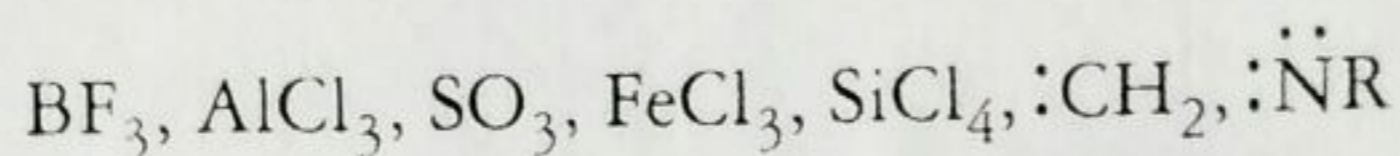


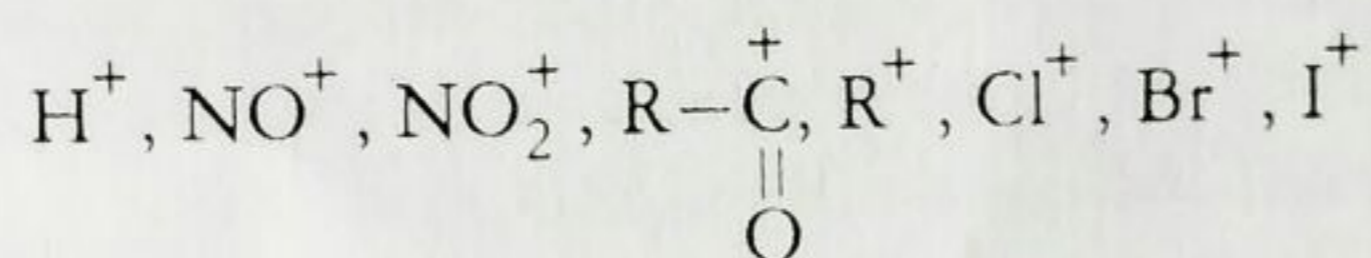
9.4 Attacking Reagents in an Organic Reaction**Electrophiles**

Electrophiles (meaning electron loving) are electron-deficient species seeking a site of high electron density. Electrophiles have an incomplete outer electron shell and are very reactive. They could be (a) neutral species in which the central atom has six electrons or (b) positively charged species, both of which are deficient in electrons.

1. Examples of neutral electrophiles are

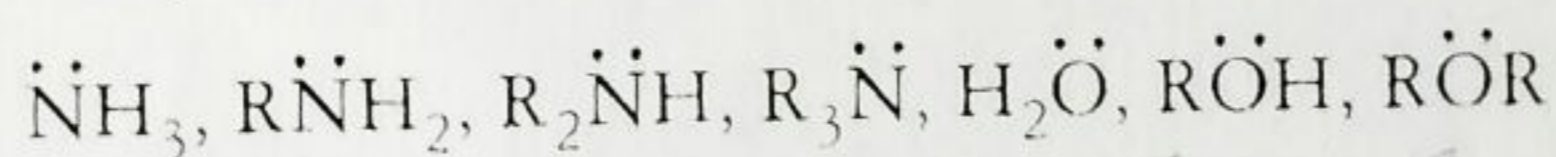


2. Examples of positively charged electrophiles are

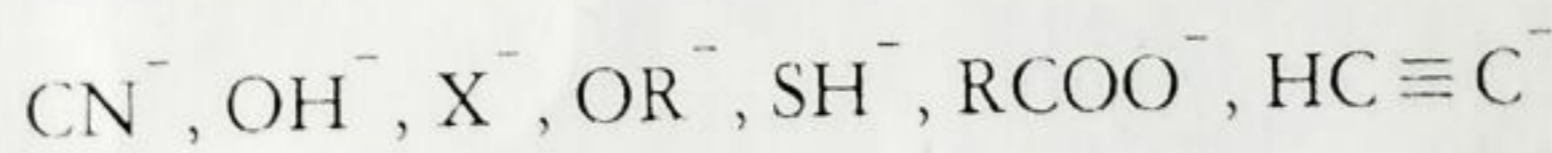
**Nucleophiles** : e⁻ rich

Nucleophiles (meaning nucleus loving) are electron-rich species with a tendency to donate a pair of electrons. They attack electron deficient sites and could be neutral or negatively charged.

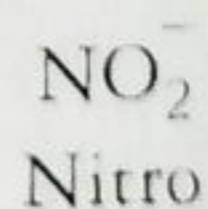
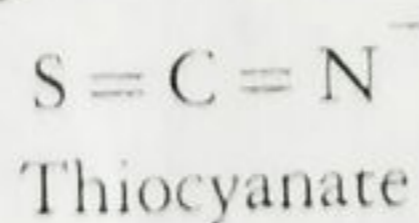
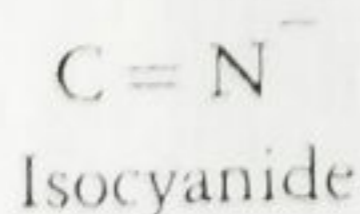
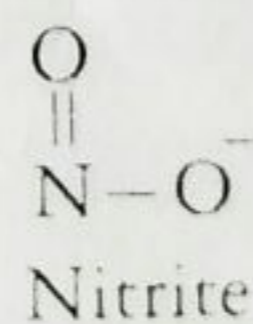
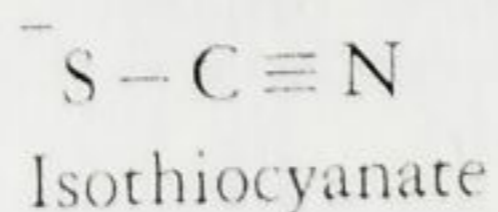
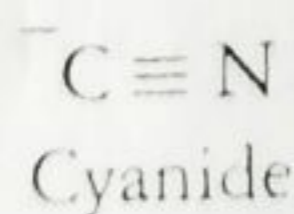
- Examples of neutral nucleophiles are



- Examples of negatively charged nucleophiles are



Nucleophiles that have more than one site for attacking the substrate are known as ambident nucleophiles. For example

**Concept Check**

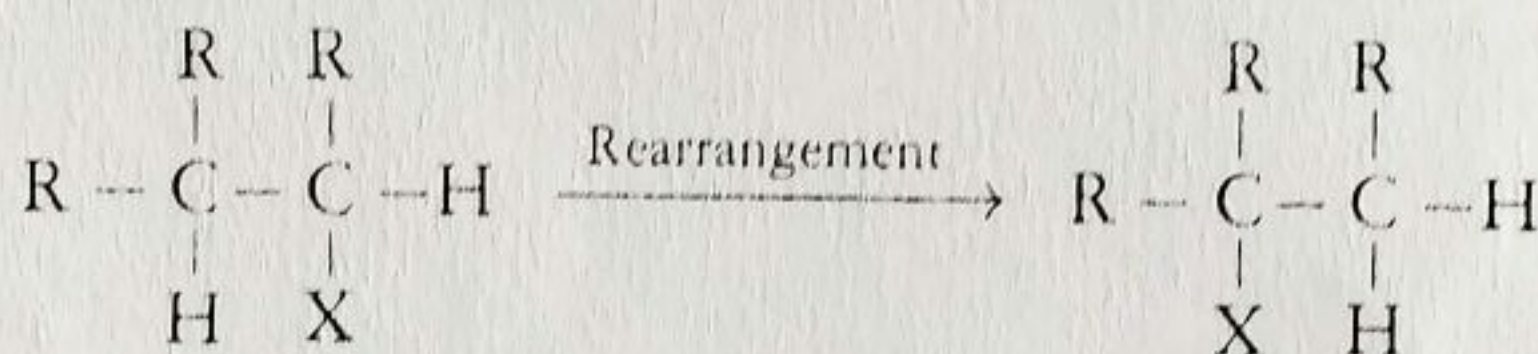
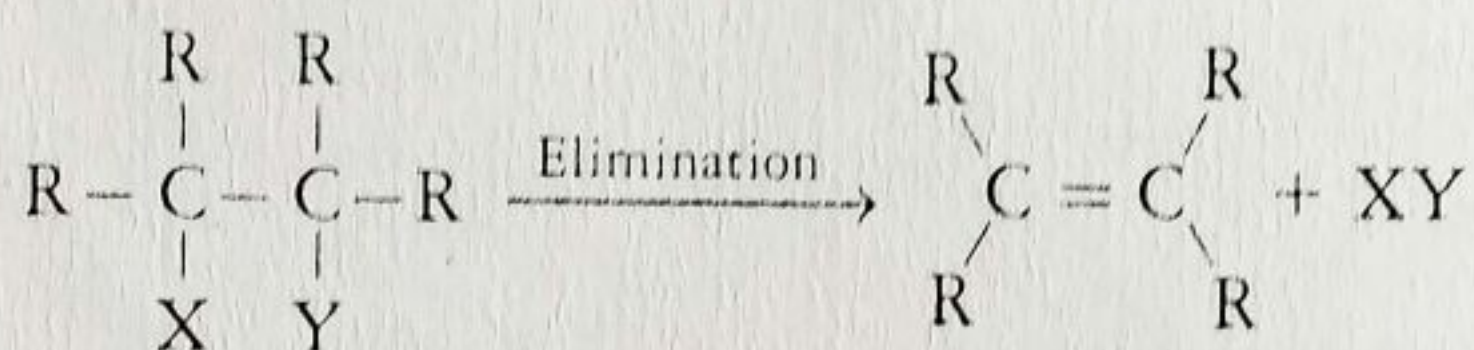
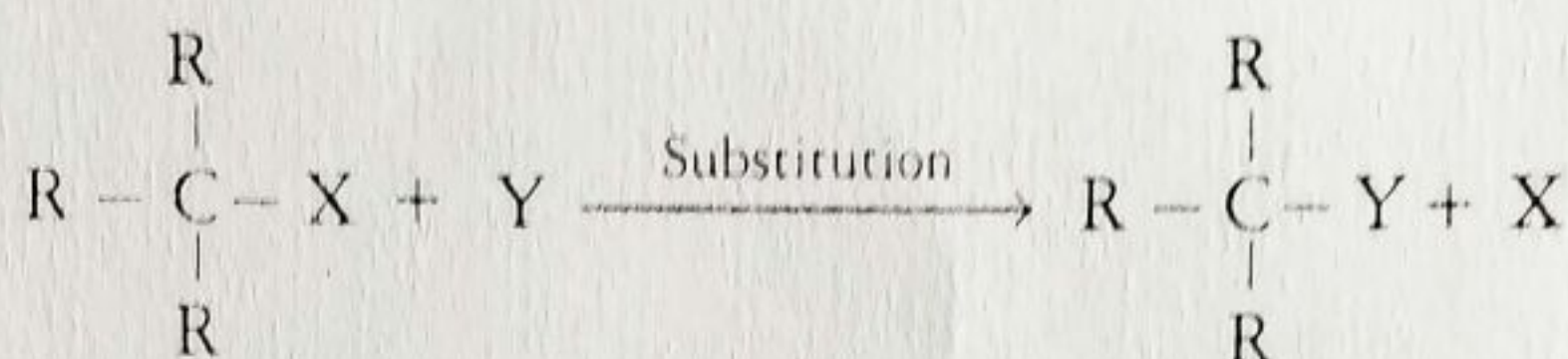
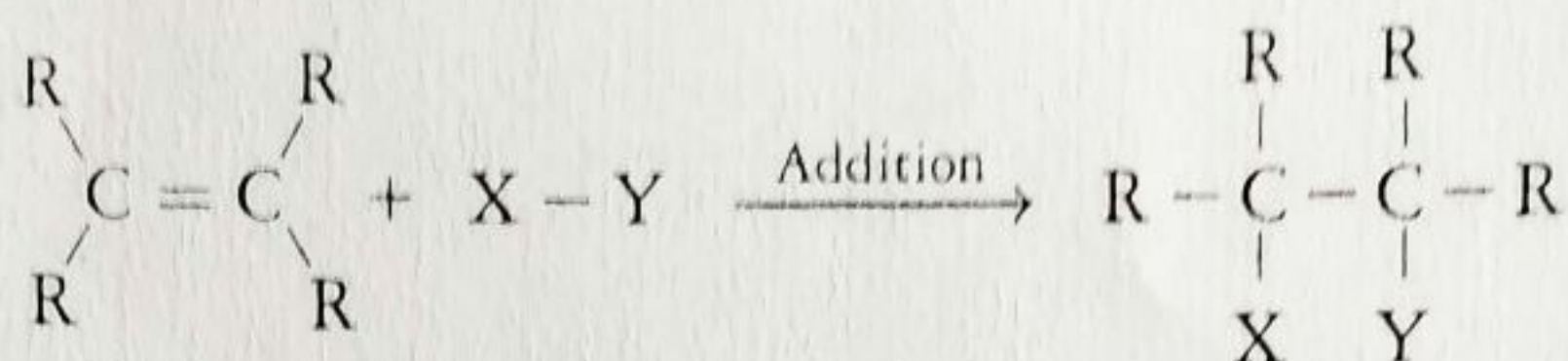
- Classify the following into electrophiles and nucleophiles:
 $\text{BF}_3, \text{RCOO}^-, \text{ROH}, \text{NO}_2^+, \text{CN}^-, \text{RNH}_2, \text{OR}^-$
- What is an ambident nucleophile? Give two examples.

9.5 Types of Organic Reactions

Organic reactions may be broadly classified into

1. Addition
2. Substitution
3. Elimination
4. Rearrangement

These may be represented as follows:



Concept Check

- What are the different kinds of organic reactions?
- Distinguish between substitution and rearrangement reactions.

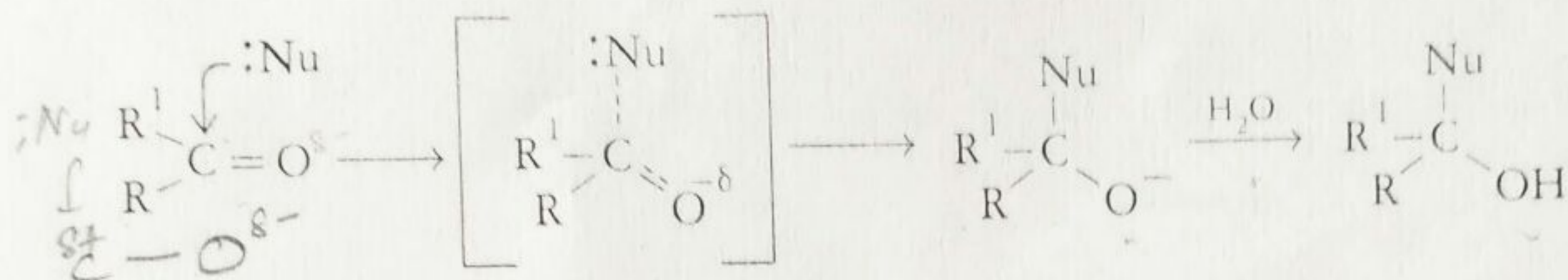
9.6 Addition Reactions

Addition reactions occur in compounds containing multiple bonds, for example, $\text{C}=\text{C}$, $\text{C}\equiv\text{C}$, $\text{C}=\text{O}$, $\text{C}\equiv\text{N}$, etc. The addition reactions can proceed through:

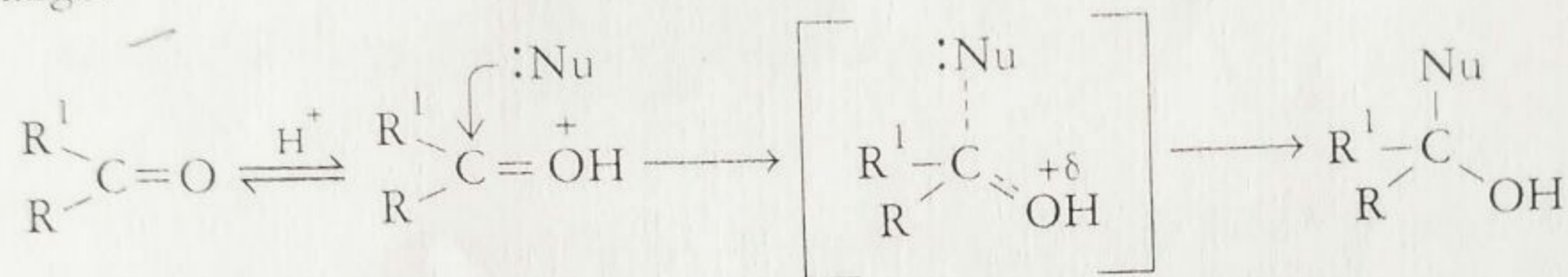
1. nucleophilic addition;
2. electrophilic addition;
3. free radical addition.

Nucleophilic Addition

Nucleophilic addition generally occurs in compounds containing polar functional groups; for example, $\text{C}=\text{O}$, $\text{C}\equiv\text{N}$, $\text{C}=\text{S}$, etc., most important of them being $\text{C}=\text{O}$.

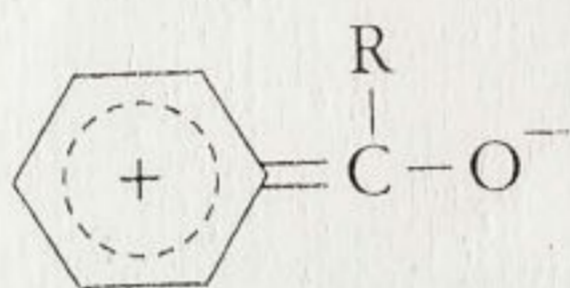


Nucleophilic addition to carbonyl compounds is catalyzed by an acid. The protonated carbonyl group undergoes nucleophilic attack more readily because oxygen can take electrons without acquiring a negative charge.



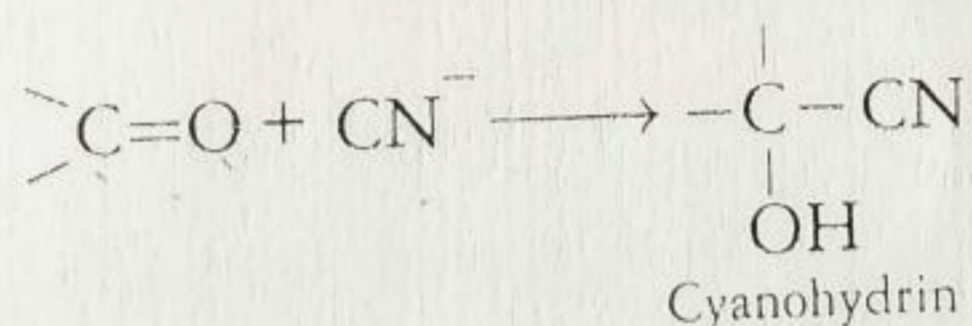
Aldehydes undergo nucleophilic addition more readily than ketones. This is because a ketone contains a second alkyl or aryl group and hence causes crowding. An alkyl group also releases electrons and thus destabilizes the transition state by intensifying the negative charge developing on oxygen.

An aryl group has an electron withdrawing inductive effect, and thus it is expected that it will stabilize the transition state and increase the rate of the reaction. However, it seems to stabilize the reactant even more by resonance and thus causes net deactivation.

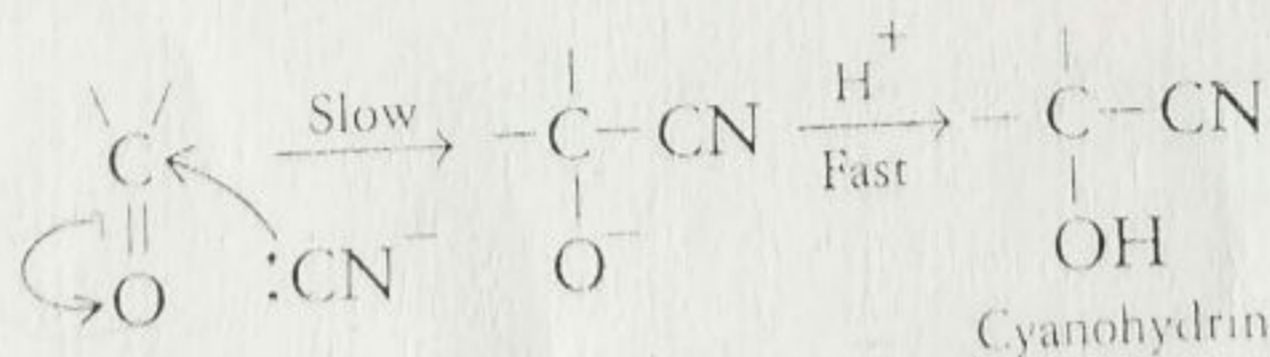


The examples of nucleophilic addition are as follows:

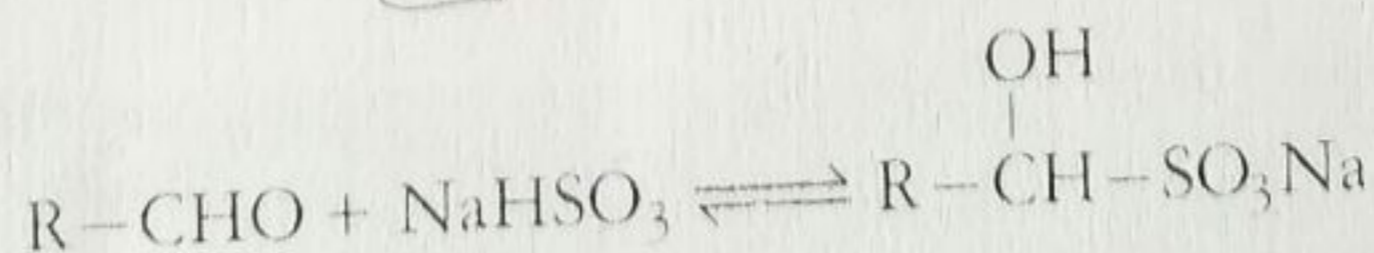
1. Addition of a cyanide to carbonyl group (cyanohydrin formation)



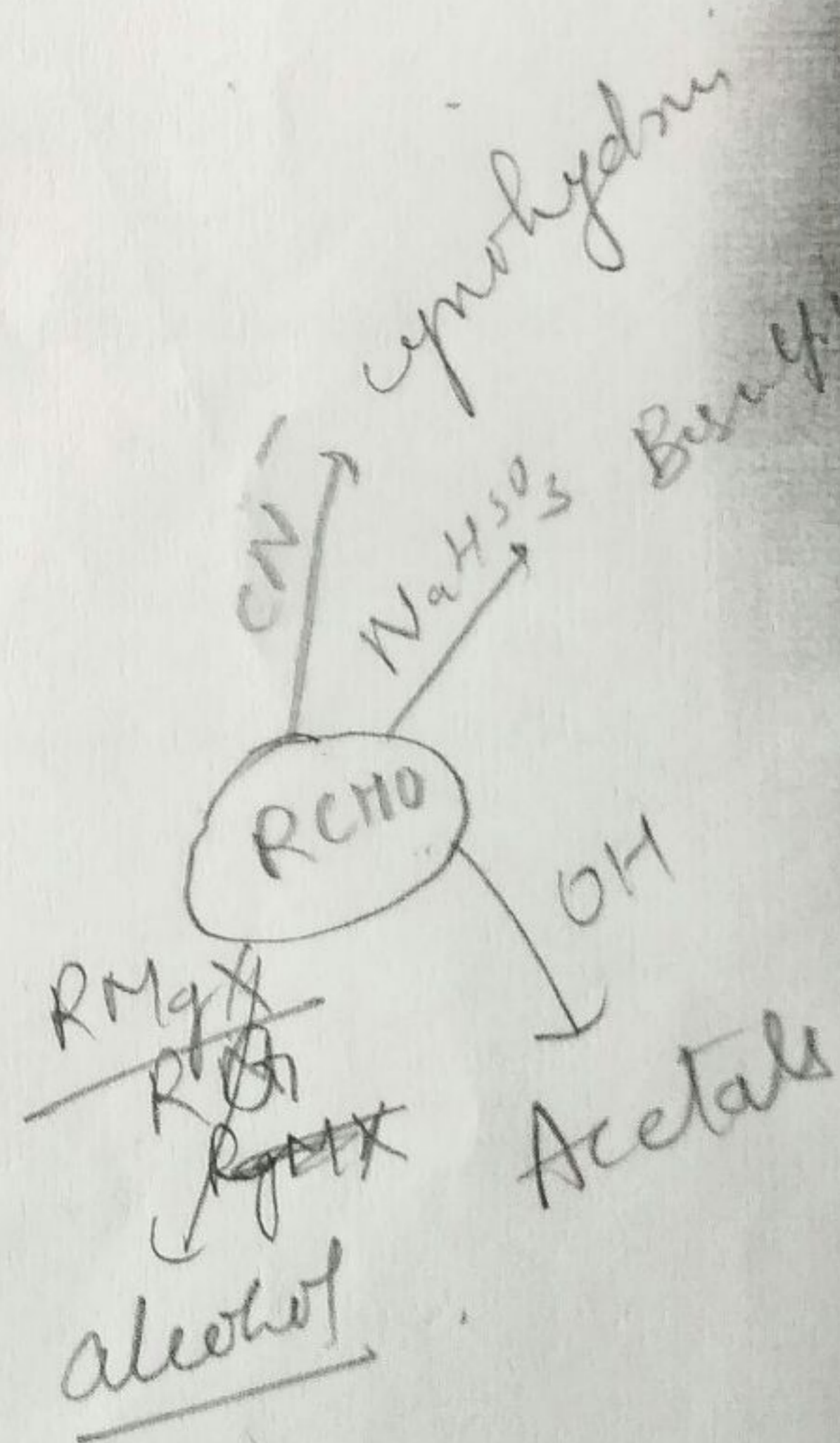
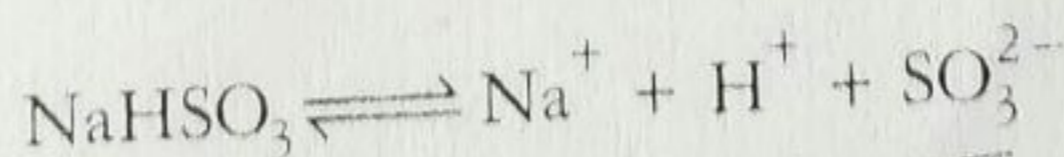
Mechanism

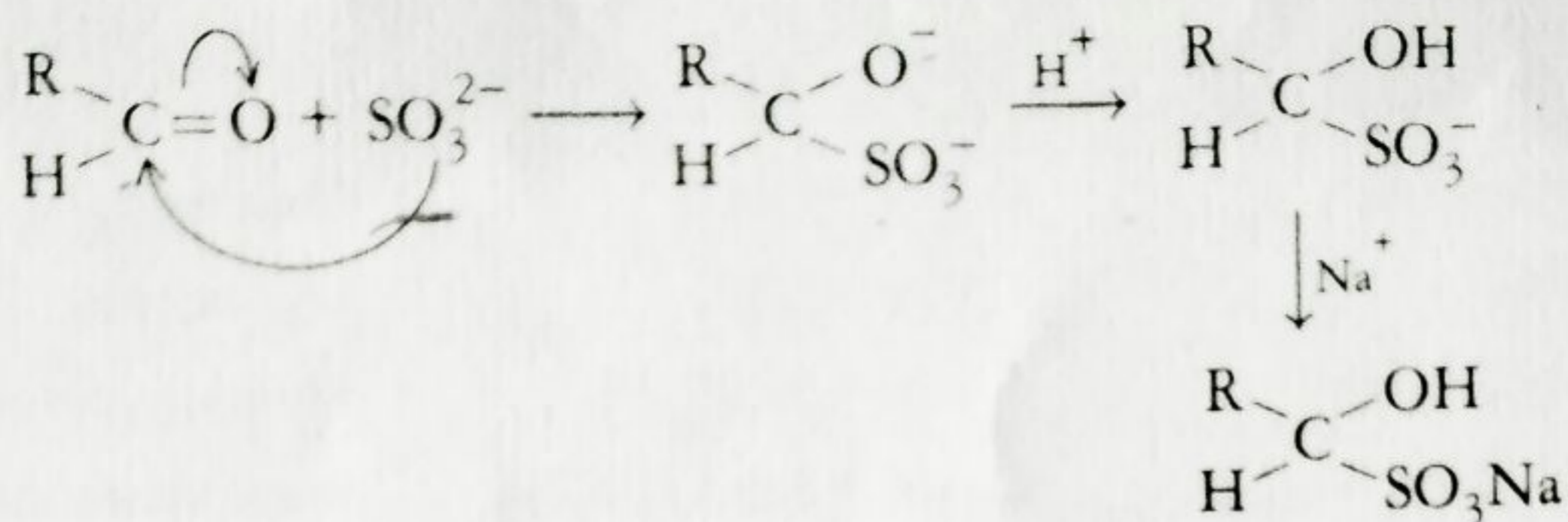


2. Addition of bisulphite to carbonyl group

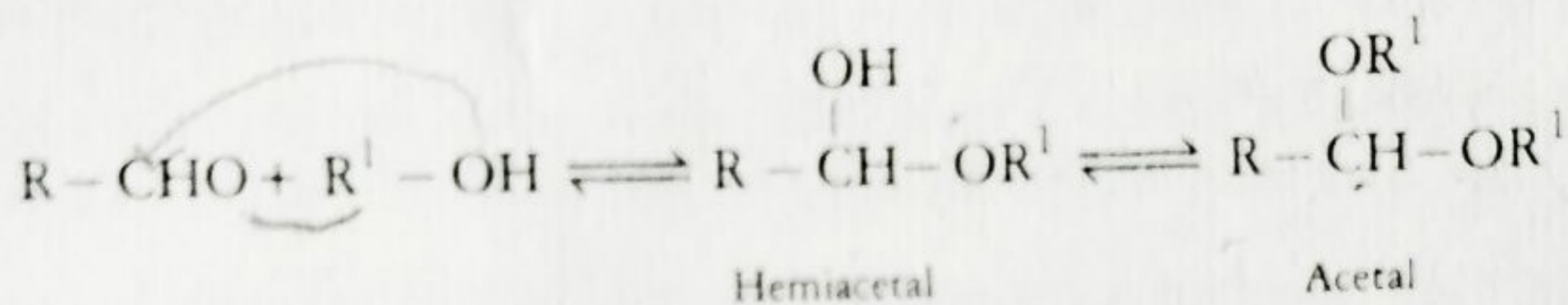
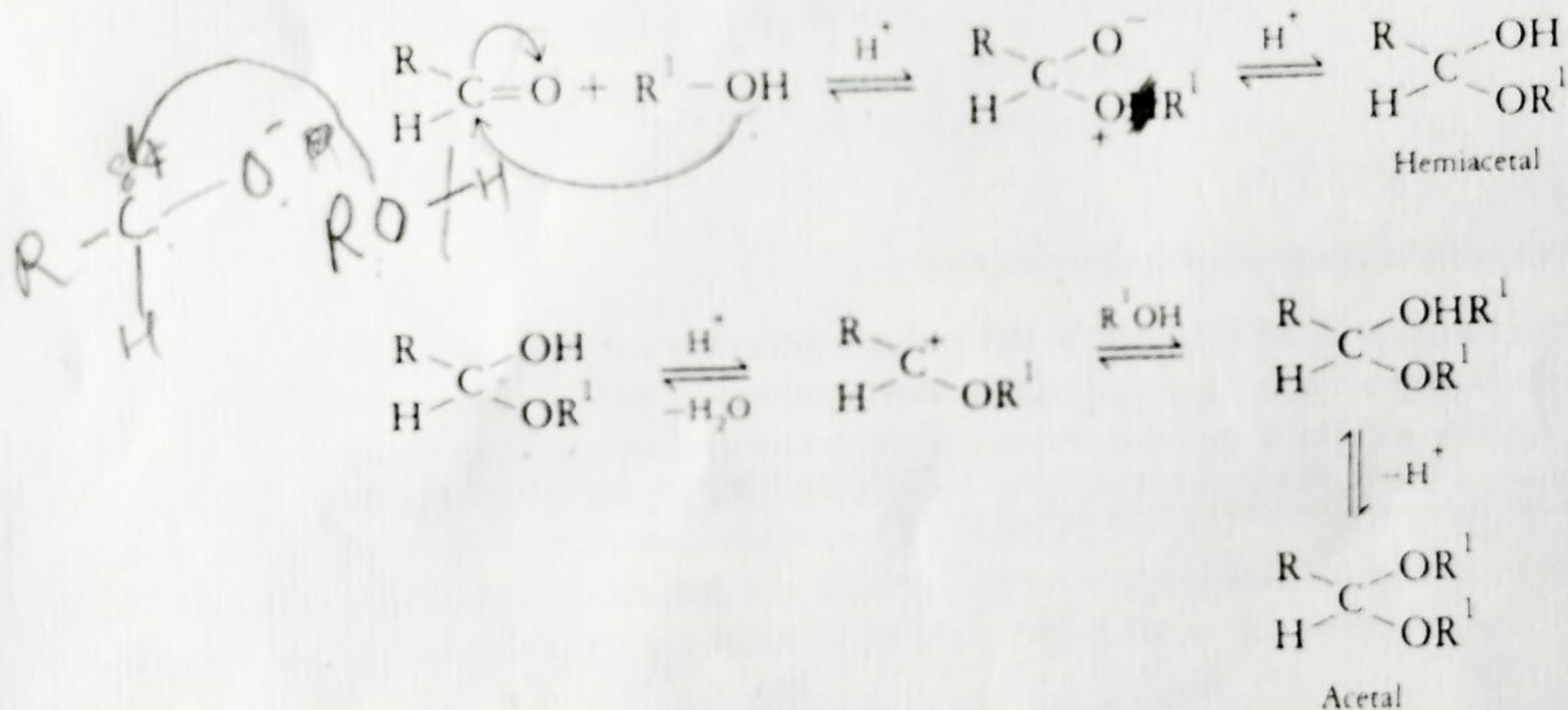


Mechanism

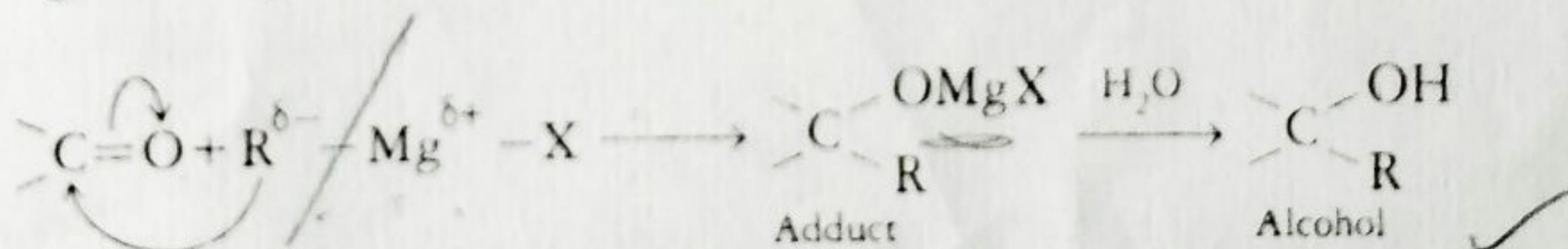




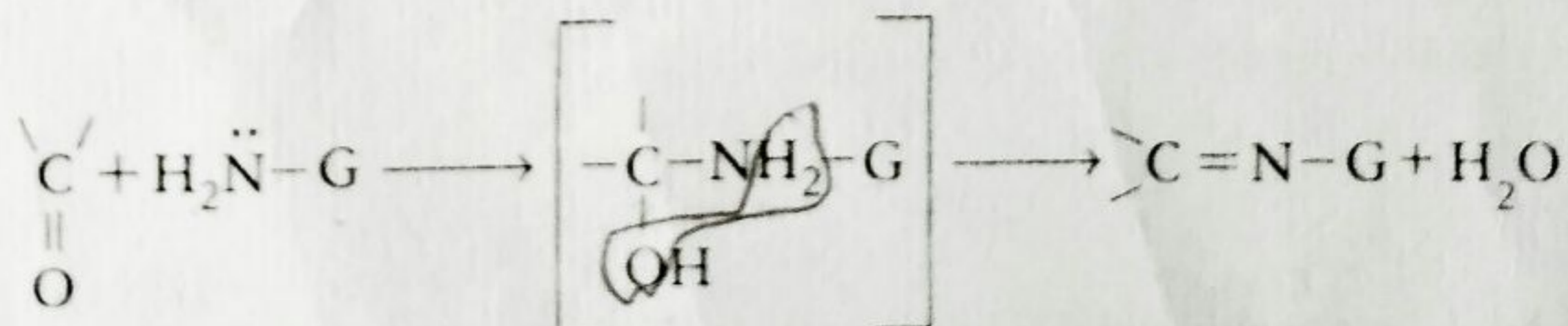
3. Addition of alcohol to carbonyl compounds

*Mechanism*

4. Addition of Grignard reagent



5. Addition of derivatives of ammonia to carbonyl compounds

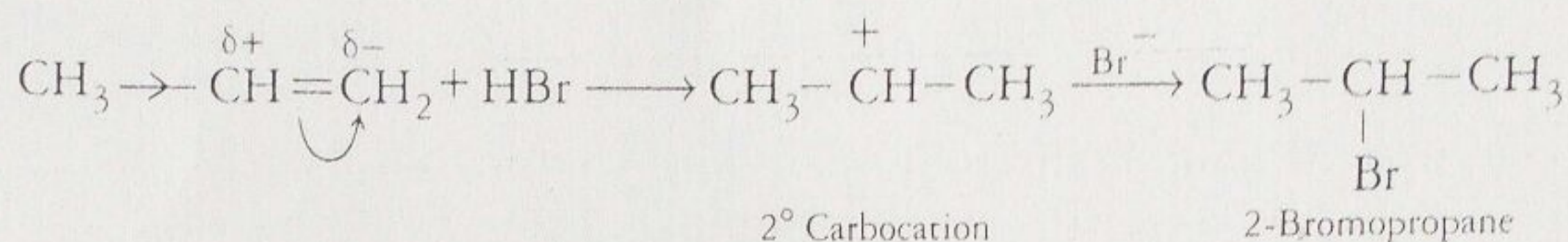


The derivatives and the products formed from them are shown as follows:

Markownikoff, a Russian chemist, formulated an empirical rule called Markownikoff's rule to explain this reaction. According to this rule, the negative end of the reagent goes to the carbon atom containing lesser number of hydrogen atoms.

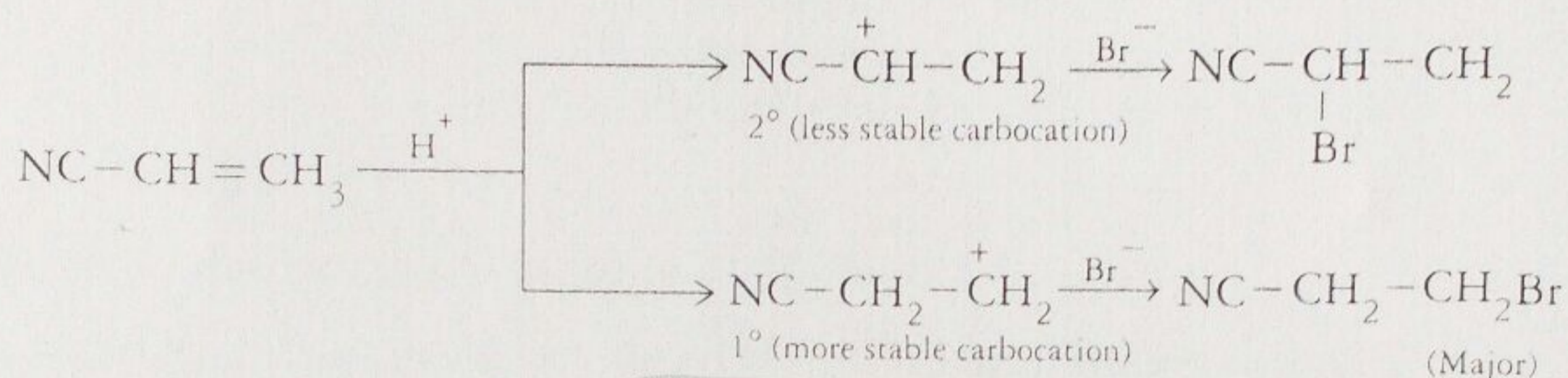
Mechanism

Mechanistically, Markownikoff's rule can be explained as follows

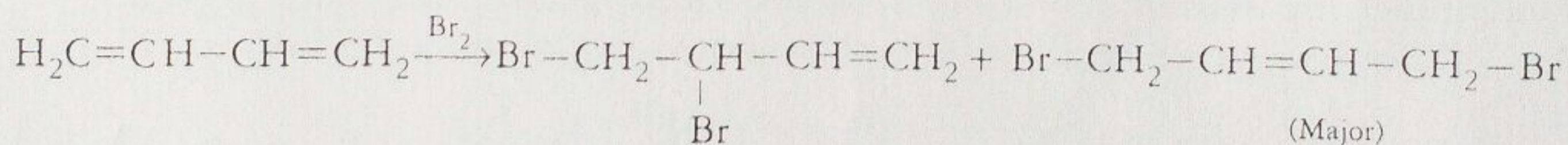


In this case, +I effect of the methyl group displaces the π electrons towards the terminal carbon atom, because of which it gets a partial negative charge. So H^+ adds to the terminal C atom, followed by addition of bromide ion.

Markownikoff's rule is, however, not applicable to alkenes which contain electron withdrawing groups. For example

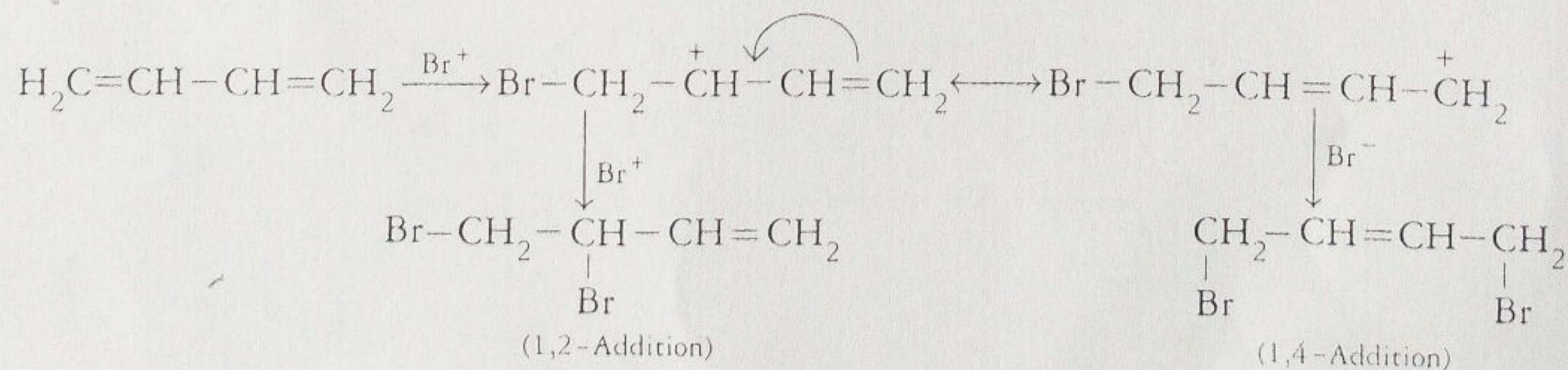


3. **Addition to conjugated dienes:** When a conjugated diene like 1,3-butadiene reacts with bromine, the major product obtained is 1,4-dibromo-2-butene.



Mechanism

Mechanistically, this can be explained as follows:



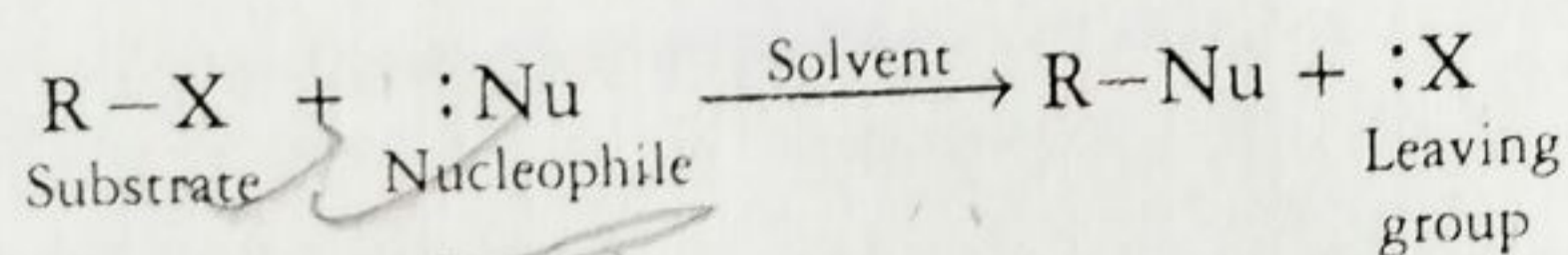
In this reaction, the 1,2-addition product predominates at lower temperatures and 1,4-addition product predominates at higher temperatures.

9.7 Substitution Reactions

In these types of reactions, an atom or group replaces another atom or group present in a compound, without causing a change in the structure of that compound. Free radicals, electrophiles or nucleophiles may be involved in these reactions as reactive intermediates to bring about free radical, electrophilic and nucleophilic substitutions, respectively.

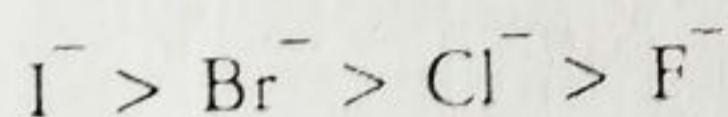
Nucleophilic Substitution (S_N)

These reactions occur in the presence of nucleophiles. Apart from nucleophiles, nucleophilic substitution reaction requires a substrate (which contains an alkyl group and a leaving group) and solvent.



Both nucleophiles and leaving groups are bases, but out of the two, the leaving group is a weaker base. Some terms related to nucleophilic substitution reactions are as follows:

- Nucleophilicity:** The interaction of the nucleophile with carbon is determined by its nucleophilicity. A good nucleophile should have a large attacking atom, high polarizability and should be weakly solvated.
- Nucleophilicity order:** Iodide ion being large, highly polarizable and weakly solvated is a strong nucleophile as compared to the small, less polarizable and strongly solvated fluoride ion. Therefore, the order is



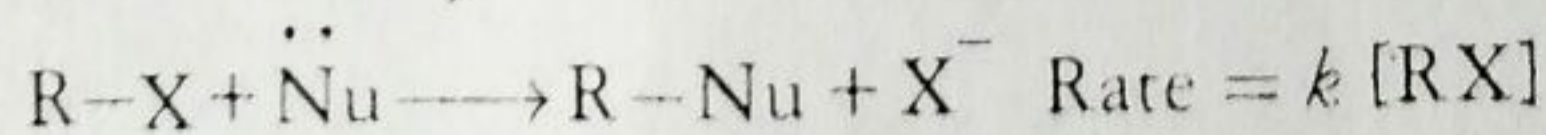
- Leaving group:** A leaving group leaves with the electrons of the σ bond. Better the leaving group, faster is the reaction. The leaving ability of the leaving group (X) depends on three factors:
 - strength of the R-X bond;
 - polarizability of R-X bond;
 - stability of X^- .

A good leaving group should be a weak base.

Nucleophilic substitutions take place mainly by two mechanisms: unimolecular and bimolecular. This can be determined by kinetic studies.

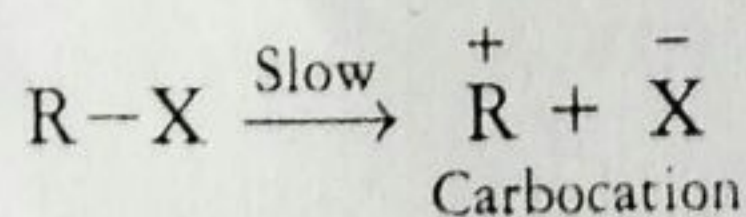
Unimolecular Mechanism (S_N1)

In S_N1 reactions, the rate of the reaction depends only on the concentration of the substrate and is independent of concentration of nucleophile.



Mechanism

It follows first order kinetics and is a two-step mechanism. The first step is the slow step and is the rate determining step.

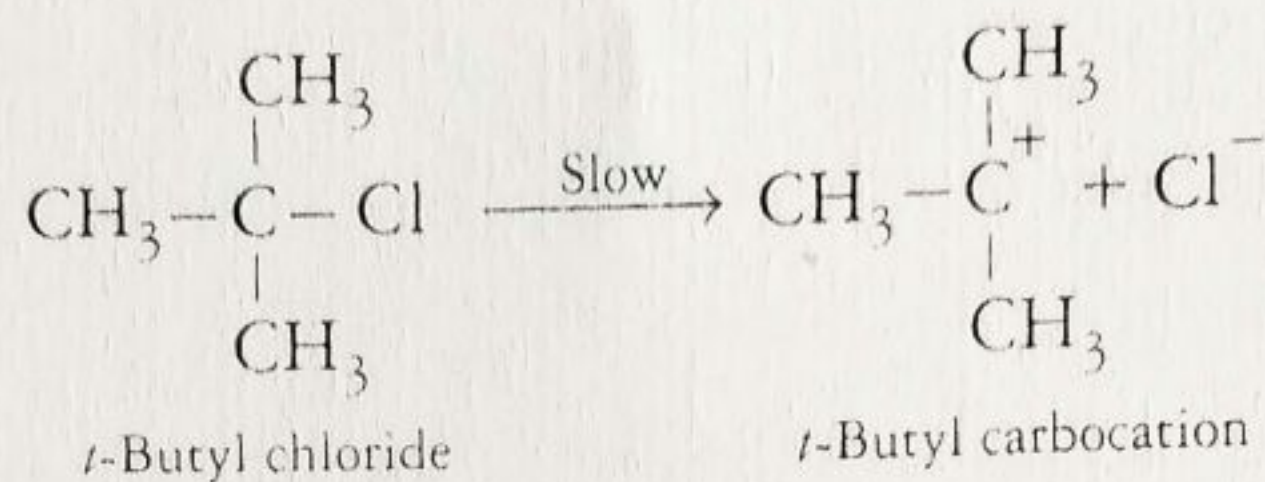


The second step, which is the fast step, involves the attack of the nucleophile on the carbocation. For example

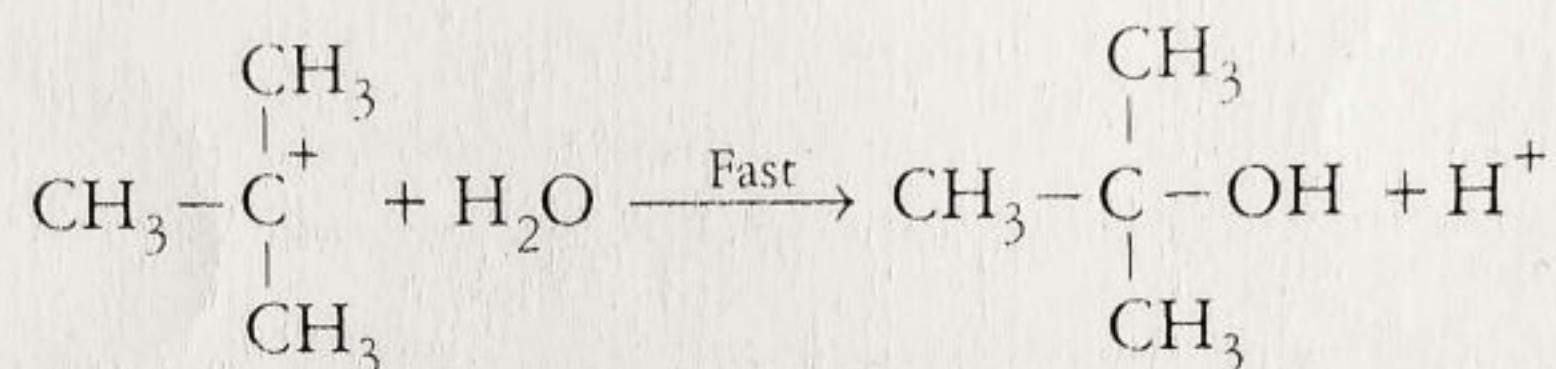


For example, consider nucleophilic substitution on *t*-butyl chloride

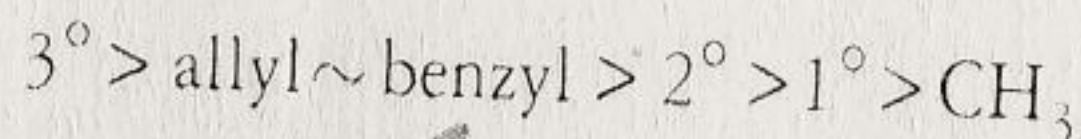
Step 1:



Step 2:

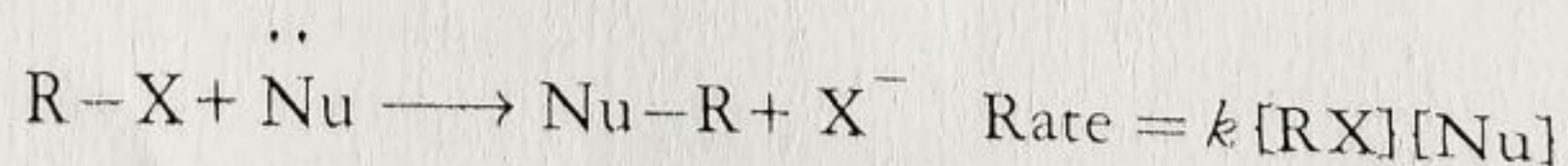


Since the nucleophile can attack the carbocation from either side, the reaction proceeds with racemization. Also, as the rate determining step in S_N1 mechanism is the formation of the carbocation, therefore, the order of reactivity of substitutes will depend on the stability of the carbocation formed after ionization of substrate. Thus, the order of reactivity of alkyl halides is similar to the order of stability of carbocations:



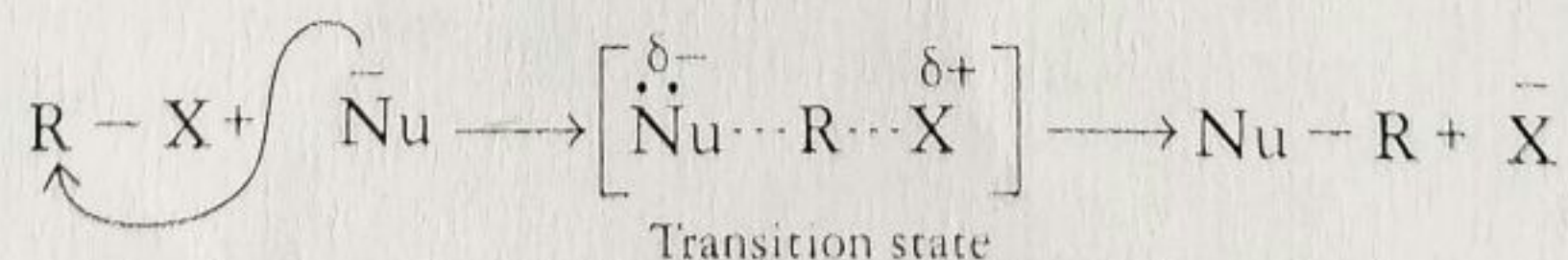
Bimolecular Mechanism (S_N2)

In an S_N2 reaction, the rate of the reaction is dependent both on the concentration of the substrate as well as the nucleophile.



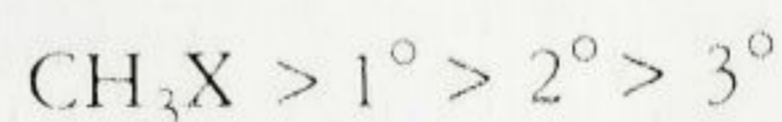
Mechanism

The S_N2 reaction proceeds in a single step via a transition state.



In an S_N2 reaction, there is a simultaneous attack by the nucleophile on the opposite side of the substrate followed by the departure of leaving group. Therefore, in the transition state the nucleophile-carbon bond is partially formed and the C-X bond is partially broken. The nucleophile cannot attack from the side of the molecule bearing the leaving group due to electrostatic repulsion and also due to steric factors. Thus, the attack will be from side opposite to the leaving group and the substitution reaction will proceed with inversion of configuration. This inversion is called Walden inversion.

Steric hindrance around the central carbon atom plays a significant role in the rate of S_N2 reaction. The reactivity towards S_N2 mechanism decreases with increase in number of substituents on the carbon bearing the leaving group. The reactivity in S_N2 mechanism follows the order:

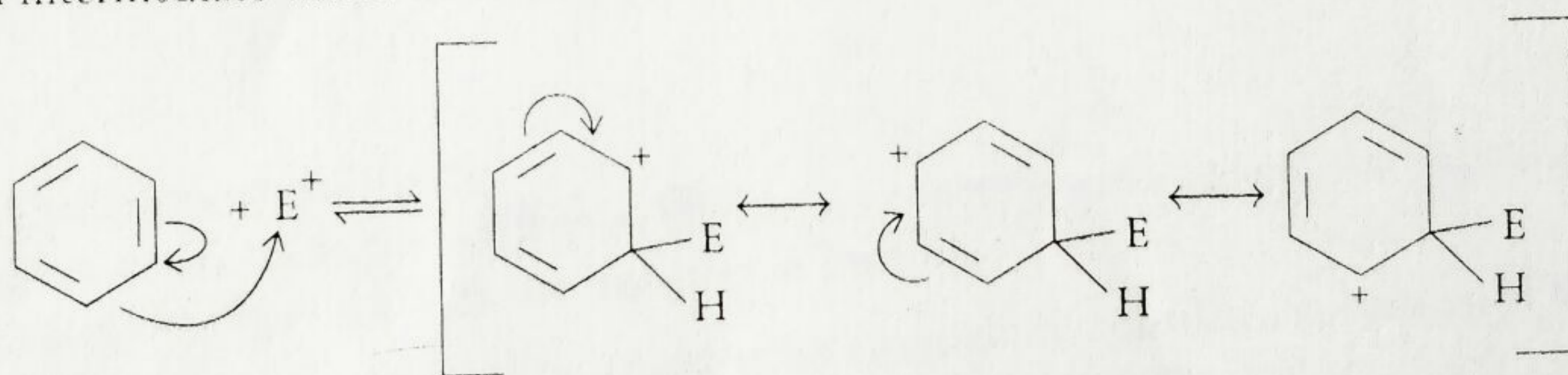


In the reactant and product, the central carbon atom is tetrahedral and in the transition state it is bonded to five atoms or groups. Therefore, we see that there is an increase in crowding moving from the reactant to the transition state. As the hydrogen atoms are replaced by the larger methyl groups, there is increased crowding about the central carbon atom and hence, it is difficult for the nucleophile to attack.

Electrophilic Substitution

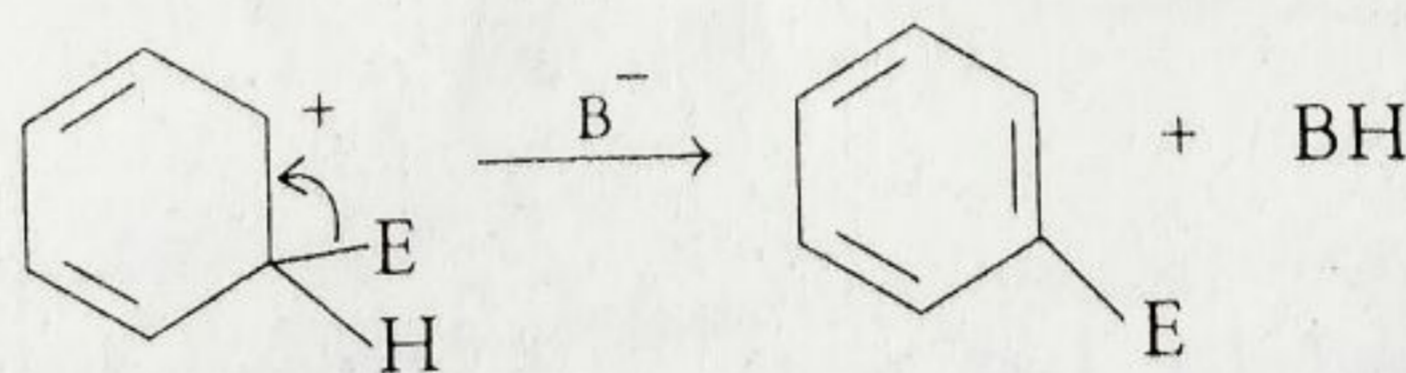
This substitution reaction occurs in the presence of an electrophile. Aromatic systems with high electrons density generally undergo substitution by this mechanism. For example, benzene has delocalized π electrons and there is a concentration of negative charge above and below the plane of the ring-carbon atoms. This promotes the attack of electrophile E^+ . The mechanism of electrophilic substitution in aromatic systems involves three steps:

1. **Generation of the electrophile:** In the first step, the reagent is ionized to generate an electrophile.
2. **Attack of electrophile on π -electron system:** The electrophile attacks on the benzene ring to give an intermediate which is resonance stabilized.



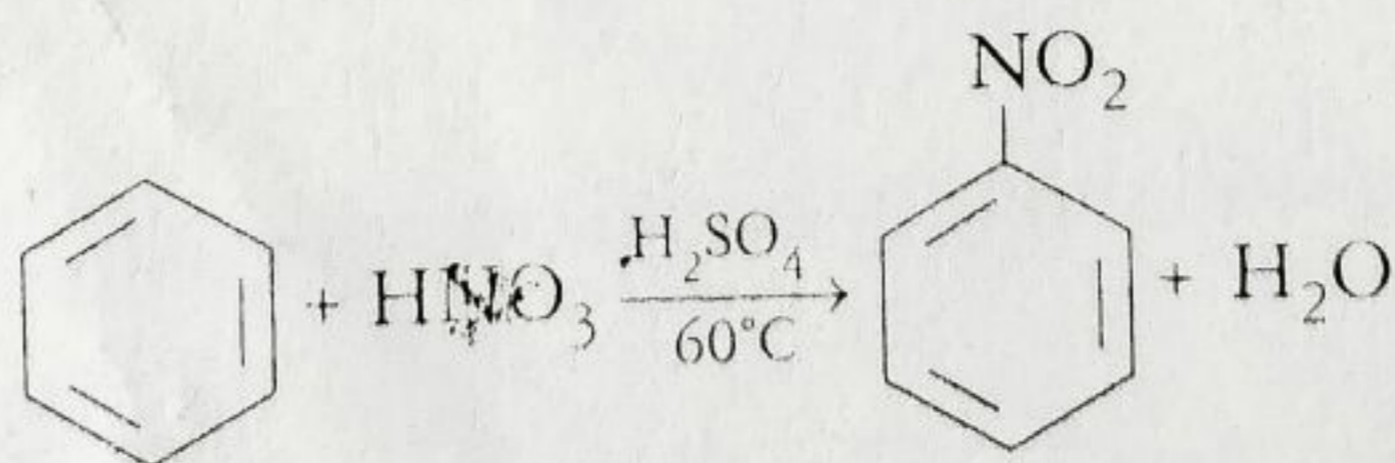
This is generally the rate determining step.

3. **Removal of proton by base:**



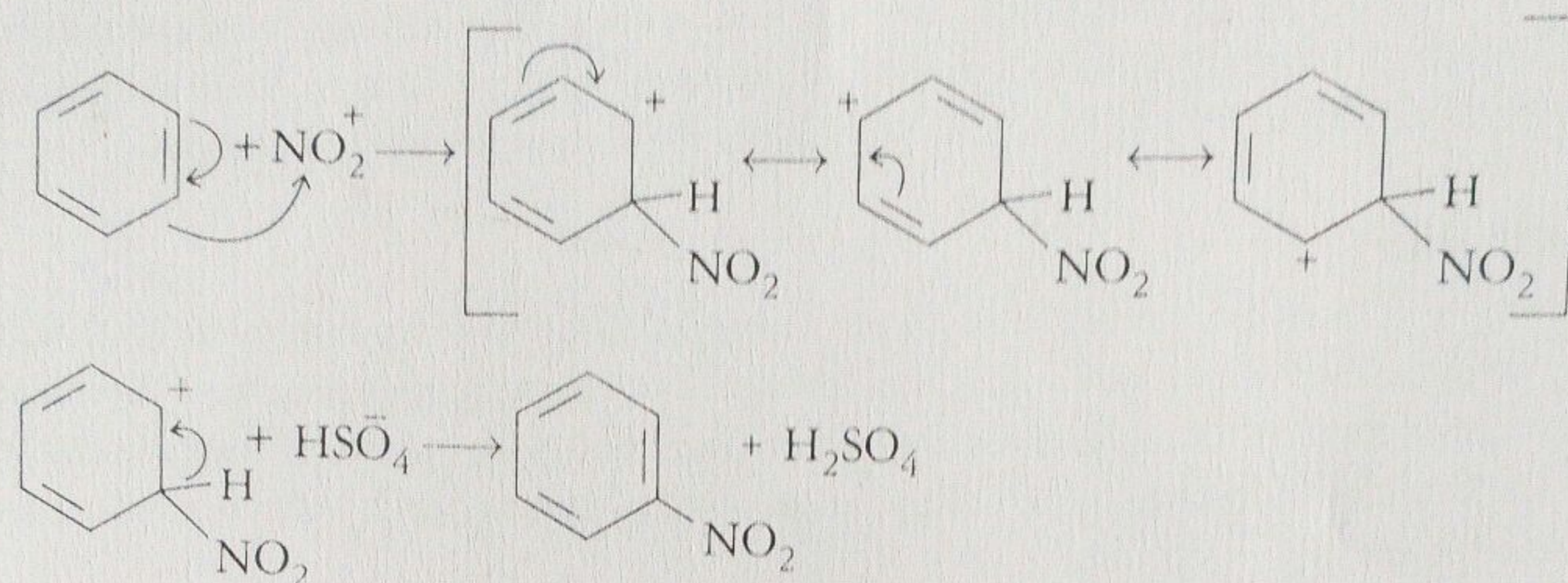
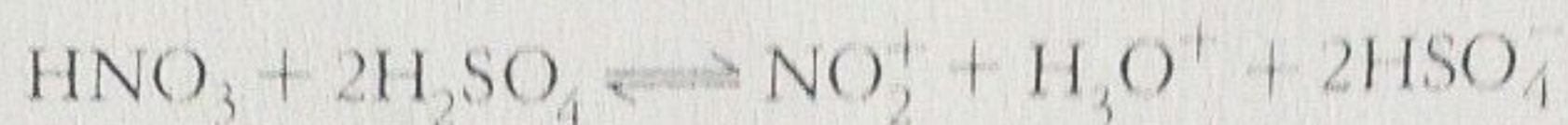
The examples of electrophilic substitution include nitration, halogenation, sulphonation of aromatic system, Friedel crafts alkylation, acidification, etc. The detailed mechanisms of a few of these are described as follows:

1. **Nitration:** This is most frequently carried out with a mixture of concentrated nitric acid and sulphuric acid called the nitrating mixture.

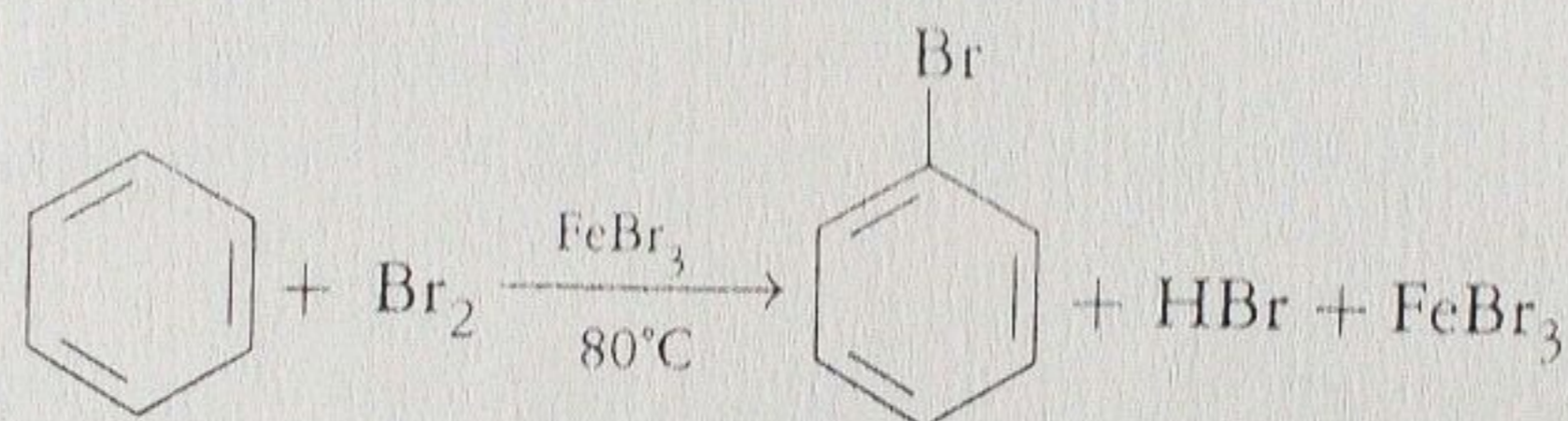


Mechanism

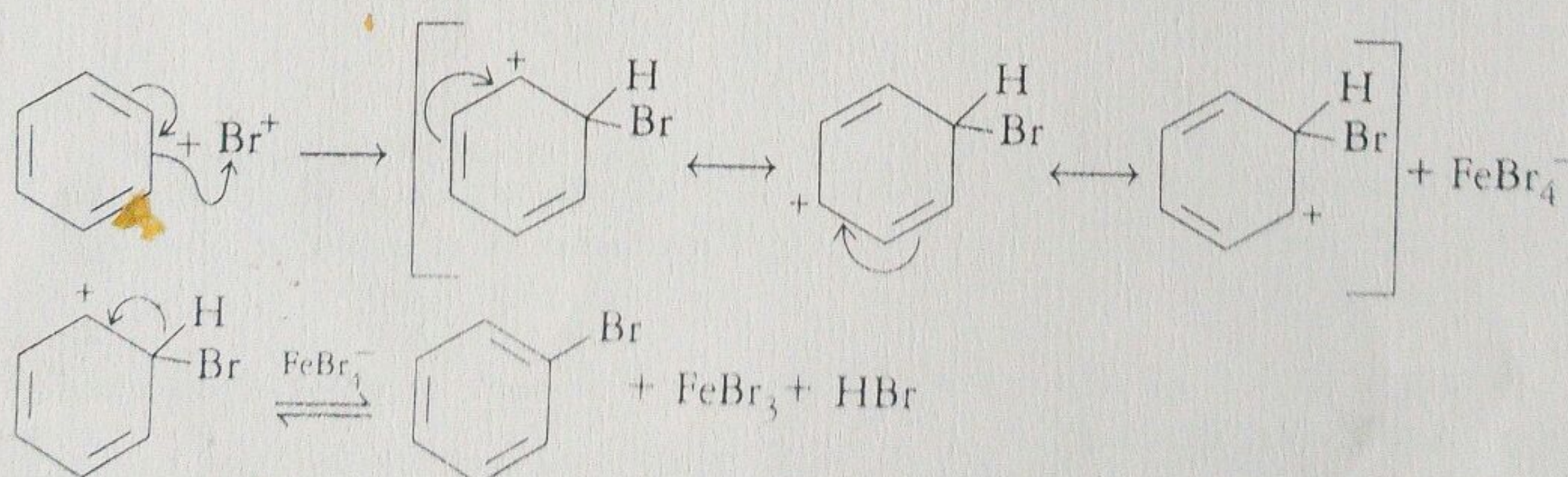
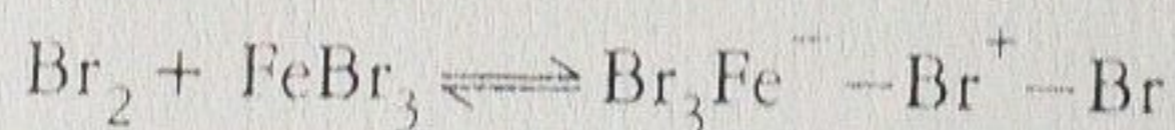
The mixture of concentrated nitric acid and sulphuric acid (1:2 ratio) gives a positive nitronium ion NO_2^+ , which is an electrophile.



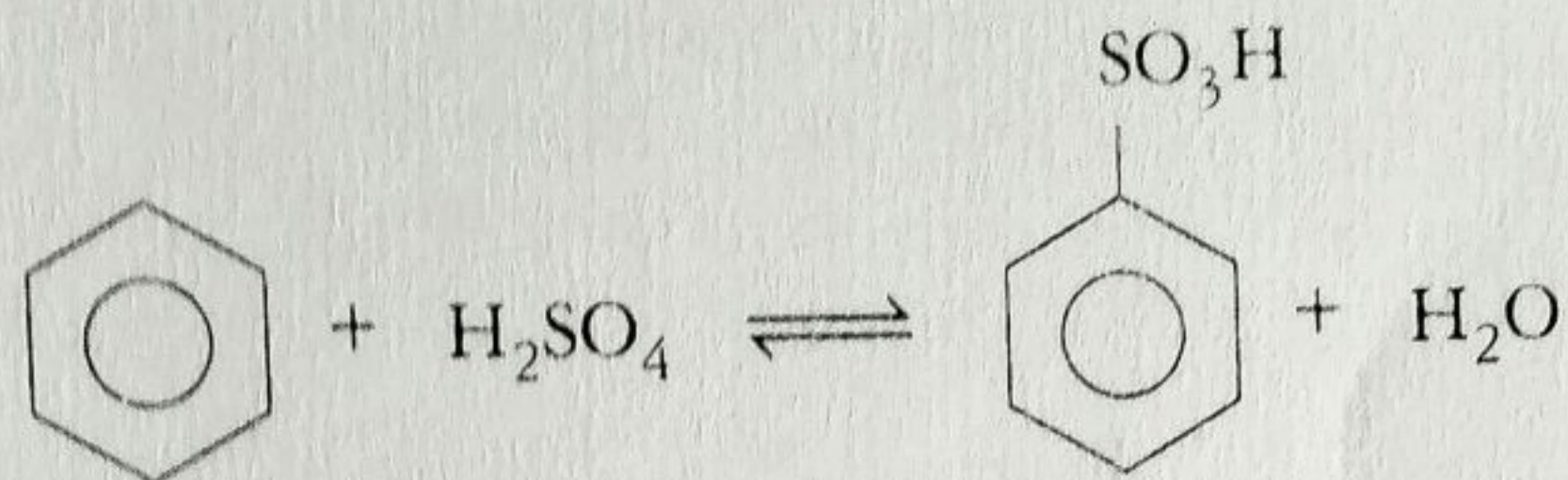
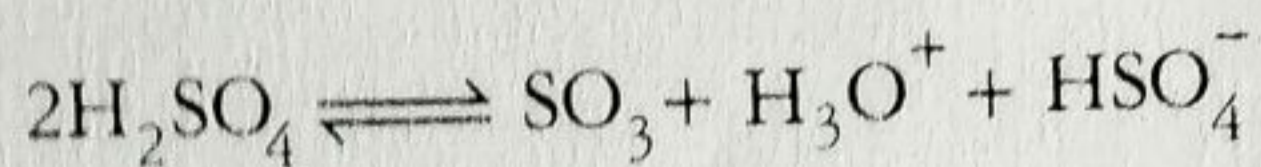
2. **Halogenation:** Benzene can be halogenated with Cl_2 or Br_2 in the presence of Lewis acids, such as FeBr_3 , FeCl_3 , AlCl_3 , etc.

*Mechanism*

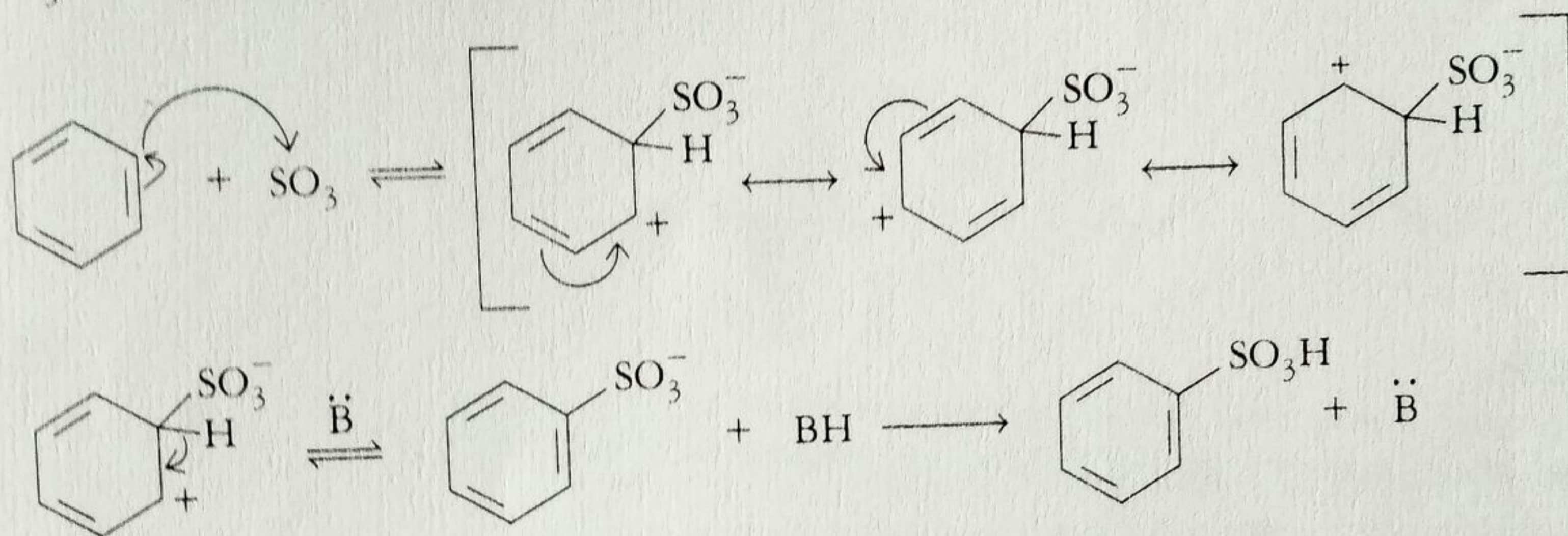
The role of FeBr_3 as a Lewis acid is to polarize the Br_2 molecule, making it more reactive.



3. **Sulphonation:** Benzene can be sulphonated slowly by hot concentrated sulphuric acid, but rapidly by oleum.

*Mechanism*

SO_3 is not positively charged, but it is a strong electrophile because S is deficient of electrons.

**Activating and Deactivating Effects**

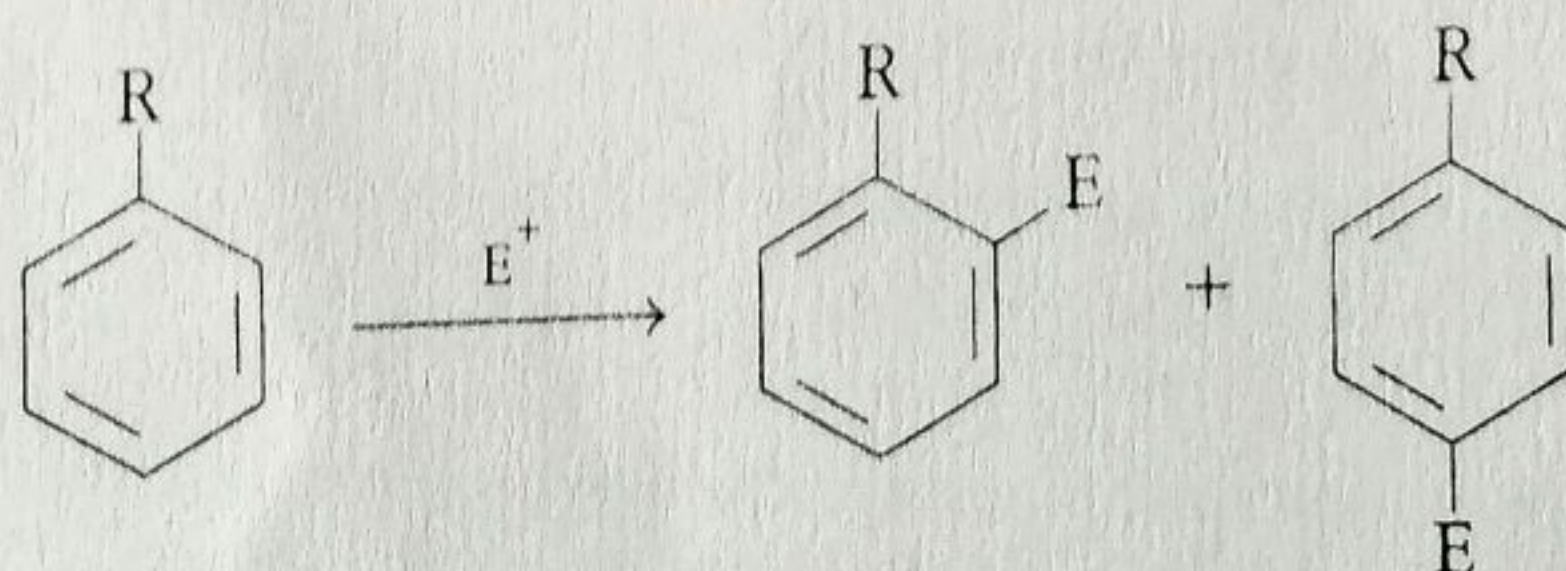
When a substituted benzene derivative undergoes further electrophilic substitution, the substituent already present on the aromatic ring affects the reactivity of the ring.

1. The electron donating groups activate the ring towards electrophilic substitution because of their resonance (+R) and inductive (+I) effects. These groups are called activating groups.
2. The electron withdrawing groups deactivate the ring towards electrophilic substitution because of their -R and -I effects. These groups are called deactivating groups.

Orientation of Electrophilic Substitution

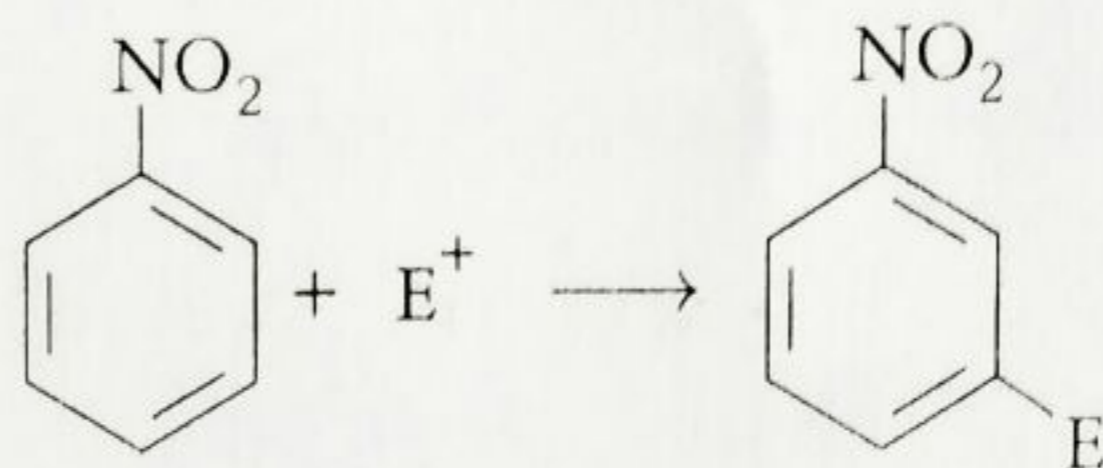
If electrophilic substitution takes place on a mono-substituted benzene ring, the incoming substituent may be incorporated either at the *ortho*, *meta* or *para* position. These substituents which decide the orientation of electrophilic substitution belong to three main categories.

1. Activating groups that direct incoming group to ortho and para position, for example, alkyl groups.

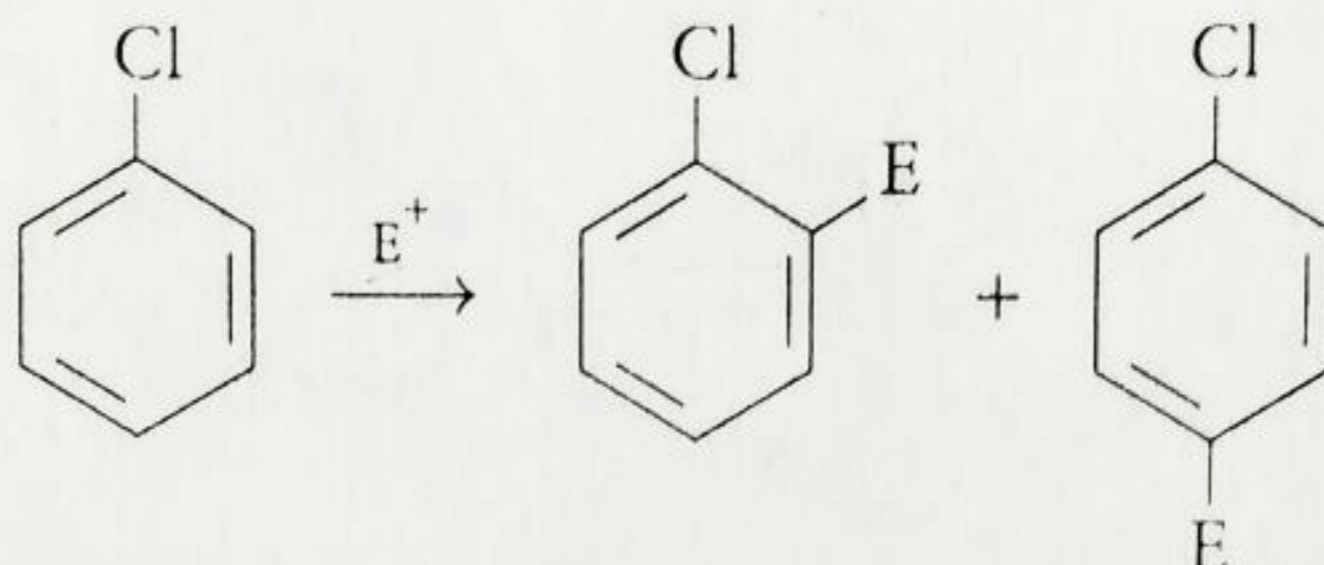


Alkyl group has a positive inductive effect and thus, it pushes the electron density to the ring. It directs the attacking reagent to the ortho and para positions of the ring. Similarly groups such as OH , $-\text{OR}$, $-\text{NHCOR}$, $-\text{NR}_2$ also direct the incoming substituent to the ortho and para positions.

2. Deactivating groups that direct the incoming group to meta positions, for example, NO_2 , COOH , COR , etc.

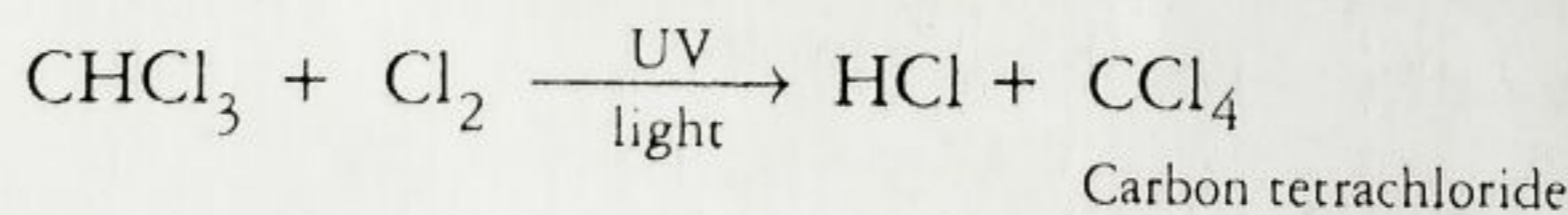
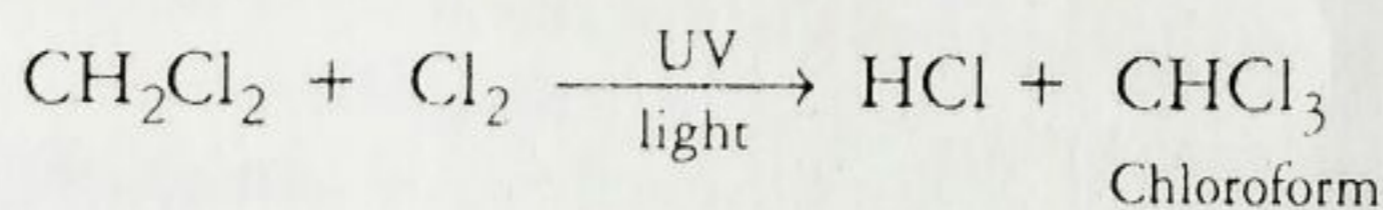
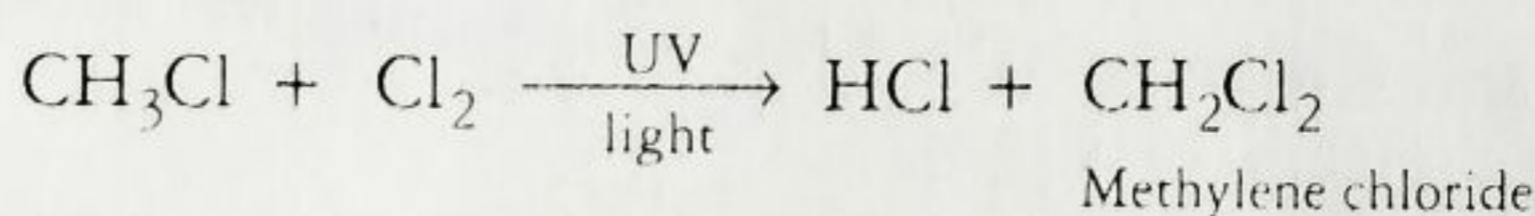
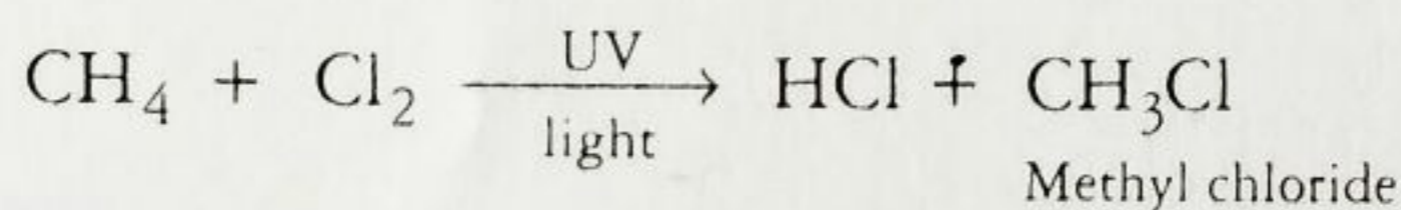


3. Deactivating groups that direct the incoming group to ortho and para positions, for example, F , Cl , Br and I .



Free Radical Substitution

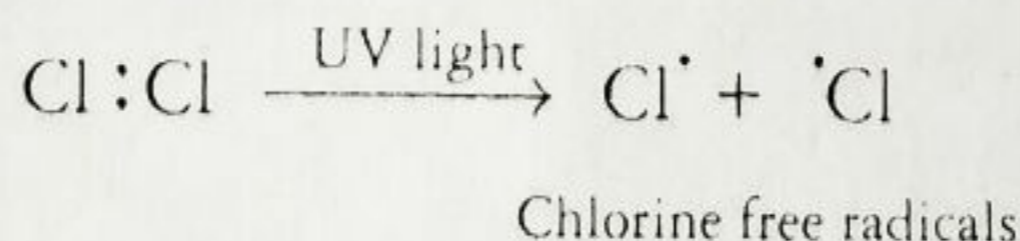
Substitution reactions that proceed through free radical formation are known as *free radical substitutions*; for example, halogenation of alkanes in the presence of light or at a temperature of $300\text{--}400^\circ\text{C}$.



The mechanism of a free radical substitution involves the following steps:

Step I: Chain initiation

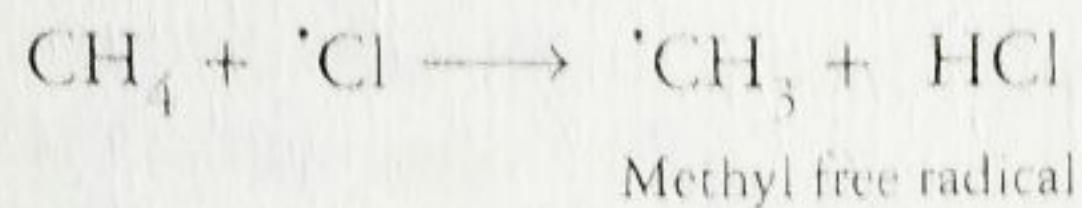
Light energy or heat splits up the chlorine molecule into two chlorine free radicals as a result of homolytic fission.



This homolytic fission is an endothermic process and requires 58 kcal mol^{-1} of energy. Hence, the free radicals produced are energy-rich chemical species.

Step II: Chain propagation

The chlorine free radical attacks the methane and abstracts the hydrogen atom from the CH_4 molecule to produce a methyl free radical ($\cdot\text{CH}_3$) and HCl .



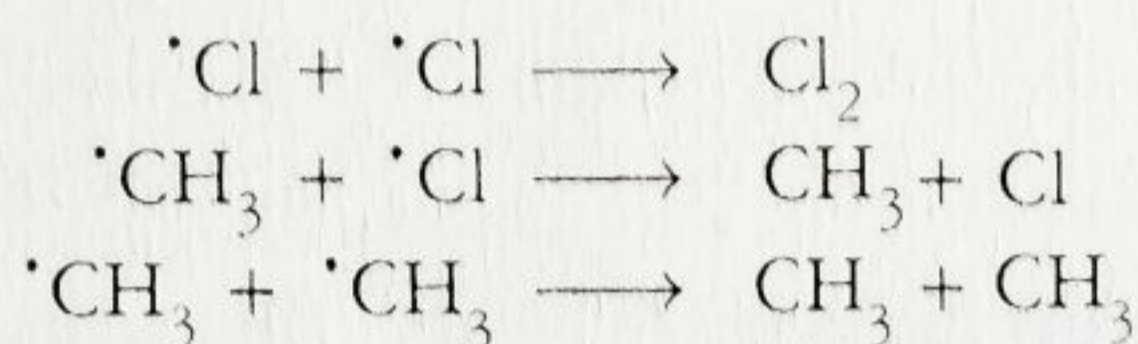
The methyl free radical then attacks the chlorine molecule to form an alkyl halide and a chlorine free radical.



The chlorine free radical thus formed, reacts again and again to create a chain reaction. Propagation steps are exothermic, so they release energy and are repeated several times.

Step III: Chain termination

The propagation of the chain continues until all the chlorine or methane is used up or until the process is terminated by any of the following reactions:

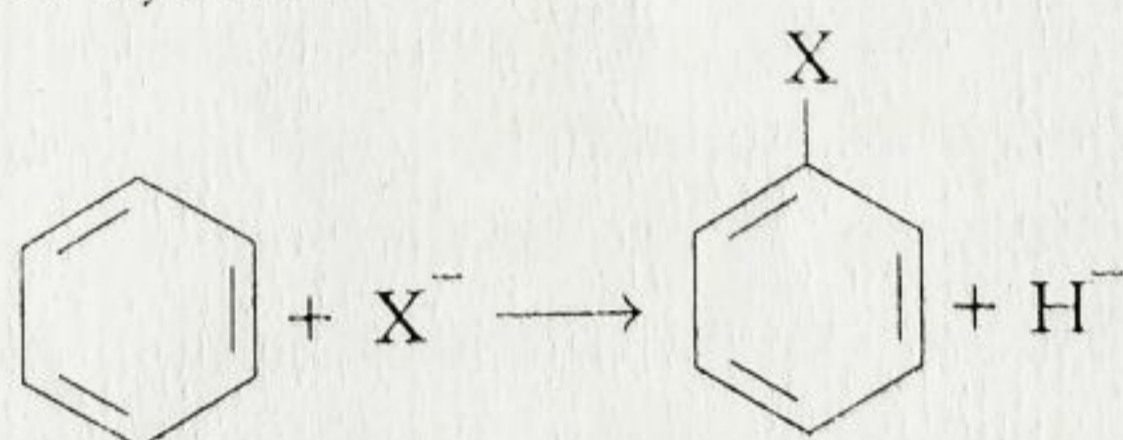


In the last reaction replace $\text{CH}_3 + \text{CH}_3$ with $\text{CH}_3\text{—CH}_3$

Nucleophilic Aromatic Substitution

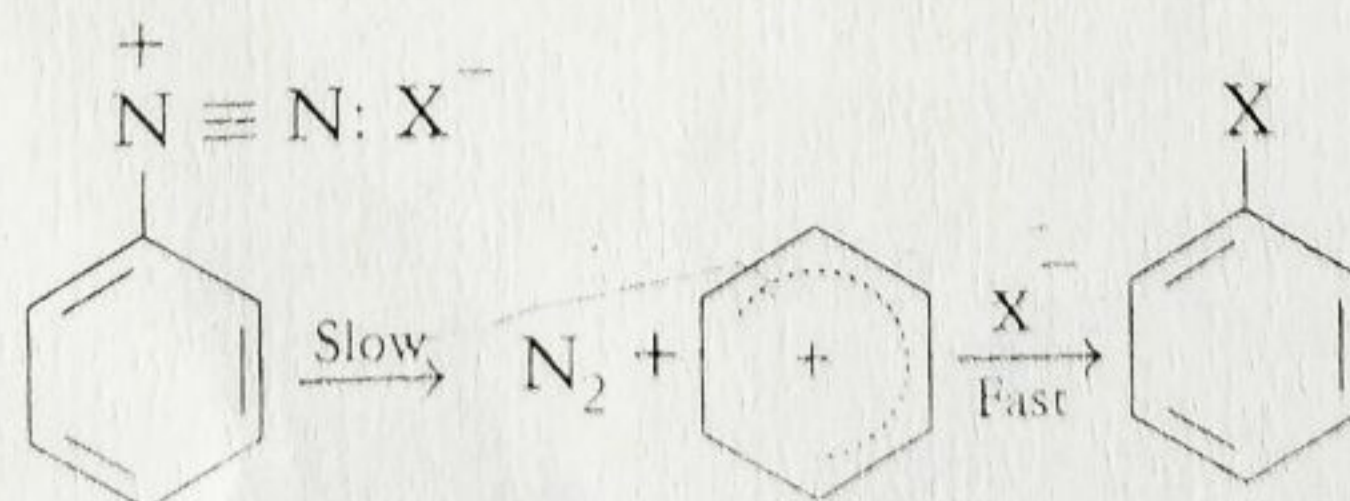
When either hydrogen or any other substituent is replaced by a nucleophilic agent in an aromatic ring, the reaction is known as *nucleophilic aromatic substitution*. Significantly, the substitution does not take place with benzene but with substituted benzene derivatives and naphthalene. Benzene does not undergo nucleophilic substitution due to

1. the concentration of a negative charge above and below the plane of the carbon atoms of the ring and
2. the formation of the less stable hydride ion.



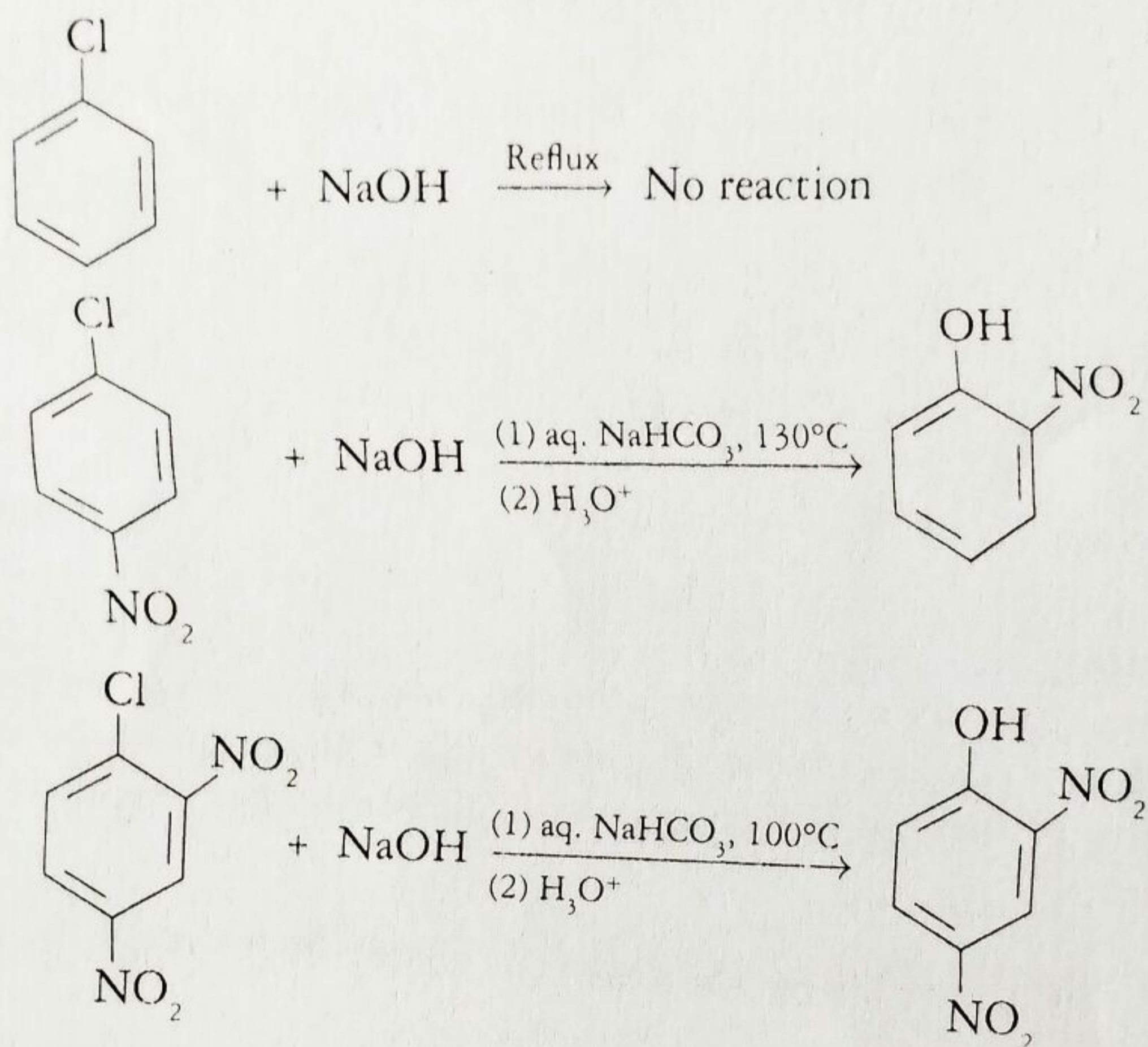
The three main mechanisms through which nucleophilic aromatic substitutions can take place are as under:

1. **Unimolecular mechanism:** Nucleophilic aromatic substitution does not usually occur by unimolecular mechanism because phenyl cations are unstable. There is only one example of such a reaction, which is the uncatalyzed decomposition of the aryl diazonium cation.

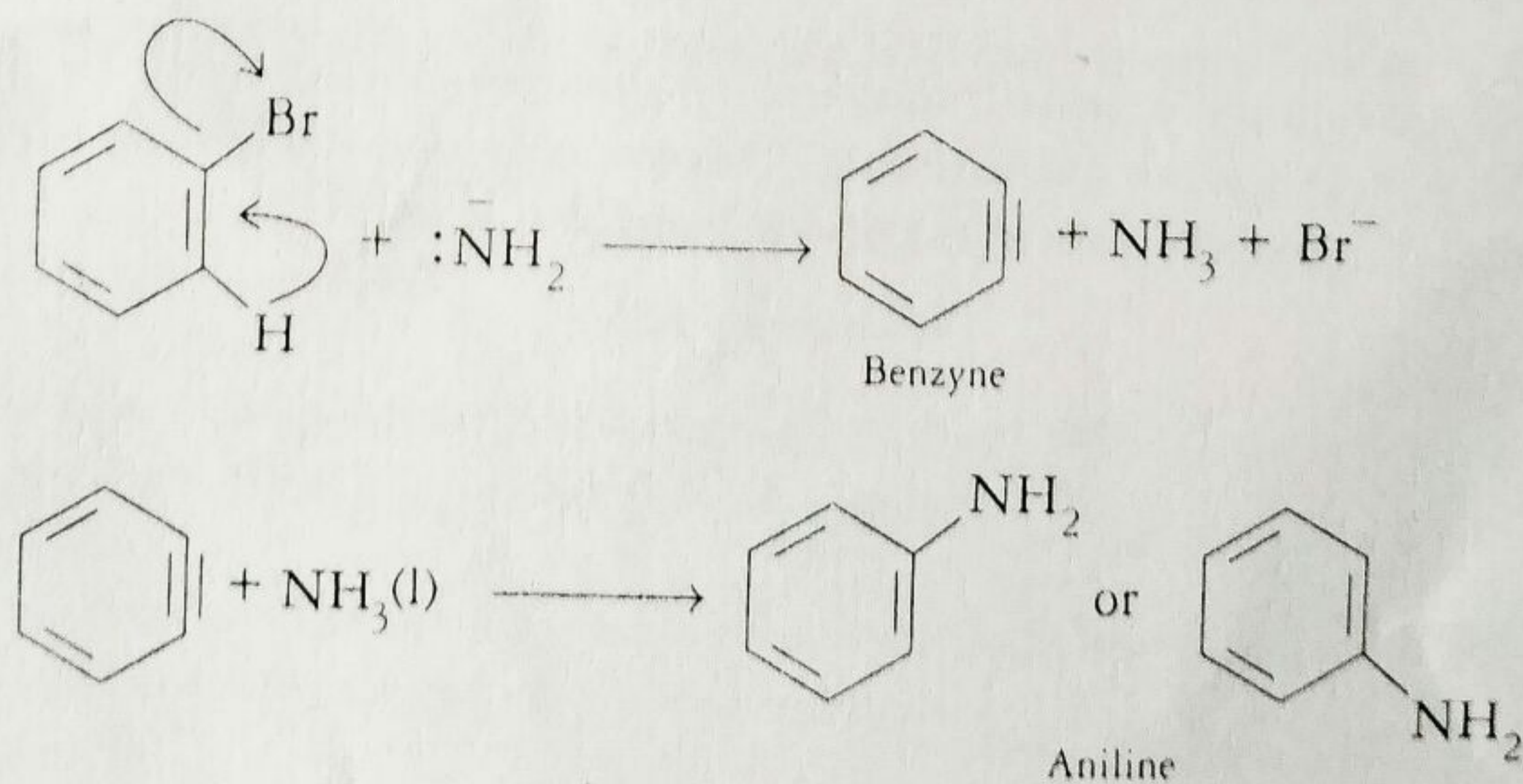


where $\text{X}^- = \text{OH}^-, \text{OR}^-, \text{Cl}^-, \text{CN}^-$ and NO_2^- .

2. **Bimolecular mechanism:** The aryl halides do not readily undergo substitution by bimolecular mechanism because the benzene ring prevents the back-side attack. Also, the carbon-halogen bond is strong and develops double bond character stabilized by resonance structures. However, they become reactive towards nucleophiles and readily undergo substitution in presence of strongly electron withdrawing groups present *ortho* or *para* to the halogen atom. For example, chlorobenzene boiled with sodium hydroxide does not produce phenol except under high temperature and pressure conditions. However, *mono-*, *di-*, and *tri-*substituted chlorobenzenes react with sodium hydroxide at increasingly milder conditions to yield phenol.



3. **Benzyne mechanism:** Although unreactive, aryl halides react with nucleophiles under extreme conditions of temperature and pressure. The reaction proceeds through an elimination-addition mechanism involving a reactive intermediate benzyne. In the first step of the reaction, hydrogen halide (HX) is eliminated from aryl halide. This leads to the formation of highly unstable benzyne intermediate with a triple bond. Finally, the product is formed by addition of the nucleophile to this intermediate. Formation of aniline from bromobenzene is one example:

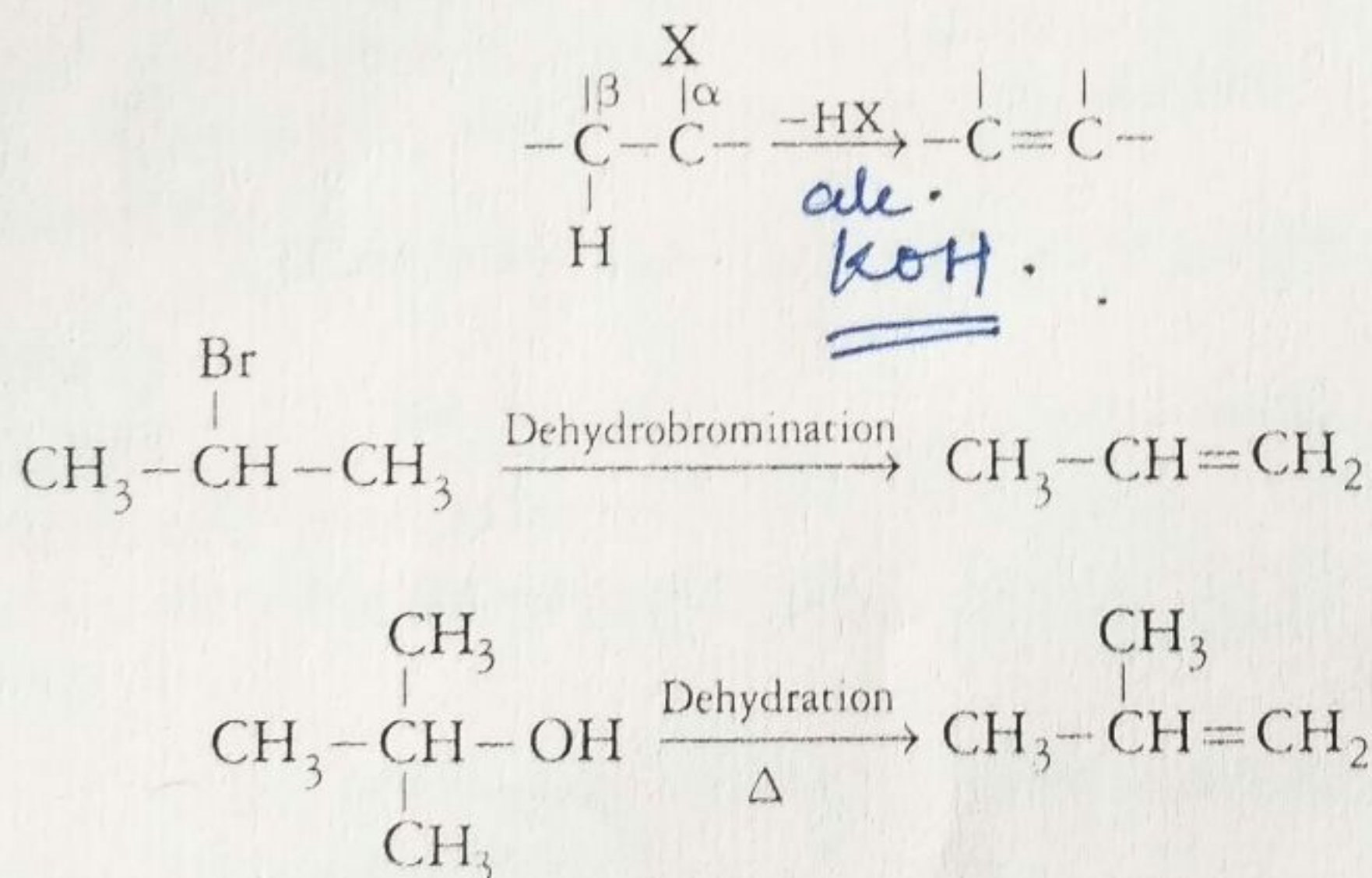


Concept Check

- The reactivity of alkyl halides towards S_N1 mechanism follows same order as stability of carbocations. Explain.
- Arrange the following in decreasing order of reactivity towards S_N2 substitution:
 CH_3-Cl , CH_3CH_2-Cl , $(CH_3)_2CH-Cl$,
 $(CH_3)_3C-Cl$
- What are the steps involved in electrophilic substitution on aromatic compounds?
- How does the presence of electron donating and electron withdrawing groups affect the reactivity and orientation of further electrophilic substitution in aromatic compounds?
- Why is an aromatic ring unreactive towards nucleophilic substitution? Give an example of nucleophilic aromatic substitution reaction.

9.8 Elimination Reactions

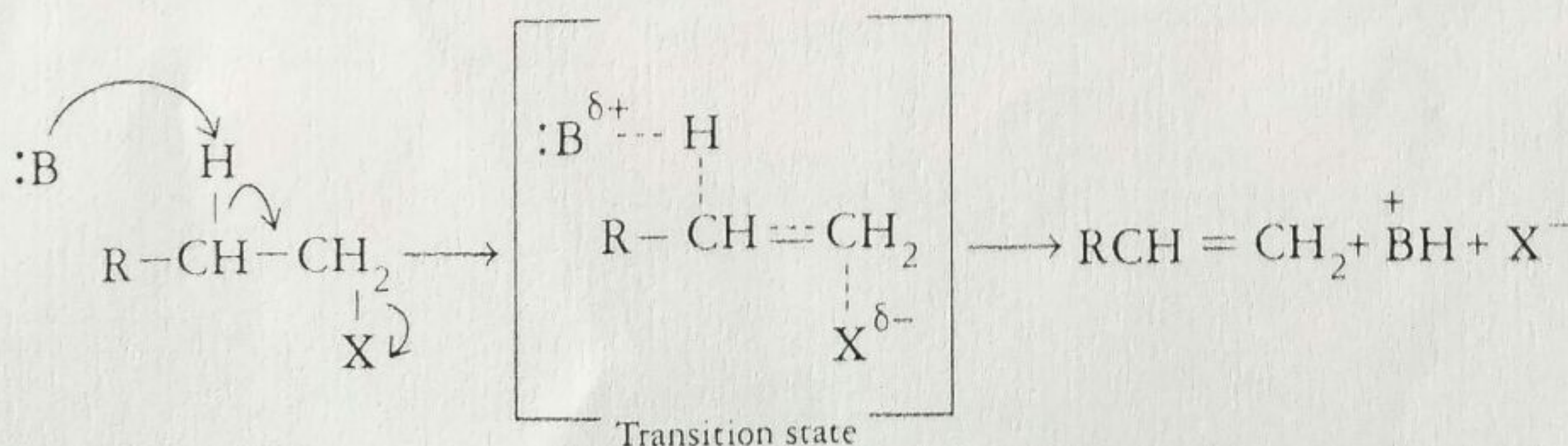
As the term suggests, elimination involves the removal of two atoms or groups. In these reactions, an atom or a group from α -carbon atom and a proton from the β -carbon are eliminated.



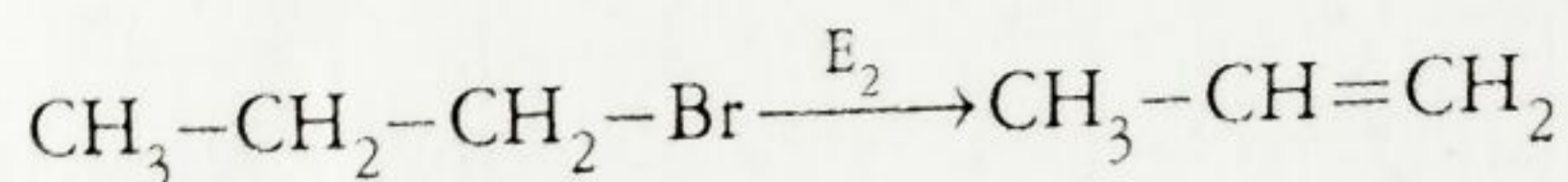
Elimination reactions proceed through two mechanisms: bimolecular and unimolecular.

Bimolecular Elimination Reactions (E_2)

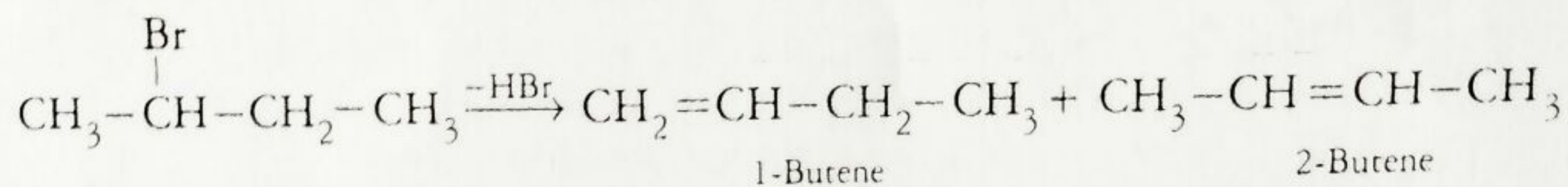
The rate of elimination depends on the concentration of the substrate and the nucleophile in these reactions. The reaction is of second order and is a one-step process just like the S_N2 reaction.



It is also called 1,2-elimination or β -elimination. For example

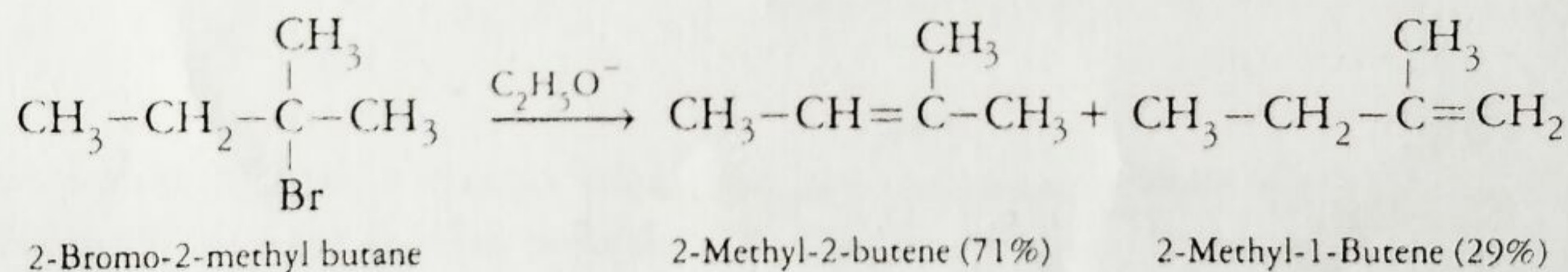
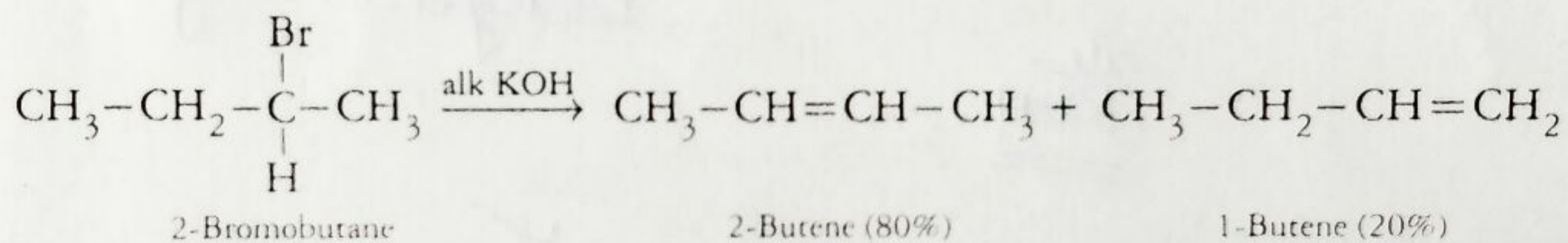
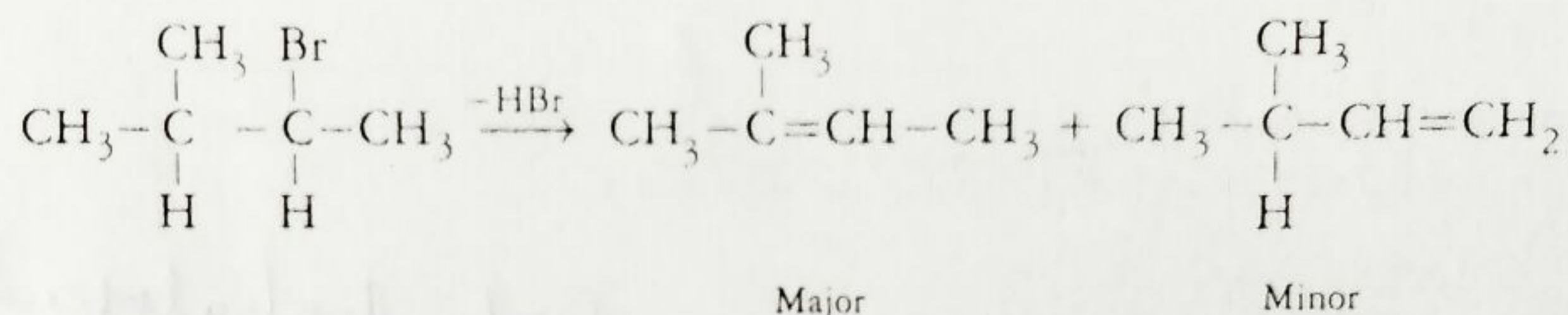


Unsymmetrical substrate, which has hydrogen attached to two different β -carbons, can afford two alkenes. For example, 2-bromobutane on dehydrohalogenation may give 1-butene or 2-butene.



The alkene, which will be obtained in major amount, in the above dehydrohalogenation is decided by Saytzeff rule.

Saytzeff rule: According to this rule, hydrogen is eliminated preferentially from the carbon atom which has less number of hydrogen atoms and so the highly substituted alkene is the major product.



Unimolecular Elimination Reactions (E_1)

The rate of elimination depends only on the concentration of the substrate. The reaction is of first order (E_1).

