# Reaction Mechanism

5.1 Addition Reactions:

5.1. (A) Addition to Carbon-Carbon multiple bond

Addition to a Carbon-carbon multiple bond may be initiated by an electrophile, a nucleophile or a free radical. All the three reaction takes place by a two-step mechanism, the second step consisting of the combination of the resultant intermediate with a negative species, a positive species or a neutral entity.

Electrophilic Addition:

In this mechanism a positive species approaches the double or triple bond and in the first step forms a bond by converting the π-pair of electrons into a σ-pair.
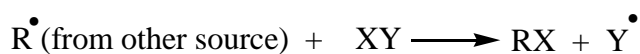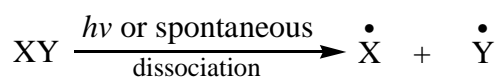
Step-1:

Step-2:
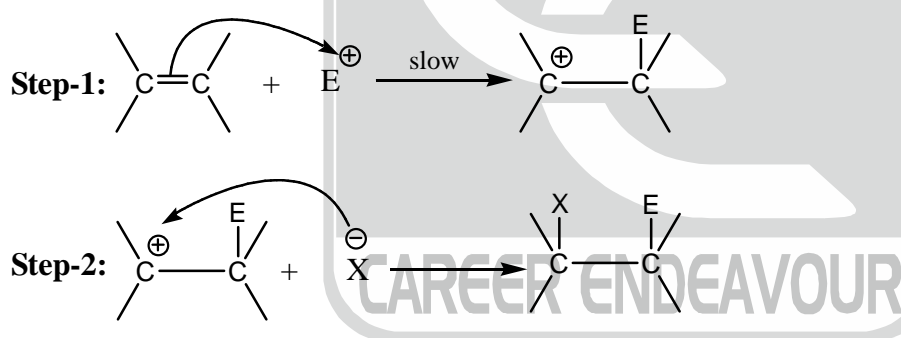
Nucleophilic Addition:

In the first step of Nucleophilic addition a nucleophile brings its pair of electrons to one carbon atom of the double or triple bond, creating a carbanion. The second step is combination of this carbanion with a positive species.
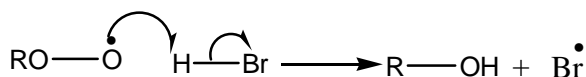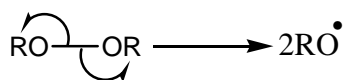
Step-1:

Z = Electron withdrawing group
Example: CHO, COOH, COOEt, CN, etc

Step-2:
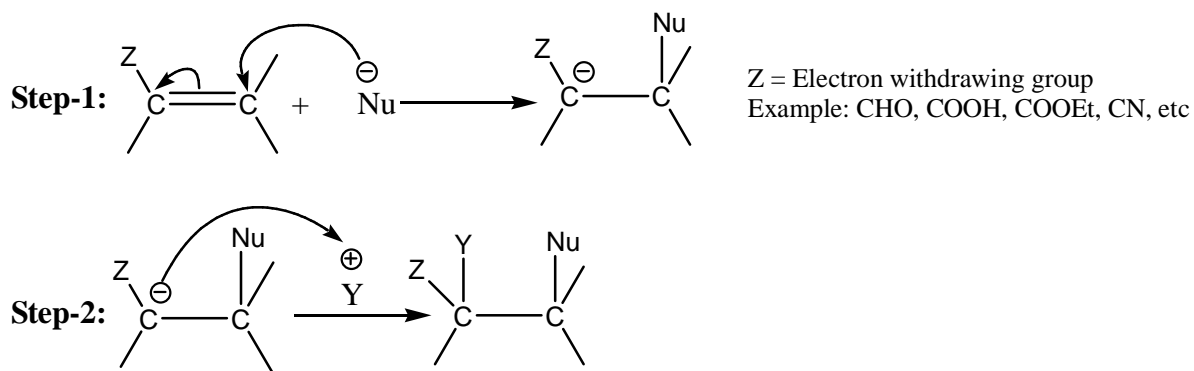
Free Radical Addition :

The mechanism of free-radical addition occur in two steps. Free radicals are generated by homolytic cleavage in the inition steps. Reactions occur through propagation steps.
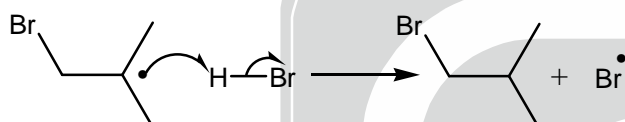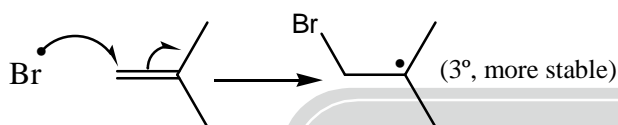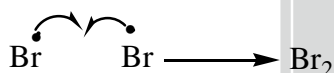
$$XY \xrightarrow[\text{dissociation}]{hv \text{ or spontaneous}} \overset{\bullet}{X} \quad + \quad \overset{\bullet}{Y}$$

$$\overset{\bullet}{R}\text{(from other source)} \quad + \quad XY \longrightarrow RX \quad + \quad \overset{\bullet}{Y}$$

Radical chain reaction consist of

- Initiation Steps:

RO—OR ⟶ 2RO•

RO—O H—Br ⟶ R—OH + Br•

- **Propagation Steps:**
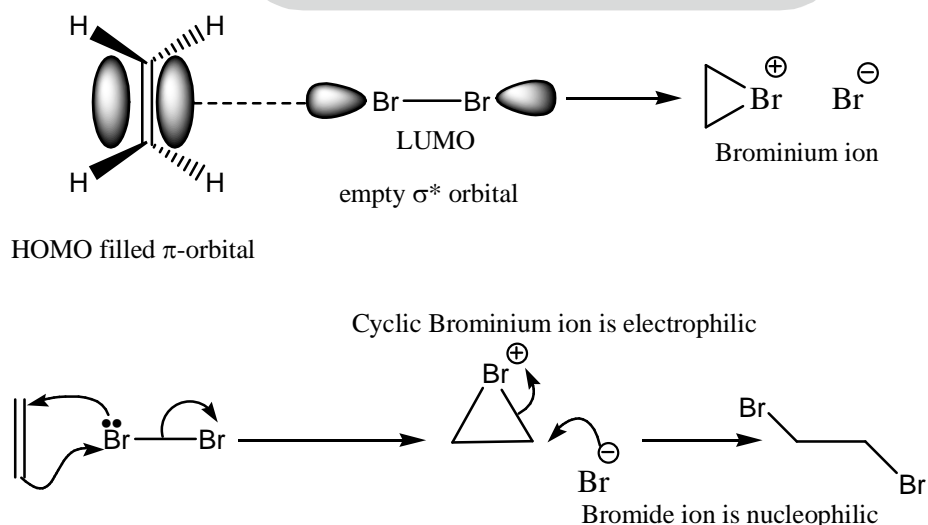

(3°, more stable)

- **Termination Step:**

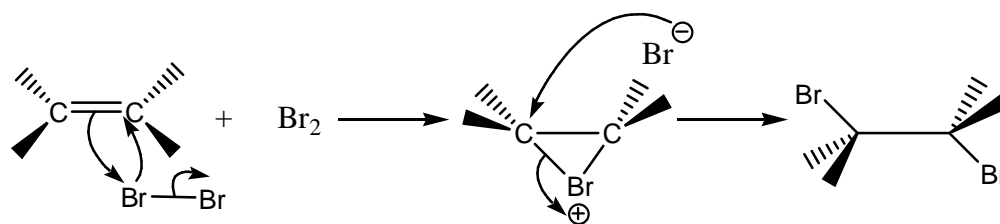Br• Br• ⟶ Br₂

5.1. (B) Addition of halogen to alkenes

In the reaction with ethylene, the alkene must be nucleophile and its HOMO is the C=C π-bond. Other simple alkenes are similarly electron rich and they typically act as Nucleophile and attack electrophiles.

Simple unconjugated alkenes are nucleophilic and react with electrophiles.

Alkene's filled π-orbital (the HOMO) will interact with the bromines empty σ* orbitals to give a product. π-HOMO can interact in a bonding manner with σ* LUMO is if the Br_2 approaches end on.

LUMO

Brominium ion

empty σ* orbital

HOMO filled π-orbital

Cyclic Brominium ion is electrophilic

Bromide ion is nucleophilic

Electrophilic Addition to Symmetrical Alkene:

In case of unsymmetrical alkene, nucleophile preferably attacks the more substituted carbon.


(±)-anti-1, 2-dibromo-cyclohexane
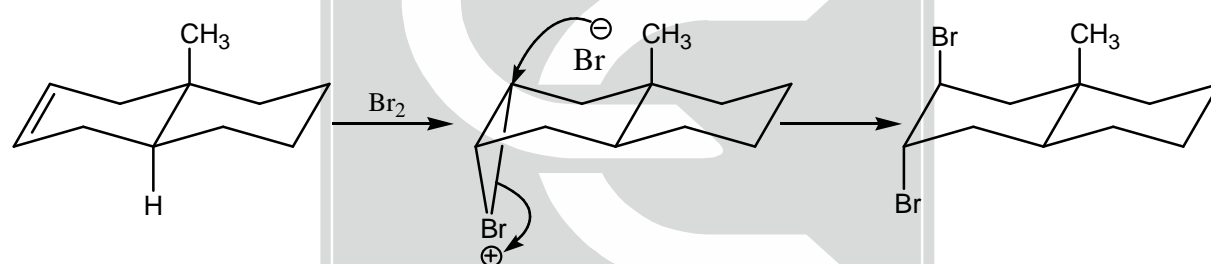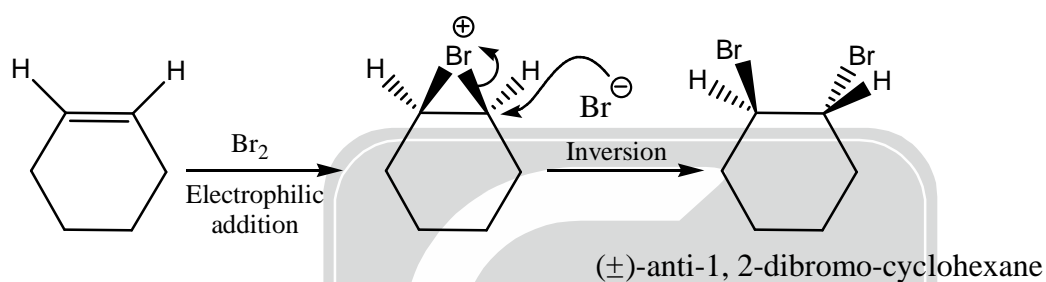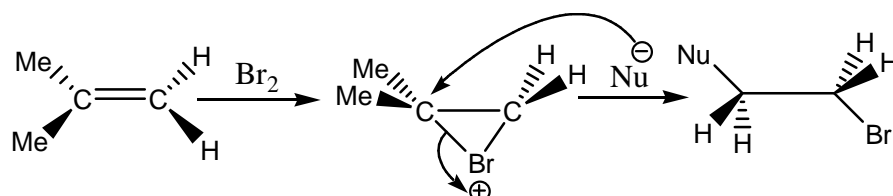
Halogenation involves elecrophilic attack, substituents on the double bond that increases electron density increases the rate of reaction, whereas electron withdrawing group substituents decreases the rate of reaction. Most simple alkenes add bromine in a stereospecific manner, giving the product of anti-addition. Cyclic positively charged brominium ion intermediate provide an explanation for the observed anti-stereospecific.

Electrophilic addition to alkenes can be stereospecific.

Bromination of alkenes is a stereospecific process as the geometry of the starting alkene determines which diastereoisomer is obtained.

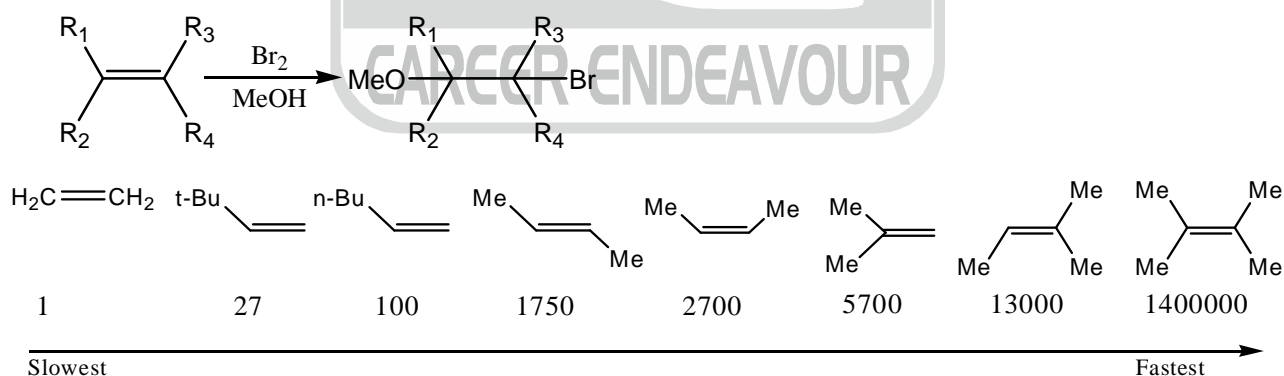On bromination *Z* but-2-ene gives *d/l* pair and *E*-but-2-ene gives *meso* compound.

Z-But-2-ene

d/l pair

Enantiomers

E-But-2-ene → Br₂ → ... → A + B → Identical, *meso* compounds
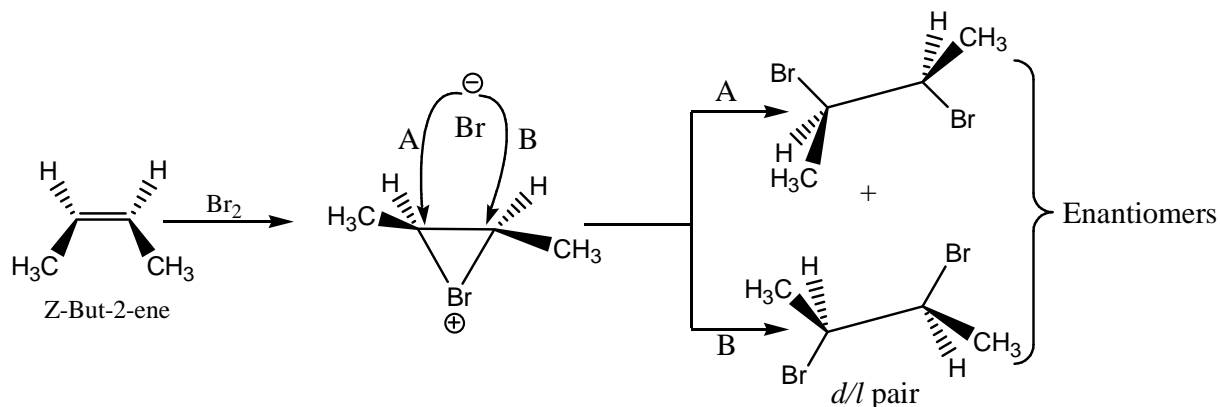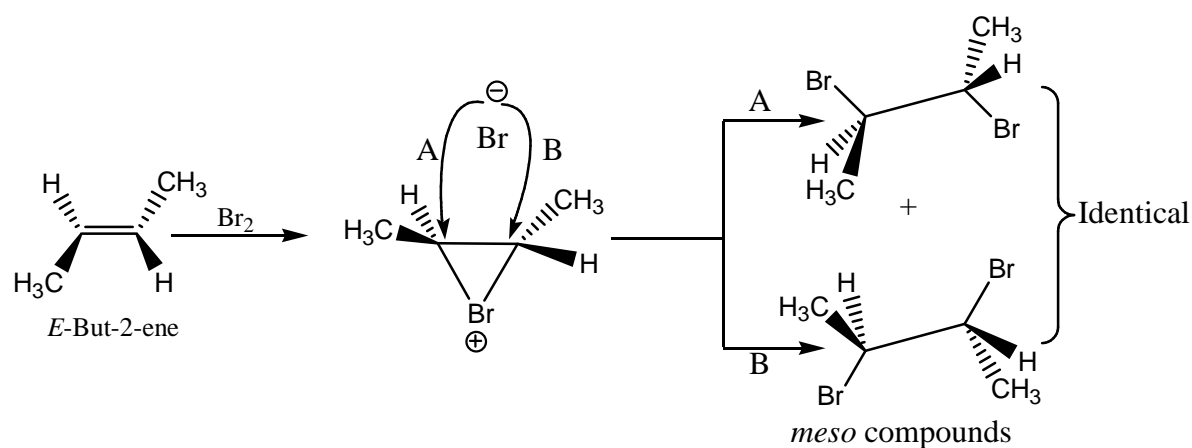
The bridging by bromine prevents rotation about the remaining bond and backside nucleophilic opening of the brominium ion leads to the observed anti-addition.

A substantial amount of syn addition is oberved for Z-1-phenylpropene (27–30% syn addition), E-1-phenylpropene (17–29% syn addition), and cis-stilbene (upto 90% syn addition in polar solvents).


28%   72%

83%   17%
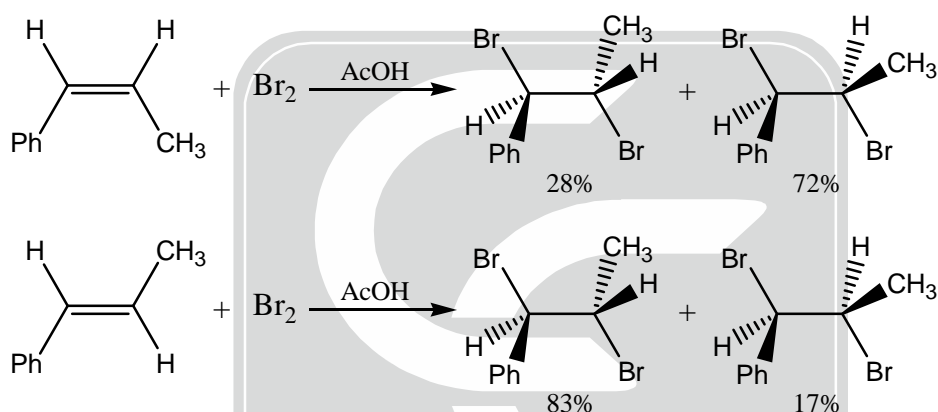
Rates of bromination of alkene:
Relative rates of reaction of alkenes with bromine in methanol.

H_2C=CH_2	t-Bu ... n-Bu	...	Me ...	Me ... Me	Me ... Me	Me ... Me	Me ... Me ... Me ... Me
1	27	100	1750	2700	5700	13000	1400000

Slowest → Fastest

Phenyl substituted double bond gives syn addition on bromination. The presence of phenyl substituent diminshes the strength of bromine bridging by stabilizing the cationic center.
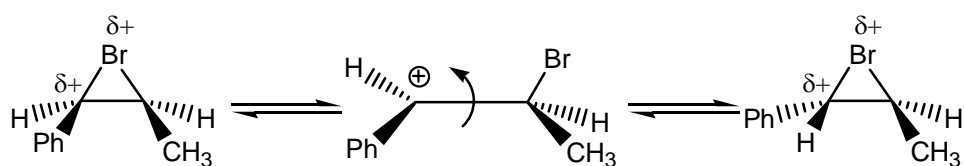

Chlorination of aliphatic alkenes usually gives anti-addition. Syn addition is often dominant for phenyl-substituted alkenes.
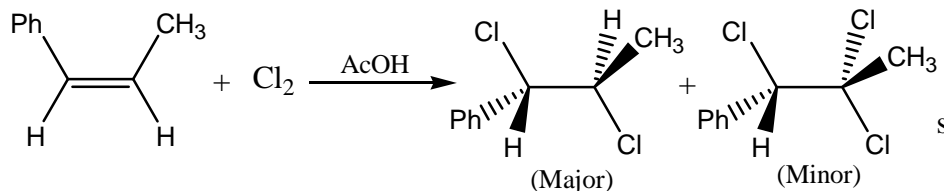
Phenyl substituted leads to cationic character at the benzylic site, and there is more syn addition.

Bromination therefore, generally gives a higher degree of anti-addition than chlorination.

Chlorination can be accompanied by other reactions that are indicative of carbocation intermediate branched alkenes can give products that are the result of elimination of a proton from a cationic intermediate.
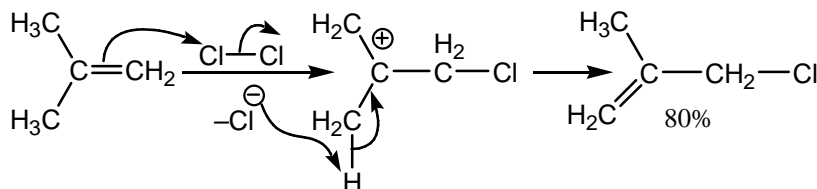
Note: Cl⁻ is a hard base and perfer the H⁺ i.e. hard acid abstraction from 3° cation.
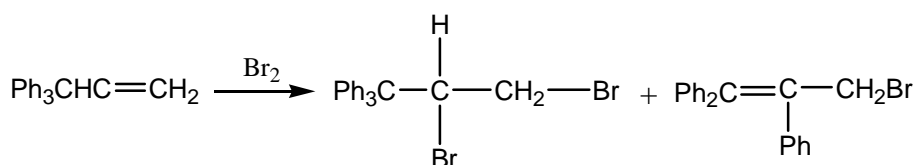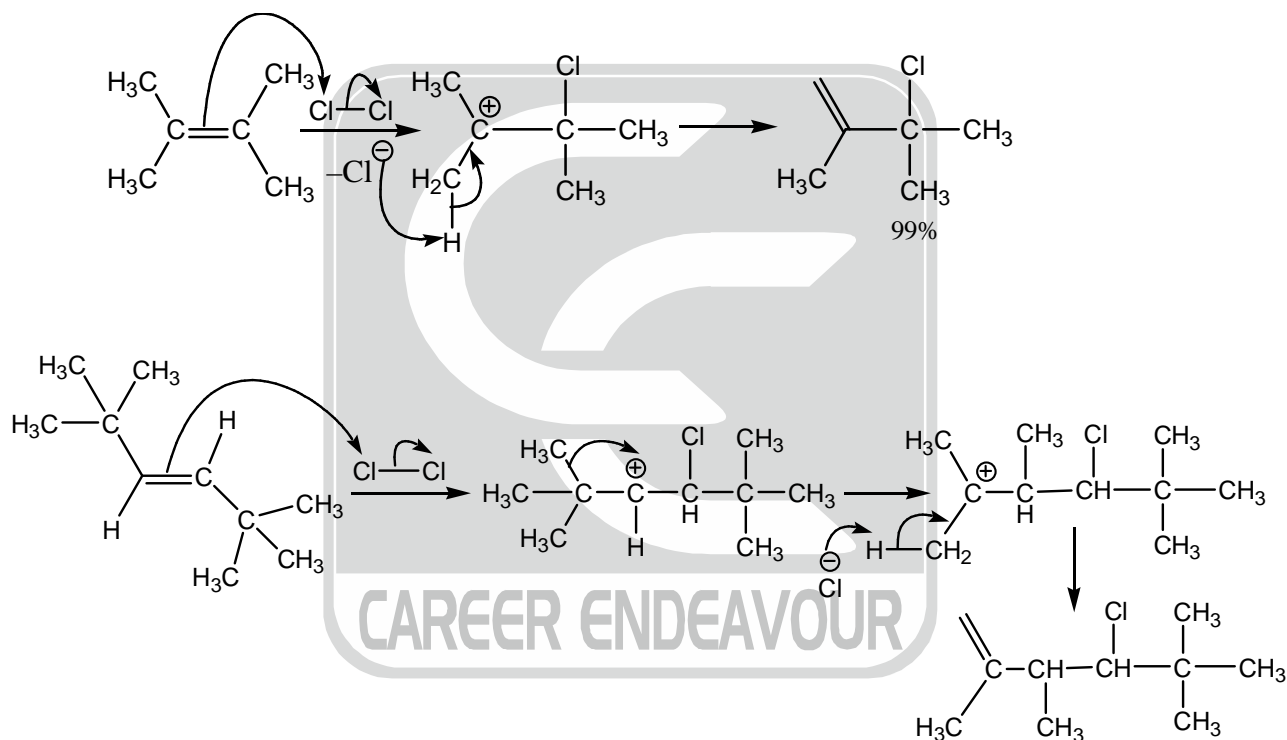
Nucleophilic solvent can complete with halide ion for the cationic intermediate.
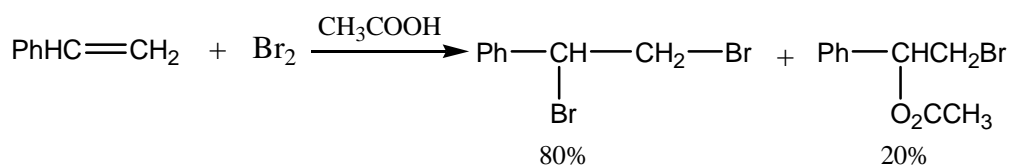
The acetoxy group is introduced exclusively at the benzylic carbon. This is in accord with the intermediate being a weakly bridged species or a benzylic cation.

Because of high reactivity, special precautions must be taken with reactions of fluorine and its use some what specialized. There is some basis for comparison with the less reactive halogen. Addition of fluorine to Z- and E-1-propenyl benzene is not stereosepecific.
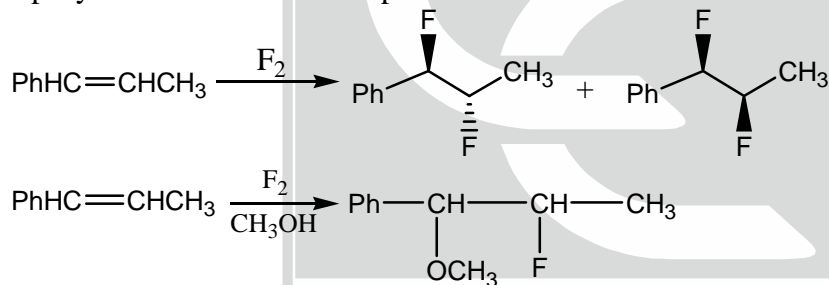
5.1. (C) Electrophilic addition to dienes
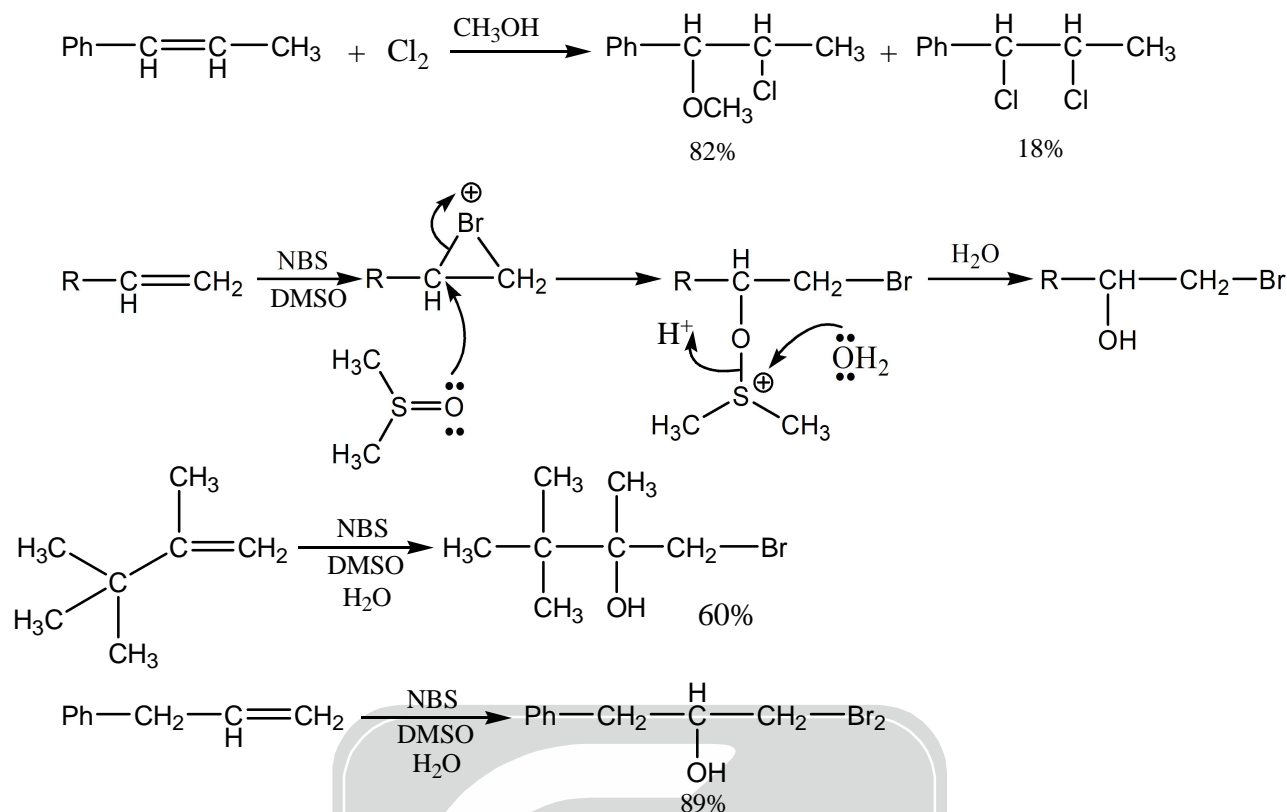
Dienes are more nucleophilic than isolated alkenes. Dienes react with electrophile in such a way that, formation of more stabilised carbocation.

More stabilised carbocation

No protonation at this double bond

due to the formation of less stabilised carbocation

Prenyl bromide
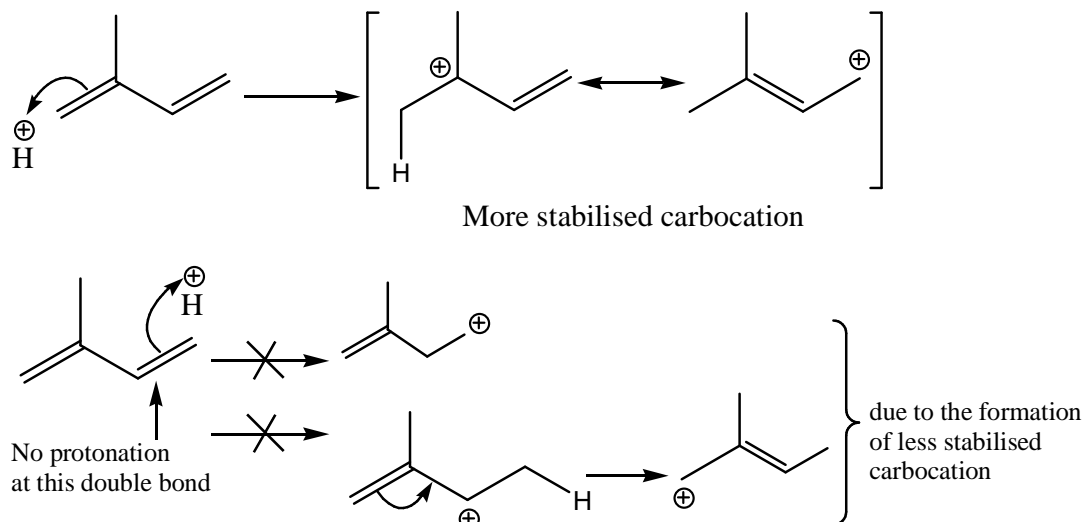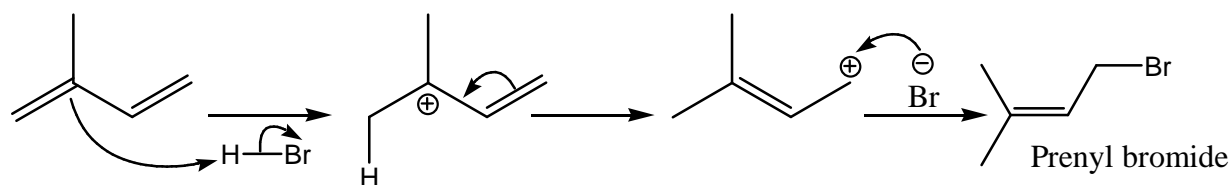
Addition of Br_2 with 1, 3-butadiene depends upon condition. At high temperature more stable alkene(product) is favoured (major) and at low temperature, less stable alkene (product) is favoured (major)

1, 4-dibromide

1, 2-dibromide

Cation intermediate

Changing the conditions slightly gives a different outcome. If the reaction is done at lower temperature, the bromine just adds across one of the double bonds to give a 1, 2-dibromide. This compound turn out to be the kinetic product of the bromination reaction. The 1, 4-dibromide is formed only when the reaction is hea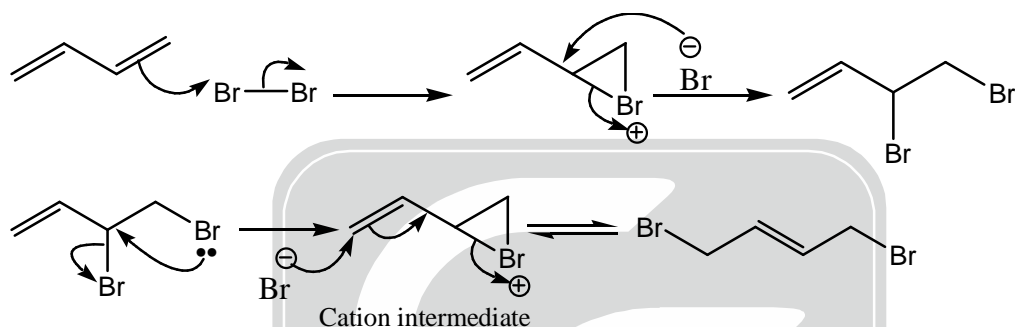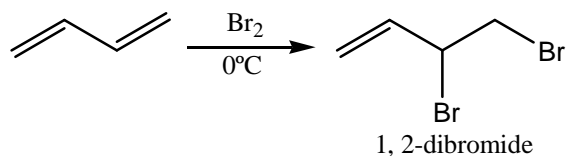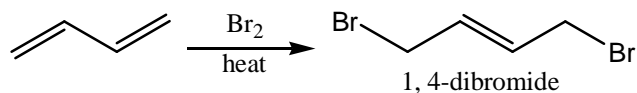ted and is the thermodynamic product. The 1, 2-dibromide can still react further because it can undergo nucleophilic substitution. At high temperature all steps are reversible so the fact that 1, 4-dibromide is formed under these conditions must mean it is more stable than the 1, 2-dibromide.

5.1. (D) Addition of hydrogen halide:

Electrophilic addition to unsymmetrical alkenes is regioselective:
In the addition of hydrogen halides to a carbon-carbon double bond, proton is electrophilic and forms a hydrogen-bridged intermediate called a protium ion which is subsequently attacked from backside by the halide ion resulting in the trans addition.

T.S.
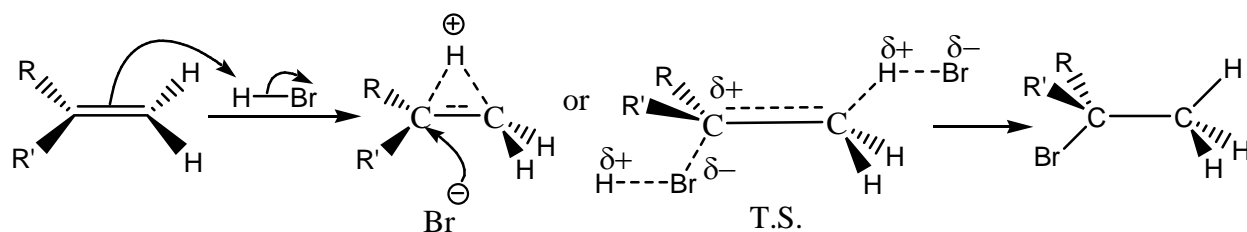
According to Markovnikov's rule: Addition of unsymmetrical alkene to unsymmetrical reagent, negative part of reagent goes to more substituted carbon atom of alkene.
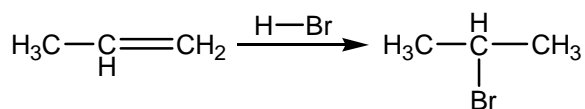
But actual addition of unsymmetrical reagent to unsymmetrical alkene, negative part of reagent goes to more stabilised carbocation of alkene.
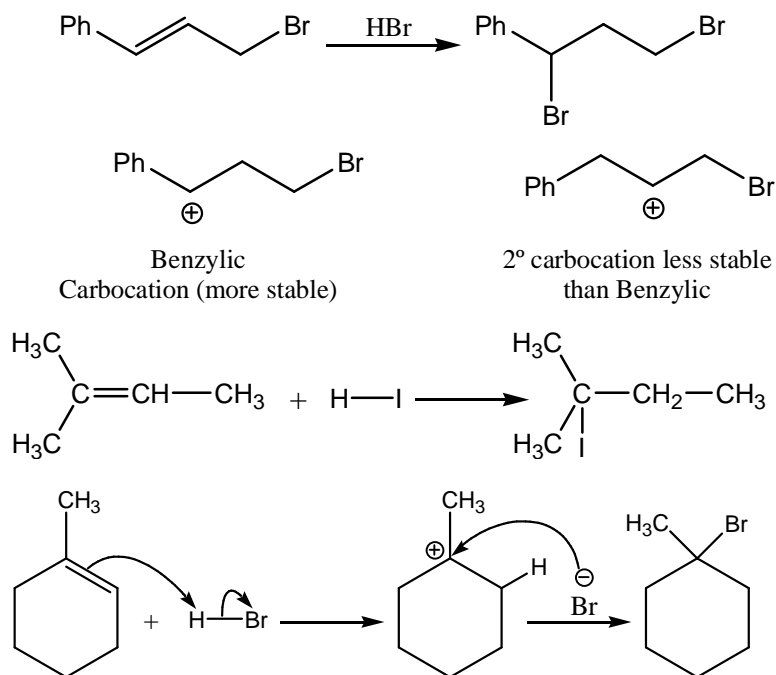
Hydrogen halide (Cl, Br) react with alkene to give addition product. Markovnikov's rule is used for the mode of addition. Addition usually takes place to give the product with the halogen atom attached to the more-substituted carbon of the double bond.

The addition involves either protonation or a partial transfer of a proton to the double bond.

The relative stability of the two possible carbocations from an unsymmetrical alkene favours formation of the more-substituted intermediate.

When a carbocation is not involved, the regioselectivity of electrophilic addition is the result of attack of the electrophile at the more electron rich carbon of the double bond.

Alkyl substituents increases the electron density of the terminal carbon by hyper conjugation.
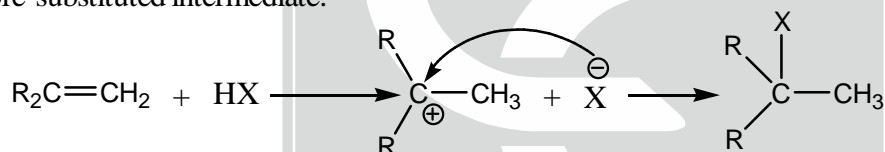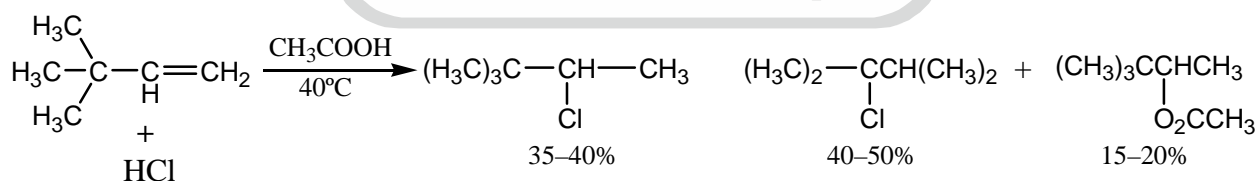
When carbocations are involved as intermediate, carbon skeleton rearrangement can occur during electrophilic addition reaction.

1, 2-Dimethylcyclohexene is an example of an alkene for which the stereochemistry of hydrogen chloride addition is dependent on the solvent and temperature. At $-78°C$ in dichloromethane, 88% of the product is the result of syn addition, whereas at $0°C$ in ether, 95% of the product result from anti-addition. The addition can proceed through an ion pair intermediate formed by an initial protonation step.

The major factor in determining which mechanism is followed is the stability of the carbocation intermediate. Alkenes that can give size to a particularly stable carbocation.

Stereochemistry of addition of hydrogen halide to alkenes:

Alkene	Hydrogen halide	Stereochemistry
1, 2-Dimethylcyclohexene	HBr	anti
1, 2-Dimethylcyclohexene	HCl	Solvent and temperature dependent
Cyclohexene	HBr	anti
Z-2-Butene	DBr	anti
E-2-Butene	DBr	anti
1-methylcyclopentene	HCl	anti
1, 2-Dimethylcyclopentene	HBr	anti
Norbornene	HBr	Syn and rearrangement
Norbornene	HCl	Syn and rearrangement
E-1-phenylpropene	HBr	Syn (9:1)
Z-1-phenylpropene	HBr	Syn (8:1)
Bicyclo [3.1.0]hex-2-ene	DCl	Syn
1-phenyl-4-(t-butyl) cyclohexene	DCl	Syn

5.1. (E) Hydration and other acid-catalysed additions of oxygen nucleophiles

Oxygen nucleophiles can be added to double bond and under strongly acidic condition. Addition to double bond under strongly acidic condition. Addition to proton occur to give the more substituted carbocation so addition is regioselective.
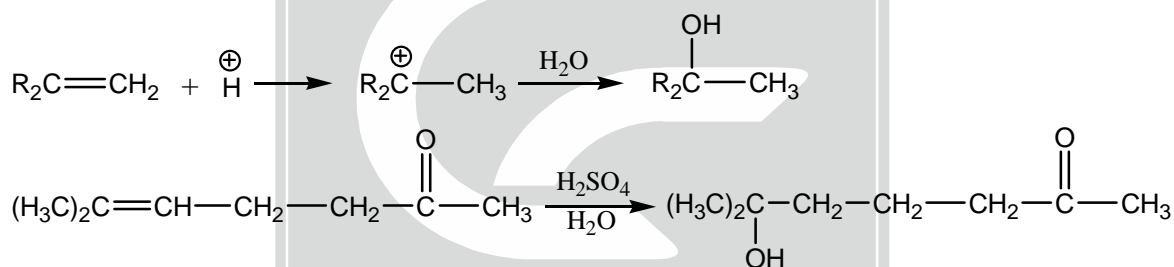
Involvement of cationic intermediate, rearrangements can occur in system in which a more stable cation can result by aryl, alkyl or hydrogen migration.

Addition of nucleophilic solvents such as alcohols and carboxylic acid can be effected by using strong acids as catalyst.
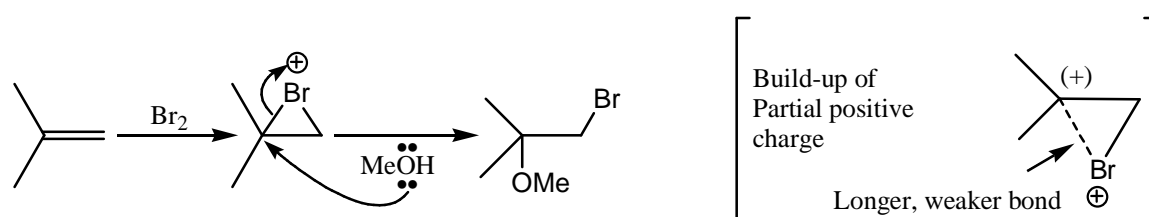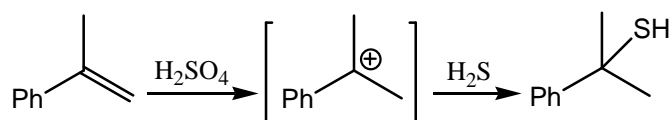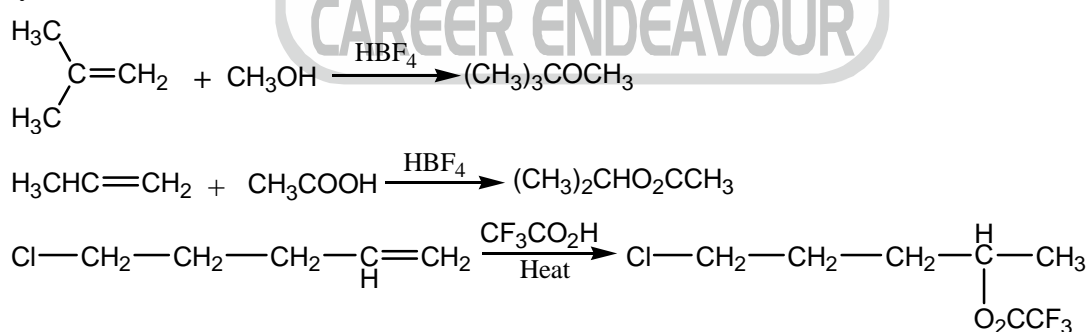
Leaving group start to leave, creating a partial positive charge at carbon atom. Which is intercepted by the nucleophile, best explaination for this mechanism.

Addition of hydroxyl group:

Stable, tertiary carbocation
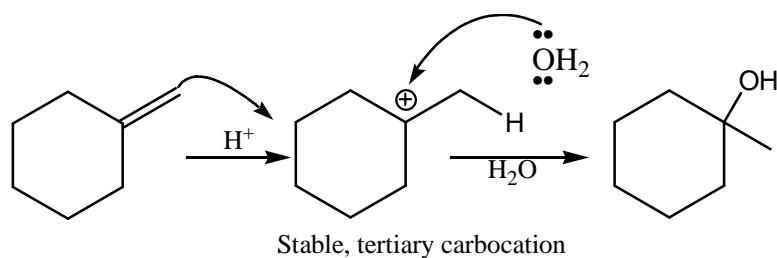
Addition of water to an alkene can be carried out using aqueous acid. There is an intial formation of carbocation by the attack of electrophile to the sp^2 carbon that is bonded to the greater number of hydrogen. Nucleophile add to the other sp^2 carbon.

Addition of HX to Unsymmetrical Alkene is often Accompanied by Rearrangement:

Let us consider the following reaction:

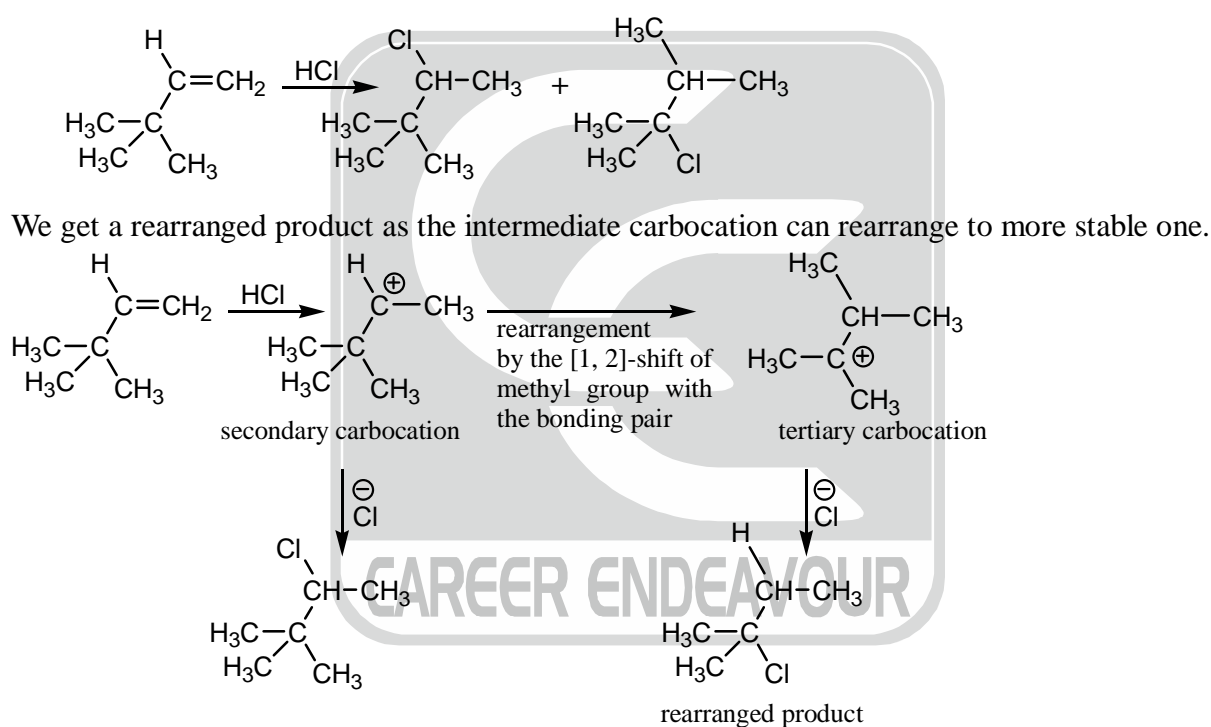We get a rearranged product as the intermediate carbocation can rearrange to more stable one.

rearranged product

Addition of Hydrogen Bromide: Peroxide Effect or Kharasch Addition:

Addition of hydrogen chloride and hydrogen iodide to alkenes happens strictly adhering the Markownikoff's rule. However, untill 1933 the situation with respect to hydrogen bromide was throughly confusing. It had been reported by some workers that addition of hydrogen bromide to a particular alkene yields a product in agreement with Markownikoff's rule; by others, a product in contradiction to Markownikoff's rule (the so-called anti-Markownikoff product); and by still others, a mixture of both products. Sporadic reports appeared which claimed that product obtained dependent upon various factors such as presence or absence of water or solvent or light or upon the nature of the surface of the reaction vessel etc. In 1933 Morris S. Kharasch and F.W. Mayo at the University of Chicago put a stop to this chemical anarchy by discovering that the orientation of addition of hydrogen bromide to the carbon-carbon double bond is determined *soley* by the presence or absence of peroxides.

Organic peroxides are the compounds containing the –O–O– linkage. They are found, generally in only very small amounts, as impurities in many organic compounds, where they are seen *slowly* formed by the action of oxygen; even an alkene may contain peroxide through aerial oxidation at the allylic position, e.g.
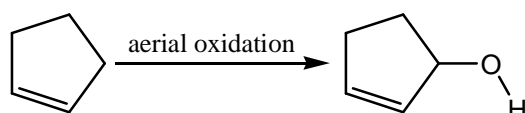
Kharasch and Mayo found that if one carefully excludes peroxides from the reaction system or if one adds certain inhibitors such as hydroquinone or diphenylamine – the addition hydrogen bromide to alkenes diligently obeys the Markownikoff's rule. On the other hand, if one does not exclude peroxides, or if one deliberately puts peroxides into the reaction system hydrogen bromide adds to alkenes in exactly reverse direction.
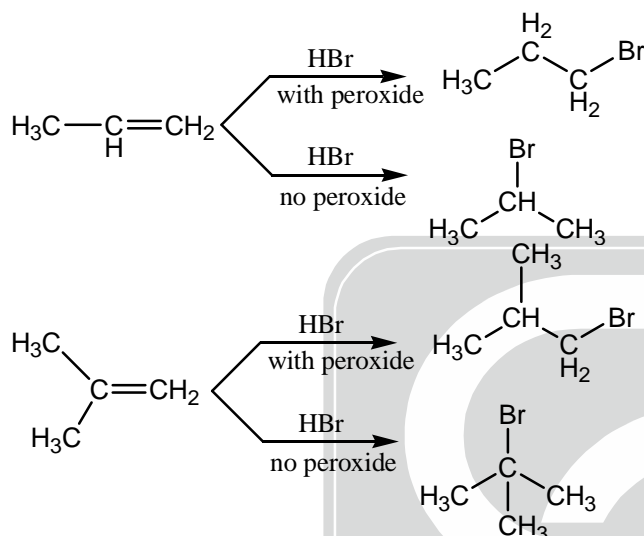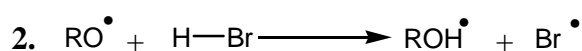

Commonly used peroxides:

di-tert-butylperoxide   dibenzoyl peroxide
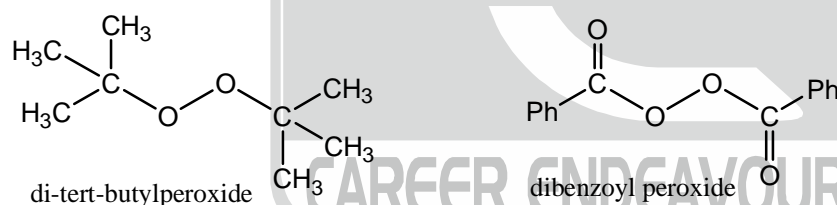
This reversal of the orientation of addition of hydrogen bromide in presence of peroxide appears to be anti-Markownikoff's type and it is often referred to as peroxide effect or Kharasch addition. During such addition usually 0.01 mole peroxide is used.

In the absence of peroxides, hydrogen bromide adds to alkenes according to Markownikoff's rule; in presence of peroxides, the direction of addition is exactly reversed. To account for this peroxide effect, Kharasch and Mayo proposed that addition can take place by an entirely different mechanism: Markownikoff's addition by ionic mechanism that we have discussed, and Kharasch addition by a free radical chain mechanism. Peroxides initiate the free radical chain in the following way:

Chain initiation:

1. $R\!-\!O\!-\!O\!-\!R \xrightarrow{\Delta} 2RO^{\bullet}$

2. $RO^{\bullet} + H\!-\!Br \longrightarrow ROH^{\bullet} + Br^{\bullet}$

Chain propagation:

3.

4.
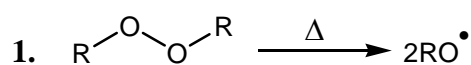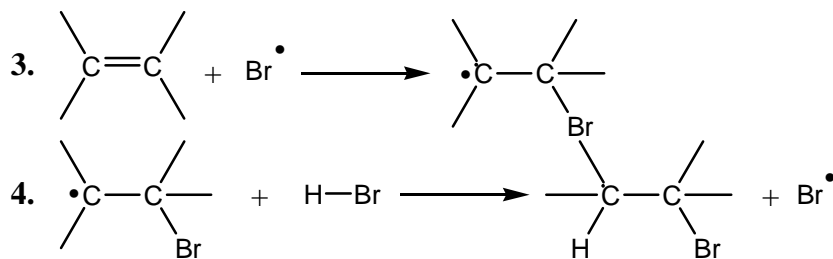
and so on .....

This mechanism is gathers support from the following facts:

- Small amount of peroxide is sufficient to change the orientation of addition of many molecules of hydrogen bromide which strongly indicates a chain reaction.
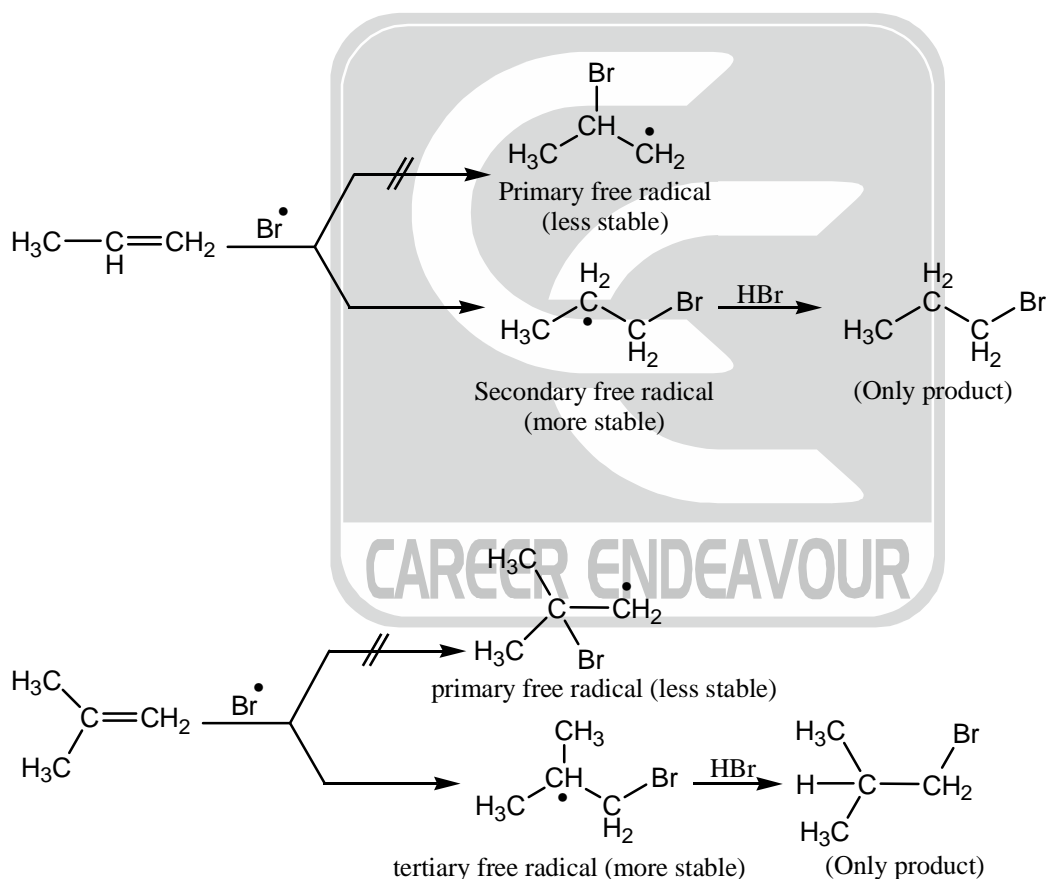
- So, too, does the fact that a very few molecules of inhibitor can prevent this change in orientation. It is not surprising to find that these same compounds are efficient inhibitors of many other chain reactions.

Let us now try to explain the orientation of addition in present of peroxides. Step determines the orientation of addition. Obviously, the reaction will proceed through the more stable transition state at a faster rate, i.e. via more stable potential free radical i.e. via the more stable free radical.

Primary free radical
(less stable)

Secondary free radical
(more stable)

(Only product)

primary free radical (less stable)

tertiary free radical (more stable)

(Only product)

Like the polar mechanism, the HBr addition through free radical mechanism also runs the risk of rearrangement in appropriate cases. Consider the following example where the HBr addition is triggered photochemically:
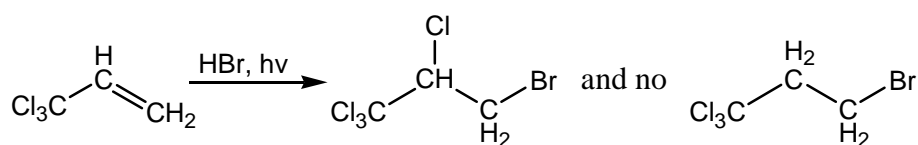
Obviously, this can be explained by taking into account the rearrangements of the initially formed radical into a more stable one:

secondary radical....

.... but, this is more stable conjugation from Cl lone pair
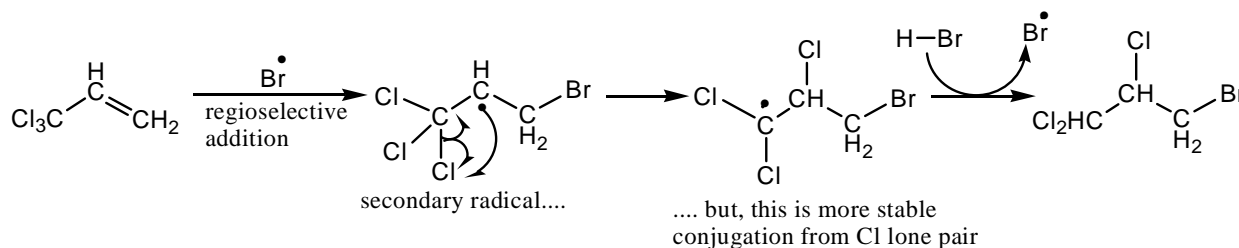
which eventually leads to the exclusive product.

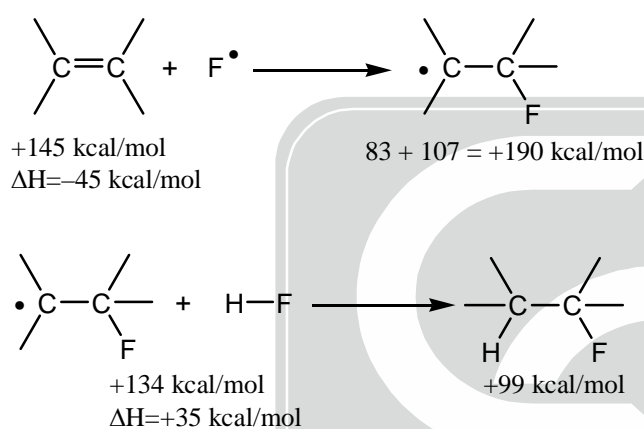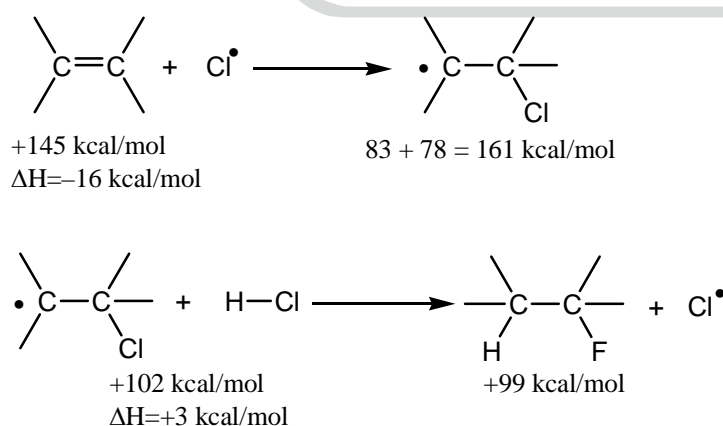Hydrogen bromide is the only hydrogen halide that will add readily to alkenes via a free radical pathway. The question therefore is – why does only hydrogen bromide show peroxide effect? The answer can be found in the ΔH values for the two steps of the chain reaction for addition of respectively hydrogen halides to the carbon-carbon double bond, for example:

HF addition:

+145 kcal/mol
$\Delta H = -45$ kcal/mol

$83 + 107 = +190$ kcal/mol

+134 kcal/mol
$\Delta H = +35$ kcal/mol

+99 kcal/mol

Second step in chain propagation for HF addition is thus highly unfavorable as this step is highly endothermic, reflecting the strength of the H—F bond and the difficulty of breaking it. As a result, HF does not participate in peroxide effect.

HCl addition:

+145 kcal/mol
$\Delta H = -16$ kcal/mol

$83 + 78 = 161$ kcal/mol

+102 kcal/mol
$\Delta H = +3$ kcal/mol

+99 kcal/mol

Second step of HCl addition in chain propagation is again unfavorable as this step is endothermic, though not to such a great extent. Thus, a few free radical addition of HCl are known, but reactions are not very rapid, and the reaction chains are short at ordinary temperature.

HBr addition:

+145 kcal/mol
ΔH=–6 kcal/mol

83 + 68 = +151 kcal/mol

+87 kcal/mol
ΔH=–12 kcal/mol

+99 kcal/mol
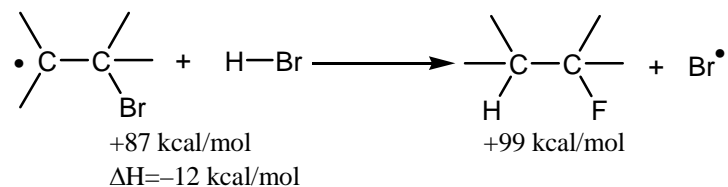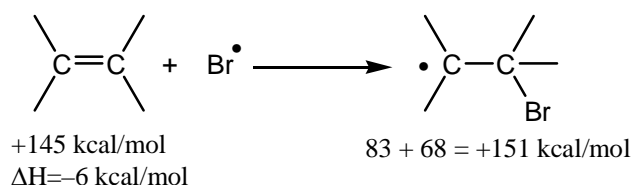
Obviously, for HBr addition both the steps are energetically favorable as both the steps are exothermic. Thus, HBr shows the peroxide effect.

HI addition:

+145 kcal/mol
ΔH=11 kcal/mol

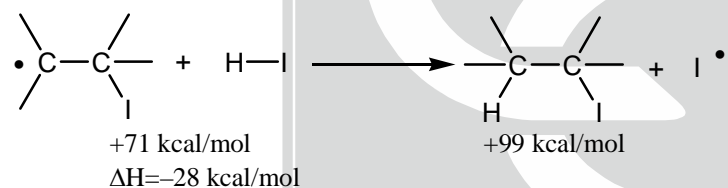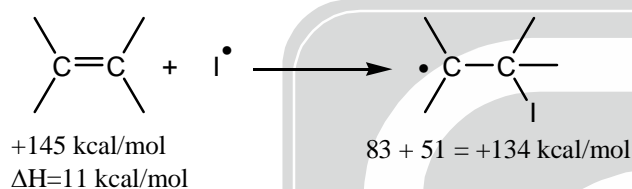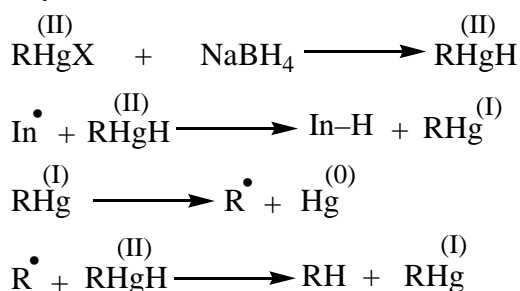83 + 51 = +134 kcal/mol

+71 kcal/mol
ΔH=–28 kcal/mol

+99 kcal/mol

The first propagation step in free radical HI addition is energetically unfavorable as this step is endothermic, reflecting the fact that energy gained in forming I–C bond is not as great as the lost in breaking the carbon-cabond double bond. Thus, HI does not show peroxide effect.
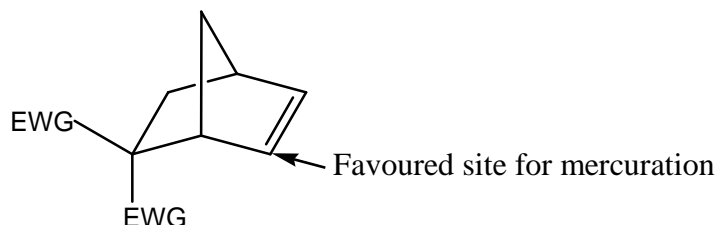
Oxymercuration-Reduction:

General mechanism depicts a mercurinium ion as an intermediate. The cation may be predominantly bridged or open, depending on the structure particular alkene. The addition is completed by attack of a nucleophile at the more-substituted carbon. The nucleophilic capture is usually the rate and product controlling step.

The reductive replacement of mercury using sodium borohydride is a free radical chain reaction involving a mercuric hydride intermediate.

$$\overset{\text{(II)}}{\text{RHgX}} + \text{NaBH}_4 \longrightarrow \overset{\text{(II)}}{\text{RHgH}}$$

$$\overset{\bullet}{\text{In}} + \overset{\text{(II)}}{\text{RHgH}} \longrightarrow \text{In–H} + \overset{\text{(I)}}{\text{RHg}}$$

$$\overset{\text{(I)}}{\text{RHg}} \longrightarrow \overset{\bullet}{\text{R}} + \overset{\text{(0)}}{\text{Hg}}$$

$$\overset{\bullet}{\text{R}} + \overset{\text{(II)}}{\text{RHgH}} \longrightarrow \text{RH} + \overset{\text{(I)}}{\text{RHg}}$$

Polar effects of EWG's favours mercuration at the carbon that is closer to the substituent which is attributed to a favourable polar effect that stabilised the negative charge on the mercurated carbon.

Favoured site for mercuration

In oxymercuration, an alkene is treated with mercuric acetate in aqueous tetrahedrofuran (THF). When the reaction is complete, sodium borohydride is added to the reaction mixture. In the first step of oxymercuration reaction, the electrophilic mercury of mercuric acetate adds to the double bond. The reaction is analogous to the addition of Br_2 to an alkene to form a cyclic brominium ion. In the second step, water attacks to the more substituted carbon of the mercurinium ion.

Sodiumborohyride ($NaBH_4$) converts the C-Hg bond into a C-H bond.
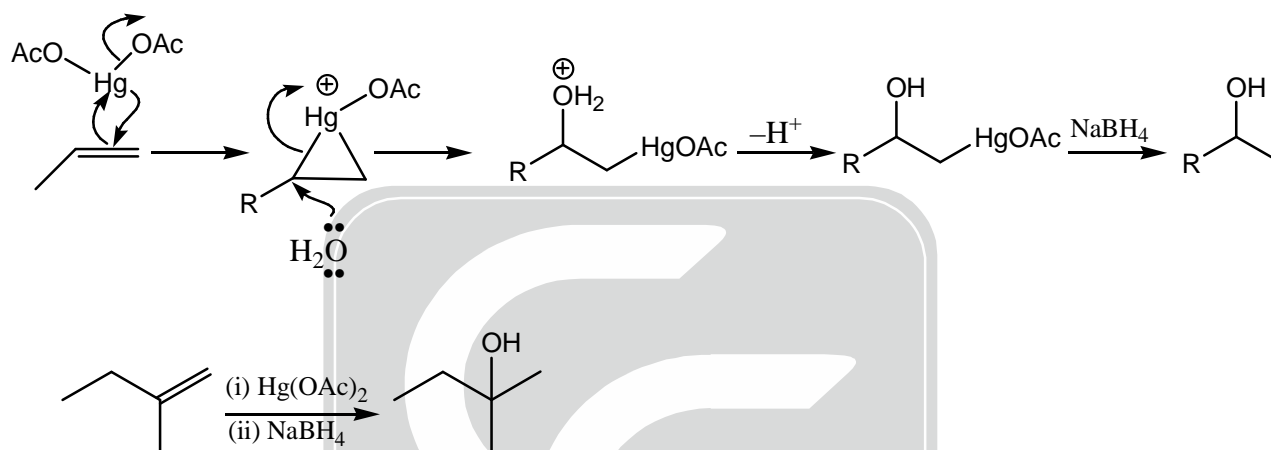
Acid catalysed hydration of the alkynes also require mercuric ions and proceeds in accordance with Markovnikov's rule. Alkynes lead to the formation of ketones.