

Mechanism

S_N1 and **S_N2** reactions

S_N2 Reactions

Mechanism of aliphatic bimolecular Nucleophilic Substitution Reactions

- A nucleophilic substitution reaction which is kinetically of second order is called S_N2 reaction

Kinetics of the reaction

Rate = k [Substrate][Nucleophile] k =rate constant.

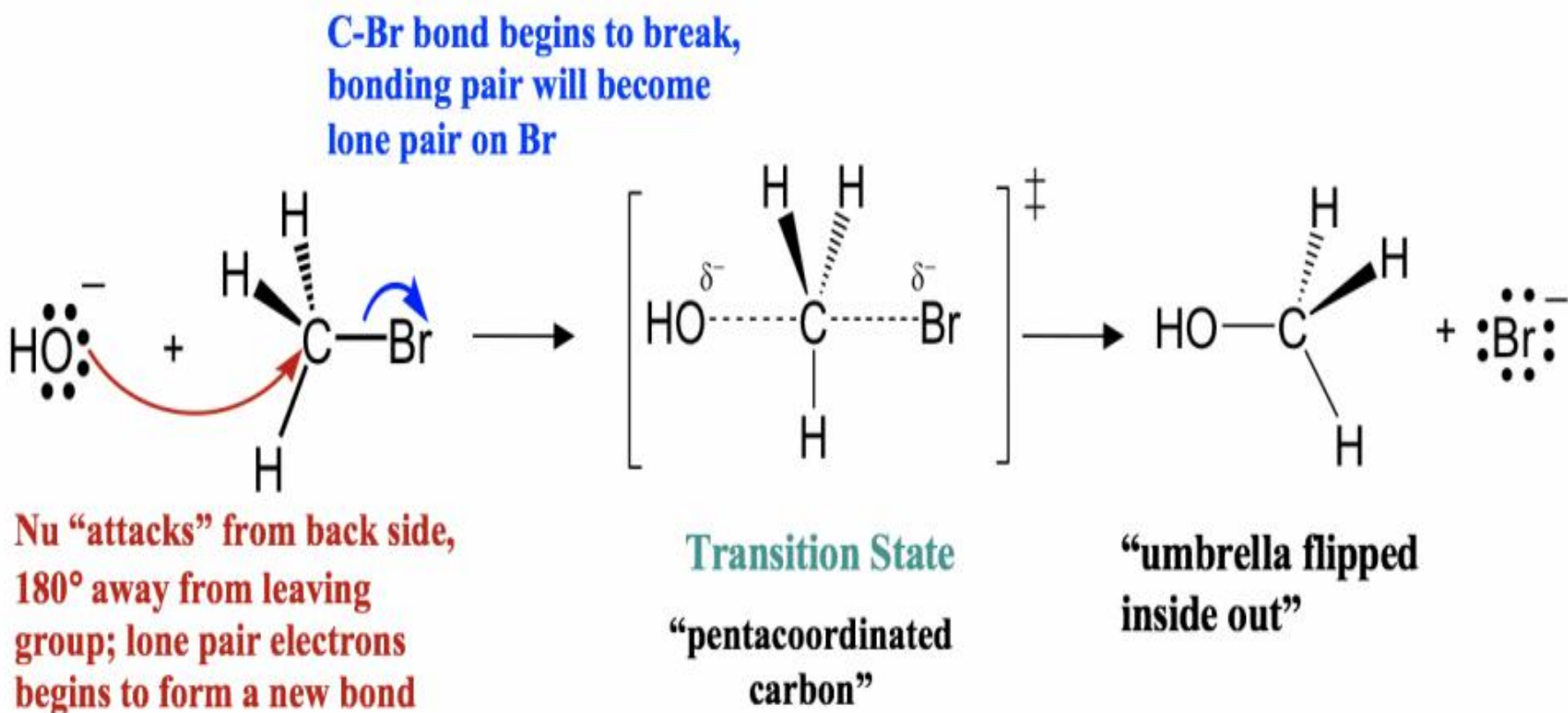
Eg: Reaction of Methyl bromide and hydroxide ion to yield methanol.



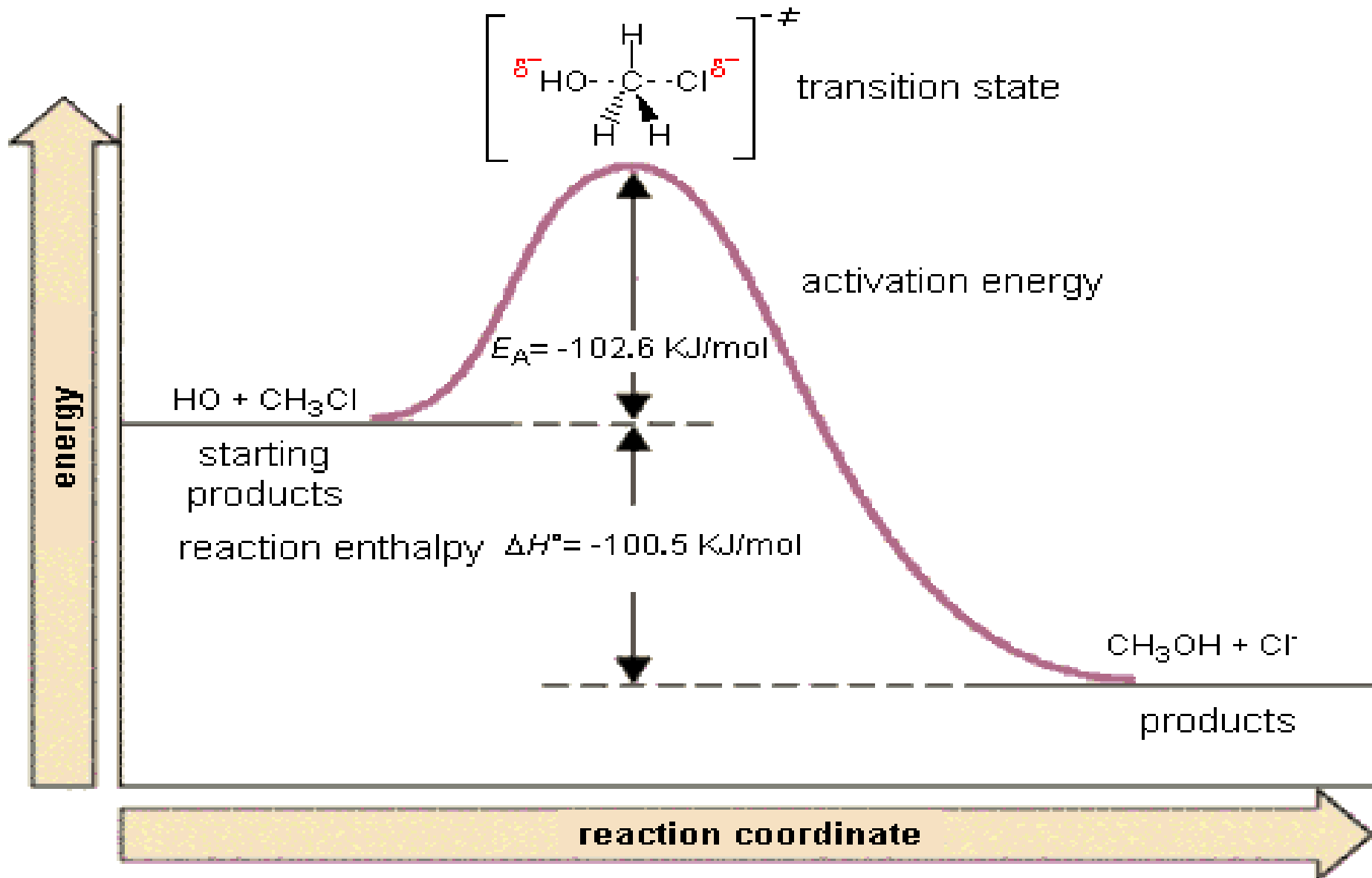
$$\text{Rate} = k[\text{CH}_3\text{-Br}][\text{OH}^-]$$

Hughes-Ingold mechanism of S_N2 reactions

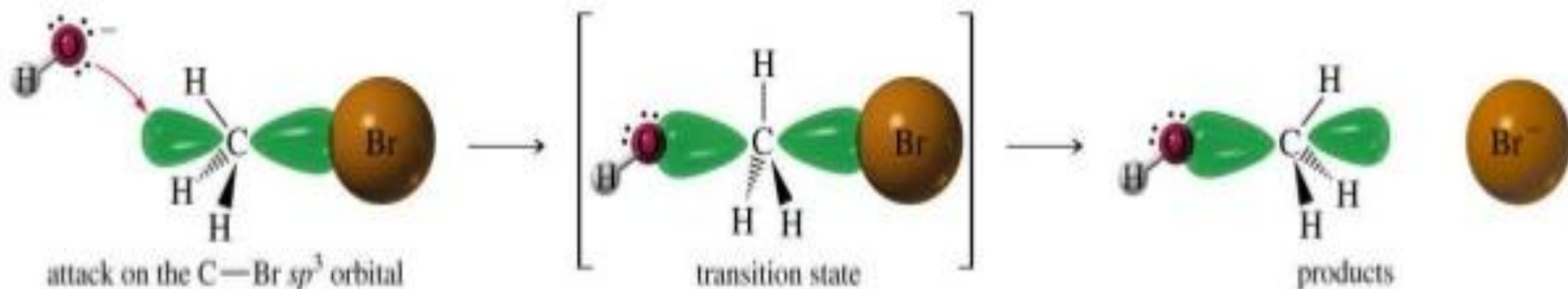
1. Single step concerted mechanism
2. Nu- attacks the Carbon from the sterically favorable rear side (side remote from Br).



Potential Energy diagram for a S_N2 reaction



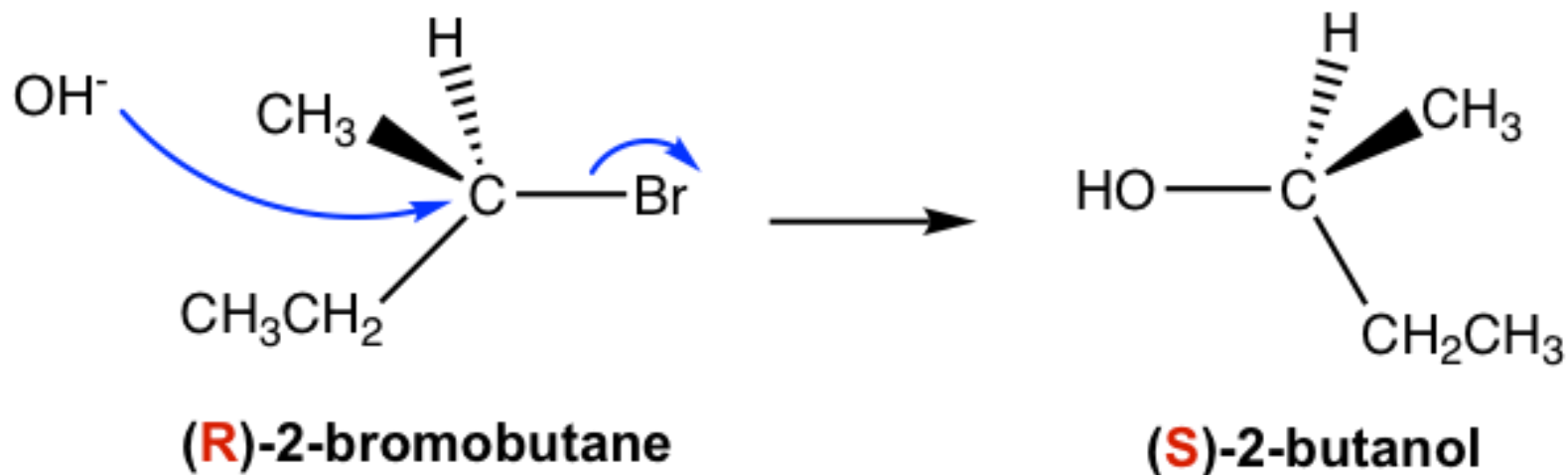
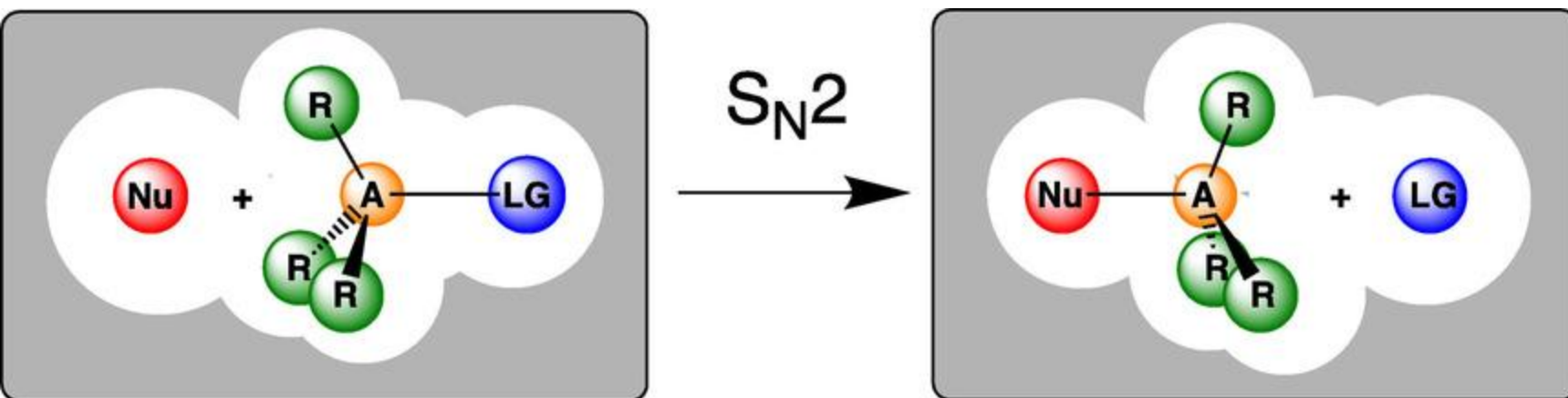
Stereochemistry of S_N2 reactions



In T.S, the C- atom is in penta co-ordinated state where C -is approximately in sp^2 hybridised with one lobe of its unhybridized p orbital partially overlapping with the Nu- orbital and other with the leaving group orbital.

An S_N2 reactions always proceeds with complete stereochemical inversion.

Walden inversion



Factors affecting reactivity in the S_N2 reactions of RX

1. Nature of the substrate

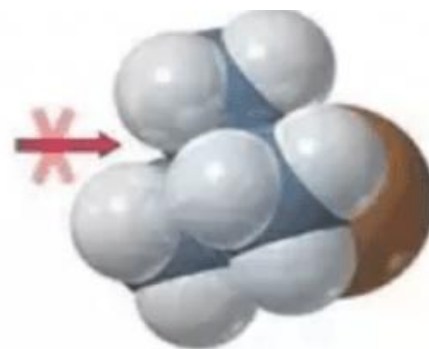
a) Nature of alkyl group-steric effect.



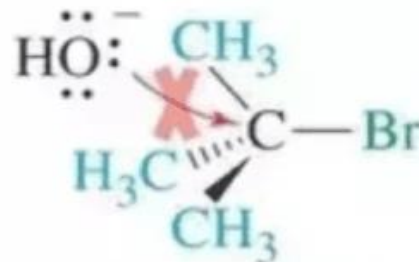
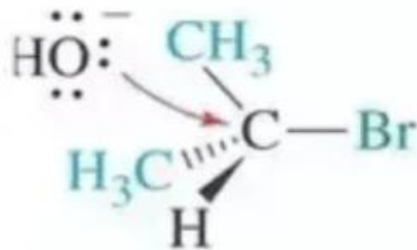
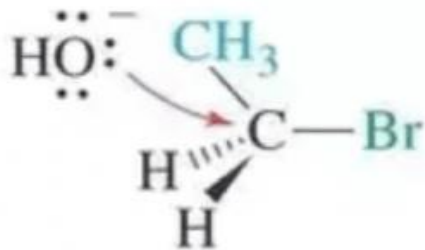
ethyl bromide (1°)
attack is easy



isopropyl bromide (2°)
attack is possible



t-butyl bromide (3°)
attack is impossible



2. Nature of leaving group

Weaker the base the better the leaving group

The relative basicities of halide ions are in the order



The relative reactivities of Alkyl halides is in the order



3. Nature of Nucleophile

Stronger bases are better nucleophiles. (Greater the nucleophilicity

better the reactivity)



4. Nature of the solvent

In polar protic solvents the nucleophiles become solvated through ion-dipole interactions. A sheath of solvent thus decreases its nucleophilicity (of strong nucleophiles) and thereby its reactivity.

Thus Polar protic solvents slow down S_N2 reactions

Ion-dipole interactions are absent when non-polar solvents are used

In polar aprotic solvents like CH_3CN , DMF, DMSO interactions are less.

Factor affecting rate of an S_N2 reaction

The ability of the leaving group to leave

The best leaving groups are:

- Lower basicity
- Electron-withdrawing, to polarize the carbon atom.
- Stable (weak base) once it has left.
- Polarizable, to stabilize the transition state.

	<u>relative rates of reaction</u>	<u>pK_a HX</u>
$\text{HO}^- + \text{RCH}_2\text{I} \longrightarrow \text{RCH}_2\text{OH} + \text{I}^-$	30 000	-10
$\text{HO}^- + \text{RCH}_2\text{Br} \longrightarrow \text{RCH}_2\text{OH} + \text{Br}^-$	10 000	-9
$\text{HO}^- + \text{RCH}_2\text{Cl} \longrightarrow \text{RCH}_2\text{OH} + \text{Cl}^-$	200	-7
$\text{HO}^- + \text{RCH}_2\text{F} \longrightarrow \text{RCH}_2\text{OH} + \text{F}^-$	1	3.2

- ❑ Iodine (-I) is a good leaving group because iodide (I⁻) is non basic and stabilize their negative charge.
- ❑ The hydroxyl group (-OH) is a poor leaving group because hydroxide (OH⁻) is a strong base.

Carbon and iodine, however, have the same electronegativity. Why, then, does an alkyl iodide undergo a substitution reaction? We know that *larger atoms are more polarizable than smaller atoms*.

S_N1 Reactions

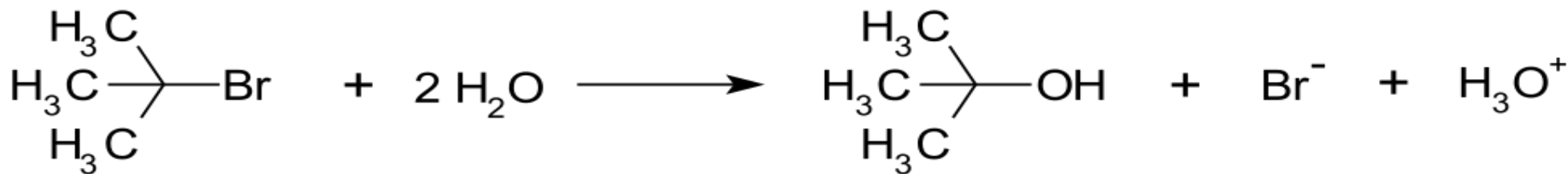
Mechanism of aliphatic uninuclear Nucleophilic Substitution Reactions

A nucleophilic substitution reaction which is kinetically of first order is called S_N1 reaction.

Kinetics of the reaction

Rate = k [Substrate] k =rate constant.

Eg: Reaction of t-butyl bromide and hydroxide ion to yield t-butyl alcohol.

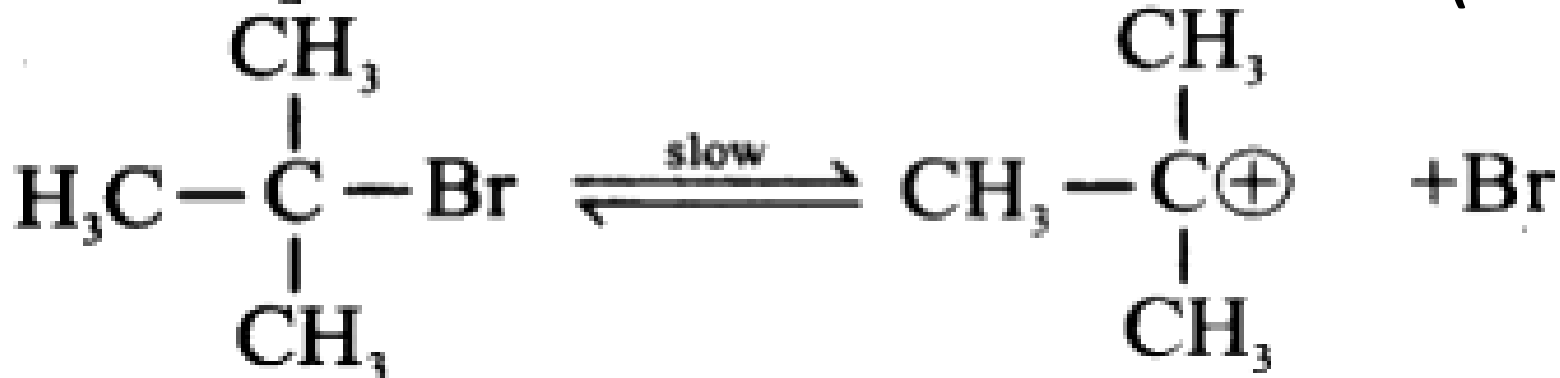


Rate = k [t-butyl bromide]

A low concentration of OH^- can bring about the S_N1 mode of hydrolysis of ter-butyl bromide.

Mechanism of S_N1 reactions (Hughes and Ingold)

Step - 1: Formation of carbocation: (Slowest step)



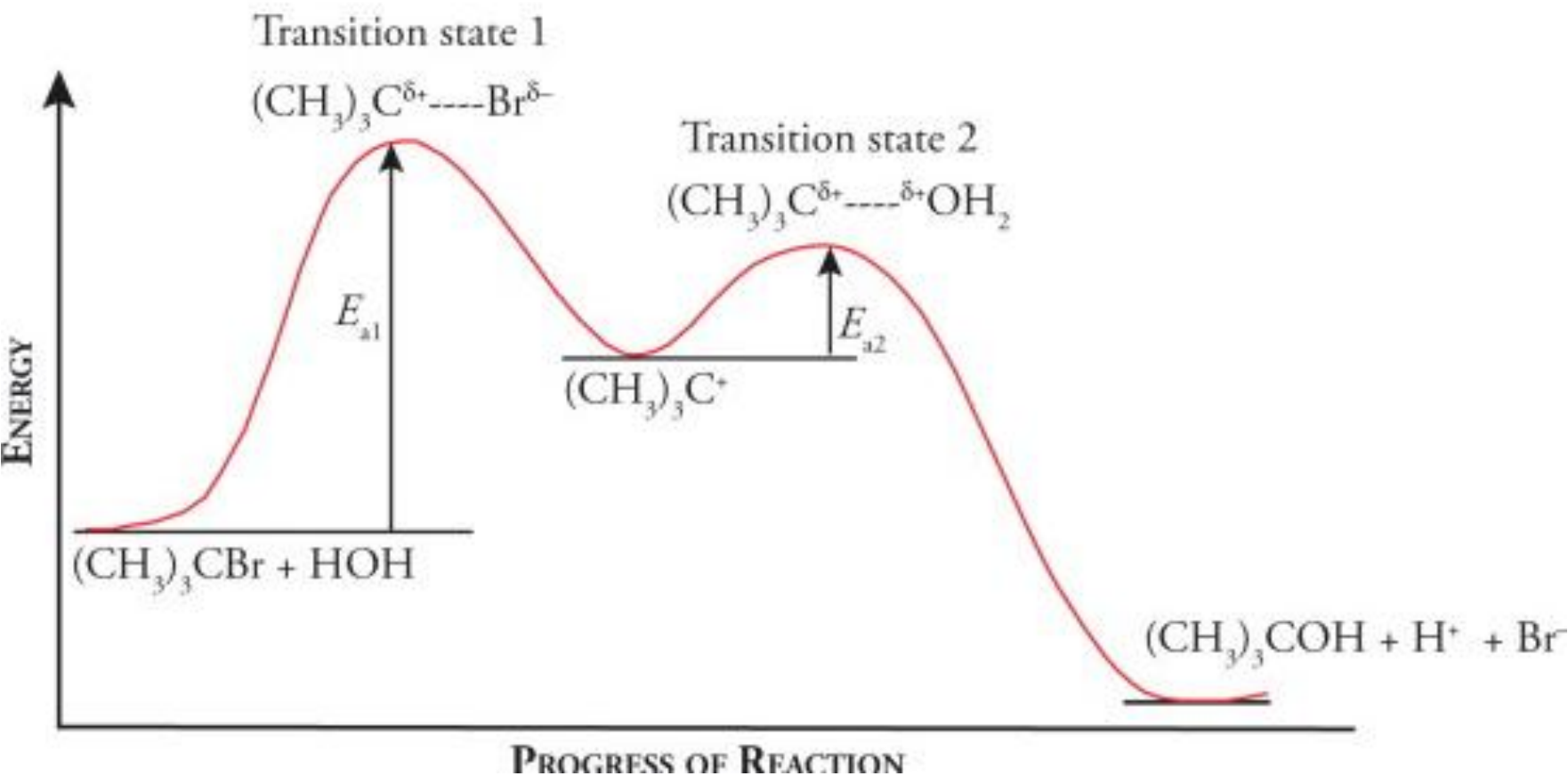
Step - 2: Attack of nucleophile on carbocation



Energy profile diagram

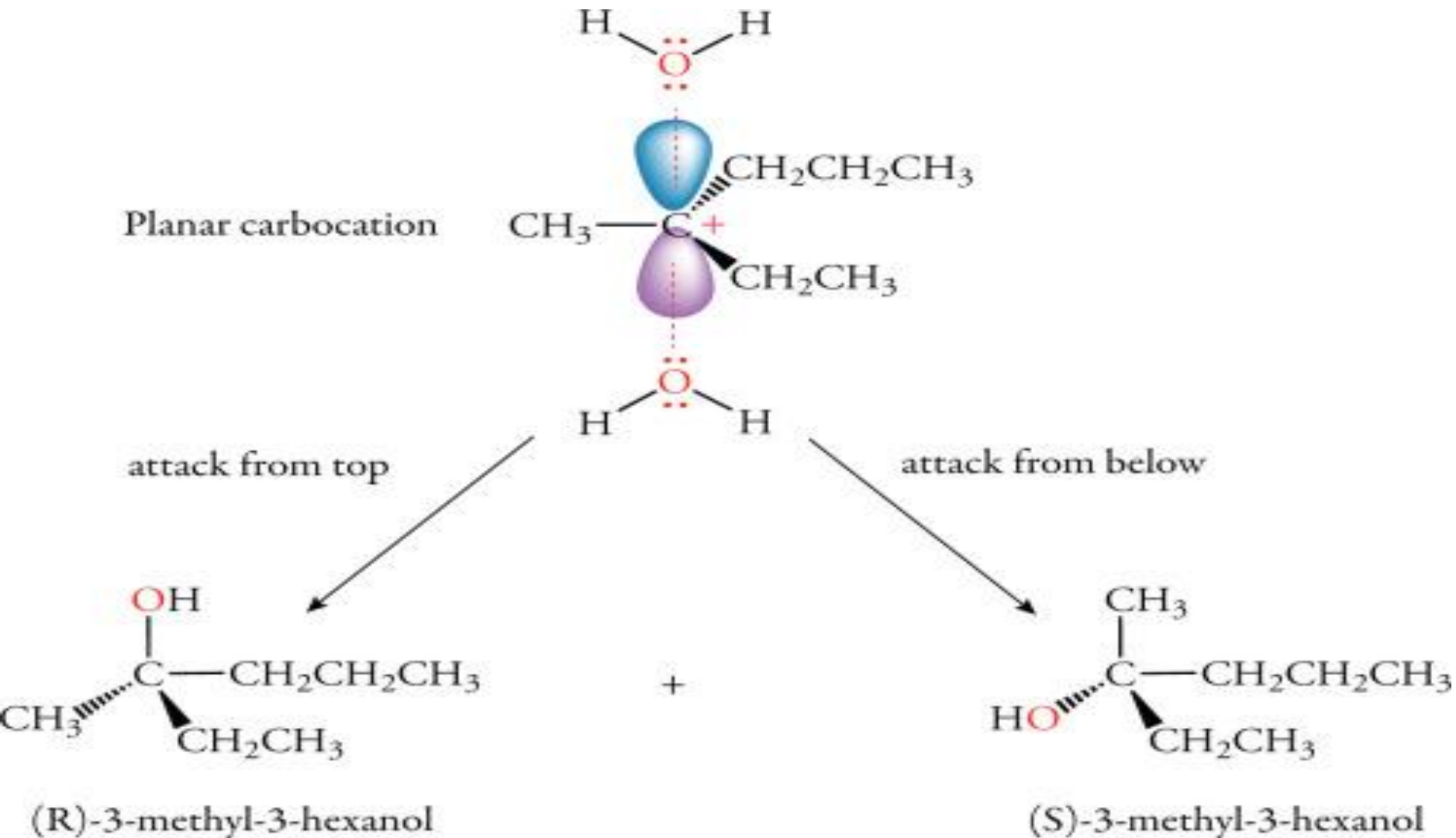
The reaction proceeds through 2 transition states with carbocations as intermediate. $\Delta H = -ve$ shows that the overall reaction is exothermic

E_{a1} is endothermic

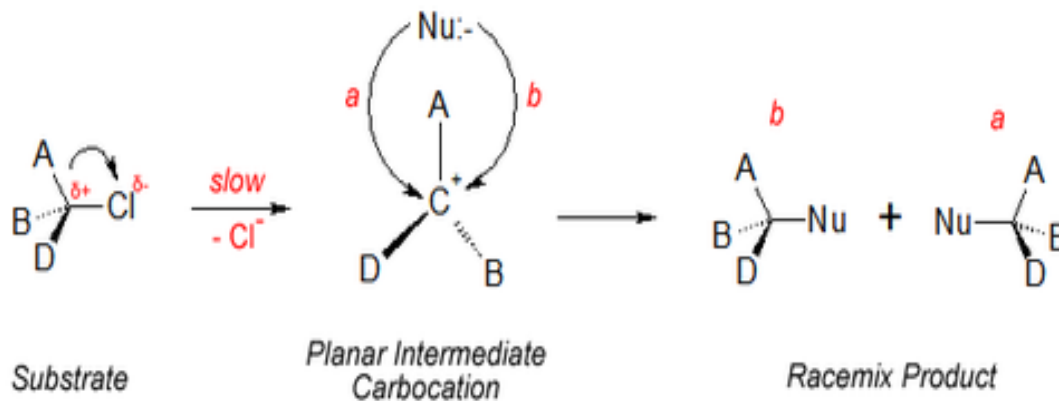
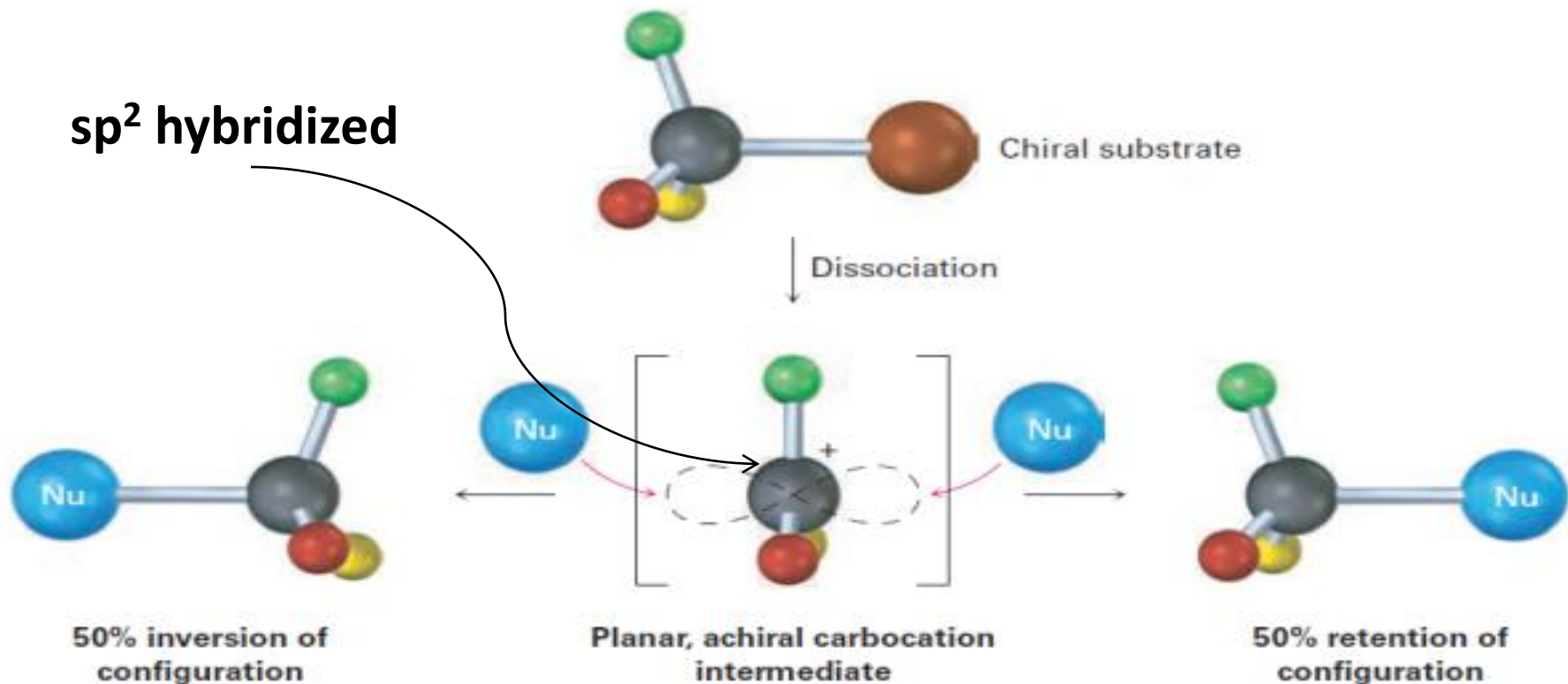


Stereochemistry of the S_N1 reaction

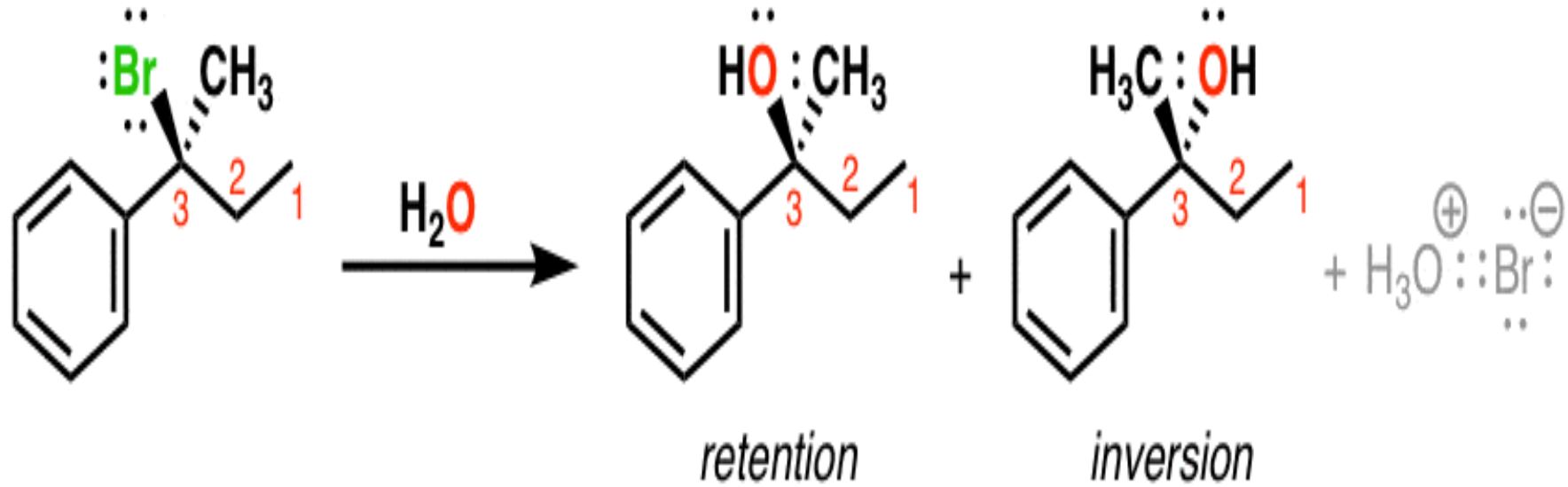
Front side attack will result in retention of configuration and back side attack will lead to inversion of configuration



Stereochemistry of the S_N1 reaction



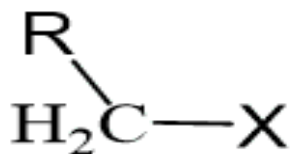
Substitution occurs with a mixture of retention and inversion at a stereocenter



Factors affecting S_N1 reaction

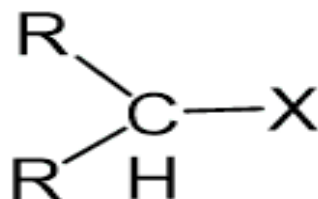
1. Nature of alkyl group

Greater the stability of carbocation formed greater would be its ease of formation .



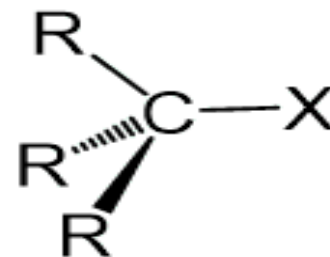
1°

<



2°

<



3°

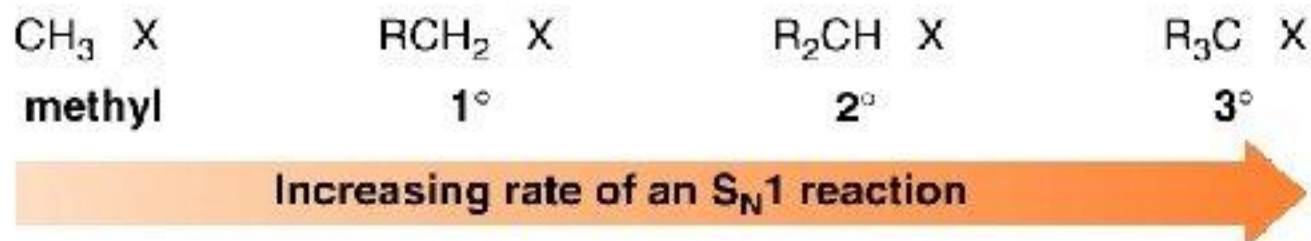
Increasing rate of an S_N1 reaction



Mechanisms for Nucleophilic Substitution

- The rate of an S_N1 reaction is affected by the type of alkyl halide involved.

As the number of R groups on the carbon with the leaving group *increases*, the rate of an S_N1 reaction *increases*.



- 3° Alkyl halides undergo S_N1 reactions rapidly.
- 2° Alkyl halides react more slowly.
- Methyl and 1° alkyl halides do *not* undergo S_N1 reactions.

- This trend is exactly opposite to that observed in S_N2 reactions.

2. Nature of leaving group

Weaker the basicity better the lg group.

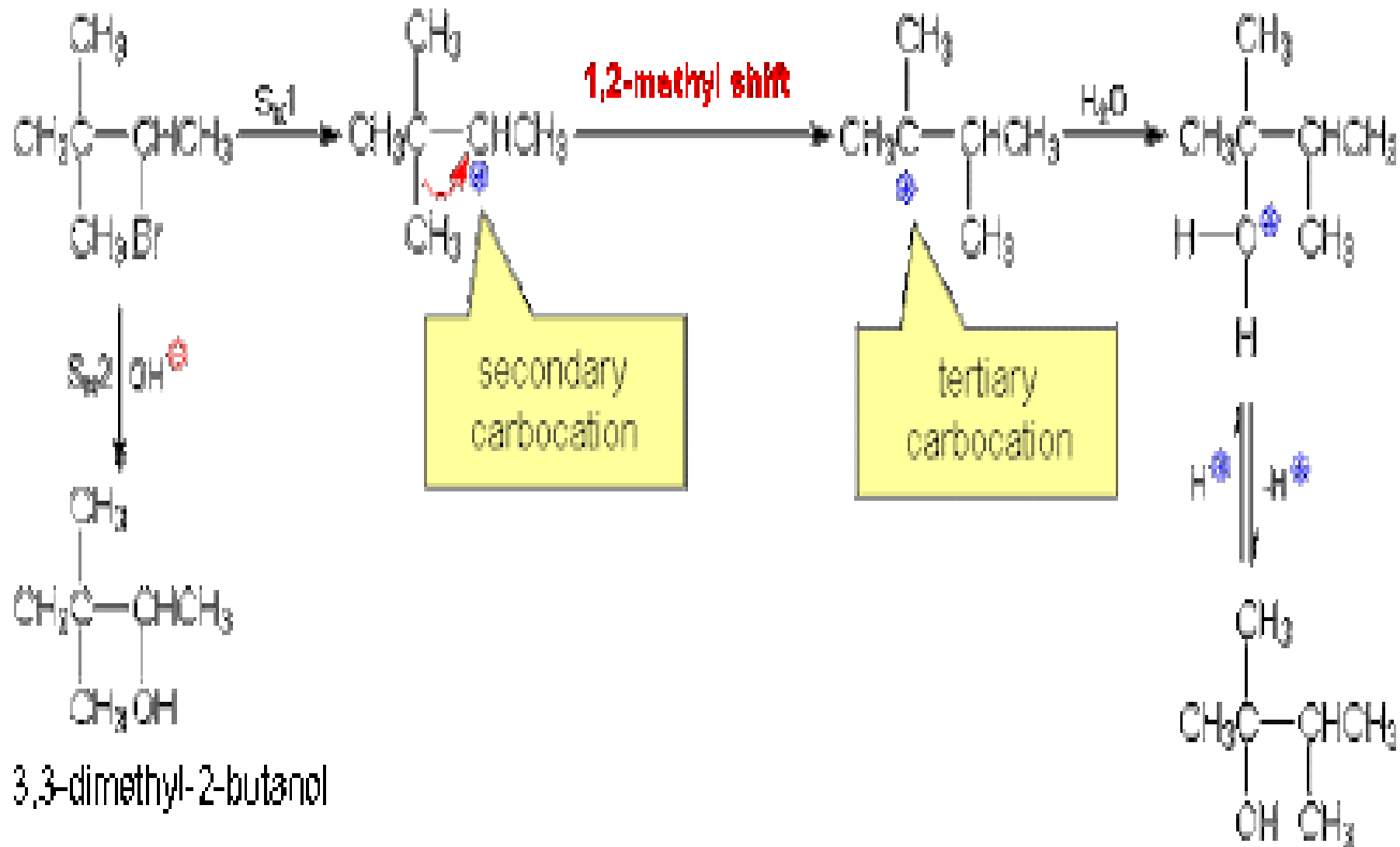
3. Nature of solvents

Polar protic solvents increases the rate of SN1

Reaction due to greater ionising power.

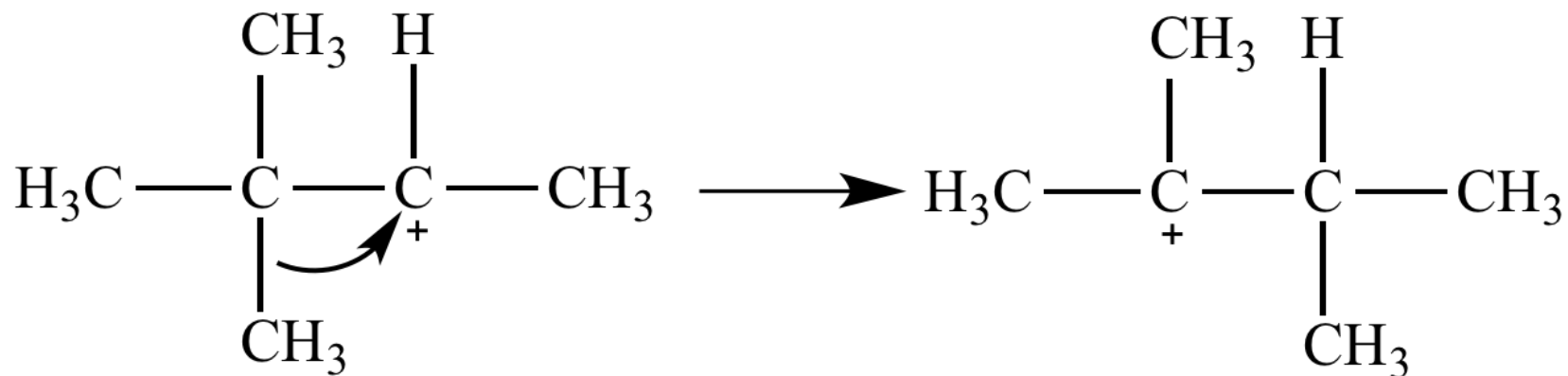
Competition between S_N1 and S_N2

The structure of substrate, the nature of the nucleophilic reagent, polarity of solvent, and other experimental conditions determine whether nucleophilic substitution will take place by S_N1 or by S_N2 mechanism. In general, primary halides undergo substitution by S_N2 mechanism and tertiary halides undergo substitution by S_N1 mechanism. Secondary halides may undergo substitution by both S_N1 and S_N2 mechanisms, however, one mechanism may be maximized by the selection of appropriate conditions. High concentration of the nucleophile and / or presence of strong nucleophile favors S_N2 , while the factors promoting the S_N1 are, lower concentration of nucleophile or the absence of strong nucleophile, solvents of great ionizing power (such as water) and substrate leading to stable carbocations. The reaction rates of both the S_N1 and S_N2 reactions are increased if the leaving group is a stable ion and a weak base.

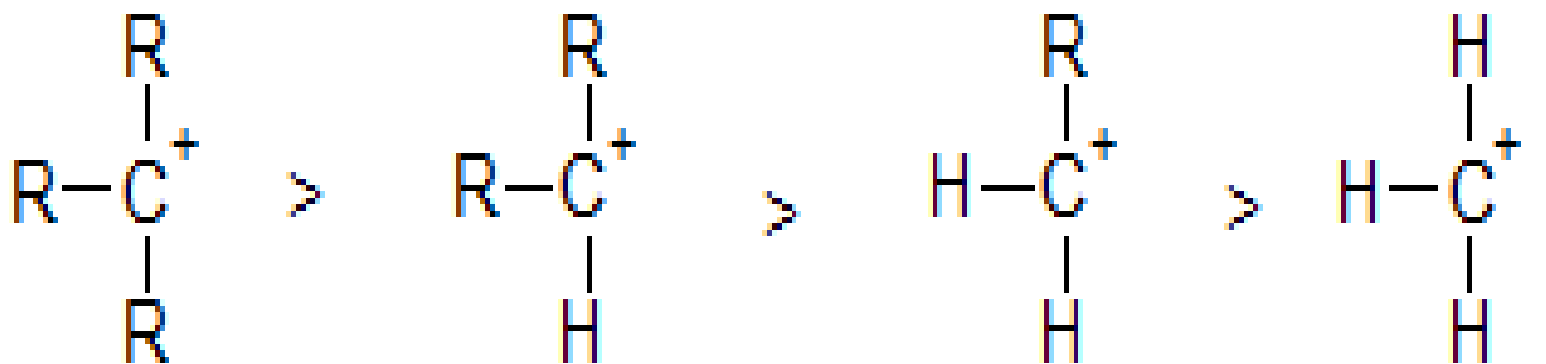


3,3-dimethyl-2-butanol

2,3-dimethyl-2-butanol



Relative Stability of Carbocations



tertiary

secondary

primary

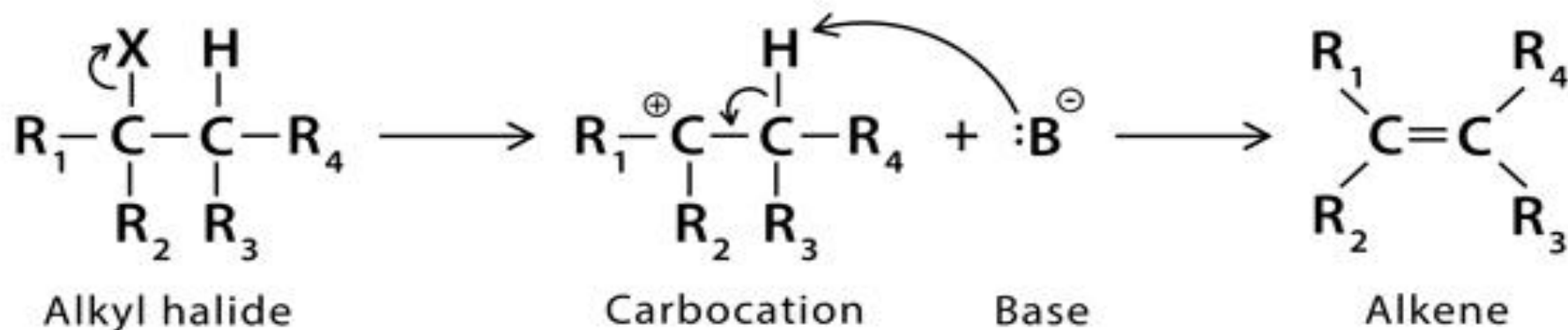
methyl

E1 mechanism

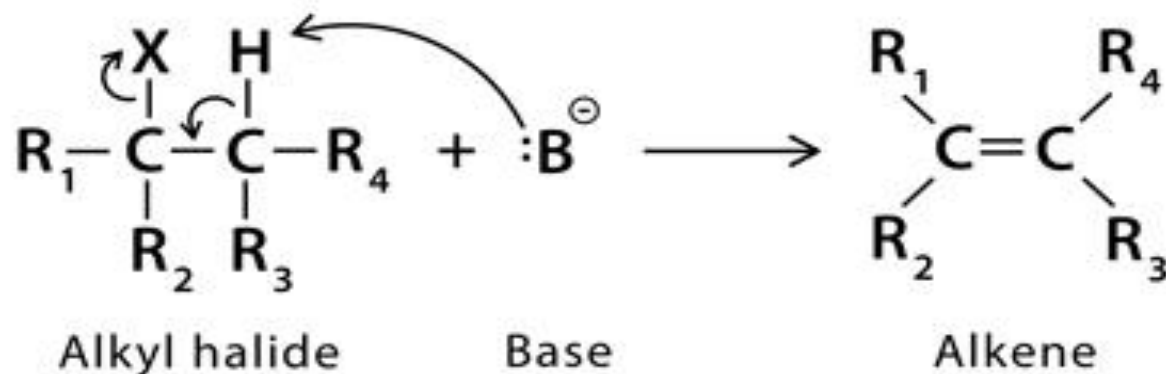
- In the **E1 mechanism** which is also known as unimolecular elimination
- Two steps involved – ionization and deprotonation.
- During ionization, there is a formation of carbocation as an intermediate. In deprotonation, a proton is lost by the carbocation.

Mechanism of Elimination Reaction for Alkyl Halide

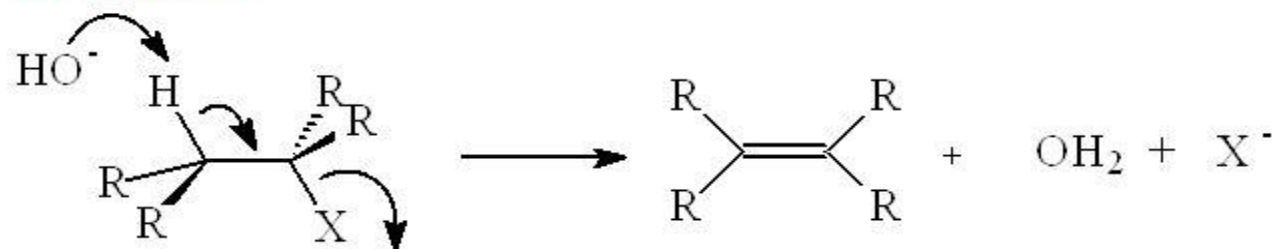
- E1 Elimination: 1. Debonding of the leaving group, followed by ionization of the molecule resulting in a carbocation
2. Removal of the hydrogen atom through deprotonation in presence of a base to form the C=C bond



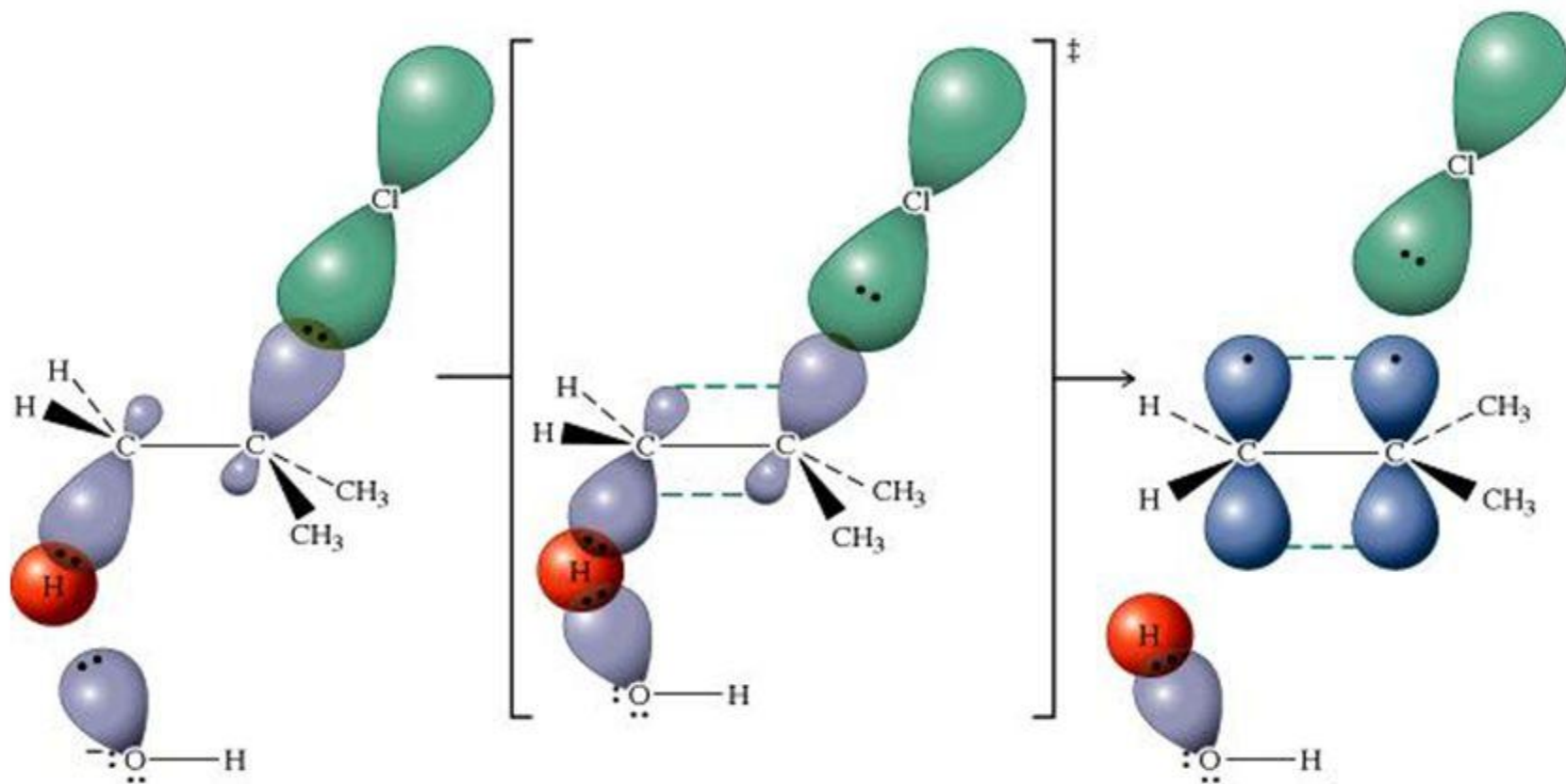
- E2 Elimination: Simultaneous removal of the leaving group and hydrogen atom in presence of a base to form the C=C bond



3) Mechanism

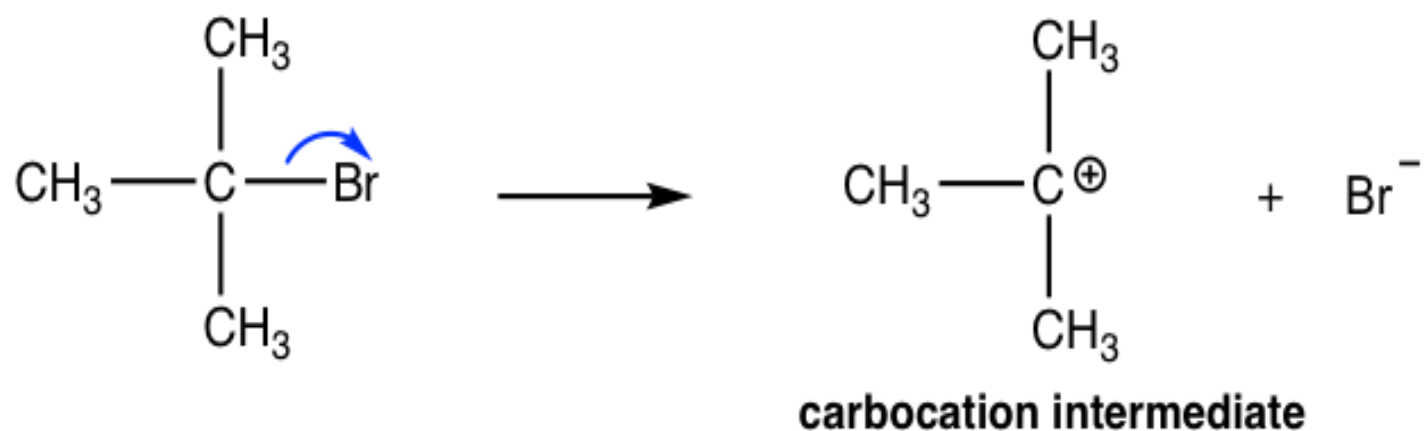


4) Orbital Picture

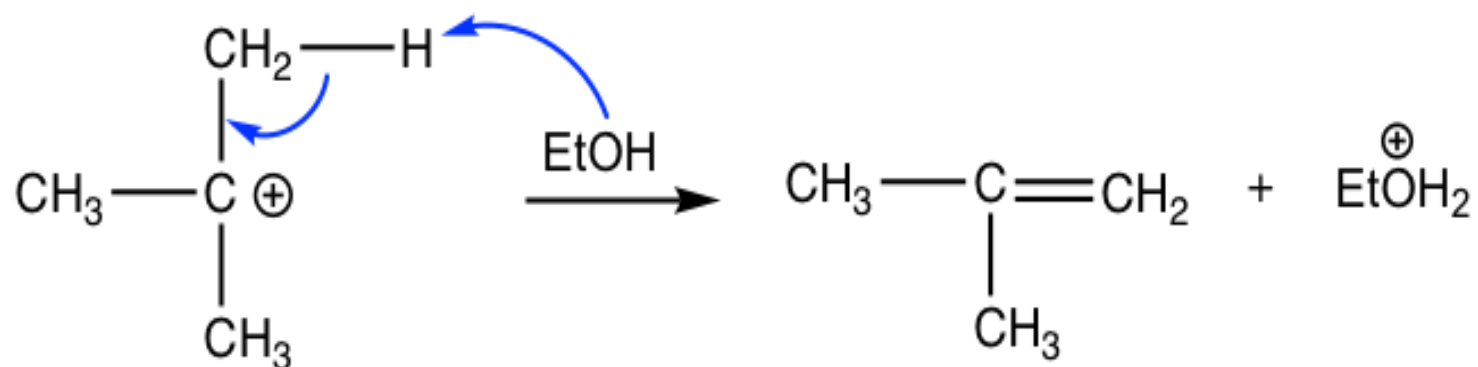


Mechanism

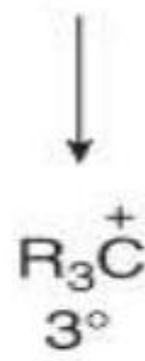
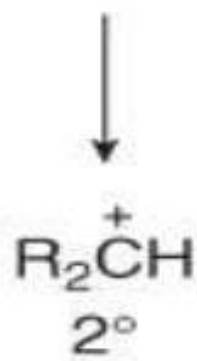
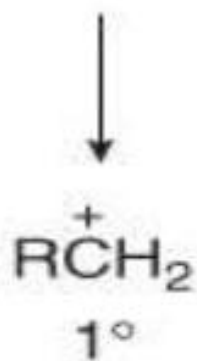
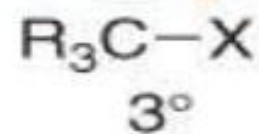
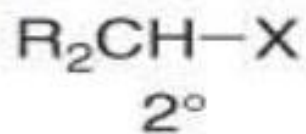
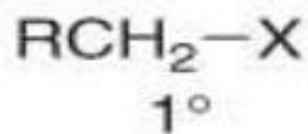
Step 1: Cleavage of C-Br bond **slowly** to form the carbocation intermediate.



Step 2: base (EtOH) removes H from a β-carbon, and double bond produced.

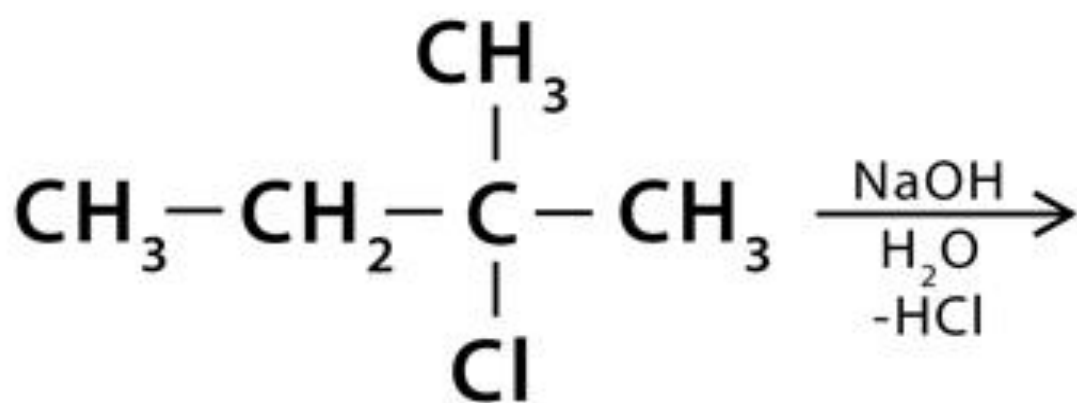


Increasing rate of an E1 reaction

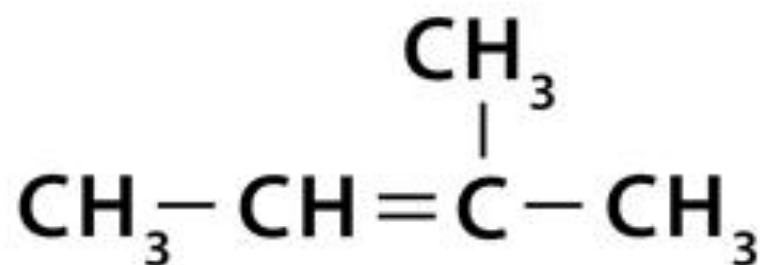


Increasing carbocation stability

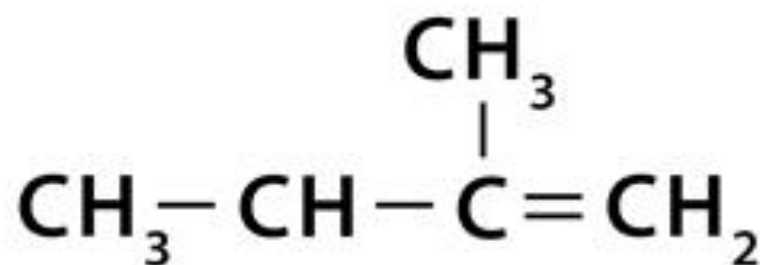
Zaitsev's Rule For Dehydrohalogenation Reaction



tert-Amyl chloride

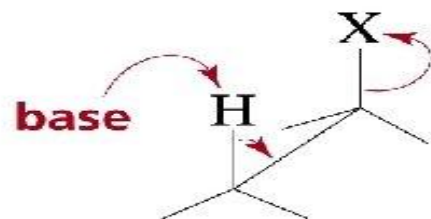


2-Methyl-2-butene
More stable, 70%

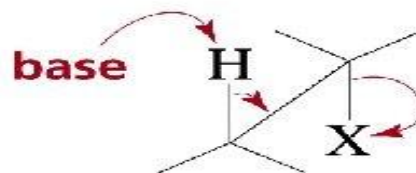


2-Methyl-1-butene
Less stable, 30%

Another view of the E2 reaction mechanism



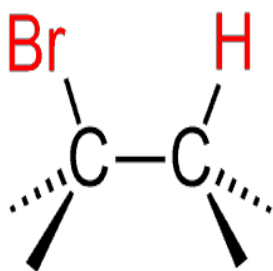
syn elimination



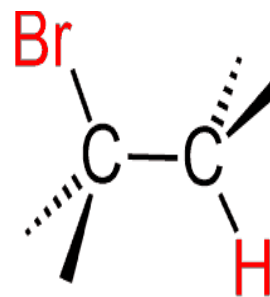
anti elimination

The best overlap of the interacting orbitals is achieved through back side attack

Anti elimination avoids repulsion of the electron-rich base



***syn* periplanar**



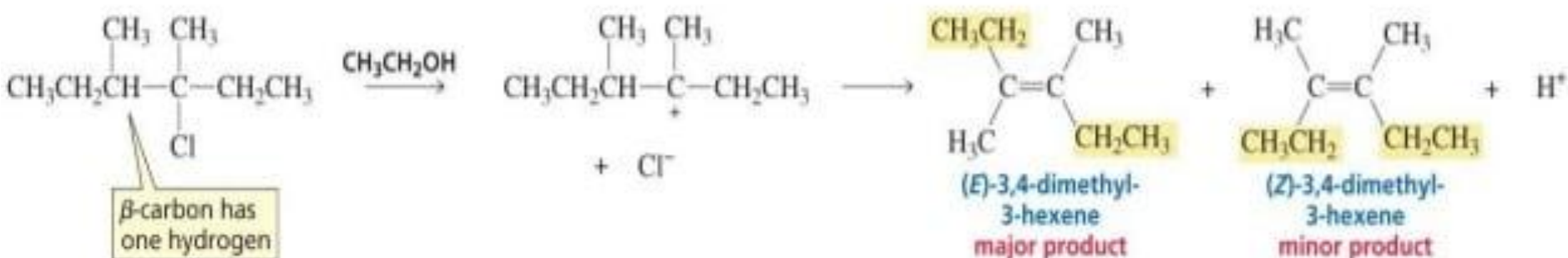
***anti* periplanar**

β -H and Br on the same side.

β -H and Br on opposite sides.

Stereochemistry of the E1 Reaction

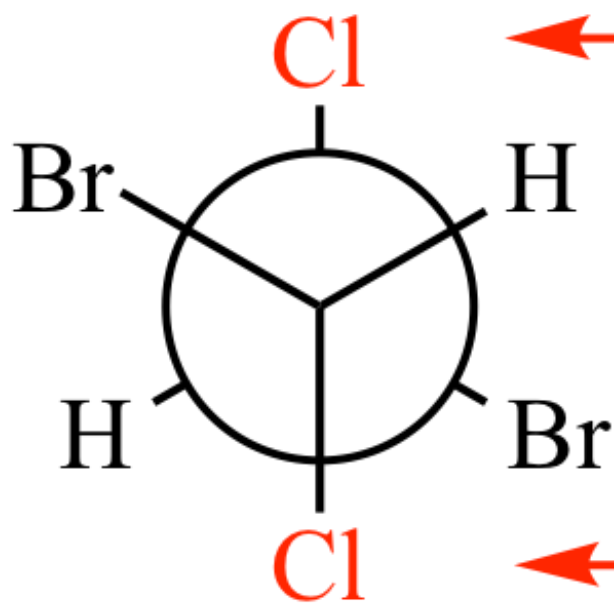
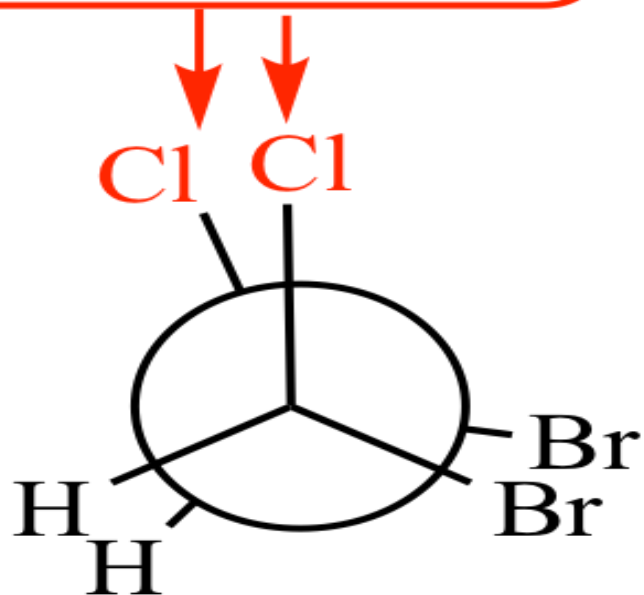
Both syn and anti elimination can occur in an E1 reaction



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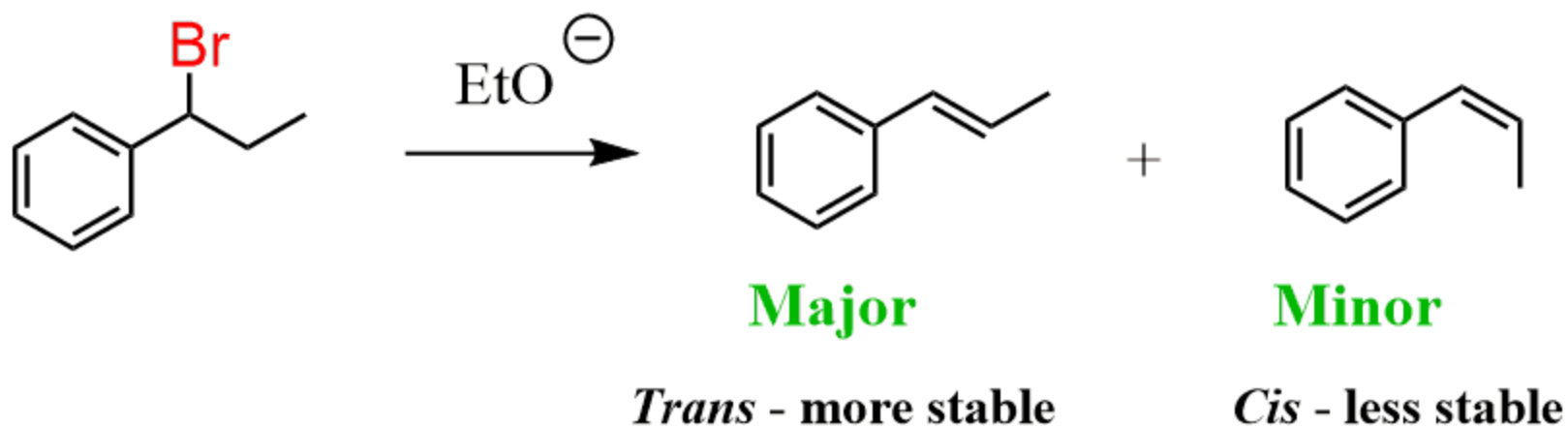
The major stereoisomer obtained from an E1 reaction is the alkene in which the bulkiest substituents are on opposite sides of the double bond

Syn-periplanar



Anti-periplanar

Stereoselectivity of the E2 elimination reactions



Two stereoisomers of an alkene are formed but one predominates.