CHEM F111 : General Chemistry
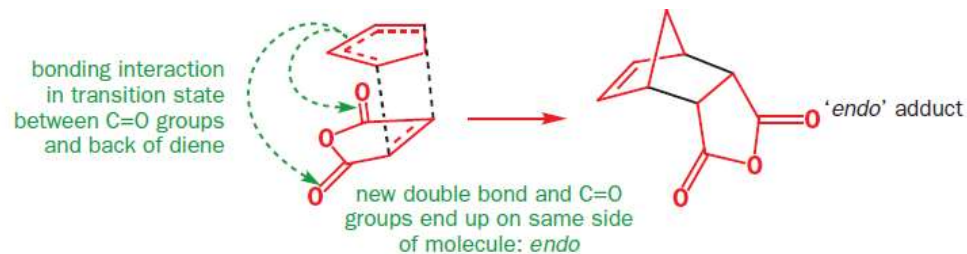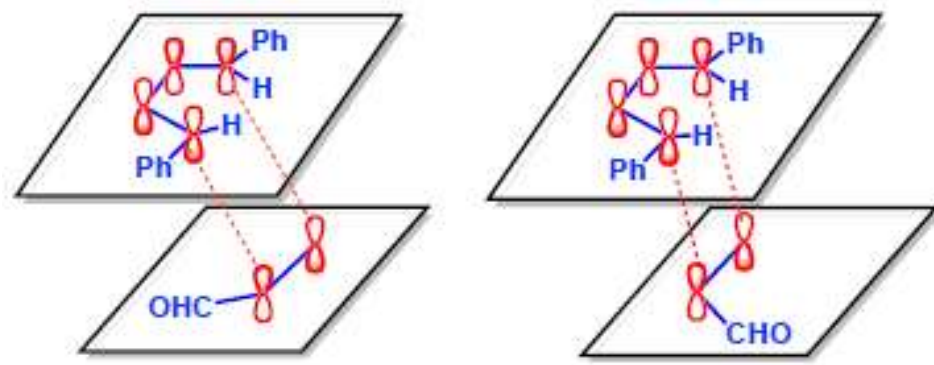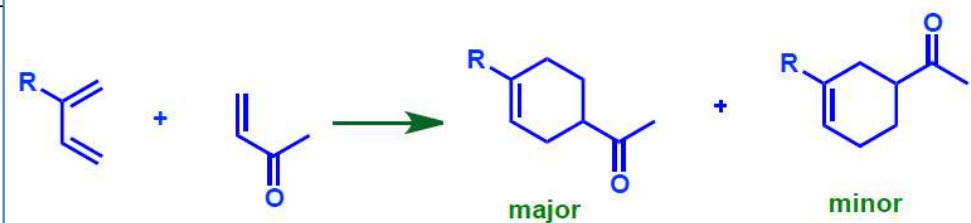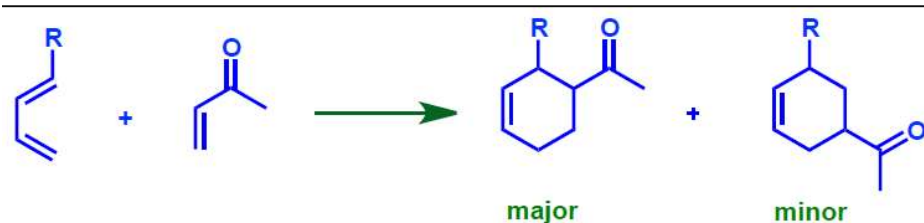# Semester II: AY 2017-18

## Lecture 38 (25-04-2018)
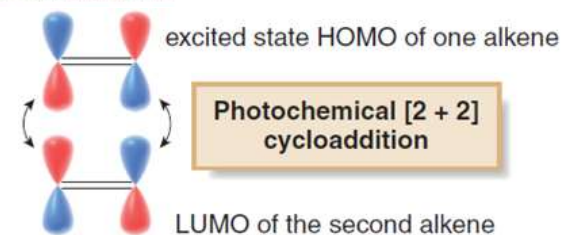
[4+2] cycloaddition under thermal conditions
[2+2] cycloaddition under photochemical conditions

bonding interaction in transition state between C=O groups and back of diene

new double bond and C=O groups end up on same side of molecule: *endo*

'endo' adduct

excited state HOMO of one alkene

Photochemical [2 + 2] cycloaddition

LUMO of the second alkene

conrotatory ring closure

HOMO is asymmetric

disrotatory ring closure

HOMO is symmetric

Electron pairs (double bonds)	Thermal reaction	Photochemical reaction
Even number	Conrotatory	Disrotatory
Odd number	Disrotatory	Conrotatory
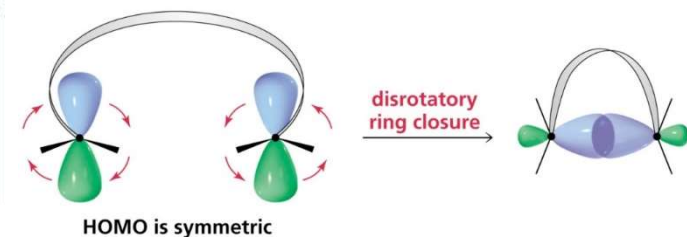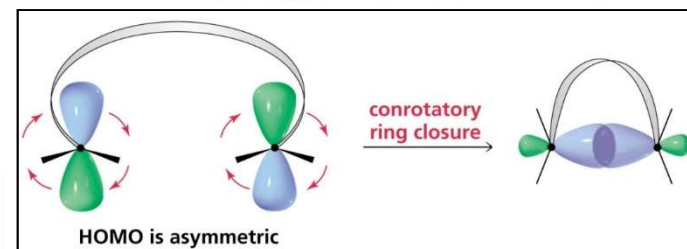
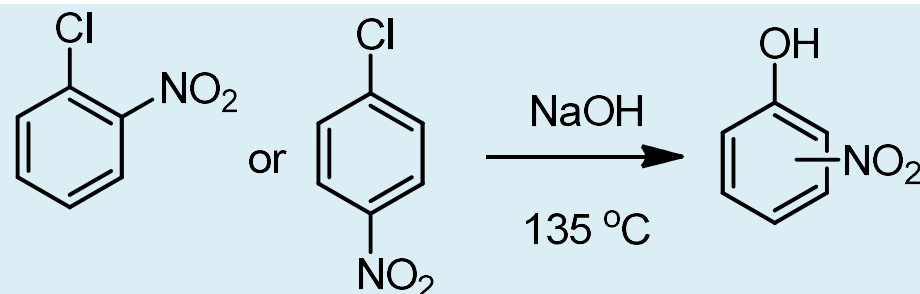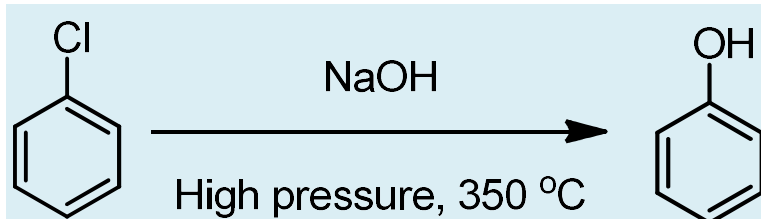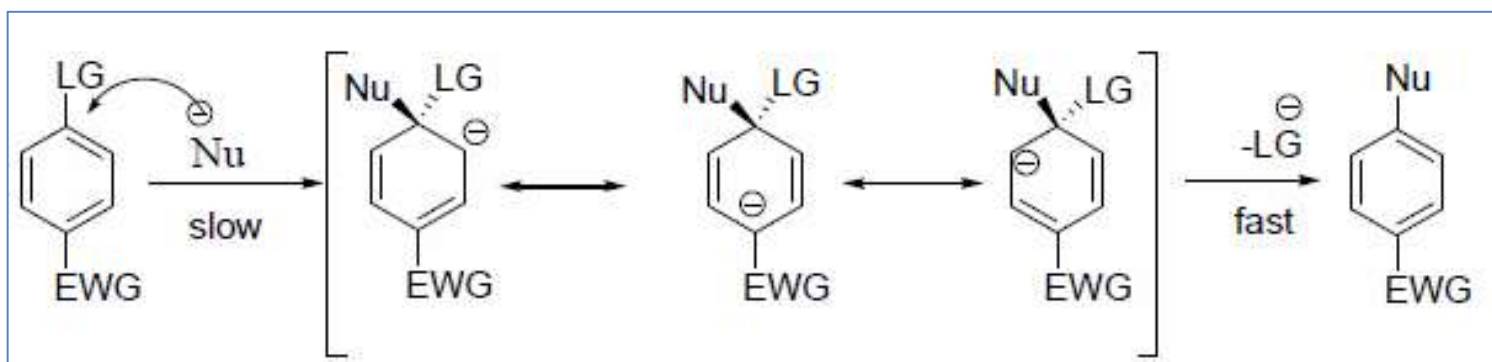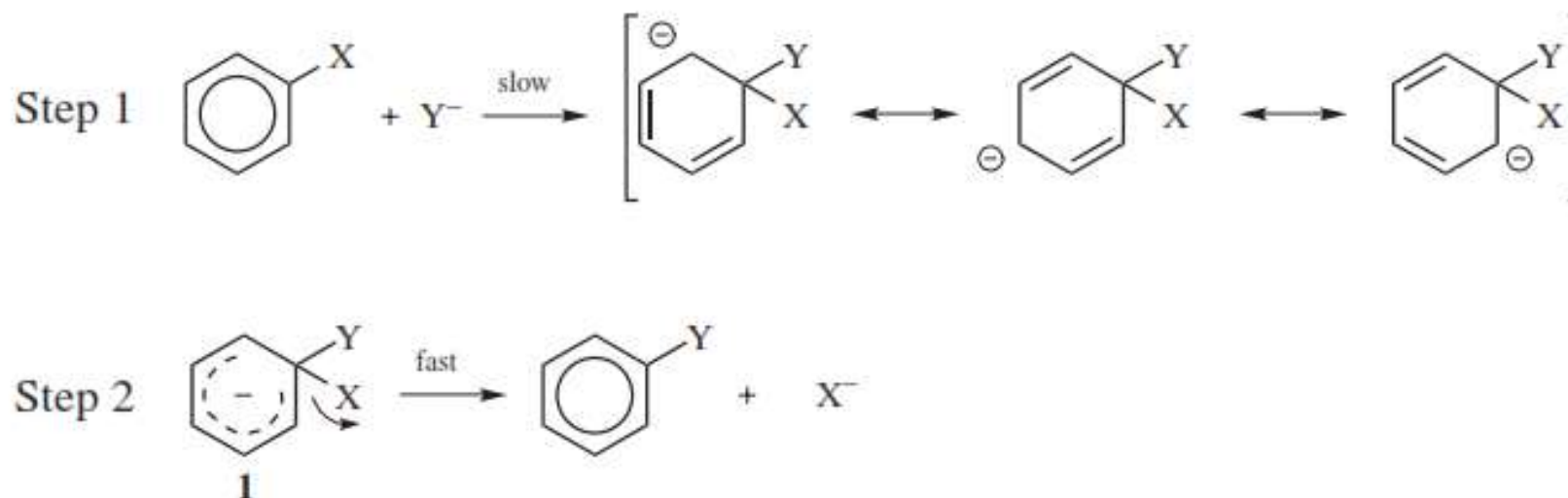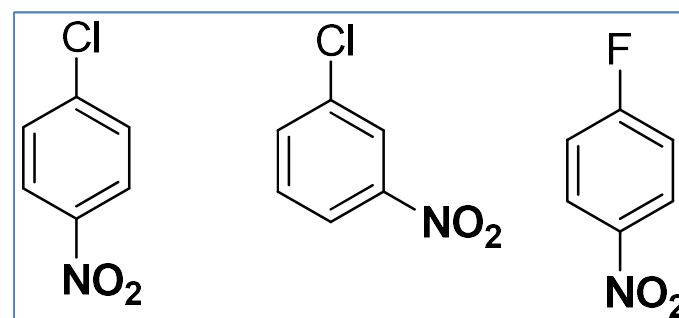# Nucleophilic Aromatic Substitution (S_NAr)

S_NAr

Addition-Elimination Mechanism (electron withdrawing group on Ar-ring)

diazonium salt method

Elimination-Addition Mechanism (Benzyne mechanism)

Nucleophilic Aromatic Substitution (S$_N$Ar)

Increasing reactivity

Step 1 and Step 2 mechanism

slow

fast
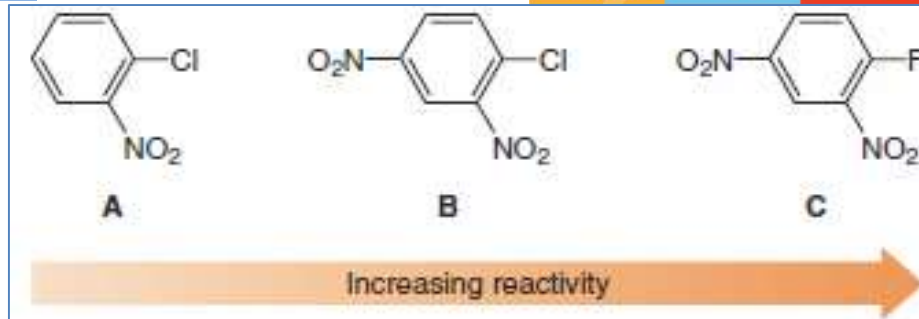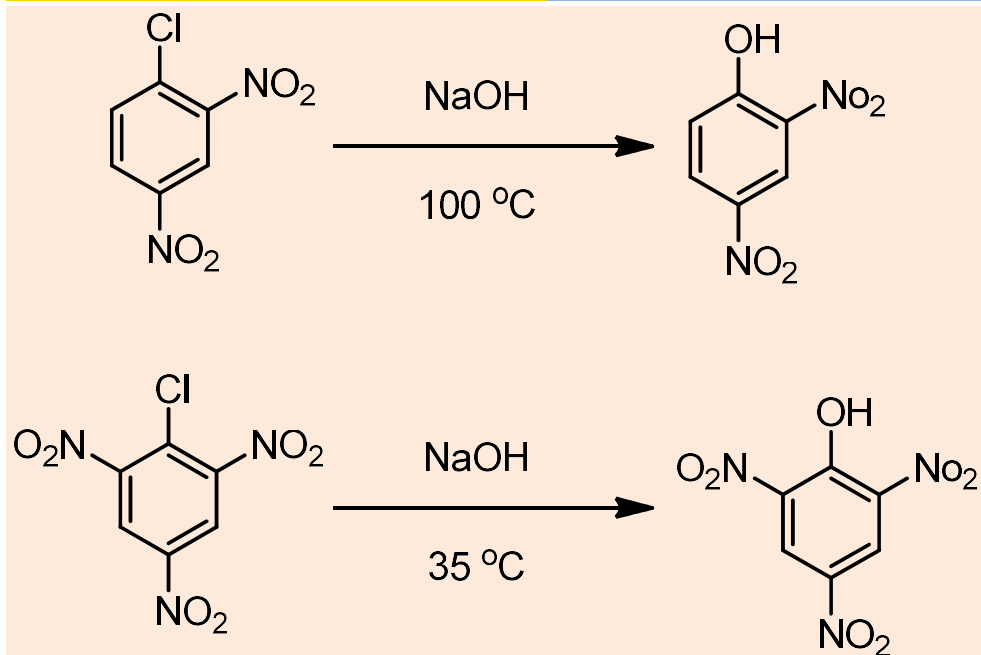
Nucleophilic Aromatic Substitution (S$_N$Ar)
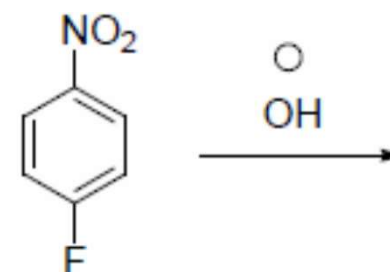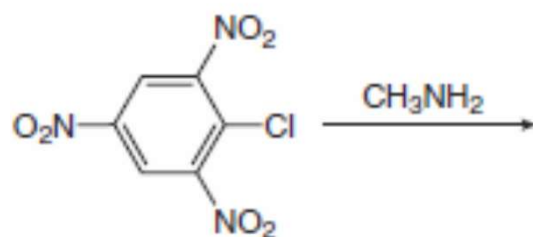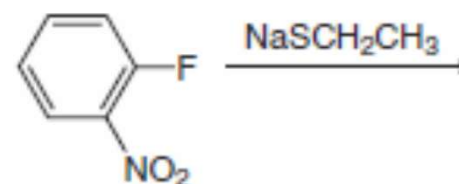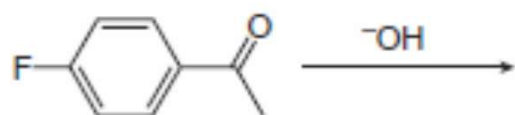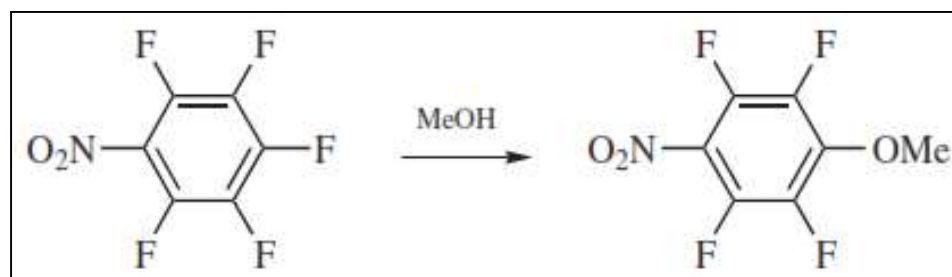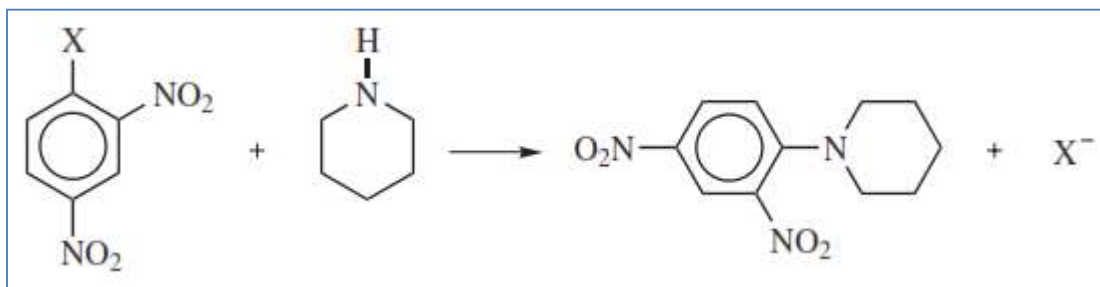
Nucleophilic Substitution Reactions

X = Cl, Br, I, OTs etc.

sp^3 C—X with $\delta+$ $\delta-$
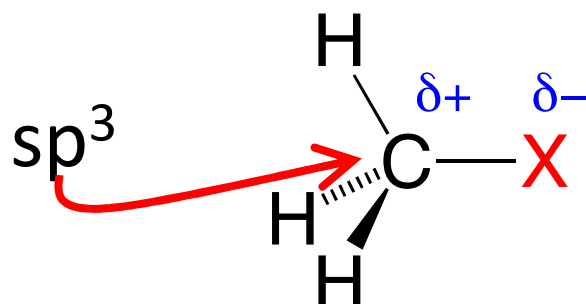
X is more electronegative than carbon Prone to undergo Nucleophilic Substitution (S_N)

sp^2

sp^2 undergo S_NAr reactions

sp
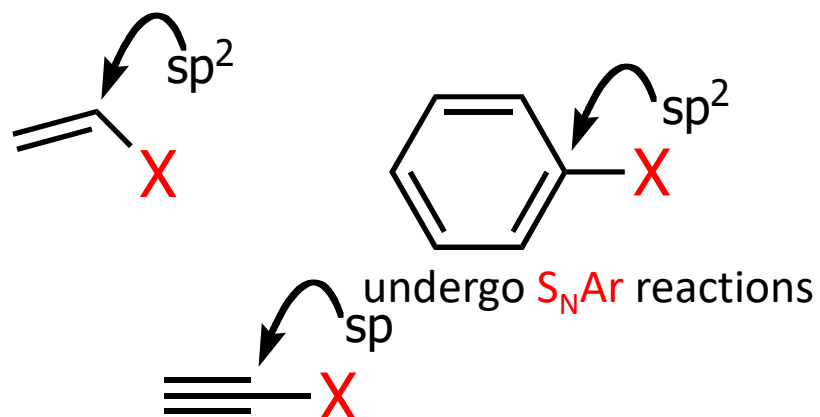
do not undergo S_N reactions

C-X is attached to:

1 carbon
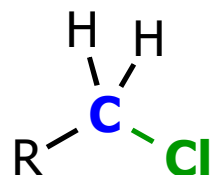
2 carbons

3 carbons

1° chloride
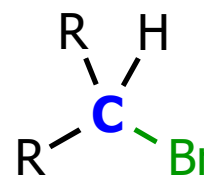
2° bromide
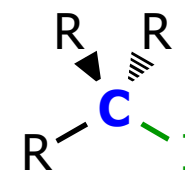
3° iodide

(R = carbon chain)

Types of Substitution Reactions

S_N2 and S_N1 mechanisms:

1st type: S_N2 (concerted mechanism)

transition state (T.S.)
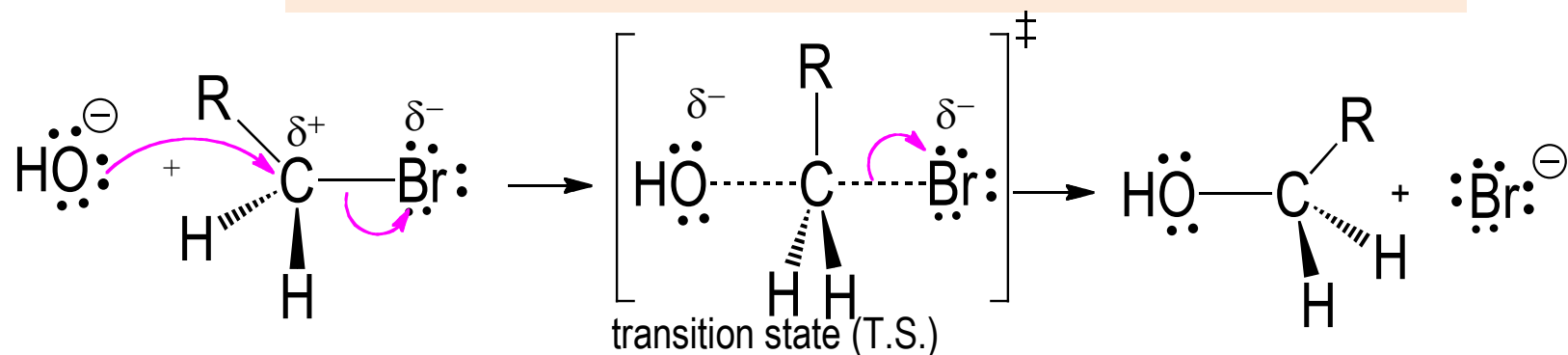
The rate (speed) of reaction is directly proportional to the concentration of either reactant. When the concentration of either reactant is doubled, the rate of reaction doubles.

Rate *dependent on* $[CH_2RBr][OH^-]$

Rate = $k[CH_2RBr][OH^-]$
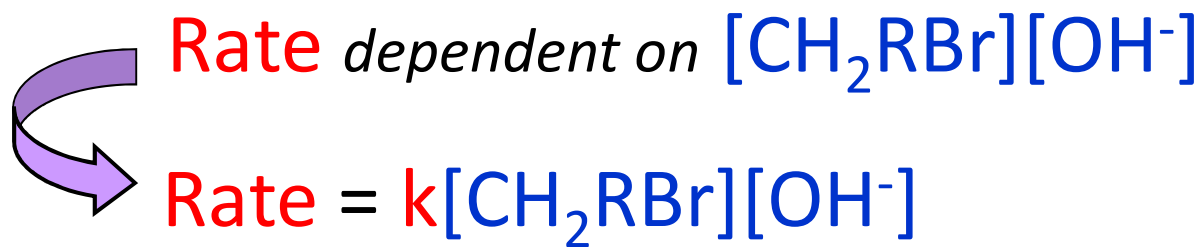
Mechanism of S$_N$2 is very well supported by three evidences.

(1) Kinetics   second order reaction - bimolecular

(2) Stereochemistry and

(3) Reactivity of substrates.

Stereochemistry

All S$_N$2 reactions results in inversion of configuration at a stereogenic center.

(inversion)

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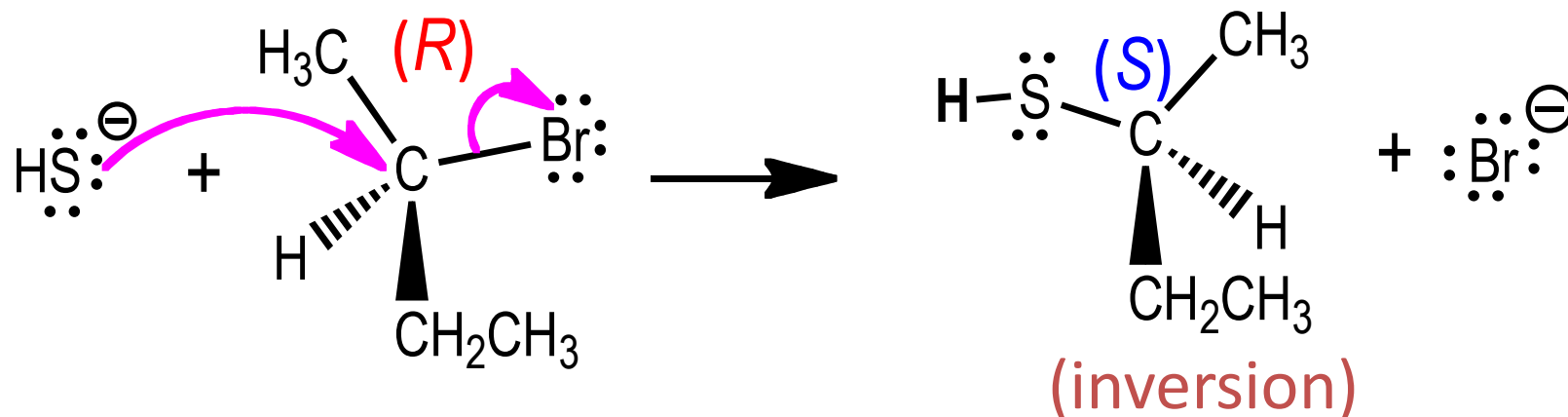
S$_N$2 Reaction

When a substrate contains more than one stereocenter, inversion takes place only at the stereocenter being attacked by the nucleophile.
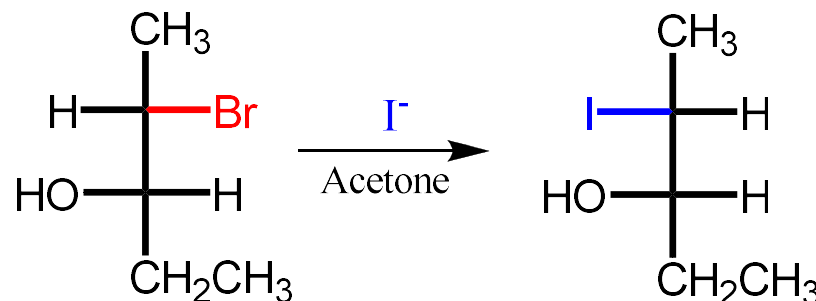
Reactivity of substrates: As the number of substituents attached to the carbon bearing the halogen is increased, the reactivity toward S$_N$2 substitution decreases.

	Methyl	1^0	2^0	Neopentyl	3^0
Relative Rates	(30)	(1)	(0.03)	(0.00001)	(~0)
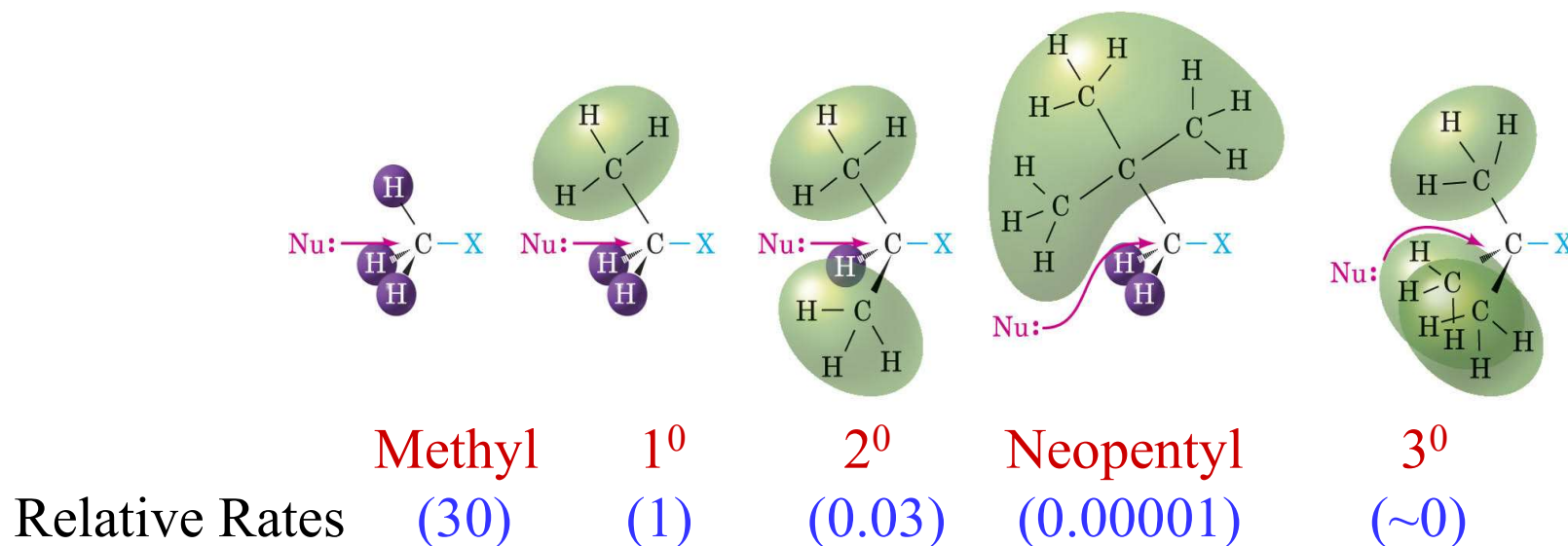
The rate of S_N1 reactions depends only on [alkyl halide]

Rate = k[RX], *first-order* reaction

$\Longrightarrow$ unimolecular nucleophilic substitution

The Structure of Carbocations:
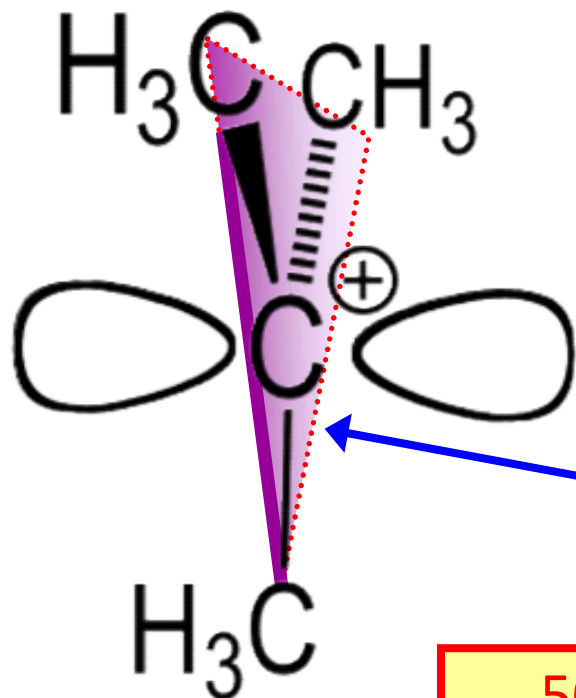
Carbocations are trigonal planar

The central carbon of carbocation is electron deficient; 6 valence shell e$^\ominus$

Empty *p* orbital is e$^{(-)}$ pair acceptor

SP^2–SP^3 σ bond

50:50 chance of attack from both side resulted racemic mixture

Factors Affecting the Rates of S$_N$1 and S$_N$2 Rxs

- The structure of the substrate
- Reactivity of the nucleophile
- Nature of the solvent
- The nature of the leaving group

LG
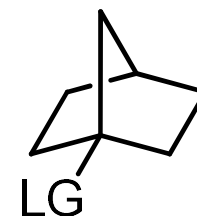
Bridged C-does not participate in S$_N$

Reactivity of Substrates towards S$_N$2 Rxn

$C_6H_5CH_2Br$ = CH_3-Br > $R-CH_2Br$ > $\underset{R}{\overset{R}{C}}CH-Br$ >>> $\underset{R}{\overset{R}{C}}\underset{R}{\overset{Br}{C}}$ >> C_6H_5-Br

$CH_2=CH-CH_2Br$

Benzyl/ Allyl   methyl   1°   2°   3° $H_2C=CHBr$

                                                                                      phenyl/ vinyl

Reactivity of Substrates towards S$_N$1 Rxn

$\underset{R}{\overset{R}{\underset{R}{C}}}Br$ > $C_6H_5CH_2Br$ > $\underset{R}{\overset{R}{C}}CH-Br$ >> $R-CH_2-Br$ >> CH_3-Br >> C_6H_5-Br

$H_2C=CHCH_2Br$ $CH_2=CHBr$

3°   Benzyl/ Allyl   2°   1°   methyl   phenyl/ vinyl

11

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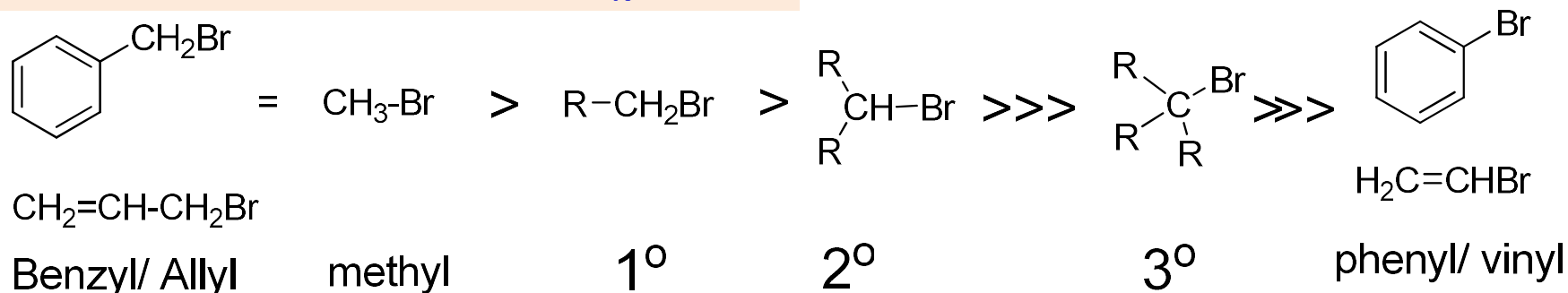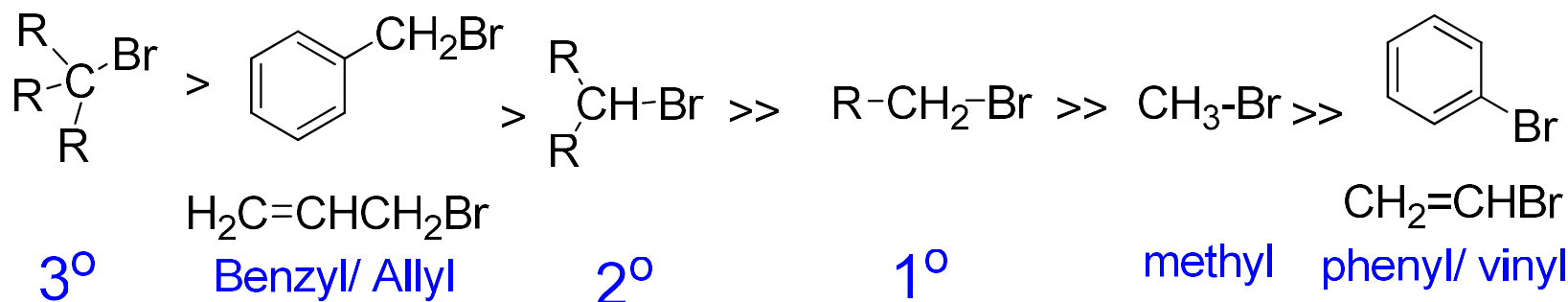
Classification of solvents

Polar protic solvents
(e.g. H_2O, MeOH, CH_3CO_2H)

Non-polar solvents
(e.g. hexane, C_6H_6)

Solvents

Polar
solvents

Polar aprotic solvents
(e.g. DMSO, HMPA)

$CH_3-C(=O)-CH_3$

(acetone)

$H-C(=O)-N(CH_3)CH_3$

(DMF)

$CH_3-C\equiv N$

(Acetonitrile)

$CH_3-S(=O)-CH_3$

(DMSO)

$Me_2N-P(=O)(NMe_2)NMe_2$

(HMPA)
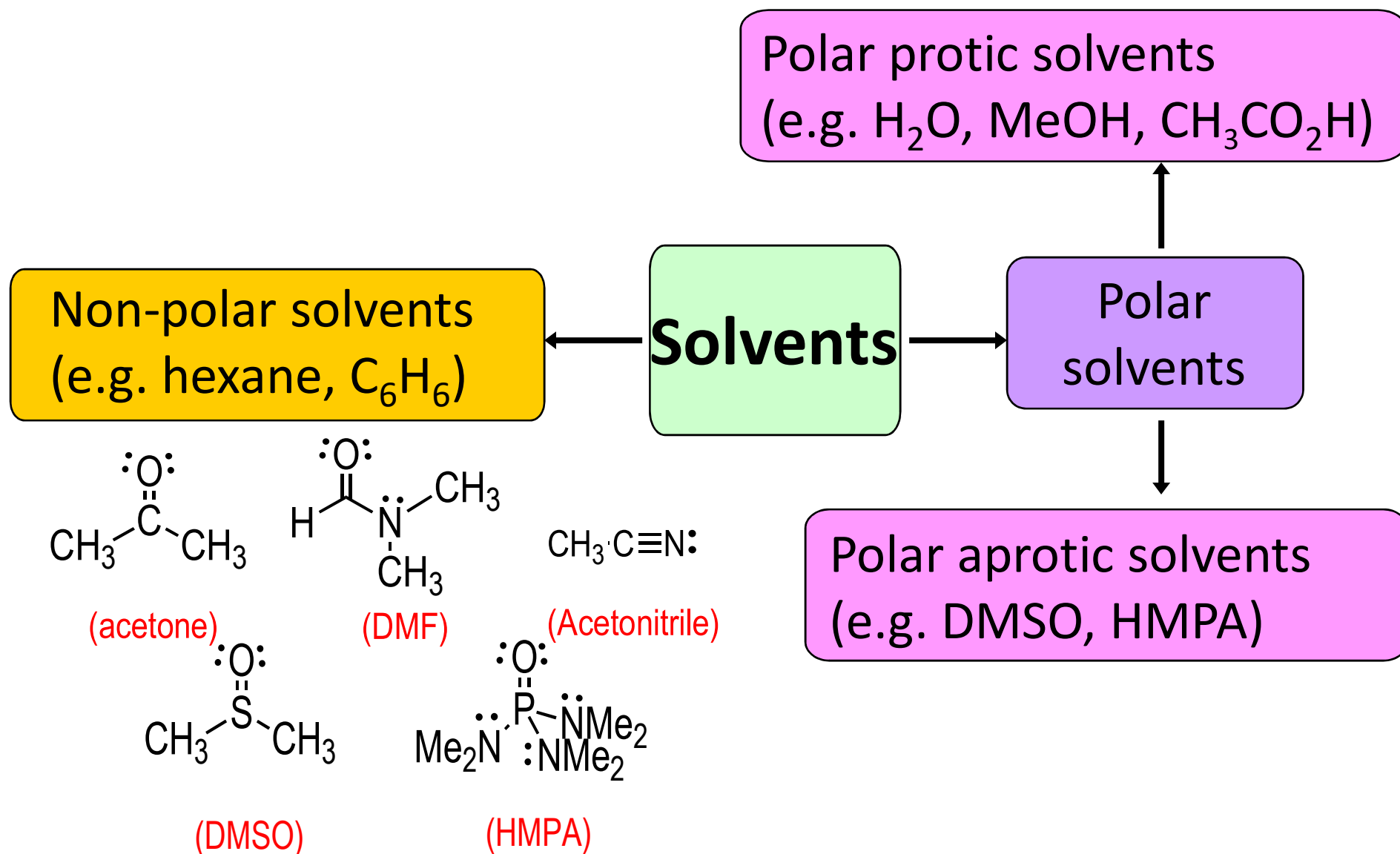
Polar APROTIC solvents solvate cations
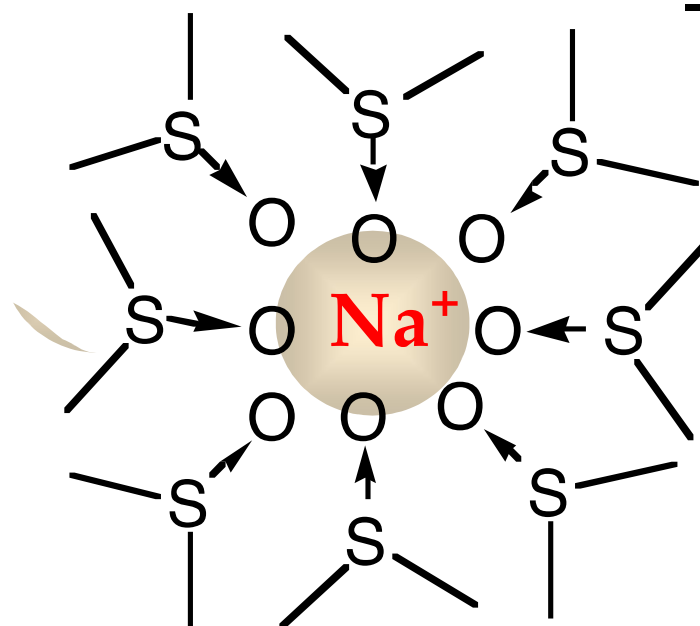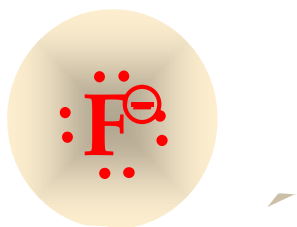
Best solvents for S_N2 rxs are

Polar Aprotic solvents

- strong dipoles

- and no OH or NH groups

$$CH_3Br + NaI \longrightarrow CH_3I + NaBr$$

Solvent	Relative Rxn Rate
MeOH	1
DMF	10^6

"naked" anion - $:\ddot{F}^{\ominus}$ e's "free" of Na$^+$

Polar protic solvents solvate cations & anions
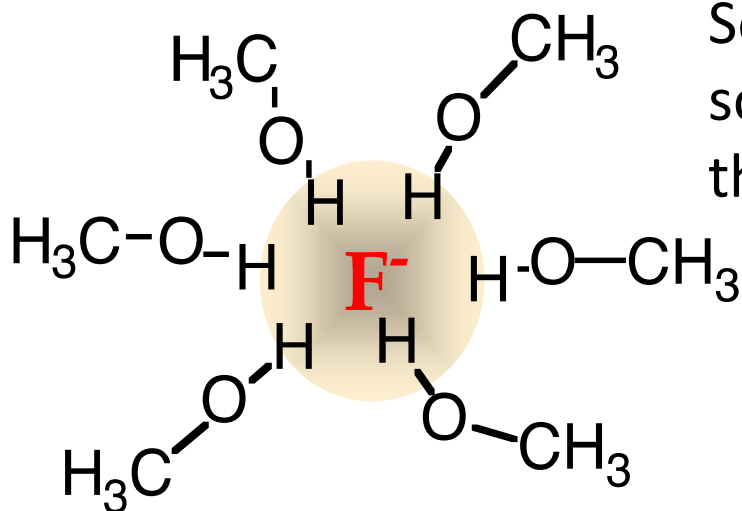
Solvation of nucleophile by Polar protic solvents, decreases its nucelophilicity. So they are not good solvent for S_N2 rexn.

S_N1 Reactions: Solvent effects are due to stabilization of the transition state. Polar Protic solvents stabilize ionization in transition state

Solvation lowers the potential energy of the nucleophile making it less reactive.
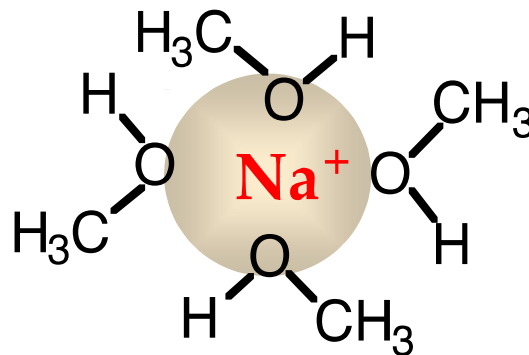
Protic solvents can form hydrogen bonds and can solvate both cations and anions.

Solvation energy is inversely proportional to the size of anion. Thus, smaller anion such as F⁻ are solvated more than I⁻ and thus are weaker nulcleophile in protic solvent.

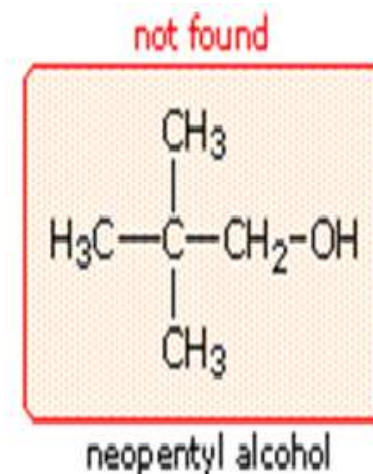innovate   achieve   lead

❑ Carbocations can rearrange to form a more stable carbocation.

Hydride shift (~H): The movement of hydrogen with its bonding pair of electrons.

Methyl shift (~CH$_3$): CH$_3$ moves from adjacent carbon if no H's are available.

Rearrangements in S$_N$1 Reactions

❑ **Increasing the stability of carbocation intermediates** is not the only factor that leads to molecular rearrangement. If angle strain, torsional strain or steric crowding in the reactant structure is relieved by an alkyl or aryl shift to a carbocation site, such a rearrangement is commonly observed.

Starting Compound
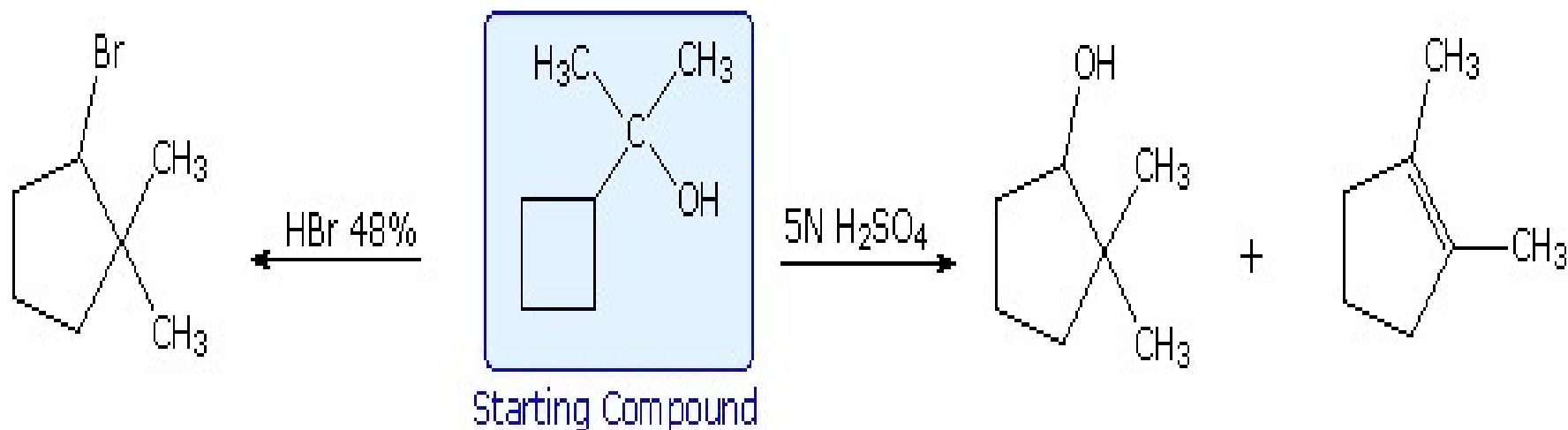
Although a 3º-carbocation is initially formed, the angle and torsional strain of the four-membered ring is reduced by a methylene group shift resulting in ring expansion to a 2º-carbocation.

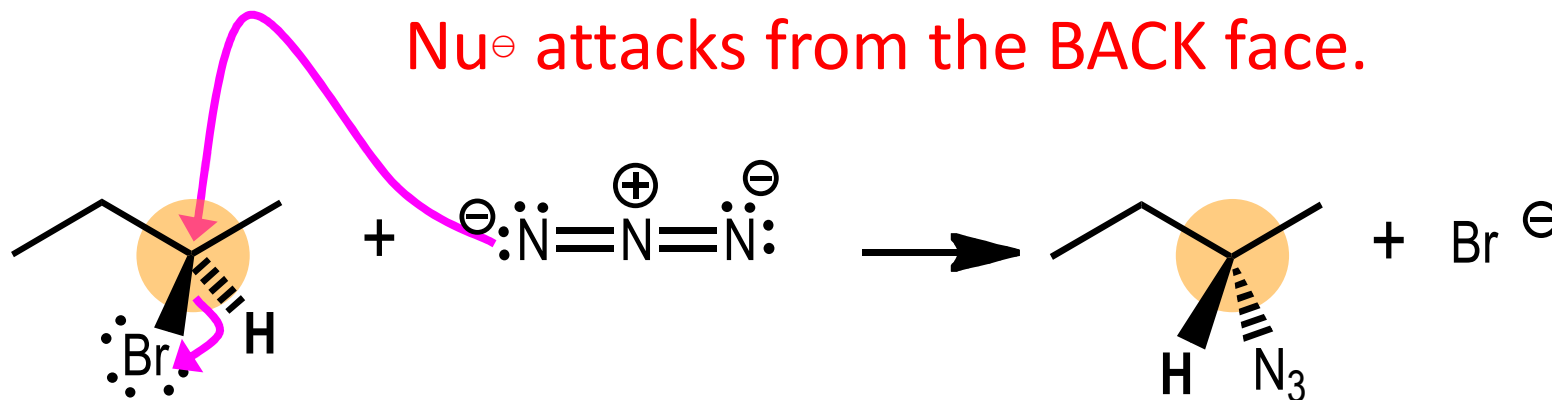# Details of S_N1 and S_N2 (Self study)

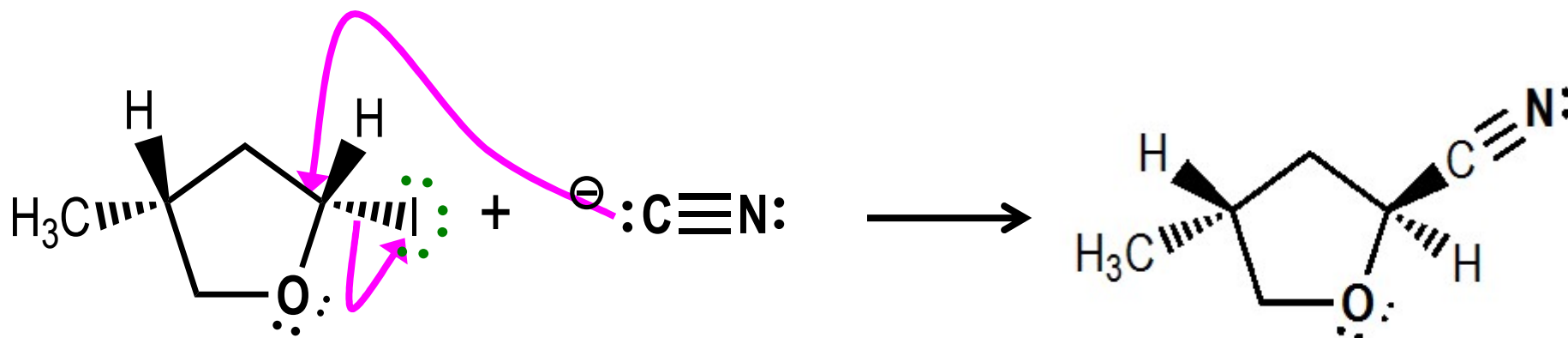## Additional slides provided

Extra class notice:
For T-07 and T-11
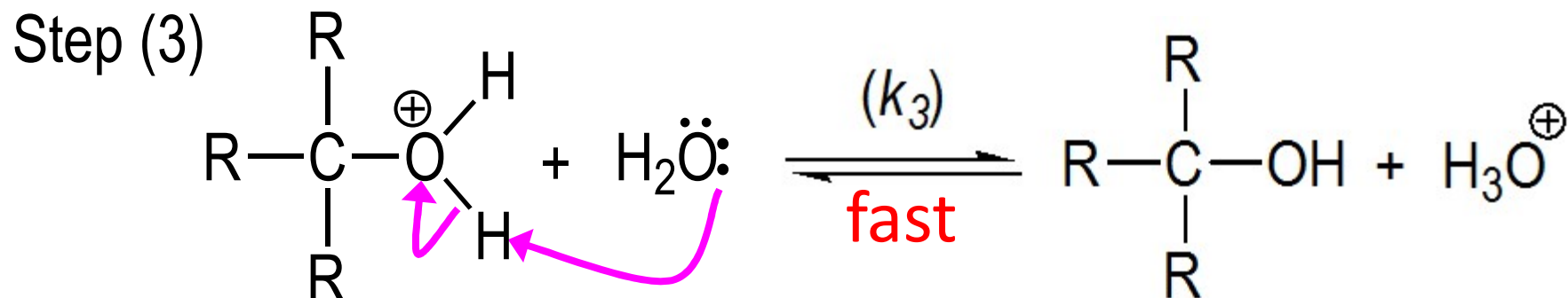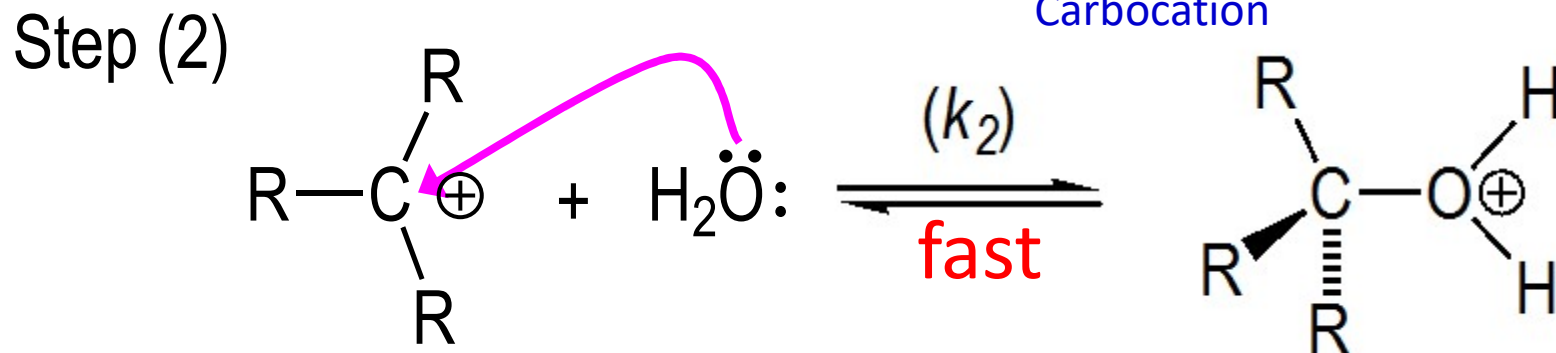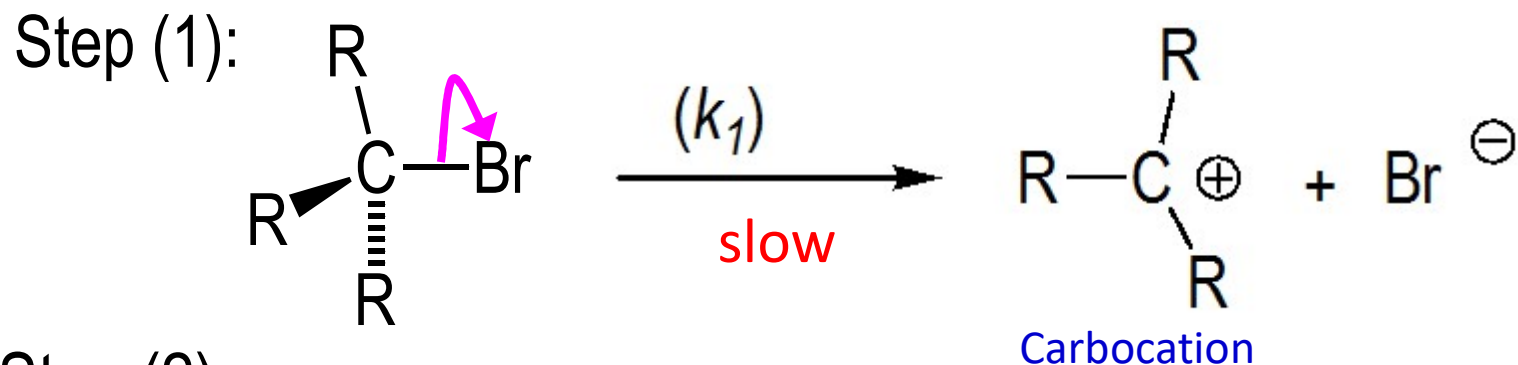Venue-6105
time- 6-7 pm

S$_N$2 Reaction

Nu⊖ attacks from the BACK face.

Nu⊖ attacks from the TOP face.

2nd type: S$_N$1 (stepwise mechanism)

Step (1):

(k_1) slow

Carbocation

Step (2)

(k_2) fast

Step (3)

(k_3) fast

Nucleophilic Substitution Reactions

(nucleophile)   (substrate)

Nu: donates e⁻ pair

(product)

new covalent bond
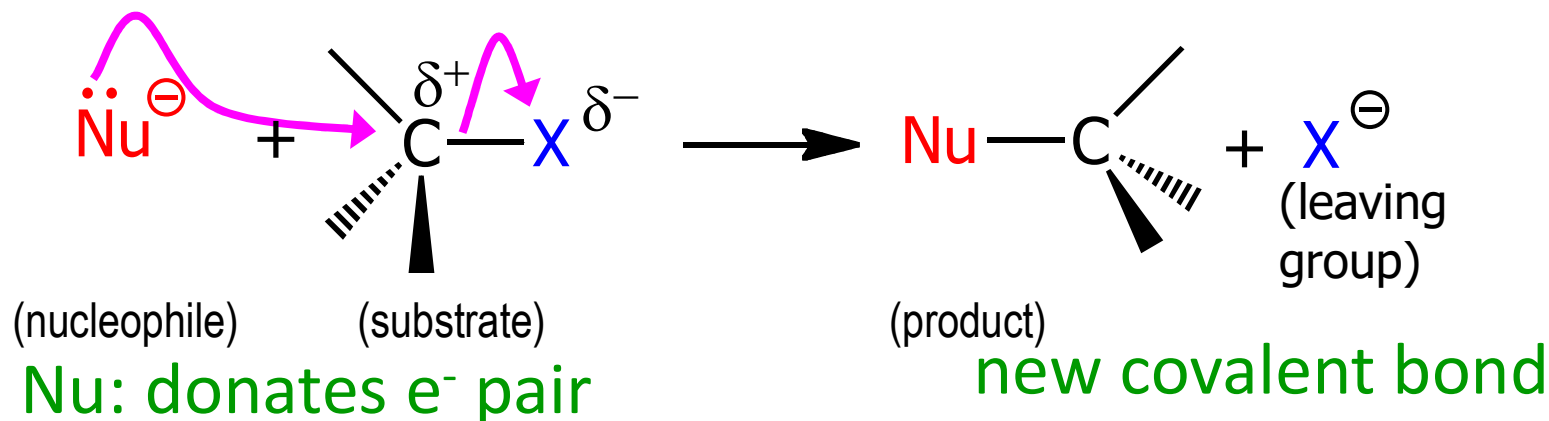
Good leaving groups:

alkyl halides   **tosylates**   **alcohols**

R—Cl

R—Br

R—I
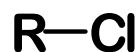
R—O—Ts
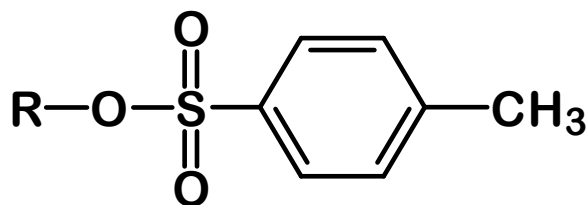
alkyl *p*-toluenesulfonate

R—OH   R—Ö—H

Alcohols require acid
and then H_2O leaves

Alcohols can also be converted to a good leaving group by making its tosylate or through protonation.

❑ In comparing two leaving groups the better leaving group is the weaker base. For example, H_2O is a better leaving group than HO^- because H_2O is a weaker base.

❑ **There are periodic trends in leaving group ability:**

Left to right across a row, basicity decreases so leaving group ability increases.

❑ Down a column of the periodic table, basicity decreases so leaving group ability increases.

Increasing basicity

Increasing basicity

:NH₃   H₂Ö:

F⁻   Cl⁻   Br⁻   I⁻

Increasing leaving group ability

Increasing leaving group ability
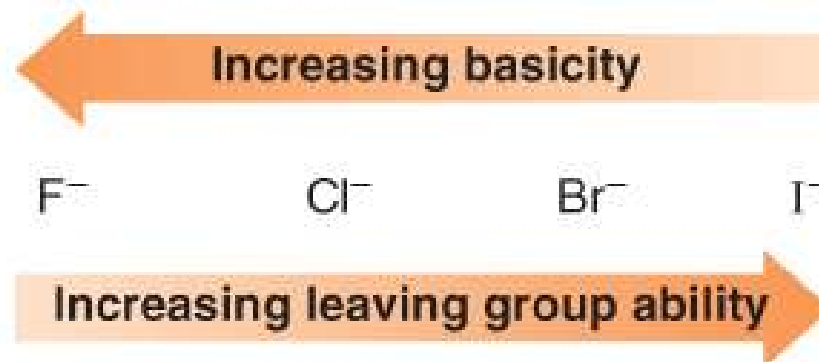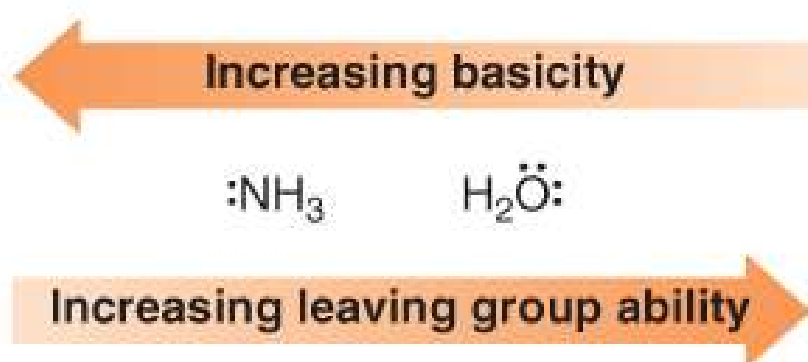
A nucleophile may be any molecule with an unshared electron pair.

Nucleophiles in general are anions ($-CN^-$, $-I^-$, $-SH^-$ etc.) or neutral molecules (H_2O, ROH, NH_3 etc.).

Although nucleophilicity and basicity are interrelated, they are fundamentally different.

Basicity is a measure of how readily an atom donates its electron pair to a proton.

It is characterized by an equilibrium constant, K_a in an acid-base reaction, making it a thermodynamic property.

Nucleophilicity is a measure of how readily an atom donates its electron pair to other atoms.

It is characterized by a rate constant, k, making it a kinetic property.

For two nucleophiles with the same nucleophilic atom, **nucleophilicity parallels basicity, i.e.** the stronger base is the stronger nucleophile.

The relative nucleophilicity of HO^- and CH_3COO^-, two oxygen nucleophiles, is determined by comparing the pK_a values of their conjugate acids (H_2O = 15.7, and CH_3COOH = 4.8). HO^- is a stronger base and stronger nucleophile than CH_3COO^-.

A negatively charged nucleophile is always a stronger nucleophile than its conjugate acid.

HO^- is a stronger base and stronger nucleophile than H_2O.

❑ Nucleophilicity does not parallel basicity when steric hindrance becomes important.

❑ Steric hindrance decreases nucleophilicity but not basicity. Sterically hindered bases that are poor nucleophiles are called non nucleophilic bases.
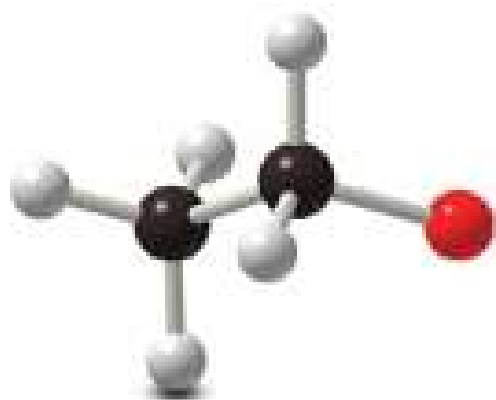
Ethoxide (Stronger nucleophile)

tert-Butoxide (Stronger base)

Relative strength of a Nucleophile

R-X   Me, 1º, 2º, 3º

strong

strong bases

Br^-, I^-, H_3CS^-, RS^-

$N \equiv C^-$, N_3^-

S_N2

HO^-, H_3CO^-, RO^-; $\overset{\ominus}{:}\overset{R'}{\underset{R}{\text{C}}}\text{--C}\overset{O}{=}$ $[H_2N^-, R\text{--}C\equiv C^-; R^-]$

S_N2

$(CH_3)_3C\text{-}O^-$

$S_N2 +$

moderate

Cl^-, F^-

$H_3CC\overset{O}{\underset{O^-}{=}}$, $RC\overset{O}{\underset{O^-}{=}}$

S_N2

H_3CSH, RSH, R_2S

H_3N, RNH_2, R_2NH, R_3N

nucleopilicity

S_N2

$S_N1 +$

weak

H_2O

H_3COH, ROH

$H_3CC\overset{O}{\underset{OH}{=}}$, $RC\overset{O}{\underset{OH}{=}}$