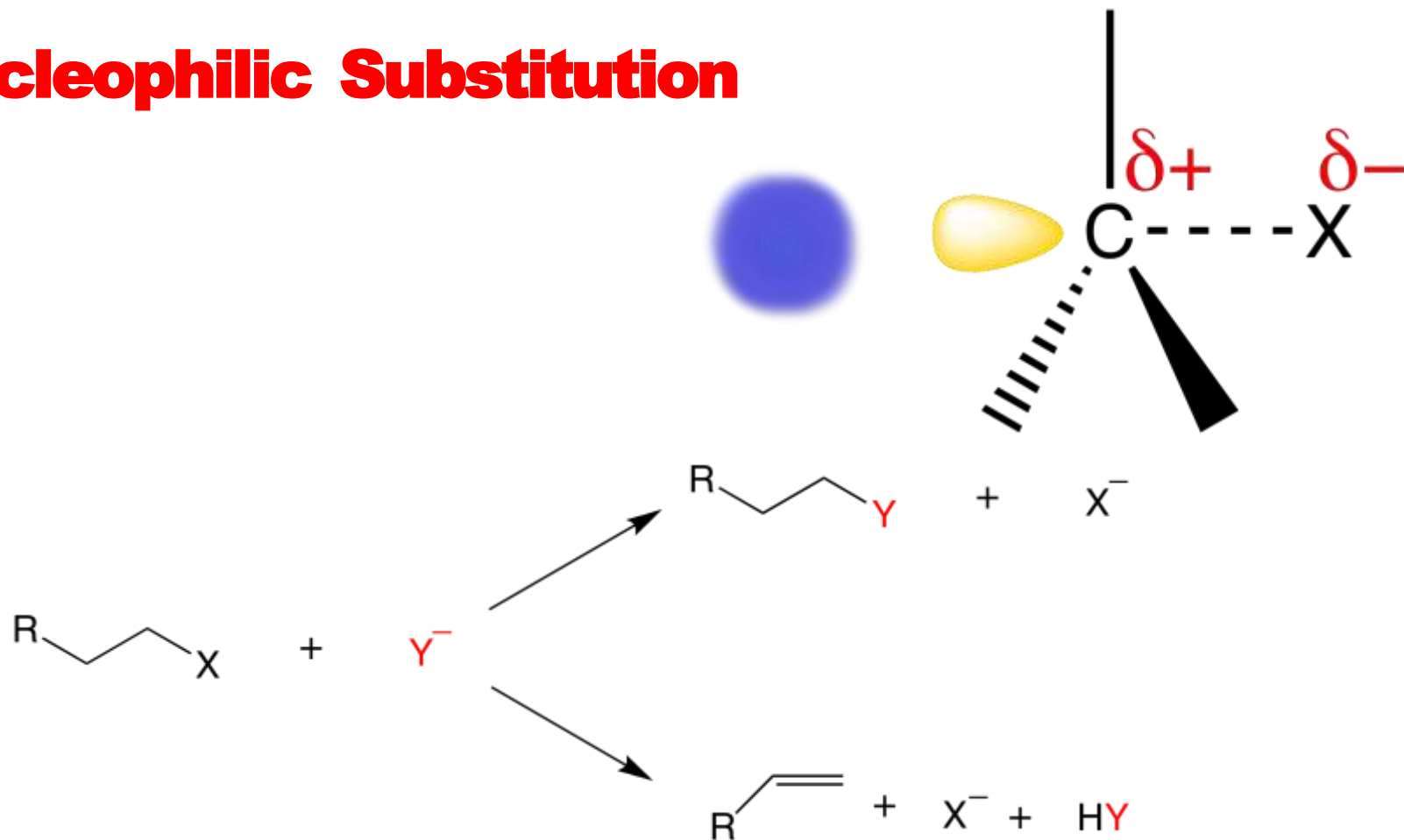


S_N2 Reaction

Nucleophilic Substitution



R = aliphatic as well as aromatic

Nucleophile + Substrate \longrightarrow Product + Leaving group

Nucleophilic Substitution

S_N1

S: Substitution
N: Nucleophilic
1: unimolecular

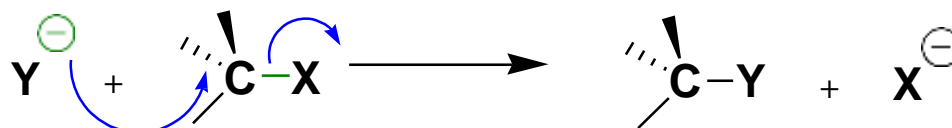
leaving group goes first and nucleophile comes later



S_N2

S: Substitution
N: Nucleophilic
2: Bimolecular

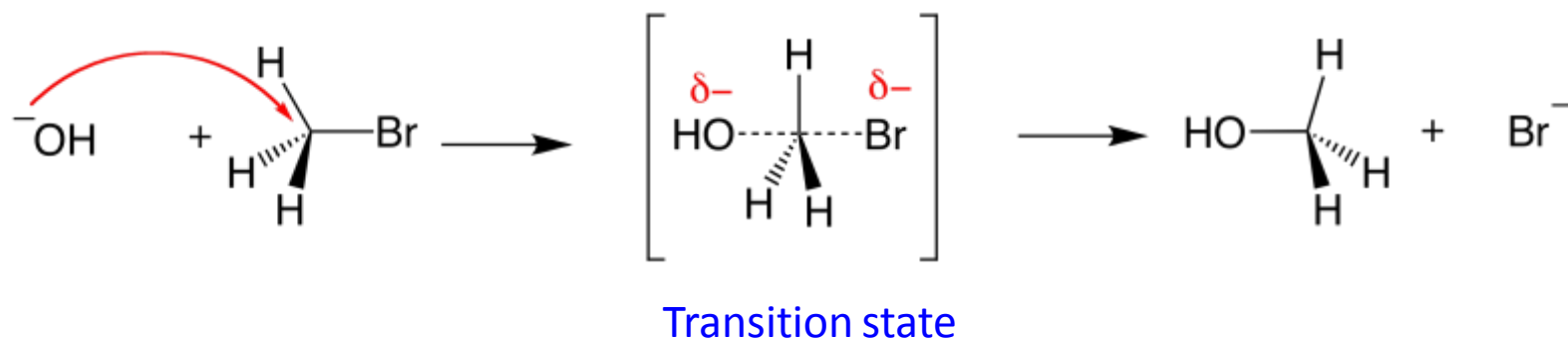
nucleophile attacks and leaving group goes simultaneously



S_N2

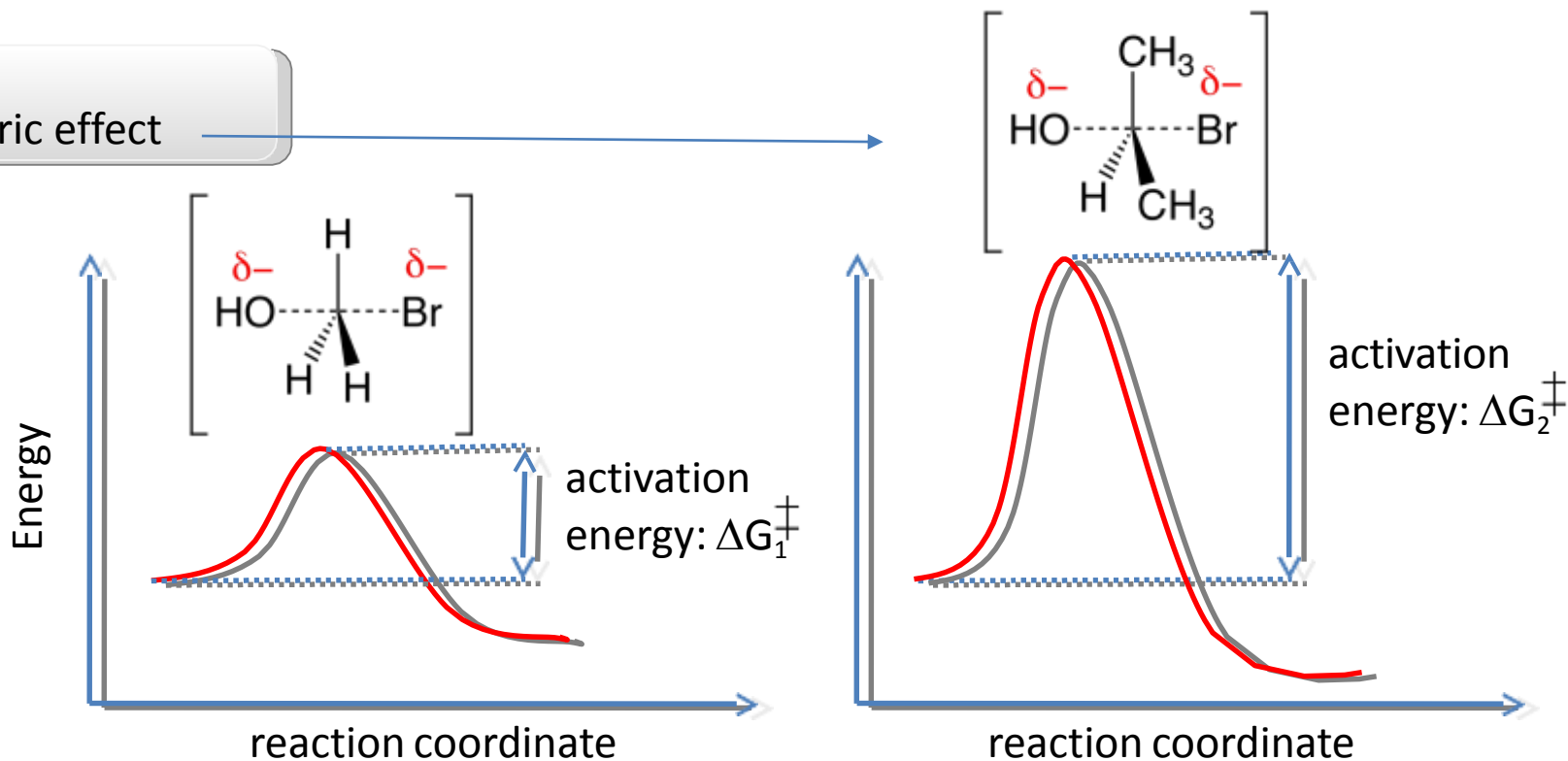
- ✓ Reaction and mechanism
- ✓ Kinetics
- ✓ Stereochemistry of S_N2 reaction
- ✓ Factors affecting S_N2 reaction-
- ✓ The structure of substrate
- ✓ Effect of nucleophiles
- ✓ Effect of leaving groups
- ✓ Effect of solvents
- ✓ Phase transfer catalysis –Role of crown ether

S_N2 reaction and mechanism

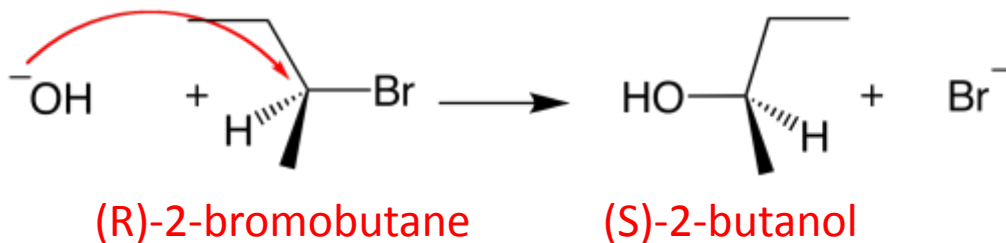


Mechanism of SN2 reaction

Steric effect



Inversion of configuration



Synthetic Utility of the S_N2 Reaction

A variety of functional groups can be prepared employing a good nucleophile and an electrophile with a good leaving group:

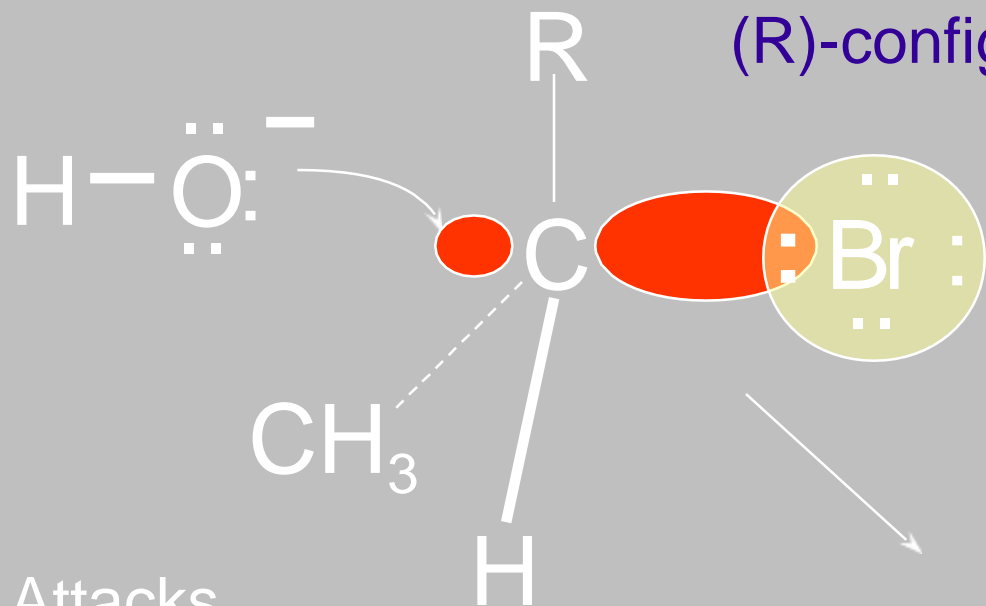


S_N2 reaction : Stereochemistry

S_N2 MECHANISM

nucleophilic attack

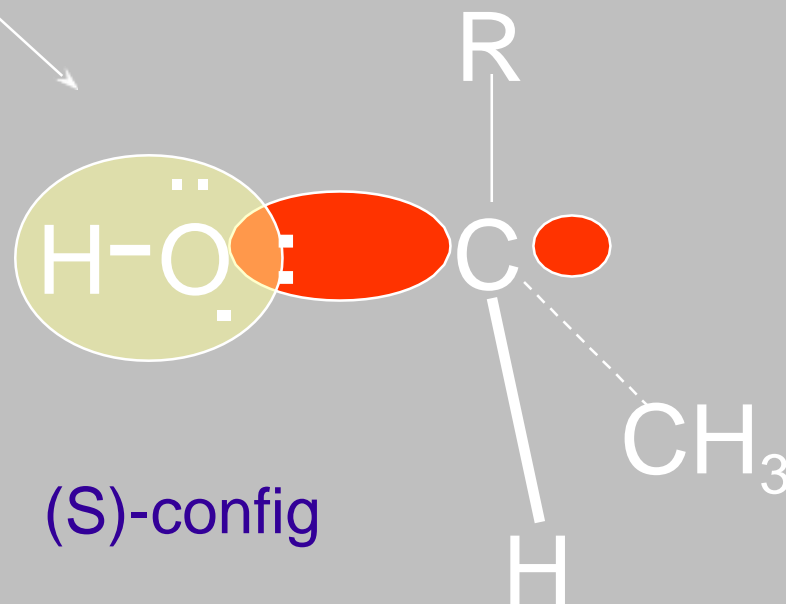
(R)-config



Attacks
back lobe

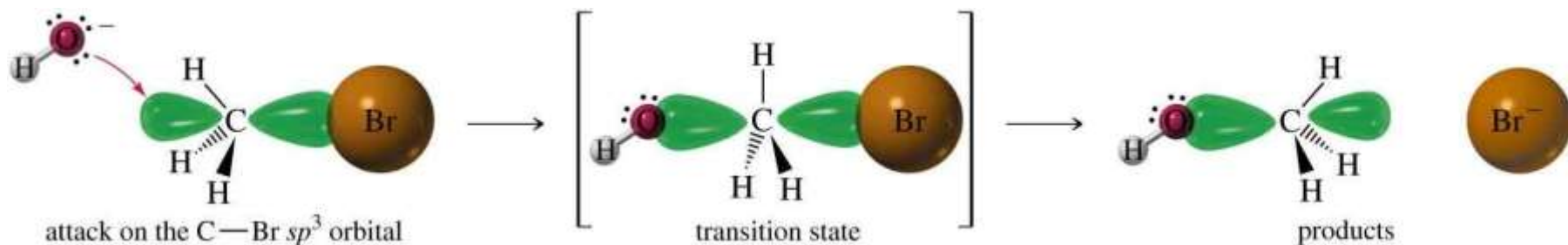
INVERSION

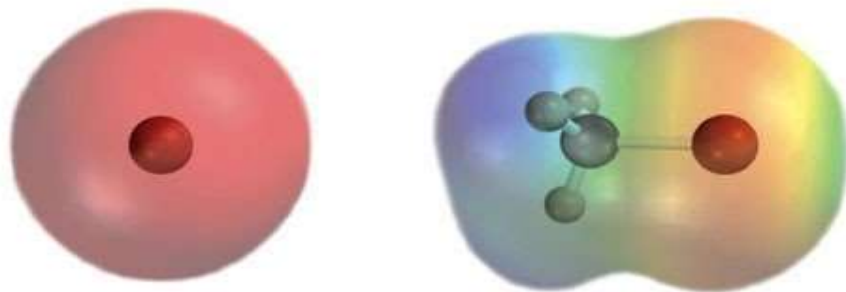
(S)-config



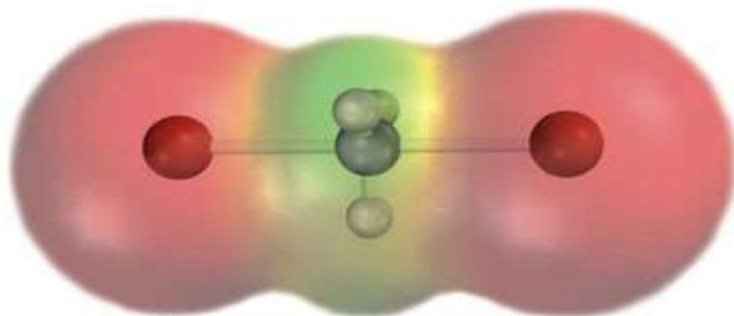
Stereochemistry of S_N2

Walden inversion

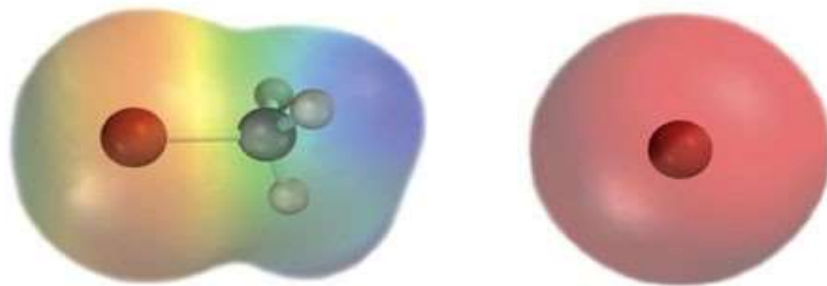
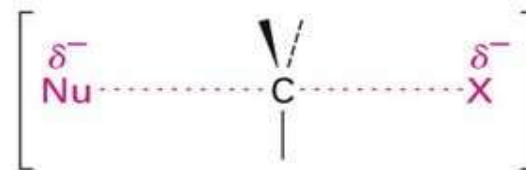




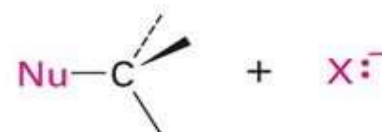
Tetrahedral



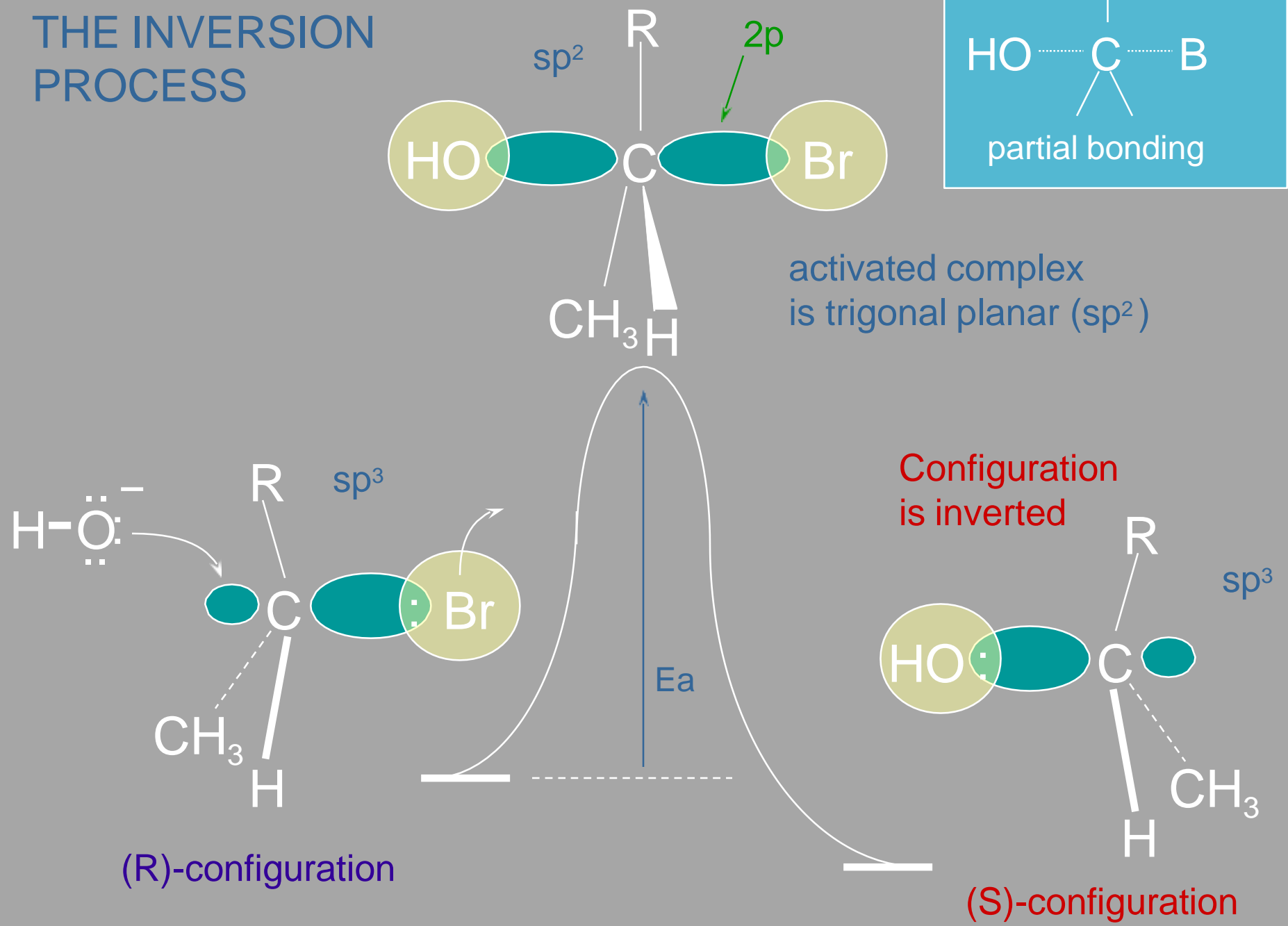
Planar



Tetrahedral



THE INVERSION PROCESS



S_N2 reaction : **substrate structure**

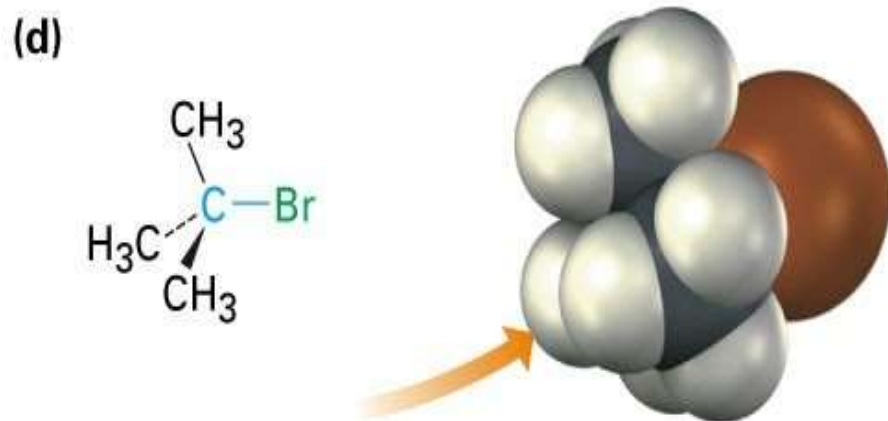
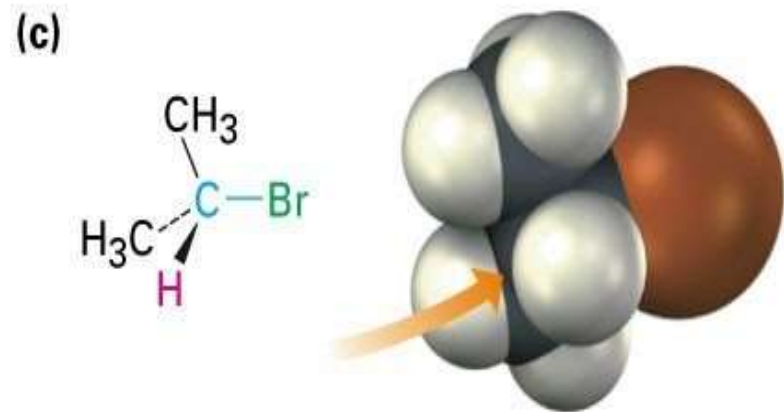
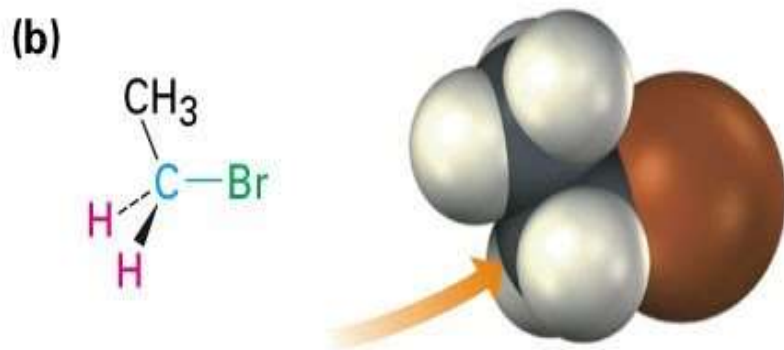
✓ Less bulky

✓ Should stabilize the transition state

S_N2 Reaction: substrate structure

KI in Acetone at 25°

	<u>k_{rel}</u>
CH_3-Br	150
CH_3-CH_2-Br	1
$\begin{array}{c} CH_3-CH-Br \\ \\ CH_3 \end{array}$	0.008
$\begin{array}{c} CH_3 \\ \\ CH_3-C-Br \\ \\ CH_3 \end{array}$	unreactive!

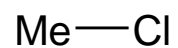


Relative rates of S_N2 reactions of alkyl chlorides with the iodide ion

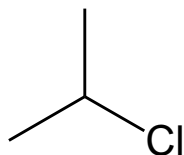
The rates are given with respect to n-BuCl

Alkyl chloride

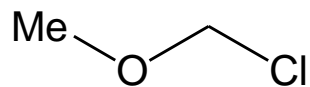
relative rate



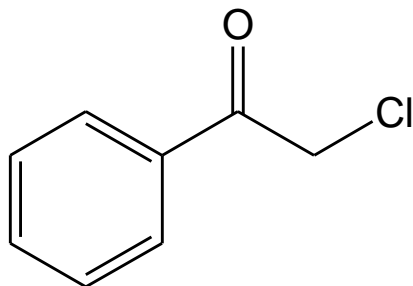
200



0.02



920



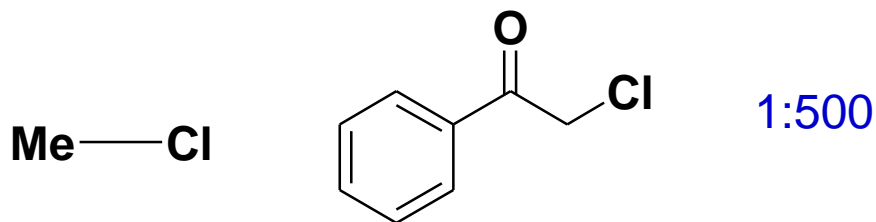
1,00,000



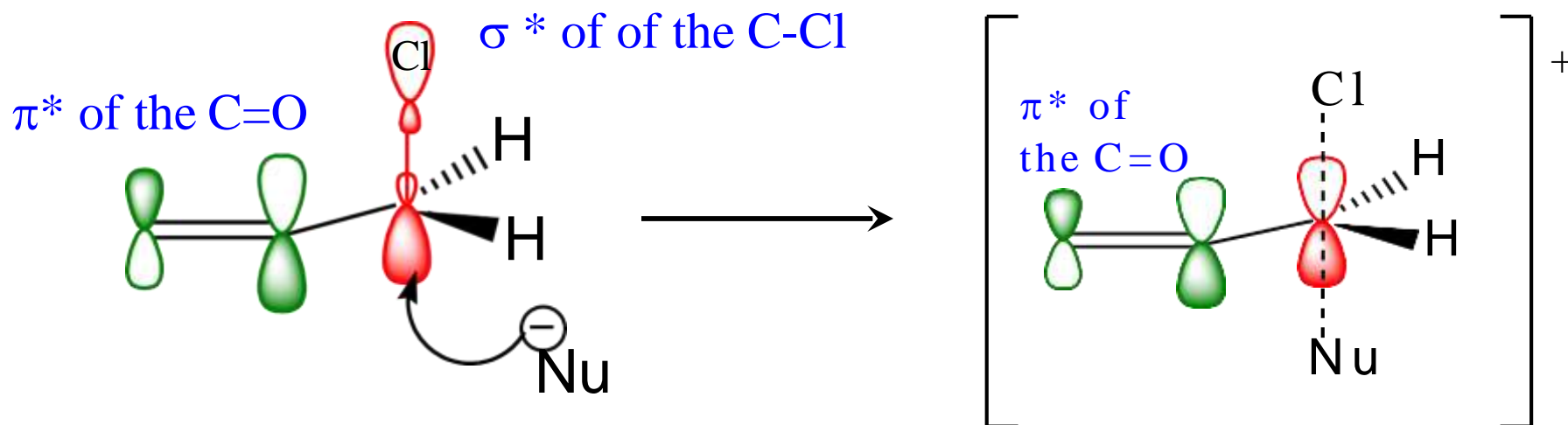
only $\text{S}_{\text{N}}2$, no $\text{S}_{\text{N}}1$

R = alkyl, aryl, OR'

Relative rates of $\text{S}_{\text{N}}2$ reactions with iodide ion



C=O group stabilizes the T.S. by
Overlap of its π^* orbital with full
P-orbital of the C-atom under attack



S_N2 reaction : **Effect of Nucleophile**

- ❑ The nucleophilicity may be correlated with the availability of the electron pairs and the ease with which it is donated

Trends in Nuc. Strength

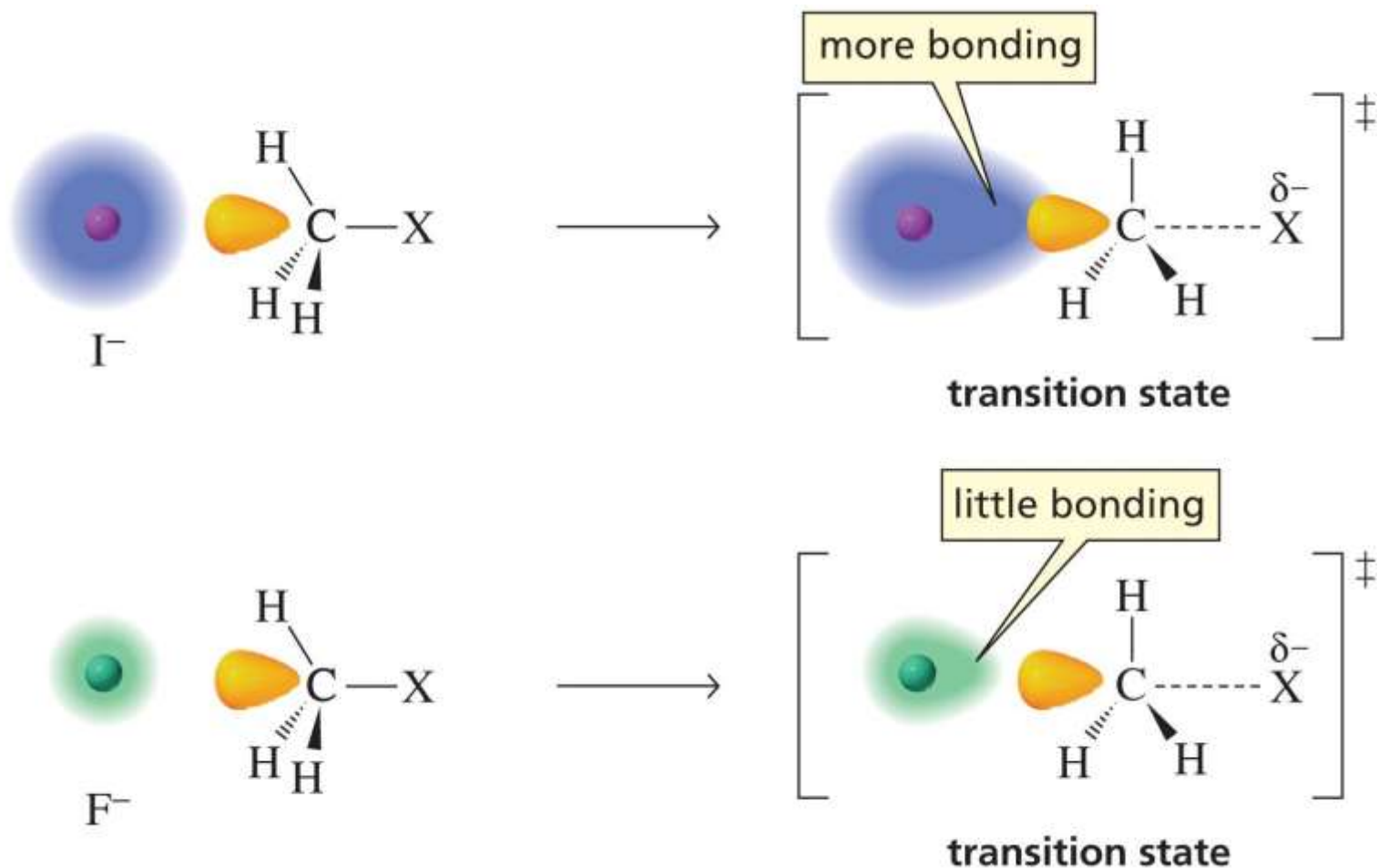
- Increases down Periodic Table, as size and polarizability increase:



- Of a conjugate acid-base pair, the base is stronger:



Polarizability and nucleophilicity - increased polarizability makes for a better nucleophile

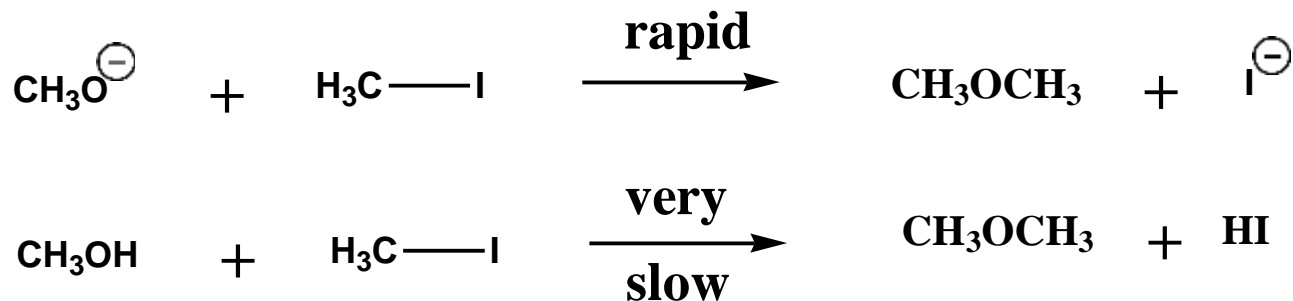


Copyright © 2007 Pearson Prentice Hall, Inc.



Effect of Nucleophile :

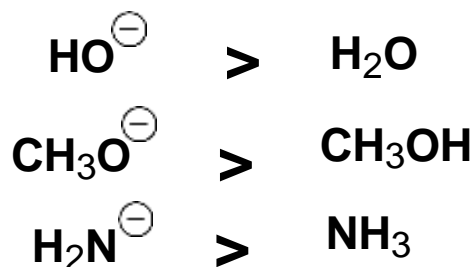
The nucleophilicity may be correlated to its basicity as both involve the availability of the electron pairs and the ease with which it is donated



Nucleophilicity of $\text{CH}_3\text{O}^- > \text{CH}_3\text{OH}$ **A negatively charged nucleophile is always stronger than its conjugate acid.**

Stronger base
better nucleophile

weaker base
poorer nucleophile



The direct relationship between basicity and nucleophilicity is maintained if the reaction occurs in the gas phase

S_N2: Nucleophilic Strength

- Stronger nucleophiles react faster.
- Strong bases are strong nucleophiles, but not all strong nucleophiles are basic.

TABLE 6-3 Some Common Nucleophiles, Listed in Decreasing Order of Nucleophilicity in Hydroxylic Solvents Such as Water and the Alcohols

strong nucleophiles	$(\text{CH}_3\text{CH}_2)_3\text{P:}$ $\text{:}\ddot{\text{S}}\text{—H}$ $\text{:}\ddot{\text{I}}\text{:}^-$ $(\text{CH}_3\text{CH}_2)_2\ddot{\text{N}}\text{H}$ $\text{:}\text{C}\equiv\text{N}$ $(\text{CH}_3\text{CH}_2)_3\text{N:}$ $\text{H—}\ddot{\text{O}}\text{:}^-$ $\text{CH}_3\text{—}\ddot{\text{O}}\text{:}^-$	moderate nucleophiles	$\text{:}\ddot{\text{Br}}\text{:}^-$ $\text{:}\text{NH}_3$ $\text{CH}_3\text{—}\ddot{\text{S}}\text{—CH}_3$ $\text{:}\ddot{\text{Cl}}\text{:}^-$ $\begin{array}{c} \text{O} \\ \parallel \\ \text{CH}_3\text{C—}\ddot{\text{O}}\text{:}^- \end{array}$ $\text{:}\ddot{\text{F}}\text{:}^-$ $\text{H—}\ddot{\text{O}}\text{—H}$ $\text{CH}_3\text{—}\ddot{\text{O}}\text{—H}$
		weak nucleophiles	

S_N2 reaction : Effect of leaving group

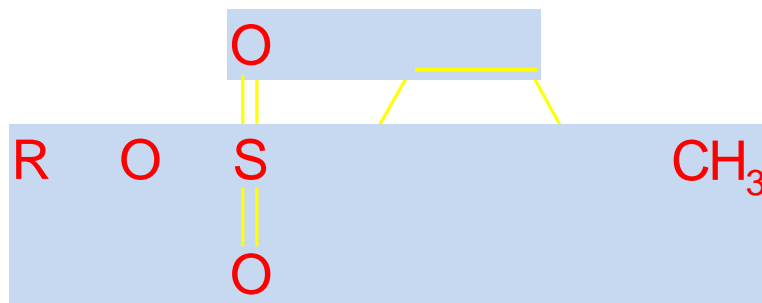
- A good leaving group needs to be a stable anion that is a weak base which can delocalize charge

The Leaving Group

Relative reactivity	$\text{OH}^-, \text{NH}_2^-, \text{OR}^-$	F^-	Cl^-	Br^-	I^-	TosO^-
	$\lll 1$	1	200	10,000	30,000	60,000

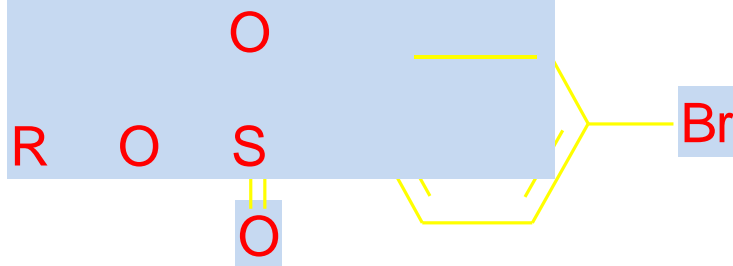
 Leaving group reactivity

Sulfonate Leaving Groups



para-Toluenesulfonate

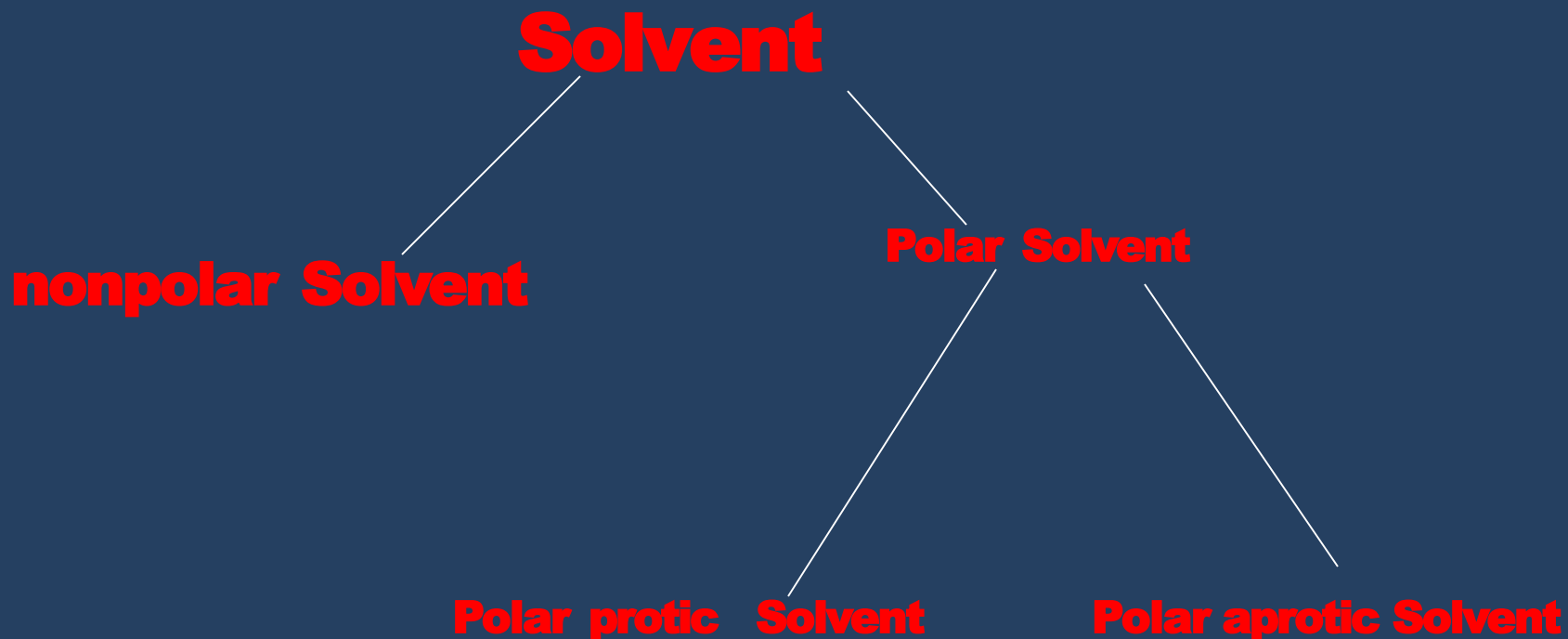
Tosylate



para-Bromobenzenesulfonate

Brosylate

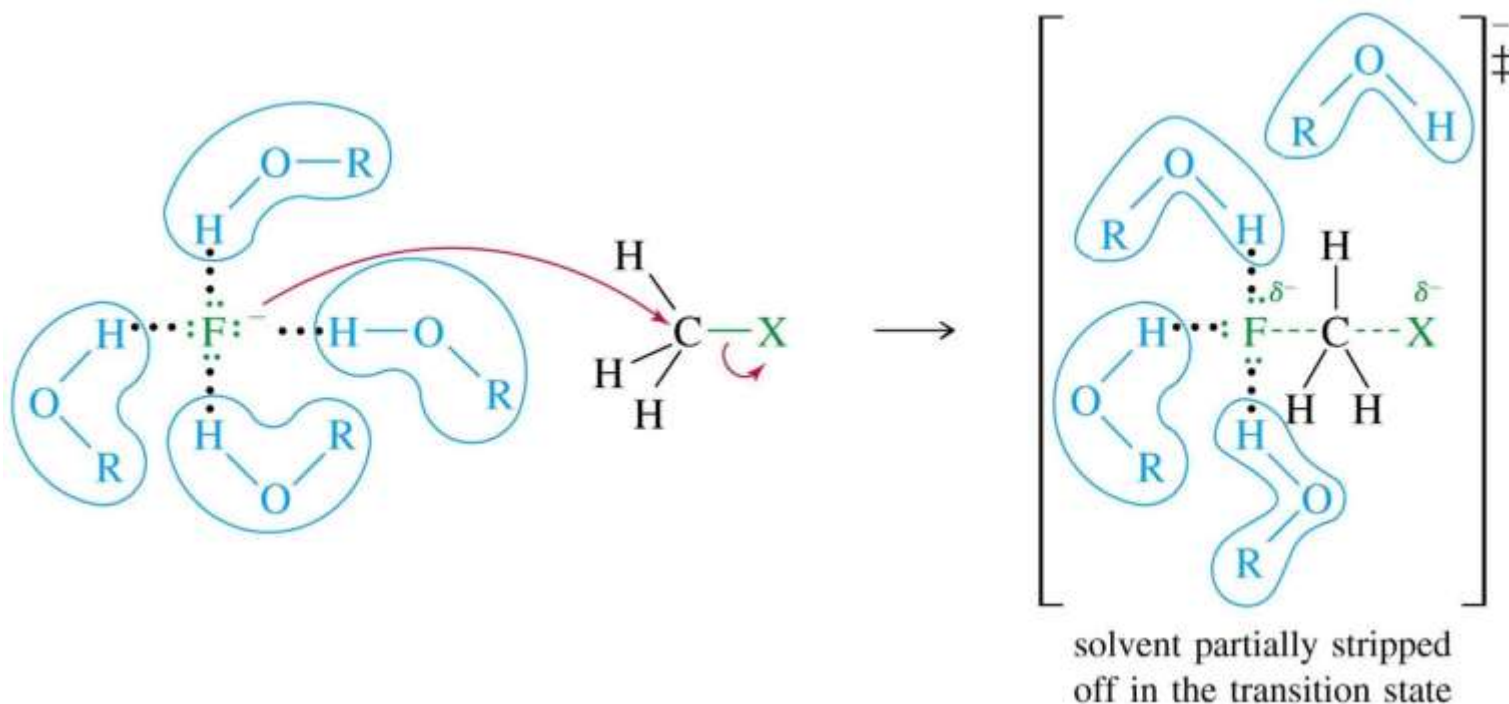
S_N2 reaction : **Effect of Solvent**



SN2 reaction prefers polar aprotic solvent

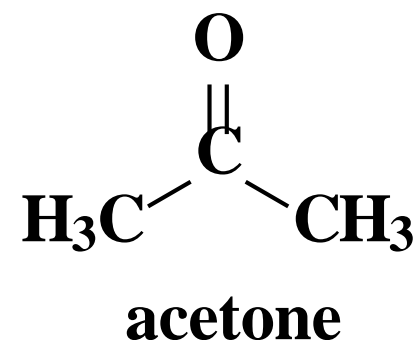
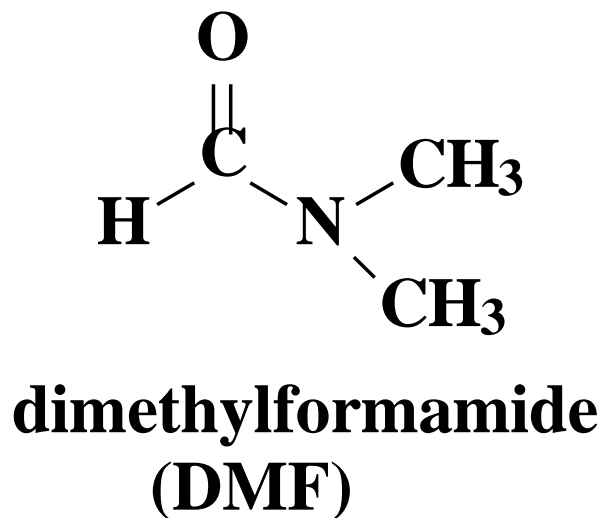
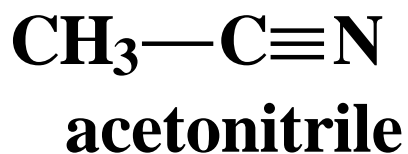
Solvent Effects (1)

Polar protic solvents (O-H or N-H) reduce the strength of the nucleophile. Hydrogen bonds must be broken before nucleophile can attack the carbon.

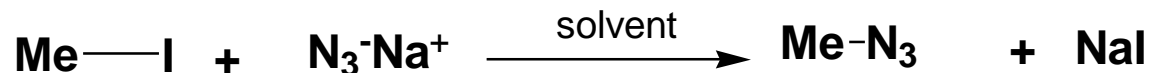


Solvent Effects (2)

- ✓ Polar aprotic solvents (no O-H or N-H) do not form hydrogen bonds with nucleophile
- ✓ Examples:



Marked effect on the rate of S_N2 reaction, when that transferred from polar protic solvent to polar aprotic solvent.



Rate in MeOH ($\epsilon = 33$) **1**

DMF ($\epsilon = 37$) **4.5×10^4**

DMSO ($\epsilon = 46$) **1×10^9**

DMF: HCONMe₂

DMSO: Me₂SO

- In MeOH both Na⁺ and N₃⁻ are solvated.**
- In DMF only Na⁺ is solvated, but not N₃⁻.**
- So, unsolvated N₃⁻ is a much more powerful nucleophile**

S_N2 or S_N1 ?

- ✓ Primary or methyl
- ✓ Strong nucleophile
- ✓ Polar aprotic solvent
- ✓ Rate = k [halide] [Nuc]
- ✓ Inversion
- ✓ No rearrangements
- ✓ Tertiary
- ✓ Weak nucleophile (may also be solvent)
- ✓ Polar protic solvent, silver salts
- ✓ Rate = k [halide]
- ✓ Racemization
- ✓ Rearranged products

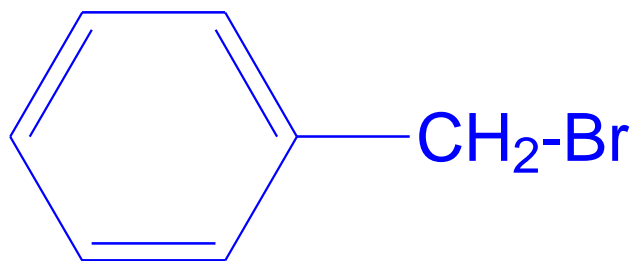
=>

Important substrates.....

Allylic and Benzylic compounds

Allylic and benzylic compounds are especially reactive in S_N1 reactions.

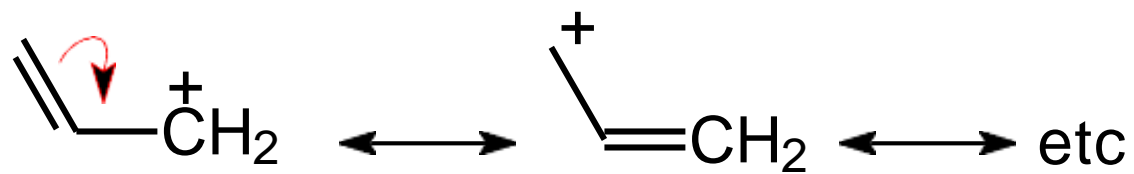
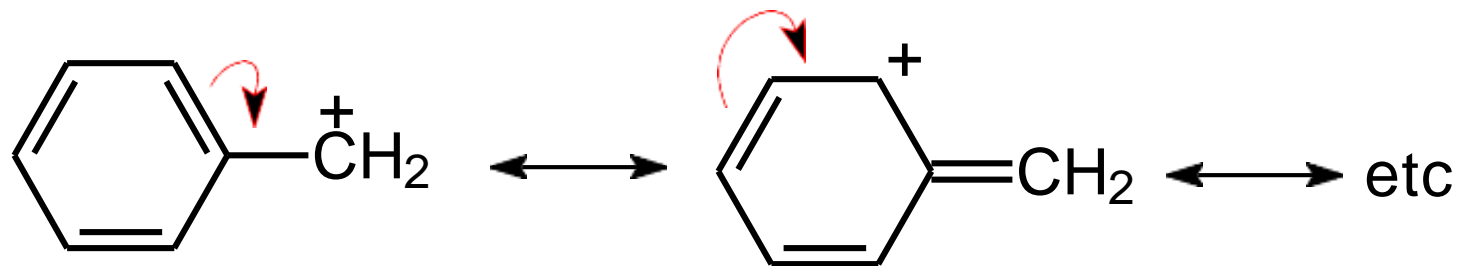
Even though they are primary substrates, they are more reactive than most other halides! They form resonance stabilized carbocations.



benzyl bromide



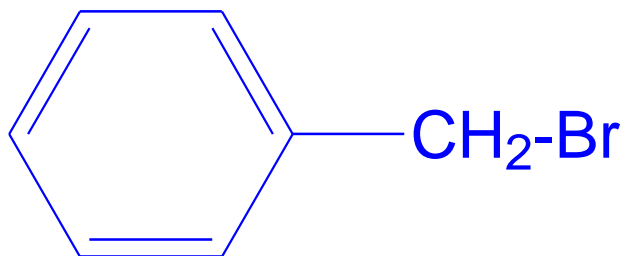
allyl bromide



Allylic and Benzylic compounds

Allylic and benzylic compounds are especially reactive in S_N2 reactions.

They are more reactive than typical primary compounds!

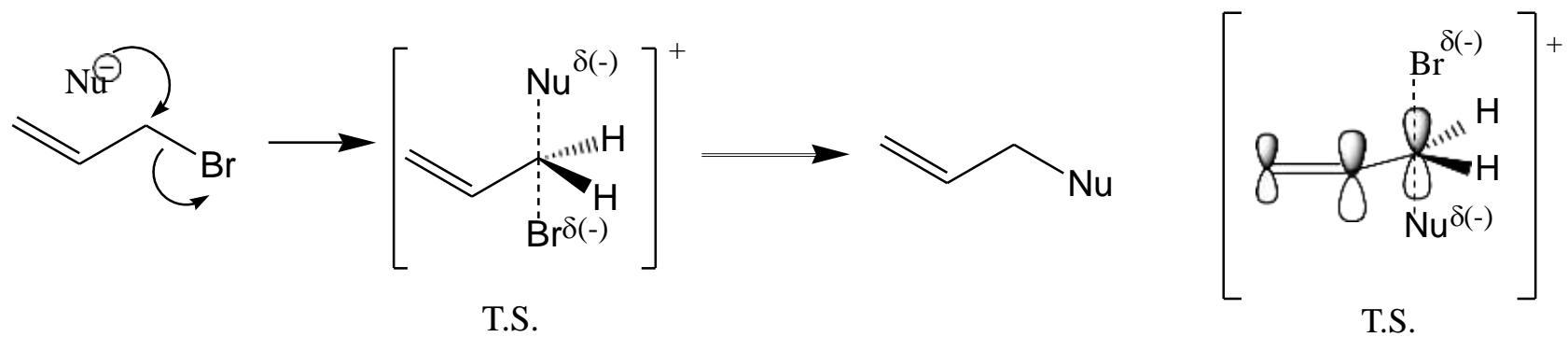


benzyl bromide



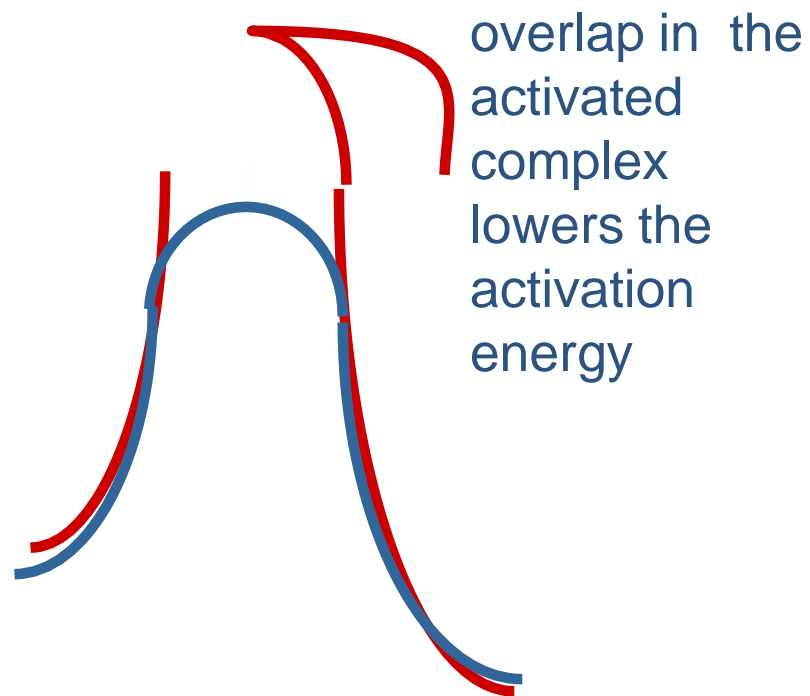
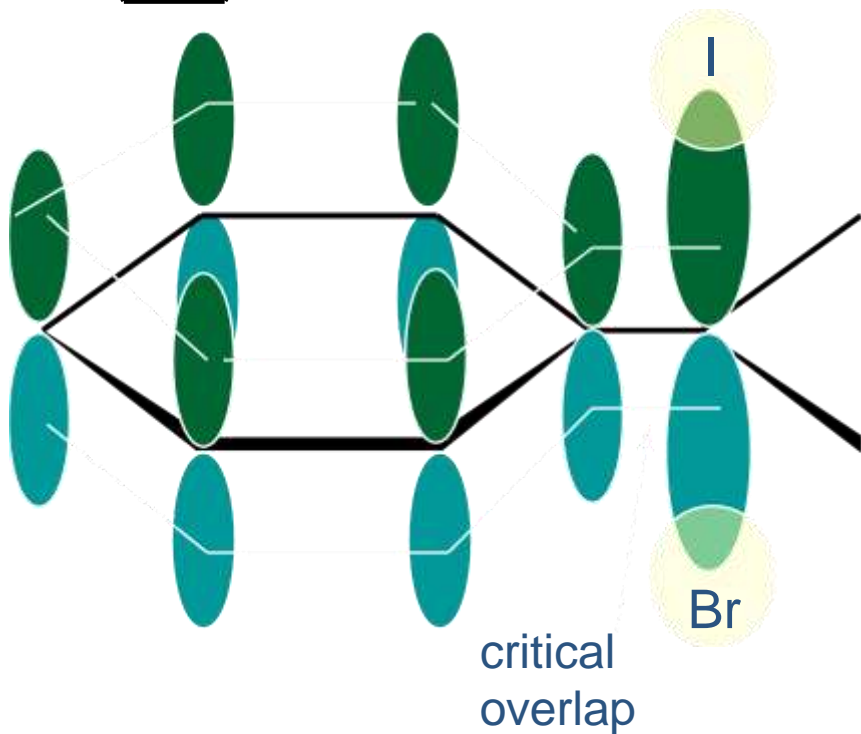
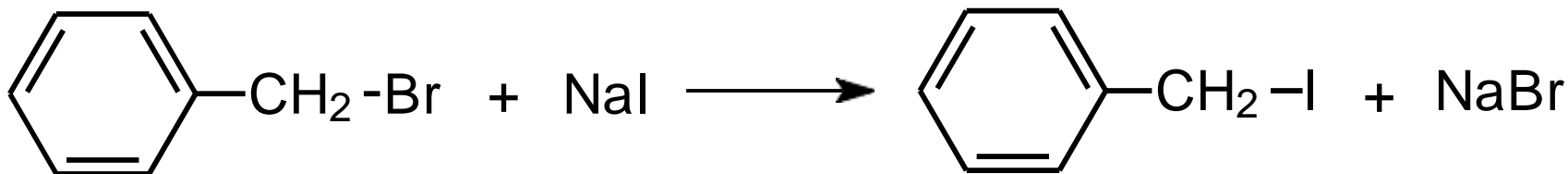
allyl bromide

For S_N2 : stabilisation of TS by conjugation with allylic π - bond



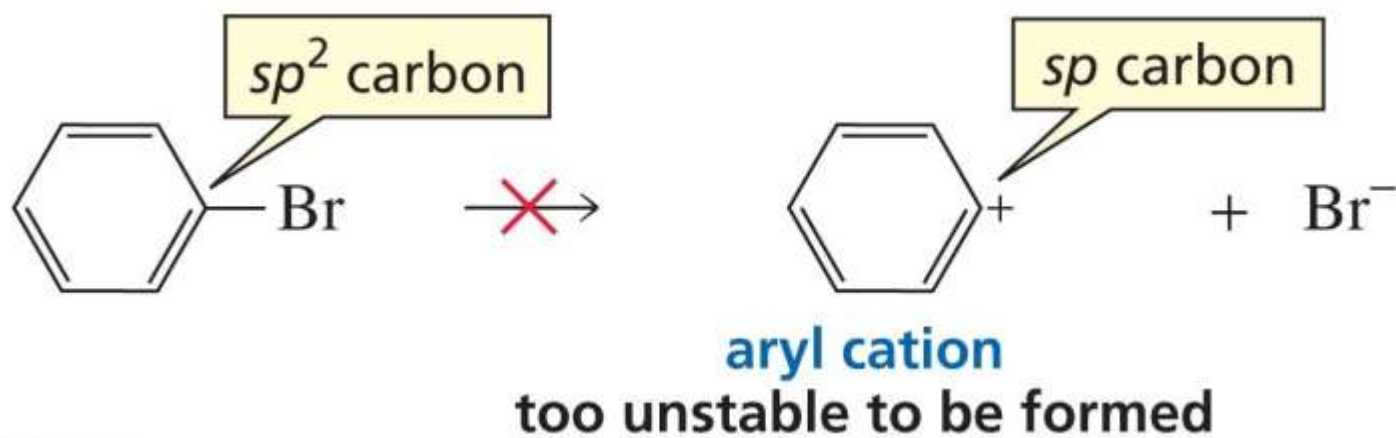
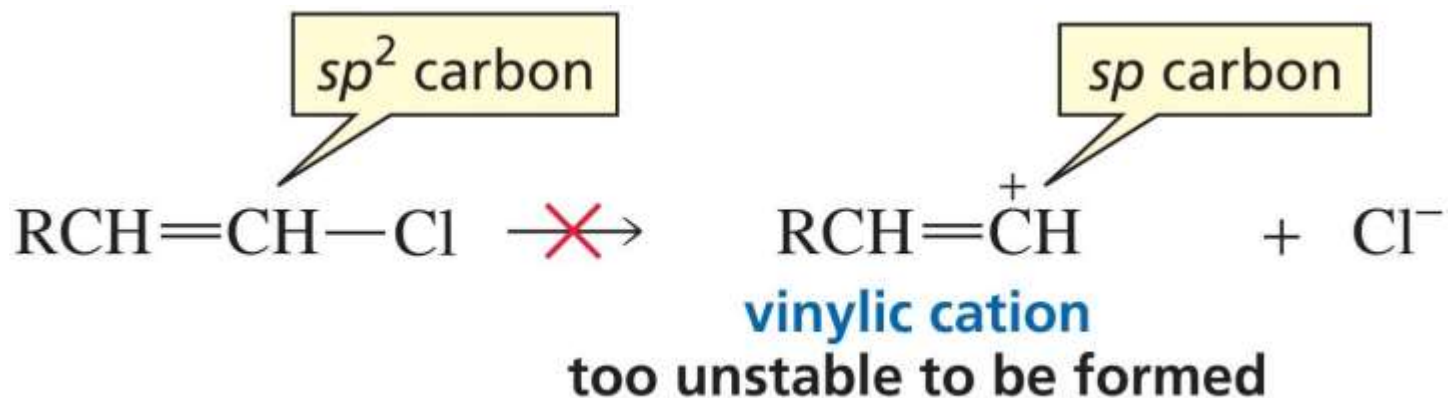
BENZYL (GOOD FOR S_N1) IS ALSO A GOOD S_N2 SUBSTRATE

primary, but faster
than other primary

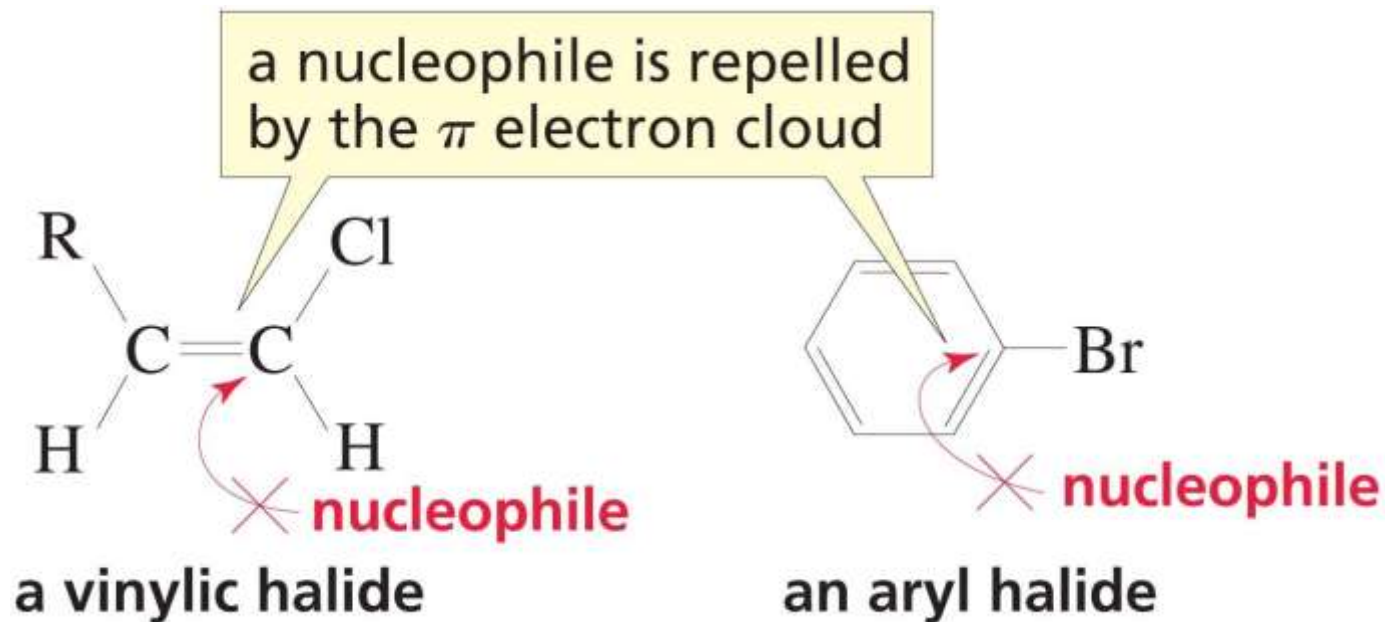


Vinyl and aryl halides

Vinyl and aryl halides do not undergo S_N1 because:



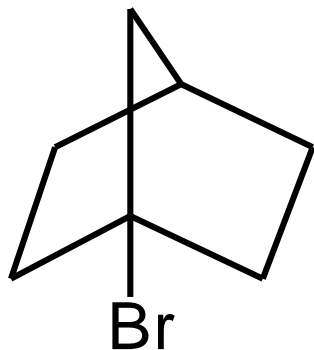
Vinyl and aryl halides do not undergo S_N2 because:



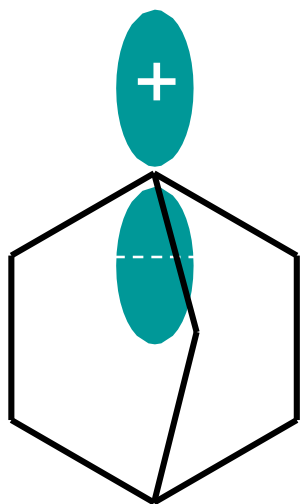
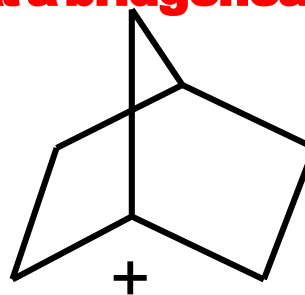
Cyclic systems

rigid bicyclic molecule.

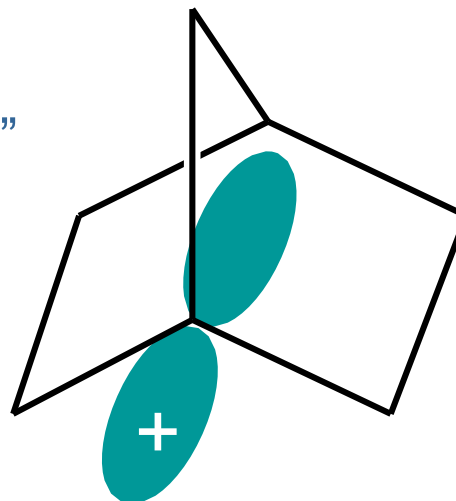
You can't have p orbitals on a bridgehead position



-- You cannot form a carbocation at a bridgehead position.



“steric rigidity”

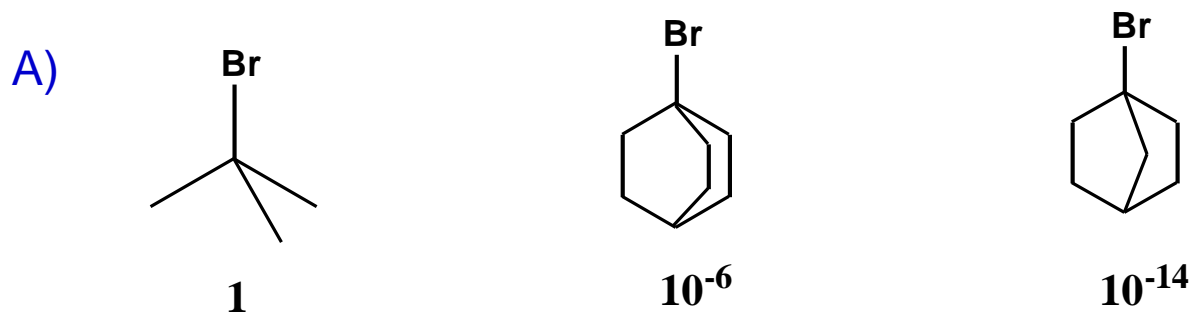


Problems :

1) S_N2 reaction by Et O⁻ in Et OH:

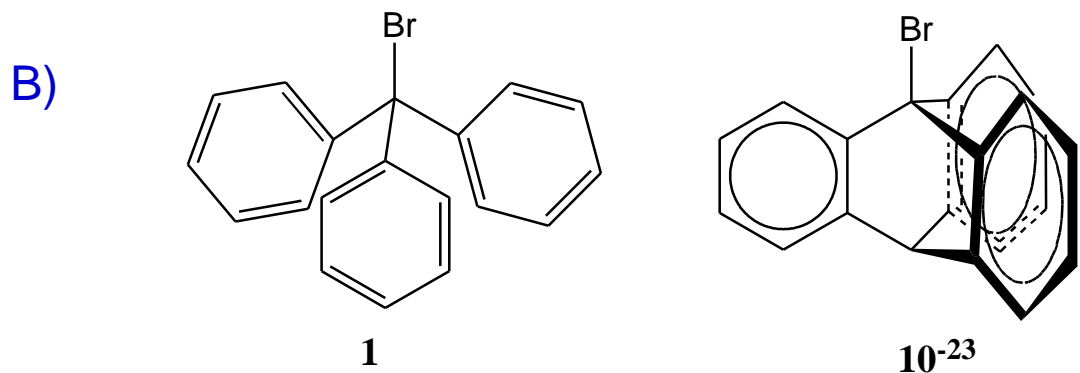
	CH ₃ CH ₂ -Br	CH ₃ CH ₂ CH ₂ -Br	Me ₂ HCCH ₂ -Br	Me ₃ CCH ₂ -Br	Explain ?
relative rate	1	2.8X10 ⁻¹	3.0X10 ⁻²	24.2X10 ⁻⁶	

2) Rate of solvolysis in EtOH :



Explain?

cc at bridge head, less stable, difficult to attain planarity due to rigidity



Explain ?

Rigid structure, cation empty p-orbitals are at right angles to π orbitals of Ph

1-bromotriptycene