ALKYL HALIDES

BY

A.CAROLINE GRACE

INTRODUCTION

- Alkyl halides (also known as haloalkanes) are compounds in which one or more hydrogen atoms in an alkane have been replaced by halogen atoms (fluorine, chlorine, bromine or iodine).

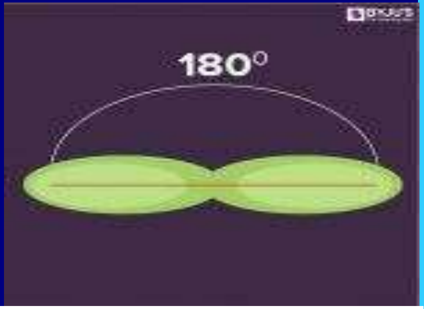
- Alkyl halides are organic molecules containing a halogen atom bonded to an *sp3 hybridized carbon atom* and exhibits a tetrahedral shape

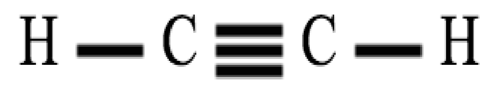
HYBRADIZATION

- Hybridization is defined as the concept of **mixing two atomic orbitals** with the same energy levels to give a degenerated new type of orbitals.
- Redistribution of the energy of orbitals of individual atoms to give orbitals of equivalent energy happens when two atomic orbitals combine together to form hybrid orbital in a molecule. This process is called hybridization.
- During the process of hybridization, the atomic orbitals **of similar energy** are mixed together such as the mixing of two ‘s’ orbitals or two ‘p’ orbital’s or mixing of an ‘s’ orbital with a ‘p’ orbital or ‘s’ orbital with a ‘d’ orbital.
- Based on the types of orbitals involved in mixing, the hybridization can be classified as sp3, sp2, sp, sp3d, sp3d2, sp3d3

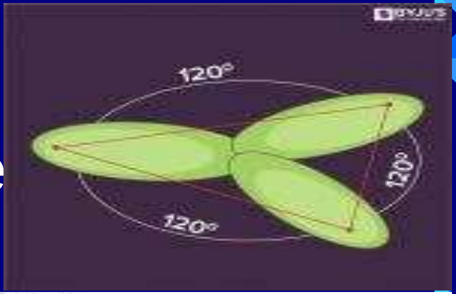
TYPES OF sp HYBRADIZATION

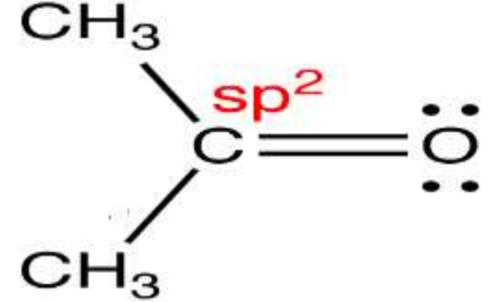
- Mixing of one ‘s’ orbital and one ‘p’ orbital of equal energy to give a new hybrid orbital known as an **sp hybridized** orbital.
- sp hybridization is also called **diagonal** hybridization.




$H-C\equiv C-H$

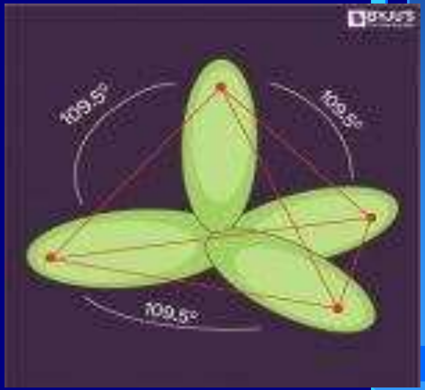
- **sp^2 hybridization** is observed when **one s** and **two p orbitals** of the same shell of an atom mix to form **3 equivalent orbital**. The new orbitals formed are called sp^2 hybrid orbitals.
- sp^2 hybridization is also called **trigonal hybridization.**

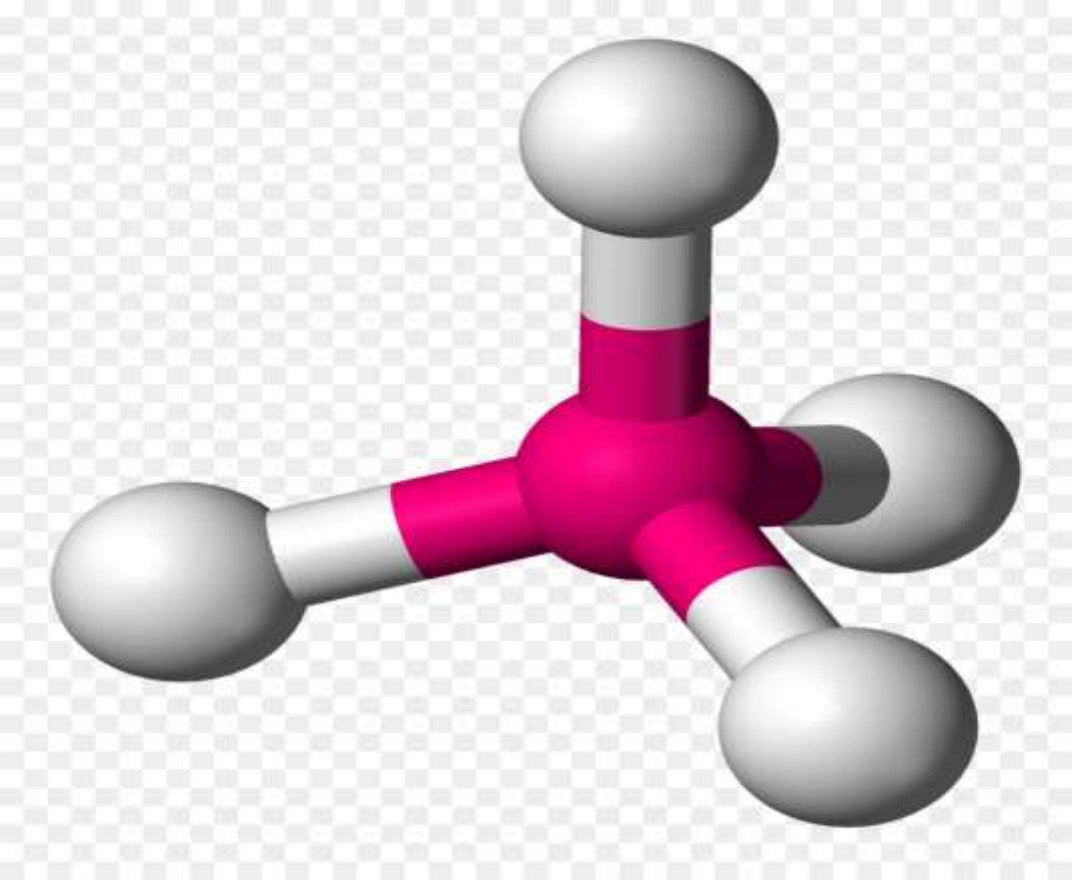


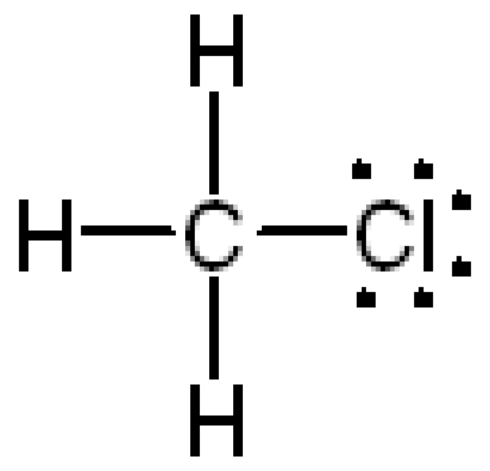


Tetrahedral shape of alkyl halide

When **one ‘s’** orbital and **3 ‘p’** orbitals belonging to the same shell of an atom mix together to form four new equivalent orbital, the type of hybridization is called a **tetrahedral hybridization or sp^3.**

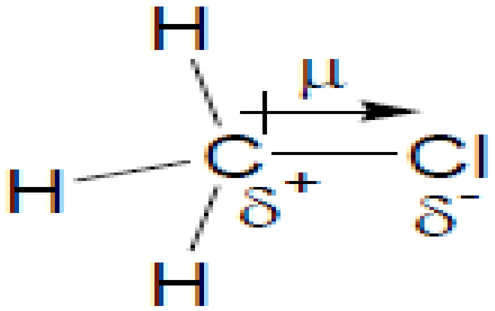






- Due to electronegativity differences between the carbon and halogen atoms, the σ covalent bond between these atoms is polarized, with the carbon atom becoming slightly positive and the halogen atom partially negative.

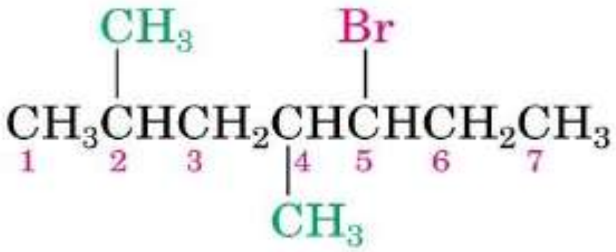
The C-X bond is polarized in such a way that there is partial positive charge on the carbon and partial negative charge on the halogen.



- The measure of the polarity of a bond is the bond moment or dipole moment.
- Hydrogen and carbon atoms have similar electronegativity values and because the dipole moment small and bond length is short. C-H is polar covalent bond.
- Due to the change in electronegativity of the C—Cl, the dipole moment is greater and the bond length is large.

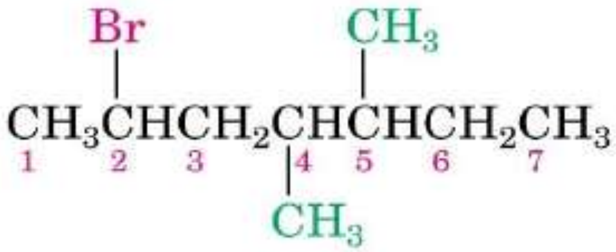
Naming Haloalkane

- Name is based on longest carbon chain (contains double or triple bond if present)
- Number the carbons of the parent chain beginning at the end nearer the first substituent, whether alkyl or halo



$$\underset{1}{CH_3}\overset{\overset{CH_3}{|}}{\underset{2}{C}}H\underset{3}{CH_2}\underset{\underset{CH_3}{|}}{\overset{4}{C}}H\overset{\overset{Br}{|}}{\underset{5}{C}}H\underset{6}{CH_2}\underset{7}{CH_3}$$

5-Bromo-2,4-dimethylheptane

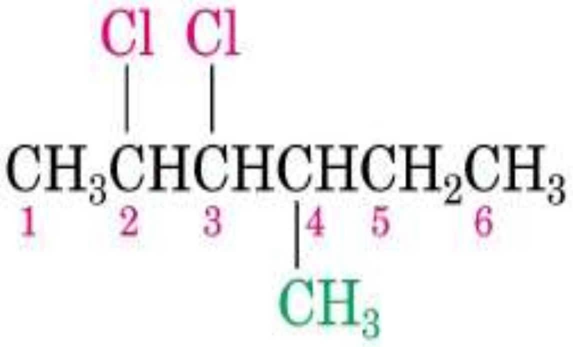


$$\underset{1}{CH_3}\overset{\overset{Br}{|}}{\underset{2}{C}}H\underset{3}{CH_2}\underset{\underset{CH_3}{|}}{\overset{4}{C}}H\overset{\overset{CH_3}{|}}{\underset{5}{C}}H\underset{6}{CH_2}\underset{7}{CH_3}$$

2-Bromo-4,5-dimethylheptane

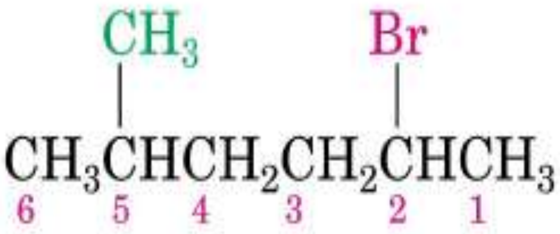
- If more than one of the same kind of halogen is present, use prefix *di, tri, tetra*
- If there are several different halogens, number them and list them in alphabetical order

Naming Haloalkane


$CH_3\overset{Cl}{CH}\overset{Cl}{CH}\underset{CH_3}{CH}CH_2CH_3$

2,3-Dichloro-4-methylhexane

© Thomson - Brooks Cole


$CH_3\overset{CH_3}{CH}CH_2CH_2\overset{Br}{CH}CH_3$

2-Bromo-5-methylhexane

(*NOT* 5-bromo-2-methylhexane)

© Thomson - Brooks Cole

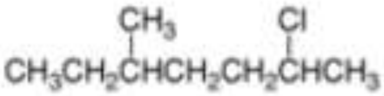
Naming if two halides or alkyl are equally distant from ends of chain

- Begin at the end nearer the substituent whose name comes first in the alphabet

Nomenclature

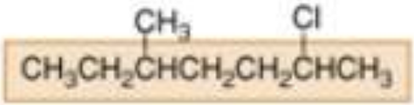
How To Name an Alkyl Halide Using the IUPAC System

Example Give the IUPAC name of the following alkyl halide:



$$CH_3CH_2\overset{CH_3}{\overset{|}{C}}HCH_2CH_2\overset{Cl}{\overset{|}{C}}HCH_3$$

Step [1] Find the parent carbon chain containing the halogen.



$$CH_3CH_2\overset{CH_3}{\overset{|}{C}}HCH_2CH_2\overset{Cl}{\overset{|}{C}}HCH_3$$

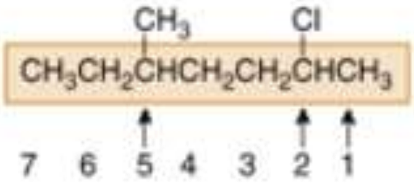
7 C's in the longest chain

7 C's ---→ **heptane**

- Name the parent chain as an ***alkane,*** with the halogen as a substituent bonded to the longest chain.

Step [2] Apply all other rules of nomenclature.

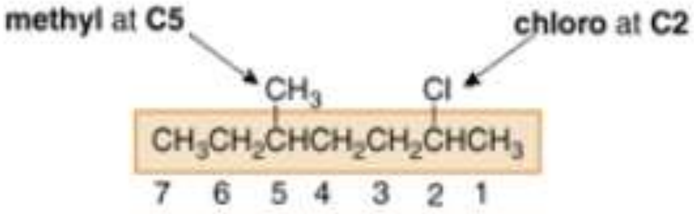
a. **Number** the chain.



$$CH_3CH_2\overset{CH_3}{\overset{|}{C}}HCH_2CH_2\overset{Cl}{\overset{|}{C}}HCH_3$$

- Begin at the end nearest the first substituent, either alkyl or halogen.

b. **Name** and **number** the substituents.



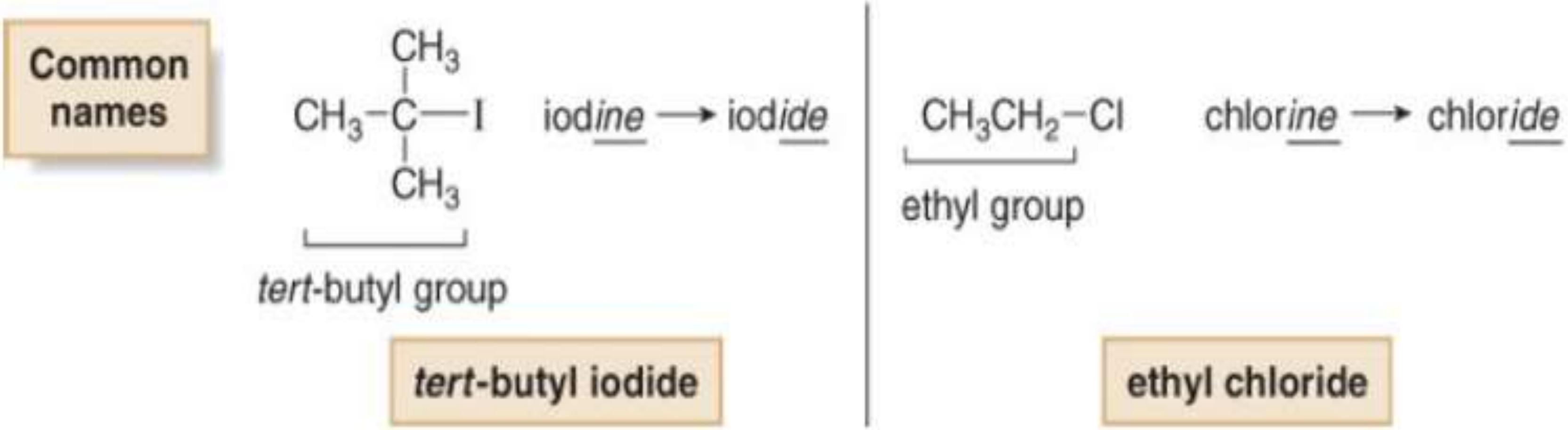
$$CH_3CH_2\overset{CH_3}{\overset{|}{C}}HCH_2CH_2\overset{Cl}{\overset{|}{C}}HCH_3$$

c. **Alphabetize: c** for **c**hloro, then **m** for **m**ethyl.

ANSWER: 2-chloro-5-methylheptane

Nomenclature

- Common names are often used for simple alkyl halides. To assign a common name:



Common names

$$\underbrace{CH_3-\overset{CH_3}{\underset{CH_3}{\overset{|}{\underset{|}{C}}}}}_{\textit{tert}\text{-butyl group}}-I$$

iod*ine* → iod*ide*

***tert*-butyl iodide**

$$\underbrace{CH_3CH_2}_{\text{ethyl group}}-Cl$$

chlor*ine* → chlor*ide*

ethyl chloride

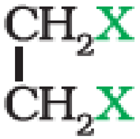
CLASSIFICATION OF ALKYL HALIDES

Based on number of halogen atom present

- classified as mono, di, or polyhalogen (tri-,tetra-, etc.) compounds depending on whether they contain one, two or more halogen atoms in their structures. For example,

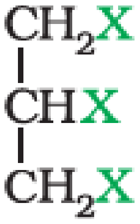
C_2H_5X

Monohaloalkane



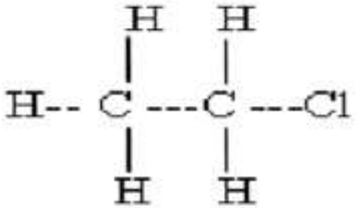
$$\begin{array}{c} CH_2X \\ | \\ CH_2X \end{array}$$

Dihaloalkane

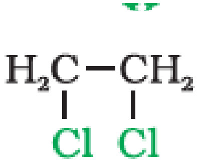


$$\begin{array}{c} CH_2X \\ | \\ CHX \\ | \\ CH_2X \end{array}$$

Trihaloalkane

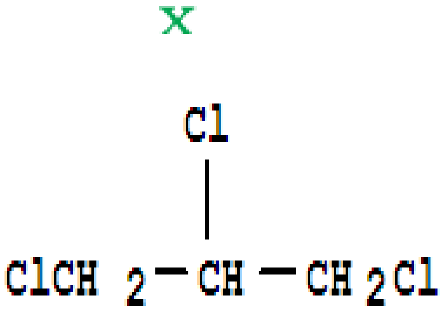


Ethyl chloride



Ethylene dichloride (*vic-dihalide*)

1, 2-Dichloroethane

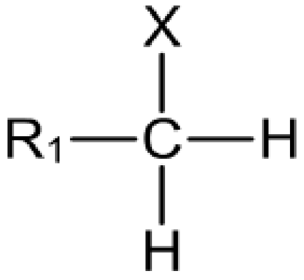


Trichloropropane

CLASSIFICATION OF ALKYL HALIDES

Based on number of alkyl groups attached

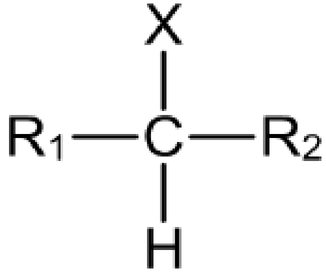
- **Primary (1°) halogenoalkanes** have one R group attached to the carbon linked to the halogen.



$$R_1-\overset{\displaystyle X}{\underset{\displaystyle H}{C}}-H$$

$R-CH_2-X$

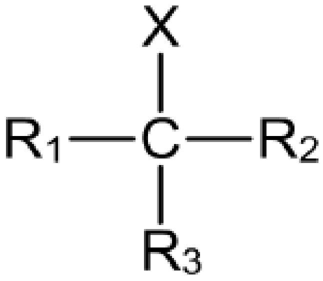
- **Secondary (2°) halogenoalkanes** have two R groups attached to the carbon linked to the halogen.



$$R_1-\overset{\displaystyle X}{\underset{\displaystyle H}{C}}-R_2$$

R_2-CH-X

- **Tertiary (3°) halogenoalkanes** have three R groups attached to the carbon linked to the halogen.



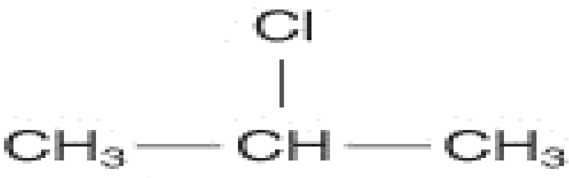
$$R_1-\overset{\displaystyle X}{\underset{\displaystyle R_3}{C}}-R_2$$

R_3-C-X

CH_3CH_2Br

bromoethane
ethyl bromide)

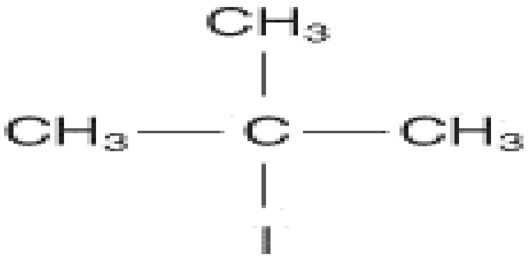
Primary alkyl halide



$$CH_3-\overset{Cl}{\overset{|}{CH}}-CH_3$$

2-chloropropane
(isopropyl chloride)

Secondary alkyl halide



$$CH_3-\overset{CH_3}{\overset{|}{\underset{\underset{I}{|}}{C}}}-CH_3$$

2-iodo-2-methylpropane
(tertiary-butyliodide)

Tertiary alkyl halide

Physical Properties

Solubility : All organic halides are insoluble in water and soluble in common organic solvents.

Boiling point : The boiling points increases with increasing in molecular weights.

Therefore, the boiling points increases in the order F<Cl<Br<I.

	M.W	bp / °C
1- Chloropropane	78.5	47
1- Bromopropane	124	71

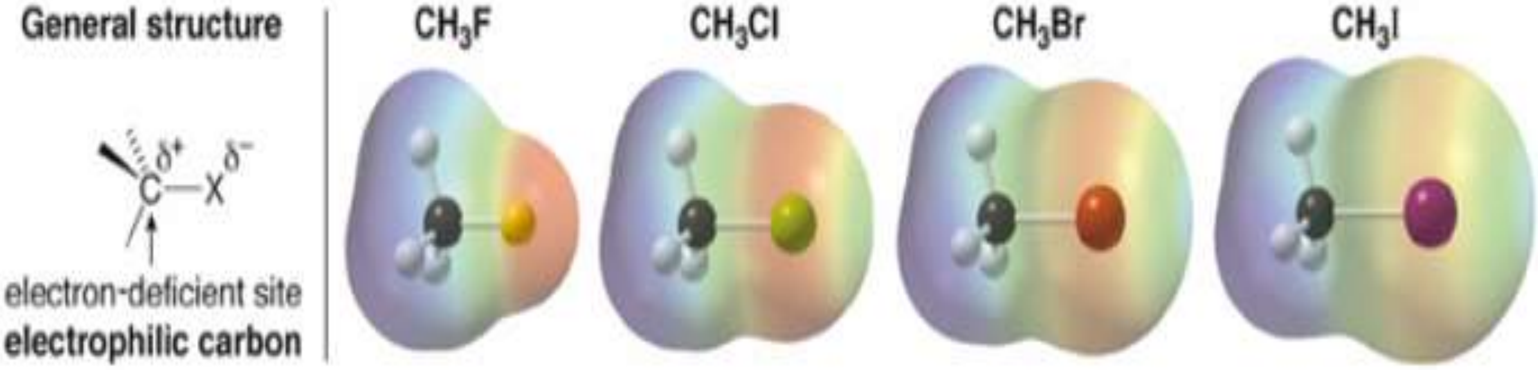
BP also increases for "straight" chain isomers.

Greater branching = lower BP

1-bromobutane	$CH_3CH_2CH_2CH_2Br$	101
2-bromobutane	$CH_3CH_2CHBrCH_3$	91
2-bromo -2-methylpropane	$(CH_3)_3CBr$	73

The Polar Carbon-Halogen Bond

The electronegative halogen atom in alkyl halides creates a polar C—X bond, making the carbon atom electron deficient. Electrostatic potential maps of four simple alkyl halides illustrate this point.



Polar bonds and nucleophiles

- The carbon–halogen bond in halogenoalkanes is polar because all halogens are more electronegative than carbon.

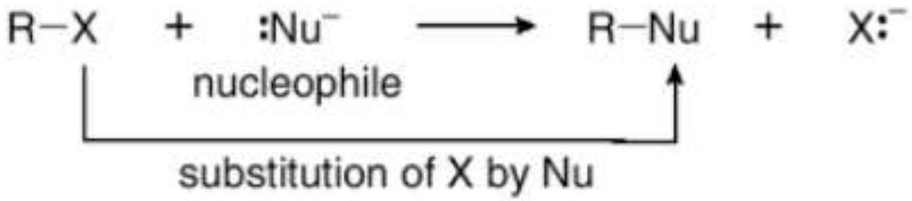
$\overset{\delta+}{\mathrm{C}}—\overset{\delta-}{\mathrm{F}}$ $\overset{\delta+}{\mathrm{C}}—\overset{\delta-}{\mathrm{Cl}}$ $\overset{\delta+}{\mathrm{C}}—\overset{\delta-}{\mathrm{Br}}$ $\overset{\delta+}{\mathrm{C}}—\overset{\delta-}{\mathrm{I}}$

- The polar bond means that the carbon atom has a small positive charge (δ+), which attracts substances with a lone pair of electrons. These are **nucleophiles**, meaning 'nucleus (positive charge) loving'. Examples include:

$:NH_3$	$:CN^-$	$:OH^-$
ammonia	**cyanide**	**hydroxide**

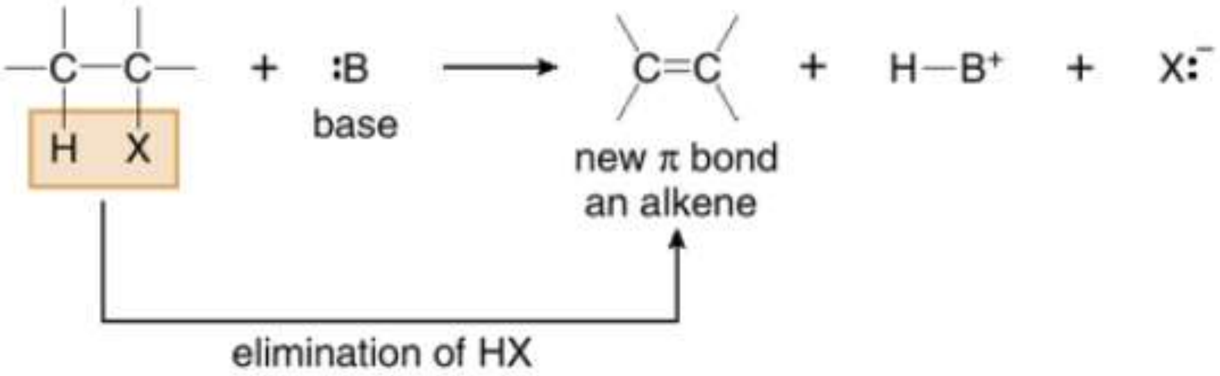
The Polar Carbon-Halogen Bond

- Alkyl halides undergo substitution reactions with nucleophiles.



$$R{-}X + {:}Nu^{-} \longrightarrow R{-}Nu + X{:}^{-}$$

- Alkyl halides undergo elimination reactions with Brønsted–Lowry bases.



Mechanism

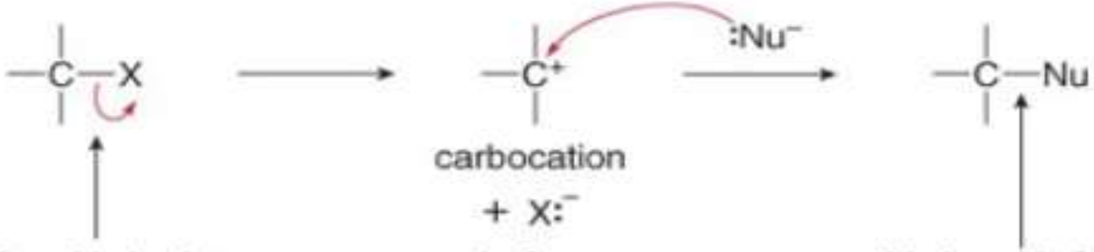
Bond making and bond breaking occur at the same time. S_N2

One-step mechanism

This bond is broken... *as* ...this bond is formed.

Bond breaking occurs before bond making. S_N1

Two-step mechanism



This bond is broken... *before* ...this bond is formed.

MCQ QUESTIONS

- Why alkyl halides are considered to be very reactive compounds towards nucleophile?

a) they have an electrophilic carbon & a bad leaving group
b) they have a nucleophilic carbon & a good leaving group
c) they have an electrophilic carbon
d) they have an electrophilic carbon & a good leaving group

- **ANSWER:** they have an electrophilic carbon & a good leaving group (d)

- The functional group in alkyl halide is ______

a) Hydroxyl group
b) Halogen atom
c) Inert gas
d) All of the mentioned

- **ANSWER:** Halogen atom **(b)**

- **When the nucleophile :OR attacks the RX, the resultant product will be _____________**

  a) R – OH
  b) ROR
  c) R:CN
  d) RNHR

- **ANSWER:** **ROR** **(b)**

- **Which of the following is the tertiary alkyl halide**

a) CH_3-X
b) $(CH_3)_2$CH-X
c) $(CH_3)_3$C-X
d) $(CH_3)_3$C-CH_2-X

- **ANSWER:** $(CH_3)_3C\text{-}X$ (c)

- SN2 reaction is a

a) Unimolecular reaction
b) Bimolecular reaction
c) Both a and b
d) None of the above

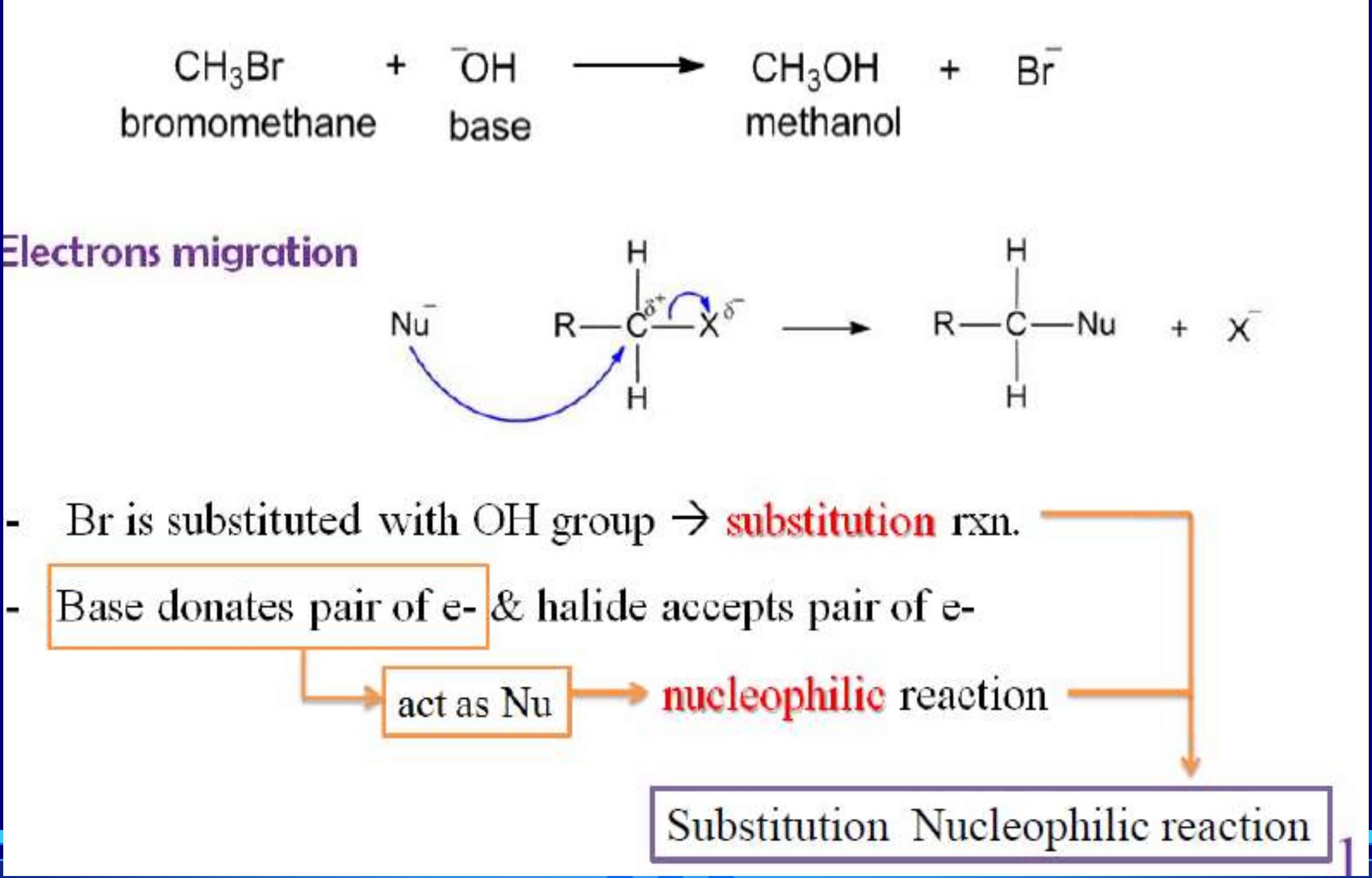
- **ANSWER:** **Bimolecular reaction (b)**

ALKYL HALDES & SN1 and SN2 Reactions

BY

A.CAROLINE GRACE

NUCLEOPHILIC SUBSTITUTION REACTION (SN)



$$\underset{\text{bromomethane}}{CH_3Br} + \underset{\text{base}}{{}^{-}OH} \longrightarrow \underset{\text{methanol}}{CH_3OH} + Br^{-}$$

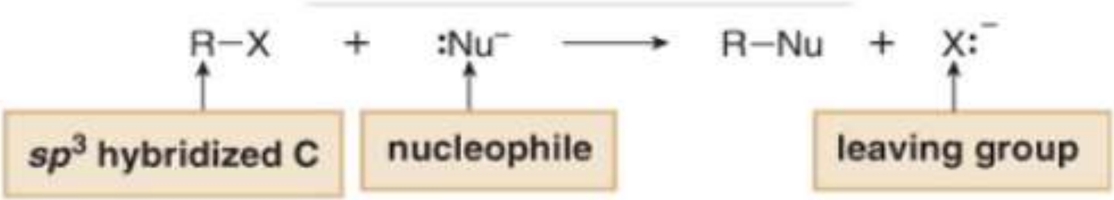
Electrons migration

- Br is substituted with OH group → substitution rxn.
- Base donates pair of e- & halide accepts pair of e-

act as Nu → nucleophilic reaction

Substitution Nucleophilic reaction

General Features of Nucleophilic Substitution



$$R{-}X \;+\; {:}Nu^- \longrightarrow R{-}Nu \;+\; X{:}^-$$

sp^3 hybridized C

nucleophile

leaving group

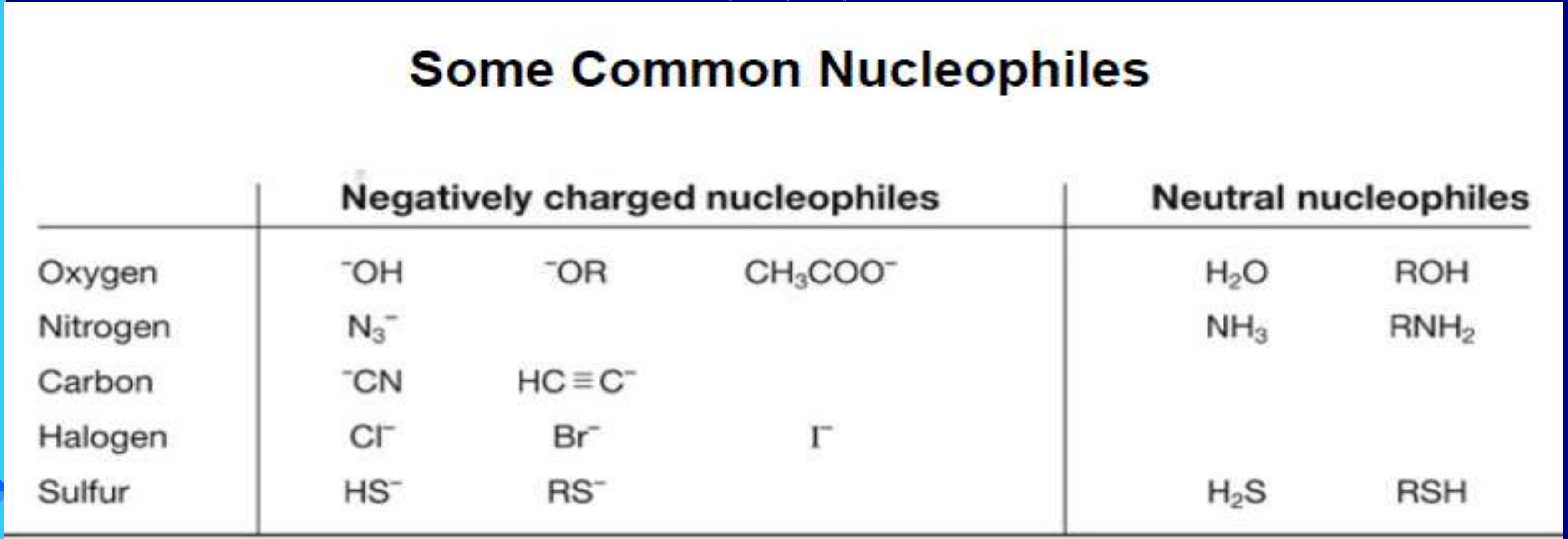
Examples

Alkyl group **Nucleophile** **Leaving group**

[1] $CH_3{-}Cl \;+\; {}^-{:}\ddot{O}H \longrightarrow CH_3{-}\ddot{O}H \;+\; Cl^-$

[2] $CH_3CH_2CH_2{-}I \;+\; {}^-{:}\ddot{S}H \longrightarrow CH_3CH_2CH_2{-}\ddot{S}H \;+\; I^-$

[3]

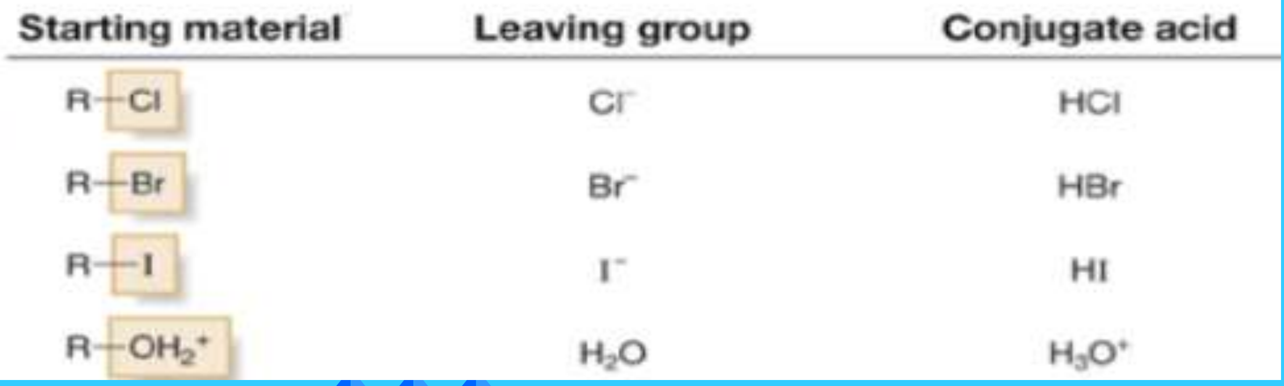


Some Common Nucleophiles

	Negatively charged nucleophiles			Neutral nucleophiles	
Oxygen	^{-}OH	^{-}OR	CH_3COO^-	H_2O	ROH
Nitrogen	N_3^-			NH_3	RNH_2
Carbon	^{-}CN	$HC\equiv C^-$			
Halogen	Cl^-	Br^-	I^-		
Sulfur	HS^-	RS^-		H_2S	RSH

The Leaving Group

These molecules undergo nucleophilic substitution



Starting material	Leaving group	Conjugate acid
R—Cl	Cl^-	HCl
R—Br	Br^-	HBr
R—I	I^-	HI
$R—OH_2^+$	H_2O	H_3O^+

Mechanism

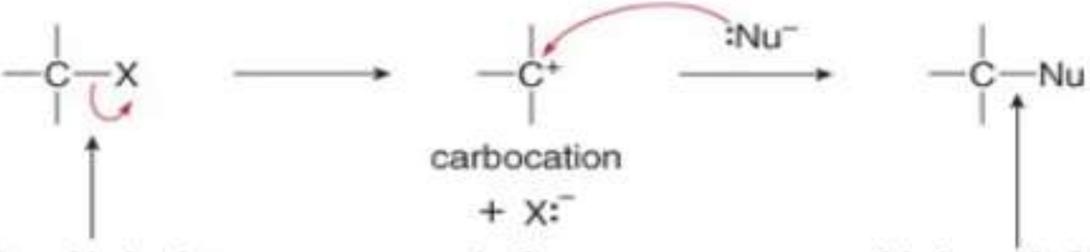
Bond making and bond breaking occur at the same time. **S_N2**

One-step mechanism

This bond is broken... *as* ...this bond is formed.

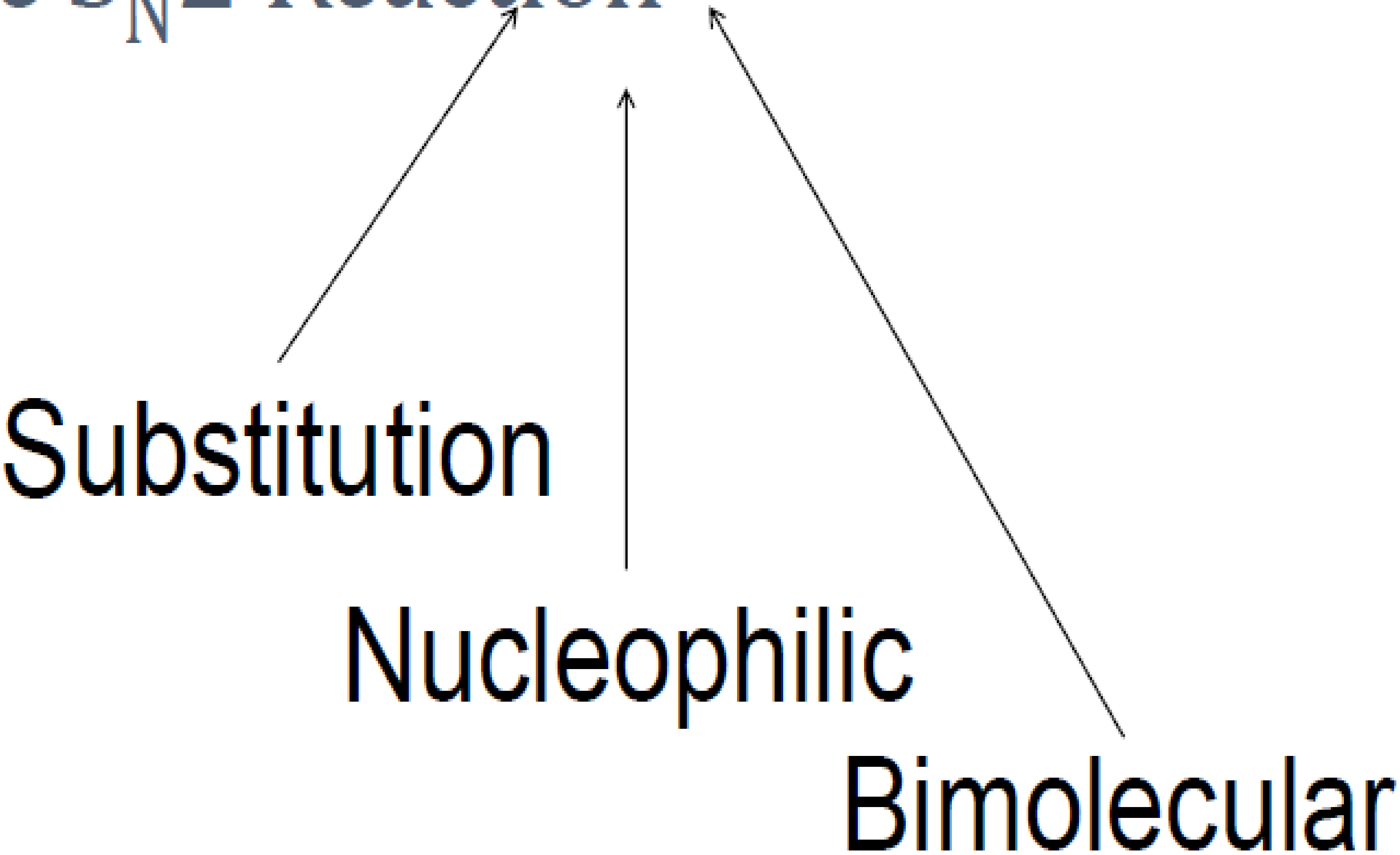
Bond breaking occurs before bond making. **S_N1**

Two-step mechanism



This bond is broken... *before* ...this bond is formed.

The S_N2 Reaction



Substitution

Nucleophilic

Bimolecular

The S_N2 Reaction

Substitution: this reaction involves a *substitution* of players – two reactants produce two products, in which some things have been switched around:

$$AB + C \longrightarrow AC + B$$

Nucleophilic: these reactions involve a nucleophile ($Nuc:^-$) replacing a leaving group.

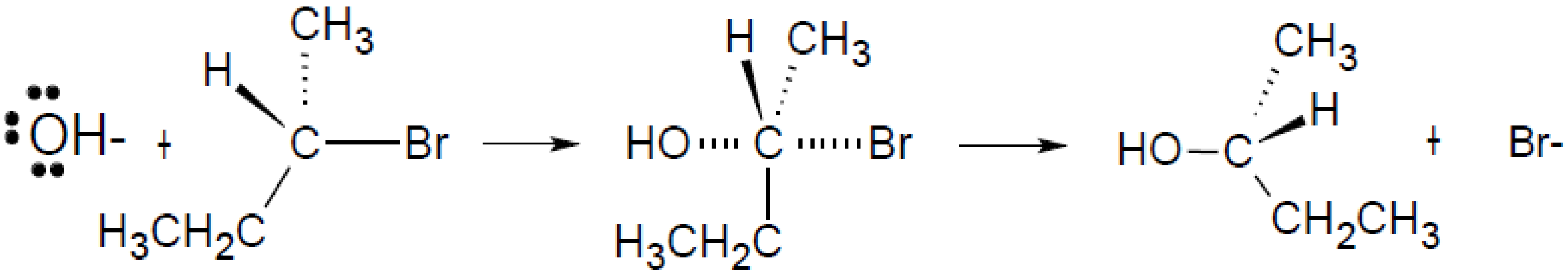
- Nucleophiles attack the substrate, donating an electron pair to the new bond, and replacing the leaving group

Bimolecular: A *bi*molecular reaction is one whose rate depends on the concentrations of *two* of its reactants.

- SN2 reactions happen in one step – the nucleophile attacks the substrate as the leaving group leaves the substrate.

Nucleophilic Substitution Bimolecular or SN2

- The rate depends on the conc. of 2 reactants: the substrate and the nucleophile.
- Takes place in one step
- No carbocation
- new bond forming and old bond breaking at same time.
- Occur most readily with methyl compounds and **primary** haloalkanes



Transition State:
As OH- attaches,
Br- leaves

S_N2 : mechanism

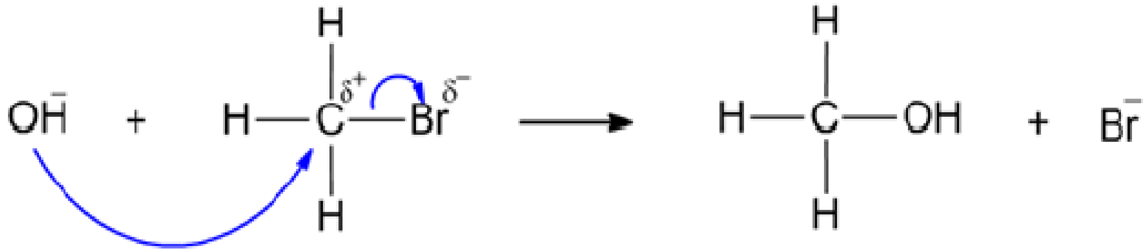
$$CH_3Br + NaOH \longrightarrow CH_3OH + NaBr$$

Observation: rate = $k\ [CH_3Br]\ [OH^-]$

rate depends on both reactants → follows *second-order kinetics.*

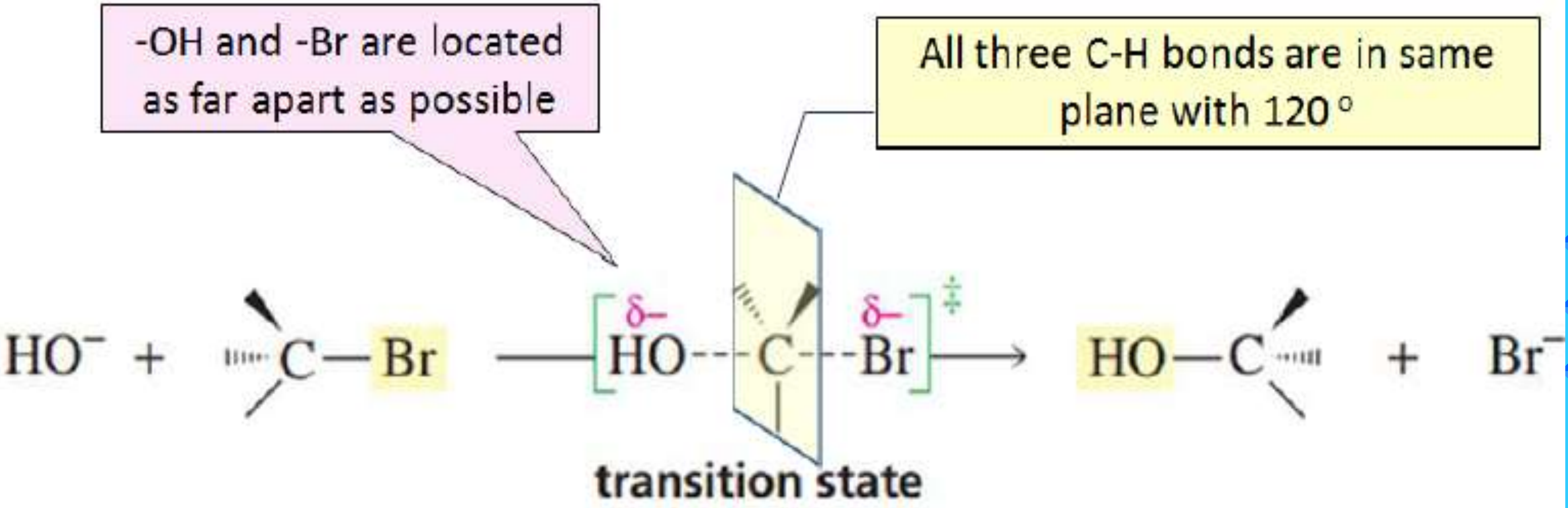
→ both substrates are in rate limiting step.

Thus, rxn have *one step* mechanism : addition of Nu. & removal of leaving group in same step.



S_N2 : mechanism

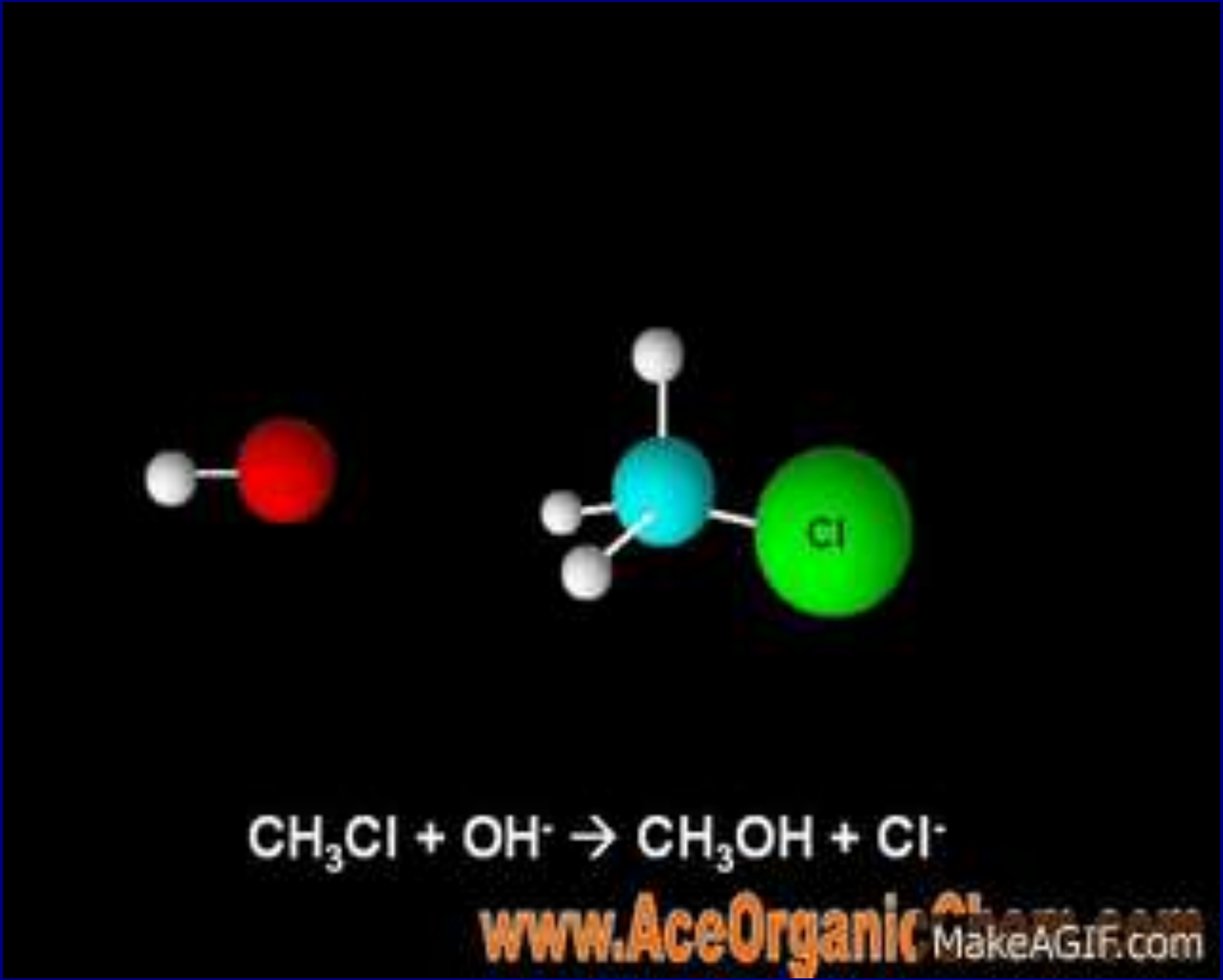
Collision btwn substrates → Nu. attacks from back side.



-OH and -Br are located as far apart as possible

All three C-H bonds are in same plane with 120 °

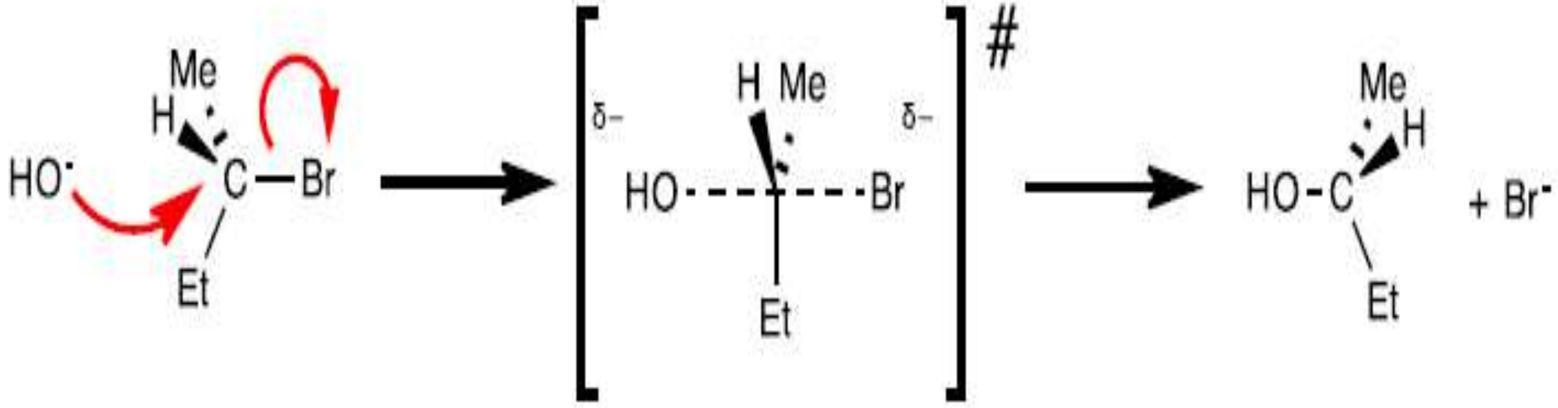
- The spokes of wheel, with C-OH and C-Br axle.
- Ts contains both substrates → bimolecular reaction → S_N2



$CH_3Cl + OH^- \rightarrow CH_3OH + Cl^-$

S_N2 Mechanism: Stereochemistry

- All S_N2 reactions proceed with backside attack of the nucleophile, resulting in **inversion of configuration** at a stereogenic center.

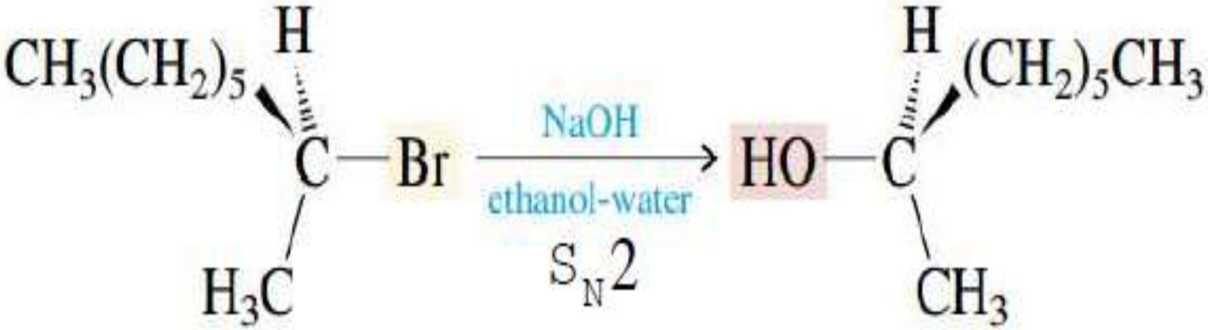


S_N2 : Stereochemistry

- Nu. attacks from back side → <u>complete</u> inversion of **configuration**

  → "back-side displacement,"

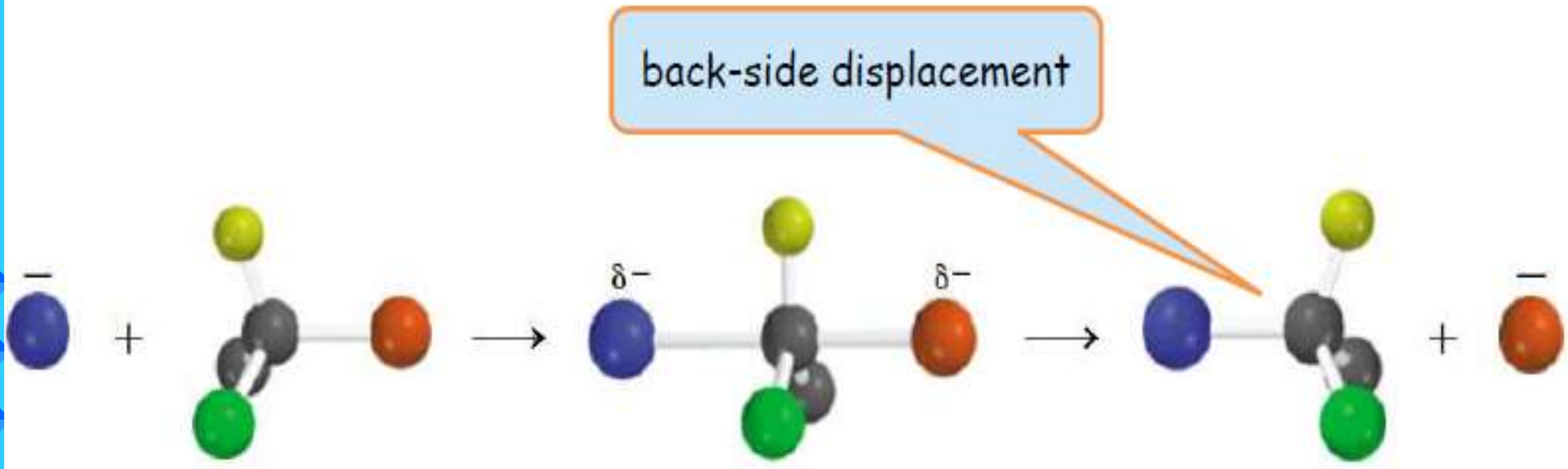
- E.g.



(*S*)-(+)-2-Bromooctane (*R*)-(−)-2-Octanol

S_N2 : Stereochemistry

Explaining mechanism with ball-stick model



back-side displacement

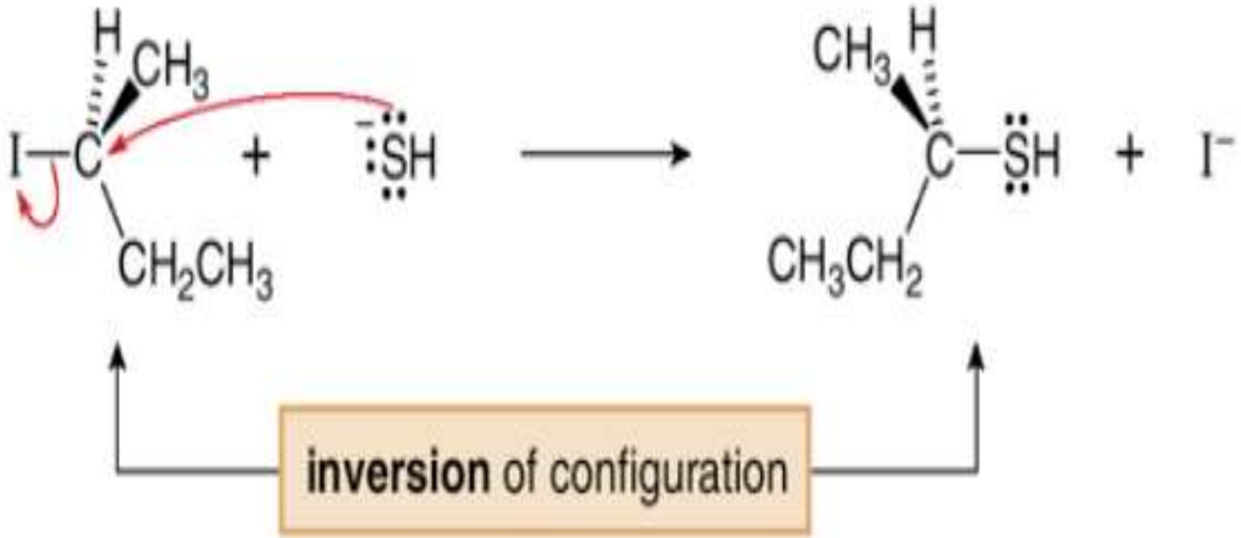
(+) isomer of reactant

(-) isomer of product

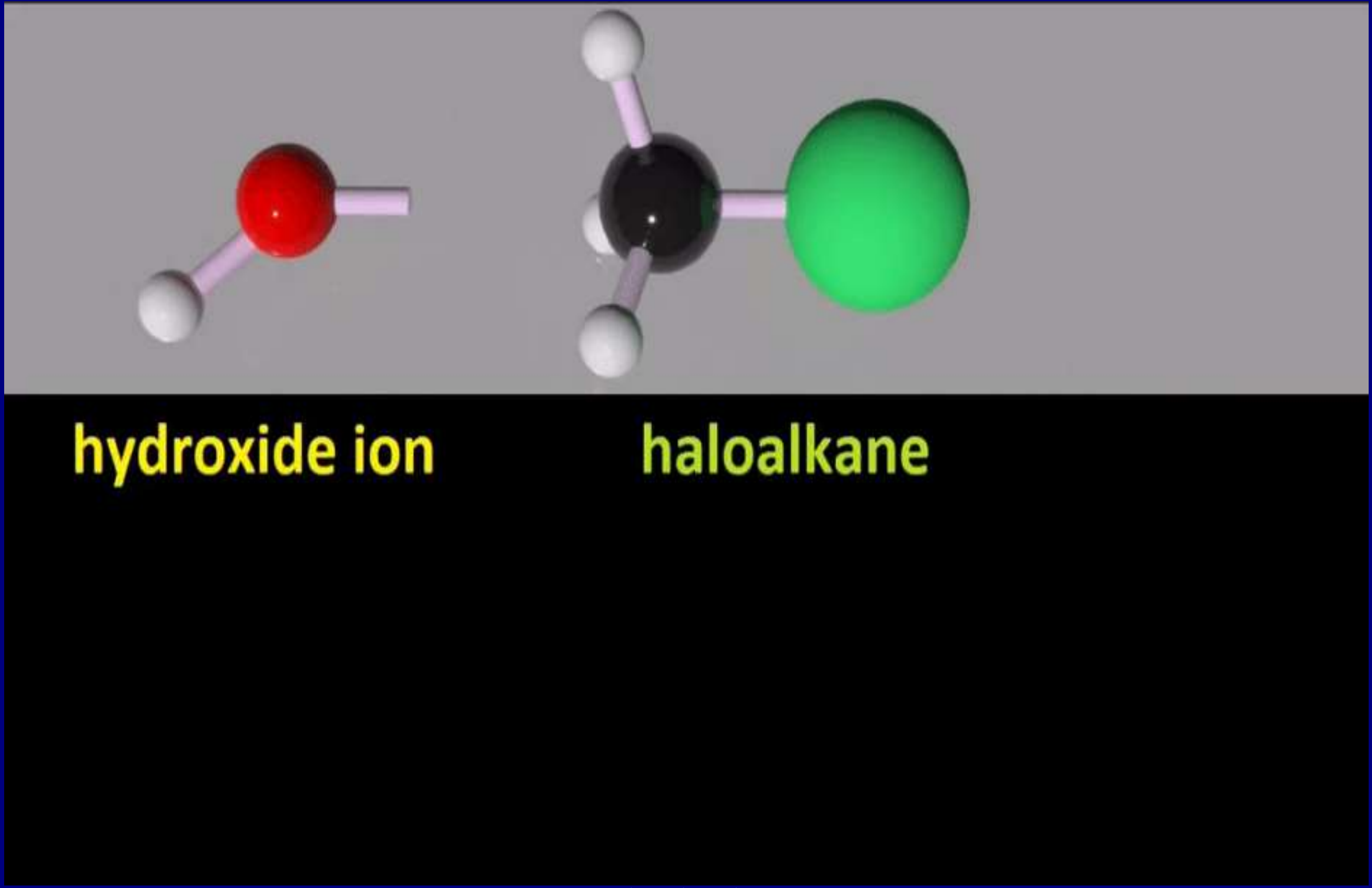
- Rxn that yields a pdct whose configuration is opp. To that of the reactant is called Walden inversion

S_N2 Mechanism: Stereochemistry

- The bond to the nucleophile in the product is always on the **opposite side** relative to the bond to the leaving group in the starting material.



Stereochemistry model



The S_N1 Reaction

Substitution

Nucleophilic

Unimolecular

The S_N1 Reaction

SN1 reactions are nucleophilic substitutions, involving a nucleophile replacing a leaving group (just like SN2).

However: SN1 reactions are **unimolecular:** the rate of this reaction depends only on the concentration of *one reactant.*

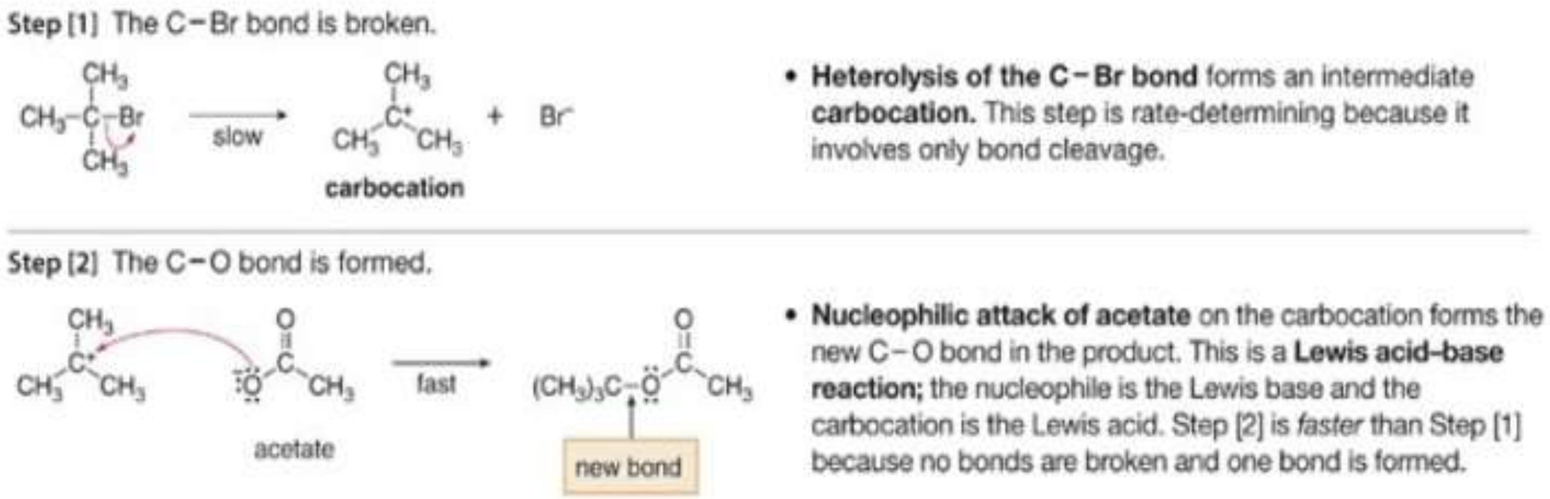
- SN1 reactions happen in two steps:

  1. The leaving group leaves, and the substrate forms a *carbocation intermediate*.
  2. The nucleophile attacks the carbocation, forming the product.

THE

S_N1 Mechanism

The S_N1 mechanism has two steps, and carbocations are formed as reactive intermediates.



Step [1] The C−Br bond is broken.

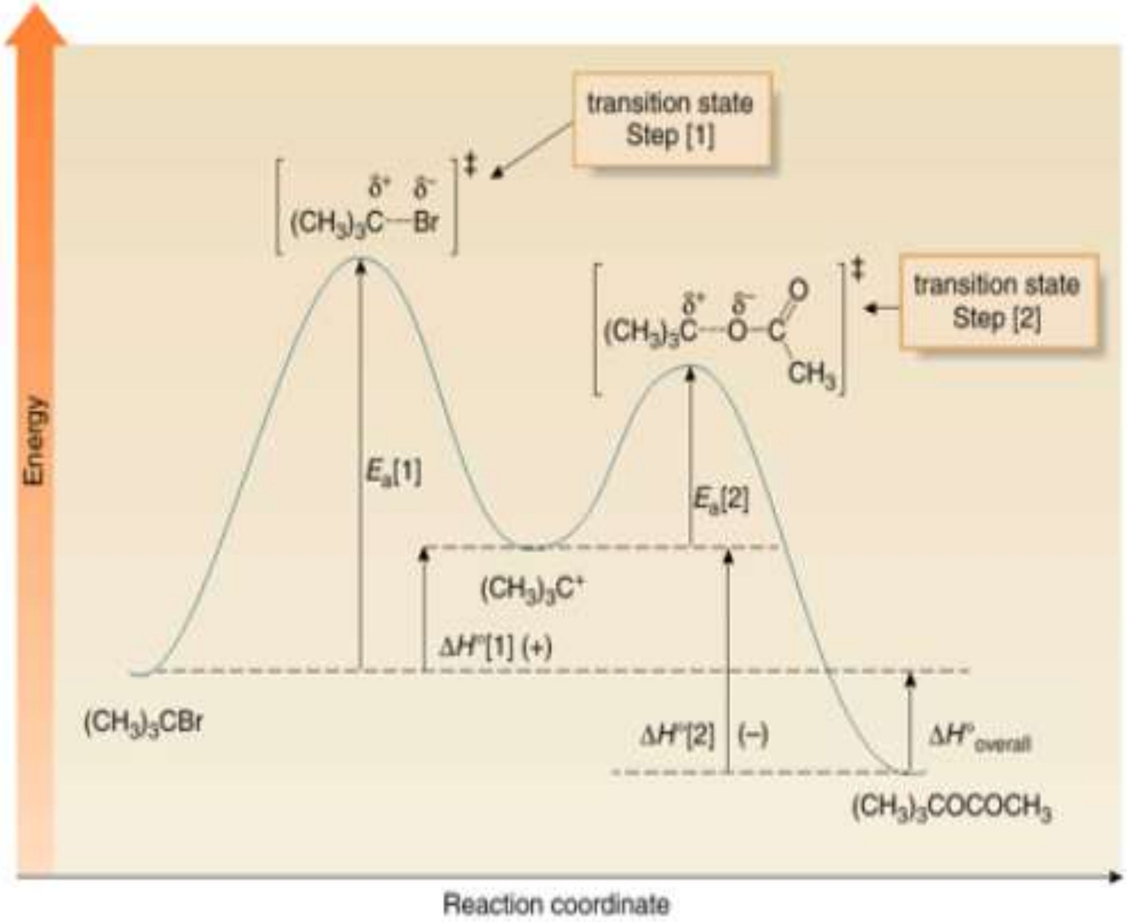
- **Heterolysis of the C−Br bond** forms an intermediate **carbocation.** This step is rate-determining because it involves only bond cleavage.

Step [2] The C−O bond is formed.

- **Nucleophilic attack of acetate** on the carbocation forms the new C−O bond in the product. This is a **Lewis acid-base reaction;** the nucleophile is the Lewis base and the carbocation is the Lewis acid. Step [2] is *faster* than Step [1] because no bonds are broken and one bond is formed.

S_N1 Mechanism: Energetics

$(CH_3)_3CBr + CH_3COO^- \rightarrow$
$(CH_3)_3COCOCH_3 + Br^-$



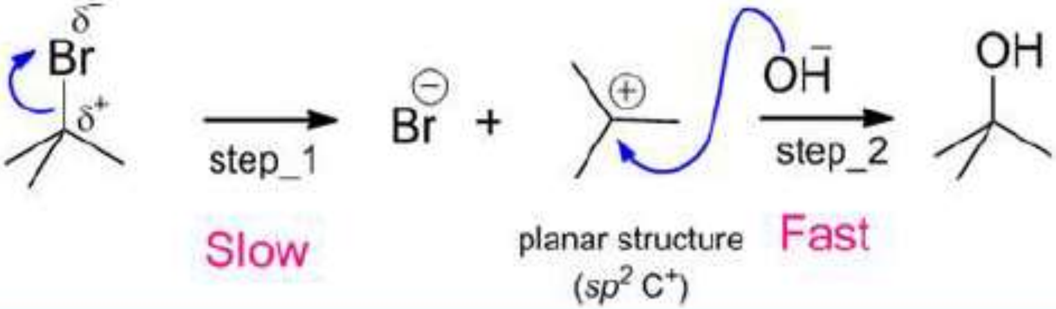
- Since the S_N1 mechanism has two steps, there are two energy barriers.

S_N1 : mechanism

$$\text{rate} = k\ [(CH_3)CBr]$$

- rate depends on RX reactant → follows *first-order kinetics*.
- rate is independent with [$^{-}$OH] → is not participating in limiting step.

Thus *two step* mechanism.



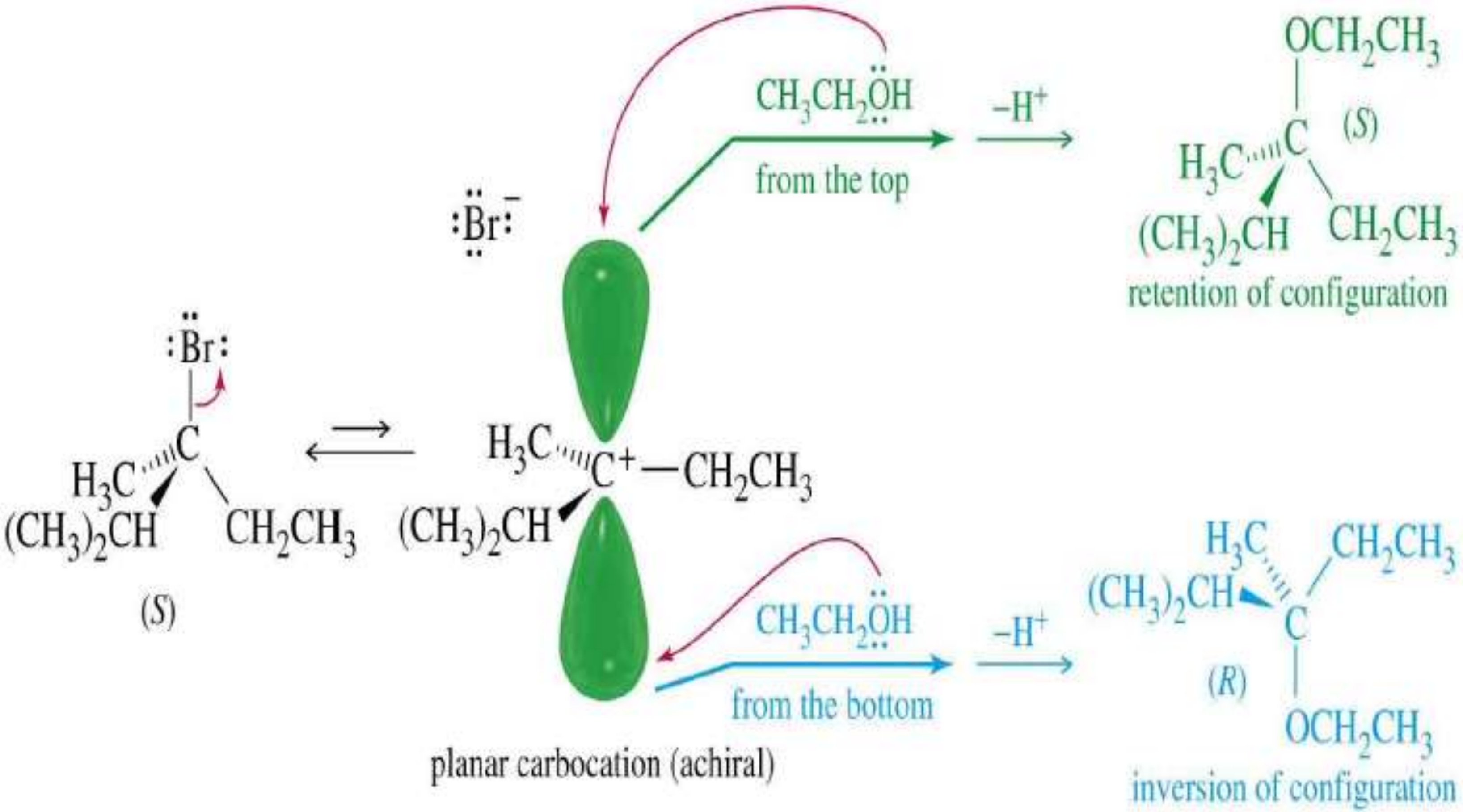
S_N1 : mechanism

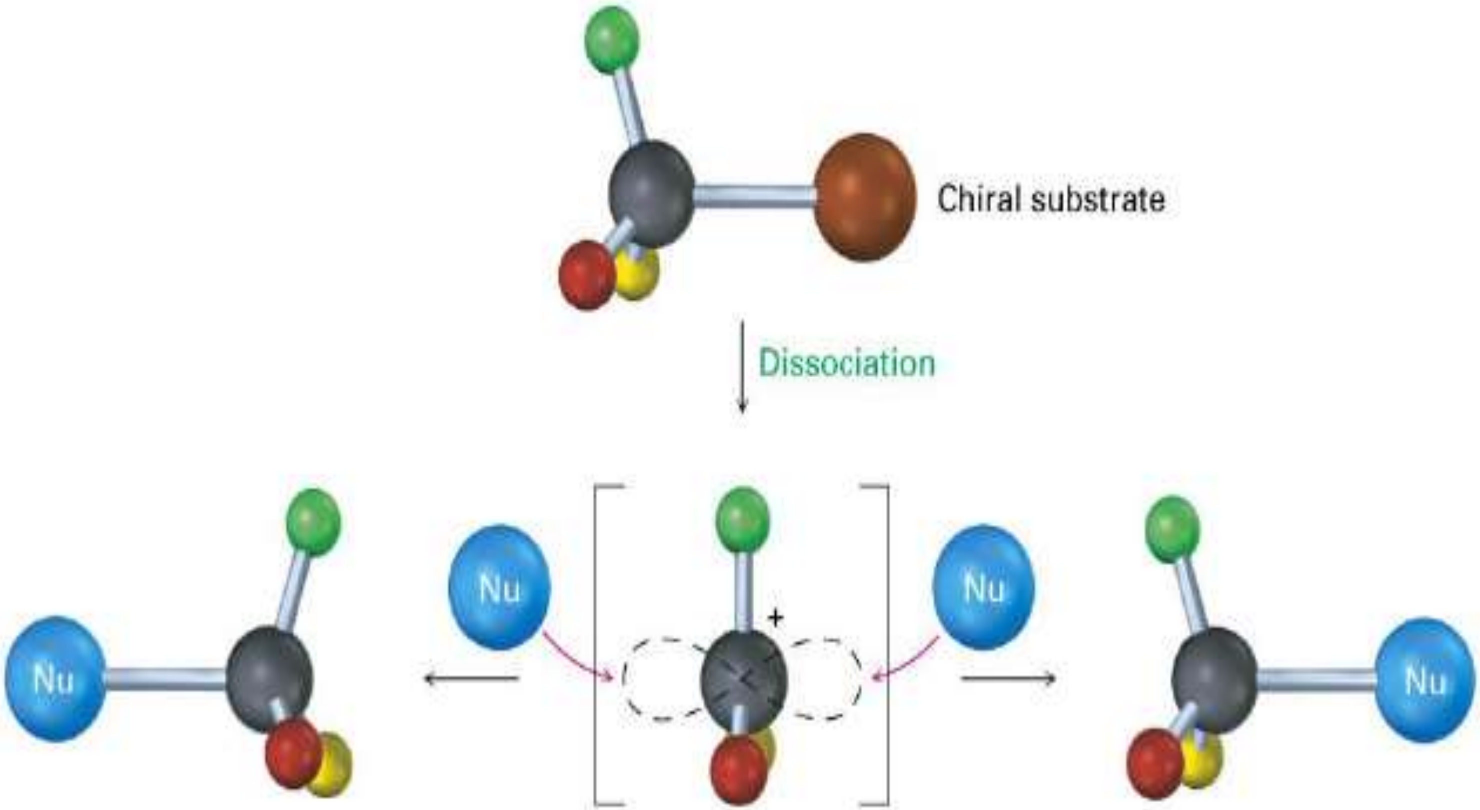
Step_1 : bond braking step = needs energy = slower step, removal of leaving group, generation of C+.

Step_2 : formation of bond = fast step

- here slower step → contains only single substrate → unimolecular reaction → S_N1

Stereochemistry of SN1 reaction





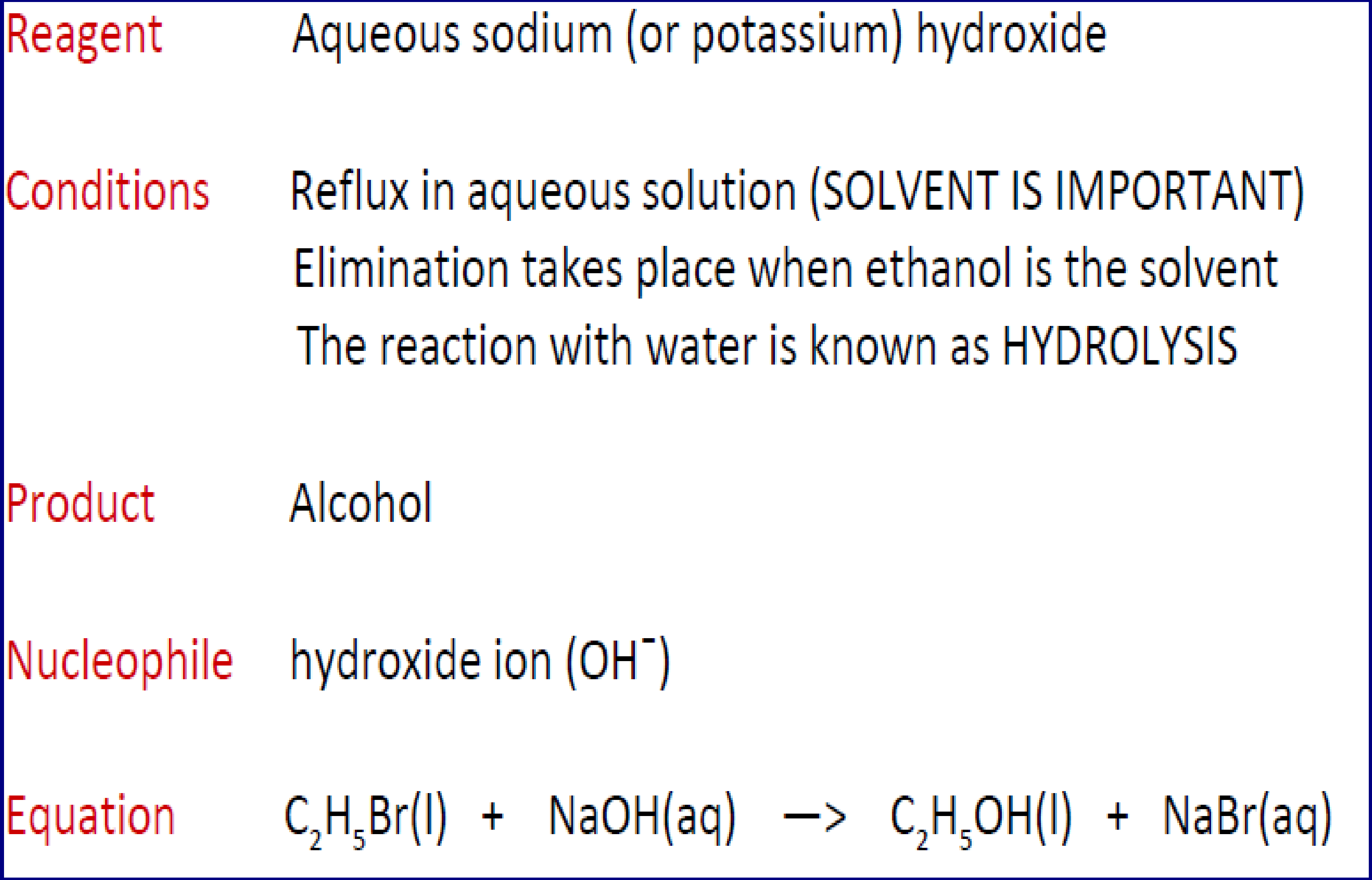
50% inversion of configuration

Planar, achiral carbocation intermediate

50% retention of configuration

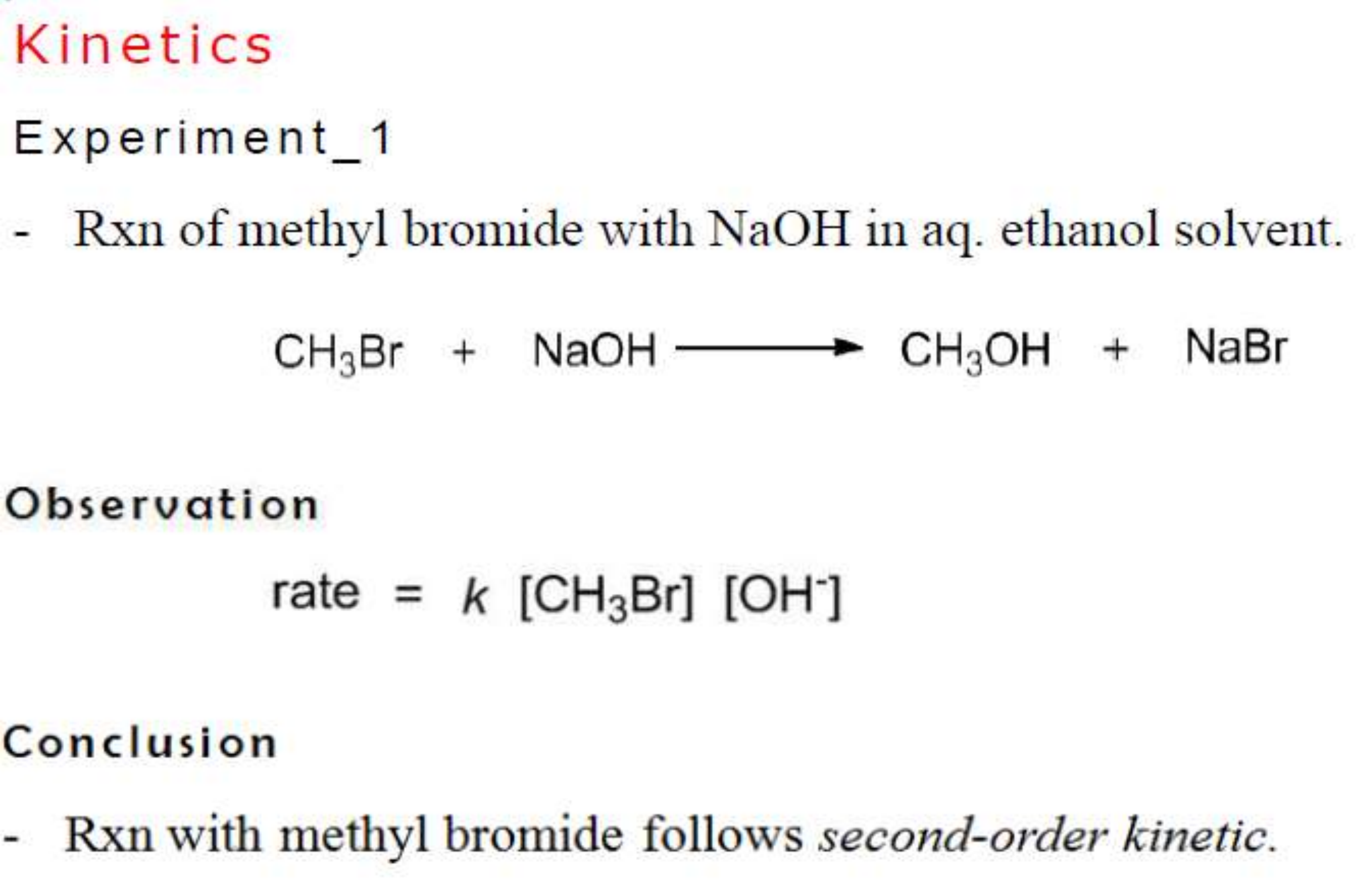
© 2007 Thomson Higher Education

KINETICS OF SN2 AND SN1 REACTIONS



Reagent	Aqueous sodium (or potassium) hydroxide
Conditions	Reflux in aqueous solution (SOLVENT IS IMPORTANT) Elimination takes place when ethanol is the solvent The reaction with water is known as HYDROLYSIS
Product	Alcohol
Nucleophile	hydroxide ion (OH^-)
Equation	$C_2H_5Br(l) + NaOH(aq) \rightarrow C_2H_5OH(l) + NaBr(aq)$

KINETICS OF SN2 AND SN1 REACTIONS



Kinetics

Experiment_1

- Rxn of methyl bromide with NaOH in aq. ethanol solvent.

$$CH_3Br + NaOH \longrightarrow CH_3OH + NaBr$$

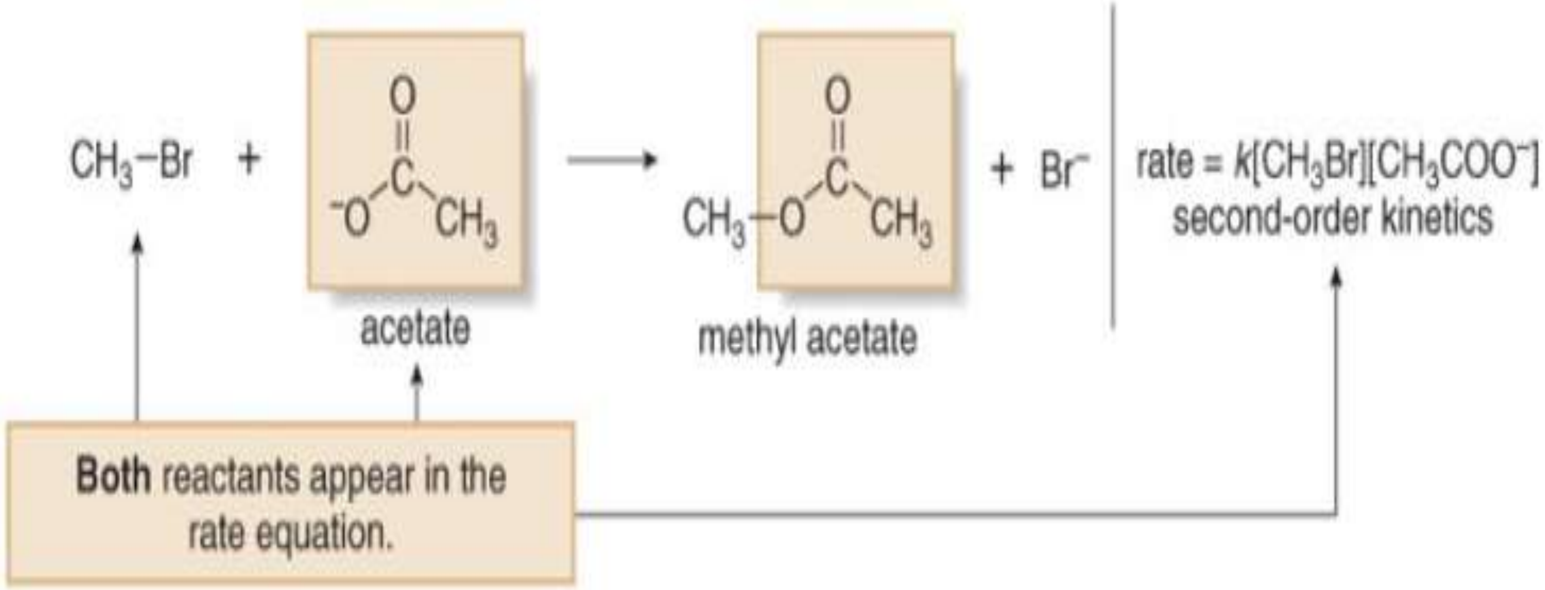
Observation

$$rate = k\ [CH_3Br]\ [OH^-]$$

Conclusion

- Rxn with methyl bromide follows *second-order kinetic.*

S_N2 Mechanism: Kinetics



acetate

methyl acetate

rate = $k[CH_3Br][CH_3COO^-]$
second-order kinetics

Both reactants appear in the rate equation.

Kinetics

Experiment_2

- Rxn of *tert*-butyl bromide with NaOH in aq. ethanol solvent.

Observation

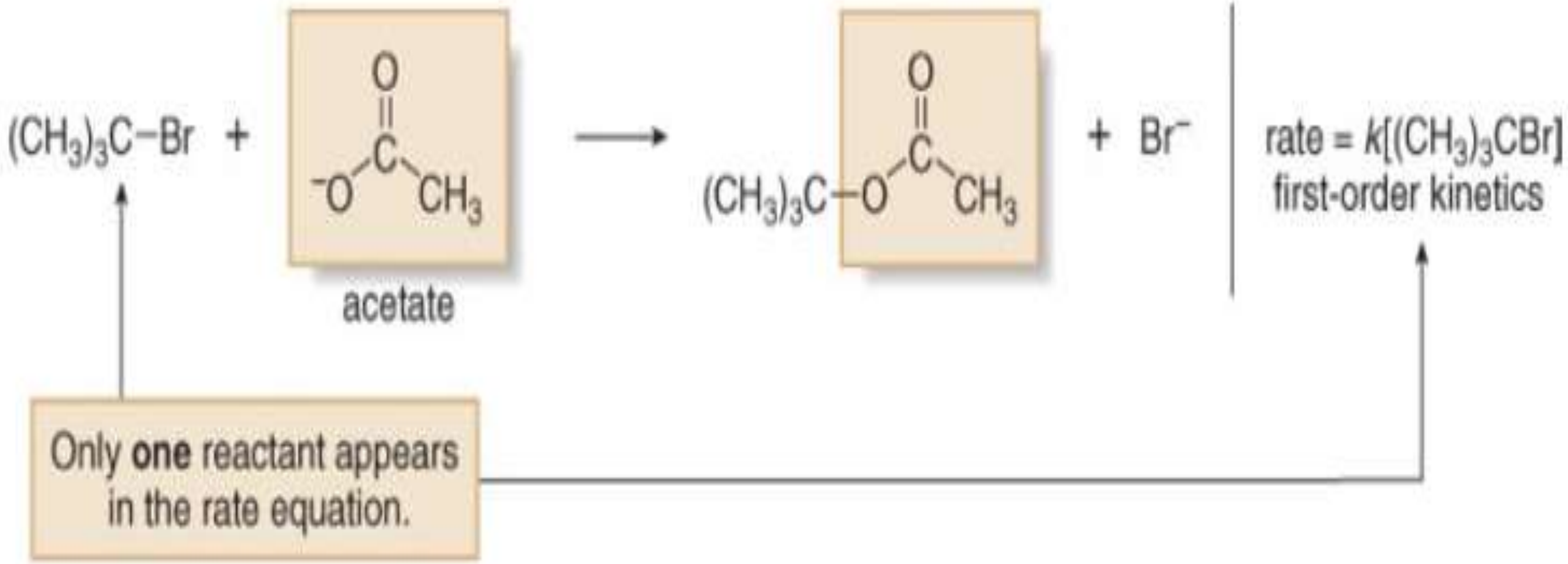
$$\text{rate} = k\ [(CH_3)CBr]$$

the rate of rxn is independent of [$^{-}$OH]

Conclusion

- Rxn with *tert*-butyl bromide follows *first-order kinetic*.

S_N1 Mechanism: Kinetics

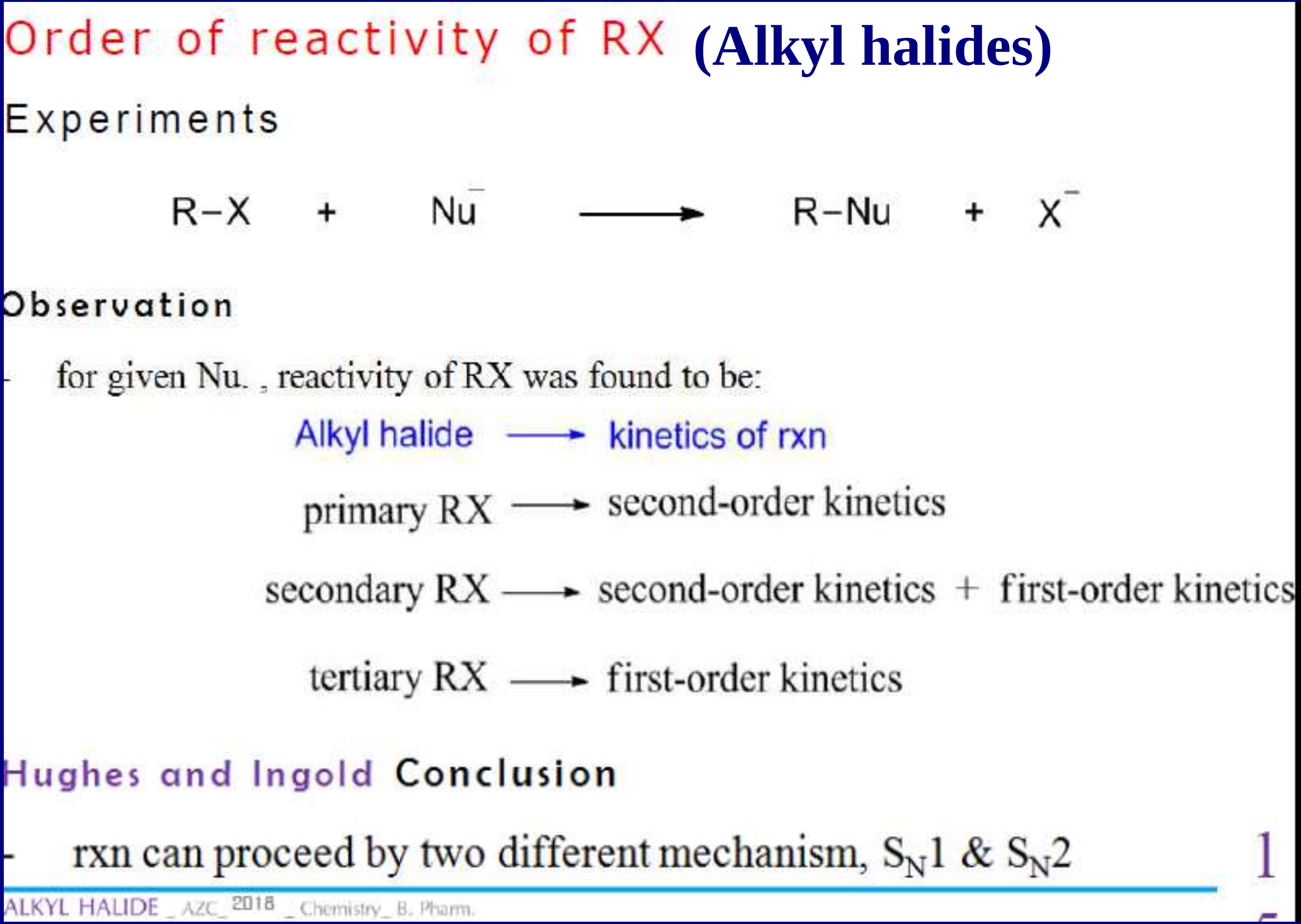


$$(CH_3)_3C{-}Br + {}^{-}O{-}\overset{\overset{\displaystyle O}{\|}}{C}{-}CH_3 \longrightarrow (CH_3)_3C{-}O{-}\overset{\overset{\displaystyle O}{\|}}{C}{-}CH_3 + Br^-$$

acetate

rate = $k[(CH_3)_3CBr]$
first-order kinetics

Only **one** reactant appears in the rate equation.



Order of reactivity of RX (Alkyl halides)

Experiments

$$R-X \quad + \quad Nu^{-} \longrightarrow R-Nu \quad + \quad X^{-}$$

Observation

- for given Nu. , reactivity of RX was found to be:

Alkyl halide ⟶ kinetics of rxn

primary RX ⟶ second-order kinetics

secondary RX ⟶ second-order kinetics + first-order kinetics

tertiary RX ⟶ first-order kinetics

Hughes and Ingold Conclusion

- rxn can proceed by two different mechanism, S_N1 & S_N2

Order of reactivity of RX

- Relation btwn RX and mechanisms

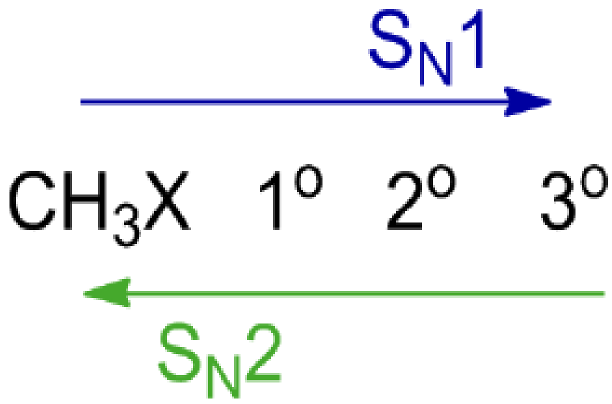
Alkyl halide → kinetics of rxn

primary RX → second-order kinetics

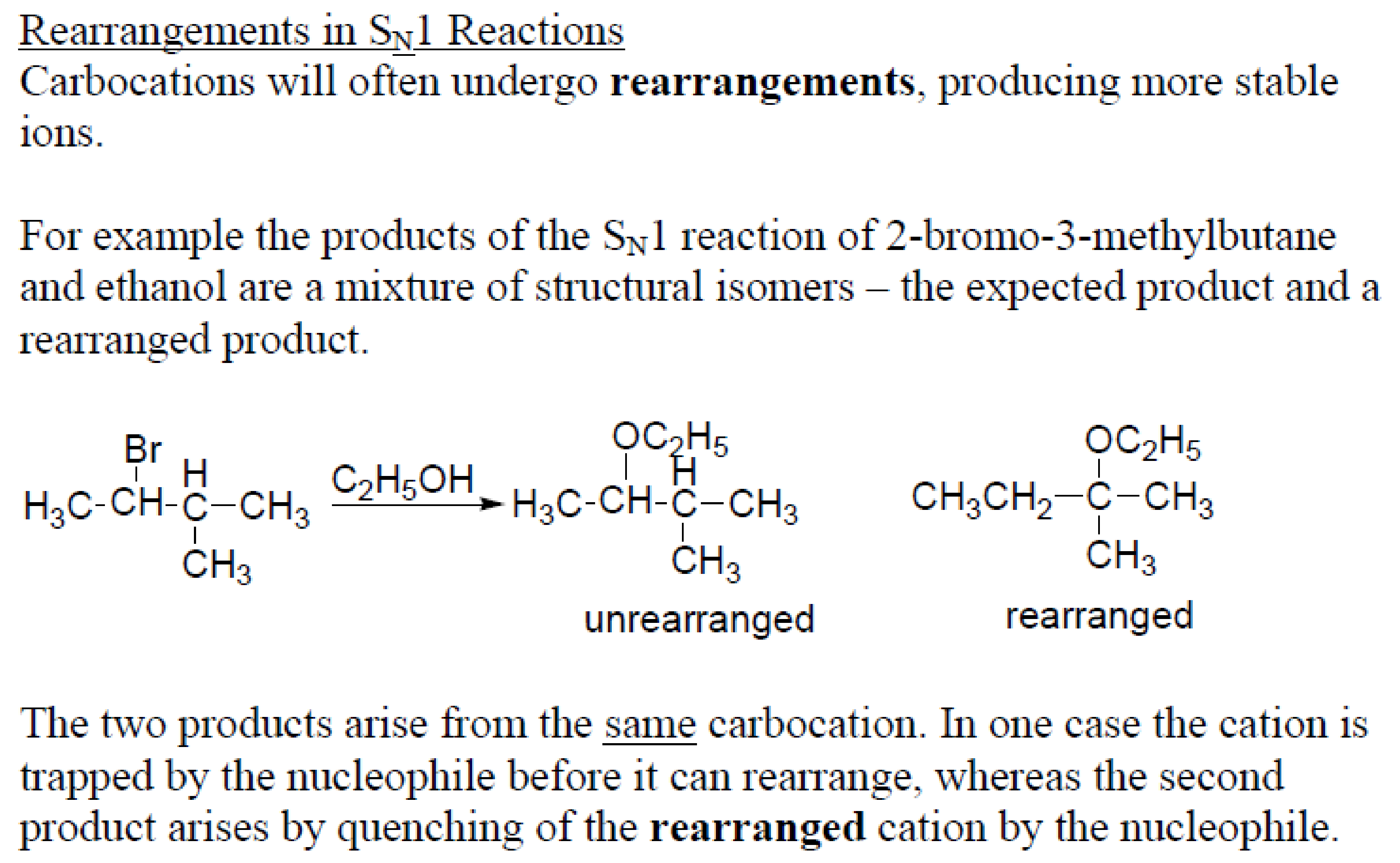
secondary RX → second-order kinetics + first-order kinetics

tertiary RX → first-order kinetics

Order of reactivity of RX is…



REARRANGEMENT OF CARBOCATION IN SN1 REACTION



Rearrangements in S_N1 Reactions

Carbocations will often undergo **rearrangements**, producing more stable ions.

For example the products of the S_N1 reaction of 2-bromo-3-methylbutane and ethanol are a mixture of structural isomers – the expected product and a rearranged product.

$$H_3C\text{-}\overset{Br}{CH}\text{-}\overset{H}{\underset{CH_3}{C}}-CH_3 \xrightarrow{C_2H_5OH} H_3C\text{-}\overset{OC_2H_5}{CH}\text{-}\overset{H}{\underset{CH_3}{C}}-CH_3 \qquad CH_3CH_2-\overset{OC_2H_5}{\underset{CH_3}{C}}-CH_3$$

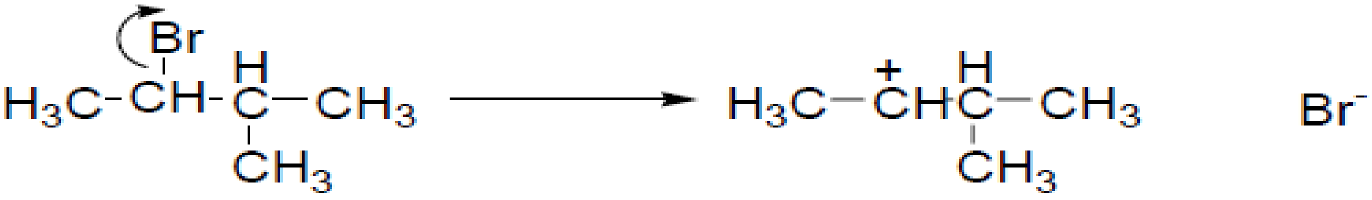
unrearranged

rearranged

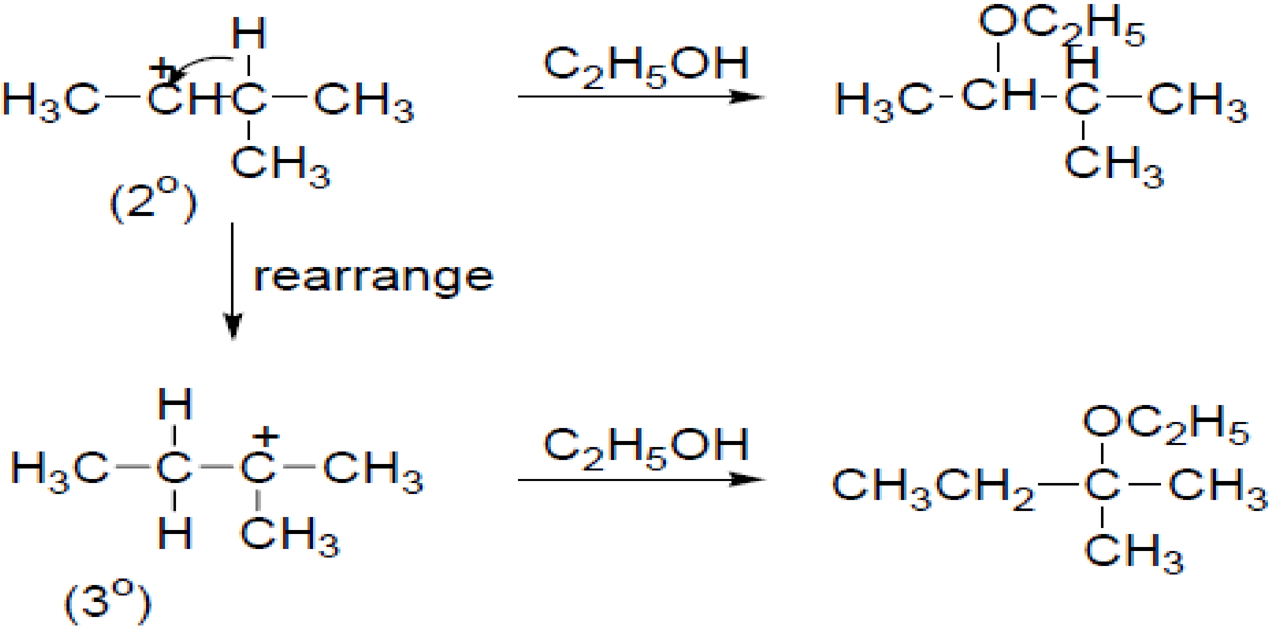
The two products arise from the same carbocation. In one case the cation is trapped by the nucleophile before it can rearrange, whereas the second product arises by quenching of the **rearranged** cation by the nucleophile.

Mechanism

Step 1: Formation of carbocation

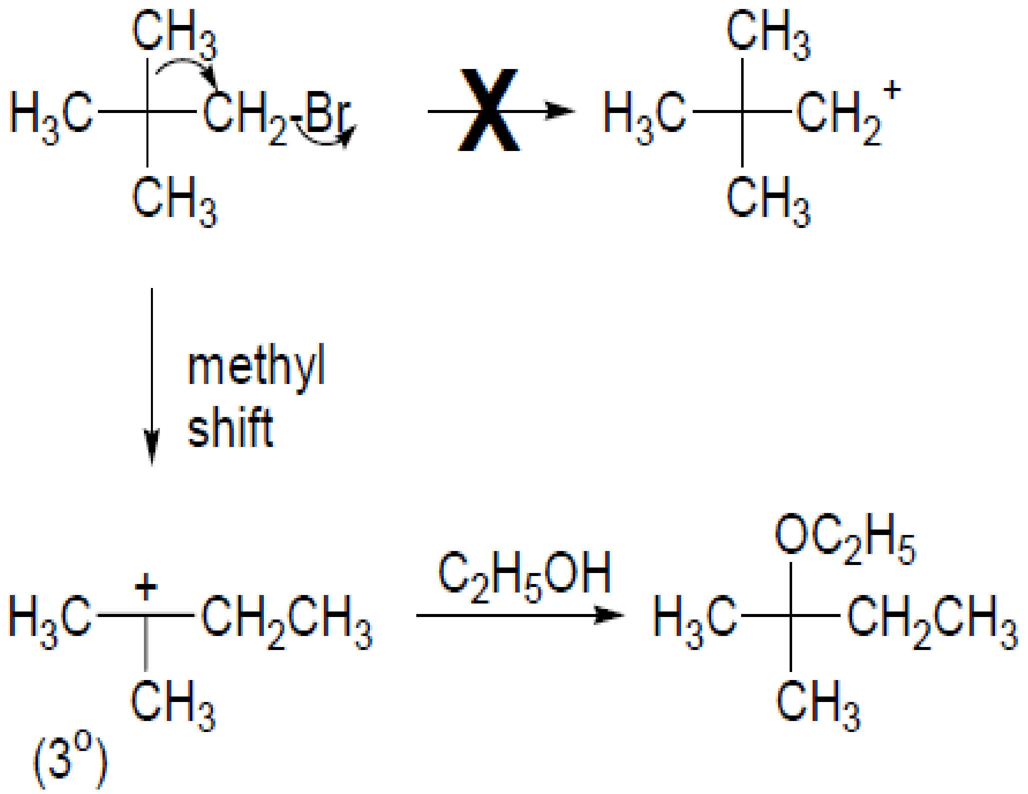


Step 2: Attack of solvent before and after rearrangement.



Another Rearrangement

Neopentylbromide gives exclusively a rearranged product, which results from a methyl shift.



This rearrangement produces a tertiary cation (stable) instead of a primary cation (unstable).

In the cationic rearrangements, the moving group (H and CH_3) take their bonding electrons with them (H^- and CH_3^-).

Rearrangements occur when a more a stable cation can be produced by a hydrogen or alkyl group shift.

(Rearrangements do not occur in S_N2 reactions since carbocations are not intermediates).

MCQ QUESTIONS

Select the correct statement from the following option.

a) S_N2 reaction follows second order kinetics
b) No intermediate is involved in S_N2 mechanism
c) S_N2 reactions are one-step reaction
d) All of the above

ANSWER: All of the above **(d)**

Which step in S_N1 reaction is a slow rate determining step?

a) Attack of nucleophile
b) Formation of a racemic mixture
c) Formation of a transition state
d) All of the mentioned

ANSWER: Formation of a transition state **(c)**

Why alkyl halides are considered to be very reactive compounds towards nucleophile?

a) they have an electrophilic carbon & a bad leaving group
b) they have a nucleophilic carbon & a good leaving group
c) they have an electrophilic carbon
d) they have an electrophilic carbon & a good leaving group

ANSWER: they have an electrophilic carbon & a good leaving group **(d)**

- The reaction which has two transition states

a) Elimination reaction
b) SN1 reaction
c) SN2 reaction
d) Both b and c

ANSWER: SN1 reaction (b)

In the stereochemistry of SN1 reaction recemaisation refers to

a) 50% inversion of configuration of reactant
b) 50% retention of configuration of reactant
c) Both a and b
d) None of the above

ANSWER: Both a and b **(c)**

FACTORS AFFECTING SN1 AND SN2 REACTIONS

FACTORS AFFECTING SN REACTIONS

- Nature of Nucleophile
- Nature of Leaving group
- Alkyl substituent
- Solvents

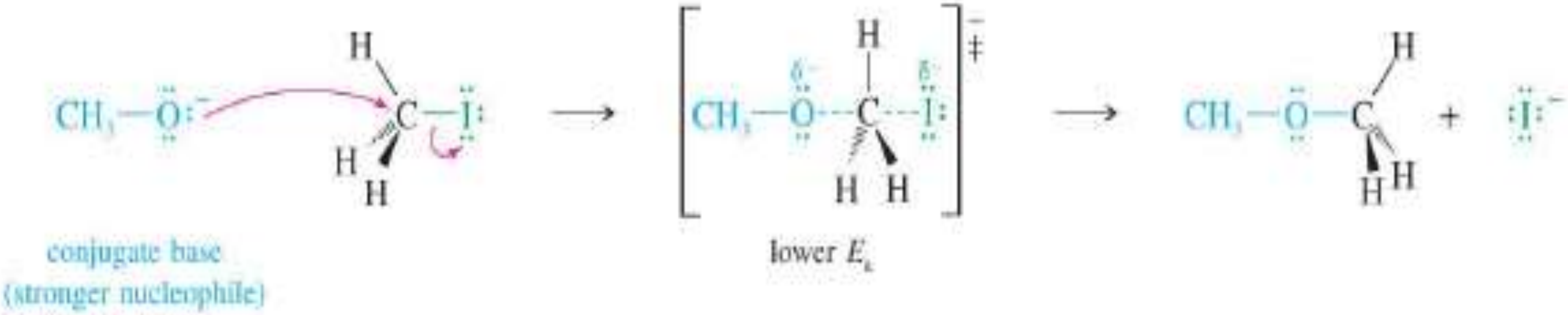
Effect of Nucleophile

Nucleophile strength (SN2 reaction)

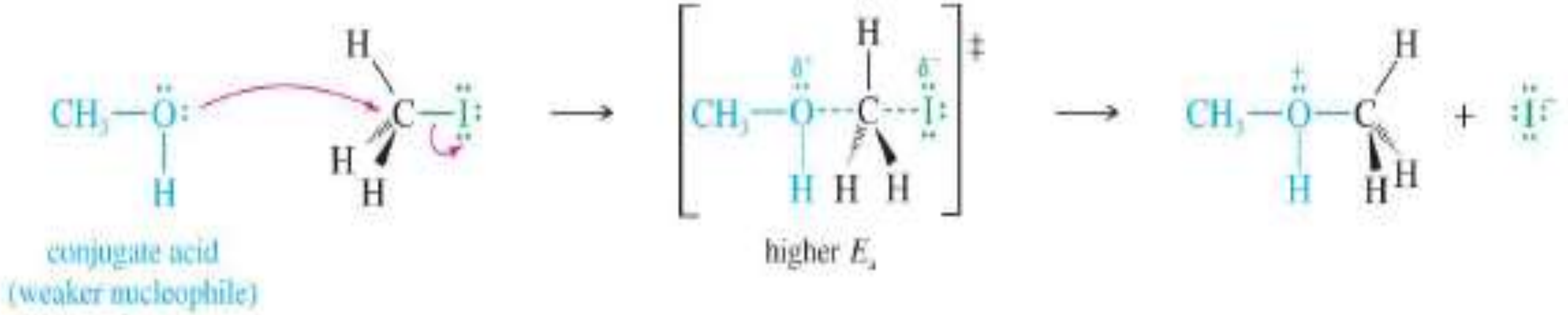
- The rate of the SN2 reaction strongly depends on the nature of the nucleophile – a good nucleophile gives faster rates than a worse nucleophile.
- Consider methanol (CH3OH) and methoxide (CH3O$^-$) reacting with CH3I.
- It is found that methoxide reacts about a *million times faster in SN2 reactions than methanol.*
- Generally, negatively charged species are much better nucleophiles than analogous neutral species.

◆ The two transition states are different energetically.

The T.S. with methoxide has the negative charge shared over the *oxygen* atom and the leaving *halide*. (Good as both are electronegative).



© 2013 Pearson Education, Inc.



© 2013 Pearson Education, Inc.

In the *methanol* case, there is no negative charge. The halide has a partial negative charge and the oxygen has a partial **positive** charge. This is of *higher* energy.

NUCLEOPHILICITY AND BASICITY

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 $CH_3O^{\ominus} > CH_3OH$

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

Stronger base	weaker base
better nucleophile	poorer nucleophile

$HO^{\ominus} > H_2O$

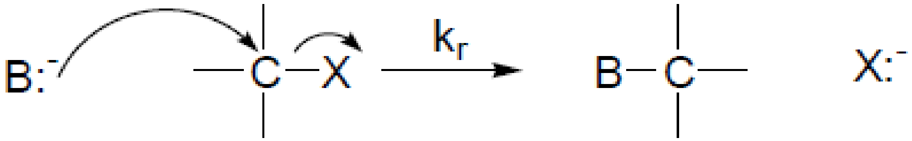
$CH_3O^{\ominus} > CH_3OH$

$H_2N^{\ominus} > NH_3$

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

Basicity and Nucleophilicity

Basicity is defined by the equilibrium constant for abstracting a proton.



Nucleophilicity is defined by the rate of attack on an electrophilic carbon atom.

Trends in Nucleophilicity

1) Species with a negative charge are stronger nucleophiles than analogous species without a negative charge. (Bases are always stronger nucleophiles than their conjugate acids).

   $^-OH > H_2O$ $^-SH > H_2S$ $^-NH_2 > NH_3$

2) Nucleophilicity decreases from left to right across the periodic table. (The more electronegative elements hold on more tightly to their non-bonding electrons).

$^{-}OH > F^{-}$ $:NH_3 > H_2O$ $(CH_3CH_2)_3P > (CH_3CH_2)_2S$

3) Nucleophilicity increases down the periodic table. (Increase in polarizability and size).

$I^{-} > Br^{-} > Cl^{-} > F^{-}$ $HSe^{-} > HS^{-} > HO^{-}$

$(CH_3CH_2)_3P > (CH_3CH_2)_3N$

As the size of an atom increases, its outer electrons get further from the attractive force of the nucleus. The electrons are held less tightly and are said to be more polarizable – they are more able to move toward a positive charge.

More polarizable atoms can form bonds at greater distances, which gives rise to stronger bonding in the T.S.

For two nucleophiles with the same nucleophilic atom, the stronger base is the stronger nucleophile.

HO^- is a stronger base and stronger nucleophile than CH_3COO^-. (pK_a: H_2O = 15.7, CH_3COOH = 4.8).

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

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

Right-to-left across a row of the periodic table, nucleophilicity increases as basicity increases:

NH_3 is a stronger base and stronger nucleophile than H_2O.

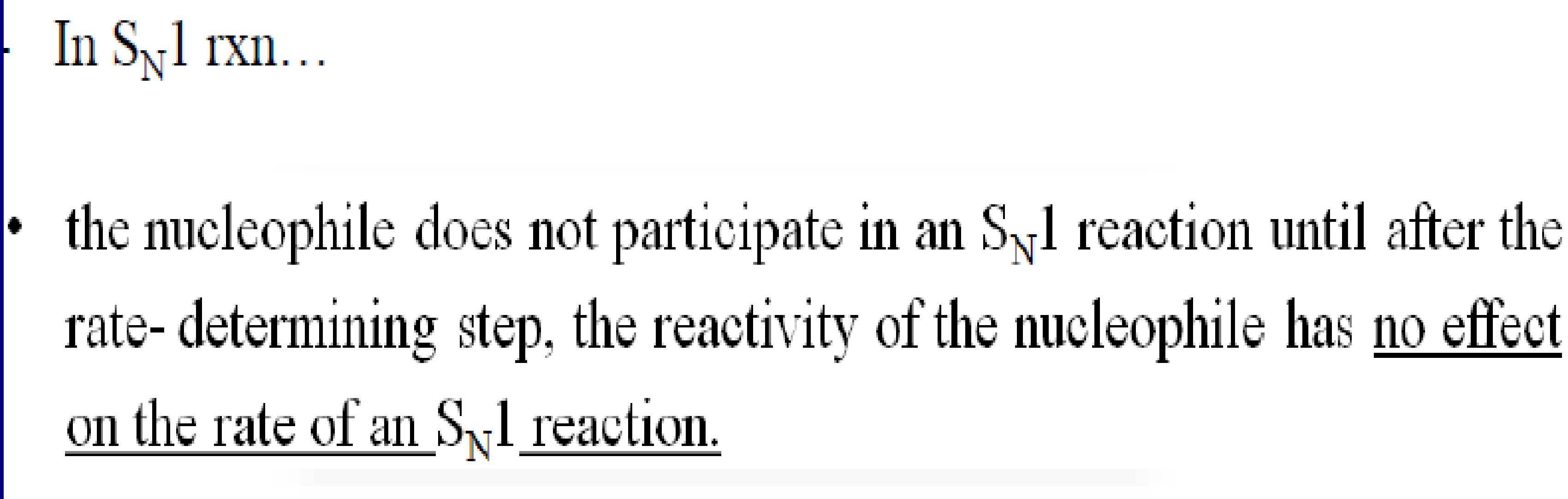
The Nucleophile

- In S_N2 rxn…
  - the nucleophile attacks an *sp*^{3} carbon in the rate-determining step of an S_N2 reaction, the rate of the reaction will depend on the strength of the nucleophile:
  - the better the nucleophile, the faster the rate of the S_N2 reaction.

$$^-NH_2 > HO^- > F^-$$

strongest base

best nucleophile

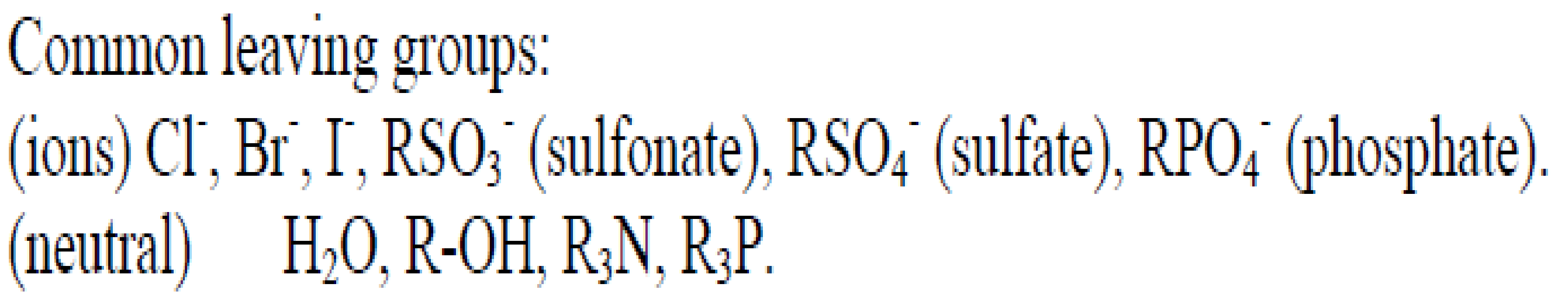


- In S_N1 rxn…

- the nucleophile does not participate in an S_N1 reaction until after the rate- determining step, the reactivity of the nucleophile has <u>no effect on the rate of an S_N1 reaction.</u>

EFFECT OF LEAVING GROUP

- A good leaving group needs to be a Stable anions that are weak bases which can delocalize charge



Common leaving groups:

(ions) Cl^-, Br^-, I^-, RSO_3^- (sulfonate), RSO_4^- (sulfate), RPO_4^- (phosphate).

(neutral) H_2O, R-OH, R_3N, R_3P.

The Leaving Group

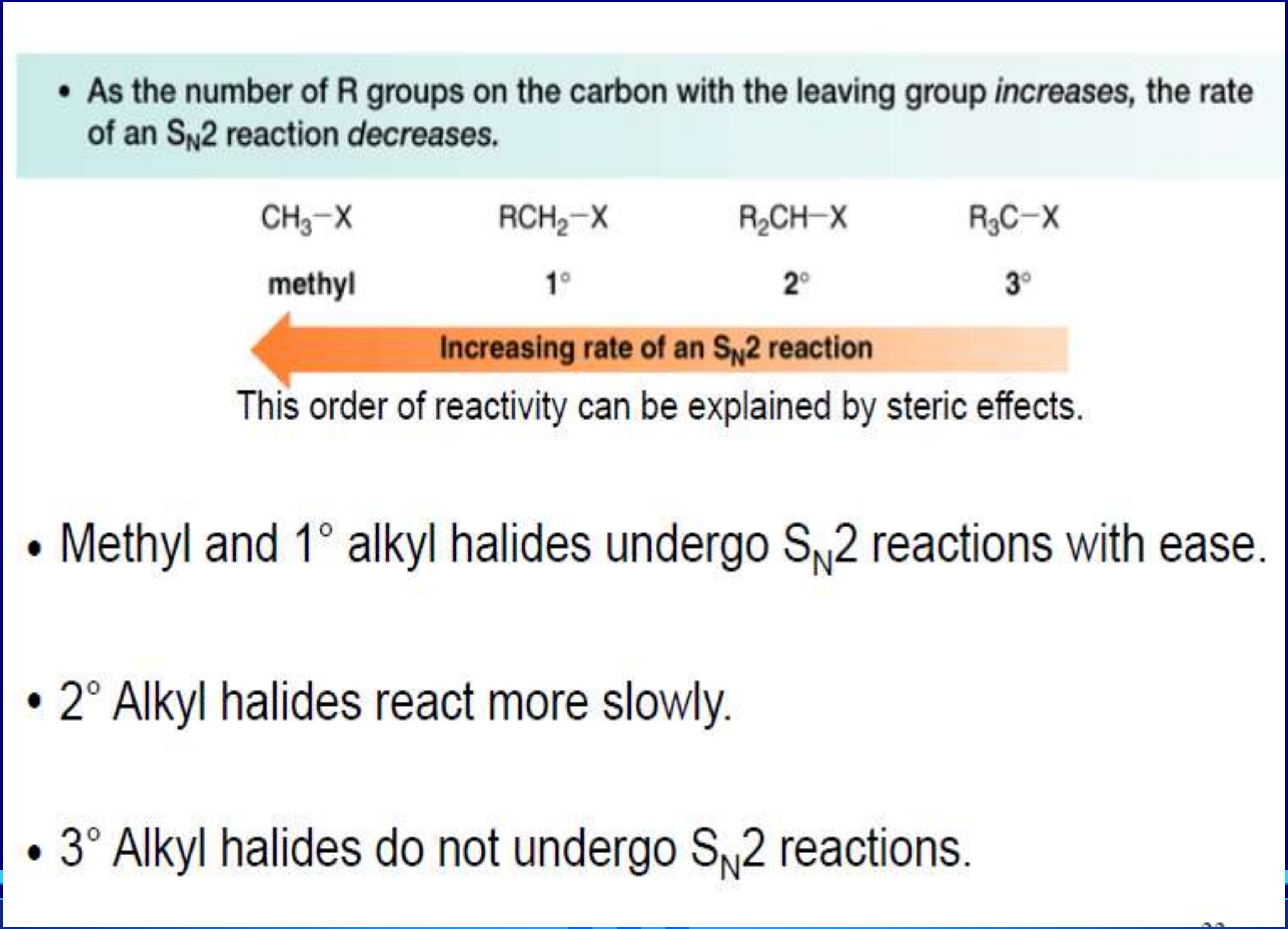
- In both SN reaction leaving group dissociates in Ts. It affects to the reaction rate.
- The weaker the C-X bond (from F to I), the better is its leaving ability.
- Thus…

relative reactivities of alkyl halides in an S_N1 & S_N2 reactions is …

C-X bond strength $\longrightarrow$

most reactive — RI > RBr > RCl > RF — too unreactive to undergo an S_N2 reaction

EFFECT OF ALKYL SUBSTRATE IN SN2 REACTION



- As the number of R groups on the carbon with the leaving group *increases*, the rate of an S_N2 reaction *decreases*.

CH_3-X	RCH_2-X	R_2CH-X	R_3C-X
methyl	**1°**	**2°**	**3°**

Increasing rate of an S_N2 reaction ←

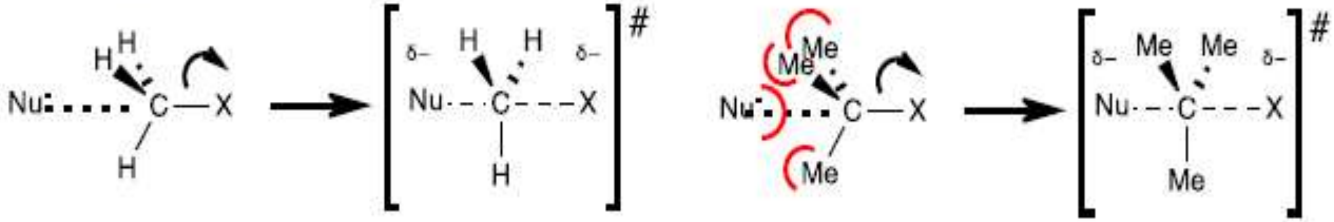
This order of reactivity can be explained by steric effects.

- Methyl and 1° alkyl halides undergo S_N2 reactions with ease.

- 2° Alkyl halides react more slowly.

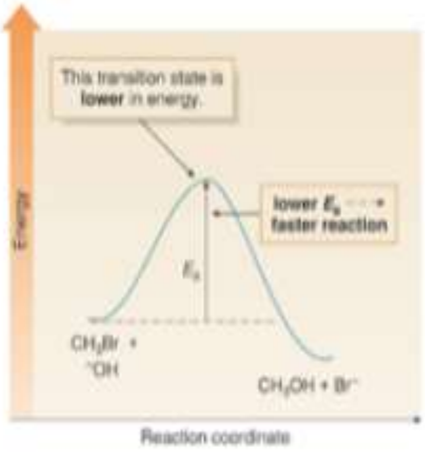
- 3° Alkyl halides do not undergo S_N2 reactions.

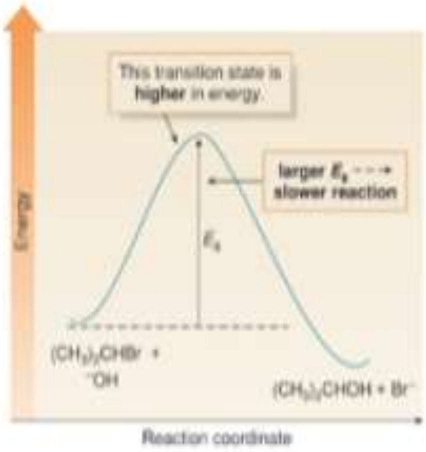
- Increasing the number of R groups on the carbon with the leaving group makes the approach of the nucleophile more difficult and increases crowding in the transition state.
- The S_N2 reaction is fastest with unhindered halides.



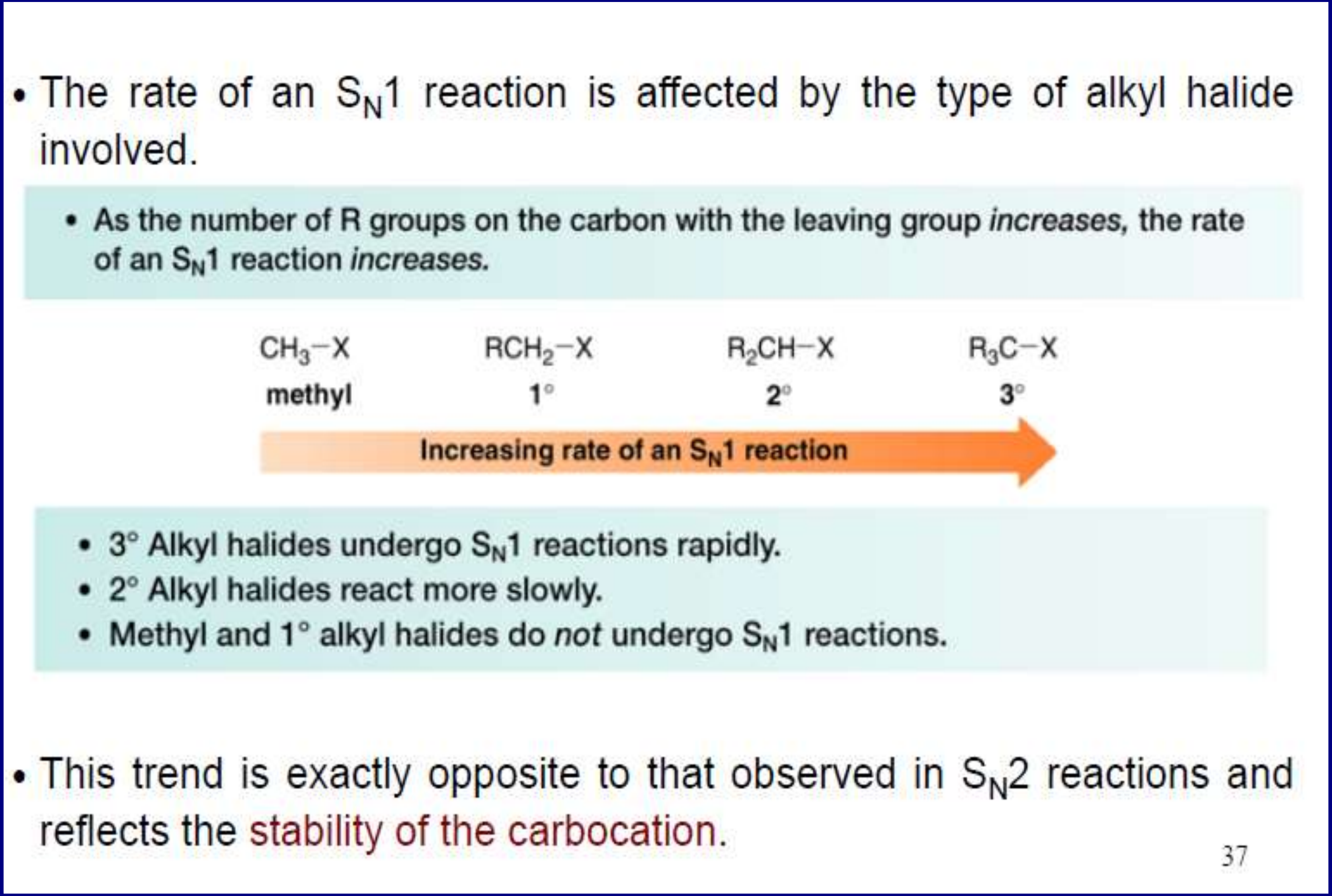
hindered approach

crowded transition state





EFFECT OF ALKYL SUBSTRATE IN SN1 REACTION



- The rate of an S_N1 reaction is affected by the type of alkyl halide involved.

- As the number of R groups on the carbon with the leaving group *increases*, the rate of an S_N1 reaction *increases*.

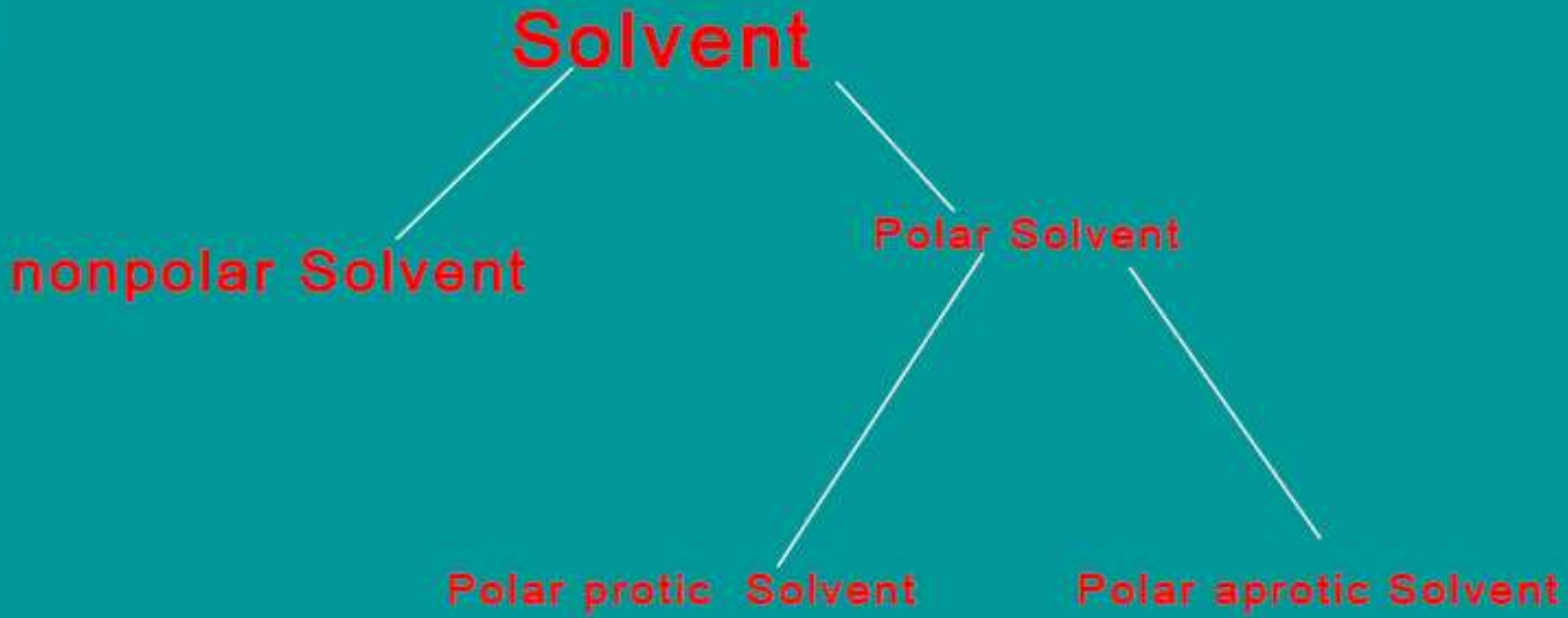
CH_3-X	RCH_2-X	R_2CH-X	R_3C-X
methyl	**1°**	**2°**	**3°**

Increasing rate of an S_N1 reaction

- 3° Alkyl halides undergo S_N1 reactions rapidly.
- 2° Alkyl halides react more slowly.
- Methyl and 1° alkyl halides do *not* undergo S_N1 reactions.

- This trend is exactly opposite to that observed in S_N2 reactions and reflects the stability of the carbocation.

EFFECT OF SOLVENT ON SN2 REACTION



Solvent

nonpolar Solvent

Polar Solvent

Polar protic Solvent

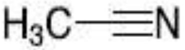
Polar aprotic Solvent

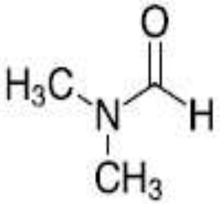
SN2 reaction prefers polar aprotic solvent

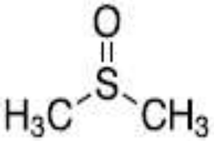
- Protic solvents slow down SN_2 reactions

H_2O	
CH_3OH	methanol
CH_3CH_2OH	ethanol
$(CH_3)_3COH$	*tert*-butanol
CH_3COOH	acetic acid

- SN_2 reations are best carried out in polar aprotic solvents


acetonitrile


N,N-dimethylformamide
DMF

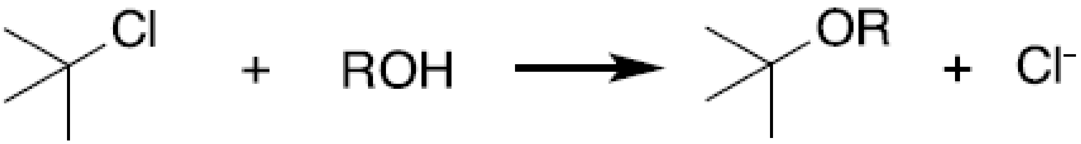

dimethylsulfoxide
DMSO

EFFECT OF SOLVENT ON SN1 REACTION

polar solvents (which stabilize ions) enhance S_N1 reactivities.

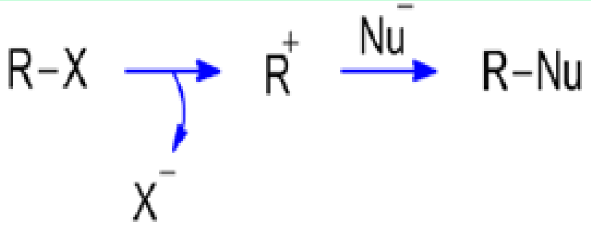
Protic solvents are especially useful since the hydrogen bonding stabilizes the anionic leaving group after ionization.

- Solvent: polar solvents favor the reaction by stabilizing the intermediate carbocation (Hammond postulate).



	ethanol	40% water/ 60% ethanol	80% water/20% ethanol	water
Relative reactivity	*1*	*100*	*14000*	*100000*

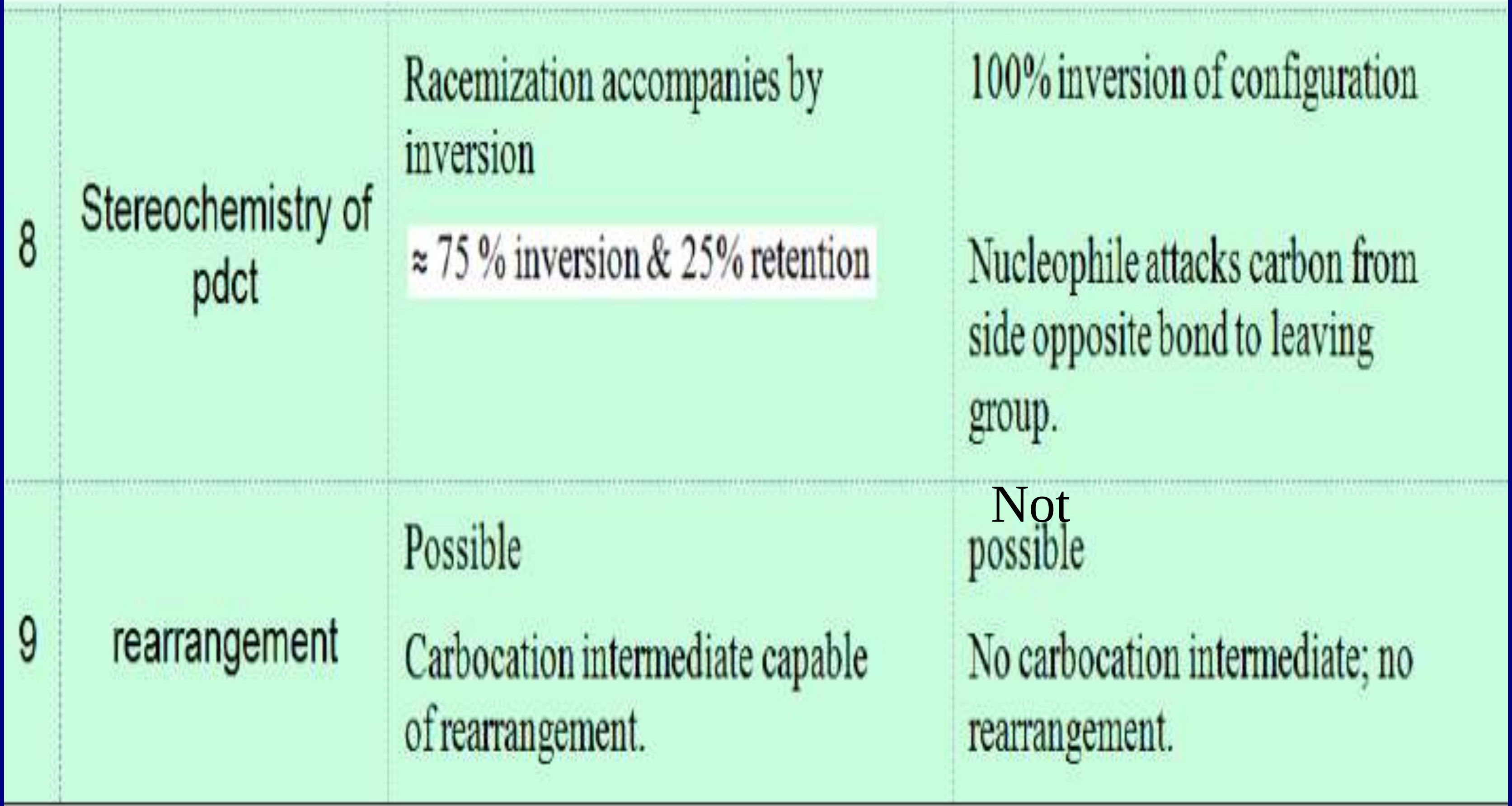
S_N1 vs S_N2 :

	Properties	S_N1	S_N2
1	mechanism	Two steps  $R-X \xrightarrow{} \overset{+}{R} \xrightarrow{\overset{-}{Nu}} R-Nu$, $\overset{-}{X}$	Single step $R-X + \overset{-}{Nu} \longrightarrow R-Nu$
2	transition state	contains only single substrate $\overset{\delta+}{R}\cdots\overset{\delta-}{X}$	contains both substrates $\overset{\delta-}{Nu}\cdots\overset{\delta+}{R}\cdots\overset{\delta-}{X}$
3	Molecularity	Unimolecular	Bimolecular

S_N1 vs S_N2 :

4	Order of Kinetics	First order Rate = k[alkyl halide]	Second order Rate = k[alkyl halide][nucleophile]
5	Reactivity of alkyl halide	$R_3CX > R_2CHX > RCH_2X > CH_3X$	$CH_3X > RCH_2X > R_2CHX > R_3CX$
6	Effect of nucleophile	Rate of rxn is independent	Rate of rxn is independent the better the nucleophile, the faster the rate of rxn
7	Effect of polar solvent	Rate increases with increasing polarity of solvent	Rate decreases

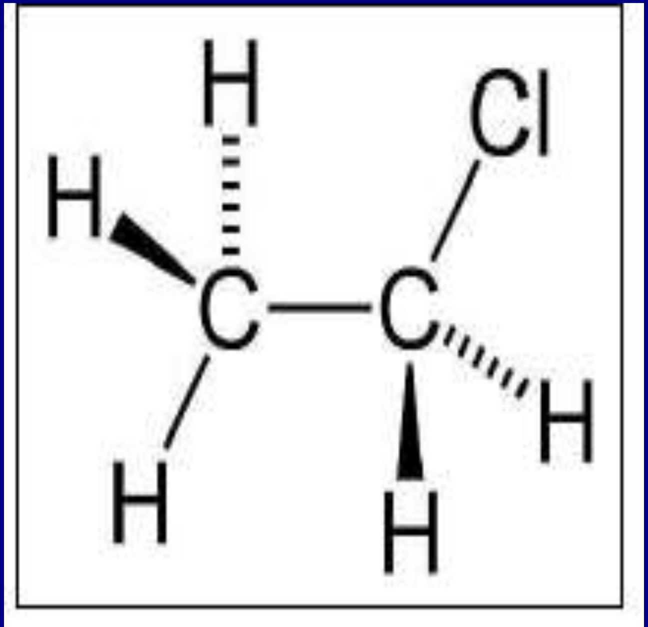
S_N1 vs S_N2 :

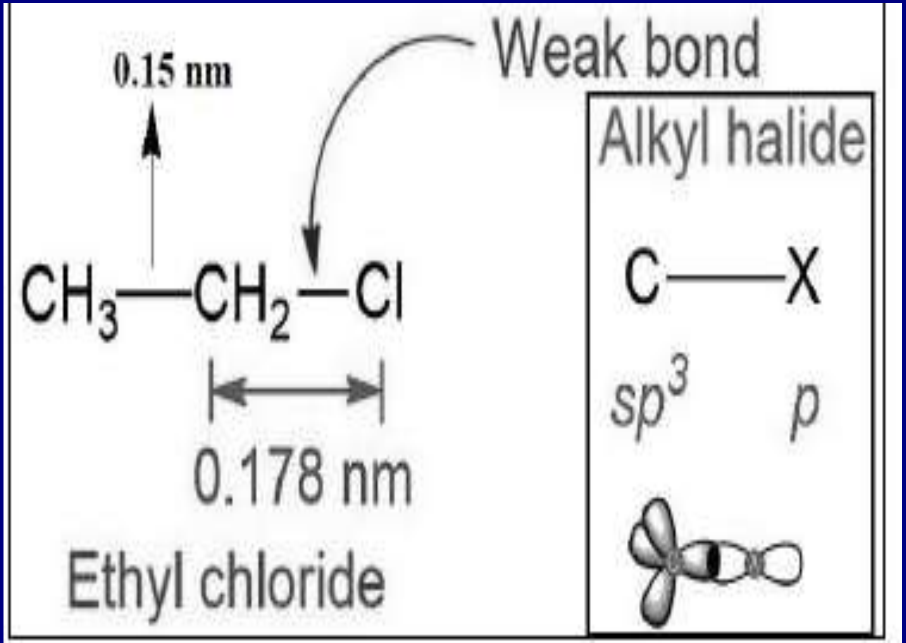


8	Stereochemistry of pdct	Racemization accompanies by inversion ≈ 75 % inversion & 25% retention	100% inversion of configuration Nucleophile attacks carbon from side opposite bond to leaving group.
9	rearrangement	Possible Carbocation intermediate capable of rearrangement.	Not possible No carbocation intermediate; no rearrangement.

ETHYL CHLORIDE

- Chloroethane or monochloroethane, commonly known by its common name ethyl chloride

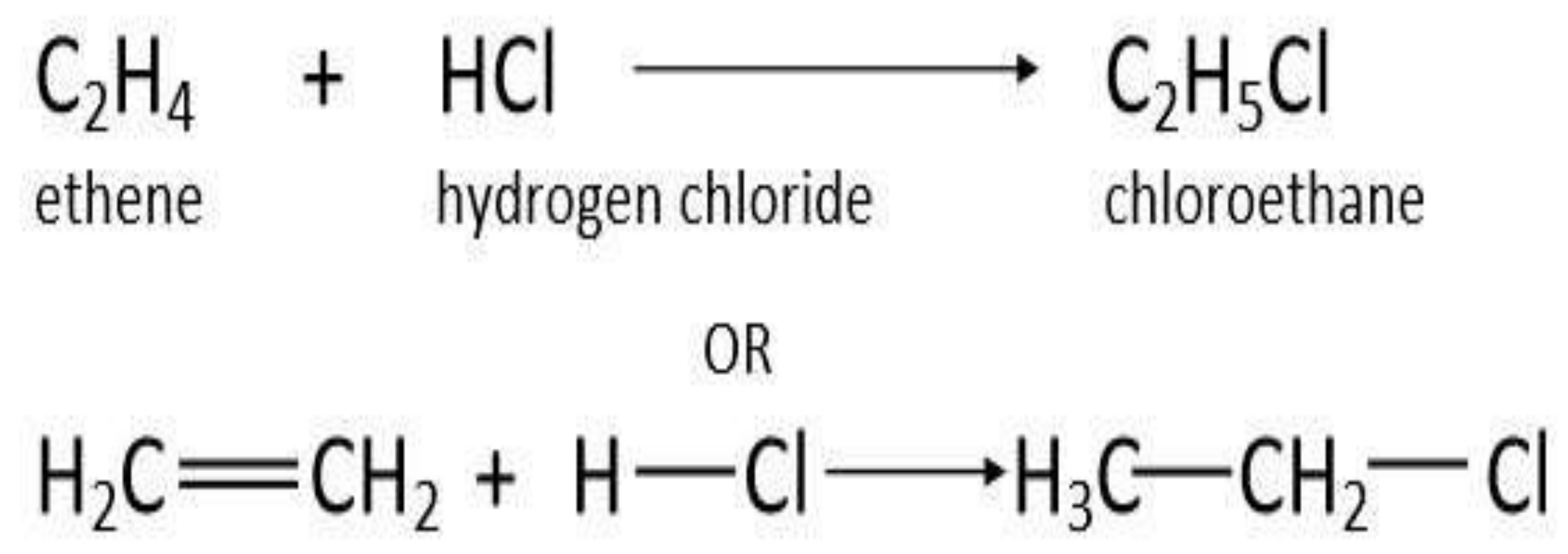




Chemical formula	C_2H_5Cl
Molar mass	64.51 g/mol
Appearance	Colorless gas
Odor	Pungent
Density	0.8898 g/cm^3 (25° C)
Melting point	−138.7 °C
Boiling point	12.27 °C decomposes at 510° C
Solubility in water	0.574 g/100 mL (20 °C)
Solubility	Soluble in alcohol, ether
Refractive index (n_D)	1.3676 (20 °C); 1.001 (25 °C)
Viscosity	0.279 cP
Dipole moment	2.06 D

PREPARATION OF ETHYL CHLORIDE

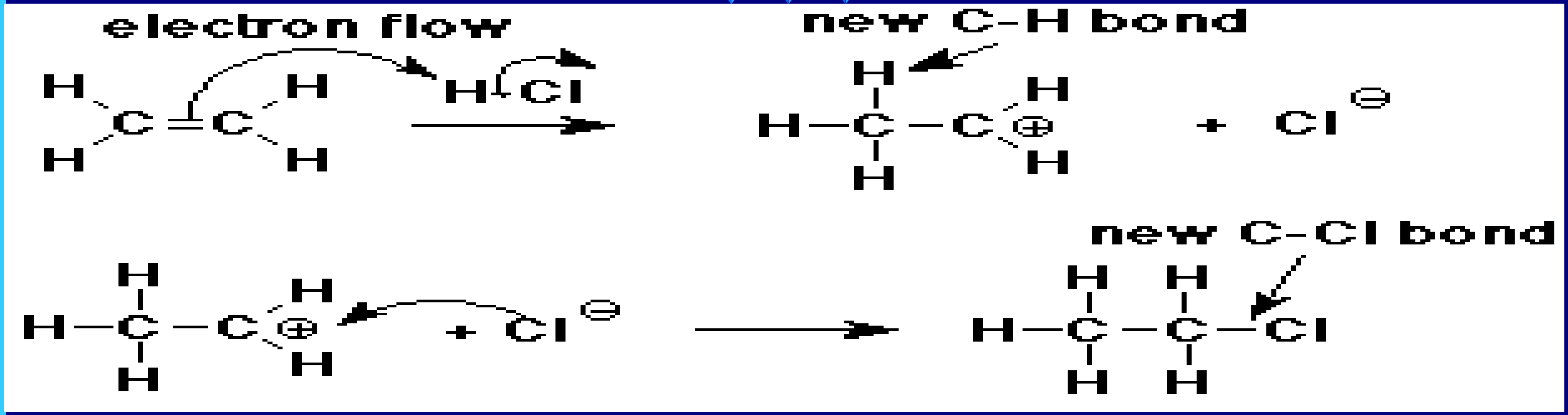
Chloroethane is produced by hydrochlorination of ethene:



$$C_2H_4 + HCl \longrightarrow C_2H_5Cl$$

OR

$$H_2C{=}CH_2 + H{-}Cl \longrightarrow H_3C{-}CH_2{-}Cl$$



The double bond in ethene is a site of high electron density (4 electrons in all). During the reaction, electrons in this site are pulled towards the partially positive H atom in HCl causing a pair of electrons to attack the hydrogen atom. This is shown by the curly full arrow beginning from the double bond and ending on the H atom. This also causes the bond between C and Cl to break by heterolytic fission.

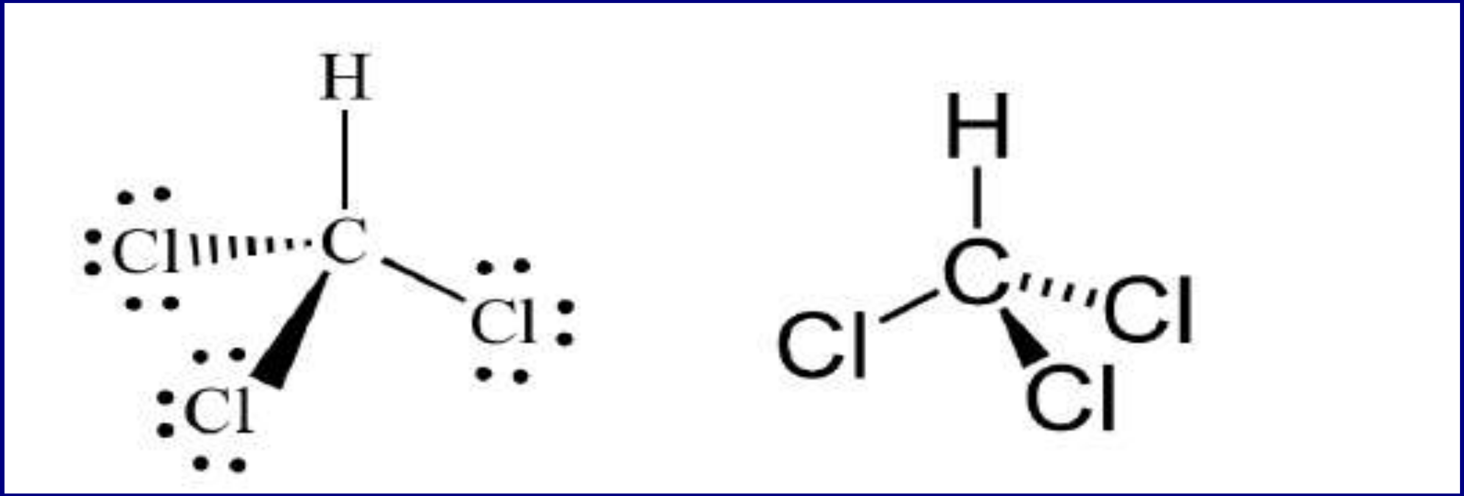
USES OF ETHYL CHLORIDE

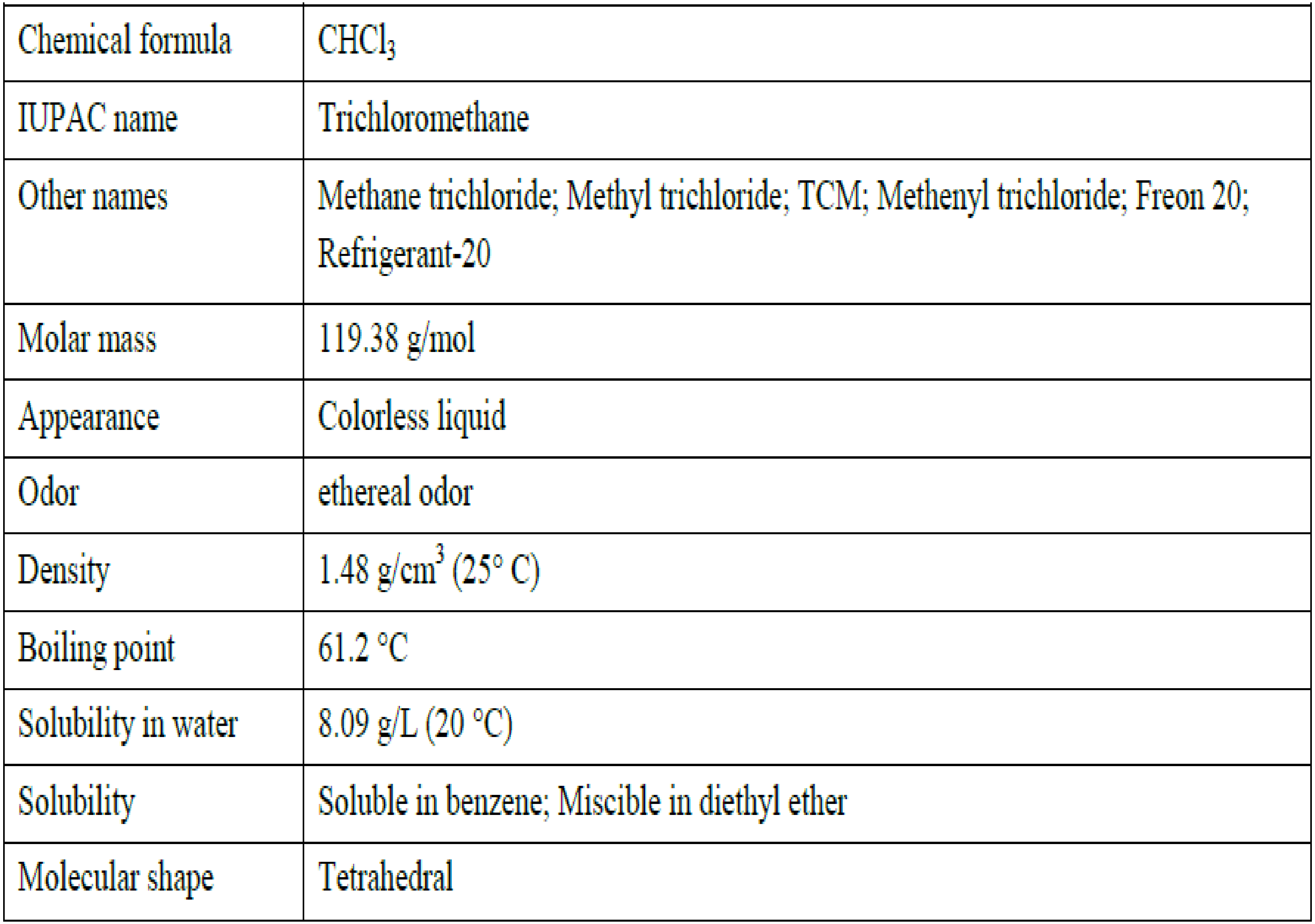
- **The major use of Chloroethane was to produce tetra ethyl lead.**
- **TEL: It is a petro-fuel additive, an anti-knock additive for gasoline.**
- **Gasoline or petrol is a transparent, petroleum-derived liquid that is used primarily as a fuel in internal combustion engines.**
- **- Chloroethane has been used as a refrigerant, an aerosol spray propellant, an anesthetic, and a blowing agent for foam packaging.**

- In dentistry, Chloroethane is used as one of the means of diagnosing a 'dead tooth', i.e. one in which the pulp has died.
- A small amount of the substance is placed on the suspect tooth using a cotton wad.
- Chloroethane's low boiling point creates a localized chilling effect.
- If the tooth is still alive this should be sensed by the patient as mild discomfort that subsides when the wad is removed.

CHLOROFORM

- Chloroform, or trichloromethane, is an organic compound with formula $CHCl_3$. It is a colorless, sweet-smelling, dense liquid





Chemical formula	$CHCl_3$
IUPAC name	Trichloromethane
Other names	Methane trichloride; Methyl trichloride; TCM; Methenyl trichloride; Freon 20; Refrigerant-20
Molar mass	119.38 g/mol
Appearance	Colorless liquid
Odor	ethereal odor
Density	1.48 g/cm^3 (25° C)
Boiling point	61.2 °C
Solubility in water	8.09 g/L (20 °C)
Solubility	Soluble in benzene; Miscible in diethyl ether
Molecular shape	Tetrahedral

Chloroform-Production

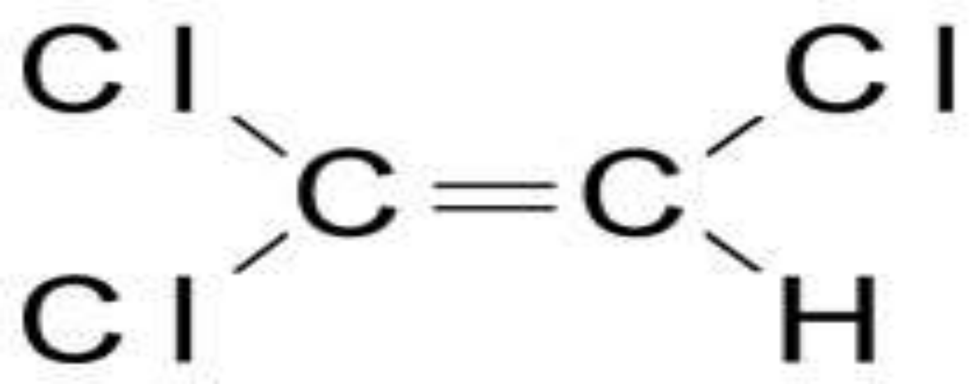
- Industrially, chloroform is produced by heating a mixture of chlorine and either chloromethane or methane to 400-500°C.
- At this temperature, a series of chemical reactions occur, converting the methane or chloromethane to progressively more chlorinated compounds.
- $CH_4 + Cl_2 \rightarrow CH_3Cl + HCl$
- $CH_3Cl + Cl_2 \rightarrow CH_2Cl_2 + HCl$
- $CH_2Cl_2 + Cl_2 \rightarrow CHCl_3 + HCl$
- $CHCl3 + Cl_2 \rightarrow CCl_4 + HCl$
- The output of this process is a mixture of the four chloromethanes, chloromethane, dichloromethane, chloroform (trichloromethane), and tetrachloromethane, which are then separated by distillation.

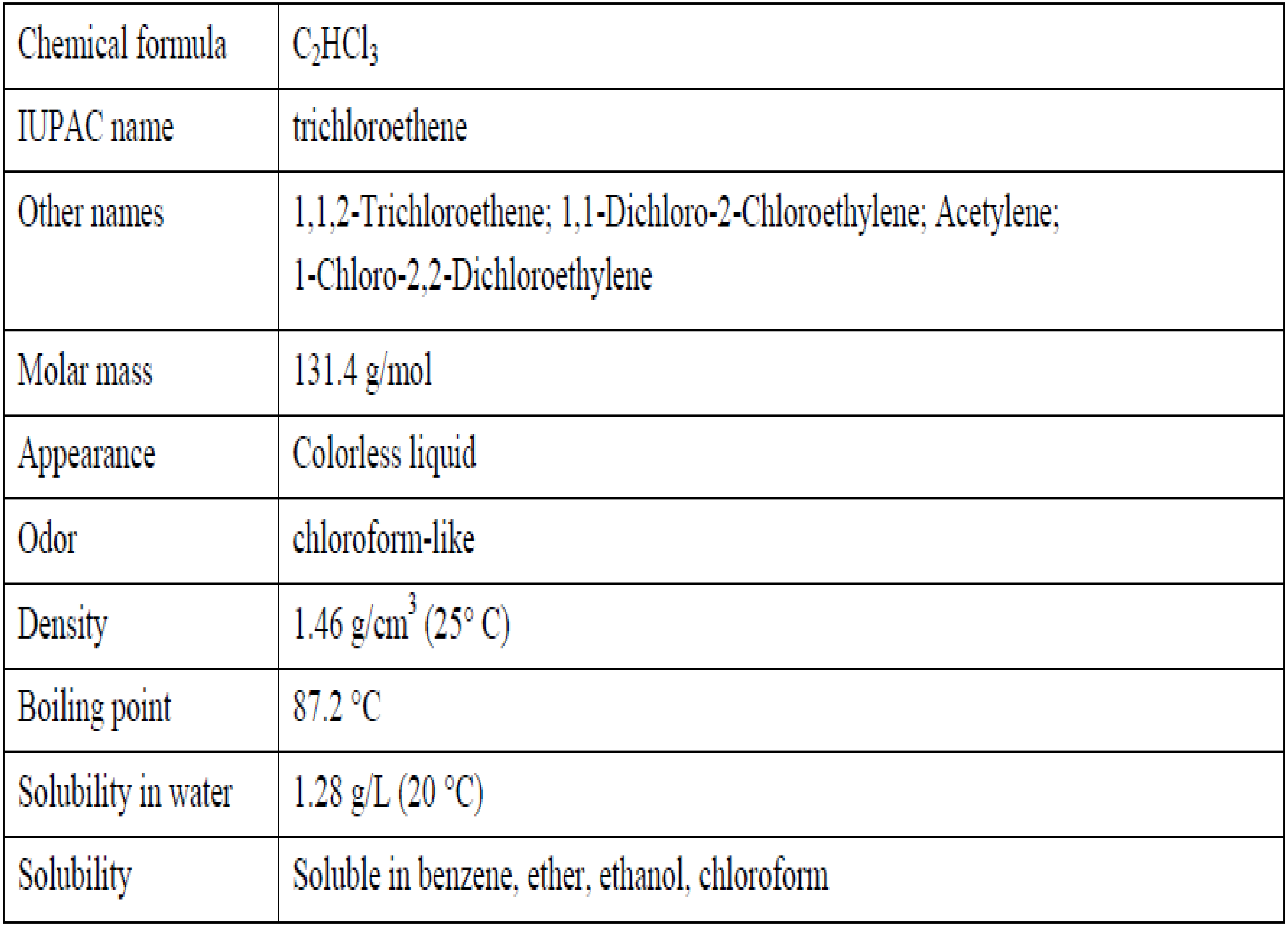
USES OF CHLOROFORM

- The hydrogen attached to carbon in chloroform participates in hydrogen bonding.
- Worldwide, chloroform is also used in pesticide formulations
- Used as a solvent for fats, oils, rubber, waxes, gutta-percha, and resins
- Used as a cleansing agent, grain fumigant, in fire extinguishers, and in the rubber industry..
- Chloroform is also used to extract and purify penicillin.
- Chloroform used for extraction and purification of Alkaloids.
- It was previously Used as anaesthetic.

TRICHLOROETHYLENE

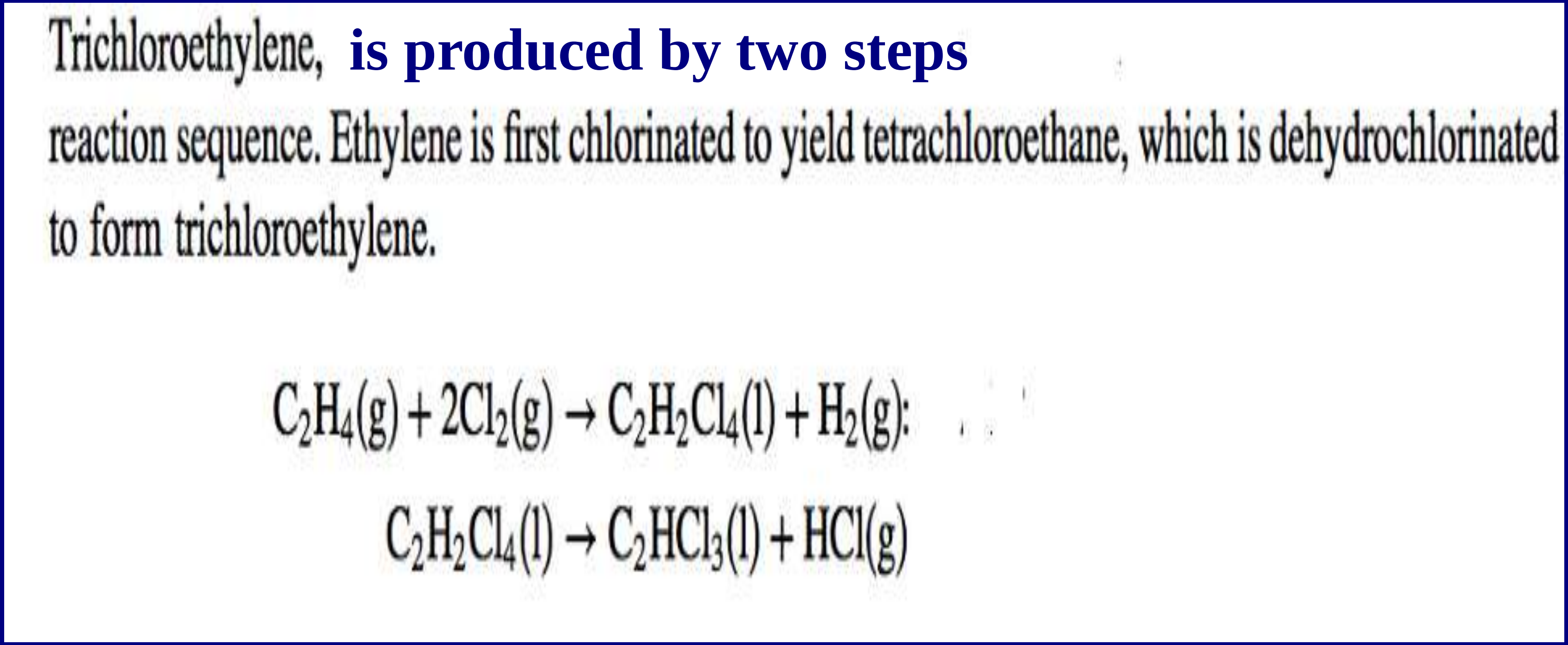
- Trichloroethylene is a halocarbon commonly used as an industrial solvent.
- It is a clear non-flammable liquid with a sweet smell.
- Trichloroethylene is not a persistent chemical in the atmosphere





Chemical formula	C_2HCl_3
IUPAC name	trichloroethene
Other names	1,1,2-Trichloroethene; 1,1-Dichloro-2-Chloroethylene; Acetylene; 1-Chloro-2,2-Dichloroethylene
Molar mass	131.4 g/mol
Appearance	Colorless liquid
Odor	chloroform-like
Density	1.46 g/cm^3 (25° C)
Boiling point	87.2 °C
Solubility in water	1.28 g/L (20 °C)
Solubility	Soluble in benzene, ether, ethanol, chloroform

PREPARATION OF TRICHLOROETHYLENE



Trichloroethylene, **is produced by two steps** reaction sequence. Ethylene is first chlorinated to yield tetrachloroethane, which is dehydrochlorinated to form trichloroethylene.

$$C_2H_4(g) + 2Cl_2(g) \rightarrow C_2H_2Cl_4(l) + H_2(g):$$

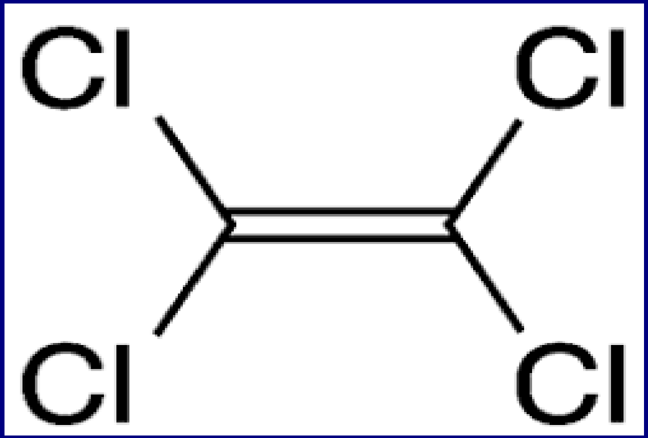
$$C_2H_2Cl_4(l) \rightarrow C_2HCl_3(l) + HCl(g)$$

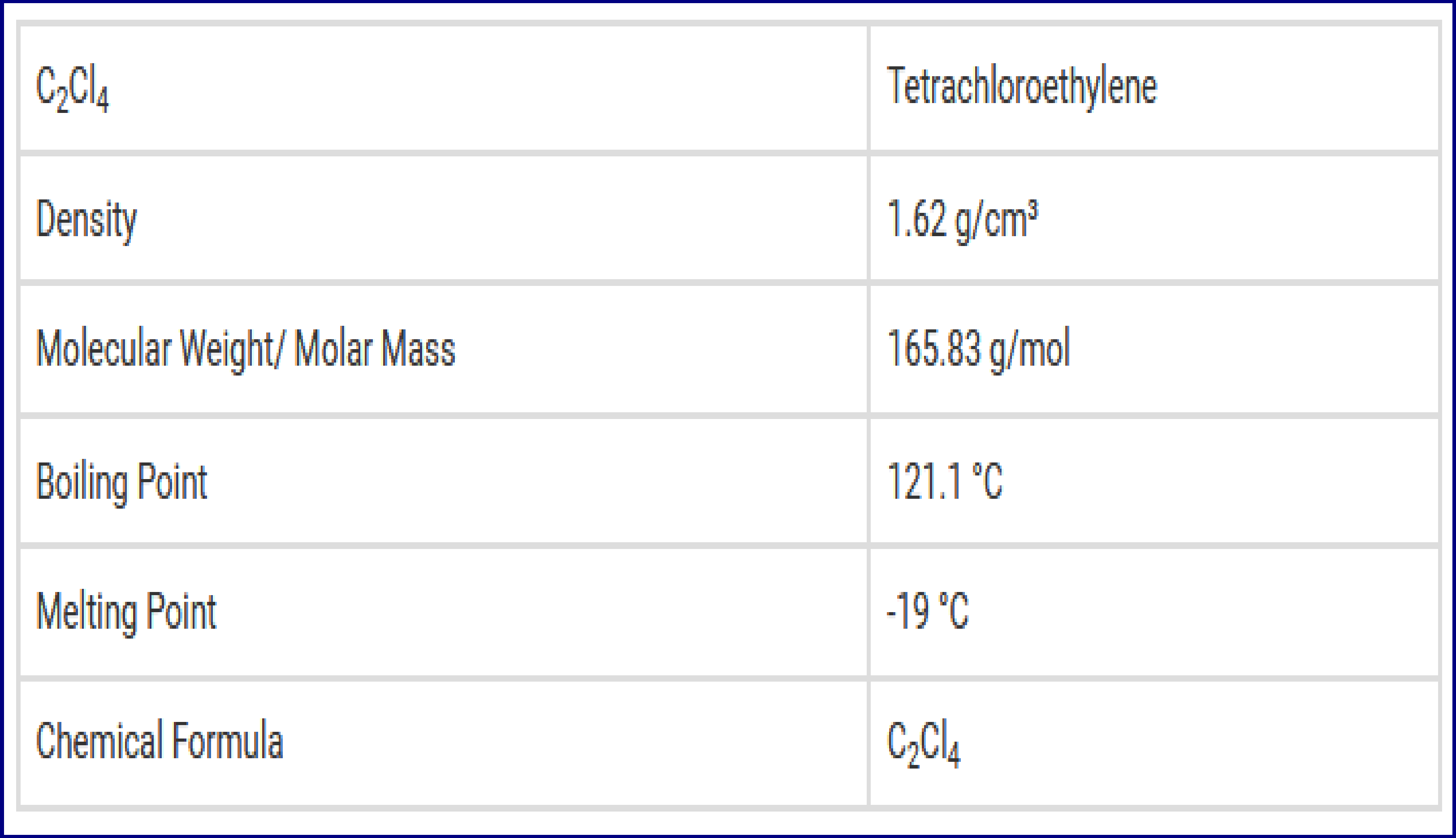
USES OF TRICHLOROETHYLENE

- The main use of trichloroethylene is vapor degreasing of metal parts.
- Trichloroethylene is also used as an extraction solvent for greases, oils, fats, waxes, and tars
- Used as a chemical intermediate in the production of other chemicals
- Used as a refrigerant.
- Trichloroethylene is used in consumer products such as typewriter correction fluids, paint removers/strippers, adhesives, spot removers, and rug (floor covering carpets)-cleaning fluids.
- Trichloroethylene was used in the past as a general anesthetic

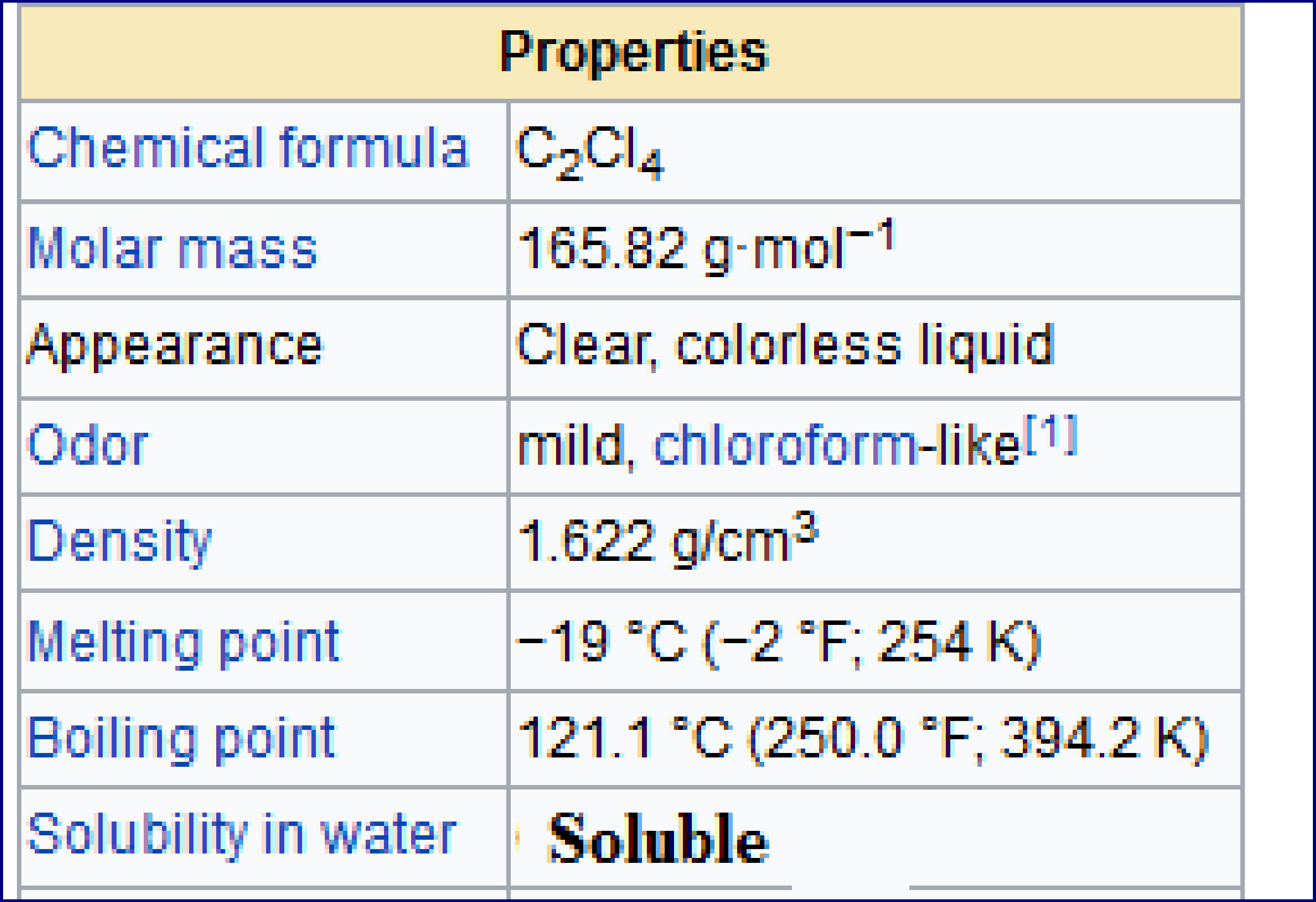
TETRACHLOROETHYLENE

- Tetrachloroethylene is a volatile chlorinated organic hydrocarbon that is widely used as a solvent
- Chemical formula C_2Cl_4.
- It is non-flammable liquid at room temperature
- Other name– Tetrachloroethene, Perchlorethylene





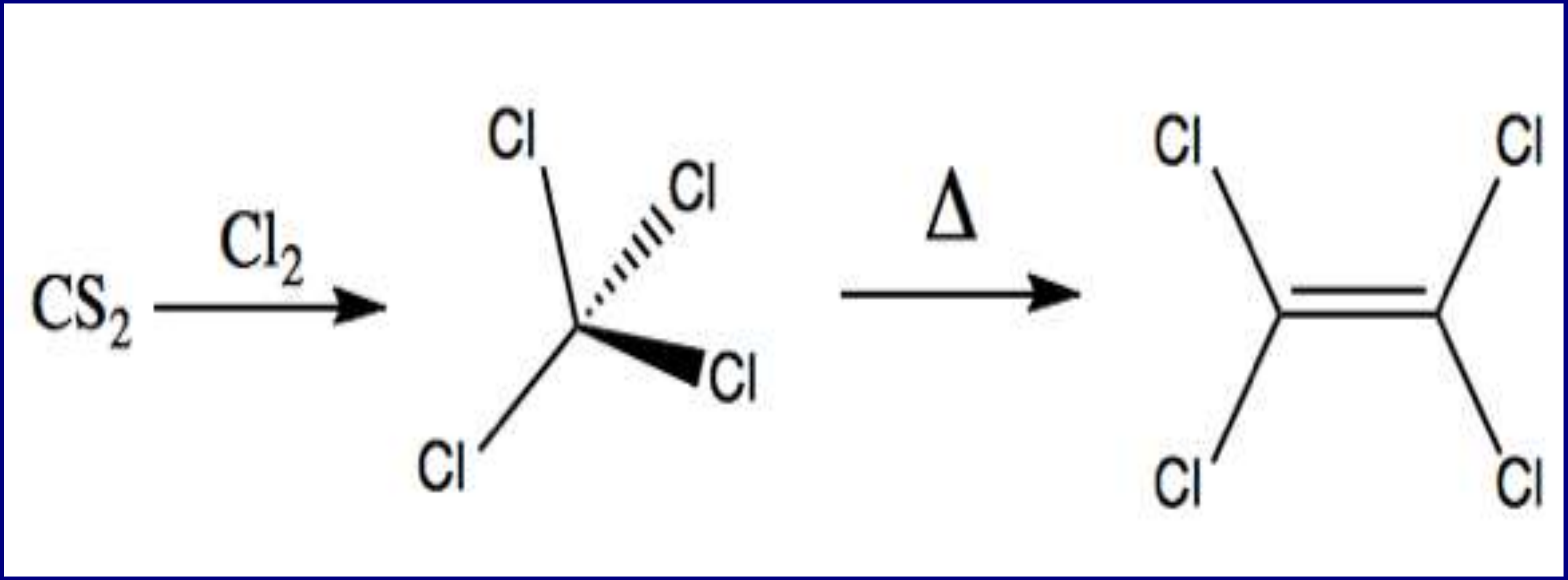
C_2Cl_4	Tetrachloroethylene
Density	1.62 g/cm³
Molecular Weight/ Molar Mass	165.83 g/mol
Boiling Point	121.1 °C
Melting Point	-19 °C
Chemical Formula	C_2Cl_4



Properties	
Chemical formula	C_2Cl_4
Molar mass	165.82 g·mol^{-1}
Appearance	Clear, colorless liquid
Odor	mild, chloroform-like[1]
Density	1.622 g/cm^3
Melting point	−19 °C (−2 °F; 254 K)
Boiling point	121.1 °C (250.0 °F; 394.2 K)
Solubility in water	**Soluble**

PREPARATION OF TETRACHLOROETHYLENE

- carbon disulfide react with chloride to obtain tetrachloroethylene

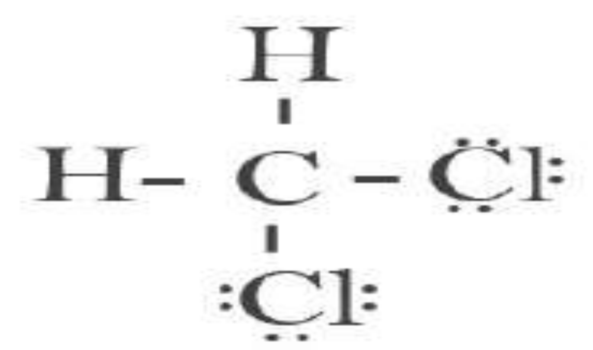


USES OF TETRACHLOROETHYLENE

- **Tetrachloroethylene is used primarily as a dry cleaning solvent, a degreasing solvent, a drying agent for metals.**
- **as a chemical precursor for fluorocarbons.**
- **It is an anthelmintic used chiefly in the treatment of hookworm infestation.**
- **Used in transformers, paint removers, inks, adhesive formulations, paper coatings and leather treatments as an insulating fluid (reduce or regulate the temperature of a system)**
- **cooling gas in aerosol (spray) formulations.**
- **Used commercially important chlorinated hydrocarbon solvent and chemical intermediate in the production of chlorofluorocarbons.**

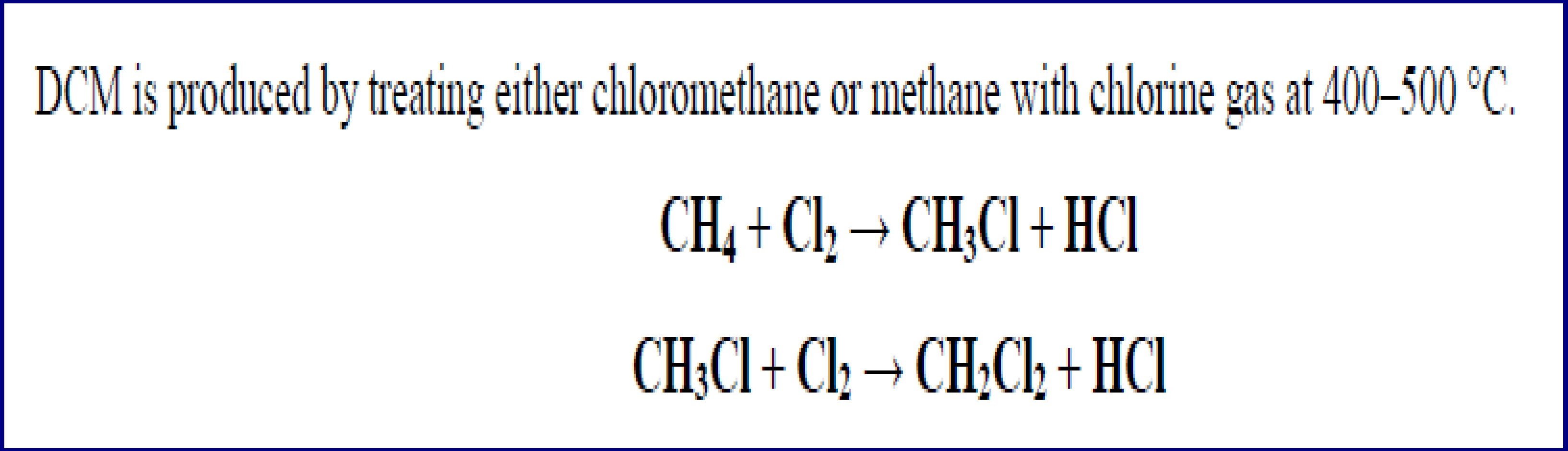
DICHLOROMETHANE

- Dichloromethane (DCM, or methylene chloride) is an organic compound with the formula CH2Cl2.
- This colorless, volatile liquid with a moderately sweet aroma is widely used as a solvent.
- Although it is not miscible with water, it is miscible with many organic solvents.
- Natural sources of dichloromethane include oceanic sources (deep ocean), *macroalgae, wetlands, and volcanoes.*
- Macroalgae are Seaweed refers to several species of macroscopic, multicellular, marine algae



Chemical formula	CH_2Cl_2
IUPAC name	Dichloromethane
Other names	Methylene chloride, methylene dichloride
Molar mass	84.93 g/mol
Appearance	Colorless liquid
Odor	chloroform-like
Density	1.32 g/cm^3 (25° C)
Boiling point	39.6 °C
Solubility in water	25.6 g/L (20 °C)
Solubility	Miscible in ethyl acetate, alcohol, hexanes, benzene, CCl_4, diethyl ether, $CHCl_3$

PREPARATION OF DICHLOROMETHANE



DCM is produced by treating either chloromethane or methane with chlorine gas at 400–500 °C.

$$CH_4 + Cl_2 \rightarrow CH_3Cl + HCl$$

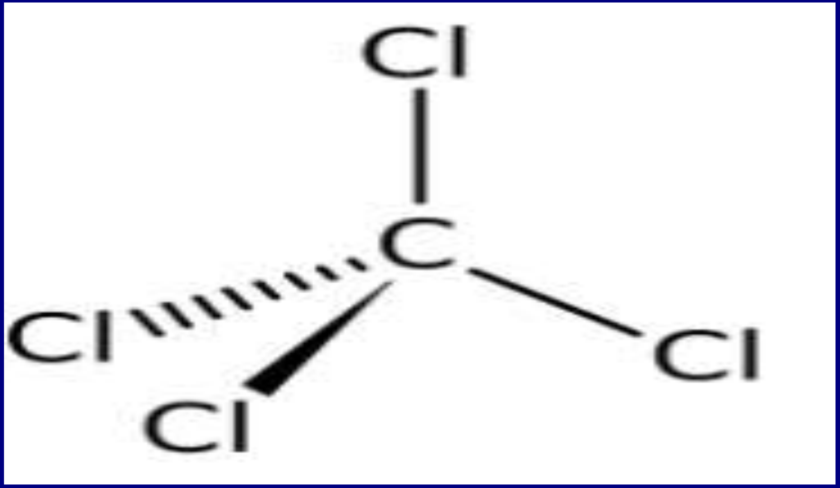
$$CH_3Cl + Cl_2 \rightarrow CH_2Cl_2 + HCl$$

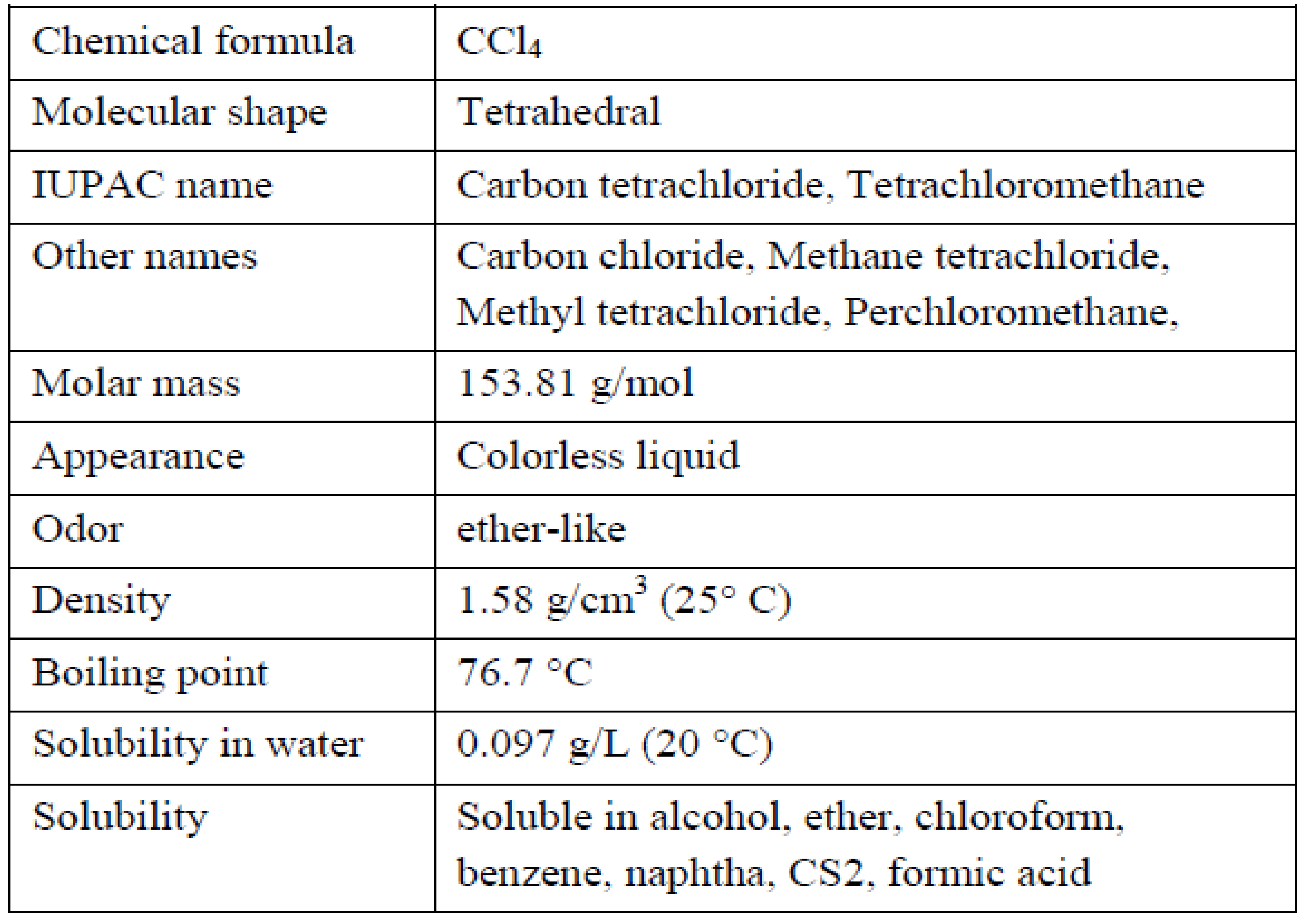
USES OF DICHLOROMETHANE

- DCM's volatility and ability to dissolve a wide range of organic compounds makes it a useful solvent for many chemical processes.
- It is widely used as a paint stripper and a degreaser.
- In the food industry, it has been used to decaffeinate coffee and tea.
- Its volatility has led to its use as an aerosol spray propellant and as a blowing agent for polyurethane foams.

TETRACHLOROMETHANE

- Tetrachloromethane also known by other name Carbon tetrachloride.
- It is a colourless liquid with a "sweet" smell that can be detected at low levels.





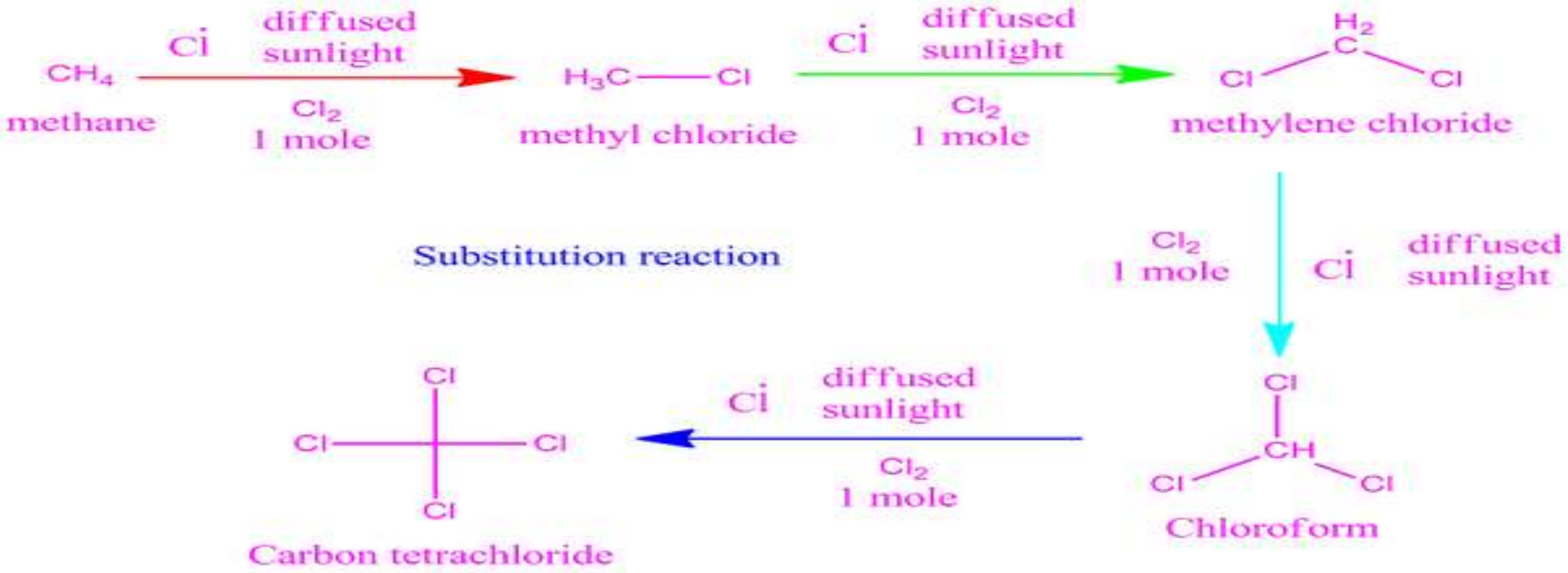
Chemical formula	CCl_4
Molecular shape	Tetrahedral
IUPAC name	Carbon tetrachloride, Tetrachloromethane
Other names	Carbon chloride, Methane tetrachloride, Methyl tetrachloride, Perchloromethane,
Molar mass	153.81 g/mol
Appearance	Colorless liquid
Odor	ether-like
Density	1.58 g/cm^3 (25° C)
Boiling point	76.7 °C
Solubility in water	0.097 g/L (20 °C)
Solubility	Soluble in alcohol, ether, chloroform, benzene, naphtha, CS2, formic acid

Preparation of Tetrachloromethane:

Cl_4 is prepared by reacting carbon disulphide (CS_2) with Cl_2 in the presence of $AlCl_3$.

$$CS_2 + 3Cl_2 \xrightarrow{\text{anhyd.}AlCl_3} CCl_4 + \underset{\text{Sulphur monochloride}}{S_2Cl_2}$$

$$2S_2Cl_2 + CS_2 \rightarrow CCl_4 + 6S$$

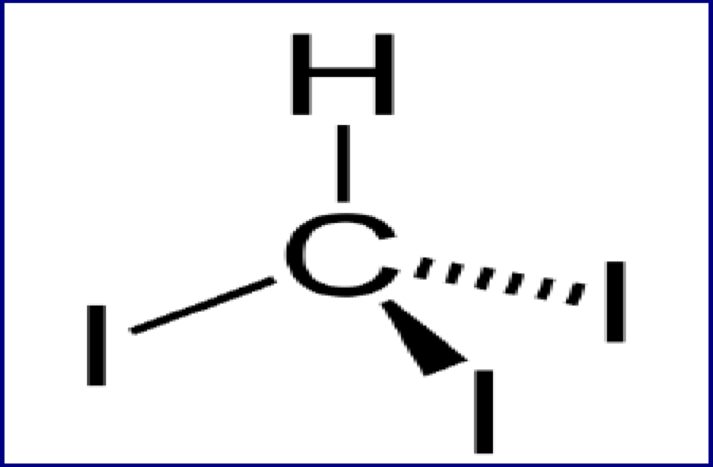


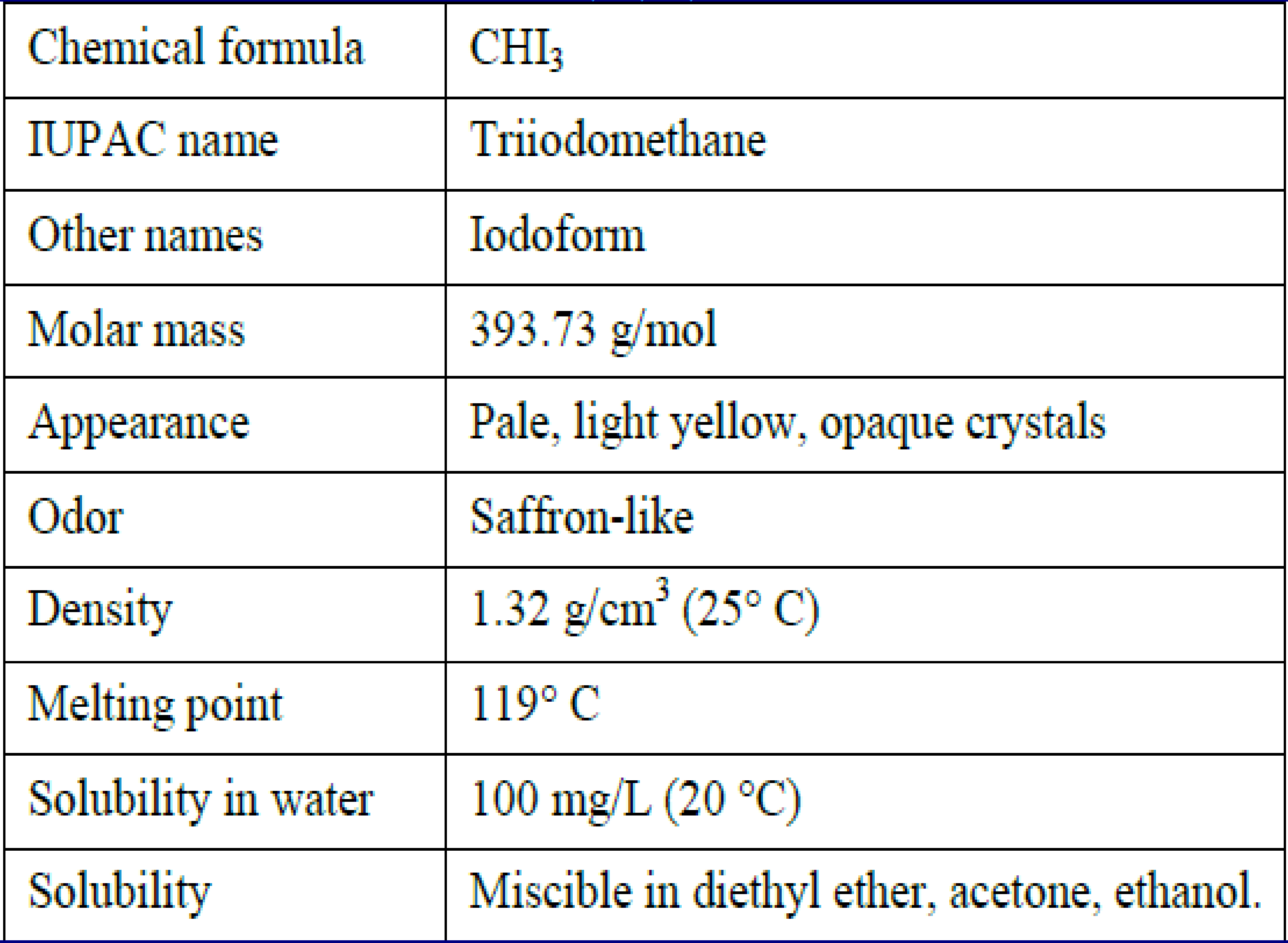
USES OF TETRACHLOROMETHANE

- Carbon tetrachloride was used to produce the chlorofluorocarbon refrigerants R-11 (trichlorofluoromethane) and R-12 (dichlorodifluoromethane).
- Carbon tetrachloride has also been used in the detection of neutrinos (neutrinos are subatomic particles produced by the decay of radioactive elements able to pass through great distances and convey astronomical information from the edge of the universe).
- It is a useful solvent for halogenations.
- Carbon tetrachloride was widely used as a dry cleaning solvent.

IODOFORM

- Iodoform is the organoiodine compound with the formula CHI3.
- A pale yellow, crystalline, volatile substance, it has a penetrating and distinctive odor and, analogous to chloroform, sweetish taste.
- It is also known as tri-iodomethane, carbon triiodide, and methyl triiodide



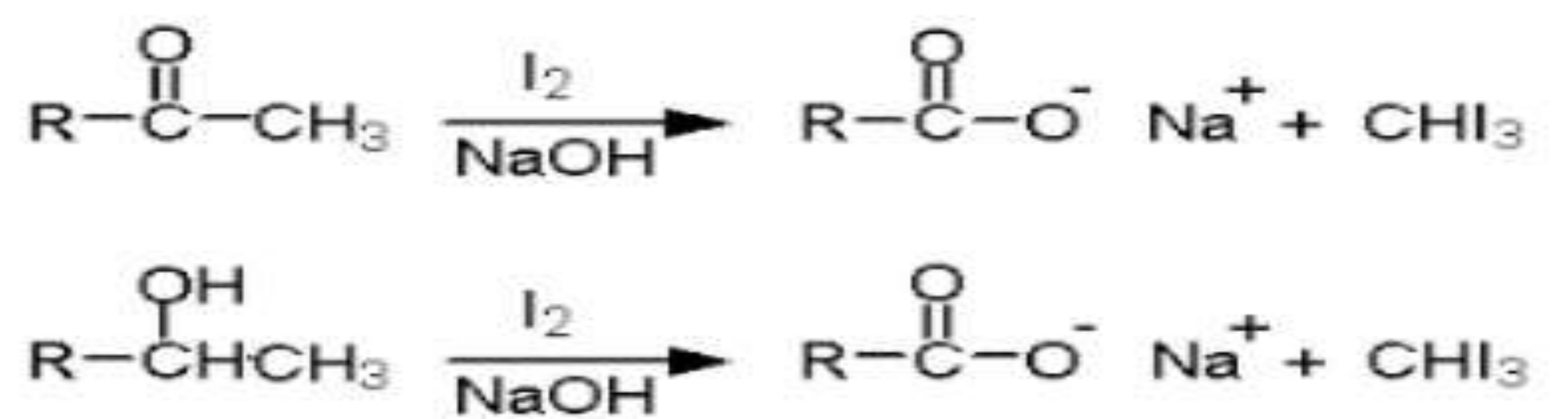


Chemical formula	CHI_3
IUPAC name	Triiodomethane
Other names	Iodoform
Molar mass	393.73 g/mol
Appearance	Pale, light yellow, opaque crystals
Odor	Saffron-like
Density	1.32 g/cm^3 (25° C)
Melting point	119° C
Solubility in water	100 mg/L (20 °C)
Solubility	Miscible in diethyl ether, acetone, ethanol.

PREPARATION OF IODOFORM

- Iodoform can be produced by the exhaustive halogenation of a methyl ketone.

- Any compound containing CH_3CO- or CH3CH(OH)– group, when heated with iodine and aqueous NaOH gives yellow precipitate of iodoform.The reaction is known as iodoforin reaction.



$$R-\overset{\overset{O}{\|}}{C}-CH_3 \xrightarrow[NaOH]{I_2} R-\overset{\overset{O}{\|}}{C}-O^- \; Na^+ + CHI_3$$

$$R-\overset{\overset{OH}{|}}{C}HCH_3 \xrightarrow[NaOH]{I_2} R-\overset{\overset{O}{\|}}{C}-O^- \; Na^+ + CHI_3$$

USES OF IODOFORM

- The compound finds small-scale use as a **disinfectant.**

- It was used in medicine as a healing and **antiseptic dressing** for wounds and sores.

- It is the active ingredient in many ear powders for dogs and cats, along with zinc oxide and propanoic acid, which are used to prevent infection and facilitate removal of ear hair.

MCQ QUESTIONS

The number of molecules taking part in the rate determining step is called

a) Order of reaction

b) Rate of reaction

c) Mole of a reaction

d) Extent of a reaction

- **Answer:** Order of reaction (a)

Nuclephile has more effect in the modification of rate of reaction of

a) SN1
b) SN2
c) Both SN1 & SN2
d) None of the above

- **Answer:** SN2 (b)

Increase in number of R groups in SN2 reaction

a) Increase the rate of reaction

b) Decrease the rate of reaction

c) No effect on the rate of reaction

Answer: Decrease the rate of reaction (b)

Rearrangement of carbocation observed in

a) SN1
b) SN2
c) Both
d) None of the above

- **Answer:** SN1 (a)

Protic solvents

a) Enhances the rate of SN1 reaction
b) Decreases the rate of SN1 reaction
c) Enhances the rate of SN2 reaction
d) None of the above

Answer: Enhances the rate of SN1 reaction (a)