

NUCLEOPHILIC SUBSTITUTION REACTIONS (Part I)

By

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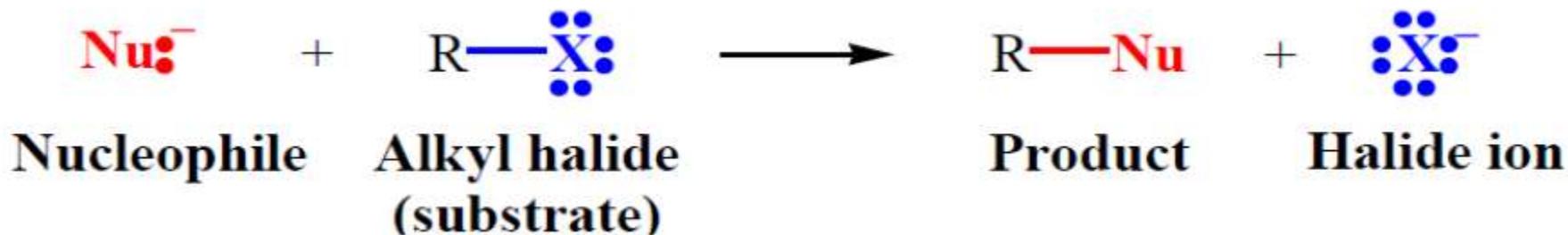
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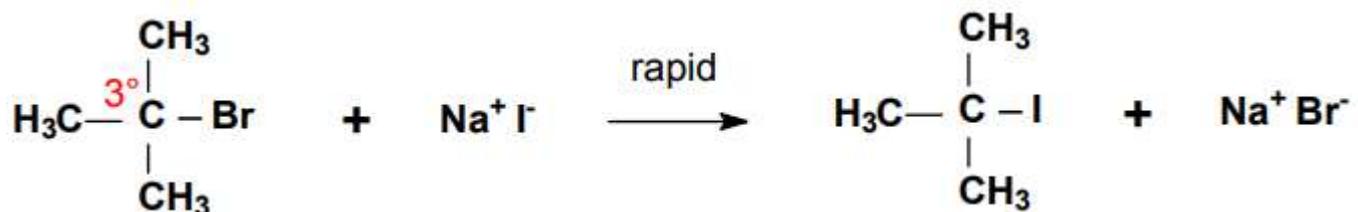


- In nucleophilic substitution reactions, the C–X bond of the substrate undergoes heterolysis, and the lone-pair electrons of the nucleophile is used to form a new bond to the carbon atom.
- A **nucleophile**, a species with an unshared electron pair (lone-pair electrons), reacts with an **alkyl halide** (substrate) by replacing the halogen substituent (leaving group).
- To be a good leaving group the substituent must be able to leave as a relatively stable, weakly basic molecule or ion.
- In alkyl halides, the leaving group is the halogen substituent — it leaves as a halide ion.
- Because halide ions are relatively stable and very weak bases, they are good leaving groups.

□ There are generally two types of nucleophilic substitution reaction.

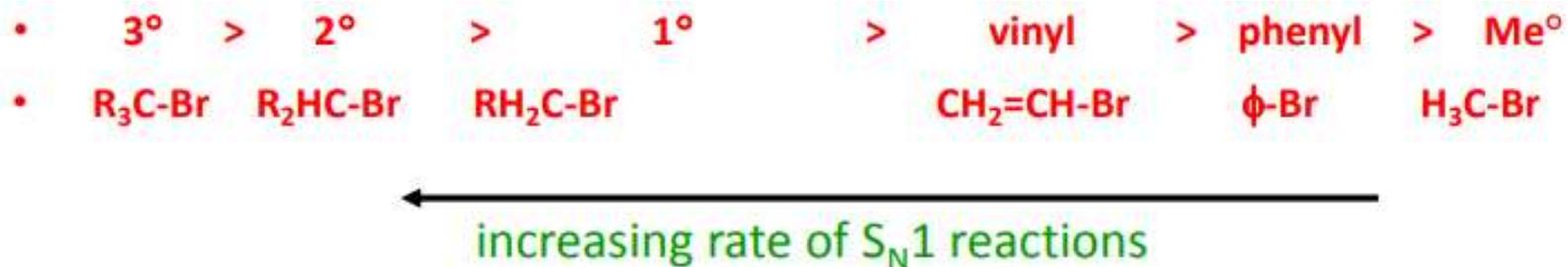
- SN^1
- SN^2

Substitution Nucleophilic Unimolecular (SN^1)



- The meaning of SN^1 reaction lies in the name itself “substitution, nucleophilic, and unimolecular.” Therefore, this reaction will follow the first order kinetics. In another term, we can say that the rate determining step in this reaction is unimolecular.
- SN^1 = Substitution, Nucleophilic, 1st order (unimolecular).
- The rate of reaction will depend upon the concentration of the one species, the alkyl halide-not the nucleophile.
- SN^1 reactions obey 1st order kinetics, i.e., Rate = k [RX].

- 3° alkyl halides do undergo nucleophilic substitution reactions quite rapidly, but by a SN¹ mechanism.
- The order of reactivity of substrates for SN¹ reactions is the reverse of SN²

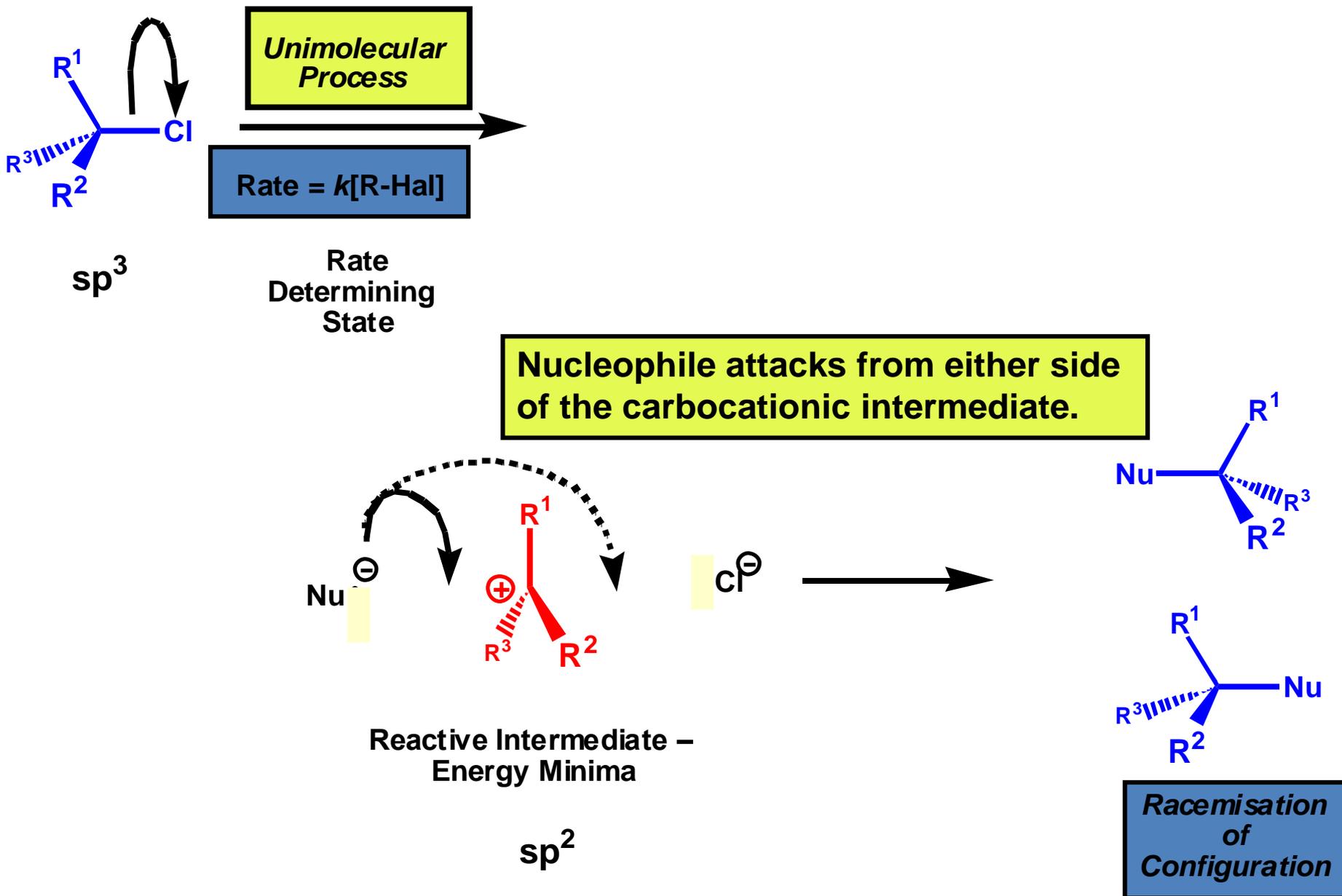


The mechanism of an SN¹ reaction occurs in 2 steps:

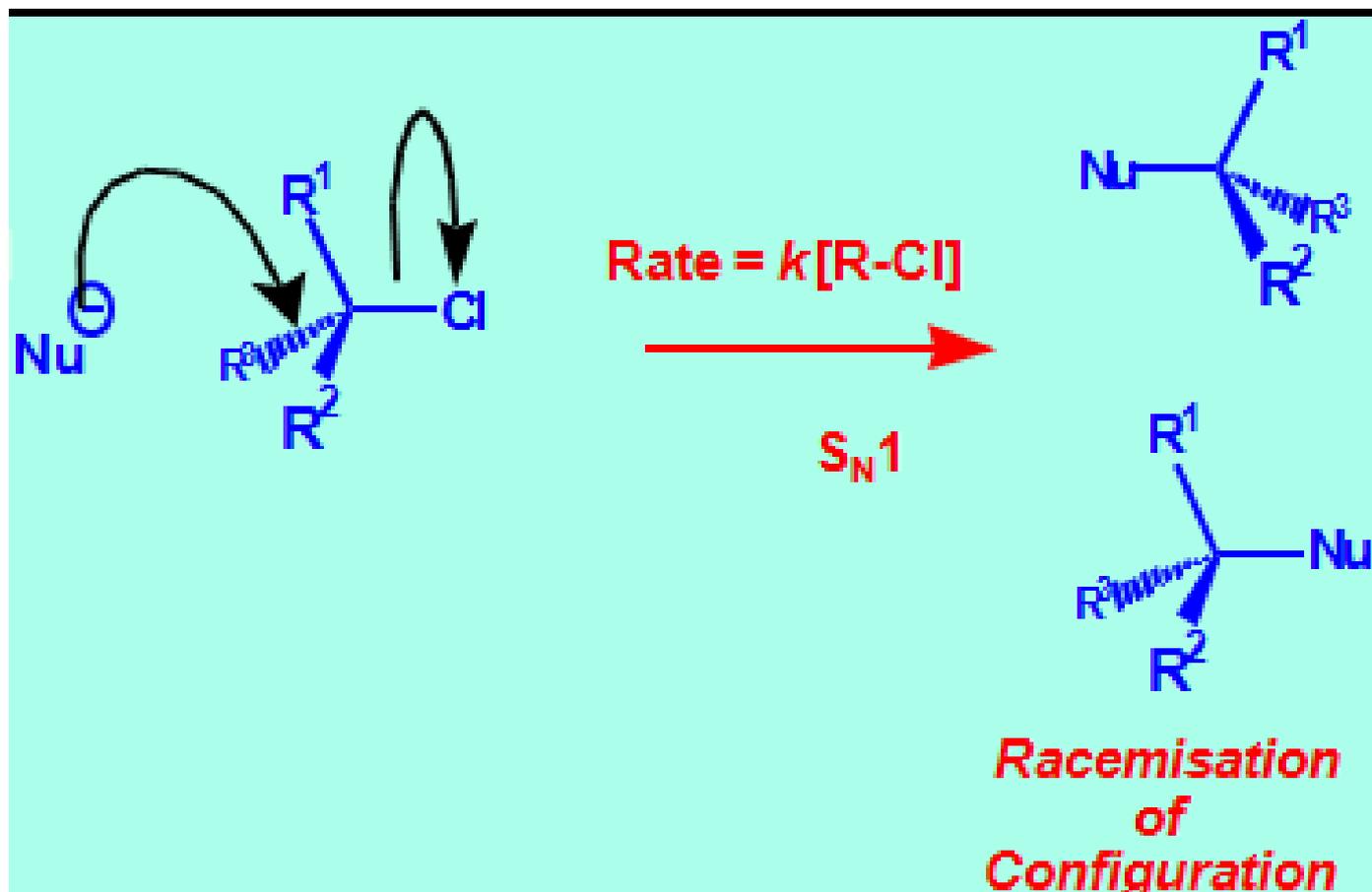
- 1) The slower, rate-limiting dissociation of the alkyl halide forming a C⁺ intermediate
- 2) A rapid nucleophilic attack on the C⁺

Note that the nucleophile is not involved in the slower, rate-limiting step

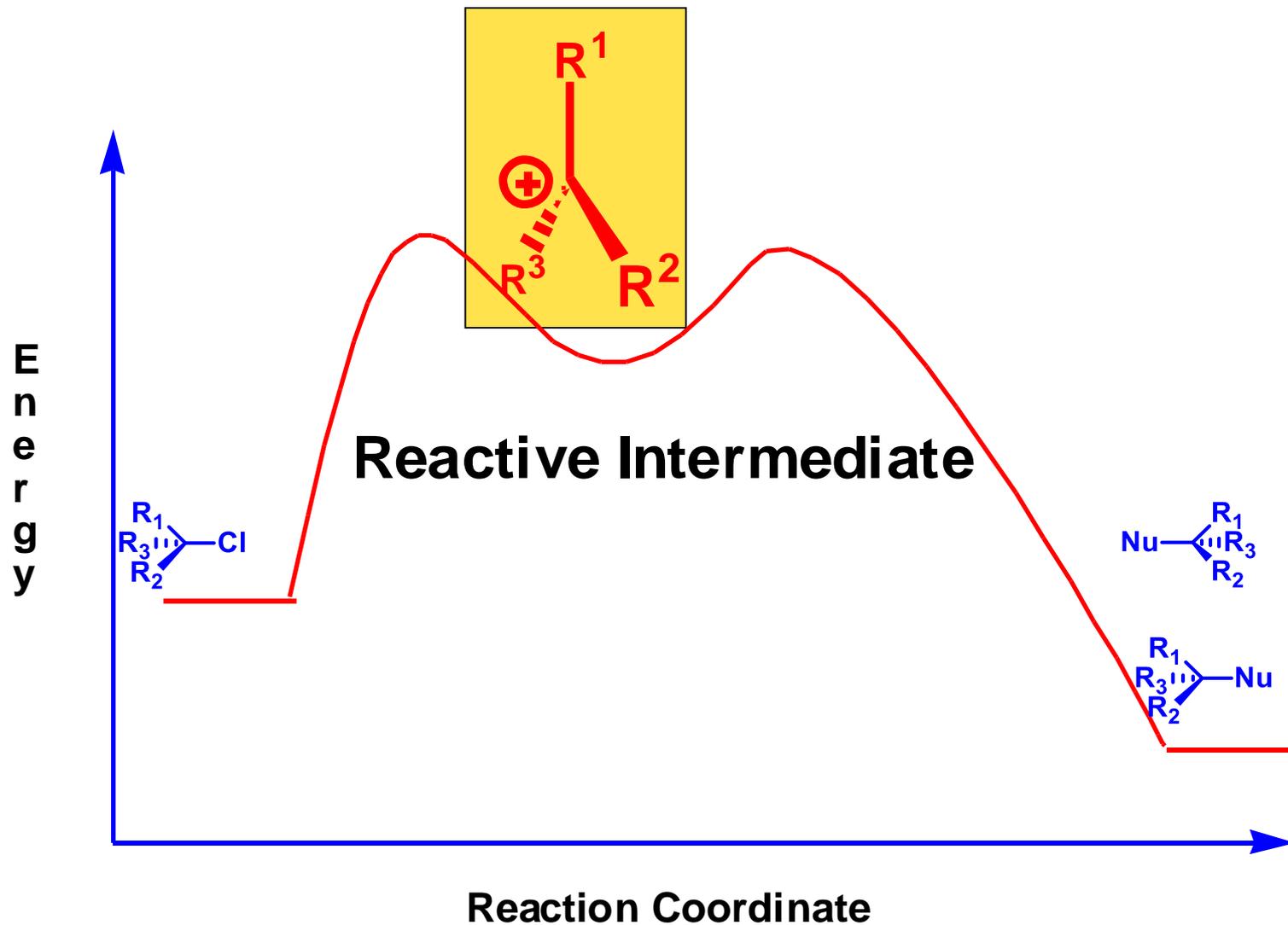
The S_N1 Reaction Mechanism



Stereo Chemistry



The Energy profile of S_N1 Reaction



- **The rate of an S_N1 reaction depends upon 3 factors:**

- 1) The nature of the substrate (the alkyl halide)

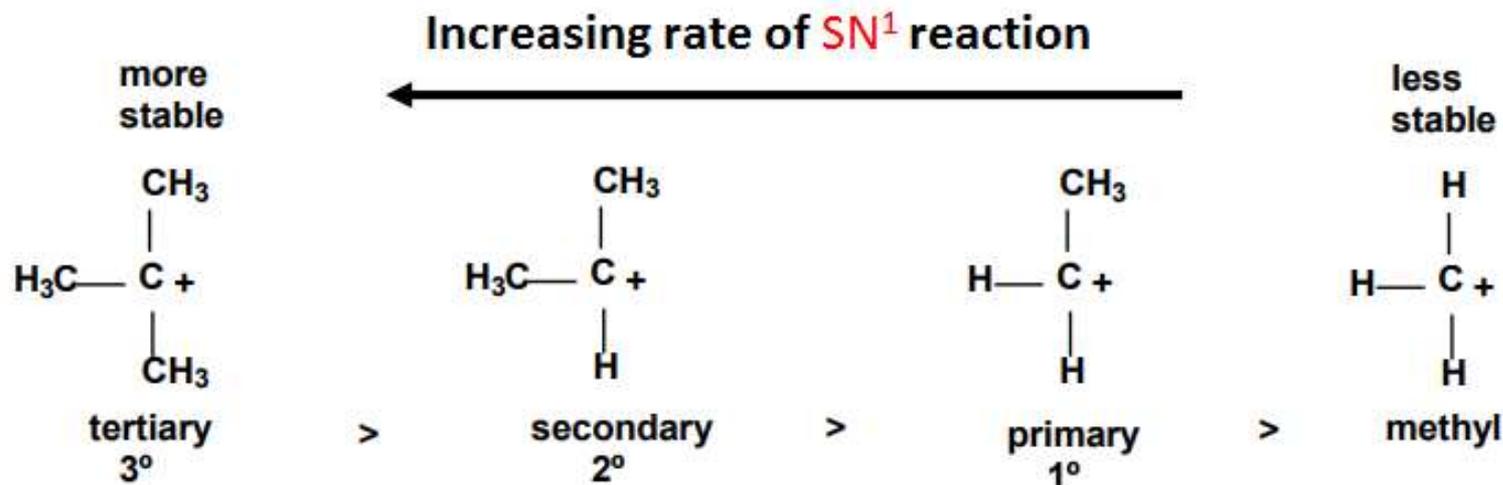
- 2) The ability of the leaving group to leave

- 3) The nature of the solvent

- The rate is independent of the power of the nucleophile

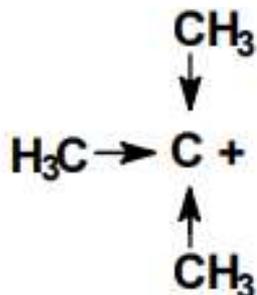
1) Nature of the substrate

Highly substituted alkyl halides (substrates) form a more stable C^+ .



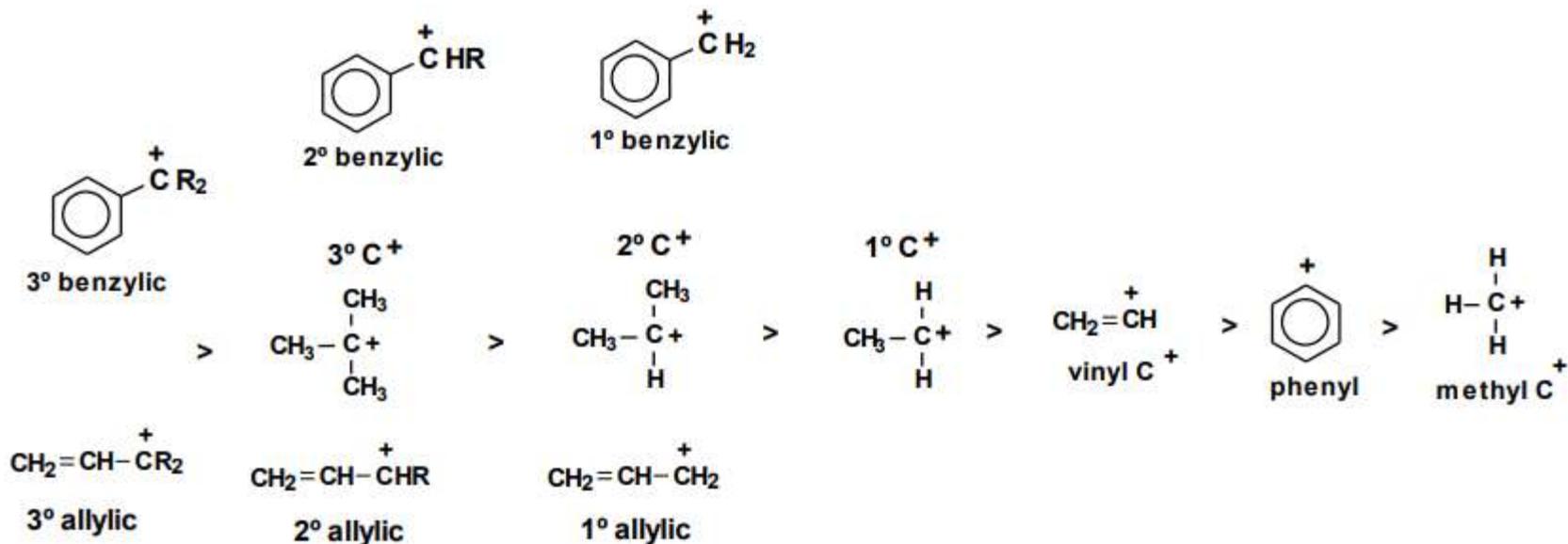
Stability of Carbocations

- Alkyl groups are weak electron donors.
- They stabilize carbocations by donating electron density by induction (through sigma bonds)

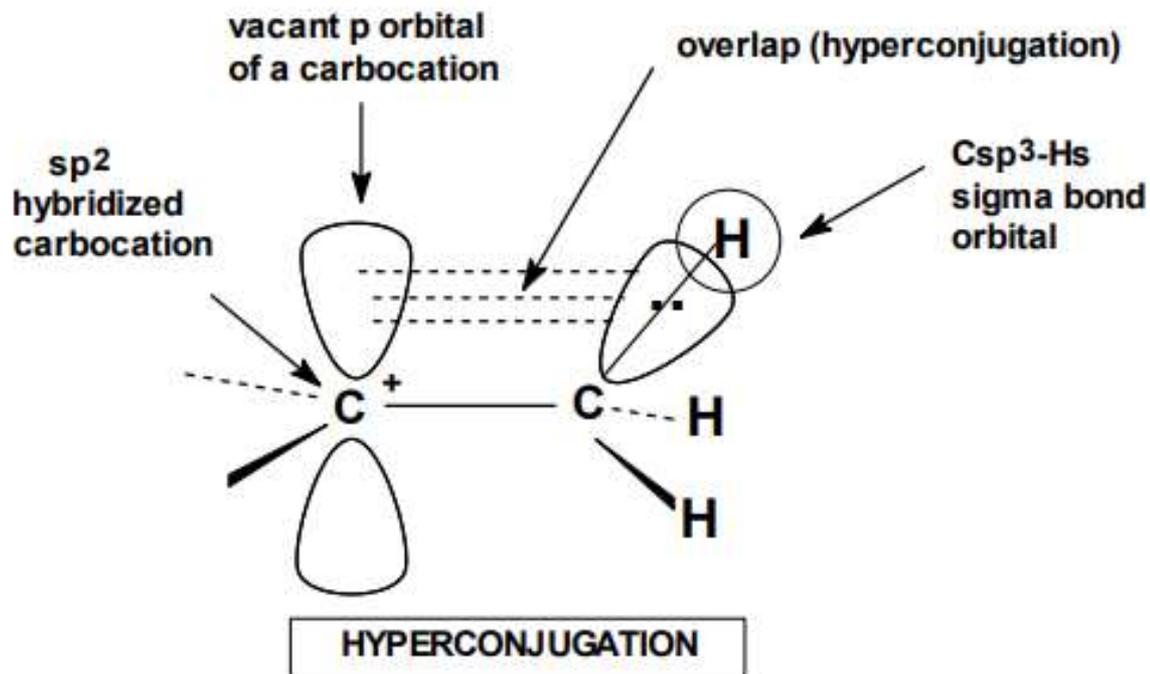


Inductive effects:
 Alkyl groups donate (shift) electron density through sigma bonds to electron deficient atoms.
 This stabilizes the carbocation.

← Increasing C⁺ stability and rate of S_N1 reaction



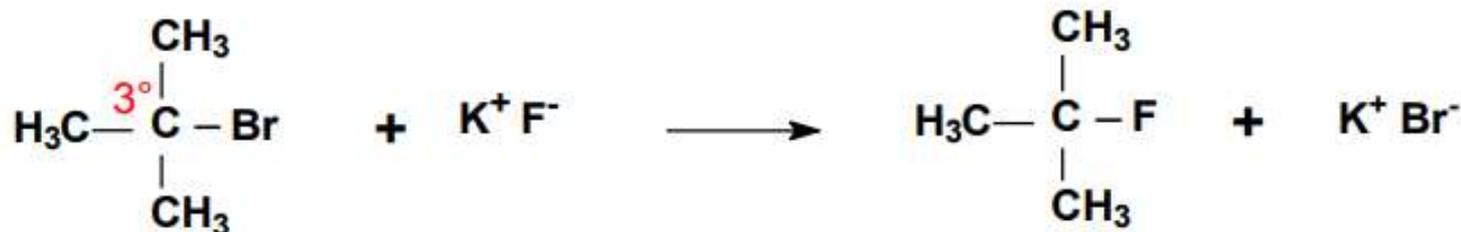
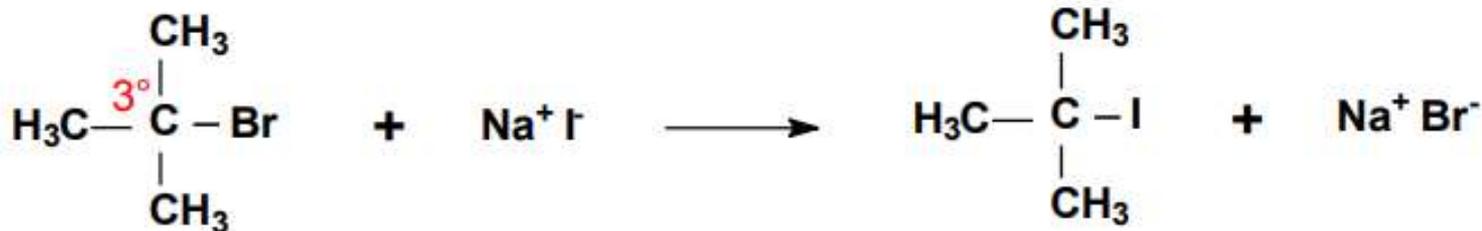
- They stabilize carbocations by hyperconjugation (by partial overlap of the alkyl C-to-H bonds with the empty p-orbital of the carbocation).



- Allyl and benzyl halides also react quickly by SN^1 reactions because their carbocations are unusually stable due to their resonance forms which delocalize charge over an extended p system.

- **Effect of the nucleophile on rate of SN¹ reactions:**

- ❑ Nature of the nucleophile has no effect on the rate of SN¹ reactions because the slowest (rate-determining) step of an SN¹ reaction is the dissociation of the leaving group and formation of the carbocation.
- ❑ All carbocations are very good electrophiles (electron acceptors) and even weak nucleophiles, like H₂O and methanol, will react quickly with them.
- ❑ The two SN¹ reactions will proceed at essentially the same rate since the only difference is the nucleophile.



2) Nature of the leaving group:

- The nature of the leaving group has the same effect on both SN^1 and SN^2 reactions.
- The better the leaving group, the faster a C^+ can form and hence the faster will be the SN^1 reaction.
- The leaving group usually has a negative charge
- Groups which best stabilize a negative charge are the best leaving groups, i.e., the weakest bases are stable as anions and are the best leaving groups.
- Iodine ($-\text{I}$) is a good leaving group because iodide (I^-) is non basic.
- The hydroxyl group ($-\text{OH}$) is a poor leaving group because hydroxide (OH^-) is a strong base.

3) Nature of the solvent

- ❑ For SN¹ reactions, the solvent affects the rate only if it influences the stability of the charged transition state, i.e., the C⁺. The Nu: is not involved in the rate determining step so solvent effects on the Nu: do not affect the rate of SN¹ reactions.
- ❑ Polar solvents, both protic and aprotic will solvate and stabilize the charged transition state (C⁺ intermediate), lowering the activation energy and accelerating SN¹ reactions.
- ❑ Non-polar solvents do not lower the activation energy and thus make SN¹ reactions relatively slower.

Effect of the solvent on rate of SN¹ reactions:

- ❑ Solvent polarity is usually expressed by the “dielectric constant”, ϵ , which is a measure of the ability of a solvent to act as an electric insulator.
- ❑ Polar solvents are good electric insulators because their dipoles surround and associate with charged species
- ❑ Dielectric constants of some common solvents are given in the following table:

name	dielectric constant	name	dielectric constant
aprotic solvents		protic solvents	
hexane	1.9	acetic acid	6.2
benzene	2.3	acetone	20.7
diethyl ether	4.3	ethanol	24.3
chloroform	4.8	methanol	33.6
HMPA	30	formic acid	58.0
DMF	38	water	80.4
DMSO	48		