl^-$/$R_4N^+Br^-$ to form $R_4N^+CN^-$. Now $R_4N^+CN^-$ is soluble in both aqueous as well as organic solvent. Hence it can come into contact with Alkyl halide present in the organic phase to produce alkyl cyanide.
- In case of crown ether the mechanism is almost same. Here crown ether binds the metal ion into its cavity. The anion associated with crown ether is thus come to the organic layer and take part in the reaction.

Elimination rxn:

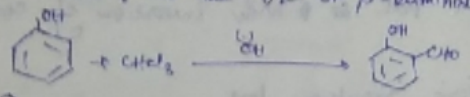
In majority of cases, elimination rxn involves removal of two atoms or group from two adjacent carbon atoms and formation of multiple bond between them.



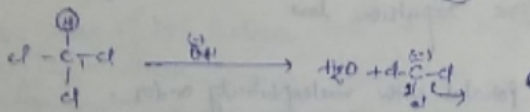
In most cases X is hydrogen (H). Y may be any other leaving group like $Br^{\ominus}$, $I^{\ominus}$ etc. Y = Br, I, Cl etc

The above type of elimination is 1,2 or β elimination. When two groups or atoms depart from the same carbon atom, it is called α-elimination. β elimination is also possible but these elimination reaction are rare. So we are mainly interested on the 1,2 or β-elimination reactions.

RT rxn:

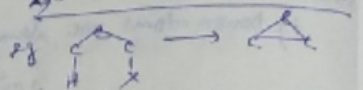


1,1 elimination
or
α elimination



:CCl_2
dichloro Carbene

1,3 elimination (δ elimination)

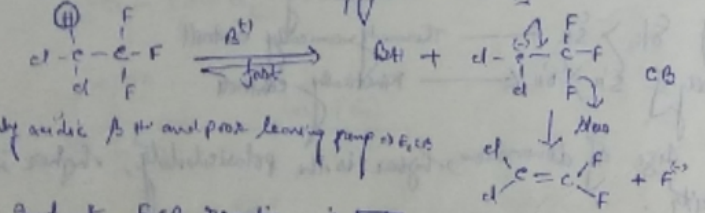


Thus eliminations is of three type
1. α-elimination or 1,1 elimination
2. β-elimination or 1,2 elimination
3. δ-elimination or 1,3 elimination

Now β elimination reactions may be classified into different ~~categ~~ catagories. In this chapter, we shall discuss the following types of β & δ elimination rxns.

i) E_1CB rxn.
ii) E_2 rxn.
iii) E_i rxn.
iv) E_i rxn (Pyrolytic syn eliminations).

c) E_1CB reaction: (Elimination from conjugate base (CB))



Highly acidic β-H and poor leaving group → E_1CB

Infact E_1CB reaction is ~~rare~~ rare. One example that almost certainly involves E_1CB path, it has been stated above. The following factors contribute E_1CB path.

i) Presence of strong electronegative halogen atom on the β carbon to make the β 'H' more acidic.
ii) Stabilisation of the carbanion or CB by -I effect of the halogen atom.
iii) Very poor leaving character of F.

Here the 2nd step is slow and rds and the first step is fast and ~~rever~~ reversible.

E_2 reaction:

Some important features of E_2 reaction may be noted as follows.

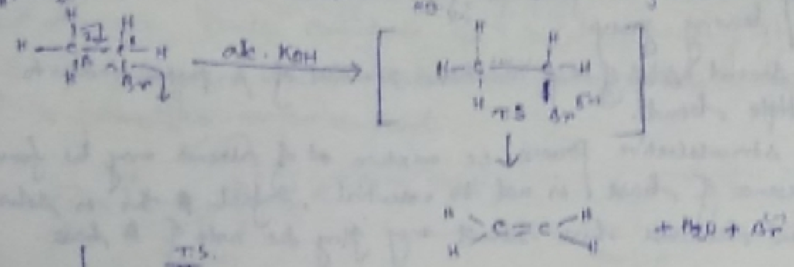
i) This is single step elimination.

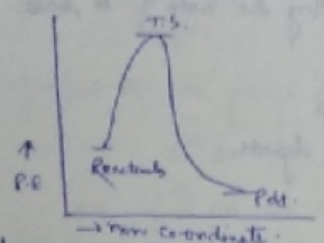
ii) Base catalysed process.

iii) Concerted mechanism.

iv) In this reaction the dihedral angle between the two leaving groups should be 180° i.e they should be anti periplanar. So this is trans or anti elimination process.

v) Stereospecific reaction. We may expect any particular product (isomeric product) from any particular stereoisomer [evidence in favour of E_2 mechanism].





Five atoms or groups involve in T.S should be co-planar.

Reaction Rate ∝ [Substrate][$B^{\ominus}$]

Bimolecular process

vi) $K_H/K_D \simeq 3\text{-}8$ which implies C–H bond breaking takes place in the T.S which is also the evidence in favour of E_2 mechanism.

Ex: Write down the product of the following reaction with proper mechanism.

$$Ph-CH_2-CH_2Br \xrightarrow[EtOH]{\overset{\ominus}{O}Et} ?$$

(β phenyl-ethyl bromide)

$$Ph-CH(H)-CH_2(Br) \xrightarrow{\overset{\ominus}{O}Et} Ph-CH=CH_2 \text{ (Styrene)}$$

E_2 path: $Ph-CH_2-CH_2Br \xrightarrow{\overset{\ominus}{O}Et} Ph-CH=CH_2 + EtOH + Br^{\ominus}$

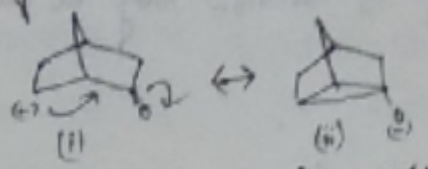
E_1cB path: $Ph-\overset{D}{C}H-CH_2Br$ (M) $\rightleftharpoons$ ($\overset{\ominus}{O}Et$) $Ph-\overset{\ominus}{C}H-CH_2Br$ (CB) $\longrightarrow Ph-CH=CH_2 + Br^{\ominus}$

CB ↓ EtOD (D^+)

✗ $Ph-CH(D)-CH_2Br$ (M+1)

In the above reaction we get styrene. But two alternative routes are possible. One of them is E_2 and another is E_1cB. The above reaction is carried out in presence of $\overset{\ominus}{O}Et$ and EtOD. It is found that D cannot enter in the substrate. This indicates CB or carbanion cannot form. So this reaction follows E_2 path but not E_1cB path.

Draw the resonating structure of the following carbanion.



(i) ↔ (ii)

(more stable)

-ve charge on more electronegative atom.

E_1 reaction:

i) Unimolecular reaction.

ii) Two step process

iii) First step involves the formation of carbocation intermediates after removal of leaving group.

iv) In the second step of this reaction removal of β-proton occurs to form multiple bond.

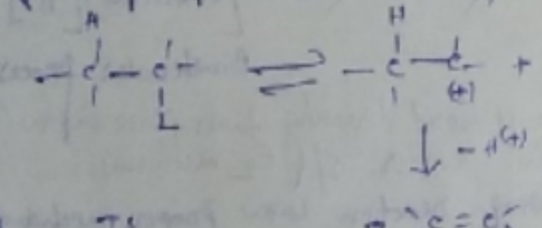
v) This is stereoselective process. i.e mixture of alkenes may be formed.

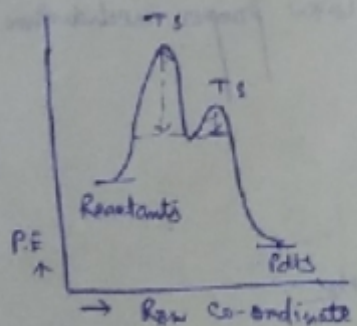
vi) Here presence of base is not so essential. Infact this is solvolytic elimination because here solvent may play the role of base.

E_2 ⇒ Two leaving groups depart simultaneously.

E_1CB ⇒ proton departs first then leaving group.

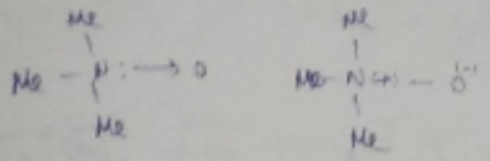
E_1 ⇒ leaving group departs first then proton departs.



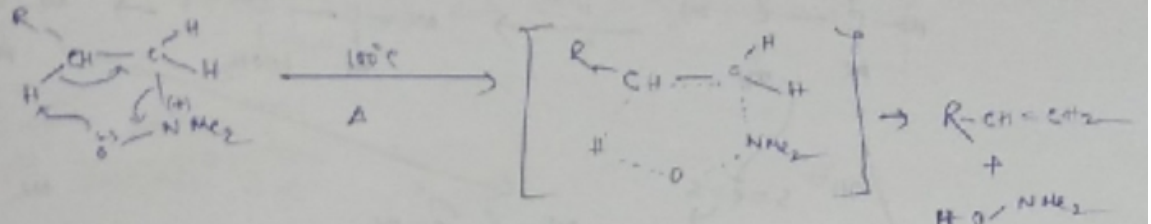


Syn elimination (Ei):

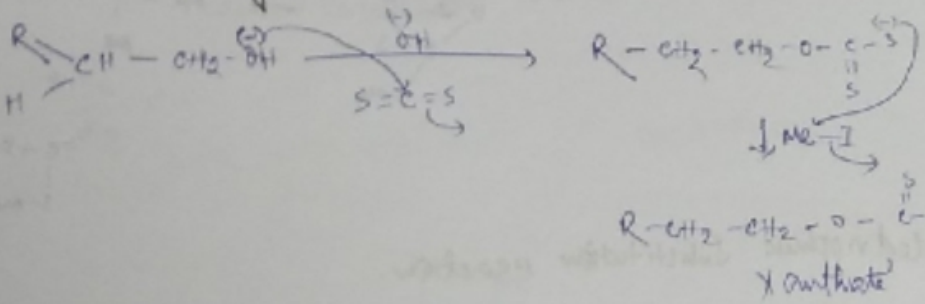
N-oxide —

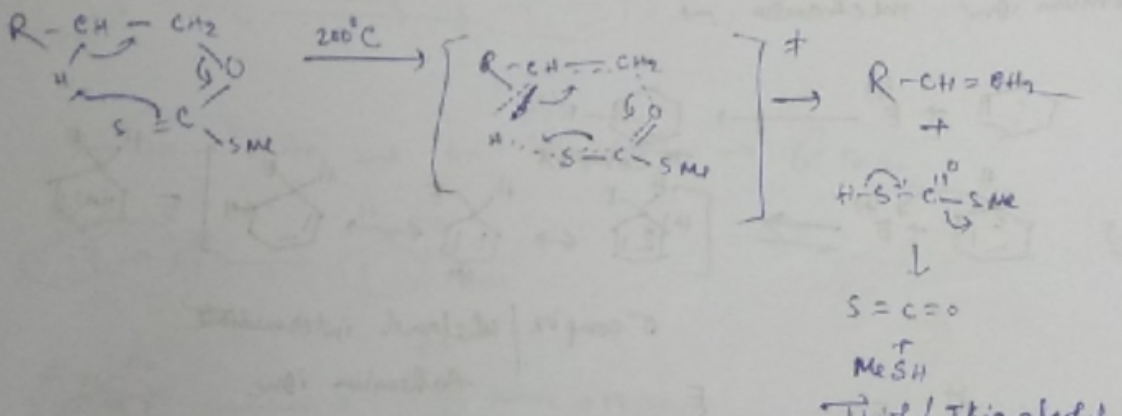


Cope reaction:

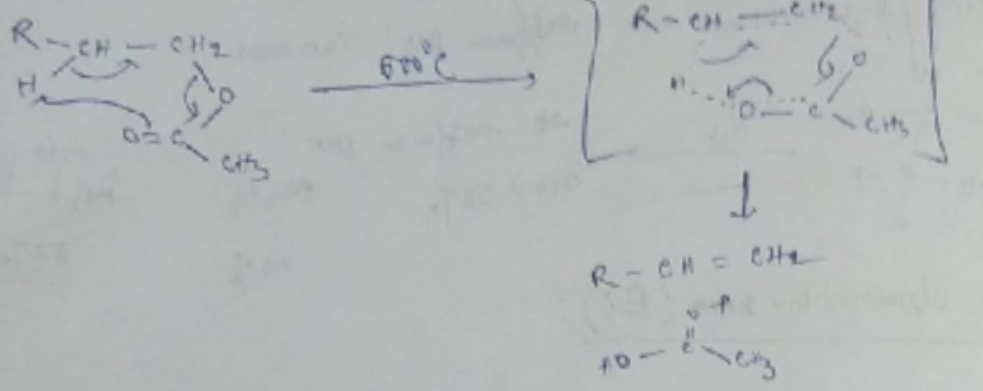


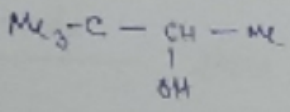
Pyrolysis of Xanthate : Chugaev reaction :

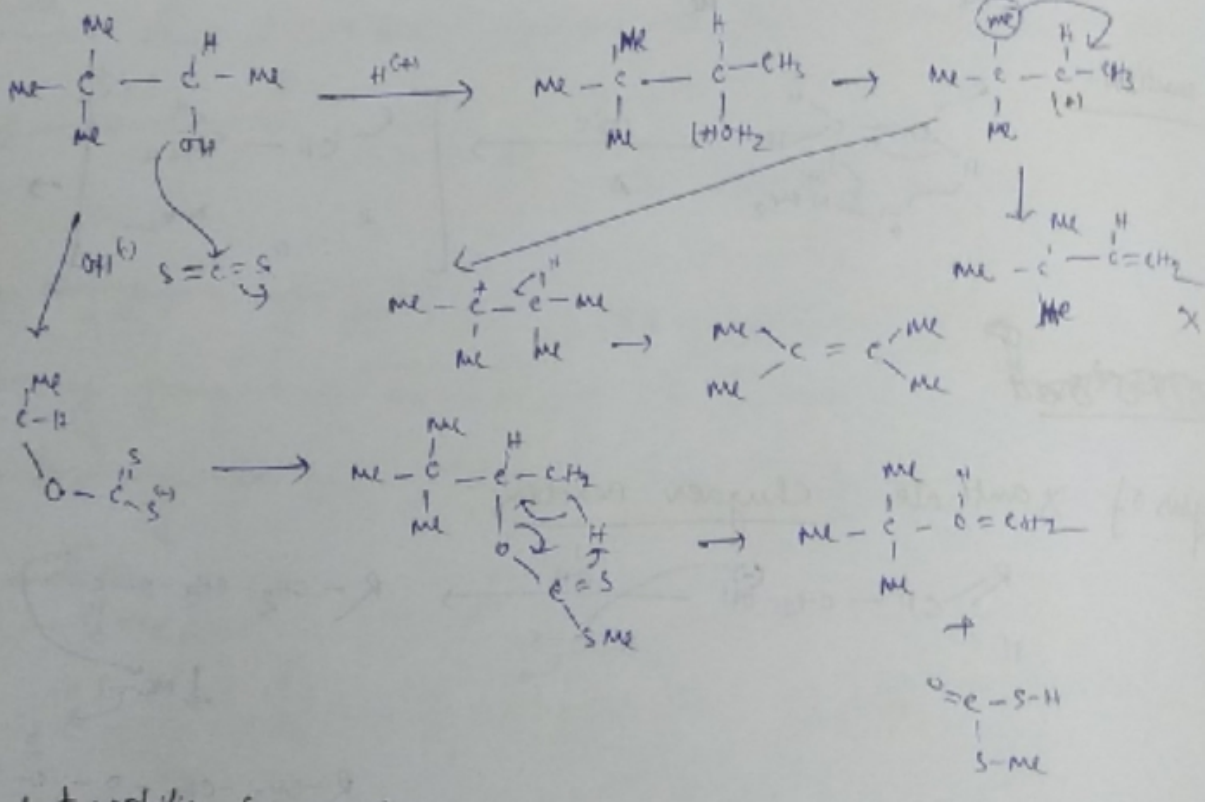




Pyrolysis of Acetate :



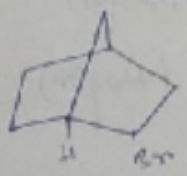


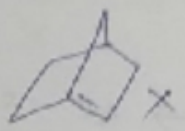


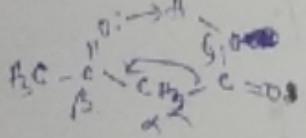
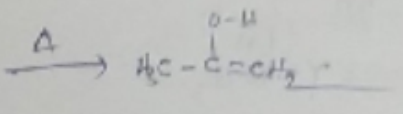
Orientation of double bond can be obtained using two rules.

1. Bredt's rule.
2. Saytzeff & Hofmann rule.

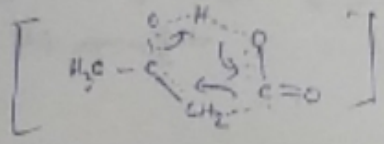
1) **Bredt's rule :** Double bond cannot be formed to the bridge head carbon atom.

1.  ✓ Possible according to Bredt's rule.

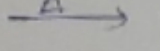
 ✗ Not possible according to Bredt's rule.

2.  

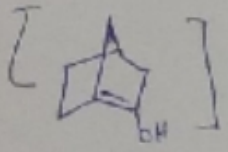
β- Keto acid



Thus  → Decarboxylation impossible according to Bredt's rule thus unreactive.

 Unreactive.

↓

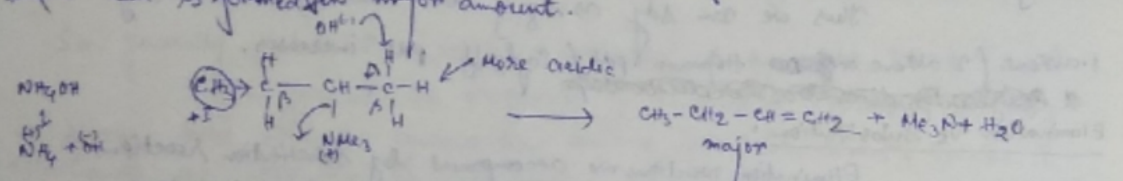


Not possible.

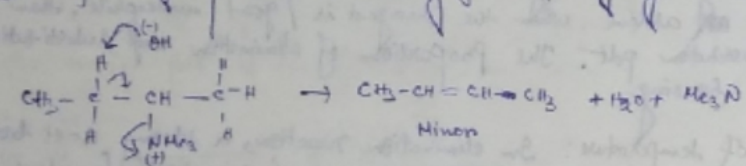
29. **Saytzeff rule**: To help ~~in forecasting~~ in forecasting the major pdt of elimination, there are two empirical rules. One of them is Saytzeff and another is Hofmann rule. Saytzeff rule states that neutral substrates lead predominantly to that alkene which is more highly substituted on the carbons of the double bond. This rule is very much applicable to E_1 type elimination involving carbocation intermediate.

* **Hofmann rule**: Hofmann rule states that [in case of charged substrates (leaving grp bearing +ve charge), the least substituted alkene will be the major pdt.]

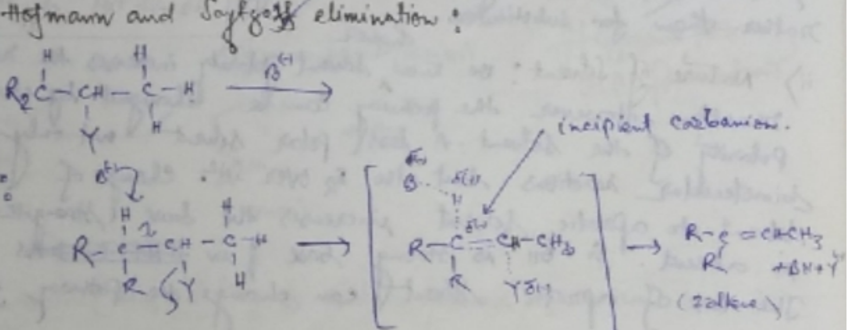
It may be noted that Saytzeff rule considers the ~~stab~~ product stability but Hofmann rule considers the relative acidity of β-hydrogen. More acidic β-hydrogen will be abstracted by base and less substituted alkene ~~[illegible]~~ is formed in major amount.



+I effect of $-CH_3$ group decreases acidity of this β-hydrogen



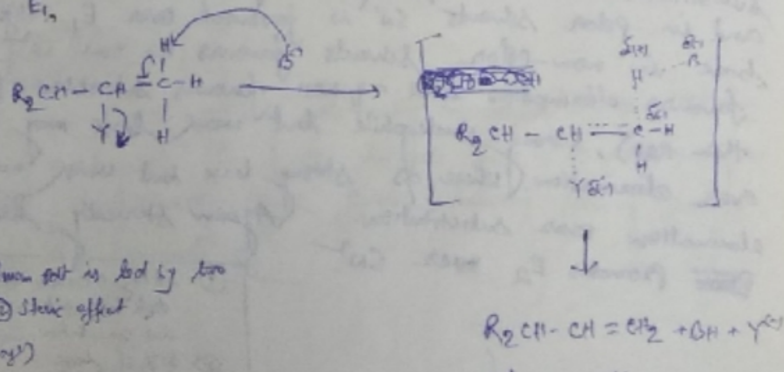
Transition state for Hofmann and Saytzeff elimination:



incipient carbanion: β-carbon occupy slightly -vely charge (E_2)

incipient carbocation: E_1

~~Hofmann~~: Hofmann:



$R_2CH-CH=CH_2 + BH + Y^{(-)}$

Hofmann pdt.

(1-alkene)

Kinetically favoured pdt is Hoffman pdt is led by two factor ① acidity of proton ② steric effect

Comparison: ① Base size (next page)
② leaving group
F → 23%. Hoffmann
Cl → 17%. "
Br → 21%. "
I → 20%. "

Size of base and ratio of 1-alkene / 2-alkene

Size of base :	$\overset{\ominus}{O}C_2H_5$ ($\overset{\ominus}{O}Et$)	$Me_3C\overset{\ominus}{O}$	$Me_2(Et)C-\overset{\ominus}{O}$	$Et_3C-\overset{\ominus}{O}$
% of 1-alkene :	30	72	77	78
% of 2-alkene :	70	28	23	22

As size of base increases, it becomes quite difficult to abstract proton from substituted position for strong steric repulsion with the alkyl group. Then bulky base will take up proton from less substituted position to form 1-alkene in major amount.

Thus we can say as size of base increases, the ratio of 1-alkene / 2-alkene or Hofmann pdt / Saytzeff pdt increases.

Elimination Vs Substitution :

Elimination reactions are accompanied by substitution reaction. When the reagent is a good base, it accepts proton to form elimination product of alkene, when the reagent is good nucleophile, then it will give substitution pdt. The proportion of elimination and substitution depends upon the following.

i) Effect of temperature: In elimination reaction, a strong C–H bond has to break, hence a higher activation energy is required for elimination rather than for substitution.

> $\Delta G = \Delta H - T\Delta S$ for elimination ΔS = (+)ve, for substitution ΔS = 0. Thus T increases for elimination – ΔH increases

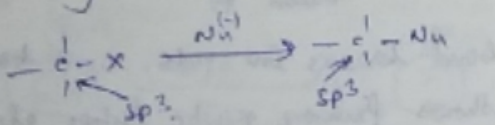
ii) Nature of Solvent : We know, higher solvent polarity increases the rate of S_N1 reaction. However the pathway can be changed by changing the polarity of the solvent. A less polar solvent not only favours bimolecular reactions but also E_2 over S_N2. Change of hydrophilic solvent to aprotic solvent increases the base strength as solvation is absent. So $\overset{\ominus}{O}H$ is strong base in ~~DMF DMSO~~ DMF or DMSO. The use of aprotic solvent can change the pathway from E_1 to E_2.

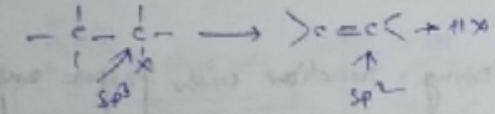
> Polar (less) → S_N1; Non polar → E_2/S_N2; Protic → [illegible] solvation, Basicity decreases, elimination [illegible]

iii) Nature of base : Generally strong base promotes elimination over substitution and in particular E_2 over E_1. In low base concentration and in polar solvents S_N1 is favoured over E_1. Higher concentration of base in non-polar solvents favours E_2 over S_N2. Hence alcoholic KOH favours elimination and aq KOH favours substitution (alcohol is less polar than H_2O). Strong nucleophile but weak base may promote substitution over elimination, whereas strong base but weak nucleophile promotes elimination over substitution. Again sterically hindered base like $Me_3C\overset{\ominus}{O}$ promotes E_2 over S_N2.

> ① Strong or weak depends on solvent
> High concentration in non polar = strong base ⇒ elimination
> Low concentration in higher polar = weak base ⇒ substitution.
> ② Size of base
> Greater size substitution < Elimination due to steric effect

Structure of the substrate : In general the proportion of elimination increases with ~~increasing~~ increase in branching of the carbon chain. So proportion of elimination increases from 1° → 2° → 3° alkyl halides. The reason is that alkene produced from branched substrate will be more stable for hyperconjugation. Again during elimination steric strain decreases in the product as ~~by~~ hybridisation state of Carbon changes from sp^3 to sp^2. But in case of substitution hybridisation state of carbon ~~in the final pdt~~ remains same in the final pdt.





So, generally substitution reaction increases in the order 3° → 2° → 1°

In general the proportion of elimination increases on using a strong base of high concentration and a low polar solvent. On the other hand the proportion of substitution increases by using a weak base of low concentration and high polar solvent

Halogenation of alkane:

$CH_4 + Cl_2 \xrightarrow{h\nu} CH_3Cl + HCl + \cdots\cdots$

Initiation → $Cl-Cl \xrightarrow{h\nu} \dot{Cl} + \dot{Cl}$

↑ chlorine radical

Propagation →
- $CH_3 - H + \dot{Cl} \longrightarrow HCl + \dot{C}H_3$ or $CH_3Cl + \dot{H}$ (X)
- $\dot{C}H_3 + Cl-Cl \longrightarrow CH_3Cl + \dot{Cl}$

Termination → $\dot{C}H_3 + \dot{C}H_3 \longrightarrow CH_3 - CH_3$

H—Cl – more ionic more stronger & more exothermic

$H-\underset{H}{\overset{H}{C}}-Cl$ – more covalent less ionic less exothermic.

$\dot{C}H_3 + O_2 \longrightarrow CH_3O_2$ – paroxy radical

The above halogenation reaction passes through several steps like initiation, propagation and termination etc. Here $\dot{C}H_3$ and HCl are formed in the intermediate step of this reaction. The alternating path is not favourable because HCl formation is more exothermic than CH_3Cl formation. If the above reaction is carried out in presence of oxygen paroxy radical is generated and naturally reaction rate becomes extreamely slow.

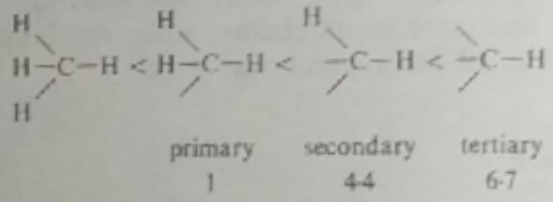
For the generation of radical some special condition like presence of peroxide, high temperature, UV radiation etc may be require.

in alkanes. The net displacement occurring at carbon on chlorination, for example, of alkanes consists (after initial formation of Cl·) of H-abstraction from R—H by Cl·, followed by Cl-abstraction from Cl—Cl by R· (this step can also be regarded as direct displacement at Cl), the two steps alternating in a very rapid chain reaction:

$$\begin{array}{ccccc} & & Cl-Cl & & \\ & & \downarrow h\nu & & \\ R-H & + \cdot Cl & \rightarrow & R\cdot & + H-Cl \\ & \uparrow & & \downarrow Cl-Cl & \\ & \cdot Cl & + & R-Cl & \end{array}$$

The chain length, i.e. number of $RH \rightarrow RCl$ conversions per Cl· produced by photolysis, is $\approx 10^6$ for CH_4, and the reaction can be explosive in sunlight. Chlorination can also be initiated thermolytically, but considerably elevated temperatures are required to effect $Cl_2 \rightarrow 2Cl\cdot$, and the rate of chlorination of C_2H_6 in the dark at 120° is virtually indetectable. It becomes extremely rapid on the introduction of traces of $PbEt_4$, however, as this decomposes to yield ethyl radicals, Et·, at this temperature, and these can act as initiators: Et· + Cl—Cl $\rightarrow$ Et—Cl + Cl·. Chlorination of simple alkanes such as these is seldom useful for the preparation of mono-chloro derivatives, as this first product readily undergoes further attack by the highly reactive chlorine, and complex product mixtures are often obtained.

Ease of attack on differently situated hydrogen atoms in an alkane is found to increase in the sequence,



i.e. in the order of weakening of the C—H bond, and of increasing stability of the product radical (*cf.* p. 310); the figures quoted are for the relative rates of abstraction of H by Cl· at 25°. This differential may often be opposed by a statistical effect, i.e. relative numbers of the different types of hydrogen atom available; thus in $(CH_3)_3CH$ there are nine primary hydrogen atoms available to every one tertiary hydrogen atom. On chlorination $(CH_3)_3CH$ is found to yield mono-chloro products in the ratio of ≈65% $(CH_3)_2CHCH_2Cl$ to 35% $(CH_3)_3CCl$—which is only roughly in accord with the rate ratios quoted above, after 'statistical' allowance has been made. If chlorination is carried out in solution, the product distribution is found to depend on the nature of the solvent, and particularly on its ability to complex with Cl·, thereby stabilising it and thus increasing its selectivity as compared with its reaction in the vapour phase.

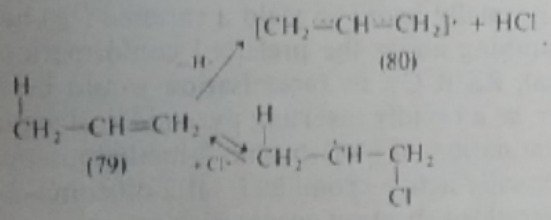
selectivity in halogenation is found to decrease with rise in temperature.

Halogenation, and particularly chlorination, unlike most radical reactions, is markedly influenced by the presence in the substrate of polar substituents; this is because Cl·, owing to the electronegativity of chlorine, is markedly electrophilic (*cf.* p. 314), and will therefore attack preferentially at sites of higher electron density. Chlorination will thus tend to be inhibited by the presence of electron-withdrawing groups, as is seen in the relative amounts of substitution at the four different carbon atoms in 1-chlorobutane (78) on photochemically initiated chlorination at 35°:

$$\underset{25\%}{CH_3}-\underset{50\%}{CH_2}-\underset{17\%}{CH_2}-\underset{3\%}{CH_2}-Cl \qquad (78)$$

The variation over the three different CH_2 groups nicely demonstrates the falling off with distance of the electron-withdrawing inductive effect of Cl. The γ-(3-)CH_2 group is behaving essentially analogously to that in $CH_3CH_2CH_2CH_3$, while the lower figure for the CH_3 group reflects the greater difficulty of breaking the C—H bond in CH_3 than in CH_2 (see above).

With propene, $CH_3CH{=}CH_2$ (79), there is the possibility of either addition of chlorine to the double bond, or of attack on the CH_3 group. It is found that at elevated temperatures, e.g. ≈450° (Cl· then being provided by thermolysis of Cl_2), substitution occurs to the total exclusion of addition. This is because the allyl radical (80) obtained by H-abstraction is stabilised by delocalisation, whereas the one (81) obtained on Cl· addition is not, and its formation is in any case reversible at elevated temperatures, the equilibrium lying over to the left:



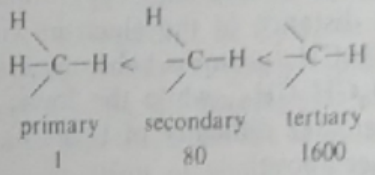
Cyclohexene undergoes analogous 'allylic' chlorination for the same reasons.

So far as the other halogens are concerned, the ΔH values—in kJ (kcal) mol^{-1}—for the two steps of the halogenation chain reaction (p. 324) on CH_4 are as follows:

	(1) $X\cdot + H{-}CH_3$		(2) $CH_3\cdot + X_2$	
F_2	−134	(−32)	−292	(−70)
Cl_2	−4	(−1)	−96	(−23)
Br_2	+63	(+15)	−88	(−21)
I_2	+138	(+33)	−75	(−18)

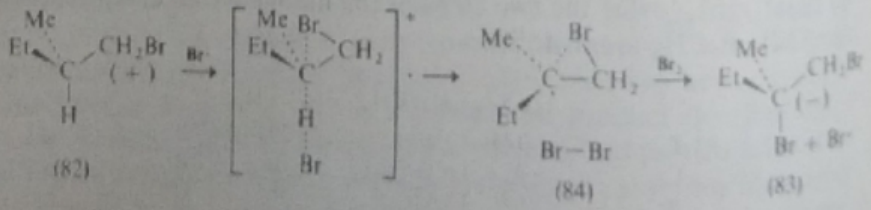
The figures for fluorination reflect the weakness of the F—F [150 kJ (36 kcal) mol^{-1}] and the strength of the H—F [560 kJ (134 kcal) mol^{-1}] bonds. Fluorination normally requires no specific initiation (*cf.* p. 324), and is explosive unless carried out at high dilution. That fluorination does proceed by a radical pathway, despite not requiring specific initiation, is demonstrated by the fact that chlorination may be initiated in the dark, and at room temperature, by the addition of small traces of F_2. Bromination is a good deal slower than chlorination, under comparable conditions, as step (1)—H-abstraction by Br·—is commonly endothermic. This step is usually so endothermic for I· that direct iodination of alkanes does not normally take place.

The markedly lower reactivity of Br· than Cl· towards H-abstraction means that bromination is much more *selective* than chlorination (the figures refer to H-abstraction by Br· at 25°):



A fact that can be put to preparative/synthetic use; thus bromination of $(CH_3)_3CH$ is found to yield only $(CH_3)_3CBr$ (*cf.* chlorination, p. 324). The effect is more pronounced when substituents are present that can stabilise the initial radical; thus across the series, CH_4, $PhCH_3$, Ph_2CH_2 and Ph_3CH the relative rates of bromination differ over a range of 10^9, but only over a range of 10^3 for chlorination. Selectivity decreases with rise of temperature, however.

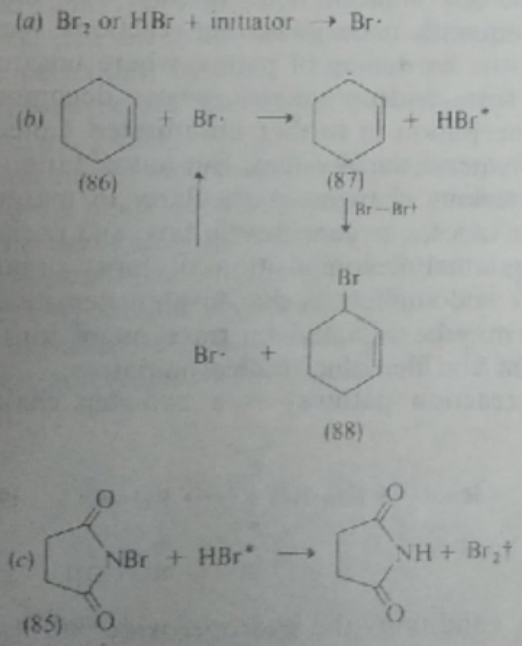
Halogenation of an optically active form of a chiral alkane, RR′R″CH, is normally found to yield a racemic (±) halide—a result that tells us nothing about the preferred conformation of the intermediate radical, RR′R″C·, as racemisation would be observed with *either* a planar, *or* a rapidly inverting pyramidal, structure (*cf.* p. 310). However, bromination of (+)1-bromo-2-methylbutane (82) is found to yield an optically active bromide, (−)1,2-dibromo-2-methylbutane (83), i.e. the overall substitution occurs with retention of configuration. This is believed to result from the original (1-)bromo substituent interacting with one side of the intermediate radical (84)—the one opposite to that from which H has been abstracted—and so promoting attack by Br_2 on the other, thus leading to retention of configuration:



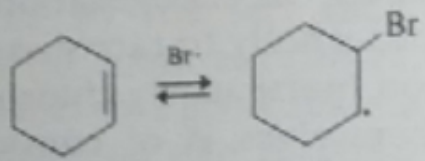
Bromination of an optically active form of the corresponding chloro compound (1-chloro-2-methylbutane) also results in an optically active product, and retention of configuration. It may be that an actual bridged radical is formed, but a somewhat less concrete interaction seems more likely, as halogenation with the more reactive chlorine is found to lead wholly to racemisation.

Radical halogenation (particularly chlorination) by reagents other than the halogens themselves is of considerable synthetic importance because of its greater stereoselectivity. Thus chlorination may be effected through reaction with alkyl hypochlorites, ROCl (e.g. R = Me_3C), in the presence of radical initiators, the latter abstracting Cl to form RO· which has been shown to be the species that abstracts H from RH; this reagent is used particularly for allylic chlorination. Another useful reagent for preparative chlorination is SO_2Cl_2, the radical initiator again abstracts Cl to yield $\cdot SO_2Cl$, and both this species and the Cl· it yields by loss of SO_2 can act as H-abstractors from RH.

Another reagent that is extremely useful synthetically is N-bromosuccinimide (NBS, 85), which is highly selective in attacking only weak C—H bonds, i.e. at allylic, benzylic, etc., positions. It requires the presence of radical initiators, and has been shown to effect bromination through providing a constant, but very low, ambient concentration of Br_2—this is maintained through reaction of the HBr produced in the reaction with NBS (*c*, below). There is usually a trace of Br_2 or HBr in the NBS that can react with the initiator to generate the initial Br· to start reaction (*a*, below):



Control of the bromine concentration is maintained by reaction (*c*) which is fast, though ionic, but can be activated only by HBr produced in the chain reaction (*b*). The alternative reaction of addition of $Br\cdot$ to the double bond to form (89) is reversible,



(86) (89)

while formation of (87) is not; overall substitution is thus favoured over addition so long as $[Br_2]$ is kept low. The radical (87) is also stabilised by delocalisation, while (89) is not (*cf.* p. 311). Support for the above interpretation of the reaction of NBS is provided: (i) by the fact that NBS shows exactly the same selectivity ratios as does Br_2, and (ii) by the fact that cyclohexene (86) is found to undergo largely addition with high concentrations of bromine, but largely allylic substitution with low (it is necessary to remove the HBr produced—as happens with NBS).

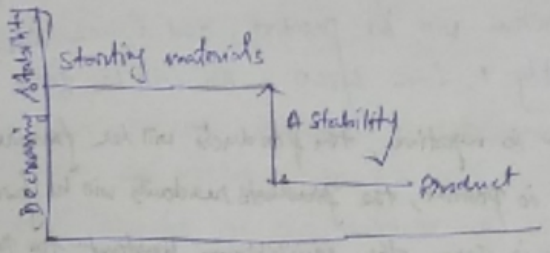
General Treatment of Reaction Mechanism II

Reaction Thermodynamics

How far and how fast a reaction can go?

$$A \rightleftharpoons B$$

$$K = \frac{[B]}{[A]}$$ where K = equilibrium Constant



Now A will move towards B when it get some stability. However it becomes apparent that the simple energy change that occurs on going from starting materials to products, and that may readily be measured as the heat of reaction, ΔH°, is not an adequate measure of the difference in stability between them, for there is often found to be no correlation between ΔH and the equilibrium constant for the reaction, K. It is often found that highly exothermic reactions having small equilibrium constants and highly endothermic reaction having high equilibrium constant. Now why this happens?

According to second law of thermodynamics, which is essentially concerned essentially with probabilities and with the tendency for ordered systems to become disordered; a measure of the degree of disorder of a system being provided by its entropy, S. In seeking their most stable condition, systems tend towards minimum energy (actually enthalpy H) and maximum entropy (disorder or randomness) a measure of their relative stability must thus embrace a comparison between H and S, and is provided by the Gibbs free energy, G which is defined by,

$$G = H - TS$$

where T is the absolute temperature. The free energy change during a reaction at a particular temperature, is thus given by

$$\Delta G = \Delta H - T\Delta S$$

and it is found that the change in free energy in going from starting materials to products, ΔG° (ΔG° refers to the change under standard conditions at unit activity; being exactly at unit, i.e. molar concentration), is related to the equilibrium constant, K, for the change by the relation,

$$-\Delta G^{\circ} = 2.303 RT \log K.$$

[P.T.O]

Now $\Delta G = -2.303\ RT \log K$ or $\Delta G = -RT \ln K$

> The sign of ΔG tells us whether products or reactants are favoured at equilibrium.

When the equilibrium lies to the side of the reactants, rather than the products K will be less than 1. This means that its logarithm must be negative and, because $\Delta G = -RT \ln K$, ΔG must be positive. Conversely, for a reaction in which products are favoured over reactants, K must be greater than 1, its logarithm will be positive, and hence ΔG must be negative. When K is exactly 1, since $\log 1 = 0$, ΔG will be zero.

Thus,

If ΔG for a reaction is negative, the products will be favoured at equilibrium.

If ΔG for a reaction is positive, the products reactants will be favoured at equilibrium.

If ΔG for a reaction is zero, the equilibrium constant for the reaction will be 1

Now from the eqn: of previous page.

$$\Delta G = \Delta H - T\Delta S$$

Now value of ΔG depends upon ΔH as well as ΔS.

Now ΔH = (-)ve for an exothermic reaction.

ΔH = (+)ve for an endothermic reaction.

ΔS = (+)ve when reaction moves towards more random state.

ΔS = (-)ve when reaction moves towards less random state.

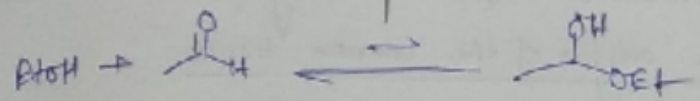
Now we will get negative ΔG most readily if,

1. ΔH is negative, ie the reaction is exothermic. and
2. ΔS is positive. (and hence $-T\Delta S$ is negative) ie, the reaction becomes more disordered.

Of course, we can still get a negative ΔG from an endothermic reaction (ie from a positive ΔH) but only if the reaction products are more disordered than the starting materials; likewise a reaction which becomes more ordered as it proceeds can still be favourable, but only if it is exothermic to compensate for the loss of entropy.

Because of the factor T multiplying the entropy term, both the equilibrium constant K (which depends on ΔG) and the relative importance of the two quantities (ΔH and ΔS) will vary with temperature. (entropy changes are more important at higher temperature).

Intermolecular and Intramolecular reactions:

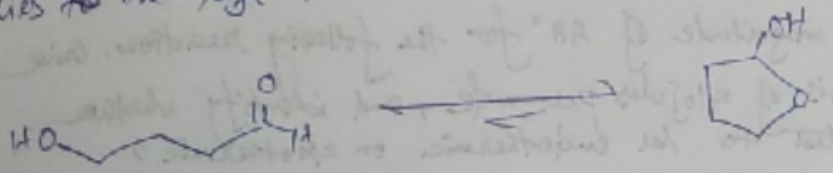


Intermolecular hemiacetal formation

ΔH is small and negative because C=O double bond is slightly less stable than 2 x C–O single bonds.

ΔS is negative because the one molecule of product is intrinsically less disordered than the two molecules of starting material.

Since $\Delta G = \Delta H - T\Delta S$, ΔG is positive and the equilibrium lies to the left.



Intramolecular hemiacetal formation

ΔH is again small and negative because C=O double bond is slightly less stable than 2 x C–O single bonds.

ΔS is no longer negative; there is no decrease in the number of molecules in this reaction.

Since $\Delta G = \Delta H - T\Delta S$; ΔG is negative and the equilibrium lies to the right.

3 Calculation of energies enthalpy using bond dissociation energies:

- Bond dissociation energies describe the strength of chemical bonds. They can be determined experimentally
- Enthalpy is the sum of bond dissociation energies of the reactions.

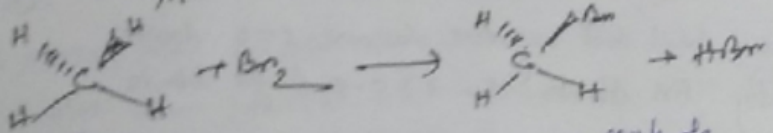
(-) = making of bonds = Exothermic (+) = breaking of bonds = Endothermic

Bond dissociation energies of the common bonds.

Bond	KJ/mol	Bond	KJ/mol	Bond	KJ/mol
H-OH	498	H_3C-H	436	H_3C-CH_3	426
H-H	436	H_3C-OH	321	HO-OH	213
H-Br	368	H_3C-Br	293	Br-Br	192
H-I	297	H_3C-I	234	I-I	151

H. bonds — Methyls — Each other

- Predict the sign and magnitude of ΔH° for the following reaction. Give your answer in units of kilojules per mole, and identify whether the reaction is expected to be endothermic or exothermic?



Breaking of bonds = CH_3-H = +436 KJ/mole

$Br-Br$ = +192 KJ/mole

+628 KJ/mole

making of bonds = CH_3-Br = (-) 293 KJ/mole

H-Br = (-) 368 KJ/mole

(-) 661 KJ/mole

~~(436) KJ/mole + (-661) KJ/mole~~

Thus ΔH° = Sum of bond dissociation energies of the reaction

= +628 KJ/mole + (-661 KJ/mole)

= -33 KJ/mole

Thus the reaction is exothermic and ΔH° = -33 KJ/mole

Chemical Kinetics :→

Thermodynamics can predict →

i) direction

& (ii) extent of a chemical rxn.

But it cannot predict

i) time required for completion

& ii) mechanism of a chemical rxn.

Rate / velocity :

It is the amount of chemical change occuring in unit time.

$R \longrightarrow P$

$$\text{rate} = v = -\frac{d[R]}{dt} = \frac{d[P]}{dt}$$ [∵ Rate is +ve quantity]

$A + B \longrightarrow C + D$

$$v = -\frac{d[A]}{dt} = -\frac{d[B]}{dt} = \frac{d[C]}{dt} = \frac{d[D]}{dt}$$

- $mA + nB \longrightarrow pC + qD$

If $d\xi$ be the advancement of the above rxn in time interval dt

∴ change in conc^{n} of $A \rightarrow m\,d\xi$

$$-d[A] = m\,d\xi \quad \text{~(i)}$$

Similarly,

$$-d[B] = n\,d\xi \quad \text{~(ii)}$$

$$d[C] = p\,d\xi \quad \text{~(iii)}$$

$$d[D] = q\,d\xi \quad \text{~(iv)}$$

Dividing both sides of eq^{n} (i) to (iv) by dt

$$-\frac{d[A]}{dt} = m\frac{d\xi}{dt}$$

$$-\frac{d[B]}{dt} = n\frac{d\xi}{dt}$$

$$\frac{d[C]}{dt} = p\frac{d\xi}{dt}$$

$$\frac{d[D]}{dt} = q\frac{d\xi}{dt}$$

$$\therefore v = \frac{d\xi}{dt} = -\frac{1}{m}\frac{d[A]}{dt} = -\frac{1}{n}\frac{d[B]}{dt} = \frac{1}{p}\frac{d[C]}{dt} = \frac{1}{q}\frac{d[D]}{dt}$$

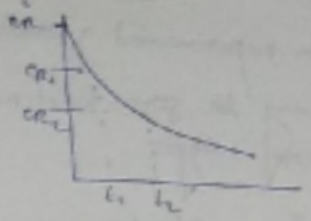
- $2A + B \longrightarrow 3C$

$$v = -\frac{1}{2}\frac{d[A]}{dt} = -\frac{d[B]}{dt} = \frac{1}{3}\frac{d[C]}{dt}$$

unit: moles $lit^{-1} s^{-1}$ / moles $lit^{-1} min^{-1}$ / moles $lit^{-1} hour^{-1}$

Rate

- Average rate $\frac{C_{A_2} - C_{A_1}}{t_2 - t_1}$
- Instantaneous rate $= \lim_{\Delta t \to 0} \frac{\Delta C_A}{\Delta t}$



Rate law / Rate equation: It is an experimentally obtained relation between rate of a rxn and conc^{n} of the reactants involved.

$2A + B \longrightarrow P$

$v = K C_A^m C_B^n$ ... Rate law

K → Rate constant

Chemical rxn

- Elementary / Single step
  $2A + B \longrightarrow P$ → $v = K C_A^2 C_B$
- Multistep / Complex
  $2A + B \longrightarrow C \longrightarrow D \longrightarrow E \longrightarrow P$

Order: It is the sum of the exponents of the conc^{n} terms used in rate law expression in multiplicative form.

$v = K C_A^m C_B^n$ Order = m+n

order is an experimental quantity.

Order may have any value, i.e. it may be zero, fraction, integer, +ve and -ve.

Molecularity: It is the no of molecules taking part in an elementary step of a chemical rxn.

Molecularity is a theoritical quantity and it is always a +ve integer.

- A zero order rxn must be multistep. Explain.

We know for a single step or elementary rxns, order and molecularity are same. Therefore if a zero order rxn be an elementary rxn its molecularity should also be zero which means no molecule is taking part in the rxn. It is this is an absurd concept. A zero order reaction must be multistep.

Order

① It is an experimental quantity.

② Order may be zero, fractional or an integer.

③ order of a particular rxn may vary with the experimental conditions. (ie; pressure, temperature, concentration of the reactants)
For eg, enzyme catalysed rxns is first order at low substrate conc^{n} and zero order at high substrate conc^{n}.

Molecularity

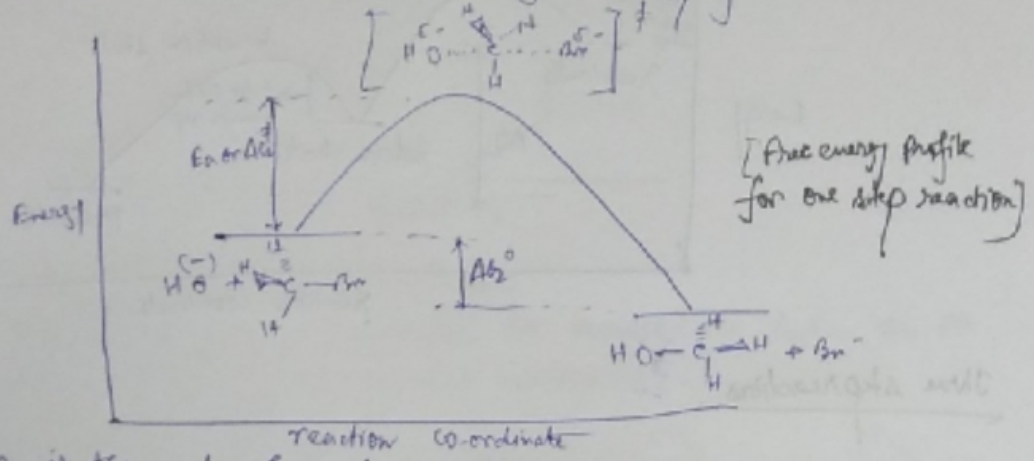
① It is a theoritical quantity.

② Molecularity is always a positive integer.

③ Molecularity of a definite rxn is always constant.

Thermodynamics is concerned with equilibria; kinetics is concerned with rates. i How fast do reactions go?

From the previous study we learn that ΔG when ΔG_2 = -ve then the reaction is feasible. But the rate at which product will form can never be predicted from this value. Formation of product is totally dependent upon an energy barrier which is generally needed to be overcome. This energy barrier is termed as $\Delta G^{\ddagger}$, ie free energy of activation.



[Free energy profile for one step reaction]

Thus higher is the value of $\Delta G^{\ddagger}$, the slower is the reaction and it can be considered as being made up of enthalpy ($\Delta H^{\ddagger}$) and entropy ($T\Delta S^{\ddagger}$) terms.

$\Delta H^{\ddagger}$ (the enthalpy of activation) corresponds to the energy necessary to effect the stretching or even breaking of bonds that is essential for reaction to take place.

$\Delta S^{\ddagger}$ term (the entropy of activation) again relates to randomness. It is a measure of the change in degree of organisation, or ordering of the reacting molecules.

The magnitude of E_{act} / $\Delta G^{\ddagger}$ for a reaction may be calculated from values of k, the rate constant, determined at ~~two~~ different temperatures, T_1 & T_2, using the Arrhenius expression which relates k to T, the absolute temperature;

$$k = Ae^{-E/RT} \quad \text{or} \quad \log_{10} k = -\frac{E_{act}}{2.303RT} + \log_{10} A$$

where R is the gas constant (8.32 Joules mol^{-1} deg^{-1}).

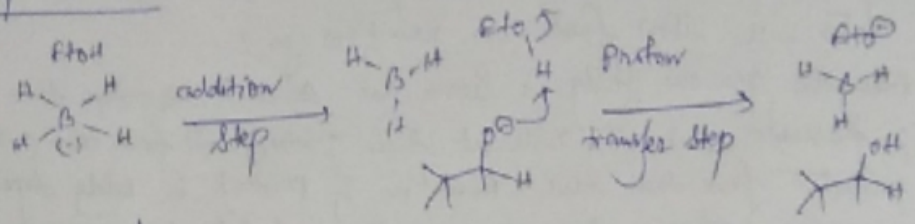
The value of E_{act} may then be obtained graphically by plotting values of $\log_{10} k$ against $\frac{1}{T}$, or by conversion of the above equation into

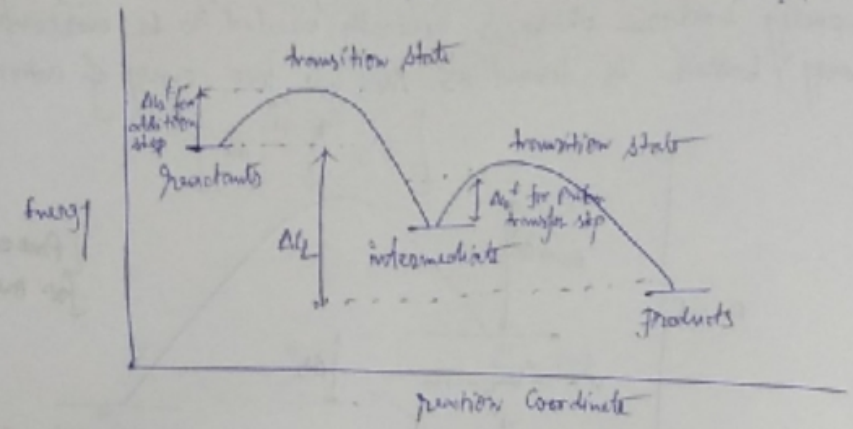
$$\log_{10} k_1/k_2 = -\frac{E_{act}}{2303R}\left[\frac{1}{T_1} - \frac{1}{T_2}\right]$$

and subsequent calculation.

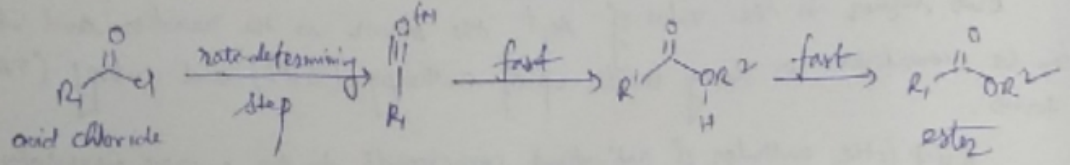
- Free energy Profiles for two and three step reactions:

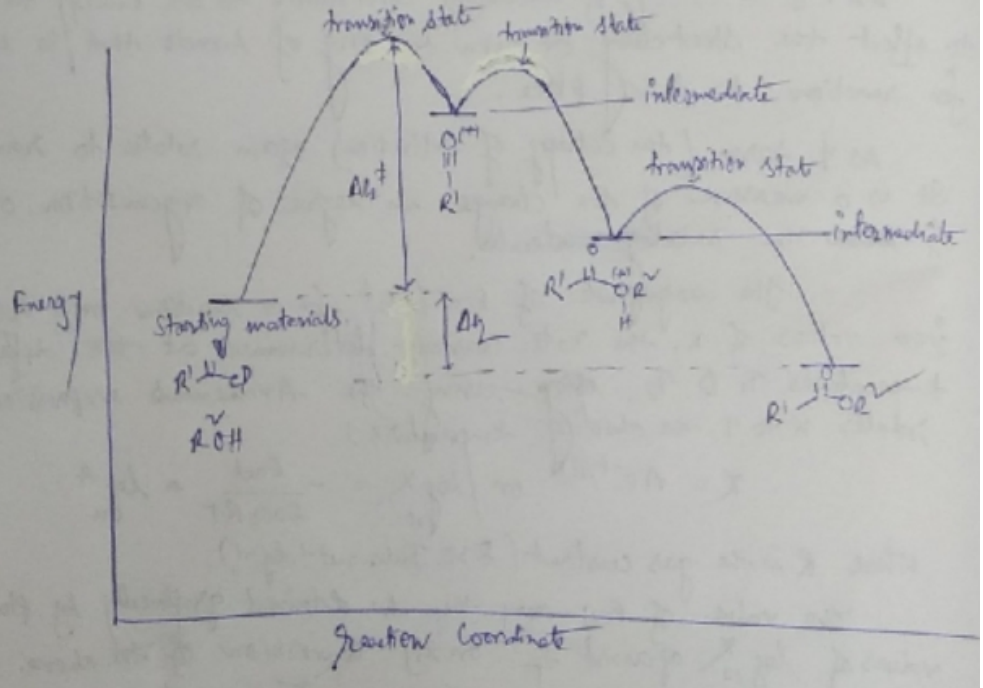
Two step reactions:





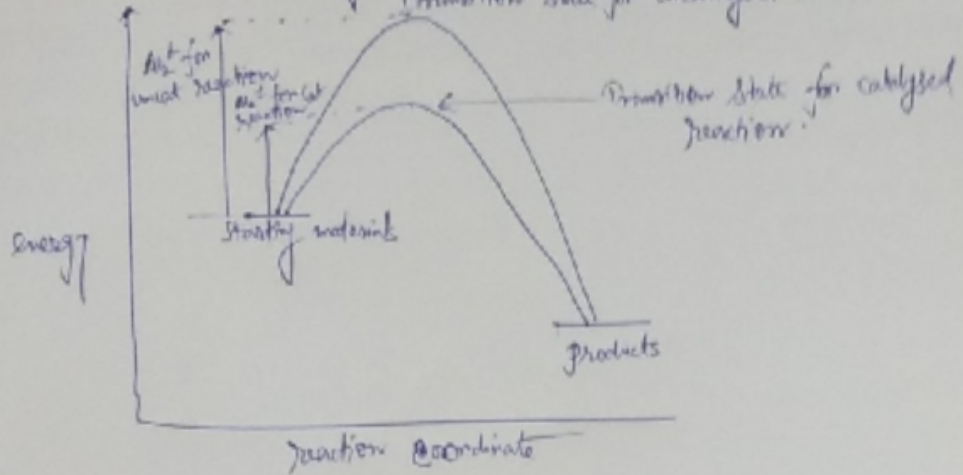
Three step reactions:





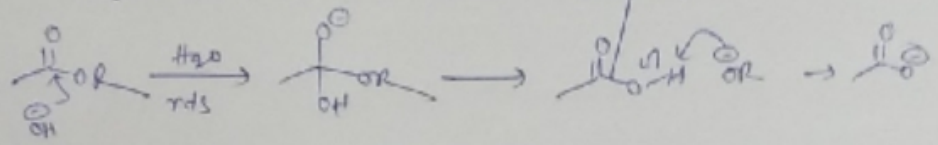
Catalysis:

Catalysts work by lowering the activation energy for a reaction.

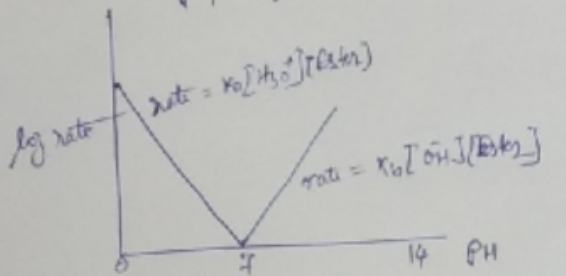


Catalysis in carbonyl substitution reactions:

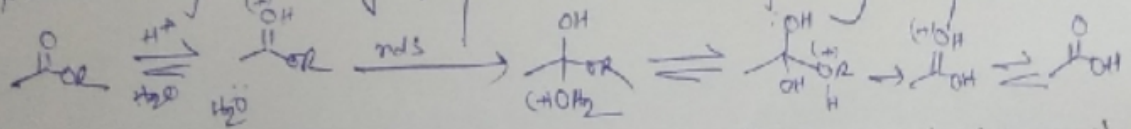
Ester hydrolysis is faster at higher pH because the higher the pH, the more hydroxide there is to act as a nucleophile.



We can plot this on a graph of rate vs pH.



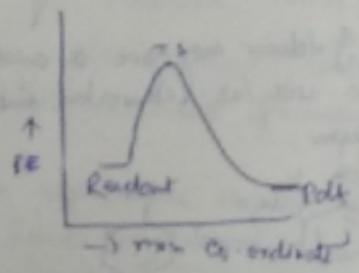
The rate equation at high pH is second order, and depends on the concentration of hydroxide and the concentration of ester. Though, below pH 7 the rate starts to increase again as the concentration of $[H^+]$ increases. This is because ester hydrolysis is also acid catalysed. At acidic pH, a new mechanism takes over in which protonation of the carbonyl group accelerates attack of weakly nucleophilic water.



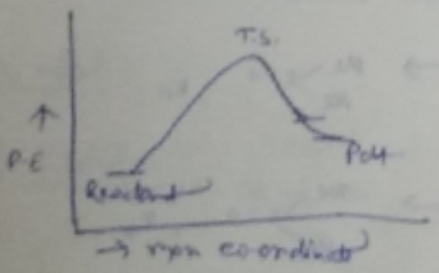
* The mechanism of a reversible reaction is exactly the same (but reversed) for both the forward and backward version of the reaction. This principle of microscopic reversibility states that - The same pathway that is travelled in the forward direction of a reaction will be traveled in the reverse direction, because it affords the lowest energy barrier for either process.

Hammond Principle:

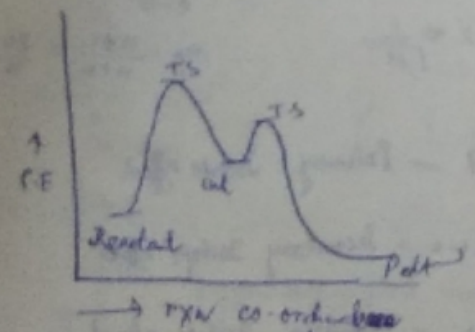
From the above energy profile diagram we can say that the position of TS must be somewhere between the position of reactants and products. Either it may be closer to the reactant or it may be closer to the product. If the reaction is strongly exothermic, then position of TS will be closer to the reactant in a single step reaction as shown below.



In case of strong endothermic single step reaction, position of T.S will be close to the product molecule as shown below.



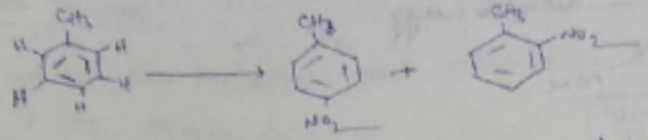
These generalisations hold good when the reaction proceeds through intermediates. Here intermediate is the product of first T.S and the reactant of the second TS as shown below.



This generalisation is known as the Hammond principle.

KCP & TCP ⇒ (Kinetic and thermodynamic Control)

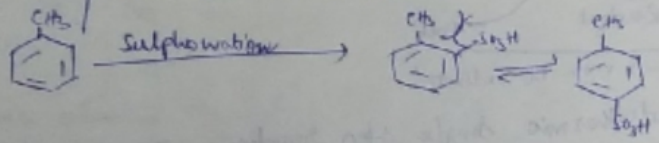
$\Delta G^{\ddagger}$ [‡ Dagger] → Activation energy



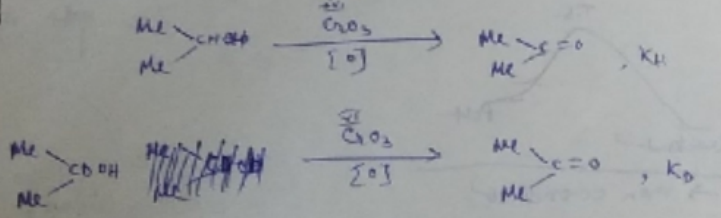
When a starting material may be converted into two or more alternative products, for example nitration of toluene where the benzene ring contains $-CH_3$ group, the proportion in which the products are formed is often determined by the relative rate of formation or relative activation energy of formation. The faster a pdt is formed, its amount will be major in the finale product mixture. This is known as Kinetic Controll and the major pdt is called KCP.

If one or more of the reactions is reversible or if the pdts are readily interconvertable under the condition of the reaction, then the composition of the finale pdt mixture may not be dictated by the relative rates of formation of the different pdts. Composition of the finale mixture will be dictated by their relative thermodynamic stabilities in the reaction system. This is called thermodynamic Controll and the major pdt is called TCP.

For example Sulphonation of toluene may give o- and p isomer but if we allow sufficient time o- will be converted into p isomer where steric repulsion will be minimum.



Isotope effect:



$K_H \neq K_D$

Hooke's law

$\bar{\nu}(\lambda) \quad \bar{\nu} = \frac{1}{2\pi c}\sqrt{\frac{K}{\mu}}$

$\bar{\nu} \propto \frac{1}{\sqrt{\mu}}$

C–H

$m_1 \quad m_2$

$\mu = \frac{m_1 m_2}{m_1 + m_2}$

$\mu_H = \frac{12 \times 1}{12+1} = \frac{12}{13} \approx 1$

C–D

$\mu_D = \frac{12 \times 2}{12+2} = \frac{24}{14} \approx 2$

$\frac{K_H}{K_D} \geq 7$ — Primary Isotope effect

$\frac{K_H}{K_D} \geq 1-2$ — Secondary Isotope effect

$\frac{K_H}{K_D} < 1$ — Inverse Isotope effect

Changes in the reaction rate due to Isotopic substitution either in the substrate or in the solvent molecules, are known as Kinetic Isotope effect. For example we may consider the Chromic acid oxidation of Isopropyle alcohol to acetone. When Isopropyle alcohol and α-deuterated Isopropyle alcohol are subjected to oxidation it is found that the rate constants, K_H and K_D are not identical. So here Kinetic Isotope effect is observed.

Depending upon the ratio of K_H/K_D isotope effects may be classified into the following three types.

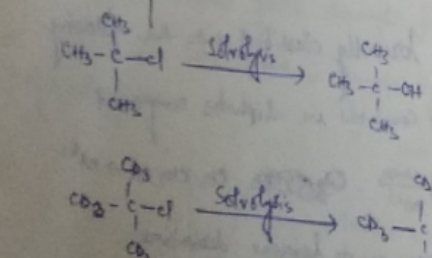
i) Primary Kinetic Isotope effect, here $K_H/K_D \geq 7$.
ii) Secondary Kinetic Isotope effect, here $K_H/K_D \geq 1-2$
iii) Inverse Isotope effect, here $K_H/K_D < 1$

K_H = rate constant of the reaction involving the breaking of C-H bond.
K_D = rate constant of the reaction involving the breaking of C-D bond.

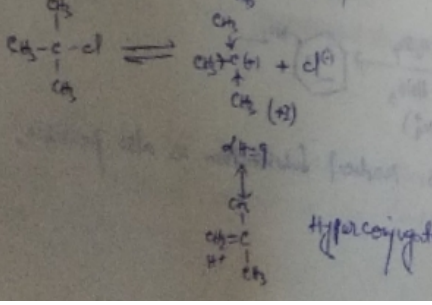
Primary Kinetic Isotope effect: If a reaction involves the breaking of C-H bond in the rds and if we replace the H by D, then primary Kinetic Isotope effect is observed. For example oxidation of Isopropile alcohol to acetone by Cr(VI) chromic acid involves breaking of C-H bond in the rds and it will exhibit primary Kinetic Isotope effect. In fact here $K_H/K_D \geq 7$.

When we replace the H atom of C-H bond by D, reduced mass increases energy level of this bond becomes low and Stability increases with decreasing vibrational wave number. So it becomes difficult to break C-D bond rather than C-H bond. Thus Isotopic substitution makes this reaction slower. In fact C-D bond is more stable than C-H bond.

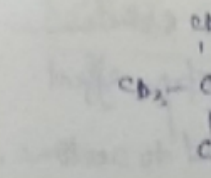
Secondary Kinetic Isotope effect:



$\frac{K_H}{K_D} \approx 1.34$



Hyperconjugation involves C-H bond breaking.



Hyperconjugation is difficult due to higher bond energy of C–D.

There are so many reactions where C–H bond does not break in the rds. C–H ~~may be~~ bond may break in other step. A Secondary Kinetic Isotope effect is the change observed in the rate of a reaction when an atom of the substrate is replaced by its isotope at a bond which is not broken or formed during the reaction.

For example Secondary Kinetic Isotope effect is observed in the above Solvolysis reaction. The exact reason behind this effect is not clear to us. But probable reason may be Hyperconjugation. As this reaction passes through carbocation intermediate and the carbocation is stabilised by hyperconjugation involving breaking of C–H bond and C–D bond as shown above. We know C–D bond is more stable than C–H bond. So, α-H is more effective than α-D in Hyperconjugation effect. So rate ~~became~~ become slower when H is replaced by D.

In case of inverse isotope effect $\frac{K_H}{K_D}$ ratio becomes < 1.