STUDY MATERIAL

Dumkal College
Basantapur Dumkal

Topic: Substitution and Elimination Reaction:Nucleophilic Substitution Reaction

Course Code: CHEMHT-4

Semester: IV (Hons)

Name of the Teacher: Md Muttakin Sarkar

Name of the Department: Chemistry

Reaction mechanism

Nucleophilic substitution reaction in aliphatic system.
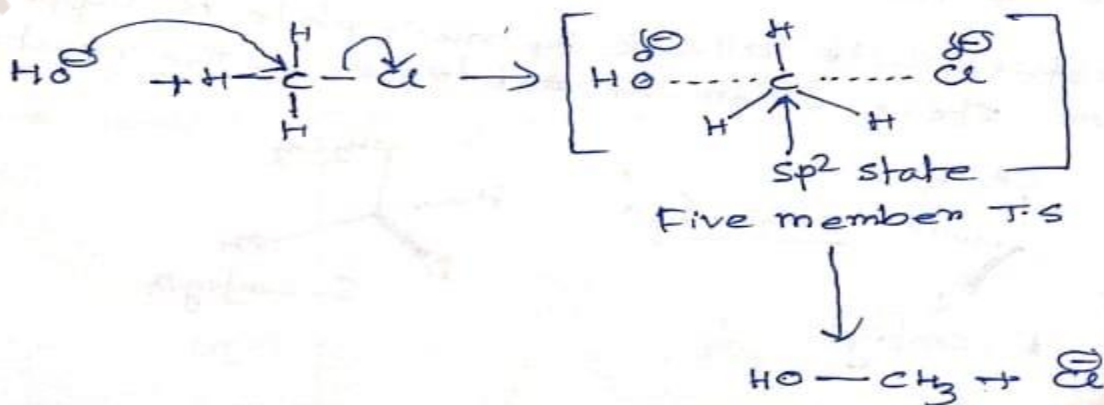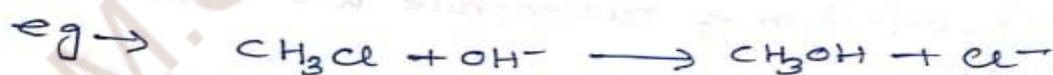
Generally represented as —

$$R-x + \overset{\ominus}{Nu} \longrightarrow R-Nu + x^{\ominus}$$

Aliphatic nucleophilic substitution reaction can be classified under three heads —

①	SN^2 reaction	$\left\{ \begin{array}{l} S \rightarrow \text{Substitution} \\ N \rightarrow \text{Nucleophile} \\ 1,2 \rightarrow \text{Order of reaction} \\ i = \text{intra molecular} \end{array} \right.$
②	SN^1 reaction	
(iii)	SN^i	

SN^2 reaction :— Main features of SN^2 reaction may be noted as follows —

① Single step process

② Bimolecular

③ Here nucleophile aproaches to the C-bearing leaving group from very back side with respect to leaving group (stereo electronic factor for SN^2 reaction)

④ If the leaving group bearing carbon is chiral, inversion of configuration occurs at this chiral carbon

eg → $CH_3Cl + OH^- \longrightarrow CH_3OH + Cl^-$

$$HO^{\ominus} \quad +H-\overset{H}{\underset{H}{C}}-Cl \longrightarrow \left[HO^{\delta\ominus} \cdots \overset{H}{\underset{H \quad H}{C}} \cdots Cl^{\delta\ominus} \right]$$

sp^2 state

Five member T.S

$$\downarrow$$

$$HO-CH_3 + \overset{\ominus}{Cl}$$

The FMO interpretation of the process is electron transfer occurs from HOMO of $\overset{\ominus}{O}H$ to LUMO of CH_3Br. The LUMO of CH_3-Cl is actually $\sigma*$ MO of $C-Cl$ bond.
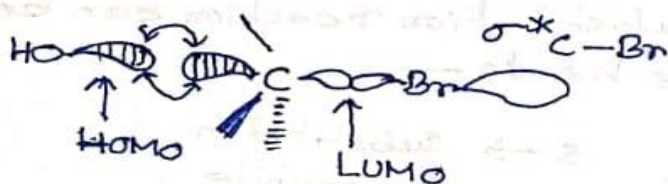
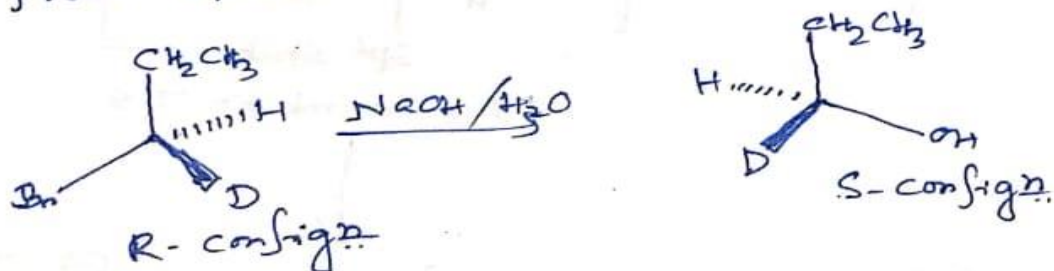If we represent the SN^2 reaction graphically, we shall get the following type of energy profile diagram:
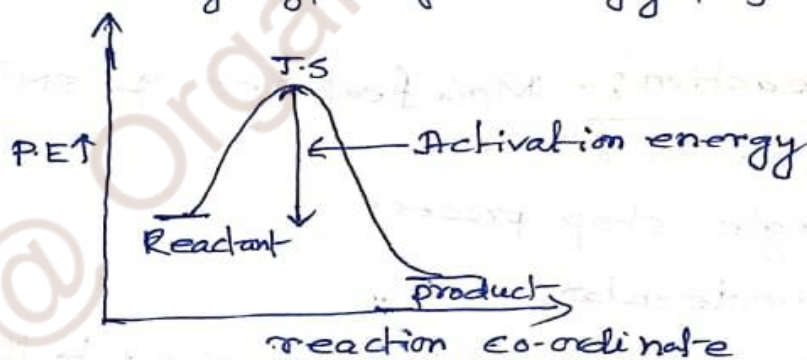

Here reaction rate α [substrate]$\times$[Nu]

$$= k\,[\text{Substrate}]\,[\text{Nu}]$$

$$k = \text{rate constant}$$

There are two concentration variables in this rate equation. Any change either concentration of substrate or in the concentration of nucleophile will alter the rate of reaction.

The back side attack by nucleophile is supported from stereo chemical evidences of the reaction—
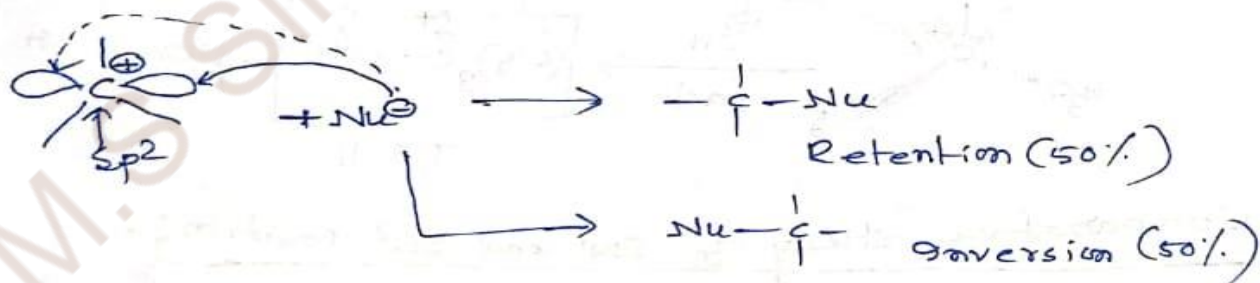
$$CH_2CH_3 \text{ (H, Me, Br) } \xrightarrow{\text{aq. NaOH}} CH_2CH_3 \text{ (H, HO, Me)}$$

S- config.   R- config.
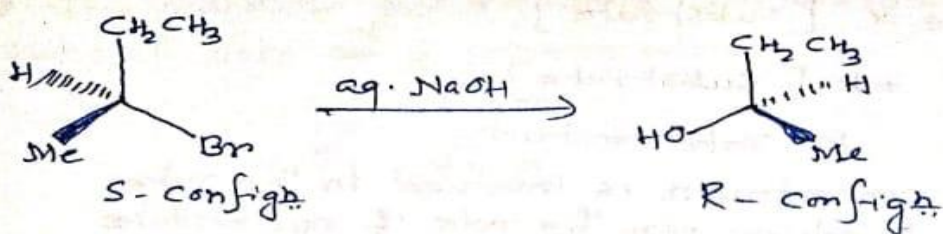
● **SN¹ reaction:—**

    ① Two steps reaction

    ⓘ Unimolecular

    ⓘⓘⓘ In the 1st 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.

    ⓘⓥ If the leaving group bearing carbon is chiral then racemisation occurs.

$$R-x \xrightleftharpoons[\text{rds}]{\text{slow}} R^{\oplus} + x^- \xrightarrow{Nu^{\ominus}} R-xu \text{ or } Nu-R$$

$$+ Nu^{\ominus} \longrightarrow -\overset{|}{\underset{|}{C}}-Nu$$
Retention (50%.)

$$\longrightarrow Nu-\overset{|}{\underset{|}{C}}- \text{ Inversion (50%.)}$$

Racemic mixture.

If we represent this reaction graphically we shall get the following energy profile diagram.

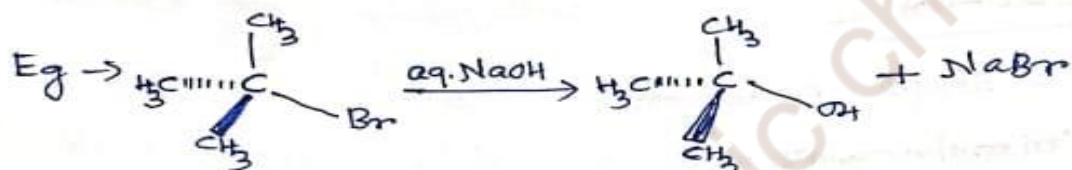P.E↑   T.S-I   T.S-II   R⁺

Reactant

product
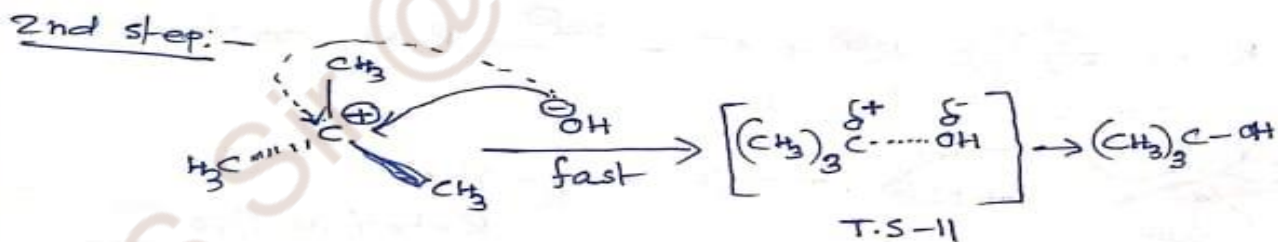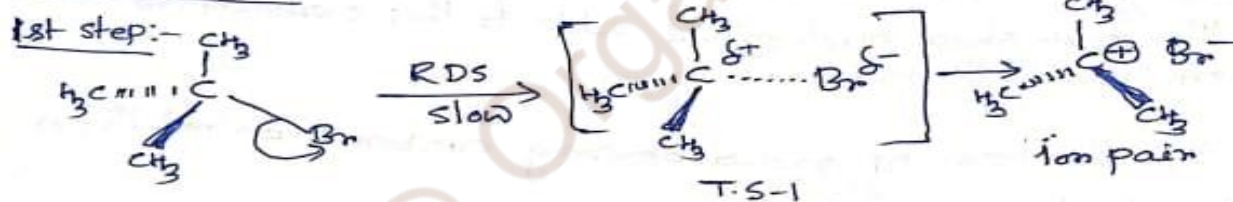
reaction co-ordinate
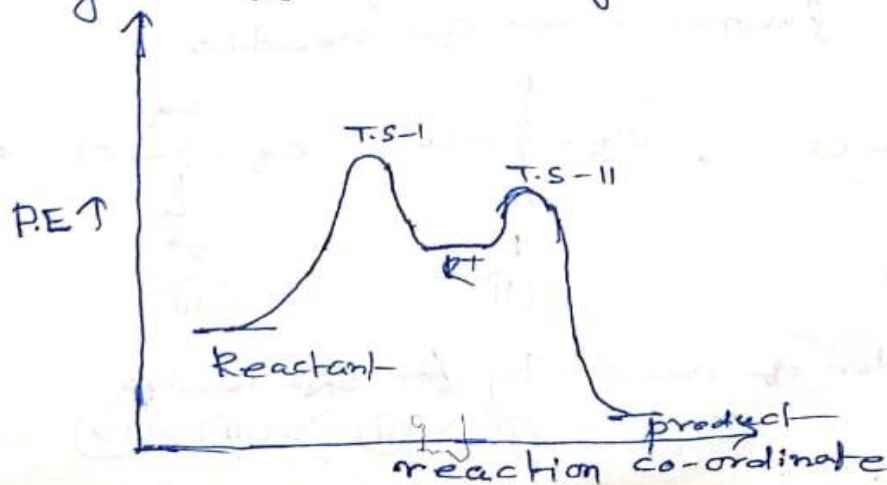
Reaction rate ∝ [substrate]

$$= k \, [\text{substrate}]$$

k = rate constant

Only substrate concentration is involved in the rate equation. In fact solvent play the role of nucleophile in absence of external nucleophile.
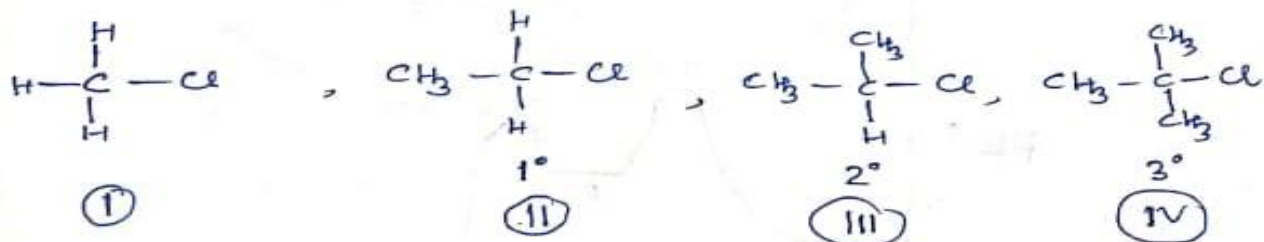
Eg →

aq. NaOH → ... + NaBr

Mechanism:-

1st step:-

RDS slow

T.S-I

ion pair

2nd step:-

$\overset{\ominus}{O}H$

fast →

$$\left[(CH_3)_3 \overset{\delta+}{C} \cdots \cdots \overset{\delta-}{O}H \right] \longrightarrow (CH_3)_3 C-OH$$
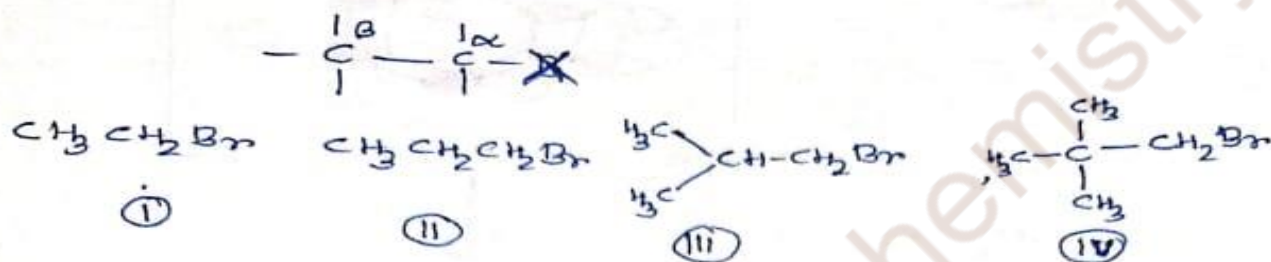
T.S-II

Comparative study of SN¹ and SN² reaction:-

In SN² reaction five member T.S is formed which is sterically crowded than substrate. For this reason sterically unhindered substrates are favorable for SN² reaction.

H—C̣—Cl	CH₃—Ç—Cl	CH₃—Ç—Cl	CH₃—Ç—Cl
	1°	2°	3°
①	⑪	⑪⑪	⑪v

Order of reactivity for SN² reaction

① > ⑪ > ⑪⑪ > ⑫v

● The rate of $SN2$ reaction decreases with increasing substituents at β-carbon atom.

$$-\overset{|}{\underset{|}{C}}^{\beta}-\overset{|}{\underset{|}{C}}^{\alpha}-\cancel{X}$$

CH_3CH_2Br $CH_3CH_2CH_2Br$ $\underset{H_3C}{\overset{H_3C}{>}}CH-CH_2Br$ $H_3C-\overset{CH_3}{\underset{CH_3}{\overset{|}{\underset{|}{C}}}}-CH_2Br$

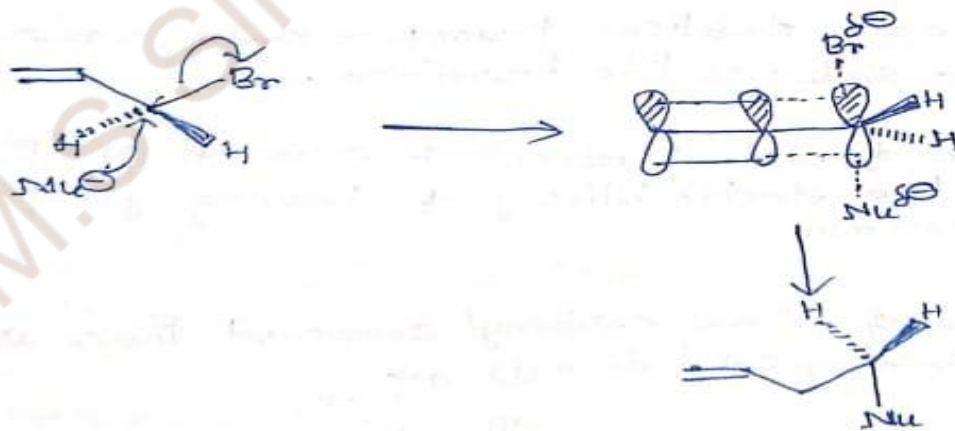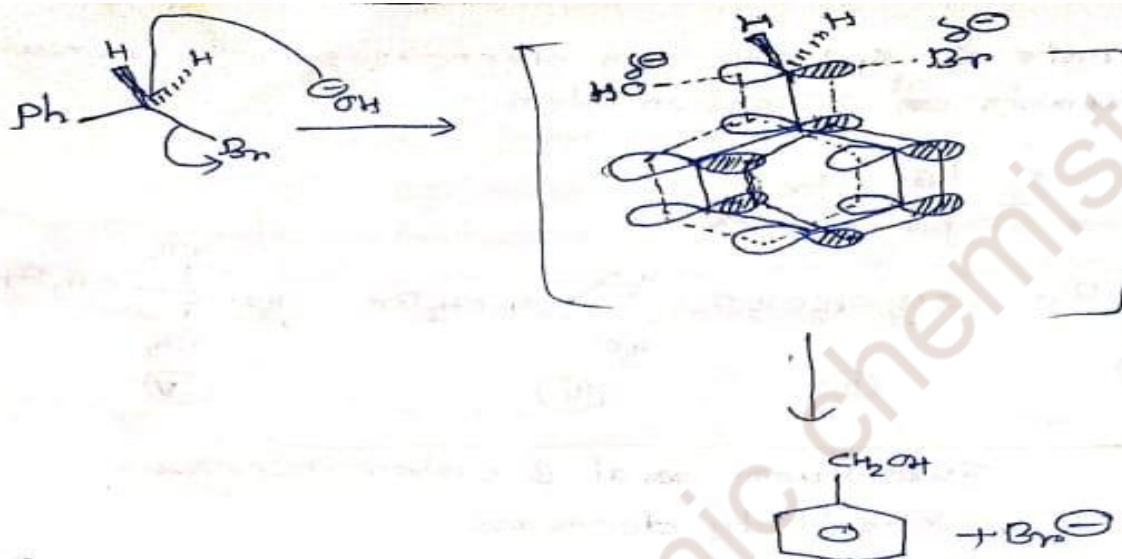   (I)   (II)   (III)   (IV)

$\xrightarrow{\hspace{6cm}}$

substituent at β-carbon increases
Reactivity decreases.

Reactivity order
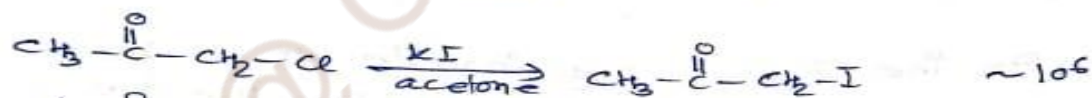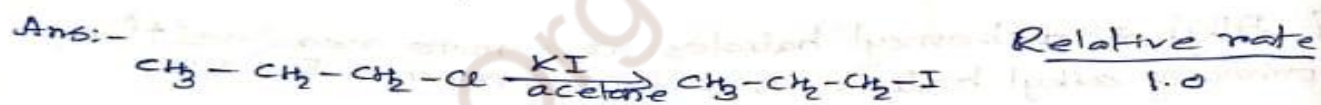
         (I) > (II) > (III) > (IV)

Q. Allyl and benzyl halides are more reactive than primary alkyl halide toward $SN2$ reaction. Explain.

Ans:- In the T.S of allyl halide, π-orbital of leaving group containing C (sp² hybridised) is in conjugation with the double bond.

$$Ph - C(H)(H) - Br \xrightarrow{\ominus OH} \left[HO^{\delta\ominus} \cdots C \cdots Br^{\delta\ominus} \right]$$

$$\downarrow$$

$$\underset{CH_2OH}{\bigcirc} + Br^{\ominus}$$

q. α-halo carbonyl compounds are highly reactive toward S_N2 reaction. Explain.

Ans:—

	Relative rate
$CH_3 - CH_2 - CH_2 - Cl \xrightarrow[acetone]{KI} CH_3 - CH_2 - CH_2 - I$	1.0
$CH_3 - \overset{O}{\overset{\|}{C}} - CH_2 - Cl \xrightarrow[acetone]{KI} CH_3 - \overset{O}{\overset{\|}{C}} - CH_2 - I$	~10^6

The higher reactivity of α- halo carbonyl compounds are due to the following reason —

① Just as $C=C$ stabilises transition state, similarly $C=O$ also stabilises the transition.

② $-I$ effect of carbonyl group increases the electrophilicity of leaving group bearing carbon.

③ In case of α-halo carbonyl compound, there are two anti-bonding orbitals — ① σ^*_{C-X}
   ② $\pi^*_{C=O}$

These ABMO's are combined to form a lower energy LUMO.

Energy

$$\left[\sigma^*_{C-X} - \pi^*_{C=O}\right]$$

σ^*_{C-X}

$\pi^*_{C=O}$

$$\left[\sigma^*_{C-X} + \pi^*_{C=O}\right]$$
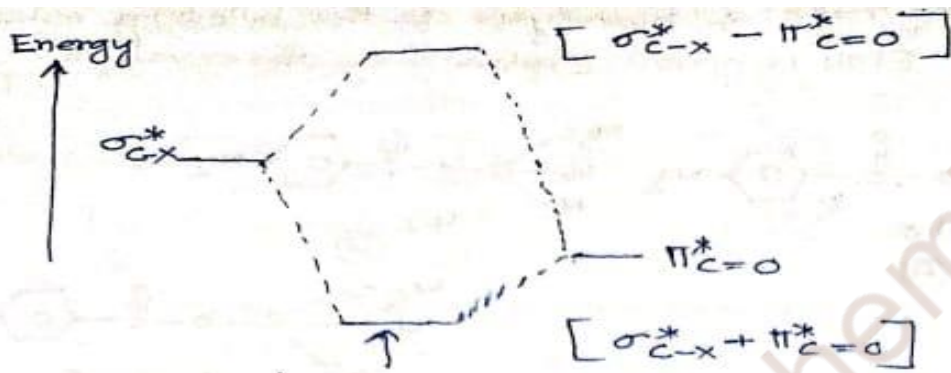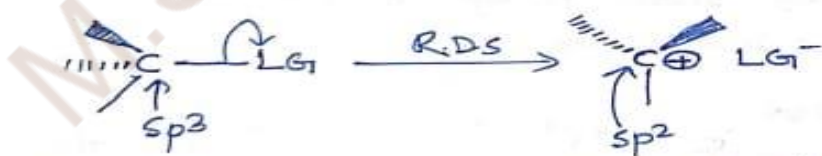
Lower energy LUMO

Due to lowering in LUMO energy of activation of reaction decreases.

⊘ SN^1 reaction occurs via formation of carbenium ion (carbocation). Therefore stability of carbocation influence the rate of reaction. If the the intermidiate carbocation is stable then rate of reaction become fast. Incase of alkyl carbocation stability order becomes following —

3° cation   2° cation   1° cation   methyl cation.
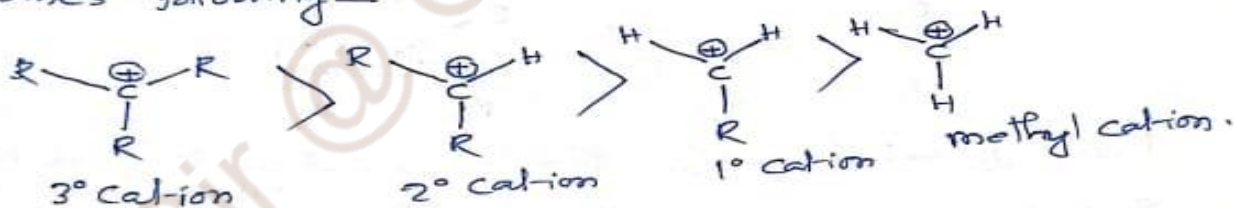
So, Rate of reaction   3° > 2° > 1° > methyl substrate

$\overset{\text{...}}{C}$—LG $\xrightarrow{R.DS}$ $C^{\oplus}$ LG$^-$

sp^3 sp^2
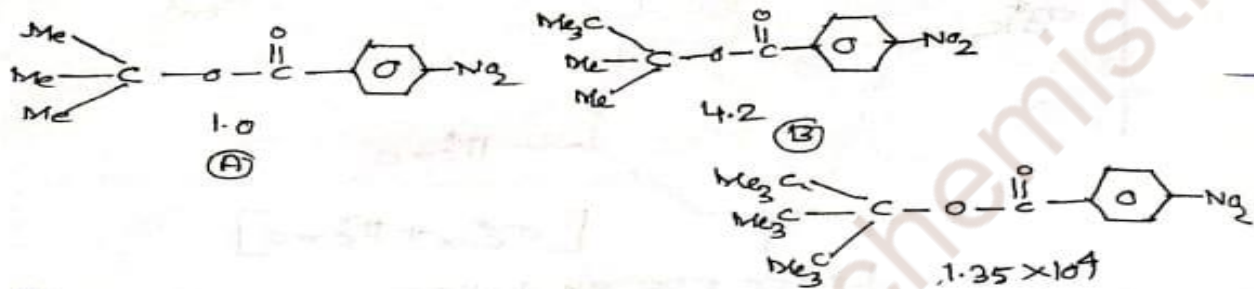
bond angle → 109°28'   bond angle — 120°

Here   hybridization state changes from sp^3 to sp^2. Steric relief occurs during formation of carbocation because bond angle changes from 109°28' to 120°. So bulky substituent favourable for SN1 reaction.

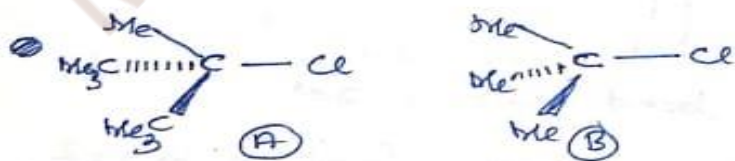9. Relative rate of hydrolysis of the following esters in 80% aq. EtOH is given. Explain the observation.

$$\text{Me}_3\text{C}\text{—}\underset{\text{Me}}{\overset{\text{Me}}{\text{C}}}\text{—}O\text{—}\overset{O}{\underset{\|}{C}}\text{—}\phi\text{—}NO_2$$

1.0 (A)   4.2 (B)   1.35 × 10⁴ (C)

All of above compounds are tertiary alkyl substrates and they undergo hydrolysis through S_N1 mechanism.

$$\xrightarrow[\text{aq. EtOH}]{RDS}$$

fast | $H_2\overset{..}{O}$.

$$\xrightarrow{-H^+}$$
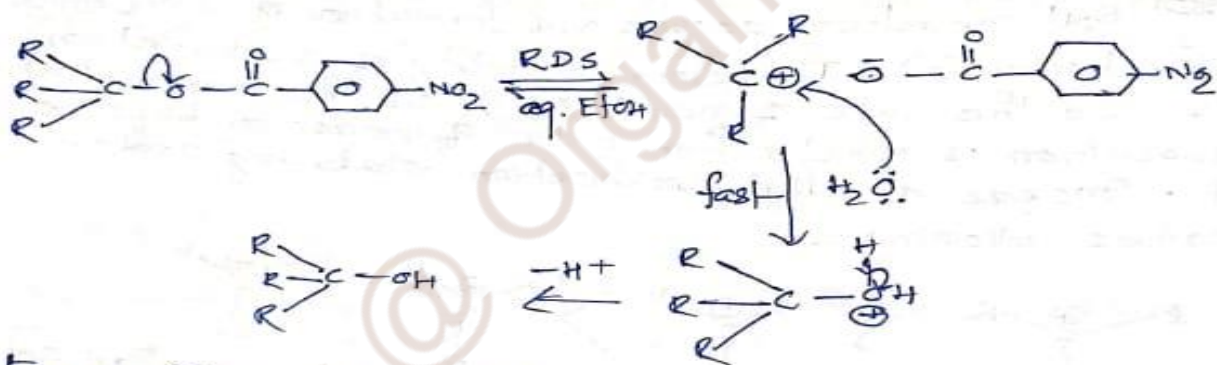
From (A) → (B) → (C) steric crowding increasing.

So rate of reaction (C) > (B) > (A)

Because with increasing steric crowding or bulkyness in the substrate, rate of reaction (S_N1) increases due to the fact of strain relief in the intermediate formation of carbocation.

(A)   (B)

For the above reason compound (A) undergoes solvolysis 600 times faster than compound B. The above reactions proceed via S_N1 mechanism.

Q. The relative rate of solvolysis of the following compounds in ethanol at 25°C are given below —

Me₃C—Br Me_3C-Br

Rate — 1.0 10^{-6} 10^{-13}

(I)   (II)   (III)
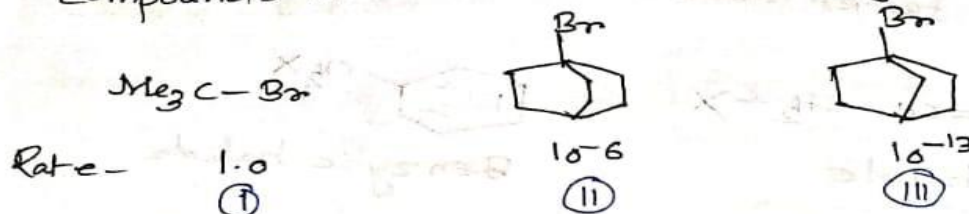
All the above compounds are tertiary alkyl substrate and they undergo solvolysis reaction via S_N1 mechanism.

Stable carbocation

(I)   (II)   unstable (III)
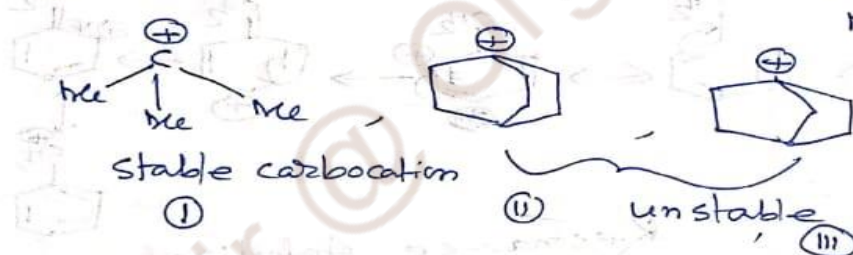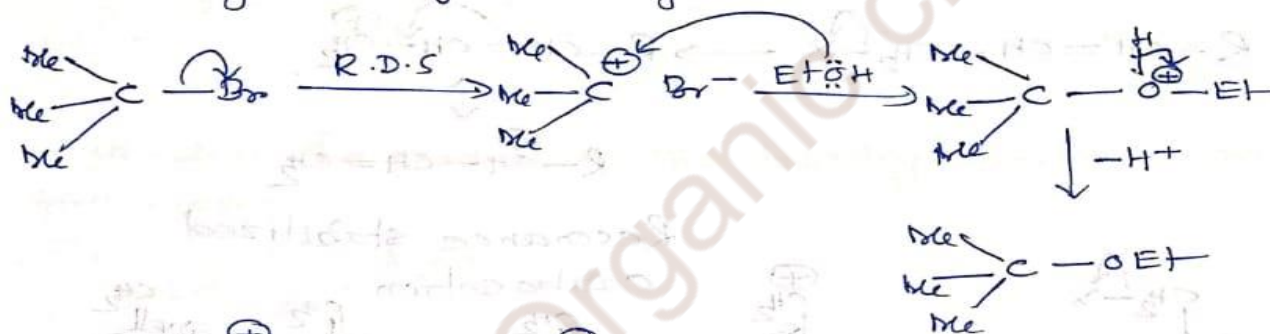
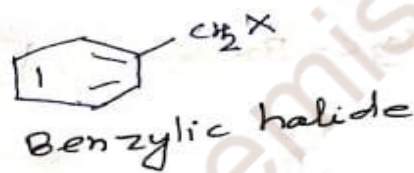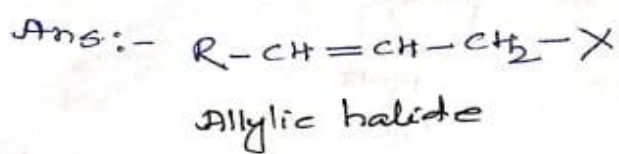Substrate (II) and (III) are rigid, bicyclic, cage-like system. They do not undergo carbocation formation due to their rigidity because ⊕ charge on the bridgehead possition is very unstable (Bredt's rule).

For bicyclic system carbocation on bridgehead possition is very unstable because here gaining of planar geometry is very difficult.
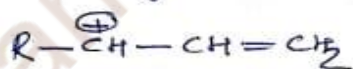
Among (II) and (III), (II) is symetric and more flexible than (III). So (II) undergoes reaction faster rate than (III).
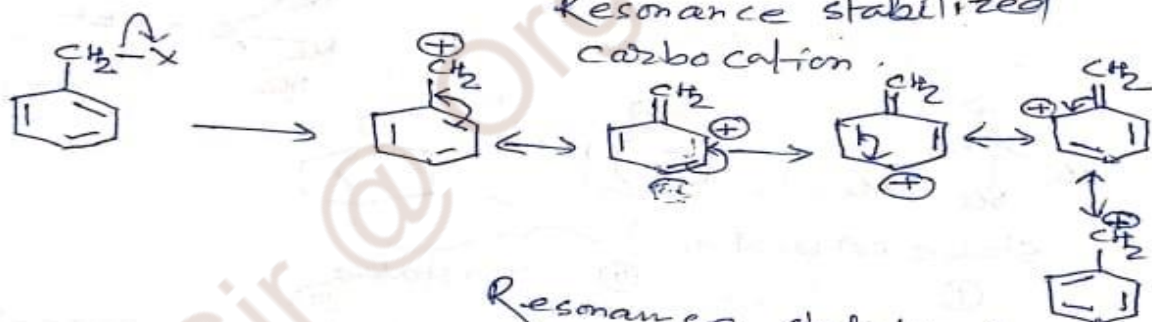
Therefore rate of reaction is (I) > (II) > (III)

Q. Allylic and benzylic halide undergo both S_N1 and S_N2 reaction faster rate. Explain.

Ans:- $R-CH=CH-CH_2-X$ $\underset{\text{Benzylic halide}}{\text{[benzene ring]}-CH_2X}$

Allylic halide

$S_N2 \rightarrow$ Explain earlier.

$R-CH=CH-CH_2-X \longrightarrow R-CH=CH-CH_2^{\oplus}$

$\updownarrow$

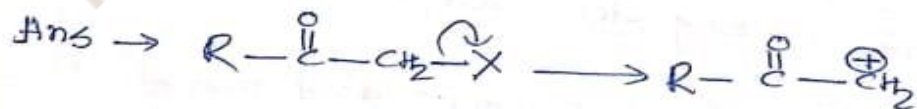$R-\overset{\oplus}{CH}-CH=CH_2$

Resonance stabilized carbocation.

Resonance stabilized carbocation.

Both allylic and benzylic halide form resonance stabilized carbocation. For this they undergo faster S_N1 reaction.

Q. α-carbonyl compounds inert toward S_N1 reaction. Explain

Ans $\rightarrow$ $R-\overset{O}{\overset{||}{C}}-CH_2-X \longrightarrow R-\overset{O}{\overset{||}{C}}-\overset{\oplus}{CH_2}$

Very unstable

Here the carbocation forms, very unstable because strong electron-withdrawing effect ($-I$ effect) of carbonyl group.

Q. CH_3OCH_2Cl undergo SN1 reaction verry faster rate - Explain

Ans:- $CH_3OCH_2-\overset{\frown}{Cl} \longrightarrow$ $\left[CH_3-\overset{..}{\overset{+}{O}}\overset{+}{\rightleftharpoons}\overset{+}{CH_2} + Cl^- \right.$

$\qquad\qquad\qquad\qquad\qquad\qquad \updownarrow$

$\qquad\qquad\qquad\qquad\qquad CH_3-\overset{\oplus}{O}=CH_2$

$\qquad\qquad\qquad\qquad\qquad$ Stable carbocation
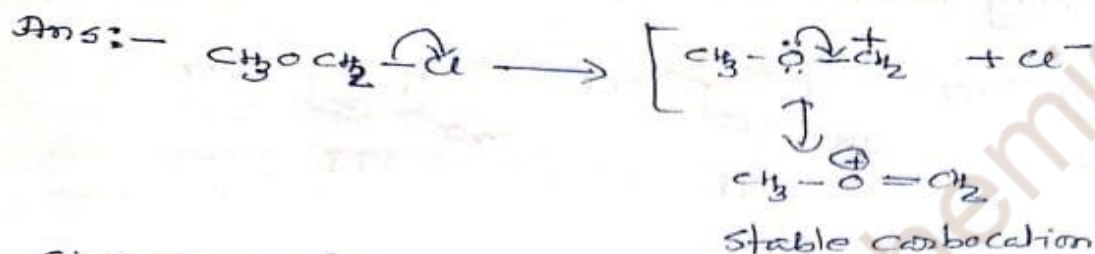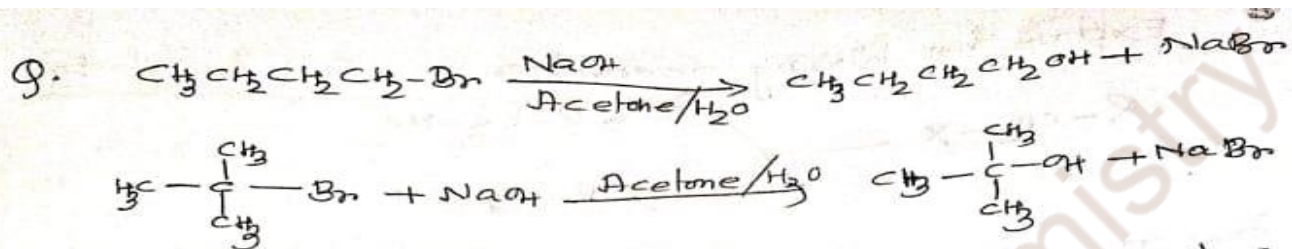
CH_3OCH_2Cl forms a resonance stabilized carbocation. For this it undergoes SN1 reaction faster rate.

Q. Predict the product of the following reaction and give reason.

Ans :-

Resonance stabilised carbocation

is
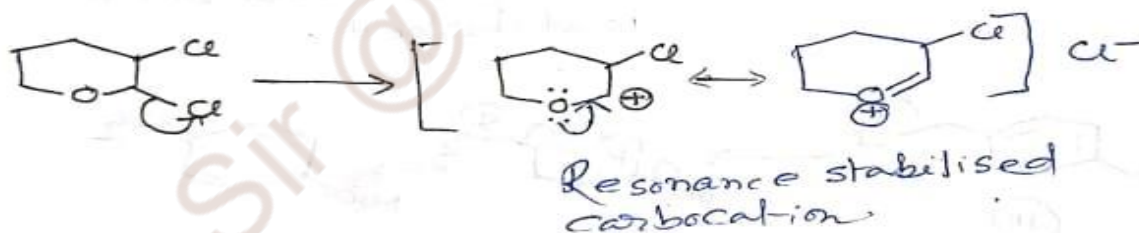
when Cl-atom adjacent to O-atom removed, then resonance stabilized carbocation is formed which shown above.

Q. $CH_3CH_2CH_2CH_2-Br \xrightarrow[Acetone/H_2O]{NaOH} CH_3CH_2CH_2CH_2OH + NaBr$

$H_3C-\underset{\underset{CH_3}{|}}{\overset{\overset{CH_3}{|}}{C}}-Br + NaOH \xrightarrow{Acetone/H_2O} CH_3-\underset{\underset{CH_3}{|}}{\overset{\overset{CH_3}{|}}{C}}-OH + NaBr$
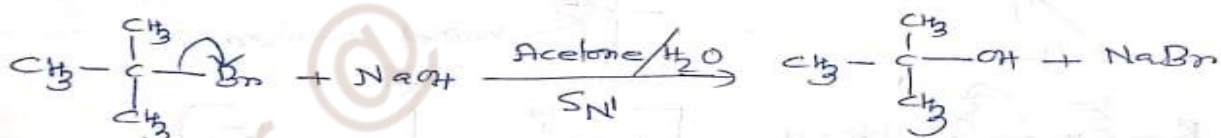
Increasing the concentration of NaOH, rate of 1st reaction increase many fold but rate of 2nd reaction remain unchanged. Explain.

Ans:-

$CH_3CH_2CH_2CH_2Br + NaOH \xrightarrow[S_N2]{Acetone/H_2O} CH_3CH_2CH_2CH_2OH + NaBr$
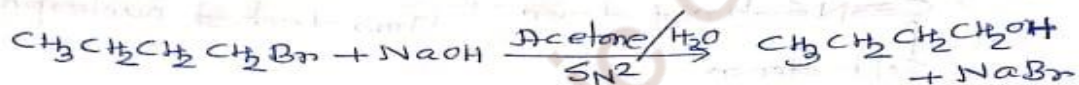
Rate, $r = k\,[CH_3CH_2CH_2CH_2Br]\,[NaOH]$

The above reaction proceed through S_N2 mechanism. Here rate of the reaction depends on concentration of NaOH. So rate of reaction increases by increasing concentration of NaOH.

$CH_3-\underset{\underset{CH_3}{|}}{\overset{\overset{CH_3}{|}}{C}}-Br + NaOH \xrightarrow[S_N1]{Acetone/H_2O} CH_3-\underset{\underset{CH_3}{|}}{\overset{\overset{CH_3}{|}}{C}}-OH + NaBr$

Rate, $r = k\left[CH_3-\underset{\underset{CH_3}{|}}{\overset{\overset{CH_3}{|}}{C}}-Br\right]$

The rate of above reaction independent on concentration NaOH. So rate of reaction remains unalter by increasing the concentration of NaOH.

For the above reason rate of 1st reaction increase many fold by increasing concentration of NaOH where as rate remain unchange incase of reaction 2nd.

Reference Books

1. Sykes, P. A guidebook to Mechanism in Organic Chemistry, Pearson Education, 2003..
2. Finar, I. L. Organic Chemistry (Volume 2) Pearson Education.
3. Maskill, H. Mechanisms of Organic Reactions, Oxford Chemistry Primer, Oxford University Press.