

Reaction Mechanism

Reaction mechanism => Each reaction has a stepwise reaction mechanism that explains how it happens i.e. how the product is gonna form step by step.

Organic reactions may be classified into the following categories:

- (i) Substitution reactions
- (ii) Addition reactions
- (iii) Elimination reactions
- (iv) Rearrangement reactions

(i) Substitution reactions:

A functional group in a particular chemical compound is replaced by another group.

Organic substitution reactions are classified in several main organic reaction types depending on whether the reagent that brings about the substitution is considered an electrophile or a nucleophile, whether a reactive intermediate involved in the reaction is a carbocation, a carbanion or a free radical, or whether the substrate is aliphatic or aromatic.

Example: photochemical chlorination of methane forming methyl chloride.

Different types of substitution reactions:

(a) Nucleophilic substitution reaction

(b) Electrophilic substitution

(c) Radical substitution

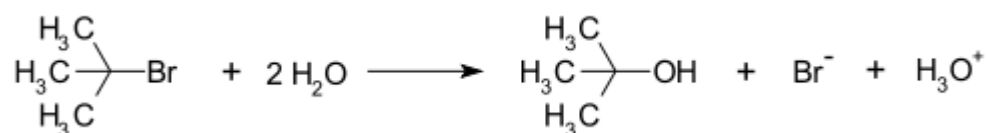
(a) Nucleophilic substitution reaction: Substitution reactions when the reagent is a nucleophile.

Depending on the nature of substrate (aliphatic or aromatic) we classify it into different category such as nucleophilic aliphatic substitution reaction, nucleophilic aromatic substitution reaction, nucleophilic acyl (derivative of carboxylic acid group) substitution etc.

The Nucleophilic substitutions can be produced by various mechanisms:

- (i) Monomolecular nucleophilic substitution (S_N^1)
- (ii) Bimolecular nucleophilic substitution (S_N^2)
- (iii) Internal nucleophilic substitution (S_N^i)

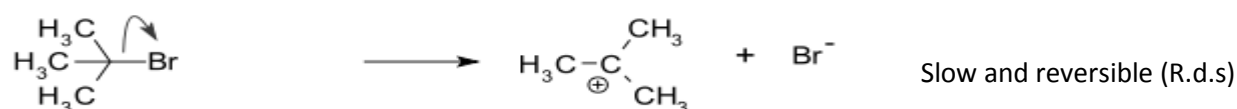
(I) Monomolecular nucleophilic substitution (S_N^1): Rate determining step (r.d.s) is unimolecular and the reaction involves formation of carbocation. Example. Hydrolysis of tert-butyl bromide with water forming tert-butyl alcohol.



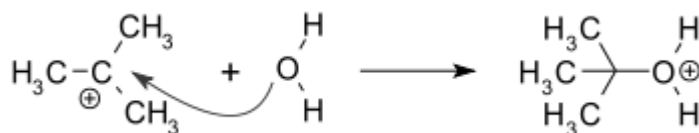
Kinetics of the reaction: Rate \propto [reactant] here reactant = t-butyl bromide

Mechanism of the reaction:

Step 1. Formation of carbocation :



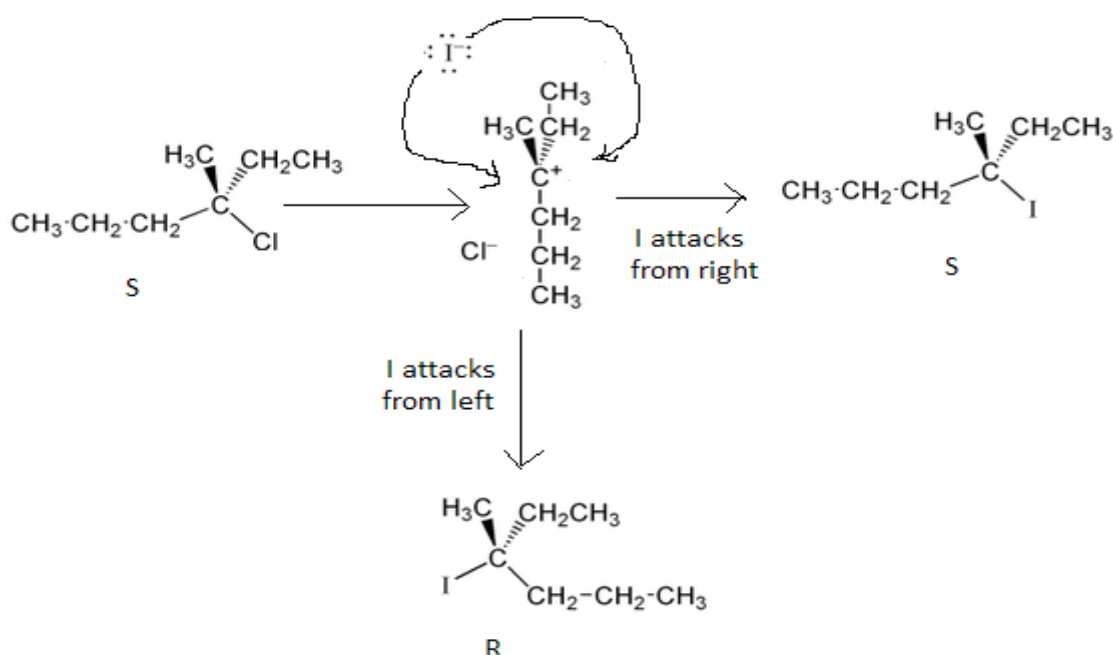
Step 2. Attack of nucleophile



Step 3. Removal of a proton on the protonated nucleophile



Stereochemistry of S_N1 reaction: Since there is formation of carbocation, which is planer in nature (Sp^2 hybridized) therefore nucleophilic attack can occur from either side of the plane, so the product formed may be racemic mixture. Example: Reaction of *S*-3-chloro-3-methylhexane with iodide ion.



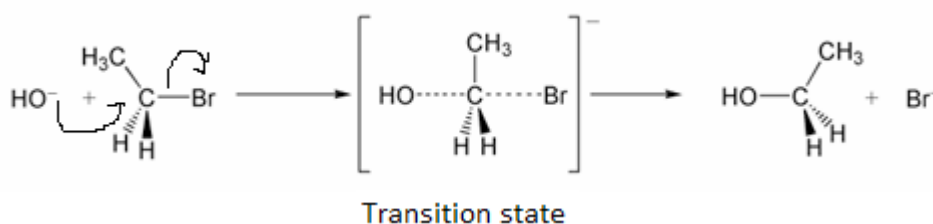
[Note: (a) S_N1 is common in reactions of secondary or tertiary alkyl halides or, under strongly acidic conditions, with secondary or tertiary alcohols. (b) Protic solvent (solvent containing dissociable H^+) will favor S_N1 reaction because it solvate the carbocation formed in r.d.s.]

(II) Bimolecular nucleophilic substitution (S_N2)

It is a one step process where two reacting species are involved in the slow, rate-determining step of the reaction. The reaction takes place via stable transition state.

Example: Formation of ethanol from bromoethane:

Mechanism of the reaction:



Kinetics of the reaction: Rate $\propto [RX][Nu^-]$

If the substrate under nucleophilic attack is chiral, this leads to an inversion of stereochemistry, called the *Walden inversion*.

[Note: (a) For leaving group in S_N2 reaction, remember that weaker the base better will be the leaving group. (b) In presence of aprotic solvent (that does not furnish H^+ in the solution) like DMF, DMSO, acetone etc. S_N2 reaction is favored.]

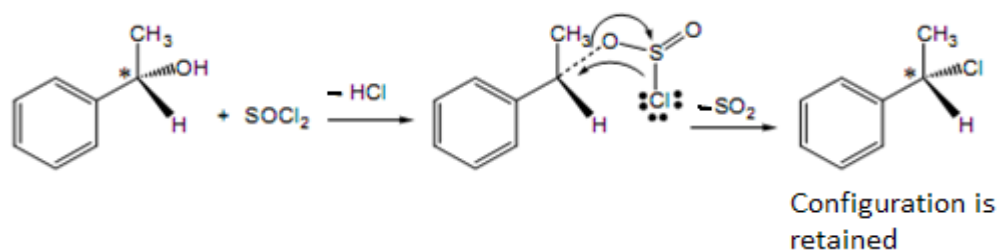
(iii) Internal nucleophilic substitution (S_Ni):

Substitution reactions proceed with retention of configuration.

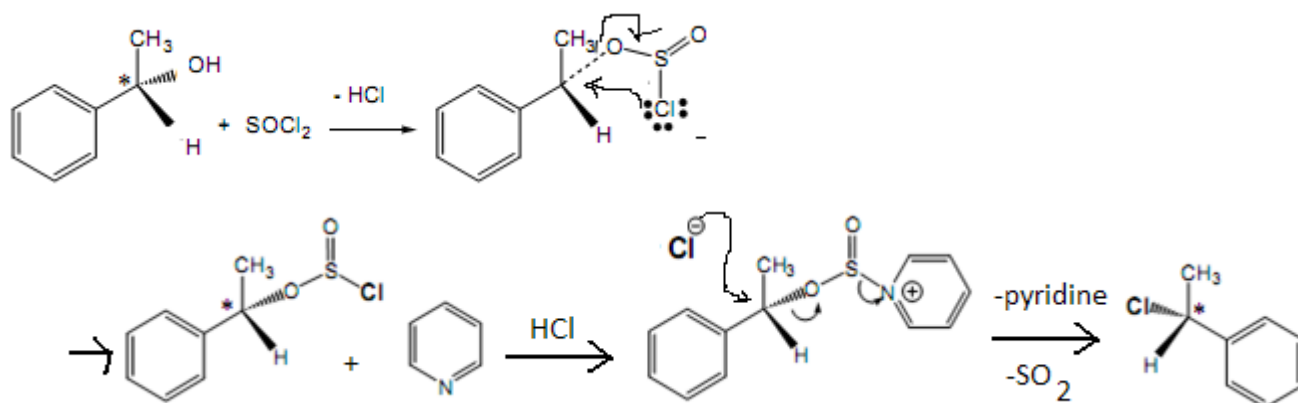
Mechanism of the reaction:

- The first step is the same as in S_N1 : ionization in which the leaving group and the residue dissociate and form a *tight ion pair*.
- In the second step, part of the leaving group attacks the incipient carbocation from the front side.

Example: Reaction of thionyl chloride with optically active alcohol.



In presence of pyridine *walden inversion* takes place according to the following mechanism:

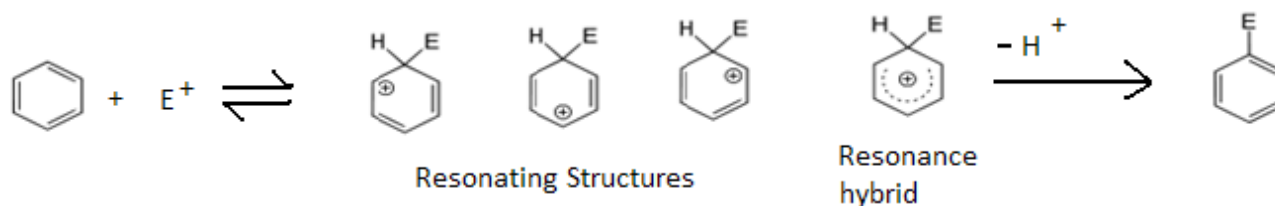


[Note: Driving force in the above example is the formation of good leaving group SO_2 .]

(b) Electrophilic substitution

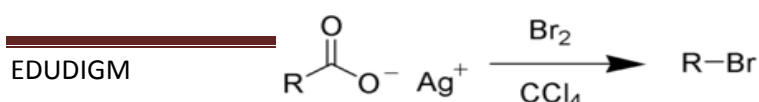
Substitution reaction in which substitution takes place by electrophile is called electrophilic substitution.

Example: Electrophilic aromatic substitution (EAS) reaction:

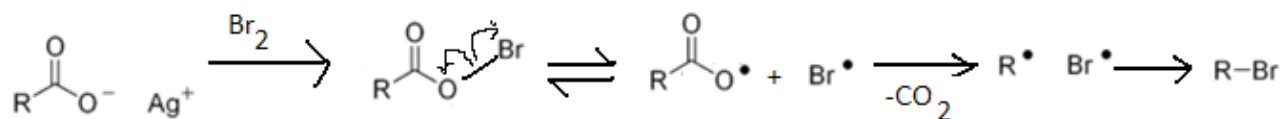


(c) Radical Substitution reaction:

Substitution reaction involving free radical is called radical substitution. Example: Hunsdiecker reaction, organic reaction of silver salts of carboxylic acids with halogens to give organic halides.

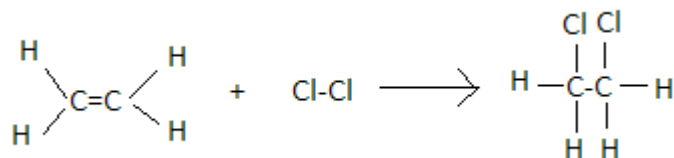


Reaction mechanism:



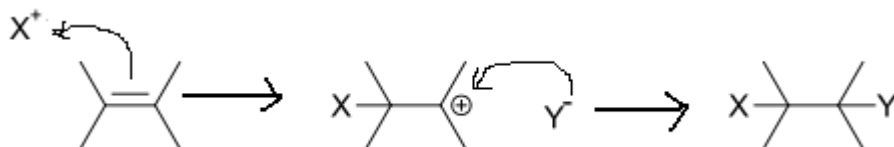
(ii) Addition reaction:

Chemical reaction in which the atoms of an element or compound react with a double bond or triple bond in an organic compound by opening up one of the bonds and becoming attached to it. For example:



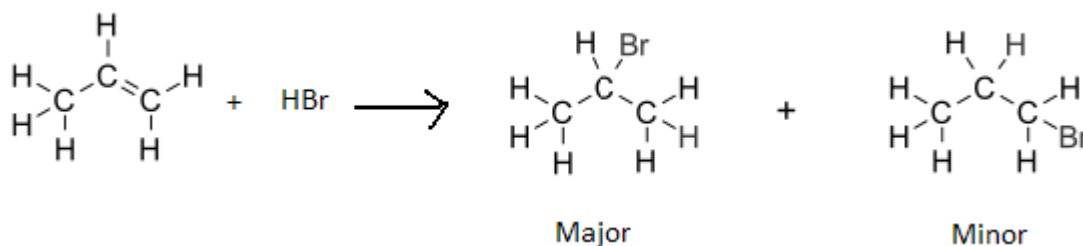
Just like substitution, addition reaction can be of different types: Electrophilic addition reaction, Nucleophilic addition reaction, free radical addition reaction.

Electrophilic addition reaction: Mechanism



Example: Hydrohalogenation reaction

Markovnikov's rule: The addition of a protic acid such as H-X to an alkene, the acid hydrogen (H) becomes attached to the carbon atom with the greatest number of hydrogens, and the halide (X) group becomes attached to the carbon with the fewest hydrogens.

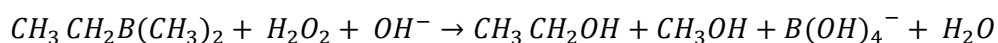
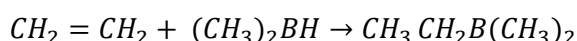


The rule may be summarized as “the rich get richer and the poor get poorer”. According to reaction mechanism this happens because of formation of stable carbocation during the addition process.

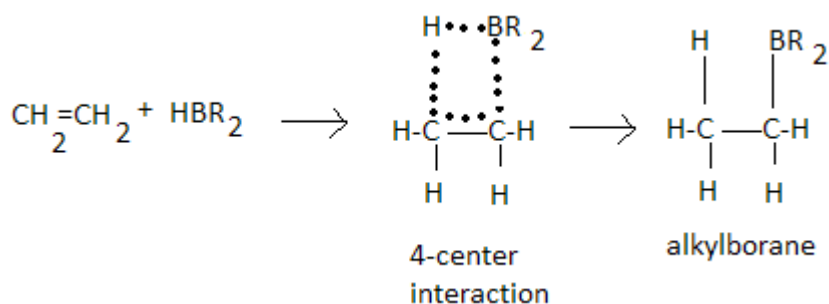
[Note: Racemic mixture may form if generation of chiral center takes place after the addition of electrophile.]

Anti-Markovnikov's rule: In presence of peroxide, unlike markovnikov's addition, reaction follows different mechanism. It follows free radical addition mechanism.

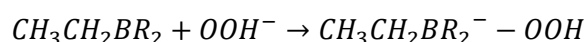
Example: *Hydroboration-Oxidation*.



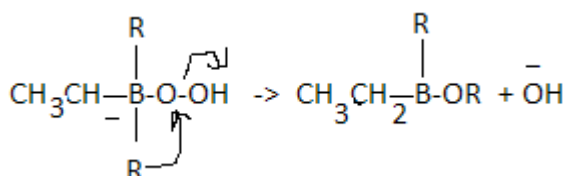
Step-wise mechanism is shown below:



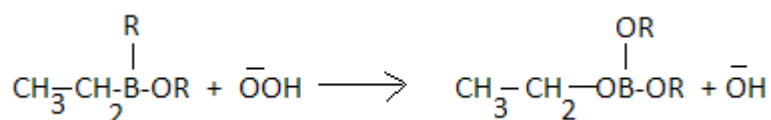
The alkylborane then undergoes a three-stage oxidation reaction to form the alcohol. In the first step, a hydroperoxide anion, formed by the reaction of a hydroxide ion with a peroxide molecule, adds to the electron-deficient boron atom.



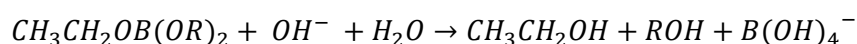
This intermediate is unstable and rearranges, losing a hydroxide ion to form a borate ester.



The borate ester then reacts with alkaline hydrogen peroxide to produce a trialkyl borate.

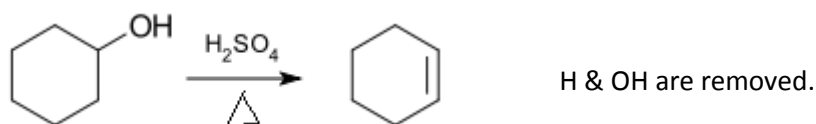


Finally, the trialkyl borate is hydrolyzed (which means split by the elements of water) to alcohols and a borate ion by the aqueous hydroxide ion.



(iii) Elimination reactions

Reactions in which two substituent are removed from a molecule in either a one or two-step mechanism. Example: Dehydration of cyclohexanol.



Elimination reaction can follow two different types of mechanism:

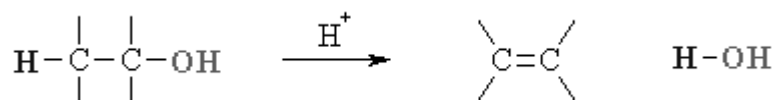
- (I) Unimolecular elimination(E1)
- (II) Bimolecular elimination (E2)

(I) E1 reaction: salient features of the reaction:

- It is a two-step process of elimination *ionization(to form carbocation) and deprotonation(of the carbocation)*.
- Reaction mostly occurs in complete absence of base or presence of only a weak base.
- Common in tertiary and some secondary substituted alkyl halides.

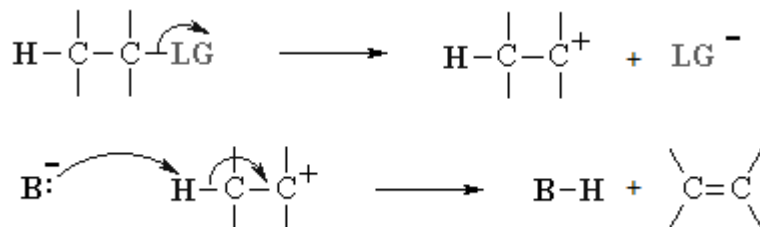
- Presence of protic solvent & high temperature favors E1.

Example: Dehydration of alcohols



Reaction kinetics: Rate = k [R-LG] where LG stands for leaving group.

Reaction mechanism:



E1 mechanistic pathway is most common with:

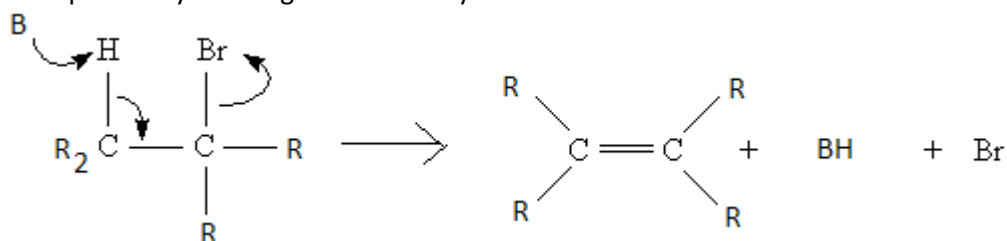
- good leaving groups (LG)
- stable carbocations
- weak bases.

[Note: E1 mechanism involves formation of carbocation, therefore rearrangement of carbocation may take place to form more stable product.]

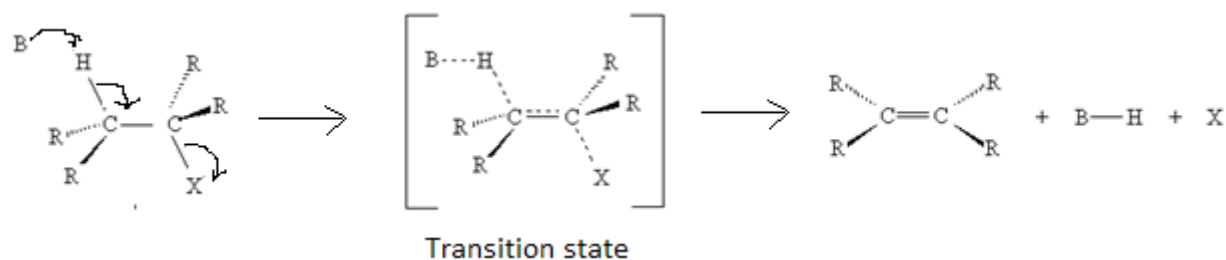
(II) **E2 reaction:** salient features of the reaction:

- Simultaneous removal of the proton, H^+ , by the base, loss of the leaving group, **LG**, and formation of the π -bond
- It is a one step reaction, therefore no rearrangement is possible.
- Reaction mostly occurs in presence of strong base. Most common bases are alc. KOH, NaNH_2 , $\text{C}_2\text{H}_5\text{O}^-$, Na^+ , $(\text{CH}_3)_3\text{CO}^- \text{K}^+$

Example: Dehydrohalogenation of alkyl halide:



Mechanism of the reaction:

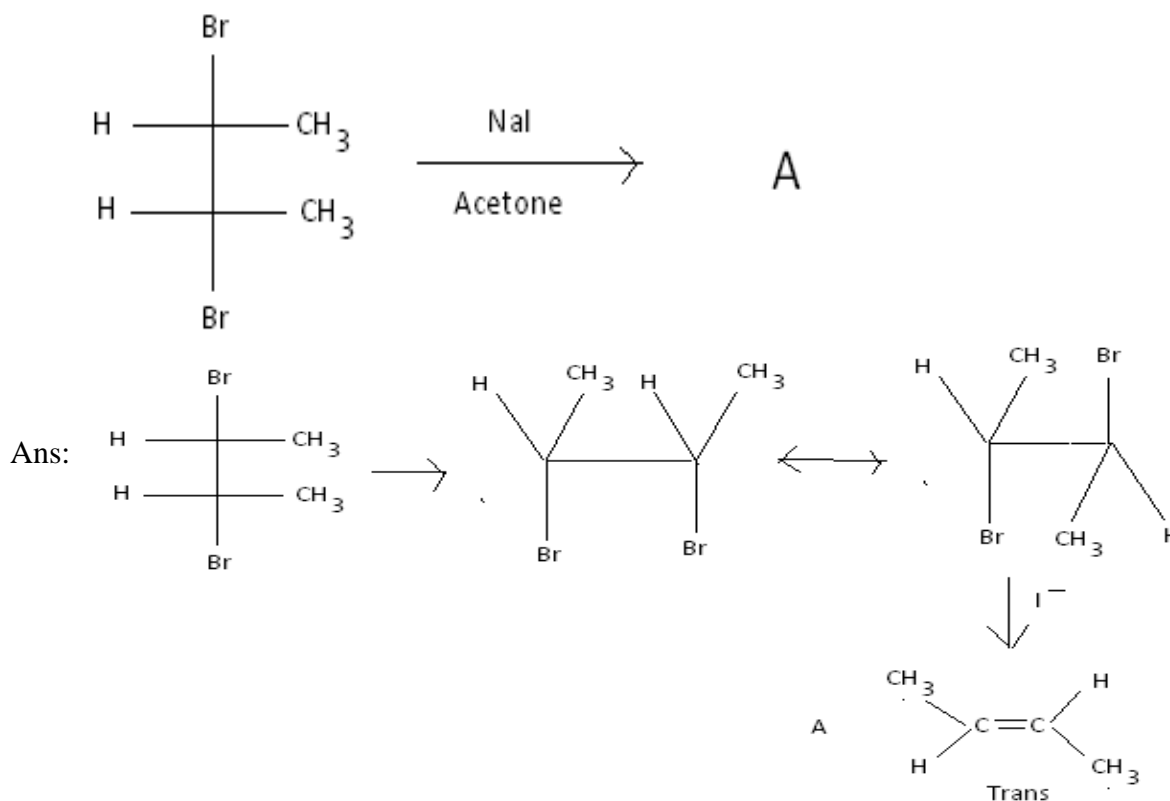


E₂ reaction proceeds via stable transition state. H and halogen will be removed from opposite sides means reaction takes place in staggered form. Hence if the substrate is given in eclipsed or fisher form, first convert into staggered form and then removal of H-X should be done.

The E₂ pathway is most common with:

- high concentration of a strong base
- poorer leaving groups
- R-LG that would not lead to stable carbocations (when the E₁ mechanism will occur).

Problem: Find the dipole moment of A



Since the product formed is trans, therefore the dipole moment = Zero.

E₂ vs. E₁ vs. S_N2 vs. S_N1 reactions

When comparing the reactivity of these four reactions, the following generalizations are useful: CH₃-X reacts always via S_N2 pathway.

Correlation of Structure and Reactivity for Substitution and Elimination Reactions

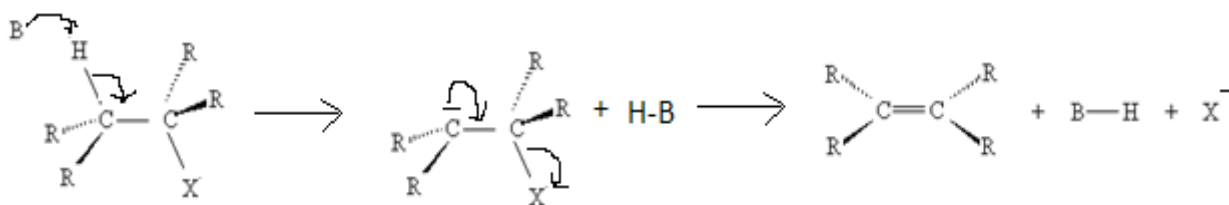
Halide Type	S _N 1	S _N 2	E1	E2
RCH ₂ X (primary)	No	Highly favored	No	Occurs when strong bases are used

R₂CHX (secondary)	Can occur with benzylic and allylic halides	Occurs when weak base are used, in competition with E2 reaction	Can occur with benzylic and allylic halides	Favored when strong bases are used
R₃CX (tertiary)	Favored in hydroxylic solvents when solvolysis occurs and favored at low temperature	No	Occurs in competition with S _N 2 reaction, favored at high temperature	Favored when strong bases are used

Special type of elimination reaction:

Elimination conjugate Base reaction (E1CB reaction) : A strong base abstracts the α proton generating a carbanion. The electron pair then expels the leaving group and the double bond is formed.

Reaction Mechanism is shown below:



(iv) Re arrangement reactions (Neighboring group participation [NGP])

In this type of reaction a carbon skeleton of a molecule is rearranged to give a structural isomer of the original molecule. Often a substituent moves from one atom to another atom in the same molecule. Example



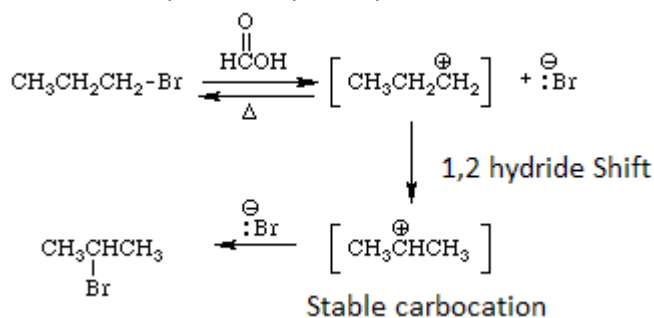
R moves from carbon atom 1 to carbon atom 2.

Some important rearrangement reactions are as follows:

- 1,2 rearrangement s
- Pericyclic reactions

1,2 rearrangement reaction: 1,2 hydride; alkyl or aryl shift

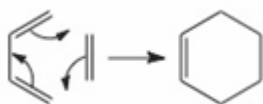
1,2 Hydride shift:



Similarly [1,3],[1,5], [1,7],[3,3],[5,5] etc. shift are also depending upon the formation of stable product.

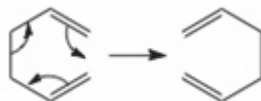
Pericyclic reaction: It can be classified into several categories:

- Cycloaddition



In this reaction two new sigma bonds are formed.

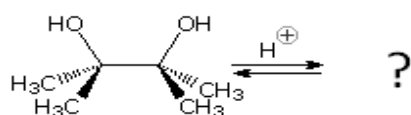
- Sigmatropic rearrangements : One new sigma bond is formed as another breaks.



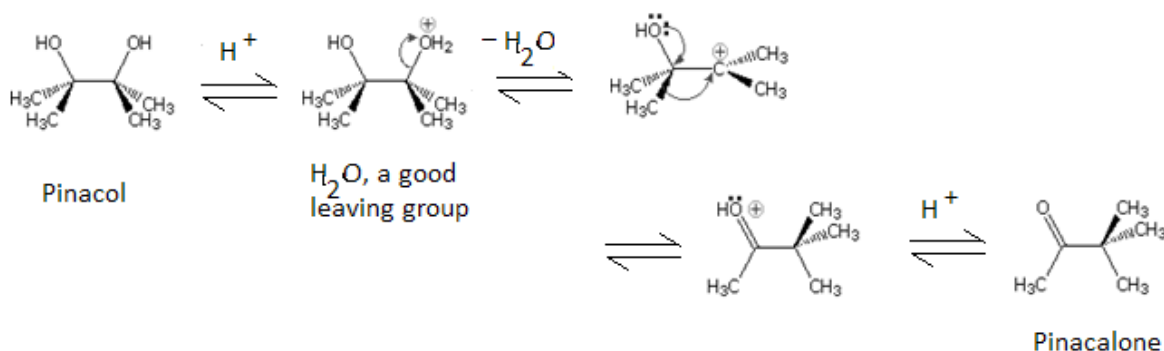
- Electrocyclic reactions: In this category of reaction, after rearrangement one new sigma bond forms or breaks.



Problem 1: Find the product formed in the following reaction:

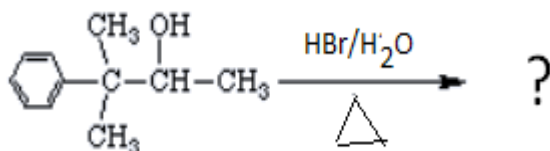


Ans.



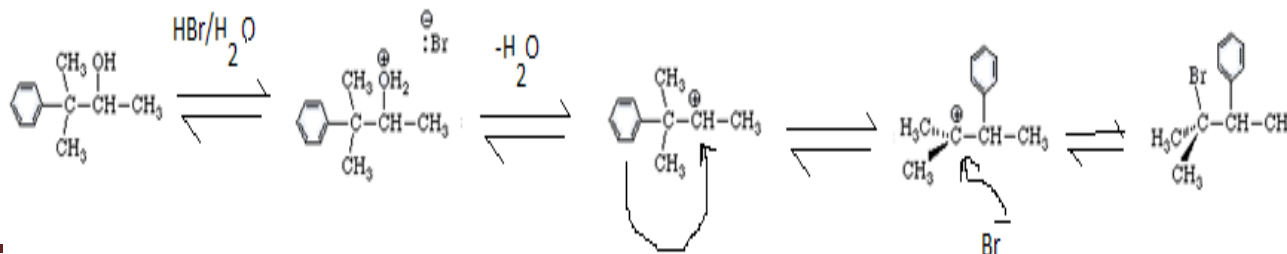
Pinacol-Pinacolone rearrangement

Problem 2:



Ans:

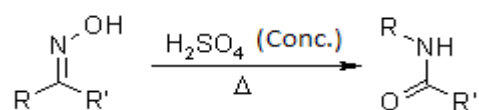
3-methyl-3-phenyl 2 butanol



Phenyl shift

Problem 3: What is Beckmann rearrangement? Explain the reaction mechanism. Suggest the mechanism of preparation of nylon 6 using cyclohexanone.

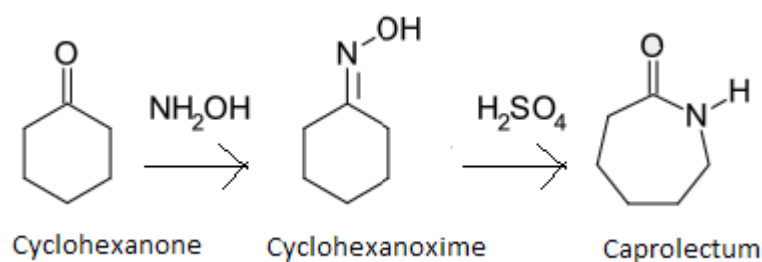
Hint: Beckmann rearrangement:



Students are advised to think of the mechanism of the reaction by themselves.

Nylon 6: Produced by ring opening polymerization of caprolectum.

Therefore first make caprolectum from cyclohexanone. i.e.



[Note: Preparation of caprolectum from cyclohexanone is an important example of Beckmann rearrangement.]

Q1) Give the reaction which lead to the formation of first organic compound inside the lab

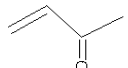
Q2) According to let –bell & vant hoff theory, what is the value of normal tetraheclran angle

Q3) in (cyclohexane) , give the hybridization of each carbon atom

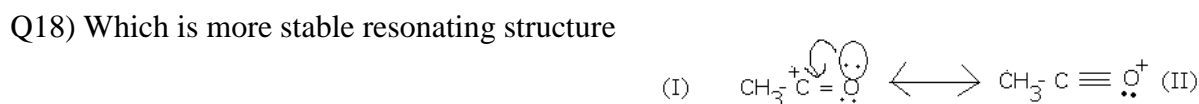
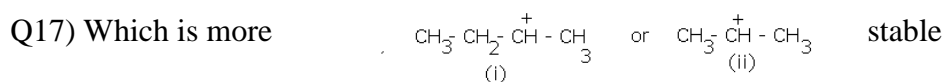
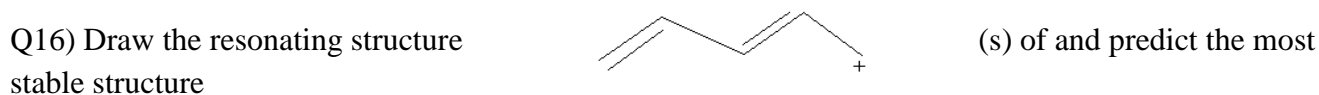
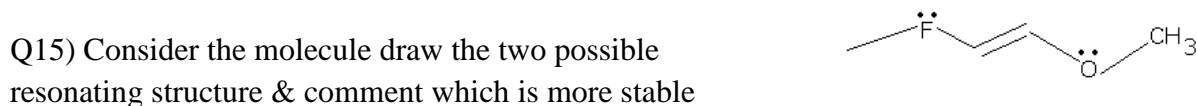
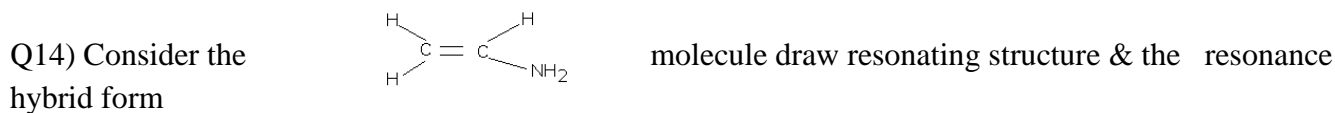
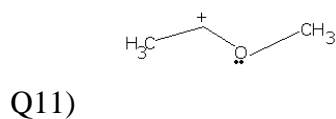
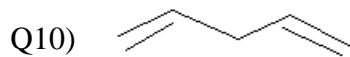
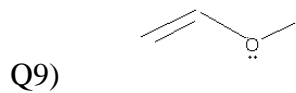
Q4) Draw the resonance  structure of with correct arrows

Draw the resonance structure of the following with correct arrows

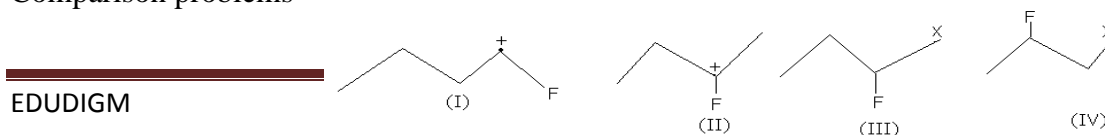
Q5) 

 Q6)

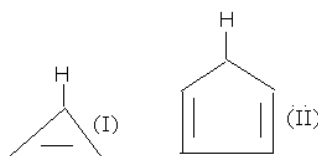
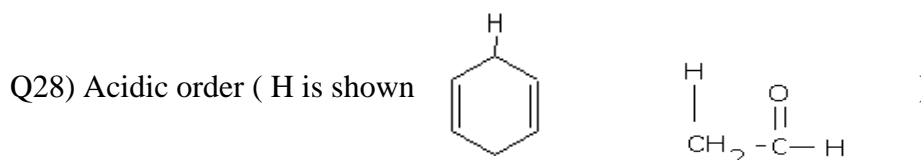
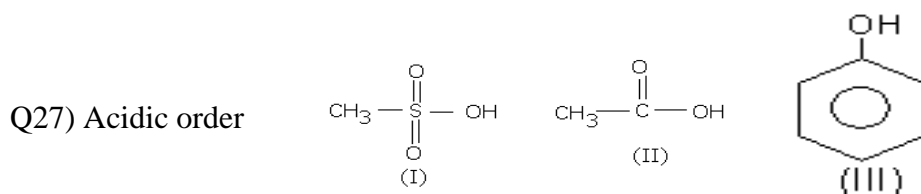
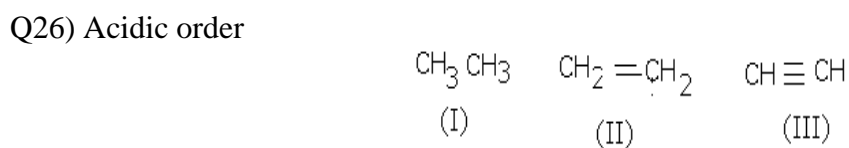
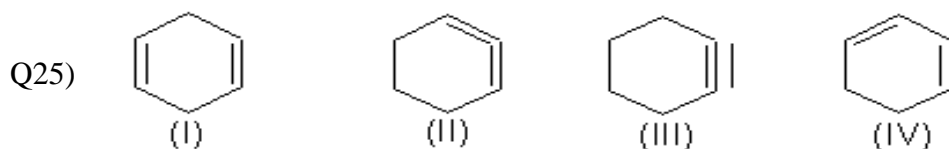
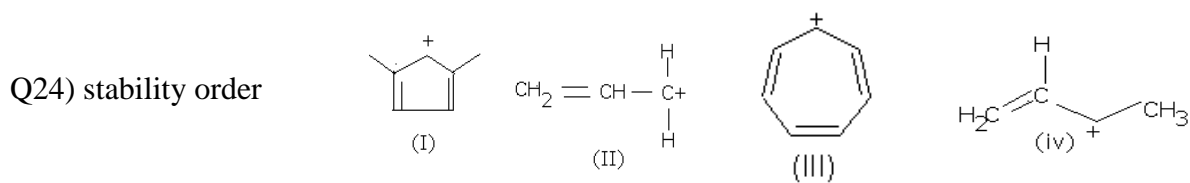
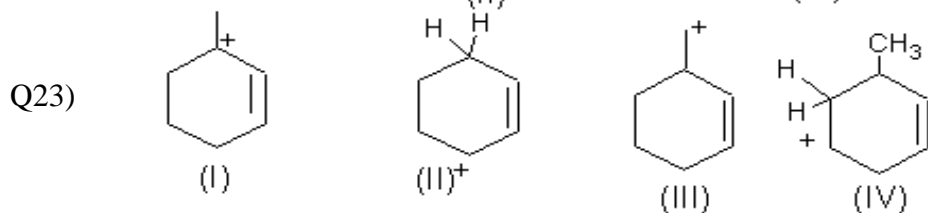
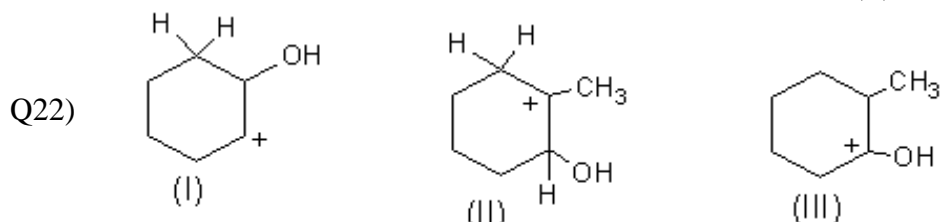
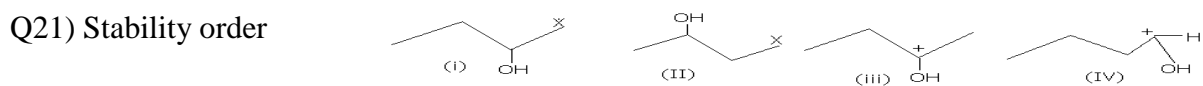
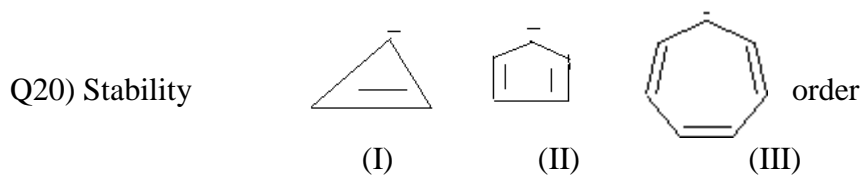
Q7) 



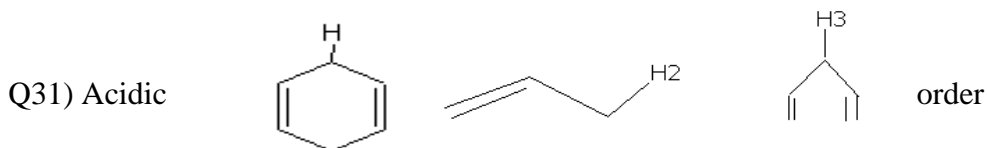
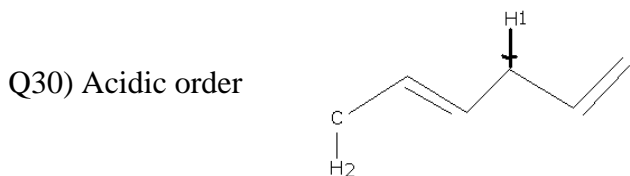
Comparison problems



Q19) Stabling order



Q29) Acidic order?



Objective problems

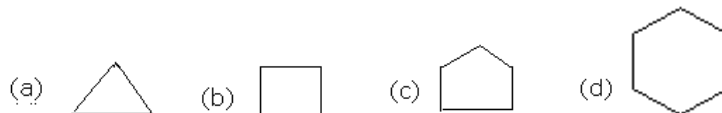
Q32) Predict the product



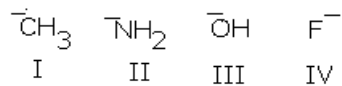
Q33) Predict the product



Q34) Which is more stable



Q35) Increasing order of basic strength of given ion



Q36) Hybridization of starred carbon is $\text{CH}_2 - \text{CH} = \text{C}^*\text{H}_2$

- (a) SP^3 (b) SP^2 (c) SP (d) no hyb.

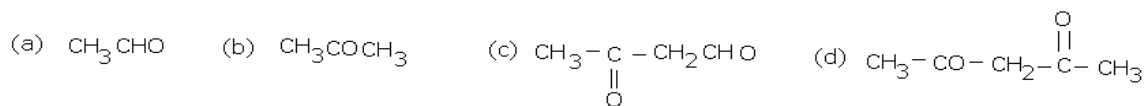
Q37) The strongest carboxylic acid is

- (a) $\text{Cl}_3\text{CCO}_2\text{H}$ (b) $\text{Br}_3\text{CCO}_2\text{H}$ (c) $\text{F}_3\text{C} - \text{CO}_2\text{H}$ (d) $\text{H}_3\text{C} - \text{CO}_2\text{H}$

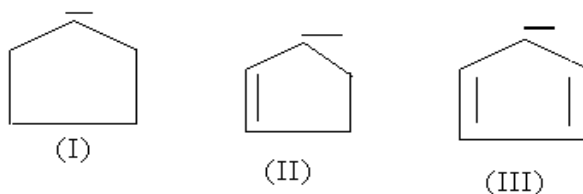
Q38) Resonance struchiry should have

- (a) identical energy (b) identical bonding (c) both (d) none

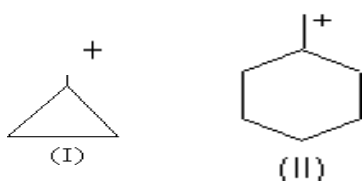
Q39) The compounds having the most acidic α - hydrogen is



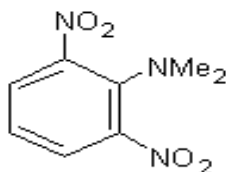
Q40) Acidic strength



Q41) Carbocation stability

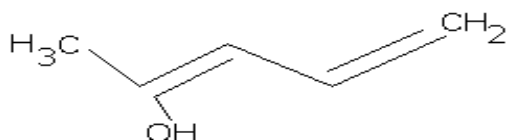


Q42) Unlike other aromatic amines why is the following amine strongly basic?



Q43) When carbene attack cis -2 - butane , single carbene gives cis product but triplet gives trans product

Q44) Write resonance structure of given compound & compare there stability.



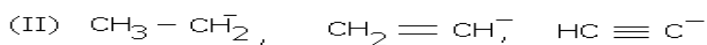
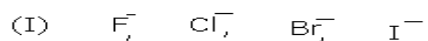
Q45) Which of the following $\text{C}-\text{Br}$ bond is weak & why?



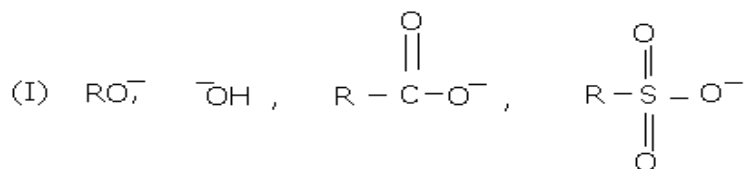
Q46) Arrange in the order of acidic strength

PhCOOH , PhSO₃H , PhOH , EtOH

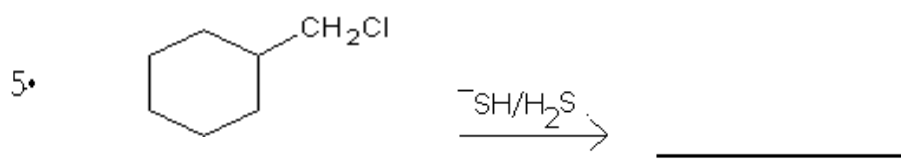
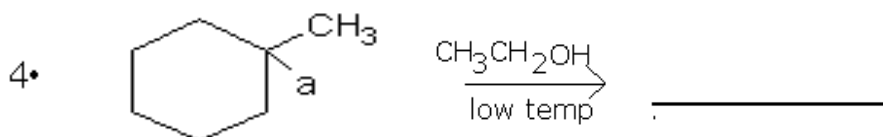
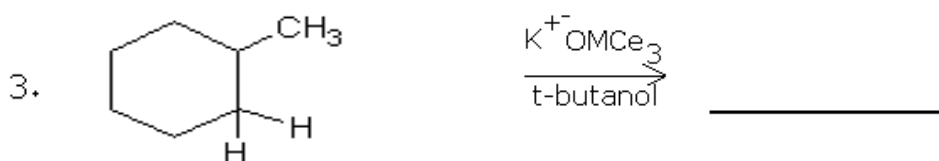
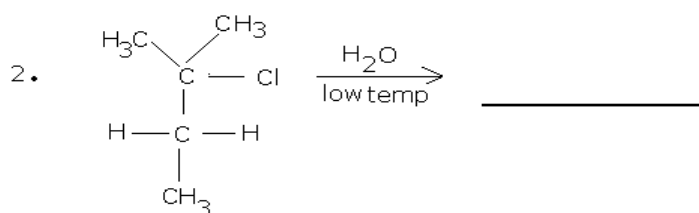
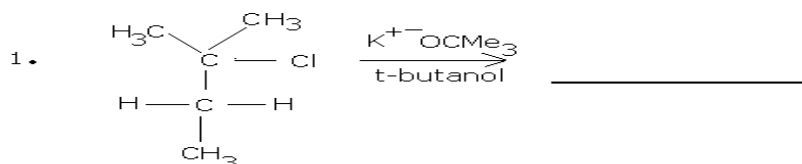
Q47) Compare the leaving tendency of following leaving group sets

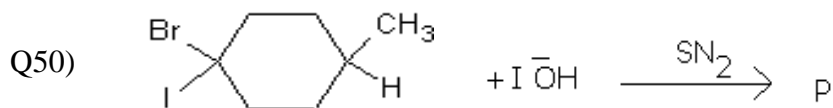


Q48) Compare the strength of given set of nucleophiles:



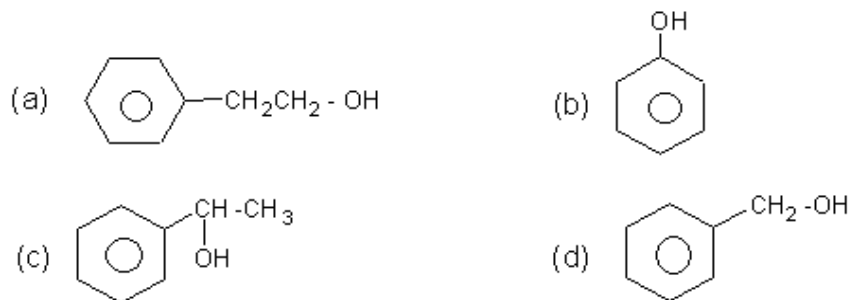
Q49) Predict the product in the following cases (major only)



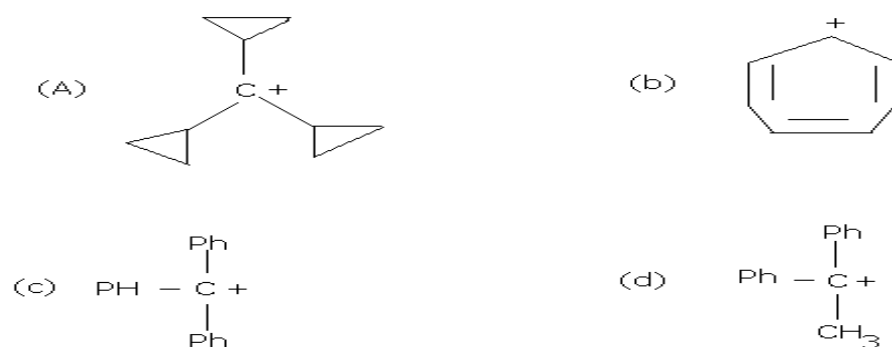


The product P will be

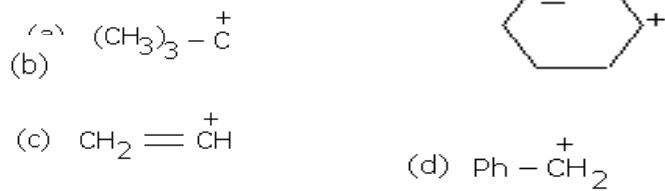
Q51) Which of the following reacts fastest with conc. HCl



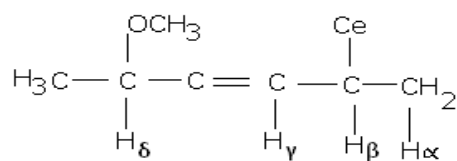
Q52) The most stable carbocation is



Q53) Most stable carbonium ion is

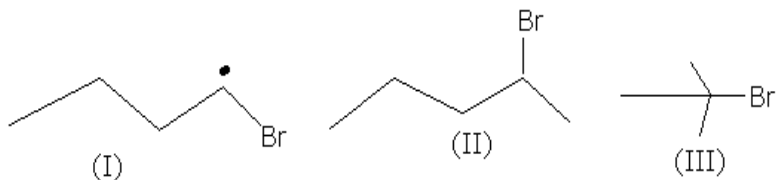


Q54) Which H is abstracted easily

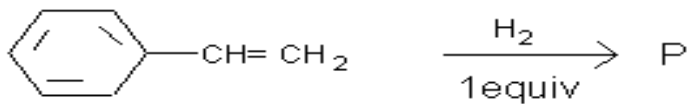


- (a) α (b) β (c) γ (d) δ

Q55) Dehydrobromination (- H Br) of the following in increasing order is

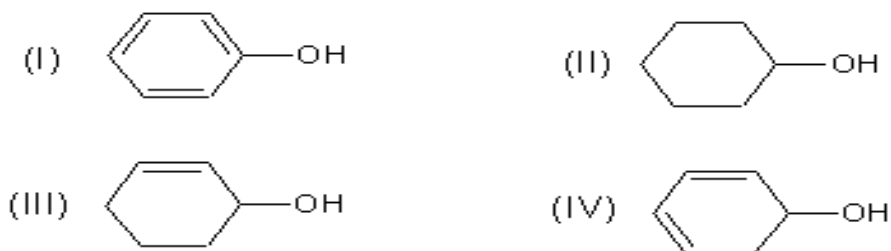


Q56)

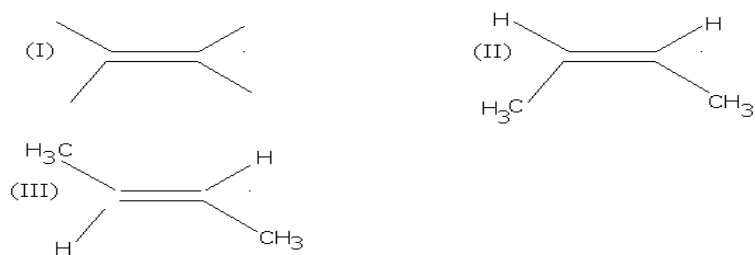


Product p is

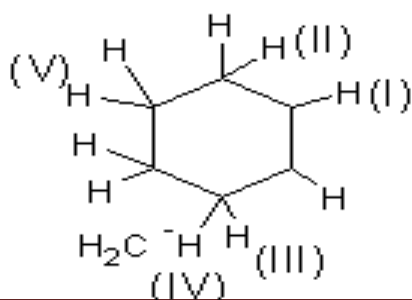
Q57) Dehydration of the following in increasing order is:



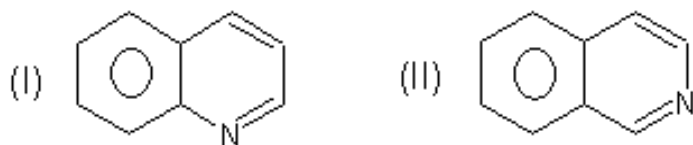
Q58) Arrange in the order of stability of double bonds (or molecules)



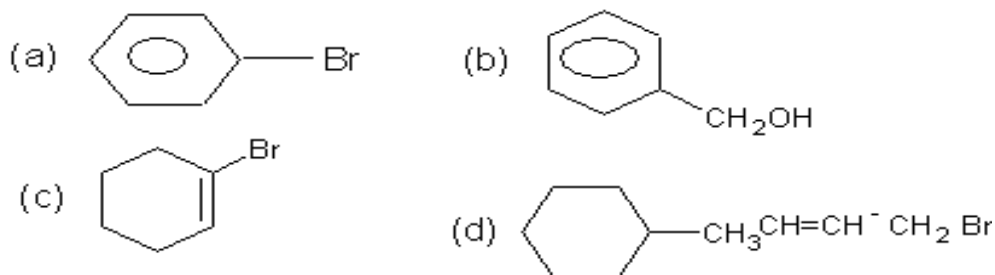
Q59) B. E of C - H bonds designated by I, II, III, IV



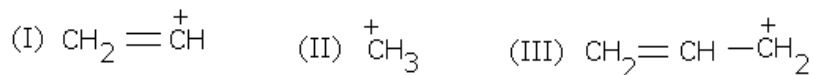
Q60) Basic strength order



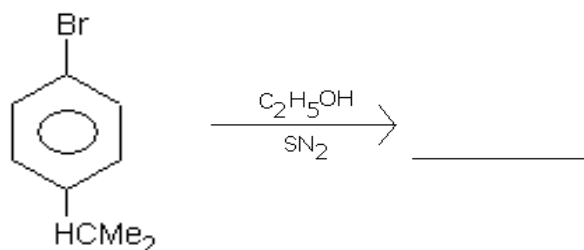
Q61) Which reacts with AgNO_3 to give ppt?



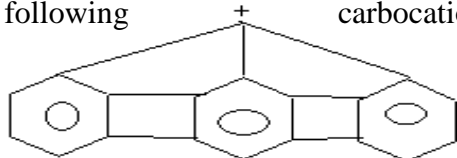
Q62) Stability of carbocation



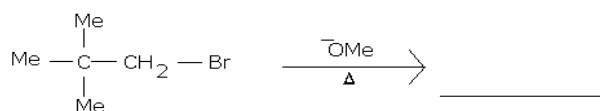
Q63) Predict the product



Q64) Is the following carbocation stable give reason



Q65) Predict the product

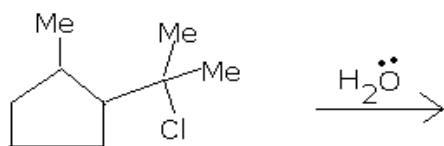


Q66) Why the formation of carbocation is the rate determining step in SN_1 reaction?

Q67) Why polar solvent prefers substitution reaction rather than elimination

Q68) Why higher temp, elimination is more preferable

Q69) Find P (major)



Q70)

