CHAPTER 4.2 – NUCLEOPHILIC SUBSTITUTION (ALKYL HALIDES)

1

OBJECTIVES

o   **Identify and classification of alkyl halides**

o   **Outline the isomerism, physical properties and preparation of alkyl halides.**

o   **Define the term S_N2 and outline in detail the S_N2 mechanism.**

o   **Define the term S_N1 and outline in detail the S_N1 mechanism.**

o   **Explain the rearrangement of carbocations in S_N1 reactions.**

o   **Relate the nature of the different leaving groups to the rate of reaction in S_N1 and S_N2 reactions.**

o   **Explain how the nature of substrate affects the S_N1 and S_N2 reactions.**

o   **Describe the effect of the nature of nucleophile on the rate of S_N2 reactions.**

o   **Compare and contrast S_N1 and S_N2 mechanisms in terms of kinetics and mechanisms, stereochemistry and reactivity.**

4.2.1 Introduction

1. General formula: $C_nH_{2n+1}X$ or R-X
   (X = F, Cl, Br or I)

2. Nomenclature and classification

- Alkyl halides are named as derivatives of corresponding alkane.

- The position of halogens are indicated by the numbering of the carbon atoms in the chain.

- Prefixes **fluoro-, chloro-, bromo**- and **iodo-** are used

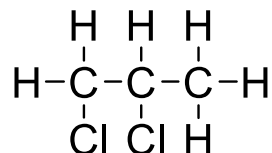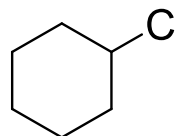- Prefixes *di-, tri-, tetra-* are used to indicate how many of each halogen are present

4.2.1 Introduction
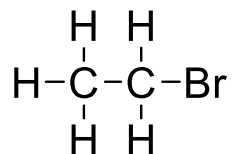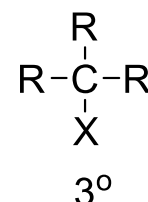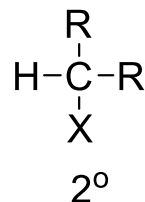

bromoethane
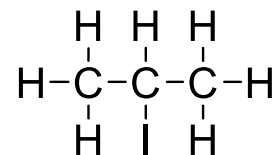
2-iodopropane
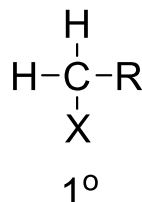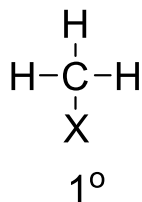

1,2-dichloropropane

chlorocyclohexane

- Alkyl halides may be classified as **primary** (1°), **secondary** (2°) or **tertiary** (3°)

1°   1°   2°   3°

At most **1 alkyl (-R)** group attached to C atom bonded to X	**2 alkyl (-R)** groups attached to C atom bonded to X	**3 alkyl (-R)** groups attached to C atom bonded to X

4

4.2.3 Physical Properties of Alkyl Halides

(a) Boiling Point (Recall: Depends on strength of intermolecular forces of attraction)

- Small amount of energy is required to overcome the ***permanent dipole–permanent dipole*** forces of attraction between the alkyl halide molecules.

- Increased boiling point with increased alkyl chain length and larger halogen size (due to higher molecular weight and stronger London dispersion forces).

- Boiling point: $CH_3Cl < CH_3CH_2Cl < CH_3CH_2CH_2Cl$

- Boiling point: $CH_3Cl < CH_3Br < CH_3I$

4.2.3 Physical Properties of Alkyl Halides

(b) Solubility and density (Recall: 'Like dissolves like')

○ Insoluble in water

- **Weak *London dispersion forces*** between R-X molecules (fairly non-polar) are incompatible to the strong hydrogen bonding between water molecules (polar).

○ Soluble in organic solvents (e.g. CCl_4 or Benzene)

- Weak London dispersion between R-X molecules (**fairly non-polar**) are compatible to the weak London dispersion forces between organic solvent molecules (non-polar).

6

Properties of some organic halogen compounds

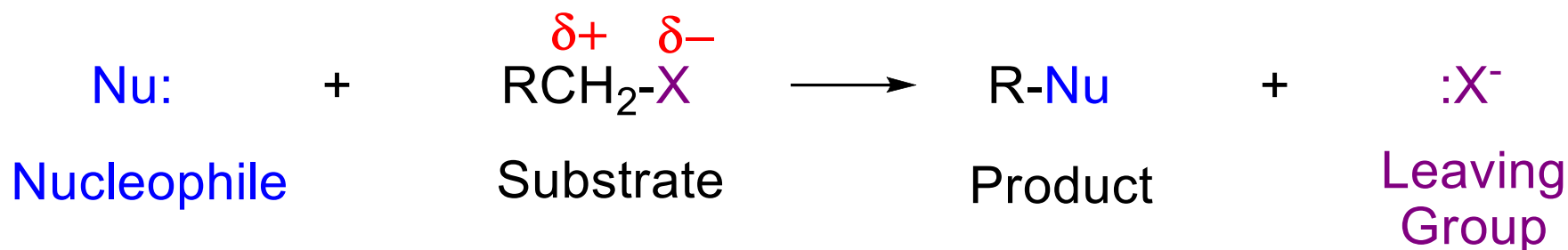| Compound	IUPAC name	b.p./°C	Density/g cm^{-3} at 20°C
CH_3F	Fluoromethane	-78.6	
CH_3Cl	Chloromethane	-24.2	
CH_3Br	Bromomethane	3.6	
CH_3I	Iodomethane	42.5	2.279
CH_2Cl_2	Dichloromethane	40.1	1.336
$CHCl_3$	Trichloromethane (Chloroform)	61.3	1.498
CCl_4	Tetrachloromethane (Carbon tetrachloride)	76.8	1.595
CH_3CH_2Br	Bromoethane	38.40	1.46
$CH_3CHClCH_3$	2-Chloropropane	35.74	0.86
$(CH_3)_3CCl$	2-Chloro-2-methylpropane	52	0.84
C_6H_5Cl	Chlorobenzene	132	1.11
$CH_2=CHF$	Fluoroethene	-72.2	
$CH_2=CHCH_2Br$	3-bromopropene	70	1.40

4.2.4 Chemical reactivity of Alkyl Halides

- The chemical reactivity of alkyl halides is due to its **polar** C – X bond.

$$H-\underset{\underset{|}{H}}{\overset{\overset{H}{|}}{C}} \xrightarrow{\overset{\delta+ \quad \delta-}{}} X$$
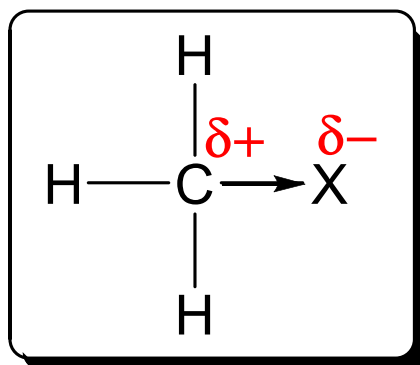
- Halogens are **electronegative** and draw the shared pair of electrons away from C towards themselves.

- The **electron deficient** $C^{\delta+}$ atom is susceptible to attack by nucleophiles.
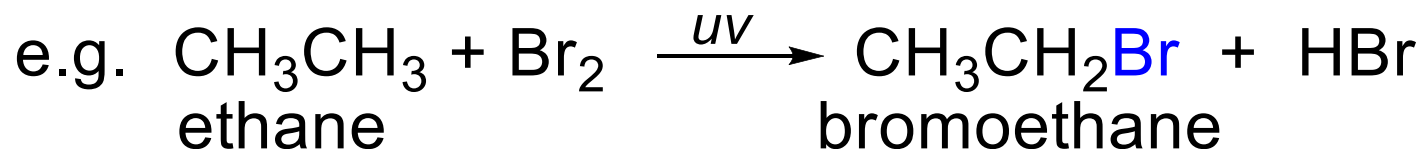
4.2.4 Chemical reactivity of Alkyl Halides

$$\text{Nu:} \quad + \quad \overset{\delta+ \quad \delta-}{RCH_2\text{-}X} \quad \longrightarrow \quad R\text{-}Nu \quad + \quad :X^-$$

Nucleophile   Substrate   Product   Leaving Group

- Alkyl halides undergo ***nucleophilic substitution*** reactions where the halogen is replaced by the *nucleophile*.

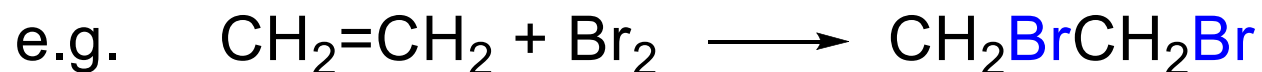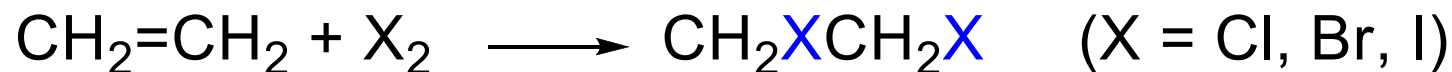# 4.2.5 Methods of Preparation

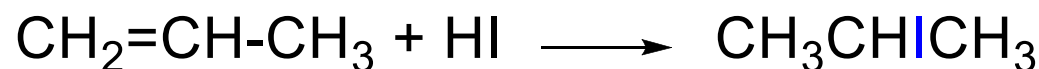**1)From alkanes (R-H → R-X)**: <u>**Free radical substitution**</u>

$$R\text{-}H + X_2 \xrightarrow{\;uv\;} R\text{-}X + HX \quad (X = Cl, Br)$$

e.g. $CH_3CH_3 + Br_2 \xrightarrow{\;uv\;} CH_3CH_2Br + HBr$

ethane   bromoethane

2)From alkenes (R-CH=CH-R' $\rightarrow$ R-X): Electrophilic Addition

(a)   Addition of halogen gas

$$CH_2=CH_2 + X_2 \longrightarrow CH_2XCH_2X \quad (X = Cl, Br, I)$$

e.g. $CH_2=CH_2 + Br_2 \longrightarrow CH_2BrCH_2Br$

2) From alkenes (R-CH=CH-R' → R-X): <u>Electrophilic Addition</u>

(b)   Addition of hydrogen halide

$$CH_2=CH_2 + HX \longrightarrow CH_3CH_2X \quad (X = Cl, Br, I)$$

e.g. $CH_2=CH_2 + HBr \longrightarrow CH_3CH_2Br$

$CH_2=CH-CH_3 + HI \longrightarrow CH_3CHICH_3$

(Recall: Markovnikov's rule)

Reactivity: HI > HBr > HCl since H-I bond is easier to break.

3)   **From alcohols (R-OH → R-X): <u>Nucleophilic Substitution</u>**

(a)   With HX

$$R\text{-}OH(l) + HX(g) \longrightarrow R\text{-}X(l) + H_2O(l) \quad (X = Cl, Br)$$

e.g. $CH_3CH_2OH(l) + HBr(g) \longrightarrow CH_3CH_2Br(l) + H_2O(l)$
ethanol   bromoethane
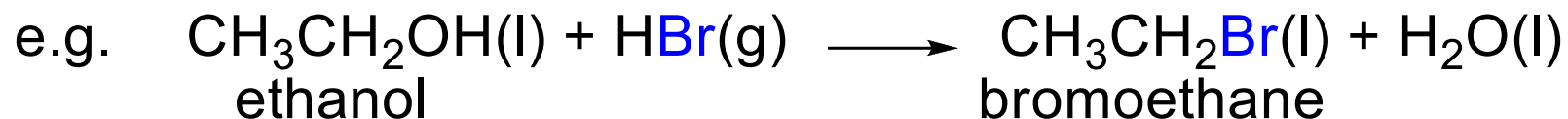
3) From alcohols (R-OH → R-X): <u>Nucleophilic Substitution</u>

(b)   With PX_3/ PX_5

$$3 \text{ R-OH } + \text{ P}X_3 \longrightarrow 3 \text{ R-}X + H_3PO_3 \quad (X = Cl, Br)$$

e.g. $3 \text{ CH}_3\text{CH}_2\text{OH } + \text{ PBr}_3 \longrightarrow 3 \text{ CH}_3\text{CH}_2\text{Br } + H_3PO_3$
       ethanol   phosphorus
                       tribromide

$$\text{R-OH } + \text{ PCl}_5 \longrightarrow \text{R-Cl} + \text{POCl}_3 + \text{HCl}$$

e.g. $\text{CH}_3\text{CH}_2\text{OH } + \text{ PCl}_5 \longrightarrow \text{CH}_3\text{CH}_2\text{Cl} + \text{POCl}_3 + \text{HCl}$
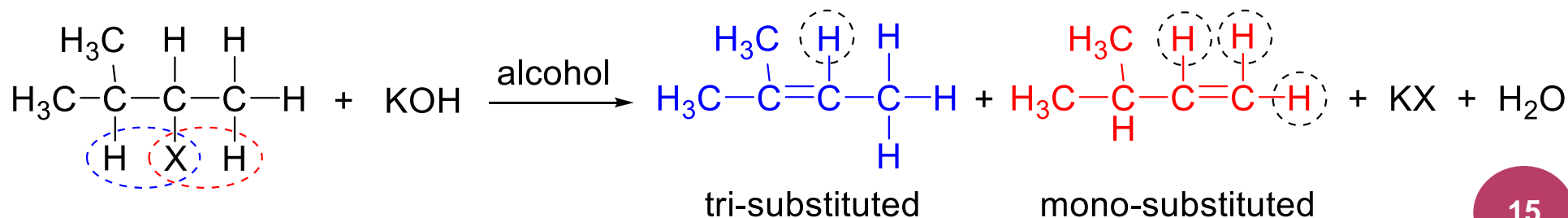   ethanol   phosphorus
                       pentachloride

14
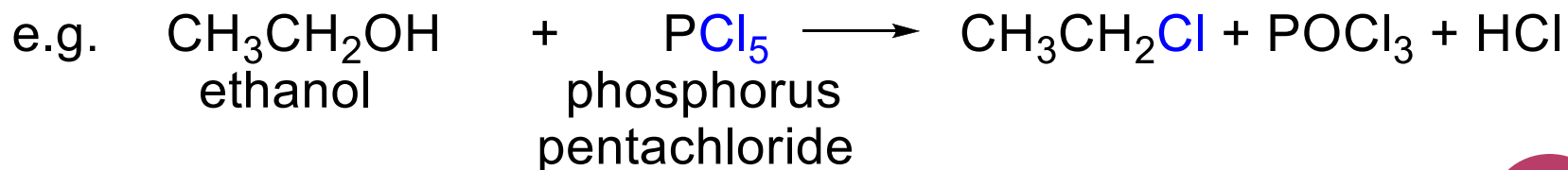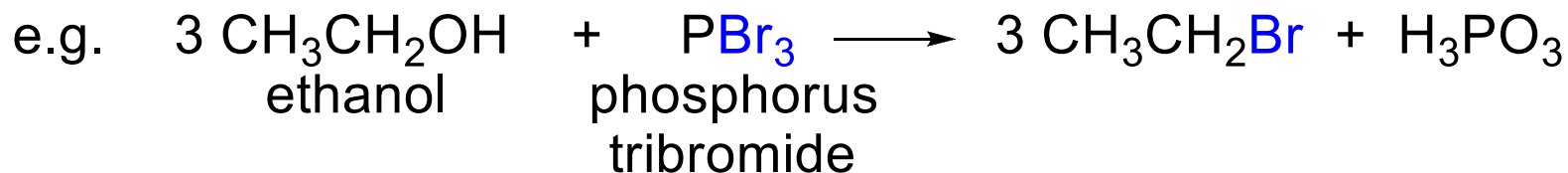
4.2.6 Reactions of Alkyl Halides

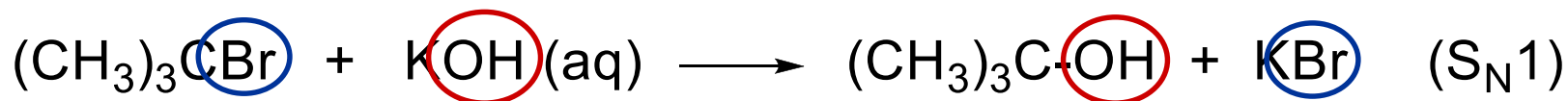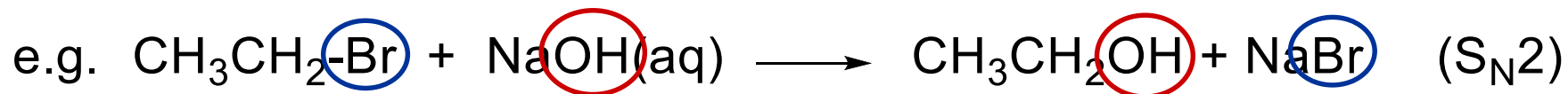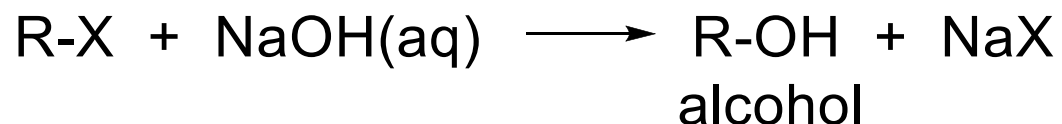## 1) Elimination (R-X → R-CH=CH-R')

Major   Minor
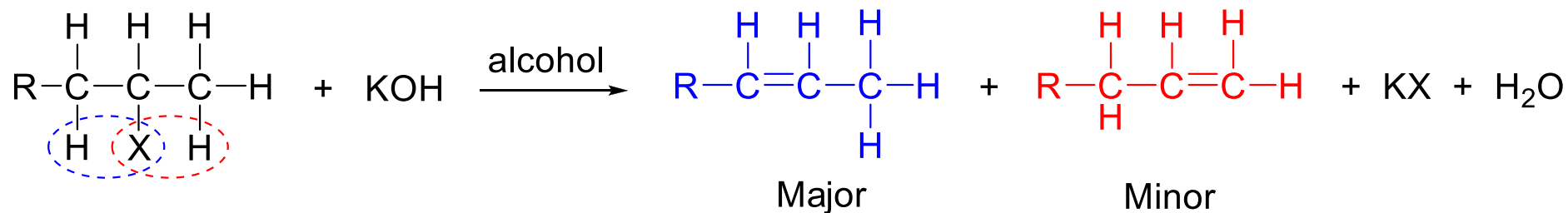
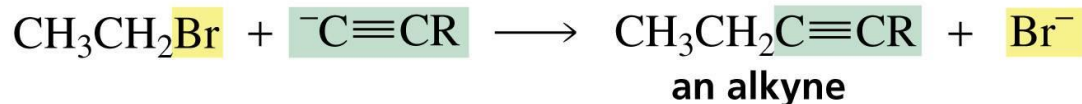Recall: Zaitsev's Rule - more substituted alkene will be preferred.

E.g
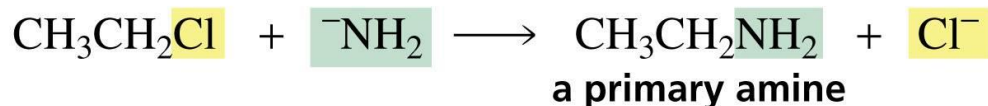

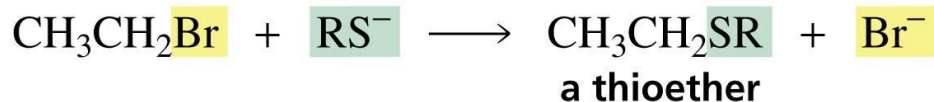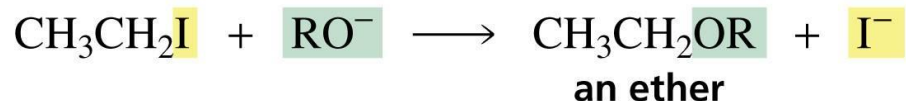tri-substituted   mono-substituted

2) Nucleophilic substitution (R-X $\rightarrow$ R-Nu)

(a)   Hydrolysis

$$R\text{-}X + NaOH(aq) \longrightarrow R\text{-}OH + NaX$$
$$\text{alcohol}$$

e.g. $CH_3CH_2\text{-}Br + NaOH(aq) \longrightarrow CH_3CH_2OH + NaBr$ (S_N2)

$(CH_3)_3CBr + KOH(aq) \longrightarrow (CH_3)_3C\text{-}OH + KBr$ (S_N1)

2) Nucleophilic substitution (R-X → R-Nu)

(b)   Other substitution reactions

$$CH_3CH_2Cl + HO^- \longrightarrow CH_3CH_2OH + Cl^-$$
an alcohol

$$CH_3CH_2Br + HS^- \longrightarrow CH_3CH_2SH + Br^-$$
a thiol

$$CH_3CH_2I + RO^- \longrightarrow CH_3CH_2OR + I^-$$
an ether

$$CH_3CH_2Br + RS^- \longrightarrow CH_3CH_2SR + Br^-$$
a thioether

$$CH_3CH_2Cl + {}^-NH_2 \longrightarrow CH_3CH_2NH_2 + Cl^-$$
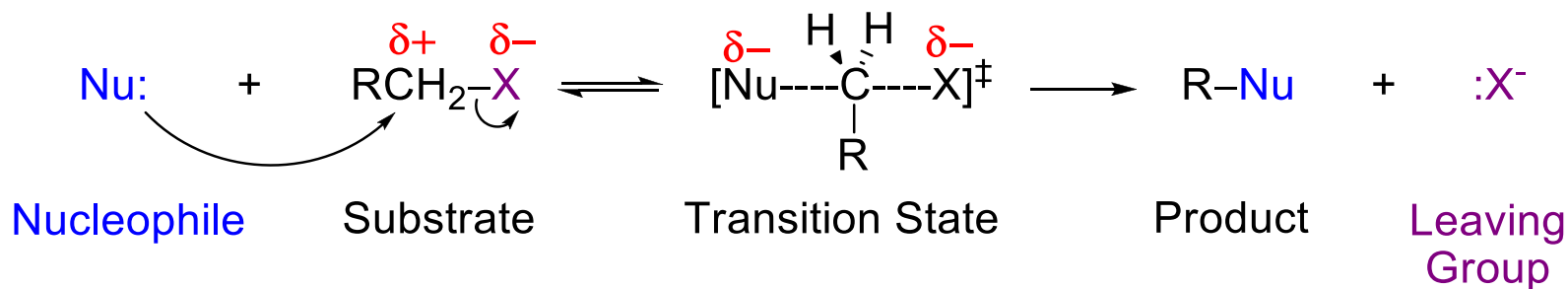**a primary amine**

$$CH_3CH_2Br + {}^-C\equiv CR \longrightarrow CH_3CH_2C\equiv CR + Br^-$$
an alkyne

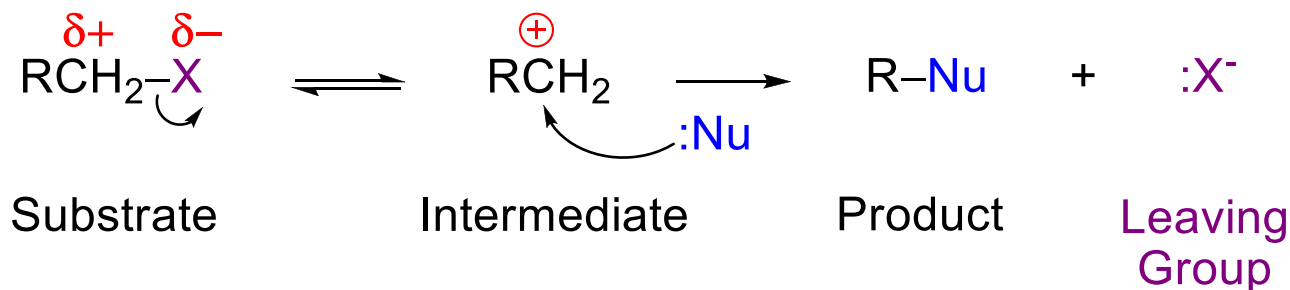$$CH_3CH_2I + {}^-C\equiv N \longrightarrow CH_3CH_2C\equiv N + I^-$$
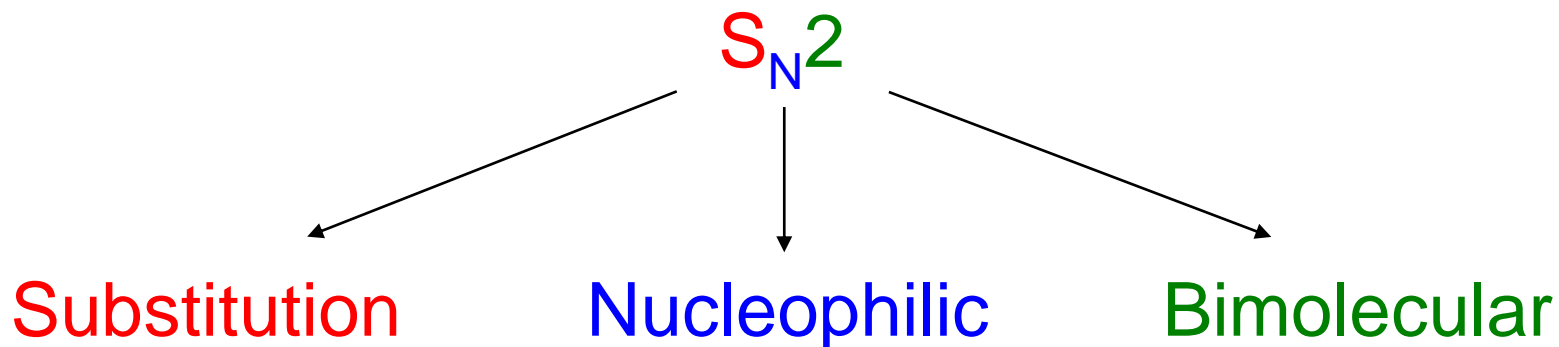**a nitrile**
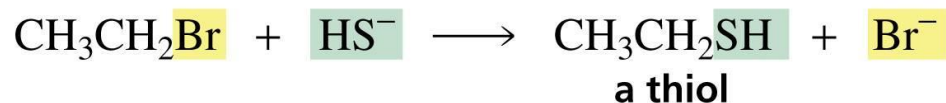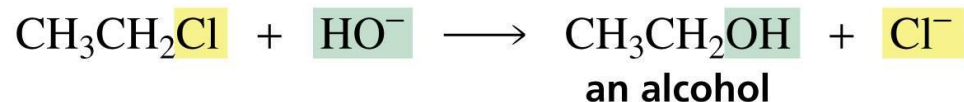
4.2.7 Nucleophilic Substitution

○ There are two possible mechanisms:

(a) **Concerted** – The carbon-halogen bond breaks at the same time as the new bond between the nucleophile and the carbon forms.
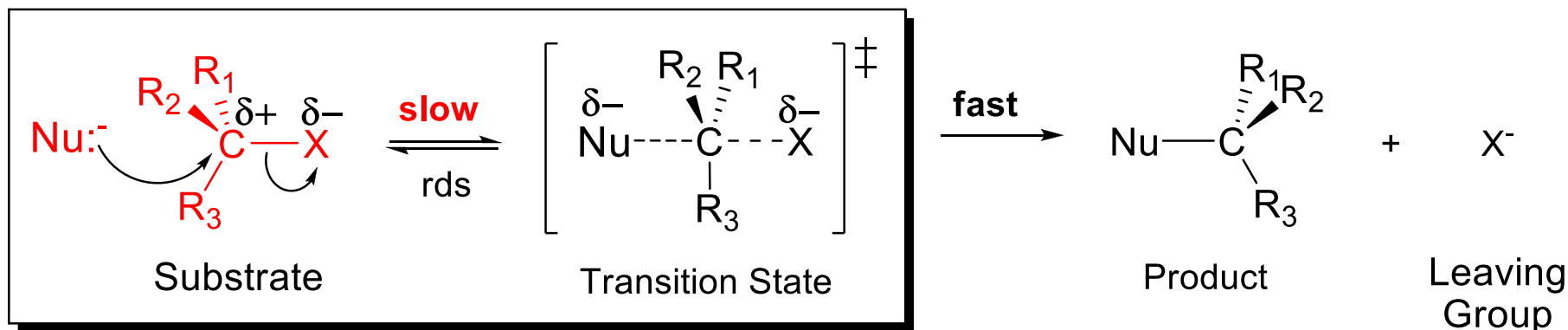
$$Nu: \quad + \quad RCH_2\overset{\delta+}{-}\overset{\delta-}{X} \quad \rightleftharpoons \quad [Nu----\overset{H}{\underset{R}{\overset{\delta-}{C}}}----X]^{\ddagger} \quad \longrightarrow \quad R-Nu \quad + \quad :X^-$$

Nucleophile   Substrate   Transition State   Product   Leaving Group

(b) **Stepwise** – The carbon-halogen bond breaks first, followed by nucleophilic attack.

$$RCH_2\overset{\delta+}{-}\overset{\delta-}{X} \quad \rightleftharpoons \quad \overset{\oplus}{RCH_2} \quad \longrightarrow \quad R-Nu \quad + \quad :X^-$$

:Nu

Substrate   Intermediate   Product   Leaving Group

4.2.8 S$_N$2 reaction

$$S_N2$$

Substitution   Nucleophilic   Bimolecular

a) Chemical kinetics

| Substrate | | Transition State | | Product | Leaving Group |

Nu:$^-$ ... C—X **slow** rds [Nu----C---X]‡ **fast** Nu—C ... + X$^-$

- Bimolecular: 2 molecules are involved in the rate-determining step (rds)
- **Rate = k [Substrate][Nu]**

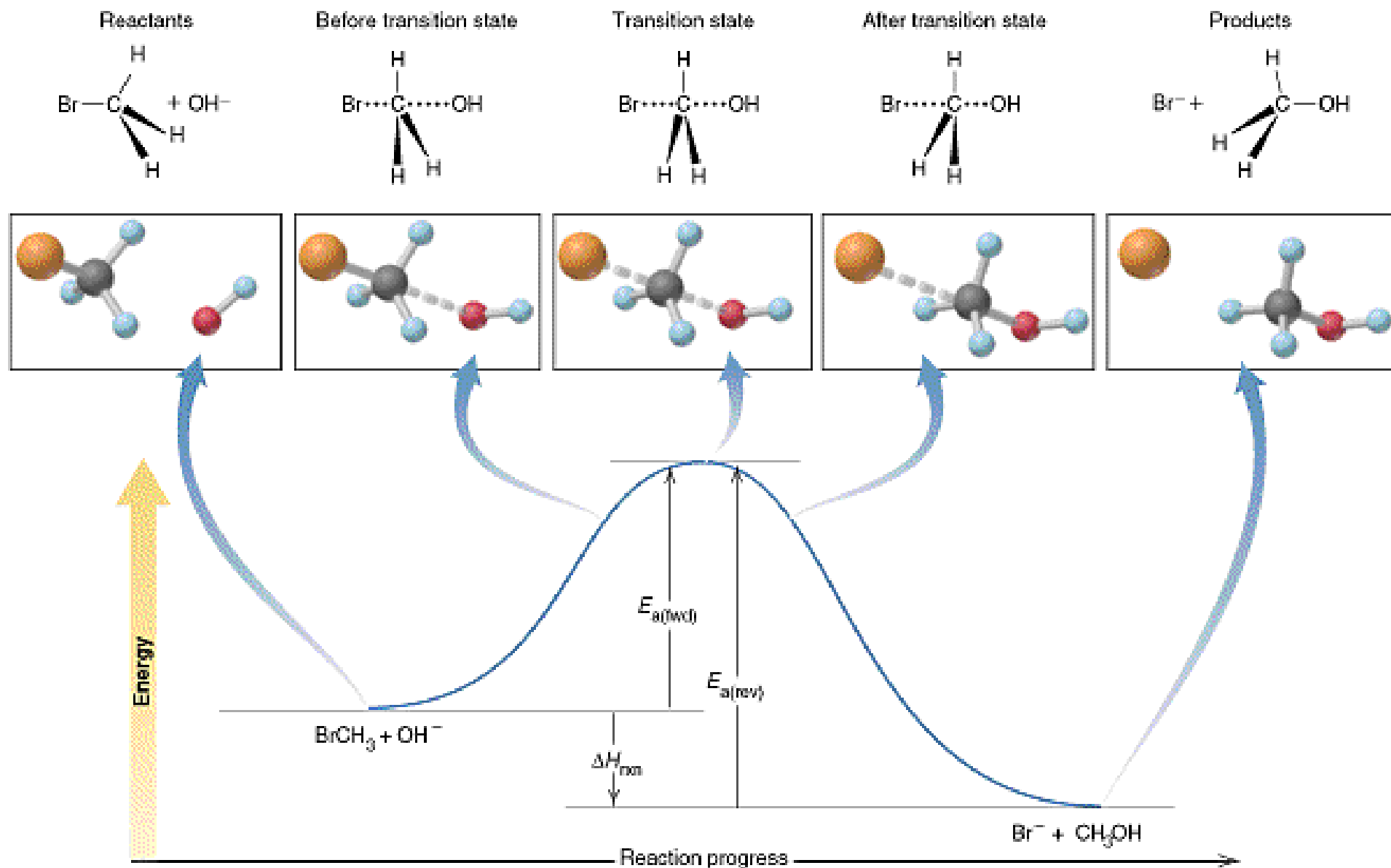**Consider the reaction between methyl chloride with hydroxide ion in aqueous solution :**

$$CH_3\text{-}Cl \ + \ OH^- \ \text{------------->} \ CH_3\text{-}OH \ + \ Cl^-$$

○ *The following kinetic results (at 60℃) were obtained:*

Expt. No.	Initial [CH$_3$Cl]/M	Initial [OH$^-$]/M	Initial Rate/Ms^{-1}
1	0.0010	1.0	4.9 x 10^{-7}
2	0.0020	1.0	9.8 x 10^{-7}
3	0.0010	2.0	9.8 x 10^{-7}
4	0.0020	2.0	19.6 x 10^{-7}

○ Above results shows that Rate $\propto$ [CH$_3$Cl] [OH$^-$]

ie.   Rate = k [CH$_3$Cl] [OH$^-$]

○ 1st order wrt CH$_3$Cl and 1st order wrt OH$^-$

○ This reaction is therefore **<u>second order overall</u>**.

(b) Energy Diagram

Reactants · Before transition state · Transition state · After transition state · Products

$E_{a(fwd)}$

$E_{a(rev)}$

$BrCH_3 + OH^-$

ΔH_{rxn}

$Br^- + CH_3OH$

Energy

Reaction progress

(c) Mechanism

| Substrate | | Transition State | | Product | Leaving Group |

The reaction scheme shows:

Nu:⁻ attacking the substrate (R_1, R_2, R_3 on carbon, $\delta+$ on C, $\delta-$ on X, C—X bond) → **slow** / rds → Transition State $[Nu \cdots C \cdots X]^{\ddagger}$ with $\delta-$ on Nu and $\delta-$ on X, (R_2, R_1, R_3) → Product Nu—C (R_1, R_2, R_3) + X^-
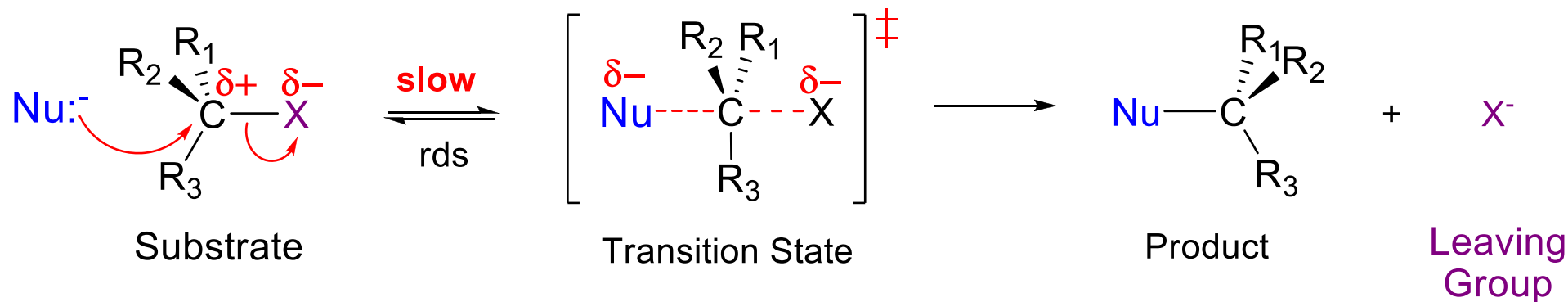
- The nucleophile approaches the α-carbon from the **backside** (the side directly opposite the leaving group) and 'kicks' out the leaving group **simultaneously** (concerted).

- The **transition state (TS)** is a fleeting arrangement of the atoms in which the nucleophile and the leaving group are both **partially bonded** (indicated with dotted lines) to the carbon atom undergoing attack.

- The carbon atom in the TS is **highly crowded** as it is bonded to five atoms.

22

(d) Stereochemistry

attack on the C—Br sp^3 orbital   transition state   products

inversion
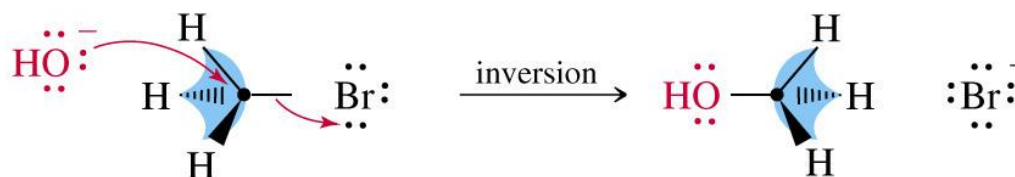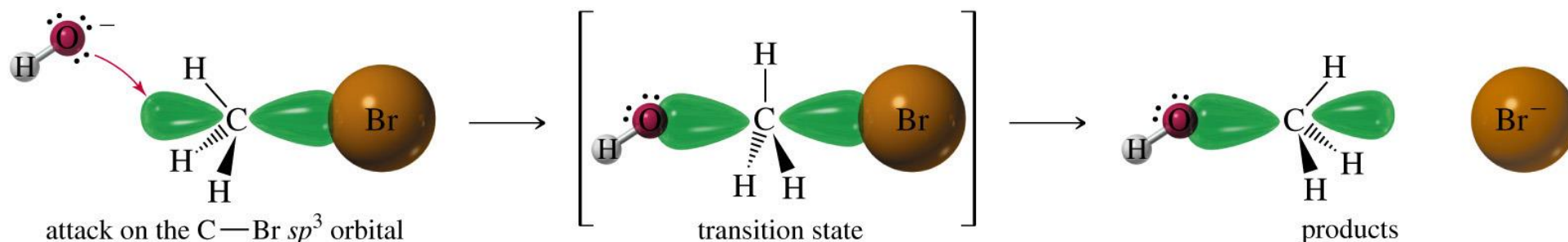
- The nucleophile attacks from the backside which causes a **change in the configuration** of the α-carbon atom (the configuration of an atom is the particular arrangement of groups around that atom in space). As the displacement occurs, the configuration of the α-carbon atom **inverts** – it is turned inside out.

$\Rightarrow$ **Inversion of configuration** is a key characteristic of S_N2 reactions.

23

Test Yourself

Name the following alkyl halide and draw the mechanism for the following reaction:
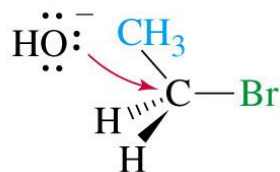

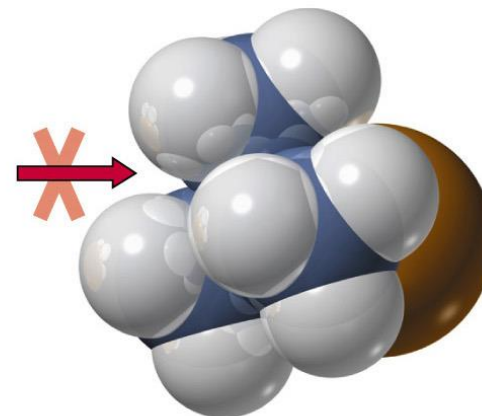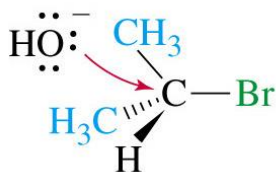$+$ OH^- $\longrightarrow$
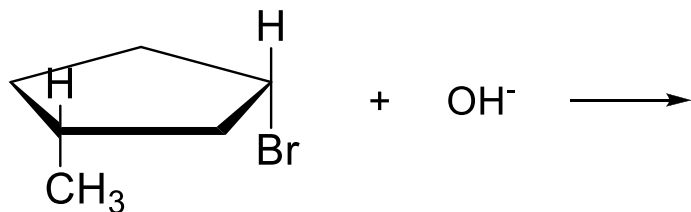
(e) Substrate

- With 2° alkyl halide in S_N2 reactions, the TS is highly crowded, and with *3° alkyl halides, crowding is so severe that the TS cannot be formed*.

- *Crowding in TS* accounts for the reactivity order of alkyl halides as **1º > 2º**.
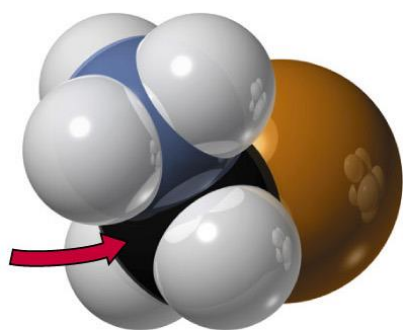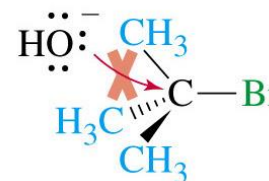
ethyl bromide (1°)
attack is easy
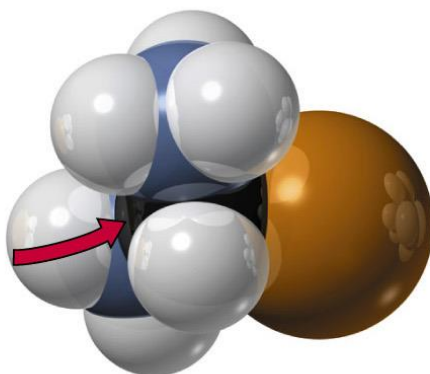
isopropyl bromide (2°)
attack is possible

*t*-butyl bromide (3°)
attack is impossible

(f) Leaving Group

- As the leaving group is normally expelled with a negative charge in most S_N2 reactions, we expect the *best leaving groups to be those that best stabilize the negative charge*.

- The stability of an anion is inversely related to its basicity, hence, **the best leaving groups should be the weakest base**.

- Relative stabilities of leaving groups:

OH^- ~ NH_2^- ~ OR^- < F^- < Cl^- < Br^- < I^- < TsO^-

Rate: <<1   1   200   10,000   30,000   60,000
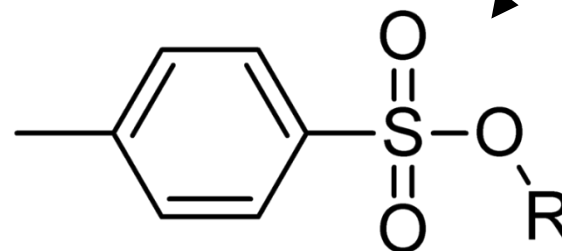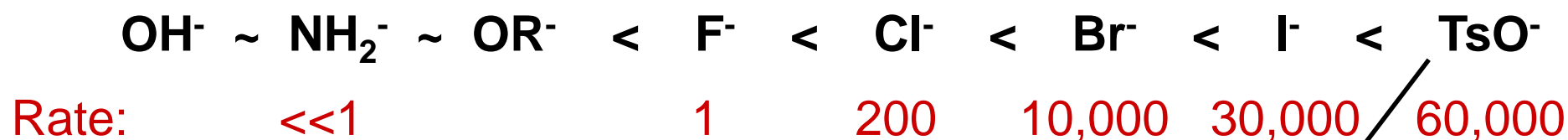
- Poor leaving groups (strong bases) like ***OH⁻, NH₂⁻, OR⁻ and F⁻*** do not undergo S$_N$2 unless they are converted into a ***weaker base***.

- This can be done via **protonation**.
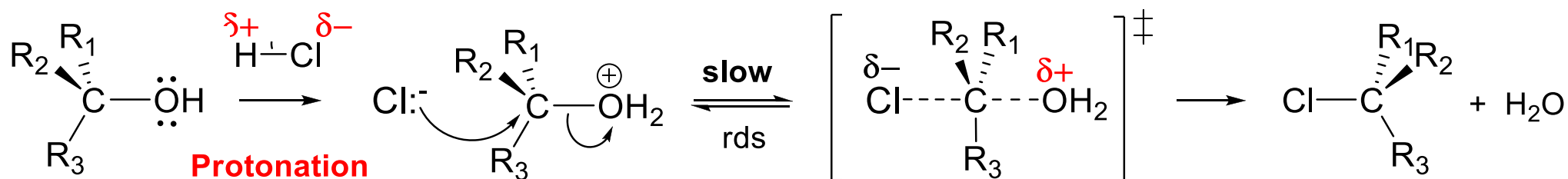
(g) Nucleophile

- Any species, either neutral or negatively charged, can act as nucleophiles as long as it has an *unshared pair or electrons for donation* (i.e. a Lewis base).

- A Lewis base is an **electron pair donor**. (c.f. Bronsted-Lowry base)

  E.g. $:OH^-$, $C_2H_5O:^-$, $H_2O:$, $:NH_3$, $R_3N:$

- A Lewis acid is an **electron pair acceptor**. (c.f. Bronsted-Lowry acid)

  E.g. $AlCl_3$, $FeCl_3$, BF_3

- Relative strength of nucleophiles:

  $H_2O < CH_3CO_2^- < NH_3 < Cl^- < OH^- < CH_3O^- < I^- < CN^- \sim HS^-$

  Rate: 1   500   700   1000   16,000   25,000   100,000   125,000

o Generally,

1) ***Nucleophilicity roughly parallels basicity*** when comparing nucleophiles having the same nucleophilic atom.

E.g. H_2O vs OH^-

- *Nucleophilicity*: the affinity of a Lewis base for the α-carbon of the substrate.

- *Basicity*: measures the affinity of a base for a proton.

2) ***Nucleophilicity usually increases down the group*** in the periodic table.

- *Increasing size* will cause the electron density to be *bound less tightly* by the nucleus, hence, *increasing ease of donation*. (c.f. solvent effect; this trend could be reversed depending on the solvent used)

3) *Negatively charged nucleophiles* are usually **more reactive** then neutral ones.

- Negatively charges nucleophiles are 'richer' in electron density and hence, *S_N2 reactions are often carried out under basic conditions.*

conjugate base
(stronger nucleophile)

lower E_a

conjugate acid
(weaker nucleophile)

higher E_a
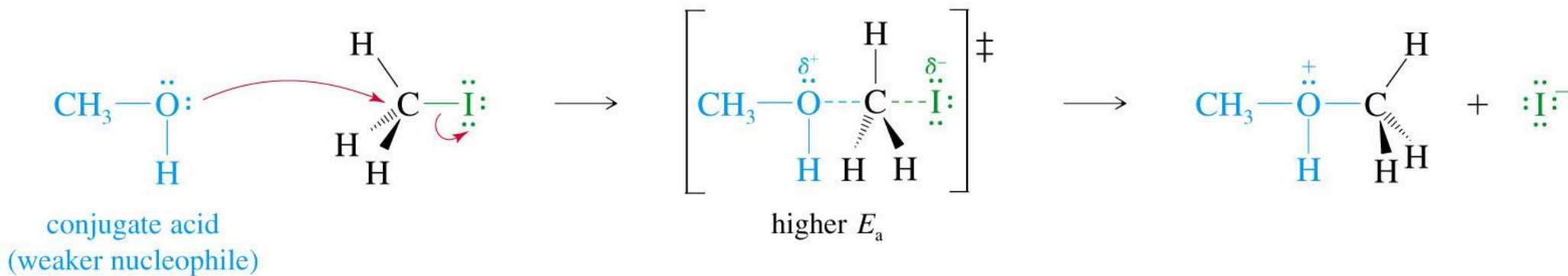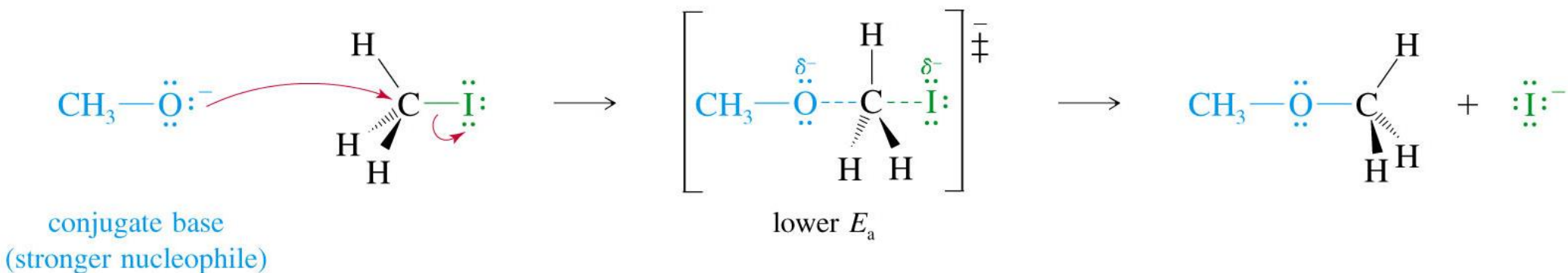
(h) Solvent effect

○ Solvent plays an important role in affecting the rate of reaction as it can either *stabilise or destabilise the intermediates/TS*.

○ There are generally two sub-categories of solvent:

- Protic solvents

- Aprotic solvents

1) **Protic solvent**

- Solvents which contain **hydrogen bonds** *(N-H, O-H or F-H)* and are capable of forming strong dipole-dipole attractions (hydrogen-bonding) with dissolved ions (both cations and anions).

E.g. H_2O, R-OH

Effect of Protic Solvents on S_N2 reaction

- Protic solvents slow down S_N2 reactions by *solvating the nucleophile* and form a "cage" around it, thereby, lowering its energy and reactivity.

solvent partially stripped off in the transition state
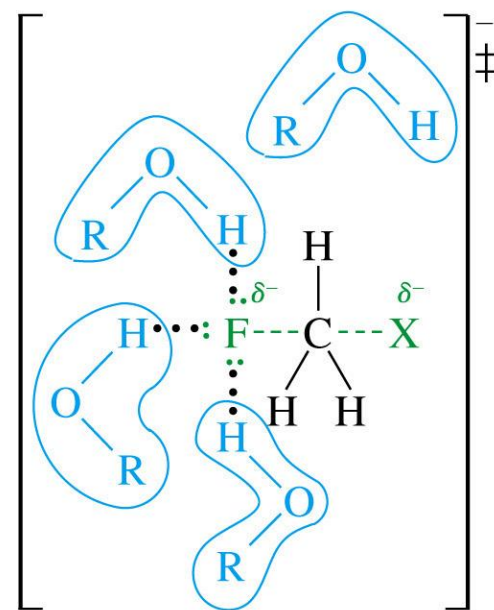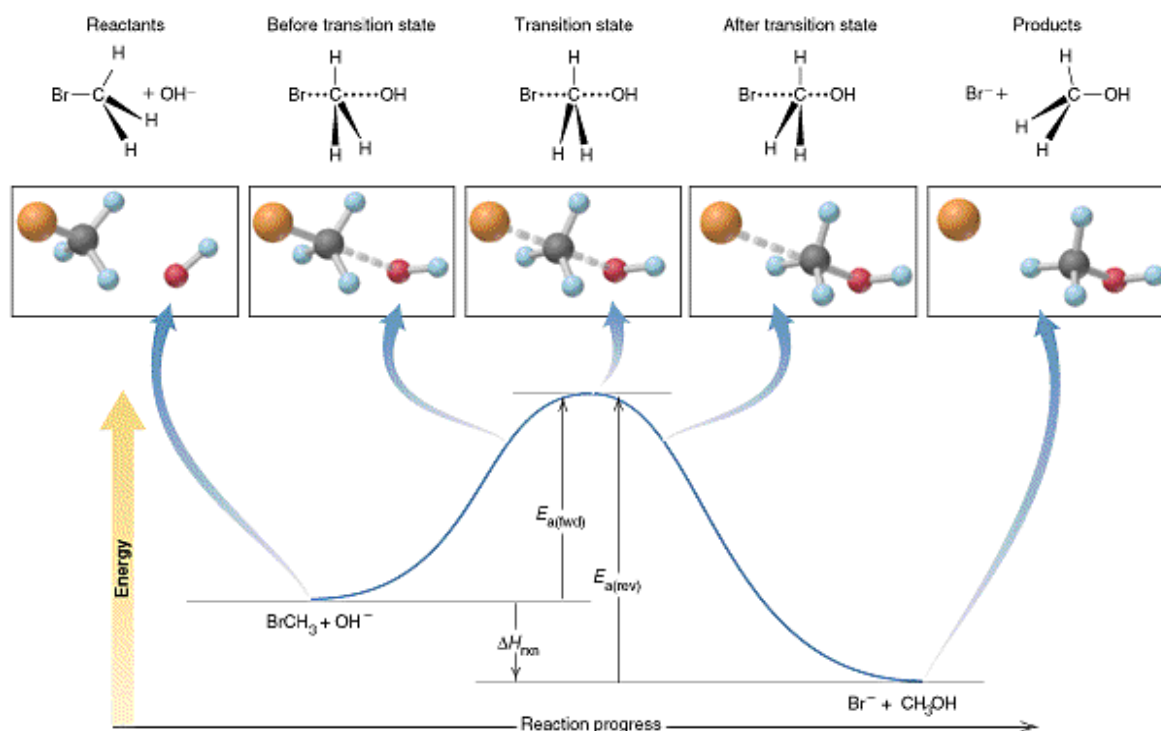
- Smaller nucleophiles with higher charge density, such as F^- ion, are more strongly **solvated** than a larger one.
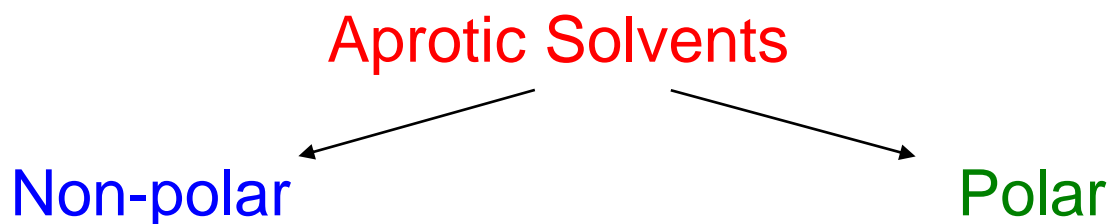
33

Nucleophilicity of Halides in Protic Solvents

○ The relative nucleophilicities of some common nucleophiles in **protic solvents** are as follows:

$SH^- > CN^- > I^- > OH^- > N_3^- > Br^- > CH_3CO_2^- > Cl^- > F^- > H_2O$

Effect of Aprotic Solvents on S_N2 reaction

○ Solvents which **do not contain *hydrogen bonds*** (no N-H, O-H or F-H) and are generally non-polar.

<div align="center">

Aprotic Solvents

Non-polar   Polar

</div>

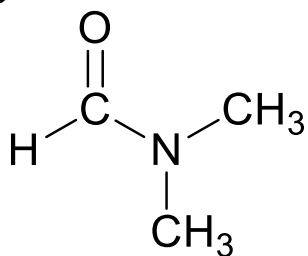○ **Non-polar Aprotic Solvents**

E.g. Hexane, CCl_4, benzene

- Ionic salt cannot dissolve well

- Nucleophile (anion) will be attracted more tightly to its countercation, M^+.

$\Rightarrow$ Substitution reactions will not be favourable.

35
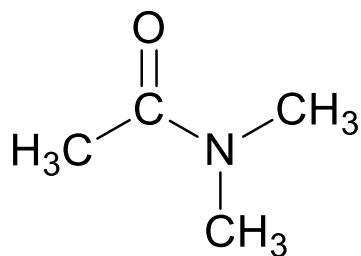
Effect of Aprotic Solvents on S_N2 reaction

o   In recent years, a number of **polar aprotic solvents** have been utilised and they can dissolve most ionic salts.

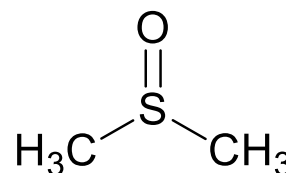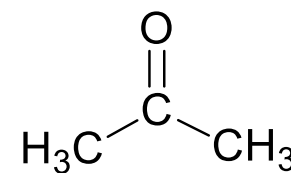o   **Polar Aprotic Solvents**

-   E.g.

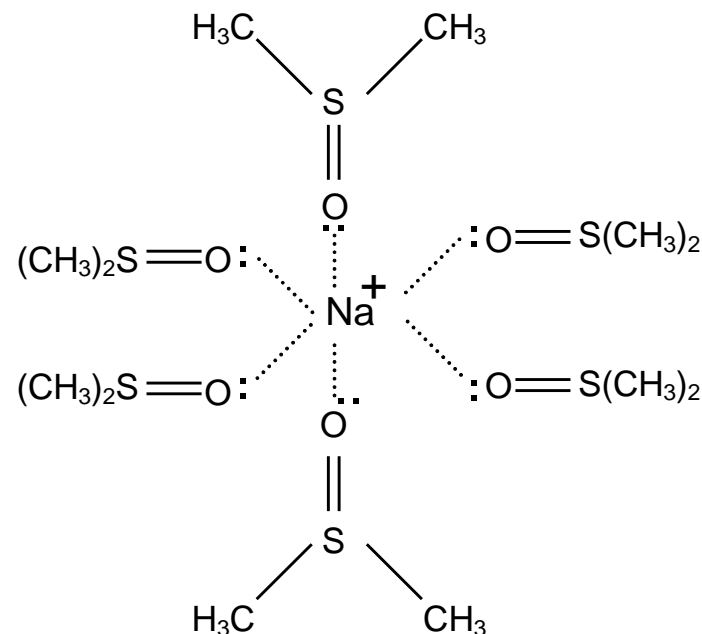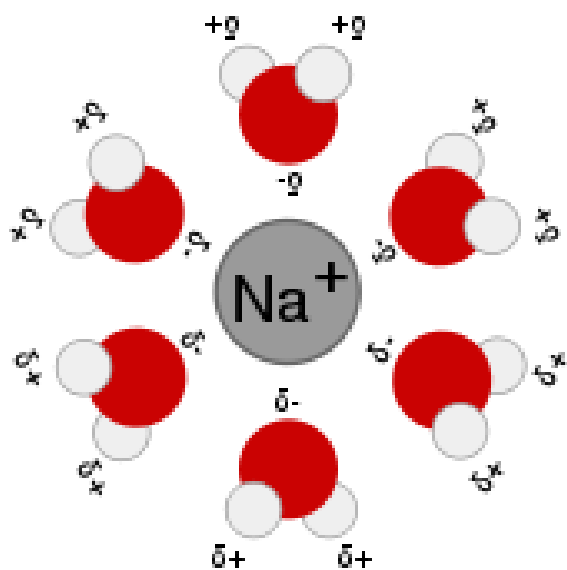N, N-dimethylformide (DMF)   Dimethylacetamide (DMA)   Dimethylsulfoxide (DMSO)   Acetone

-   Polar aprotic solvents solvate *cations* by orientating their negative ends around them and donating unshared electron pairs their vacant orbitals.
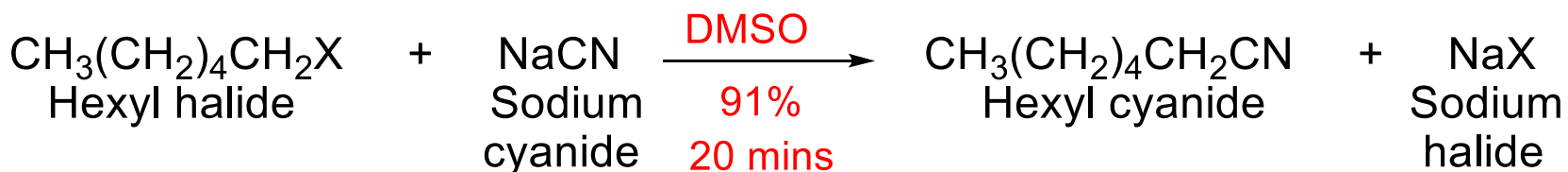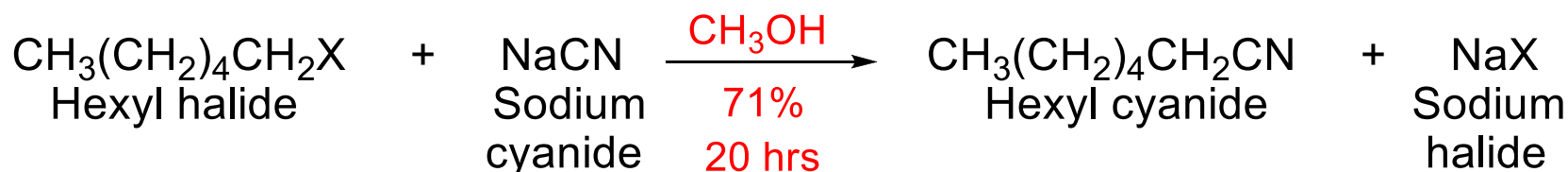
Solvation by Aprotic Solvents

o   Polar aprotic solvents *solvate cations* by orientating their negative ends around them and donating unshared electron pairs their vacant orbitals.

o   In these solvents, *anions are unencumbered* by a layer of solvent molecules and they are poorly stabilised by solvation. These *"naked" ions* are highly reactive both *as bases and nucleophiles*.

Nucleophilicity of Halides in Aprotic Solvents

○ the strength of the nucleophiles depends on its stability and basicity. The stronger the base (smaller the size), the more reactive it is as a nucleophile.

$$F^- > Cl^- > Br^- > I^-$$

○ The rates of S_N2 reactions are vastly increased when they are carried out in polar aprotic solvents. The increase in rate can be as large as a millionfold.

$$CH_3(CH_2)_4CH_2X + NaCN \xrightarrow[\substack{71\% \\ 20\ hrs}]{CH_3OH} CH_3(CH_2)_4CH_2CN + NaX$$

Hexyl halide   Sodium cyanide   Hexyl cyanide   Sodium halide

$$CH_3(CH_2)_4CH_2X + NaCN \xrightarrow[\substack{91\% \\ 20\ mins}]{DMSO} CH_3(CH_2)_4CH_2CN + NaX$$

Hexyl halide   Sodium cyanide   Hexyl cyanide   Sodium halide

38

Test Yourself

Test yourself

Label each of the solvents as polar/non-polar protic/aprotic solvent:

a) CH_2Cl_2

b) NH_3 (aq)

c) $CH_3CH_2OCH_2CH_3$

d) CH_3CN

e) CH_3COOH

f) CCl_4
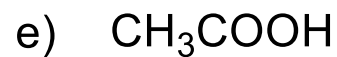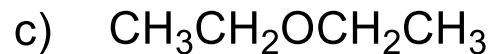
Re-cap: Characteristics of S_N2 mechanism

- Chemical Kinetics: Rate = k [Substrate][Nu]

- Bimolecular, 1st order wrt substrate, 1st order wrt Nu, 2nd order overall.

- Energy diagram: One peak, one TS.

- Mechanism: concerted, crowded 5-membered TS, one product.

- Stereochemistry: Complete inversion of configuration

- Substrate: $1^o > 2^o > 3^o$ due to crowding in TS.

- Leaving Group: Best LG is the weakest base.

- Nucleophile: Best Nu are the stongest base, larger size, -ve.

- Solvent effect:

- Aprotic solvents favour S_N2 by leaving Nu 'naked'

4.2.9 S$_N$1 reaction

S$_N$1

Substitution   Nucleophilic   Unimolecular

a) Chemical kinetics

Substrate   Intermediate   Product
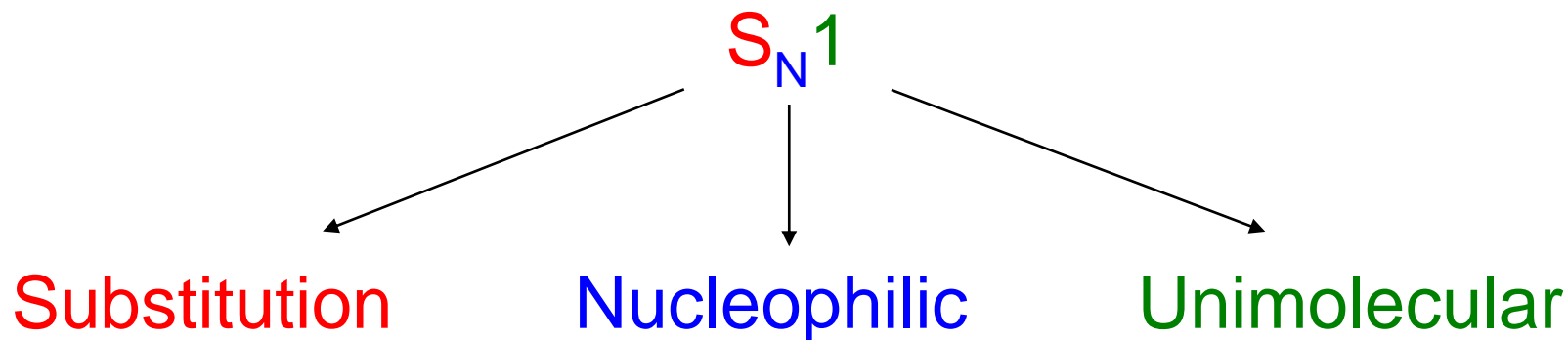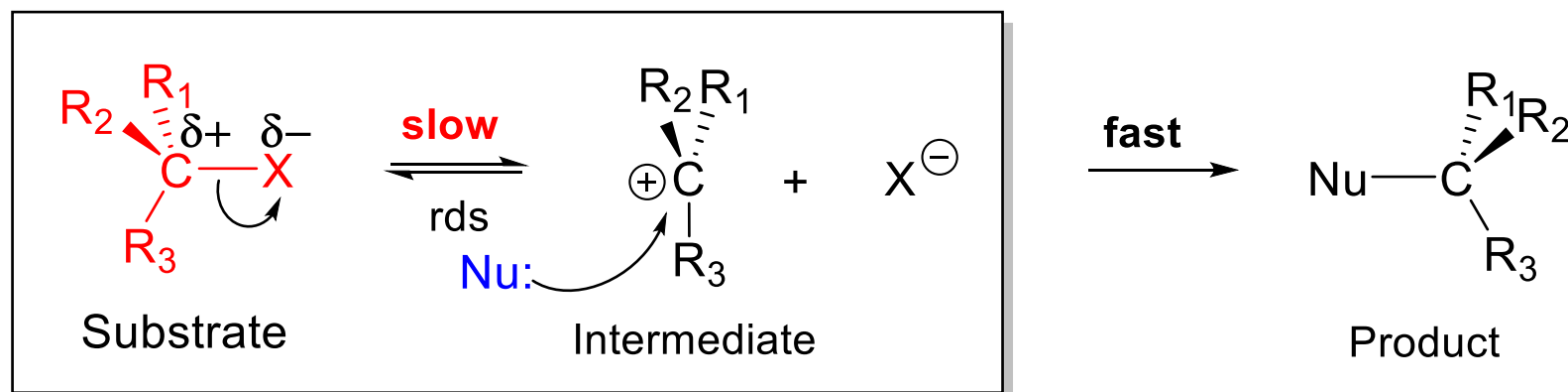
- Unimolecular: 1 molecule is involved in the rds
- **Rate = k [Substrate]** $\Rightarrow$ Rate depends on [substrate] only
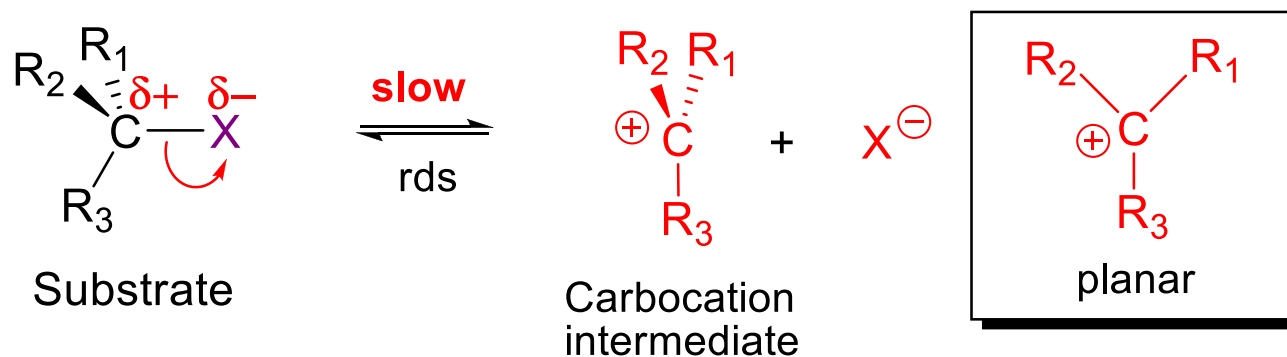
(b) Energy Diagram

- S_N1 reaction $\Rightarrow$ stepwise $\Rightarrow$ each of these steps will go through a TS (1 and 2) with an E_a.

- In the slow rds, the dissociation of the C-X bond will give a carbocation, R+, as the first intermediate. *Intermediates* are generally more stable than transition states and therefore, it appears as a 'valley' in between two 'humps' (TS).
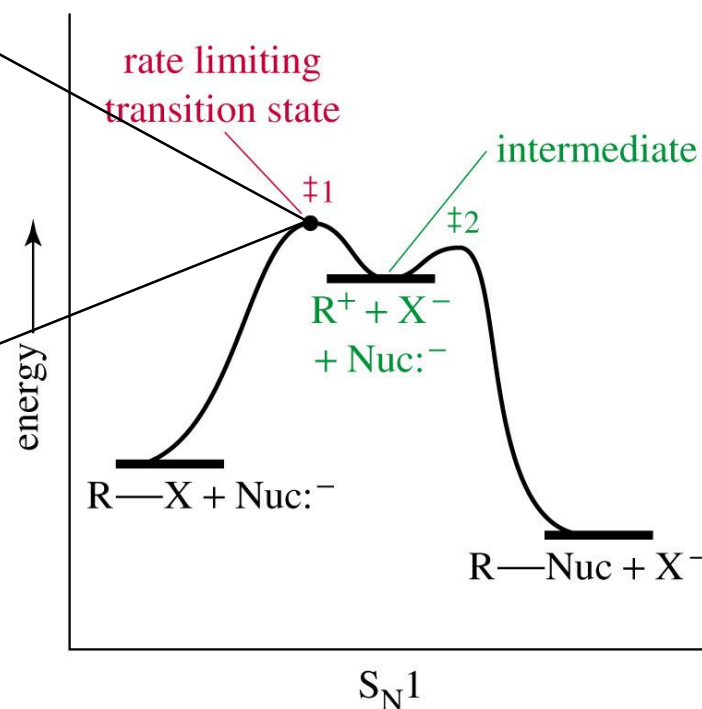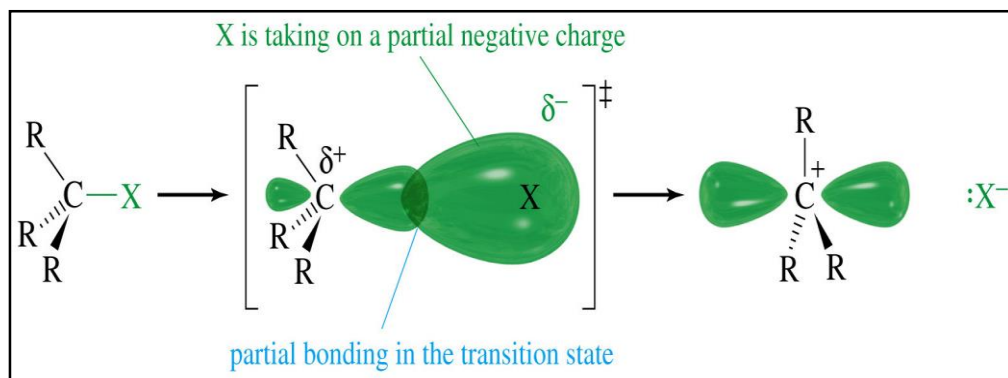
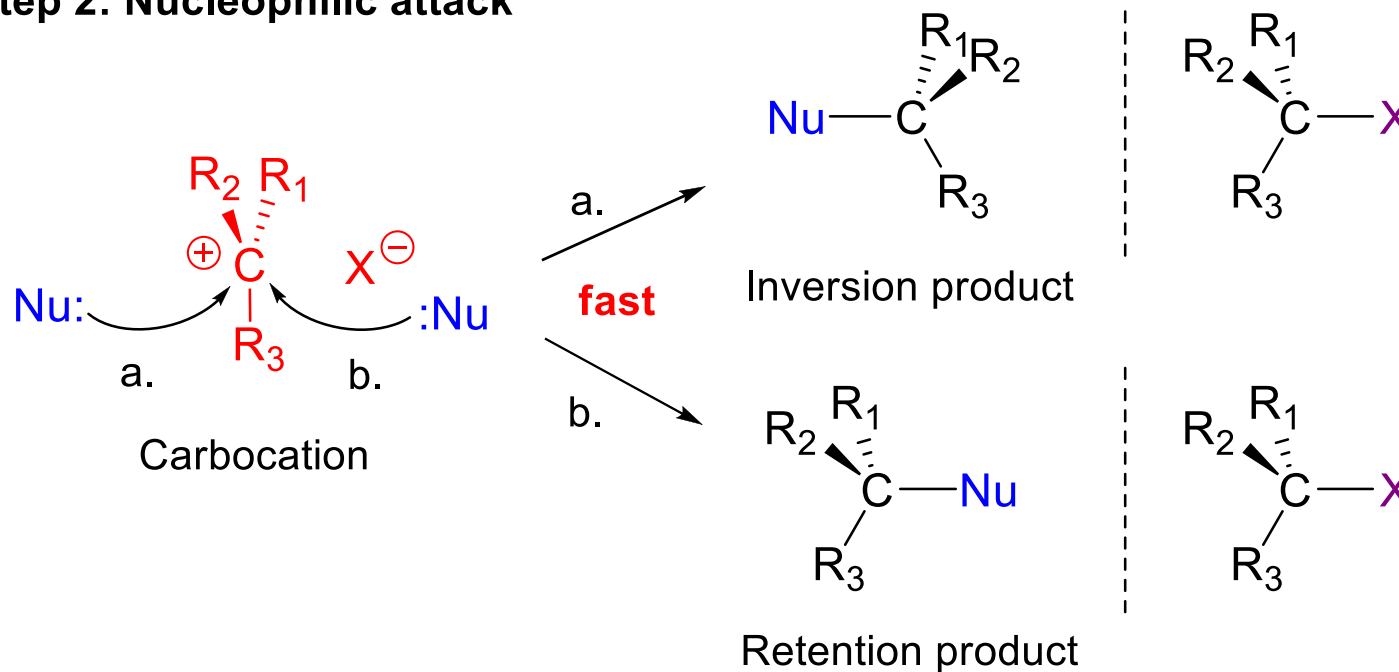Generally, the **number of steps** in the mechanism equals to the **number of peaks** in the energy diagram which represents no. of **transition states**.

42

(c) Mechanism

Step 1: Formation of the carbocation intermediate (rate-limiting)

Substrate   Carbocation intermediate   planar

Step 2: Nucleophilic attack

Carbocation

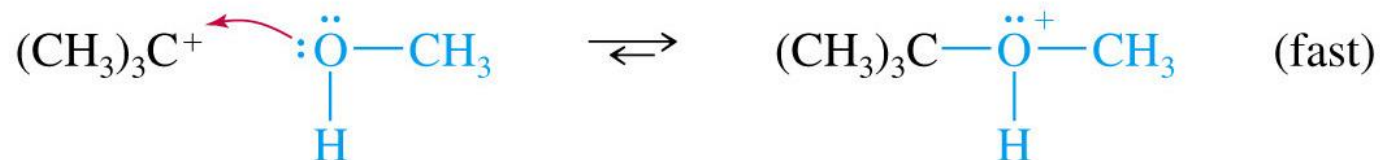a. Inversion product

b. Retention product

43

(c) Mechanism

- In the 2nd step of the S_N1 mechanism, If the nucleophile is a neutral molecule (e.g. H_2O, R-OH, R-NH_2), ***deprotonation*** will have to occur in order to obtain a neutral product.
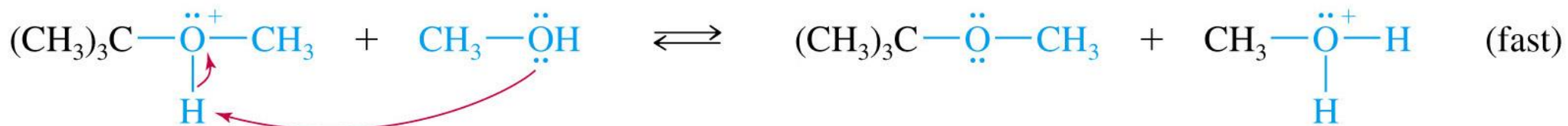
Step 1: Formation of carbocation (rate limiting)

$$(CH_3)_3C-\ddot{B}r: \quad \rightleftharpoons \quad (CH_3)_3C^+ \quad + \quad :\ddot{B}r:^- \quad (slow)$$

Step 2: Nucleophilic attack on the carbocation

$$(CH_3)_3C^+ \quad :\ddot{O}-CH_3 \quad \rightleftharpoons \quad (CH_3)_3C-\overset{..}{\overset{+}{O}}-CH_3 \quad (fast)$$
$$\quad\quad\quad\quad\quad H \quad\quad\quad\quad\quad\quad\quad\quad\quad\quad\quad H$$

Final Step: Loss of proton to solvent

$$(CH_3)_3C-\overset{..}{\overset{+}{O}}-CH_3 \quad + \quad CH_3-\ddot{O}H \quad \rightleftharpoons \quad (CH_3)_3C-\ddot{O}-CH_3 \quad + \quad CH_3-\overset{..}{\overset{+}{O}}-H \quad (fast)$$
$$\quad\quad H \quad\quad\quad\quad\quad\quad\quad\quad\quad\quad\quad\quad\quad\quad\quad\quad\quad\quad\quad\quad\quad\quad\quad\quad H$$
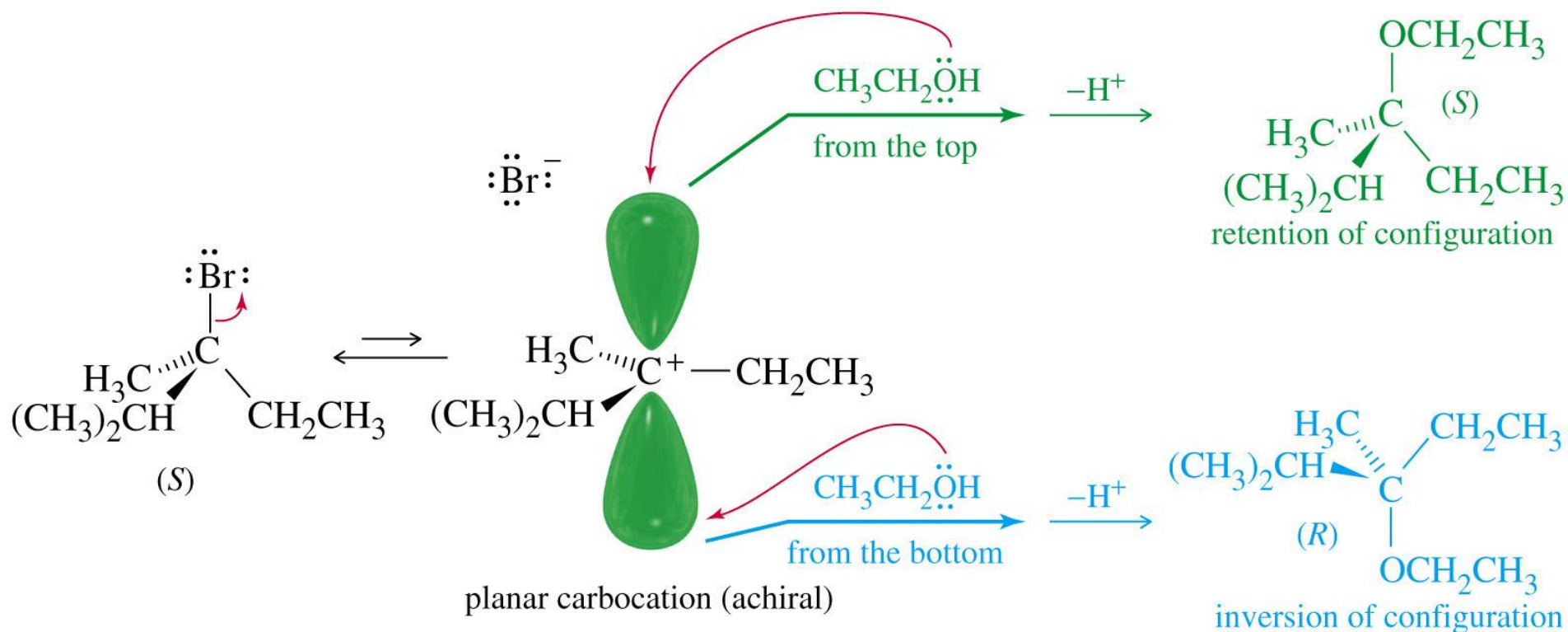
Test Yourself

Test yourself

Draw the energy level diagram for S_N1 reaction between $C(CH_3)_3Br$ and H_2O, showing all the intermediates and transition states.
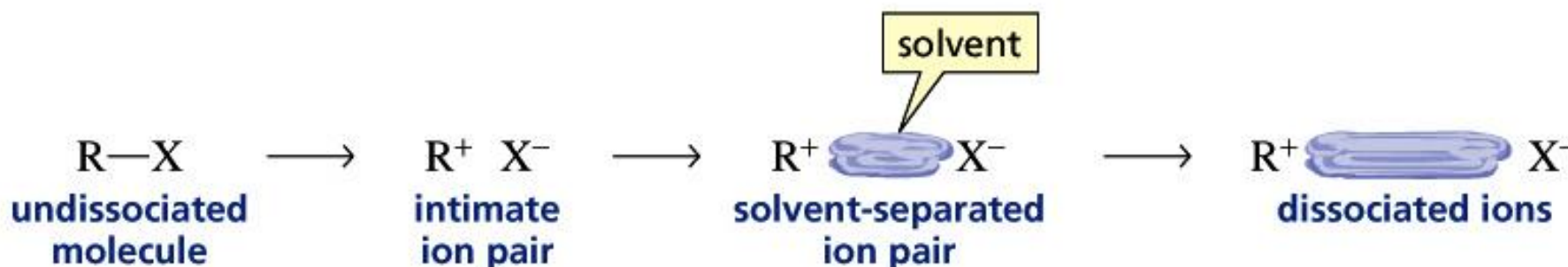
(d) Stereochemistry

planar carbocation (achiral)

retention of configuration

inversion of configuration

- As the carbocation intermediate formed has a *__trigonal planar structure__* (flat), the nucleophile (H_2O) can attack from either face, giving either enantiomer of the product.

46

(d) Stereochemistry

- If the nucleophile attacks on the same side of the leaving group, there will be *retention* of configuration, but if the nucleophile attacks on the opposite side of the leaving group the configuration will be *inverted*.

- However, experimental results showed that the **inversion product predominates** as the top face is shielded by the leaving group (formation of an **intimate ion pair**).
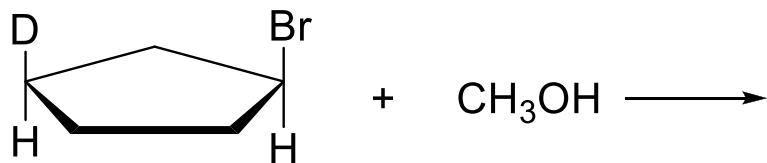
$$R{-}X \longrightarrow R^+ \ X^- \longrightarrow R^+ \bigcirc X^- \longrightarrow R^+ \bigcirc X^-$$

solvent

| undissociated molecule | intimate ion pair | solvent-separated ion pair | dissociated ions |

- *Racemization (with majority inversion)* **is a key characteristic of S$_N$1 reactions.**

Test Yourself

Test yourself

Draw the mechanism for the following reaction:

D—[cyclopentane ring]—Br, H, H   + CH_3OH ⟶

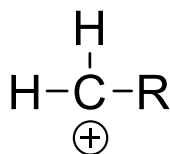# (e) Substrate / carbocation intermediate

- Since the rds in an S_N1 reaction is the spontaneous, unimolecular dissociation of the substrate to yield a *carbocation*, the reaction to be favoured whenever a stabilized carbocation is formed.

⇒ *The substrate that gives the most stable carbocation will give a faster S_N1 reaction.*
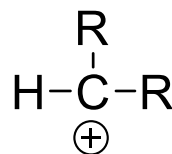
But… what kind of carbocations are stable?

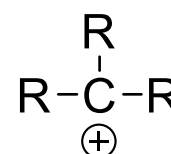- Carbocations are classified as primary, secondary or tertiary:
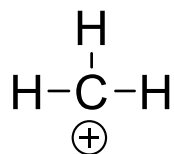
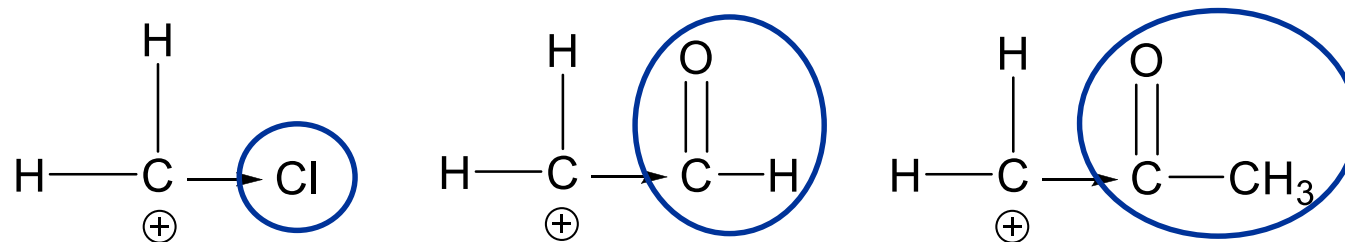| H | H−C−H ⊕ 1º	H | H−C−R ⊕ 1º	R | H−C−R ⊕ 2º	R | R−C−R ⊕ 3º
At most **1 alkyl (-R)** group attached to C atom bonded to X		**2 alkyl (-R)** groups attached to C atom bonded to X	**3 alkyl (-R)** groups attached to C atom bonded to X

(e) Substrate / carbocation intermediate

- A charged species is ***destabilized*** when the charge is ***intensified or concentrated***.

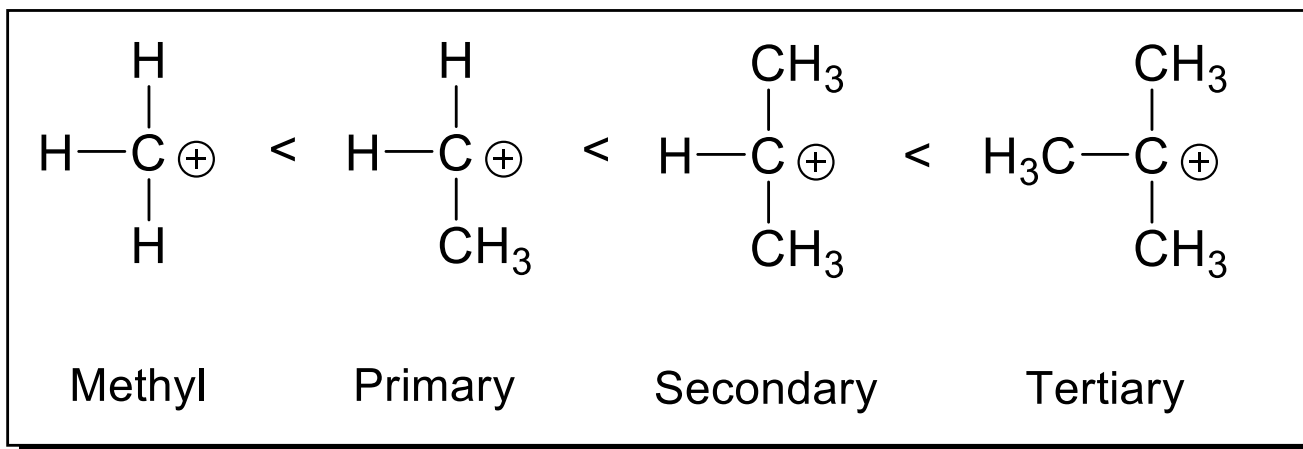 E.g. Carbocations attached to EWGs (-X, -CN, -NO$_2$, -CHO, -COR)

- A charged species is ***stabilized*** when the charge is ***dispersed or delocalised***.

  E.g. Carbocations attached to EDGs (-R, -OH, -NH)

50
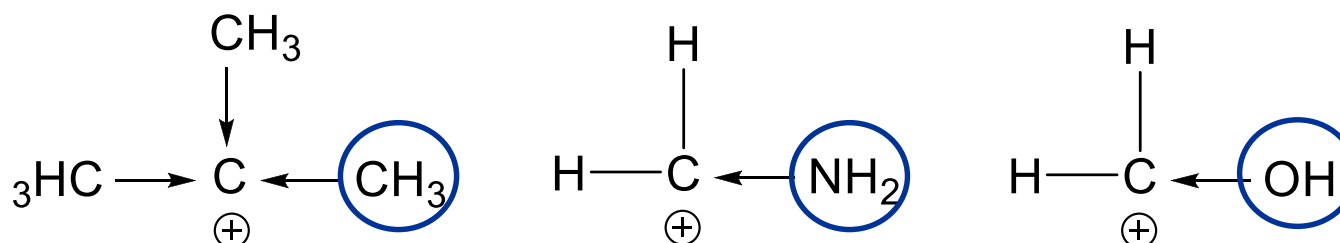
(e) Substrate / carbocation intermediate

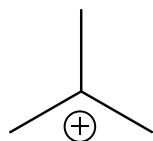o The relative stability of carbocations is as follows:

$$H-\overset{\overset{\displaystyle H}{|}}{\underset{\underset{\displaystyle H}{|}}{C}}\oplus \quad < \quad H-\overset{\overset{\displaystyle H}{|}}{\underset{\underset{\displaystyle CH_3}{|}}{C}}\oplus \quad < \quad H-\overset{\overset{\displaystyle CH_3}{|}}{\underset{\underset{\displaystyle CH_3}{|}}{C}}\oplus \quad < \quad H_3C-\overset{\overset{\displaystyle CH_3}{|}}{\underset{\underset{\displaystyle CH_3}{|}}{C}}\oplus$$

Methyl   Primary   Secondary   Tertiary

o This is exactly the same order of S_N1 reactivities for the corresponding substrates.
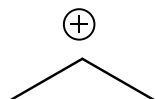
Test Yourself

Test yourself

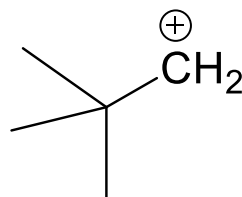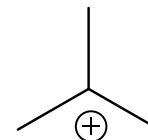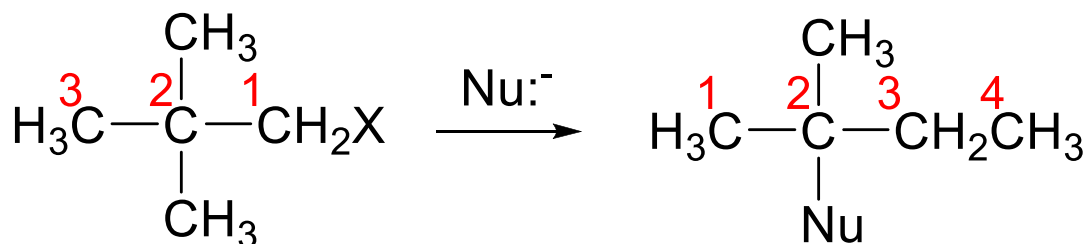Which carbocation in each of the following pair is more stable?

a)   or

b)   or

52
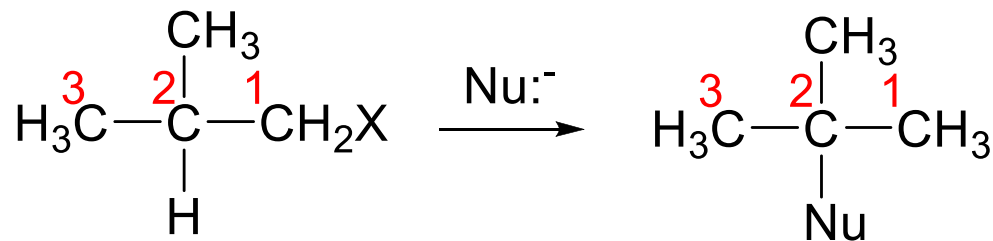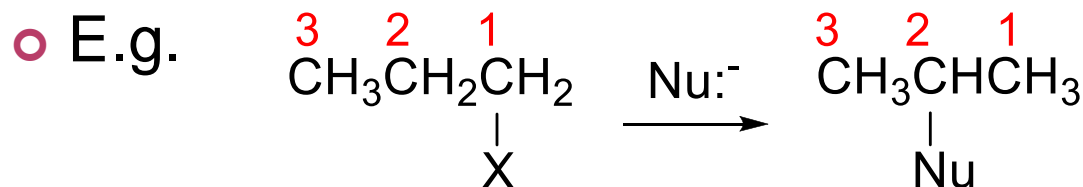
(e) Carbocations – Rearrangement

- In nucleophilic substitution, it is sometimes observed that the entering group, *Nu:-, becomes attached to a different carbon atom* than the one that originally held the leaving group, X.

- E.g.

$$\overset{3}{C}H_3\overset{2}{C}H_2\overset{1}{C}H_2\!-\!X \xrightarrow{\;Nu:^-\;} \overset{3}{C}H_3\overset{2}{C}H\overset{1}{C}H_3$$
$$\underset{Nu}{|}$$

(e) Carbocations – Rearrangement
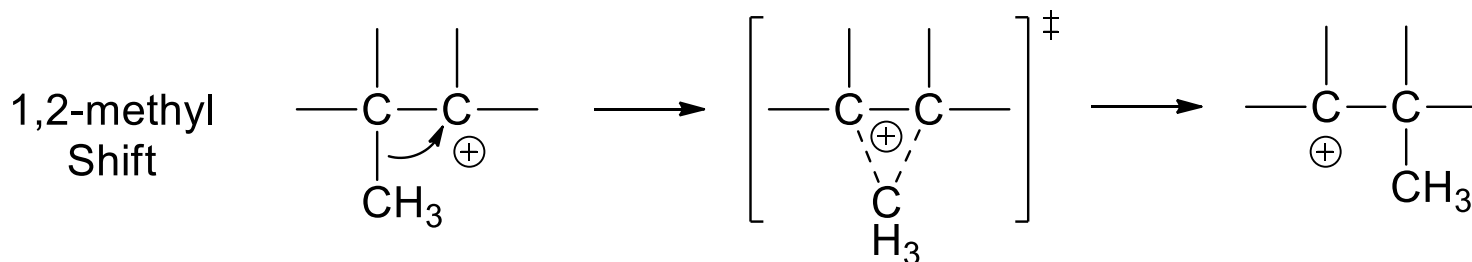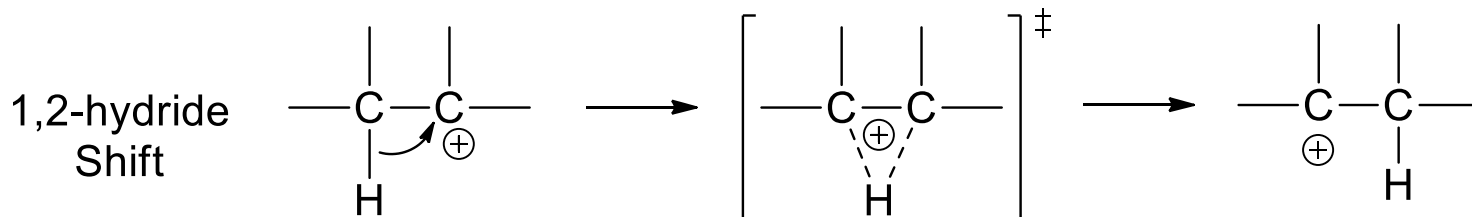
○ Only reactions proceedings by S_N1 are accompanied by these characteristic *rearrangements*. **Rearrangements is generally taken as evidence for S_N1 reactions.**

⇒ **Why?**

⇒ S_N1 involves a carbocation intermediate, S_N2 doesn't.
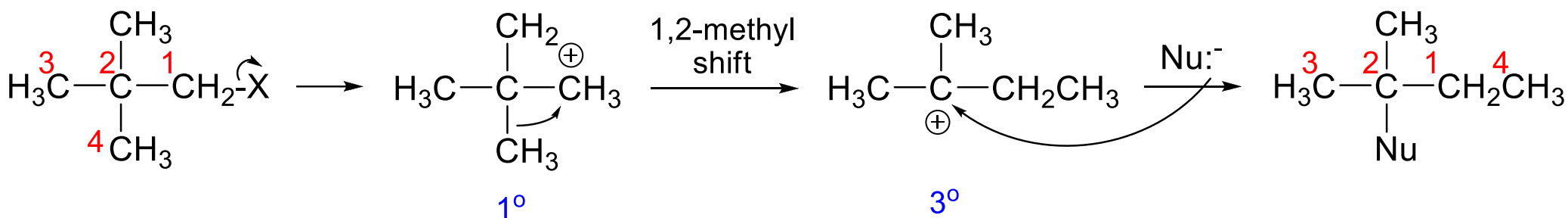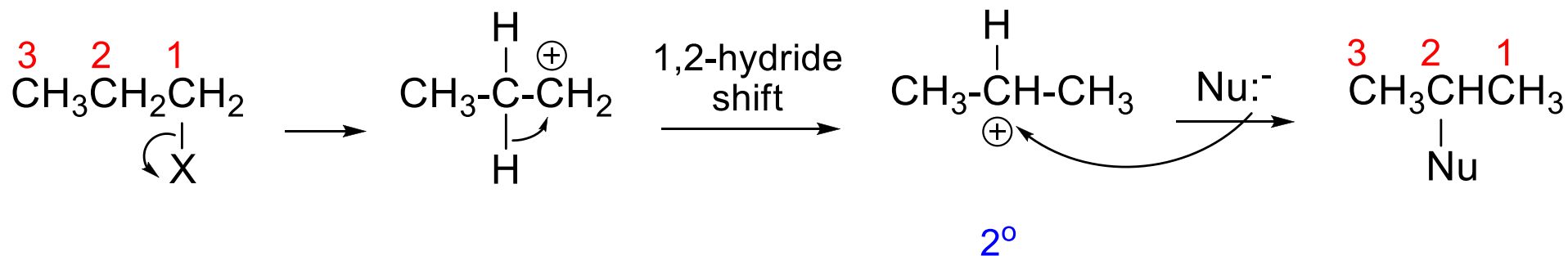
⇒ Less stable carbocation is converted into a more stable one

○ Two types of rearrangements:

1,2-hydride Shift

1,2-methyl Shift

(e) Carbocations – **Rearrangement**

○ **Examples**

$\overset{3}{C}H_3\overset{2}{C}H_2\overset{1}{C}H_2 - X$ → $CH_3-\overset{H}{\underset{H}{C}}-CH_2^{\oplus}$ →[1,2-hydride shift] $CH_3-\overset{H}{C}-CH_3$ (⊕) →[Nu:⁻] $\overset{3}{C}H_3\overset{2}{C}H\overset{1}{C}H_3$ with Nu

2°

$H_3\overset{3}{C}-\overset{2}{\underset{4\,CH_3}{\overset{CH_3}{C}}}-\overset{1}{C}H_2-X$ → $H_3C-\overset{CH_2}{\underset{CH_3}{C}}-CH_3$ (⊕) →[1,2-methyl shift] $H_3C-\overset{CH_3}{\underset{(⊕)}{C}}-CH_2CH_3$ →[Nu:⁻] $H_3\overset{3}{C}-\overset{2}{\underset{Nu}{\overset{CH_3}{C}}}-\overset{1}{C}H_2\overset{4}{C}H_3$

1°   3°

(f) Leaving Group

- S_N1 reactions have the same reactivity order for leaving groups as S_N2 reactions because the leaving groups are directly involved in the rate-determining step.

- *The best leaving groups should be the weakest base* **(bcos it can stabilise the negative charge better)**
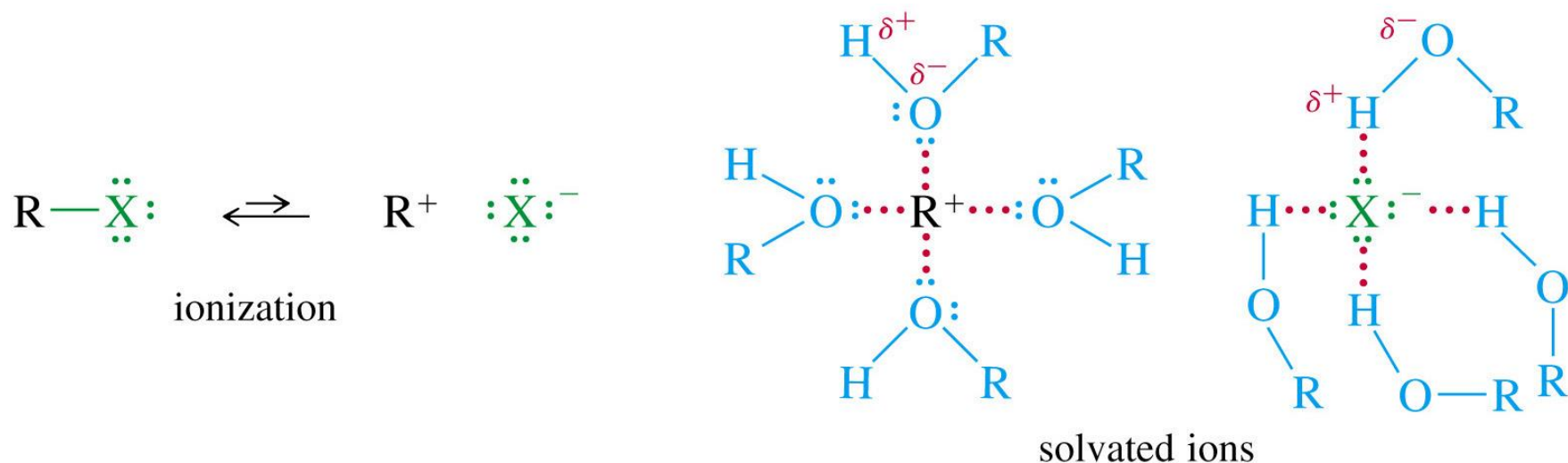
- Relative stabilities of leaving groups:

$$OH^- \sim NH_2^- \sim OR^- < F^- < Cl^- < Br^- < I^- < TsO^-$$

Rate: <<1   1   200   10,000   30,000   60,000
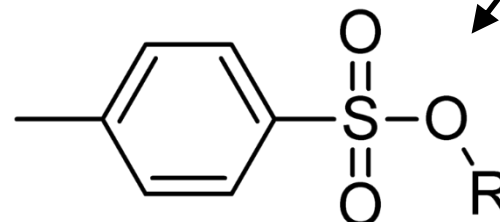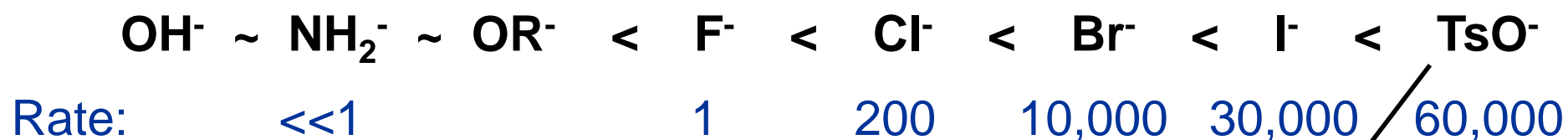
(g) Nucleophiles

- **Recall: Rate = k [Substrate]**
- Nucleophiles are not involved in the rds of S_N1.
- $\Rightarrow$ Therefore, presence of **weak** nucleophiles often suggests S_N1 mechanism and the strength/concentration of the nucleophiles do not affect the reaction rates.

(h) Solvent effect

- S_N1 reactions goes much more readily in polar solvents which stabilize ions.

- The rate-determining step in an S_N1 reaction forms an intimate ion pair, carbocation and leaving group.

- Polar protic solvents (like alcohol and water) stabilise these ions by separating the ion pair and then solvating both the cations and anions via ion-dipole interactions. i.e. ***both cations and anions are solvated***.

ionization

solvated ions

58

4.2.10 Comparison between S_N2 and S_N1 reactions

o Summary of characteristics

	S_N2	S_N1
Kinetics		
Mechanism		
TS of slow step		
Intermediates		
Configuration		
Rearrangement		

4.2.10 Comparison between S_N2 and S_N1 reactions

○ Summary of factors affecting S_N1 and S_N2

Factor	S_N2	S_N1
Substrate		
Determining factor		
Nature of Leaving Group		
Nucleophile		
Solvent		