

Alkyl Halides

Nucleophilic Aliphatic Substitution and
Elimination

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For 1st Stage Students

Reactions

Nucleophilic Substitution

A halide ion is an extremely **weak base** (conjugate base) (Good leaving group).



When attached to carbon,

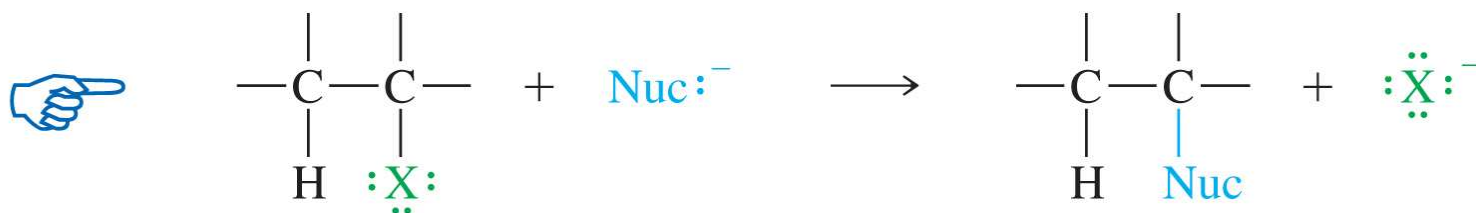
X-C

halogen can be readily displaced as halide ion by other, **stronger bases**.

These **bases** possess an **unshared pair of electrons** and are seeking a relatively **positive site**, that is, are seeking a nucleus with which to share their electrons.

Called **Nucleophilic Reagents** Nuc^-
(from the Greek, **nucleus-loving**)

Nucleophilic substitution



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- * The halogen atom on the alkyl halide is replaced with a nucleophile (Nuc^-).
- * Since the halogen is more electronegative than carbon, the $\text{C}-\text{X}$ bond breaks heterolytically and X^- leaves.

Elimination

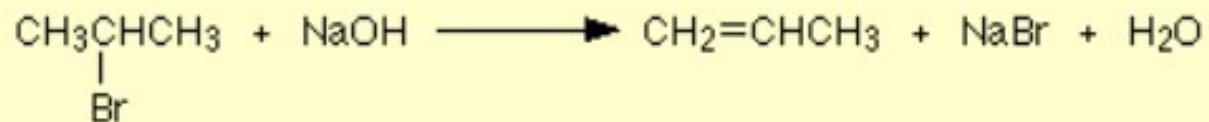
This reaction is important in the synthesis of alkenes by basic reagents

Elimination



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- * Elimination reactions produce double bonds.
- * The alkyl halides loses a hydrogen and the halide.
- * Also called dehydrohalogenation (-HX).



Kinetics of nucleophilic aliphatic substitution. Second-order and first-order reactions

1- Nucleophilic Substitution Bimolecular, S_N2

Let us take a specific example, the reaction of methyl bromide with sodium hydroxide to yield methanol:

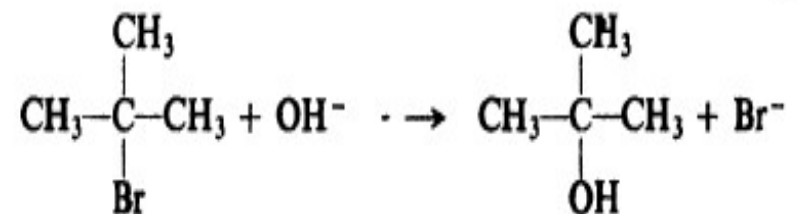


We say that the **rate of reaction** depends upon both $[\text{OH}^-]$ and $[\text{CH}_3\text{Br}]$, and we indicate this by the expression:

$$\text{rate} = k[\text{CH}_3\text{Br}][\text{OH}^-] \quad \text{Second-order kinetics}$$

Nucleophilic Substitution Monomolecular, S_N1

Ex: Reaction between *tert*-butyl bromide and hydroxide ion:

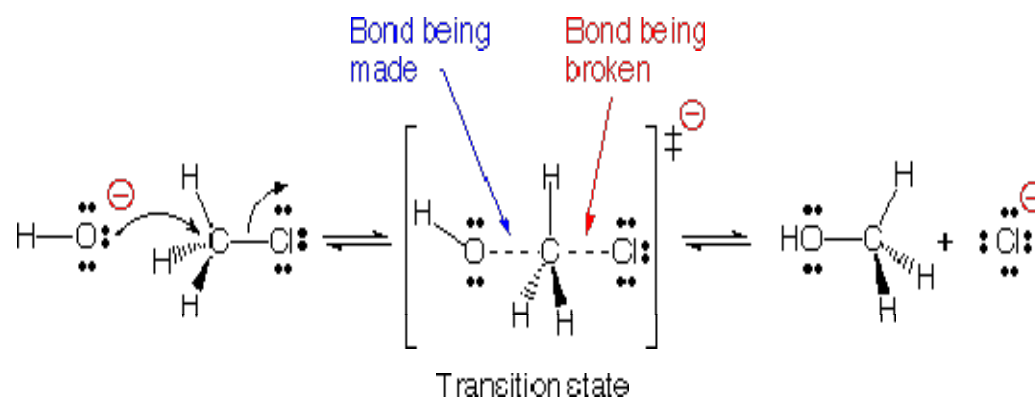


The rate of reaction of *tert*-butyl bromide depends only upon [RBr].

This is indicated by the expression

$$\text{rate} = k[\text{RBr}] \quad \text{First-order kinetics}$$

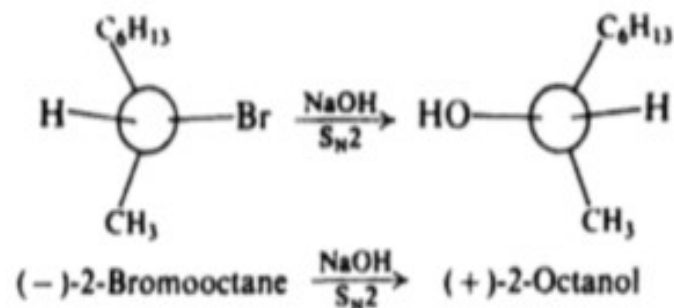
Mechanism, stereochemistry and stability (S_N2)



Features:

- * Attack from backside
- * T.S. formation
- * Inversion in configuration

When (-)-2-bromooctane is allowed to react with sodium hydroxide under conditions where second-order kinetics are followed, there is obtained (+)-2-octanol.

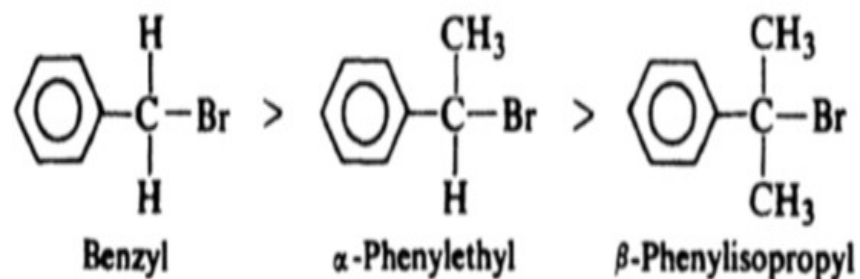
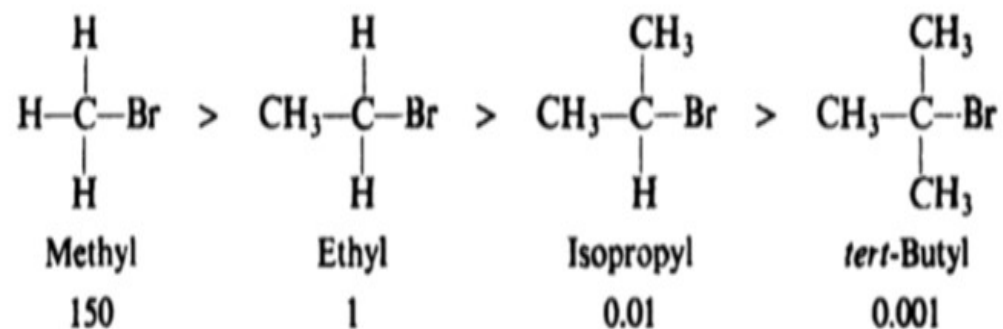


*A reaction that yields a product whose configuration is opposite to that of the reactant is said to proceed with **inversion of configuration**.*

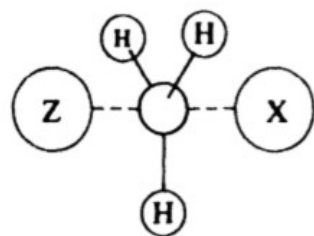
Differences in rate between two S_N2 reactions seem to be due chiefly to *steric factors*.

As the **number of substituents attached to the carbon bearing the halogen is increased**, the reactivity toward S_N2 substitution **decreases**.

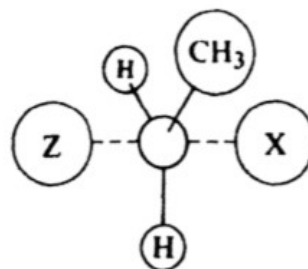
S_N2 substitution: relative reactivity toward I^-



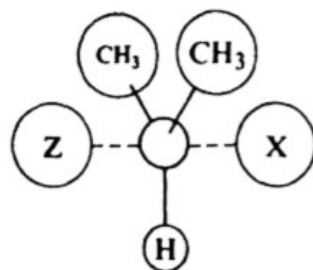
Increasing the bulk of substituents led to raises the energy of transition state (T.S) and slows down reaction.



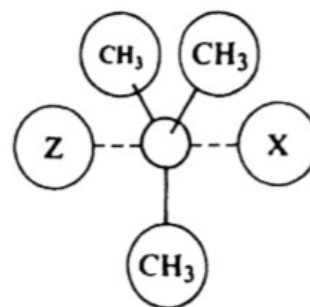
Methyl



Ethyl

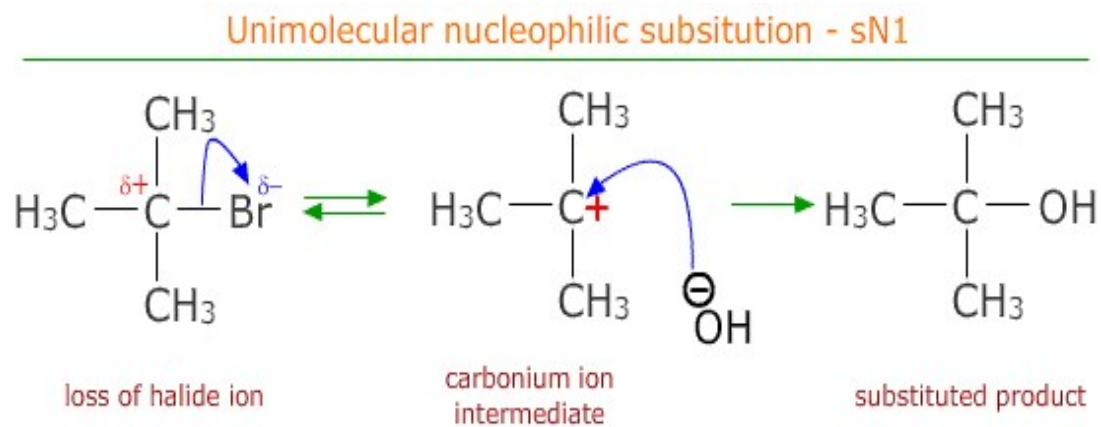


Isopropyl



tert-Butyl

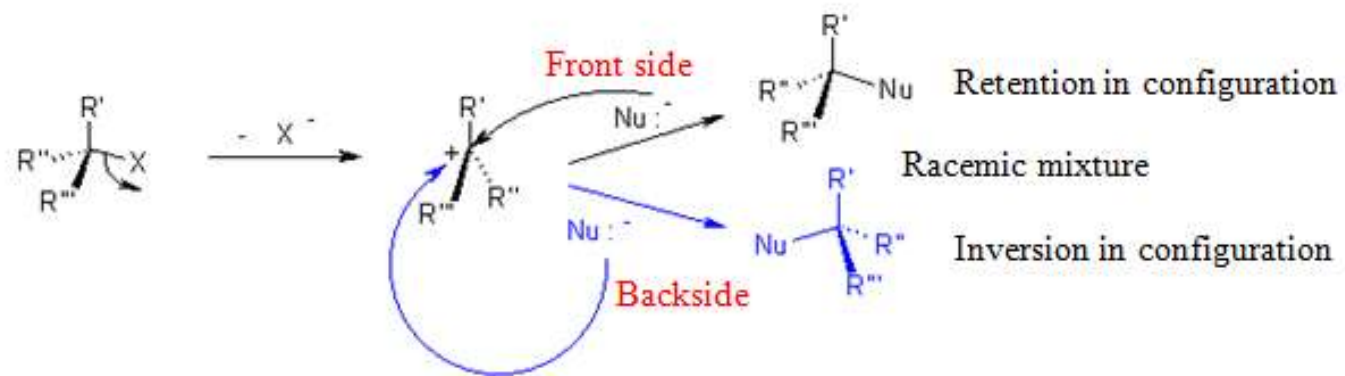
Mechanism, stereochemistry and stability (S_N1)



Features:

- * Attack from two sides
- * Carbonium ion (carbocation) formation
- * Racemic mixture

Stereochemistry

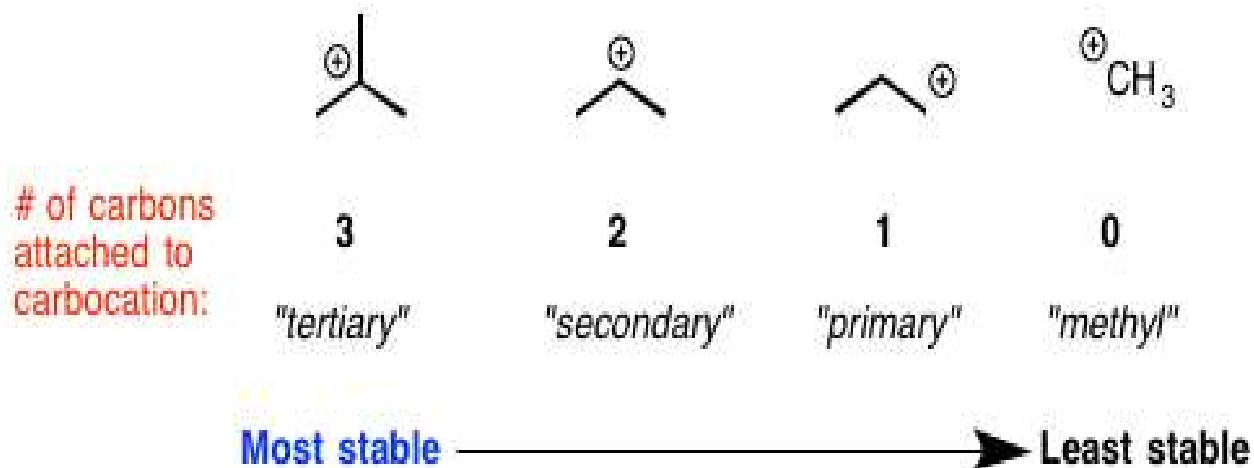


Reactivity

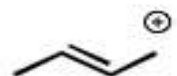
The order of reactivity of alkyl halides in S_N1 reactions is the same as the order of **stability of carbonium ions**.

In S_N1 reactions the order of reactivity of RX is **allyl, benzyl > 3 > 2 > 1 > CH_3X** .

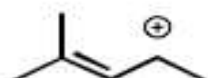
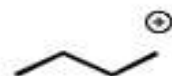
1. Increasing substitution by carbon stabilizes carbocations



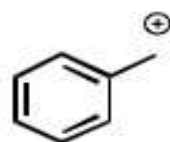
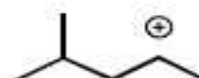
2. Adjacent carbon-carbon π bonds stabilize carbocations



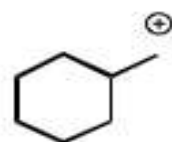
is more stable than



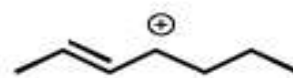
is more stable than



is more stable than



is more stable than



(note how the effect is additive)

Why? Resonance.



Resonance allows for the positive charge to be distributed over multiple carbons, which is a stabilizing influence.



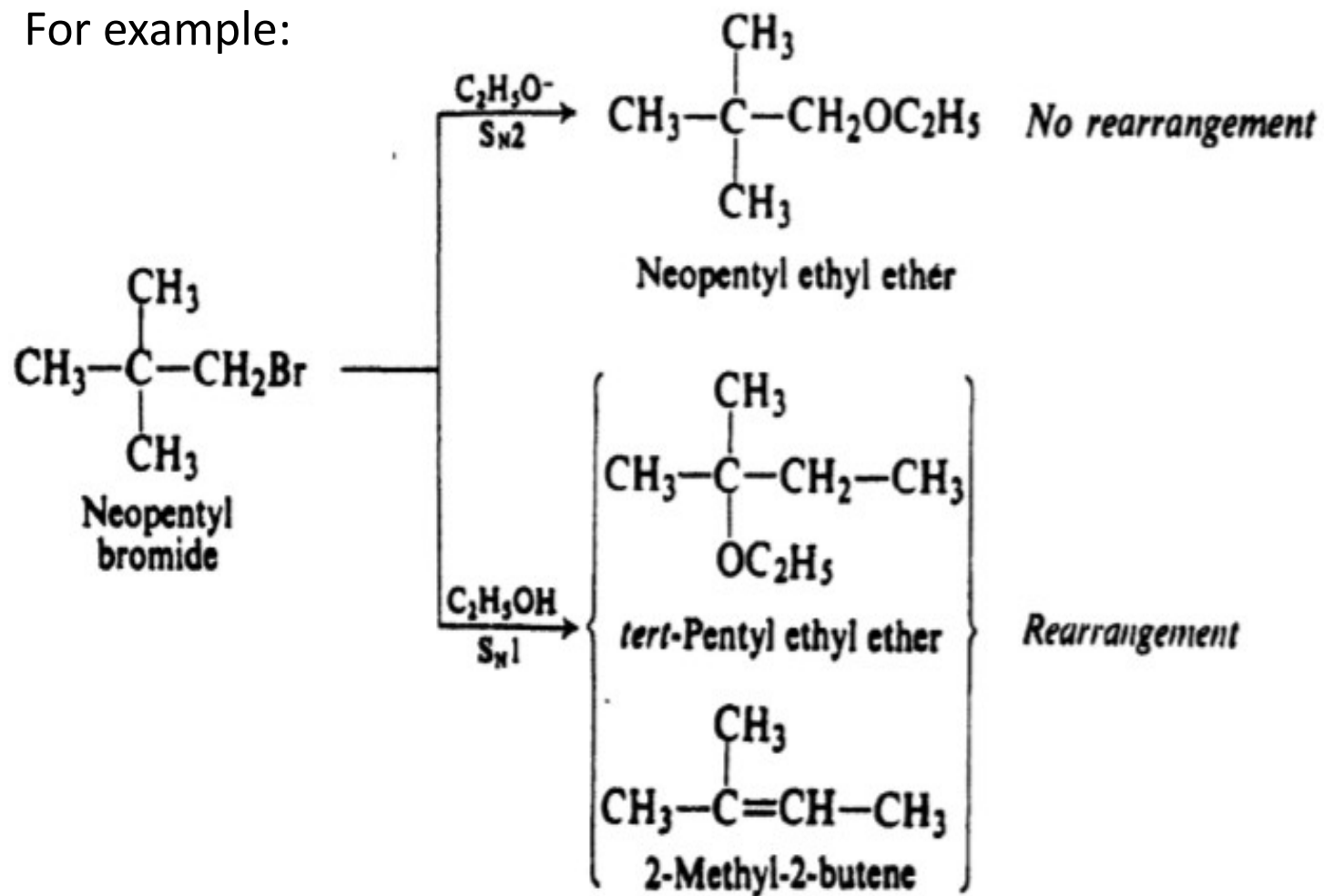
This carbocation cannot be stabilized by resonance.

S_N1 , Rearrangement

If the S_N1 reaction involves intermediate **carbonium ions**, we might expect it to show one of the characteristic features of carbonium ion reactions: **rearrangement**.

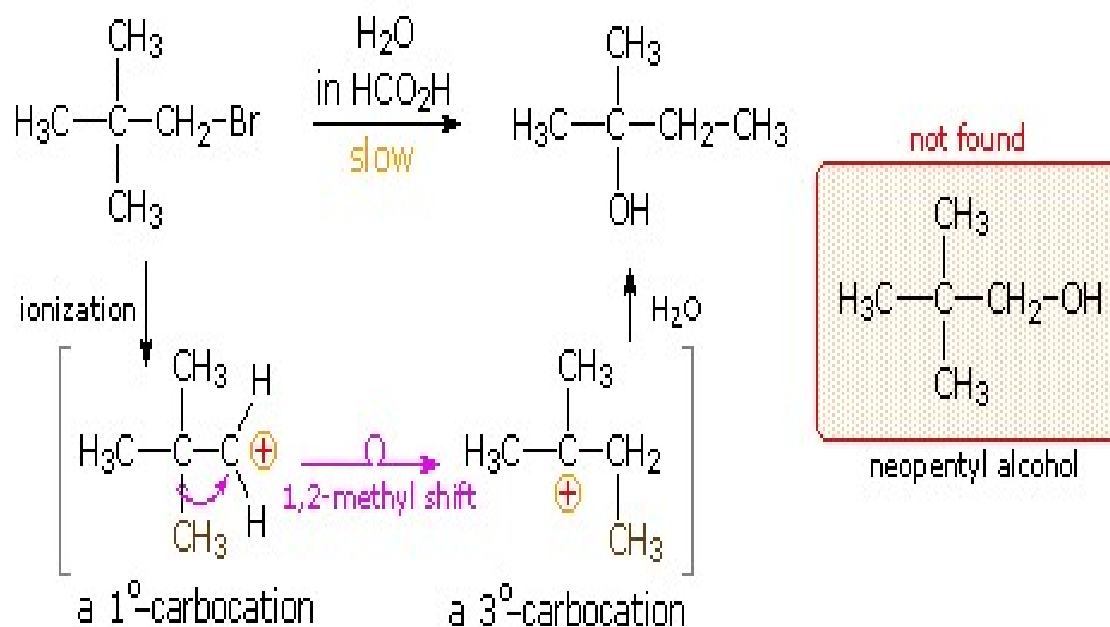
In an S_N2 reaction, on the other hand, the halide ion does not leave until the nucleophilic reagent has become attached; there is **no free intermediate** particle and hence we would expect **no rearrangement**.

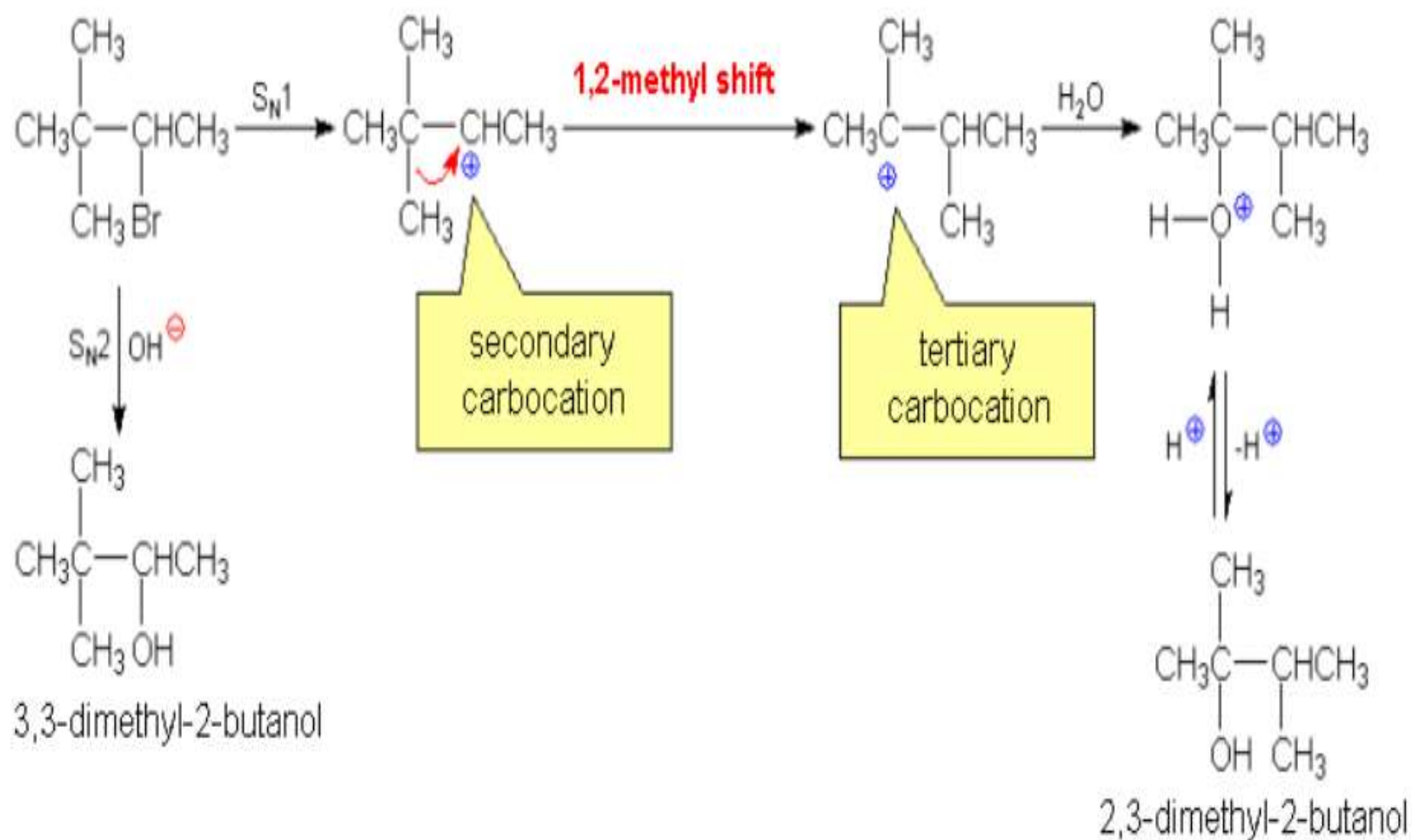
For example:



Mechanism:

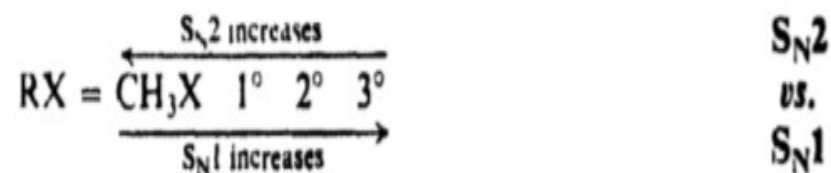
In the case of the neopentyl cation, however, the initially formed 1°-carbocation may be converted to a more stable 3°-carbocation by the 1,2-shift of an adjacent methyl group with its bonding electrons.





S_N2 vs. S_N1, Competition

* Nucleophilic substitutions that follow first-order kinetics the reactivity sequence $3 > 2 > 1 > \text{CH}_3\text{X}$,



* **Concentration of nucleophilic reagent**, high concentration of the nucleophilic reagent favors the S_N2 reaction; low concentration favors the S_N1 reaction.

* **The nature of the nucleophilic reagent (strong or weak)**, neopentyl bromide reacts with **ethoxide** ion by the S_N2 mechanism and with **ethyl alcohol** by the S_N1 mechanism

The polarity of the solvent: The more polar the solvent, the stronger the solvation forces and the faster the ionization. For example, from 80% ethanol to the much more polar water should speed up ionization and hence the rate of the S_N1 reaction.

