Elimination Reaction

Mane mam

DATE 1

Introduction :→

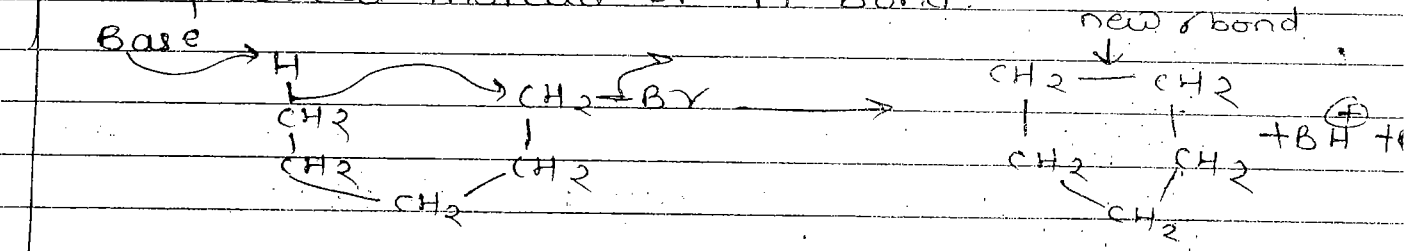
The most common type reaction is elimination reaction in which two group are lost from a substrate to produce a modified substrate and two small units.

- Elimination usually produce a new pi-bond

$$CH_3-\underset{H}{CH}-CH_2-L.G \longrightarrow CH_3-CH=CH_2 + H^{\oplus} + L^{\ominus}$$

π bond is formed

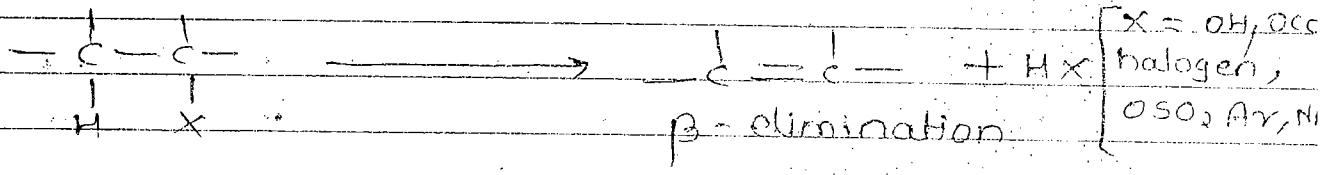
In some elimination reactions a new sigma bond is produced instead of Pi-bond.



- Elimination reactions are classified under two general headings.

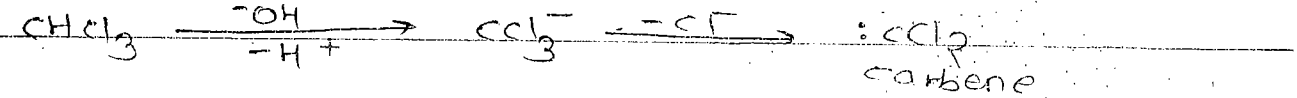
① β-elimination :→ β-elimination (1,2 elimination) are the most common elimination reaction in which groups on adjacent atom are eliminated with the formation of an unsaturated bond.

β-elimination include acid catalysed dehydration of alcohols, solvolytic and base induced elimination reaction from sulphonates, alkyl halides and Hofmann elimination from quaternary ammonium salts.



② α-elimination :→ α-elimination involves two groups departing from the same atom.

1,1 or α-eliminations are used for generating the reactive intermediates called carbenes.



β-elimination reactions occur a three mechanistic pathways. these are E_1, E2 and E_1cb mechanism.

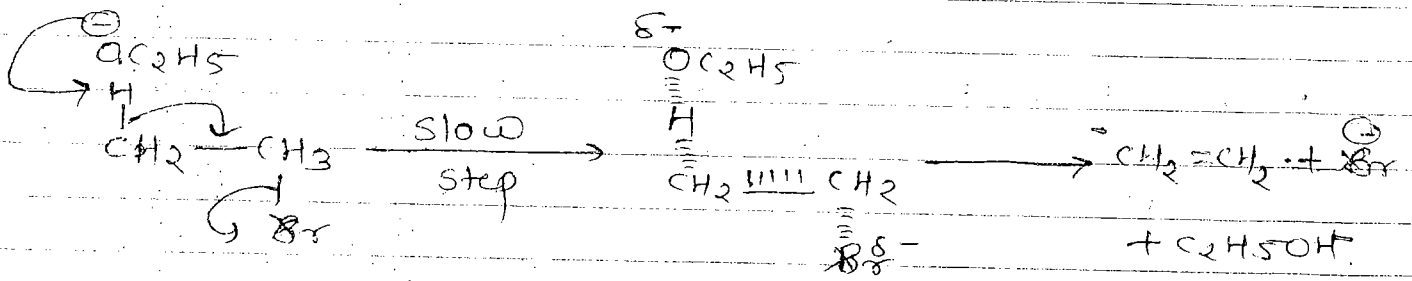
(1) E2 mechanism :→

The reaction of ethyl bromide with ethoxide ion is an example of E2 reaction. It is a second order reaction because the rate of reaction depends on the concentration of both alkyl halide and base. It is called E_2 reaction. E for elimination and 2 for biomolecular.

$$CH_3-CH_2-Br + C_2H_5-O^{\ominus} \longrightarrow CH_2=CH_2 + C_2H_5OH + Br^{\ominus}$$

$$\text{Rate} = K[\text{alkyl halide}][\text{base}]$$

The rate law tells us that ethyl bromide and ethoxide ion are both involved in the transition state of the rate determining step of the reaction. The following mechanism agree with the observed second order kinetics.

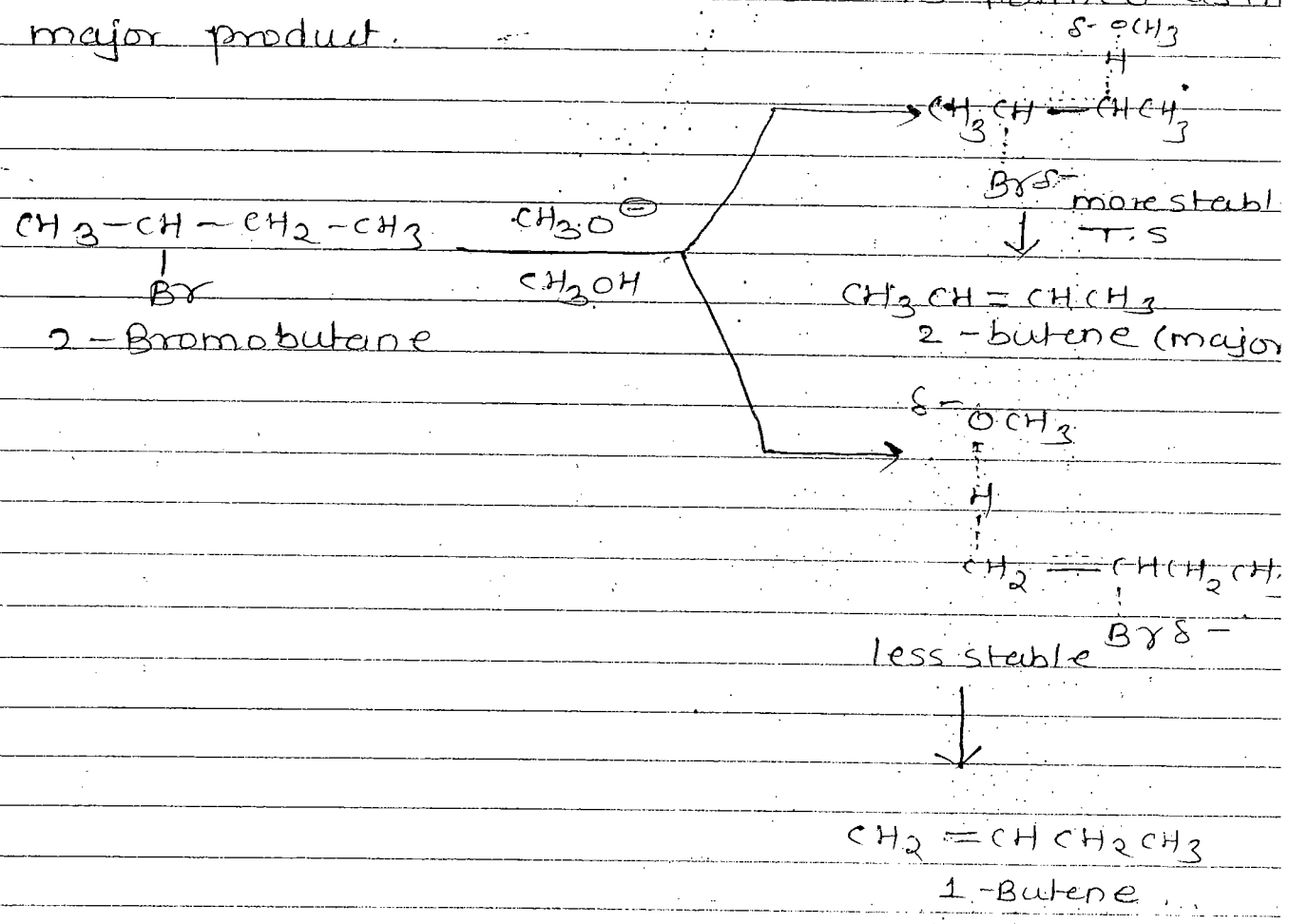


E_2 reaction is a concerted, one step reaction. proton and the bromide ion are removed in the same step. i.e the rate determining step.

Direction of elimination :→

A study of the spectrum of E2 transition states helps to explain the orientation of the double bond

With several substrates the elimination can take plac in more than one way. generally the more substituted alkene is formed as the major produ -ct. This is called as the saytzeff rule. When 2-bromobutane react with base, one expects two elimination products, since in the transition state both the C-H as well as C-Br bonds are breaking. The transition state has alkene like structure. and two factors which stabilize an alkene (the larger number of alkyl substituents bonded to the sp^2 carbons) also stabilize the transition state. thus 2-butene is formed as th major product.



The relative reactivities of alkyl halides in an E2 elimination follows the order

tertiary alkyl halide > 2° alkyl halide > 1° alkyl halides

This is due to the predominant formation of a more substituted alkene

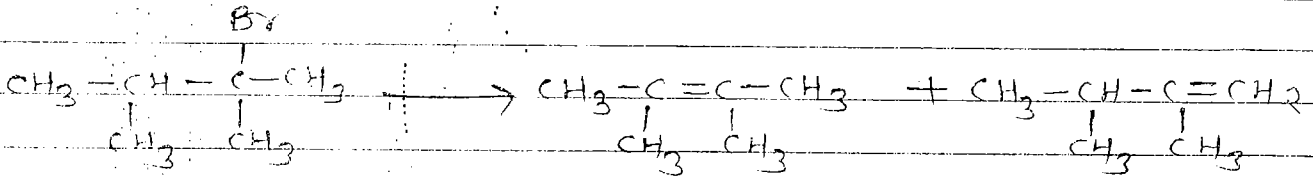
In most of the dehydrohalogenation reactions the major products are the saytzeff product But the In some cases the major alkene product is least substituted alkene.

- Elimination in which least substituted alkene is the major product is known as Hofmann elimination & the rule is known as Hofmann rule.
- Hoffmann elimination reaction takes place in the following four cases.

i) When the base is bulky
ii) When the leaving group is poor L.G such as F, $\overset{\oplus}{N}R_3$, $\overset{\oplus}{S}R_2$.
iii) steric hindrance at β-carbon
iv) When the alkyl halide contains one or more double bonds

① size of attacking base :→

When a highly branched base such as $(CH_3)_3CO^{\ominus}$ is used alkyl halides give Hofmann elimination rather than saytzeff elimination.



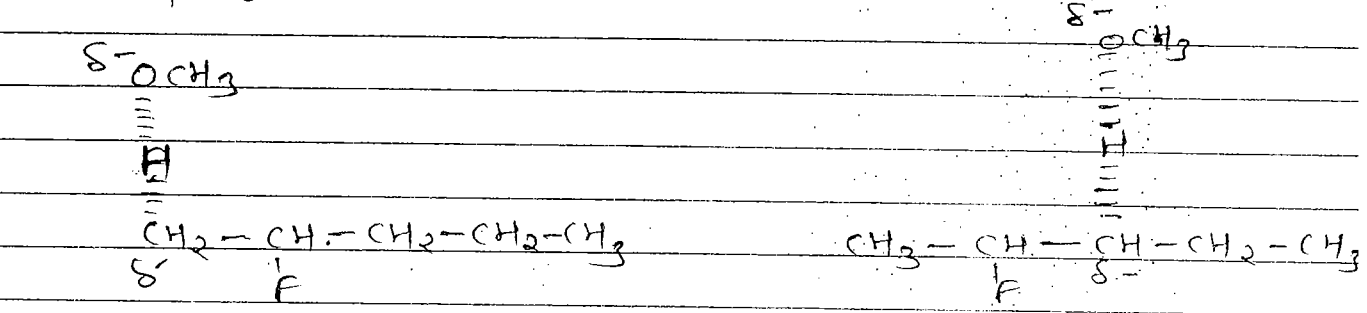
$C_2H_5O^{\ominus}$	79	21
$t\text{-}BuO^{\ominus}$	17	73
$(CH_3)_3CO^{\ominus}$	8	92

② Poor leaving group :→

Why alkyl fluoride gives Hofmann elimination?

In the case of chloride, bromide and iodide the the halogen starts to leave as soon as the base begins to remove the proton. departure of the halogen and its bonding electrons prevents the build up of negative charge on the carbon that

is losing a proton, giving the transition state alkene character rather than carbanion character. The fluoride ion is the strongest base and hence, very poor leaving group. the fluoride ion has less tendency to leave. as a result negative charge develops on the carbon that is losing the proto giving the transition state. a carbanion character rather than an alkene. this carbanion transitio state is stabilised by the strong e⁻ withdrawing group fluorine.

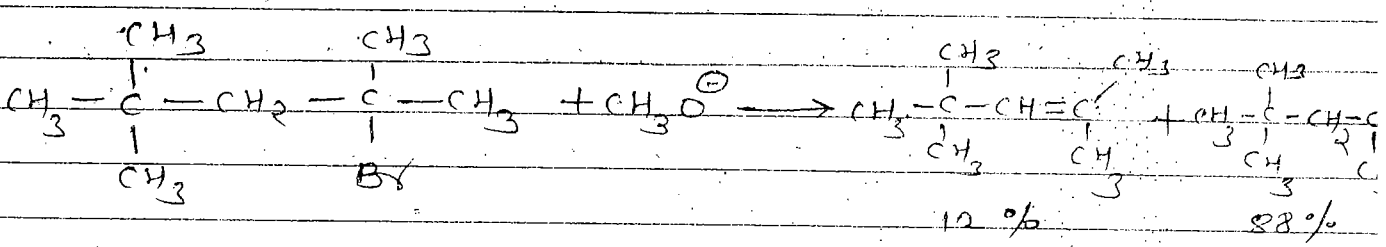


Transition state leading to 1-butene (more stable) — 1° carbanion character

T.S leading to 2-butene (less stable) — 2° carbanion cha

iii) Steric hindrance at β-carbon :→

The hindered β-hydrogen yields the less substi-tuted alkene in E2 reaction even with a small base like the methoxide ion.



12 %

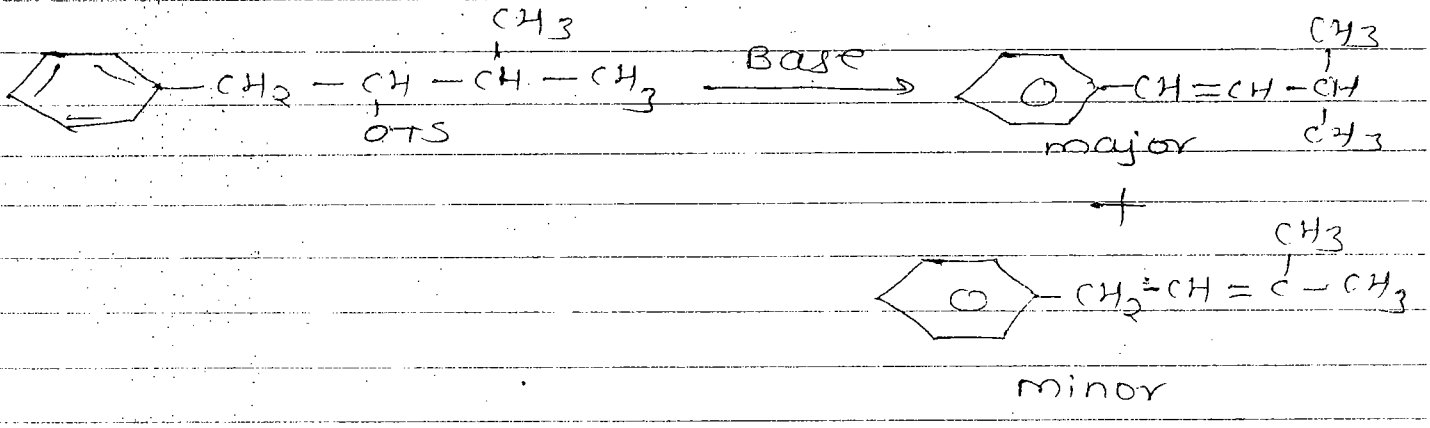
88 %

In such cases also base preferentially attacks on less hindered β-hydrogen giving more stable T.S

iv) When the alkyl halide contains one or more double bonds :→

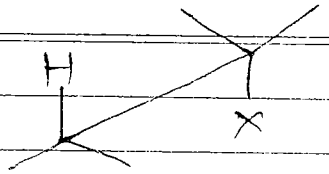
A conjugated alkene is more stable. even thoug it may not be the most substituted alkene.

A conjugated product is more stable than a nonconjugate product due to resonance. The transition state in such cases has a partial development of conjugation which provides it enough stabilization. thus the elimination gives the conjugated product as the major alkene though it is not highly substituted.

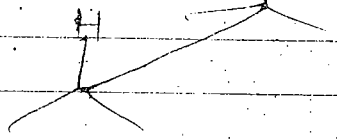


Stereochemistry of E2 elimination :→

- E2 mechanism is stereospecific.
- The five atoms involved in the transition state must be in one plane, there are two ways for this to happen.
- The H & X may be trans to each other with a dihedral angle of 180° or they may be cis with a dihedral angle of 0°. conformation (A) is called antiperiplanar, and this type of elimination in which H & X depart in opposite direction is called 'anti elimination'.
- conformation (B) is syn periplanar and this type of elimination with H & X leaving in the same direction is called syn elimination.
- In the absence of special effects, anti elimination is usually greatly favored over syn elimination, because antiecoplannar is a staggered conformation and the molecule requires less energy to reach this transition state than it does to reach the eclipsed transition state (B)



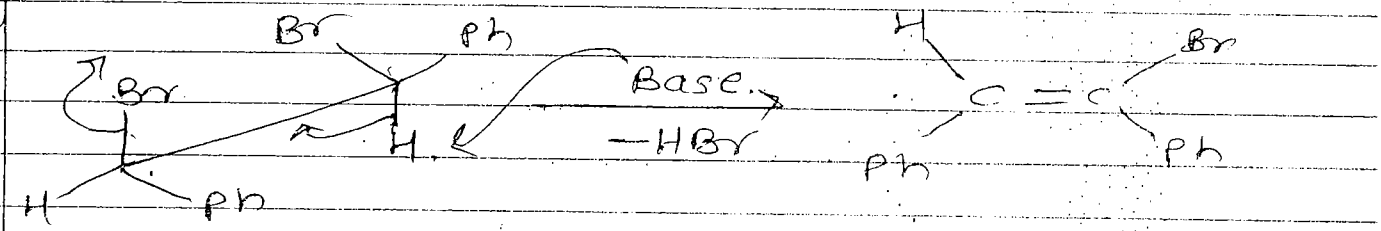
(A)

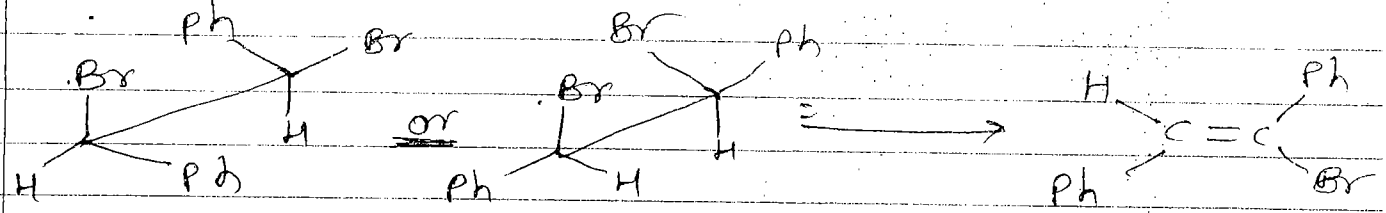


(B)

A few of the many known examples of predominant anti elimination follow.

(1) Elimination of HBr from meso-1,2-dibromo-1,2-diphenylethane gave cis-1-bromo-1,2-diphenylethane, while the (+) or (−) isomer give the trans olefin.

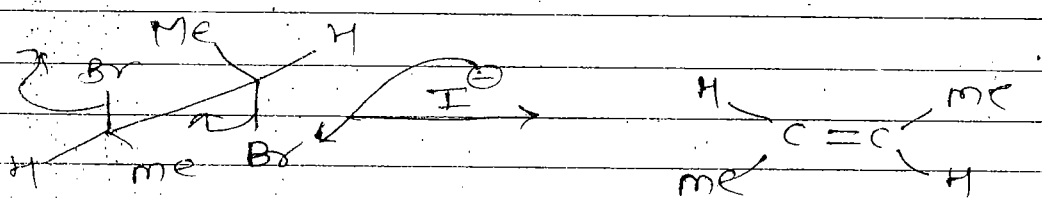




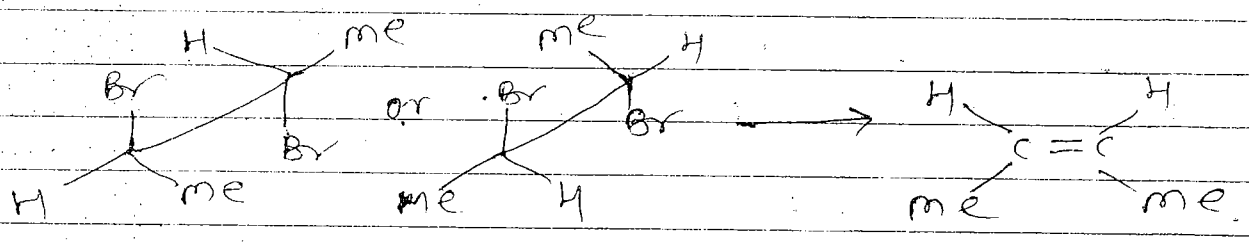
The molecule has two stereocentre and therefour four stereoisomers can exist the compound has only three stereoisomers, a (±) pair and a meso form. elimination of H and Br with base from the meso isomer give cis. while (+) or (−) pair give trans product because elimination can occur only via a conformation of the starting compound in which H & Br atom are in an antiperiplanar arrangement.

(2) dehalogenation of 2,3-dibromobutane with iodide ion. the molecule has two stereocentre and therefore four stereoisomers can exist. the compound has however only three stereo isomers. a (±) pair and meso form.

- elimination of two bromines with iodide ion from the meso isomer give trans 2-butene. while (±) pair give cis-2-butene. because elimination can occur only via a conformation of the starting comp. in which the two bromine atoms are in an antiperiplanar rearrangment. this is the most stable conformation. the reaction on (±) isomer involves less stable transition state compared to the meso isomer.



meso (erythro form) trans.



cis.

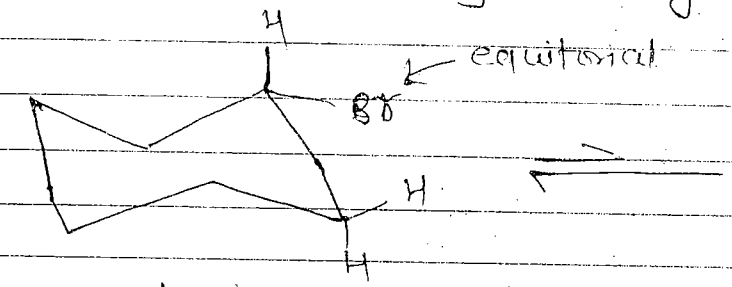
Reactions in cyclohexane system :→

generally all cyclohexanes are most stable in their chair conformation

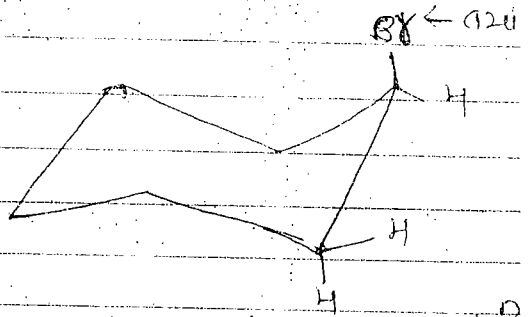
- In a chair cyclohexane any two adjacent axial bonds (trans-diaxial) are in an anti-peripl-anar conformations.
- A chair cyclohexane molecule can flip to bring about an anti-coplanar relation between the departing group for the succes of E2 reaction

When HBr eliminates from bromocyclohexane to give cyclohexene, the initial more stable conformation in which the bromine atom is equitorial undergoes chair-chair interconversion. This process inverts the axial position and equitorial relationships. this flip can now bring the leaving group in the desired axial position to have an anti-coplanar relationship with an axial hydrogen on the adjacent carbon.

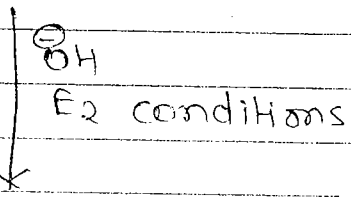
The more stable conformer of bromocyclohexane does not undergo E2 reaction. the less stable conformation radily undergoes an E2 reaction



more stable conformation

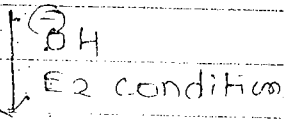


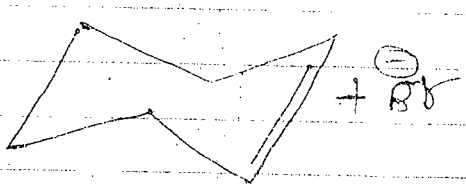
less stable. conf



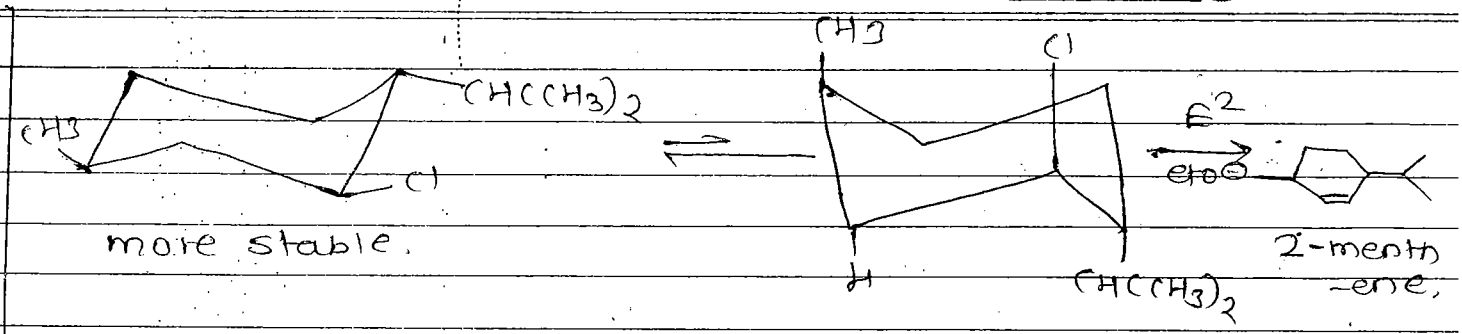
No reactions.

Favourable for E2

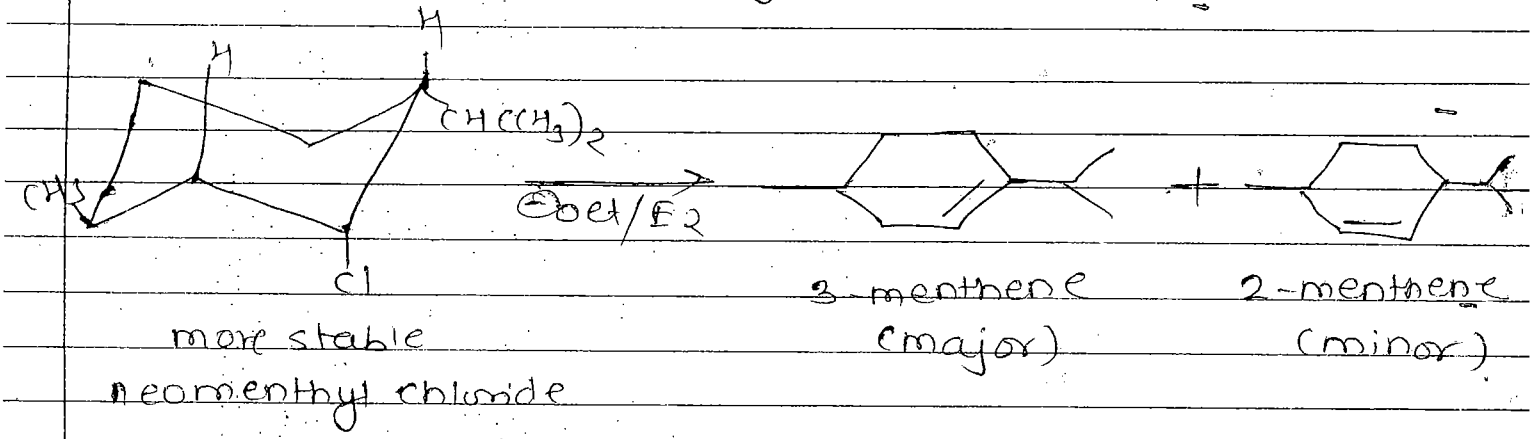




Another example to show that the E2 elimination in a six membered ring proceeds when the adjacent trans group can adopt an anti-periplanar conformation. menthylchloride can have two conformations I + II In (I) the chlorine is equitorial and as such anti-periplanarity with an adjacent hydrogen cannot be achieved. For the E2 elimination methyl chloride undergoes a ring flip unfavourable conformation. reaction occurs through an unfavourable conformation



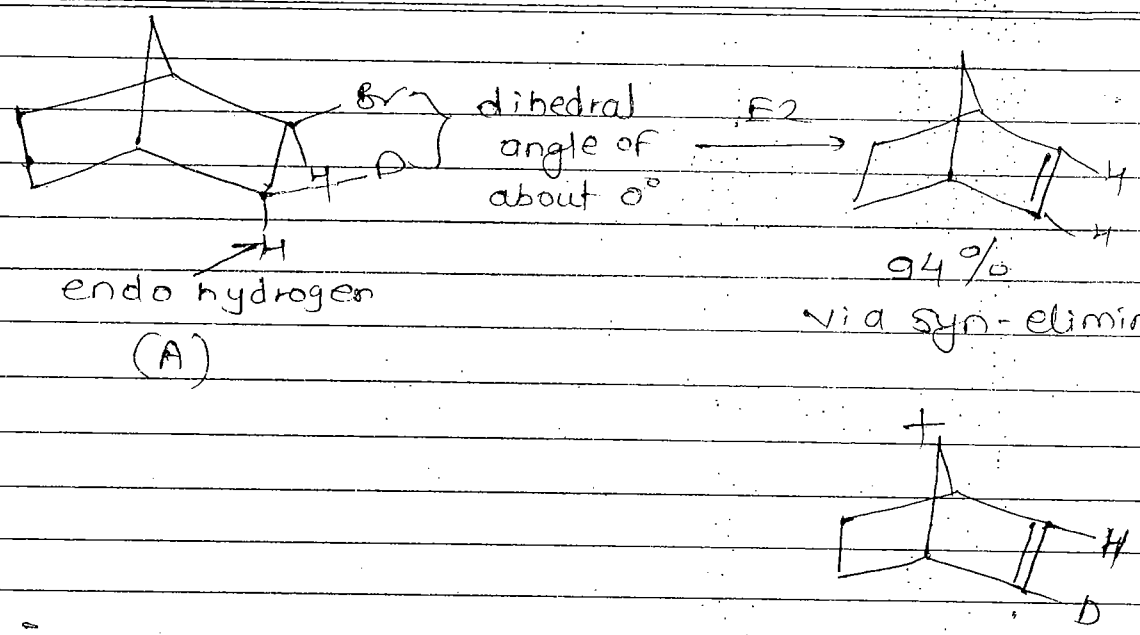
In neomenthyl chloride the chlorine is axial on neighbouring carbon on both sides. thus a facile elimination occurs to give two olefins. The olefin being the saytzeff product predominates



Eliminations in bridged compound – Syn Elimination

In most of these systems syn-eliminations are common.. In these compounds anti elimination is disfavoured both by conformational & steric reasons. deuterated norbornyl bromide on E2 elimination give almost exclusive product containing no deuterium.

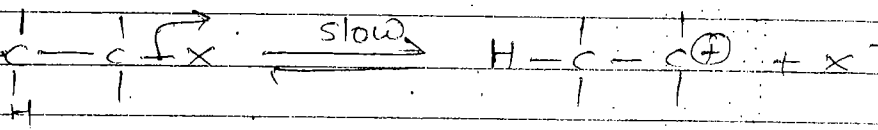
firstly the rigid ring system prohibits attainment of an anti-elimination process i.e the leaving group endo Br group cannot achieve a dihedral angle of 180° with endo hydrogen (the angle being only 120°). Thus the leaving groups (O & Br) prefer syn elimination with dihedral angle of about 0° to anti-elimination



E^1 (unimolecular elimination) reaction :→

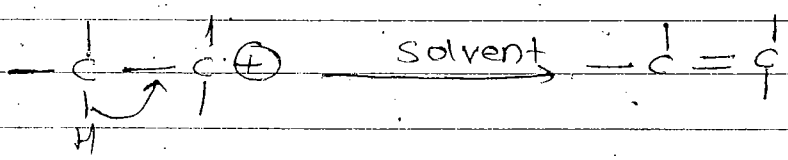
The reaction of tertiary butyl bromide with sodium hydroxide. It is first order elimination reaction because the rate of the reaction depends only on the concentration of the alkyl halide it is called E^1 reaction.

- E^1 reaction is a two step reaction
- This mechanism normally operates without an added base. E1 mechanism related to SN1. Infact; the first step of E1 is exactly the same as that of SN1 mechanism.

Step :I :→ 

The second step differs in that the solvent pulls a proton from the β-carbon of the carbocation to form alkene.

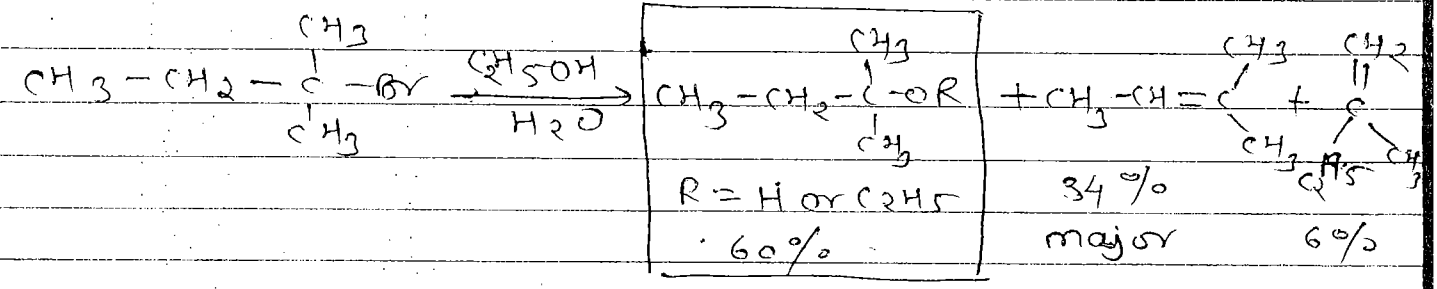
Step - 2 :→



Direction of Elimination :→

E1 elimination reaction is stereoselective.

- The E1 eliminations from the intermediate carbocation give rise to the more substituted alkene as the major product (saytzeff rule).
- 2-Bromo-2-methylbutane on reaction with water in ethanol give substitution as the major product when both water and ethanol can act as nucleophiles to give an alcohol or an ether. the major alkene formed is more highly substituted.

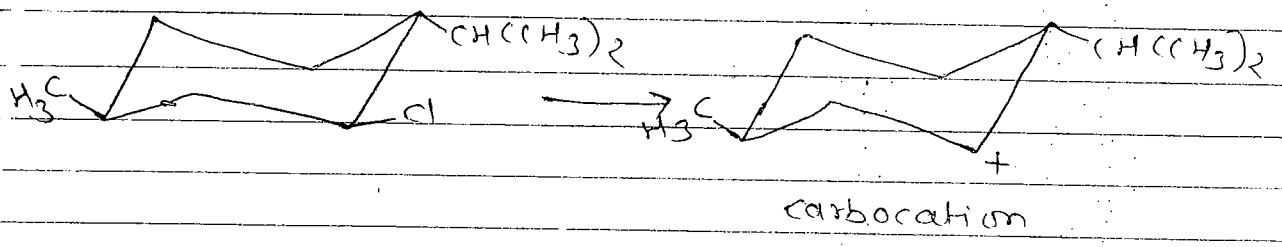


E1 elimination from cyclic compounds :→

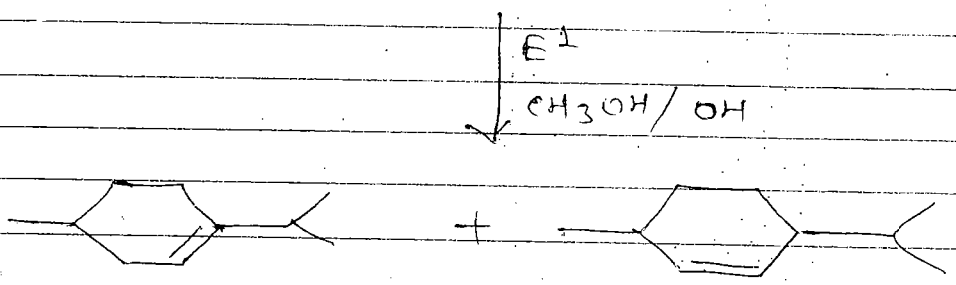
Since a carbocation is formed in the first step of E1 reaction. the relative stereochemistry of the leaving group is not important.

When menthyl chloride undergoes E2 reaction only one alkene is formed in 100% yield due to the need for the departed groups to attain diaxial positions. when menthyl chloride is subjected to E1 reaction condition two alkenes are formed. the major product is in accord with Saytzeff rule.

- If carbocation are intermediates, we should expect rearrangements. With suitable substrate



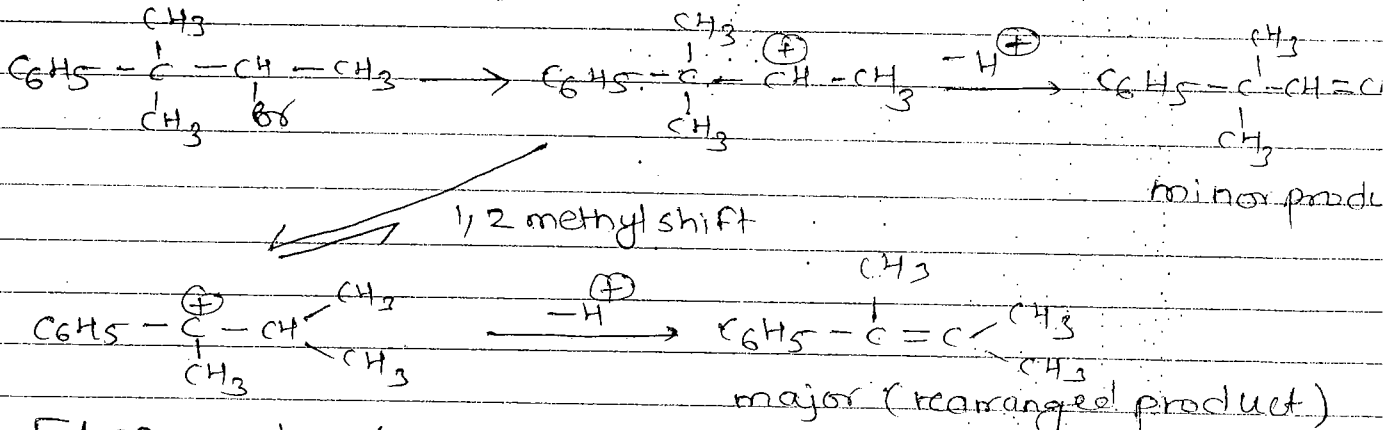
carbocation



3-menthene (major)

2-menthene minor

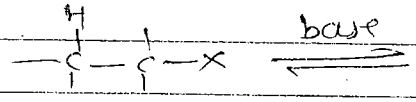
for example 3-bromo-2-methyl-2-phenyl butane gives mixture of two alkenes. one alkene is normal and other is rearranged product.



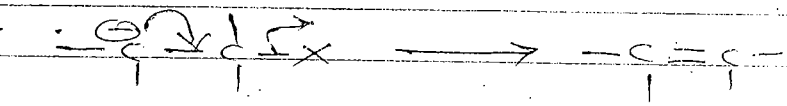
major (rearranged product)

E1CB mechanism :→

In E1 mechanism. X leaves first and then H, In E2 mechanism the two groups leave at the same time there is third possibility. the H leaves first and then X. this is two step process is called E1CB mechanism or carbanion mechanism. since the intermediate is a carbanion

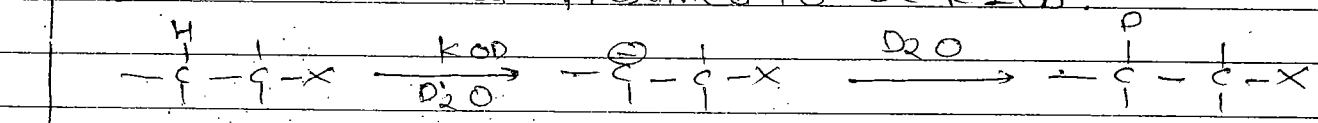
step-I :→ 

conjugate base of substrate

step-II :→ 

this elimination proceed through the conjugate base of the starting material. E1cb reaction competes with the E2 reaction. However E1cb reactions are much less common than are E2 reaction.

Any reaction which involves a carbanion as intermediate, on other hand, should produce recovered starting material labelled with deuterium. It is precisely such deuterium incorporation which occurs in those reaction presumed to be E1cb.



thus, i) E1cb mechanism is limited to substrates which can stabilise the carbanion intermediate, i.e β carbon should contain carbonyl, nitro, cyano or other $\overset{\ominus}{C}$ stabilising group ii) Product formation generally takes place by Hofmann iii) leaving group of substrate is generally poor leaving group iv) Reaction takes place in the presence of a strong base.

Reactivity :→

In this section we examine the effects of changes in the substrate, base, leaving group and medium on E1, E2, E1CB

① effect of substrate :→

It has been found that branching at α & β carbons increases the rate of the E2 reaction. because as the number of substituents increases on the carbon atom of the developing double bond, the stability of the transition state increases. reactivity of alkyl halide in E2 reaction is $3^\circ > 2^\circ > 1^\circ$ alkyl halide

E1 reaction can takes place by the formation of carbocation as reaction intermediate. thus rate of the E1 reaction depends on the stability of carbocation since +I effect, hyperconjugation effect and conjugative effect stabilise carbocation

Any structure which forms stable carbocation will be reactive. steric strain around leaving group also favours the formation of carbocation. thus the order of reactivity in decreasing order as follows

$3^\circ > 2^\circ > 1^\circ$ alkyl halide

thus, alkyl and aryl substitution on α & β carbon with respect to leaving group increase the rate of E1 reaction as strain increases. the yield of the E1 product increases. all electron withdrawing group in β position shift the mechanism towards E1cB.

(2) Effect of attacking base :→

In E1 reaction, external base is not required. The solvent act as base. the strength and concentration of the base have nothing to do with the rate of E1 reaction. when external bases are added the mechanism is shifted towards E2. with increasing basicity of the added base, the rate of the E2 reactive have been found to increase. the order of basicity among $^{\ominus}OH$, $C_2H_5O^{\ominus}$, $^{\ominus}NH_2$ is

$$^{\ominus}NH_2 > C_2H_5O^{\ominus} > ^{\ominus}OH$$

stronger bases and higher base concentrations cause the mechanism to move toward the E1cB. strong bases not only benefit E2 as against E1.

(3) Effect of leaving group :→

Better leaving groups shift the mechanism toward the E1 reaction. reactivity of the substrate depends mainly on the nature of the leaving group. the best leaving groups are those which are least basic and more polarisable. thus the decreasing order of the leaving group reactivity is $I^{\ominus} > Br^{\ominus} > Cl^{\ominus} > F^{\ominus}$

In general the better leaving group, the higher is the rate of E2 reaction. Poor leaving group and positively charged leaving groups shift the mechanism toward the E1cB end of spectrum

Effect of the medium :→

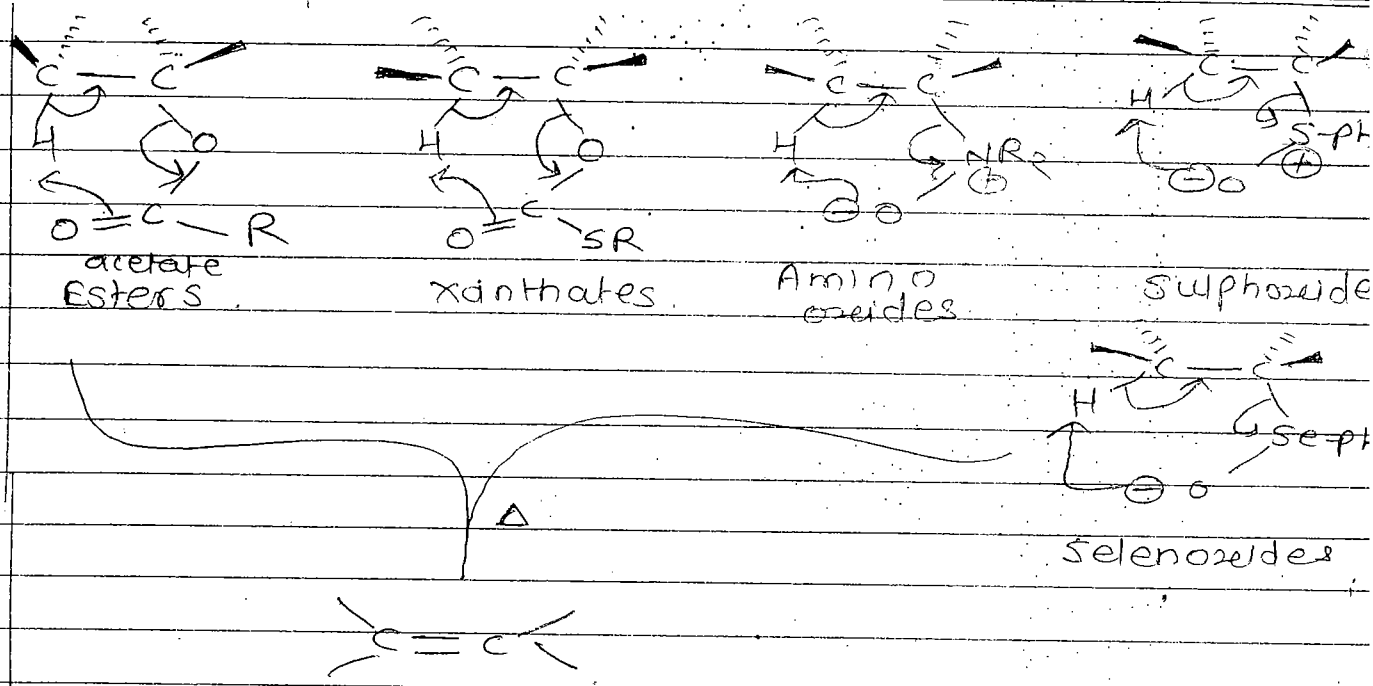
With any reaction a more polar environment enhances the rate of mechanisms that involve ionic intermediates. the rate of the E1 & E1cB mechanism increases with increasing polarity of solvent E2 reactions increases with decrease in solvent polarity because this favours the formn of the transition state of the reaction.

elimination is favoured over substitution by increasing temperature. , whether the mechanism is first or second order . the reason is that the activation energies of elimination are higher than those of substitution.

Pyrolytic syn elimination reaction. (Ei-elimination internal)

These thermal eliminations occur within a small family of compounds, like acetate esters, xanthate esters, tertiary amine oxides, sulphoxides and Selenoxides which contain atleast one β-hydrogen atom with the formation of olefins (and are the reverse of ene reaction)

- These eliminations have a common mechanistic feature: a concerted reaction via a cyclic transition state involving only one molecule of the substrate. the stereospecific syn elimination and the first order kinetics of the reaction make the chemists to classify the reaction as intramolecular or internal elimination reaction involving five or six membered cyclic Transition state, thus they are designated as Ei reaction.
- These elimination do not involve acidic or basic catalyst there is wide variation in temperatures at which these eliminations proceed.



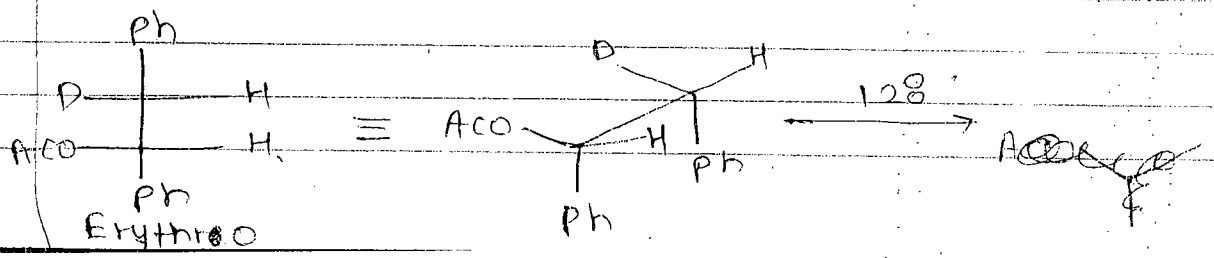
Pyrolytic syn-elimination reactions

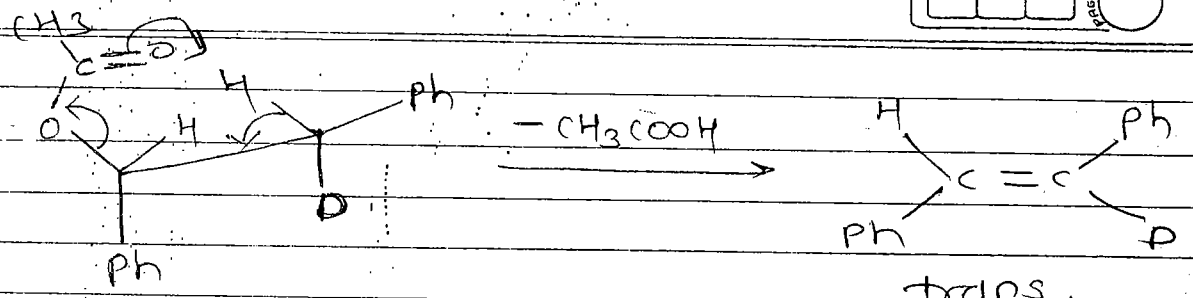
(A). Stereochemistry of thermal elimination (from acetat esters)

As already said these eliminations occurs with syn stereochemistry

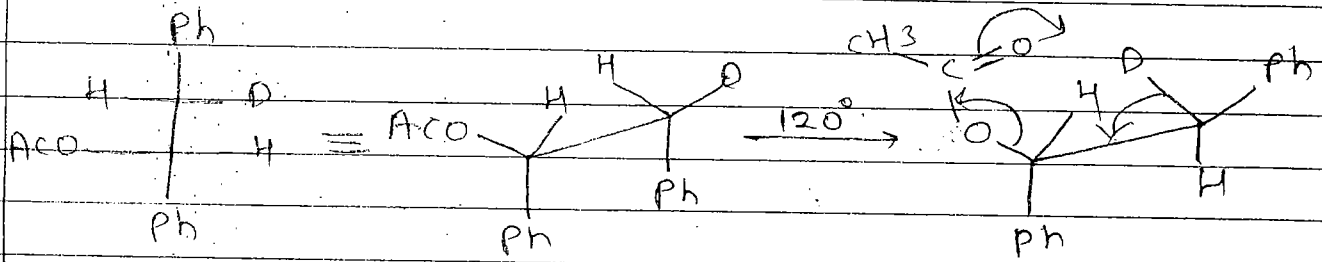
- on pyrolysis - erythro and threo isomers of 1-acetoxy - 2 deutero - 1,2-diphenylethane give in each case trans - stilbene. the syn elimination is proved by retention of deuterium in the product from erythro isomer and its loss from the threo isomer.

for this syn process either the hydrogen or the deuterium could be syn to the acetoxy group. However in the preferred conformations have the phenyl groups as far apart as possible. the molecu has two stereocenters and therefore, four stereo -isomers are possible. i.e a pair of enatiomers in each erythro and threo isomers. in eclipsed conformations Ph/Ph $\theta = 0°$. the elimination thus takes place from conformation with Ph/Ph far removed.



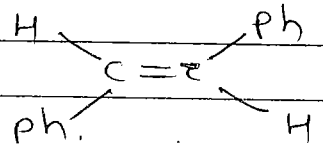


trans.



Threo isomer

$-CH_3COOD$

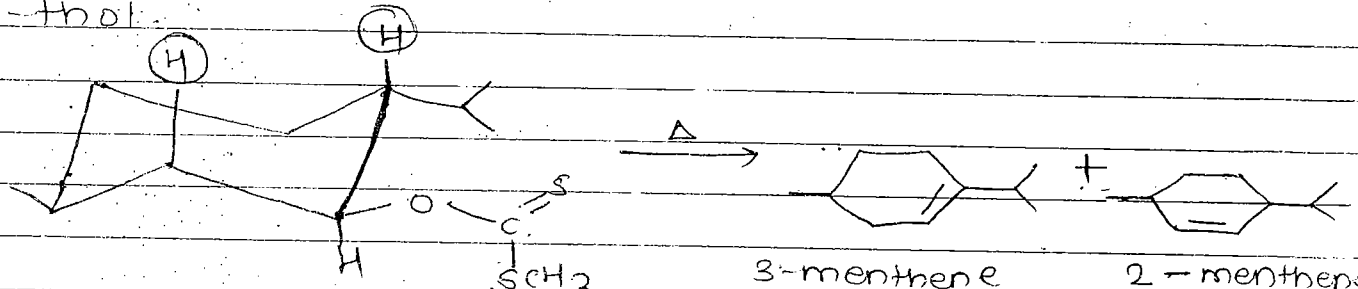


Trans.

B) Thermal Elimination reaction in cyclohexanes (From xanthate esters) -

Pyrolytic eliminations, for example involving carboxylic esters and xanthates are important group of alkene-forming reactions. these syn-eliminations proceeds by a concerted pathway.

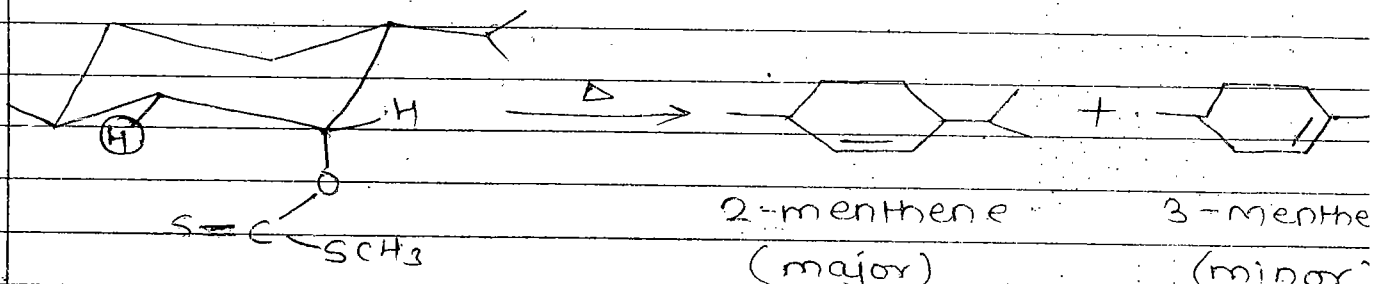
- In cyclohexane systems if a leaving group is axial then for cis relationship a β-placed equitorial hydrogen on the ring should be available for syn elimination. This is explained by considering the methyl xanthate esters from menthol & neomenthol.



menthol

3-menthene (major)

2-menthene minor



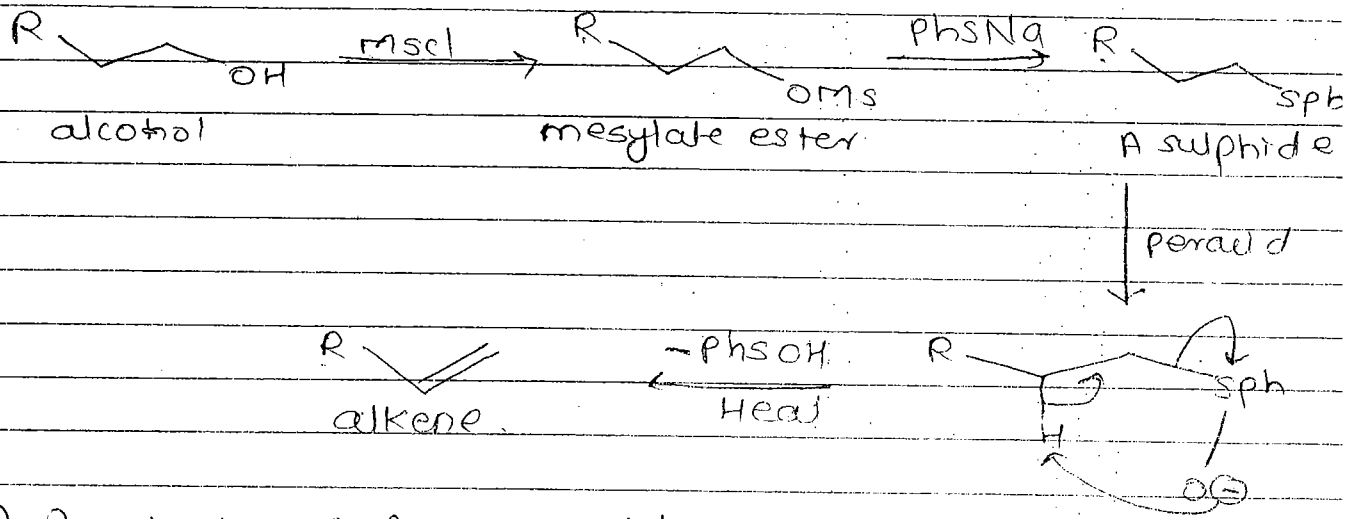
neomenthol

2-menthene (major)

3-menthe (minor)

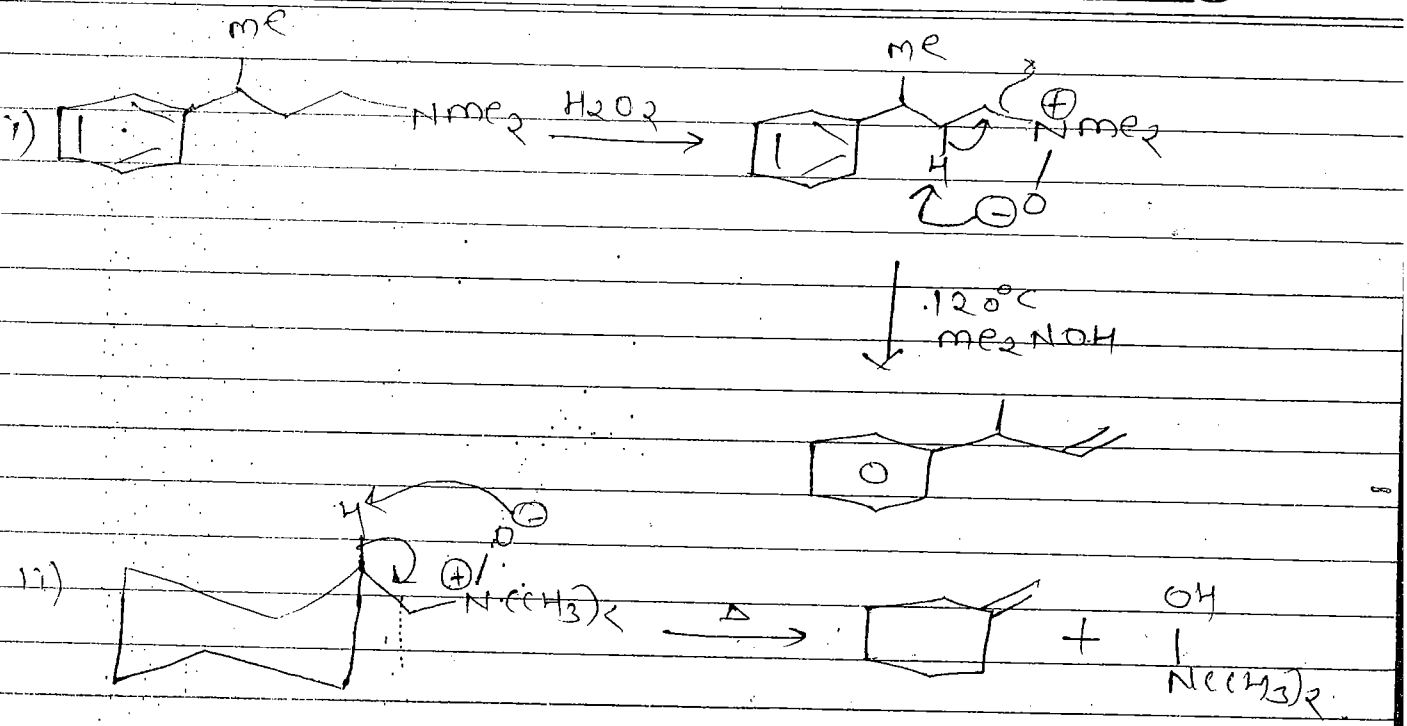
c) Pyrolysis of sulphoxides :→

- sulphoxides are easily made by oxidation of sulfid- with peracids or potassium periodate.
- the sulfides can be made by nucleophilic displacem -nt of tosylate or mesylate esters with sodium -alkyl or phenyl sulfides. the reaction of enolates with dimethyl disulphides (messme) or diphenyl disulphides (phssph) leads to corresponding sulphides. since sulphoxides are easily made by oxidation of sulphides



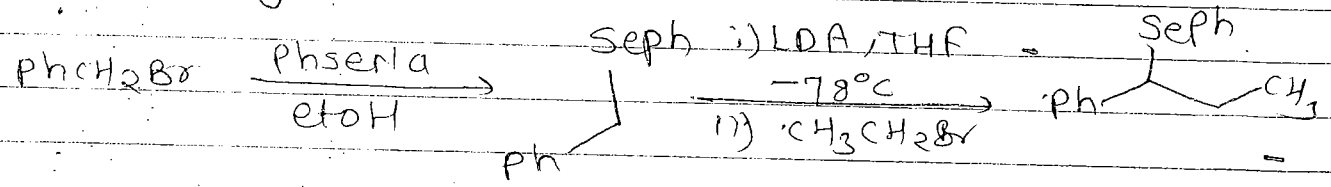
d) Pyrolysis of Amino oxides :→

The cope reaction involves the pyrolysis of amine oxides having a hydrogen atom β to the amine group. The syn elimination affords alkene & dialkylhydroxylamine.



E) Elimination from selenoxides.

selenoxide are more reactive and give better results than sulphoxides toward β-elimination & undergo thermal syn elimination to form alkenes under room temp.). The selenoxides can be easily made from the selenides by oxidⁿ with peroxide. A selenide is formed from alkyl halides or tosylates by reaction with phenyl selenide anion.



The formⁿ of α,β-unsaturated carbonyl compounds from carbonyl compounds - Lithium enolates from ketones react with benzene selenide bromide to give selenides. The treatment of selenide with H_2O_2 give α,β-unsaturated ketone.