

Organic Chemistry

244 CHEM

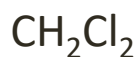
ORGANIC HALOGEN COMPOUNDS

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5

Classes of Organohalogen Compounds (Organohalides):

1) **Alkyl halides:** a halogen atom is bonded to an sp^3 -hybridized carbon.



dichloromethane trichloromethane iodomethane dichlorodifluoromethane

methylene chloride

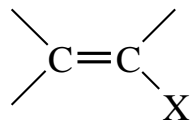
chloroform

methyl iodide

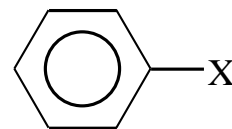
Freon-12

2) **Vinyl halides:** a halogen atom is bonded to an sp^2 -hybridized carbon.

3) **Aryl halides:** a halogen atom is bonded to an sp^2 -hybridized aromatic carbon.

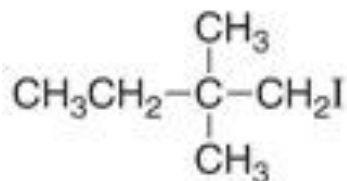


A vinylic halide

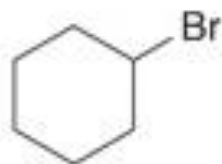


A phenyl halide or aryl halide

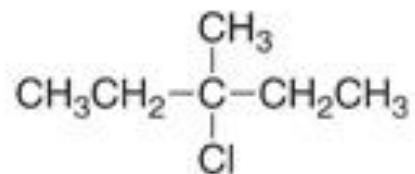
Examples of 1°, 2°, and 3° alkyl halides



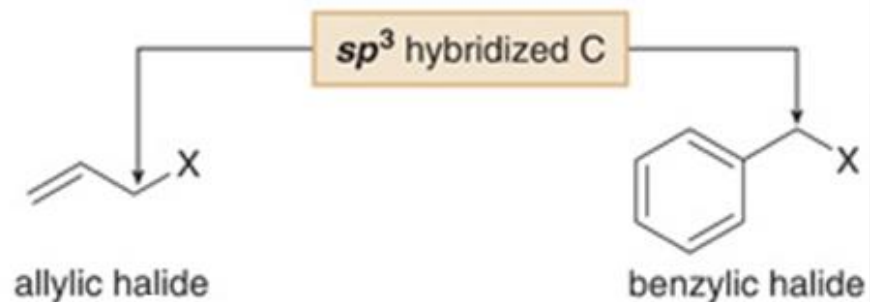
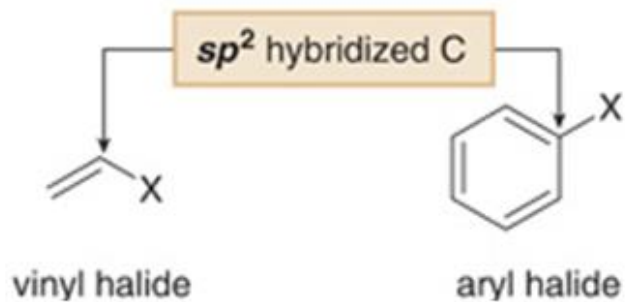
1° iodide



2° bromide



3° chloride



Importance of Organohalogen Compounds

a) Solvents: Alkyl halides are used as **solvents** for **relatively non-polar compounds**:

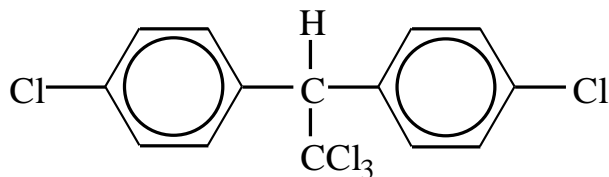


b) Reagents:

- Alkyl halides are used as the **starting materials** for the **synthesis of many compounds**.
- Alkyl halides are used in **nucleophilic reactions, elimination reactions, formation of organometallics, and etc.**

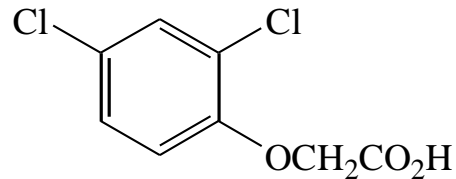
c) Refrigerants: Freons (**ChloroFluoroCarbon**)

d) Pesticides: DDT, Aldrin, Chlordan



DDT:
[1,1,1-trichloro-2,2-
bis(*p*-chlorophenyl)ethane]

e) Herbicides: Kills broad leaf weeds but allow narrow leaf plants to grow unharmed and in greater yield



2,4-D
2,4-dichlorophenoxyacetic acid

Carbon-Halogen Bond Lengths, Bond Strength and Dipole Moment

Bond	Bond Length (Å)	Bond Strength (Kcal/mol)	Dipole Moment (D)
CH ₃ -F	1.39	109	1.82
CH ₃ -Cl	1.78	84	1.94
CH ₃ -Br	1.93	70	1.79
CH ₃ -I	2.14	56	1.64

The size of the halogen atom increases going down the periodic table \Rightarrow the C-X bond length increases going down the periodic table.

Physical Properties of Organic Halides

Group	Flouride		Chloride		Bromide		Iodide	
	bp (°C)	Density (g mL ⁻¹)	bp (°C)	Density (g mL ⁻¹)	bp (°C)	Density (g mL ⁻¹)	bp (°C)	Density (g mL ⁻¹)
Methyl	-78.4	0.84 ⁻⁶⁰	-23.8	0.92 ²⁰	3.6	1.73 ⁰	42.5	2.28 ²⁰
Ethyl	-37.7	0.72 ²⁰	13.1	0.91 ¹⁵	38.4	1.46 ²⁰	72	1.95 ²⁰
Propyl	-2.5	0.78 ⁻³	46.6	0.89 ²⁰	70.8	1.35 ²⁰	102	1.74 ²⁰
Butyl	32	0.78 ²⁰	78.4	0.89 ²⁰	101	1.27 ²⁰	130	1.61 ²⁰
CH ₂ =CH-	-72	0.68 ²⁶	-13.9	0.91 ²⁰	16	1.52 ¹⁴	56	2.04 ²⁰
CH ₂ =CHCH ₂	-3		45	0.94 ²⁰	70	1.40 ²⁰	102-103	1.84 ²²
C ₆ H ₅ -	85	1.02 ²⁰	132	1.10 ²⁰	155	1.52 ²⁰	189	1.82 ²⁰
C ₆ H ₅ CH ₂ -	140	1.02 ²⁵	179	1.10 ²⁵	201	1.44 ²²	93 ¹⁰	1.73 ²⁵

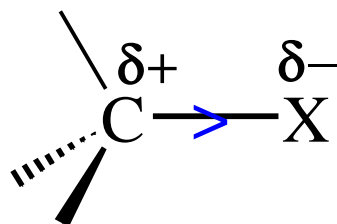
Solubilities:

- ❑ Many alkyl and aryl halides have very low solubilities in water, but they are miscible with each other and with other relatively nonpolar solvents.
- ❑ Dichloromethane (CH_2Cl_2 , *methylene chloride*), trichloromethane (CHCl_3 , *chloroform*), and tetrachloromethane (CCl_4 , *carbon tetrachloride*) are often used as solvents for nonpolar and moderately polar compounds.

Boiling points:

- Methyl iodide (bp 42 °C) is the only monohalomethane that is a liquid at room temperature and 1 atm pressure.
- Ethyl bromide (bp 38 °C) and ethyl iodide (bp 72 °C) are both liquids, but ethyl chloride (bp 13 °C) is a gas.
- The propyl chlorides, propyl bromides, and propyl iodides are all liquids.
- In general, higher alkyl chlorides, bromides, and iodides are all liquids and tend to have boiling points near those of alkanes of similar molecular weights.
- **Polyfluoroalkanes** tend to have **unusually low boiling points**.
- Hexafluoroethane boils at -79 °C, even though its molecular weight (MW = 138) is near that of decane (MW = 144; bp 174 °C).

Polarity of C–X bond:

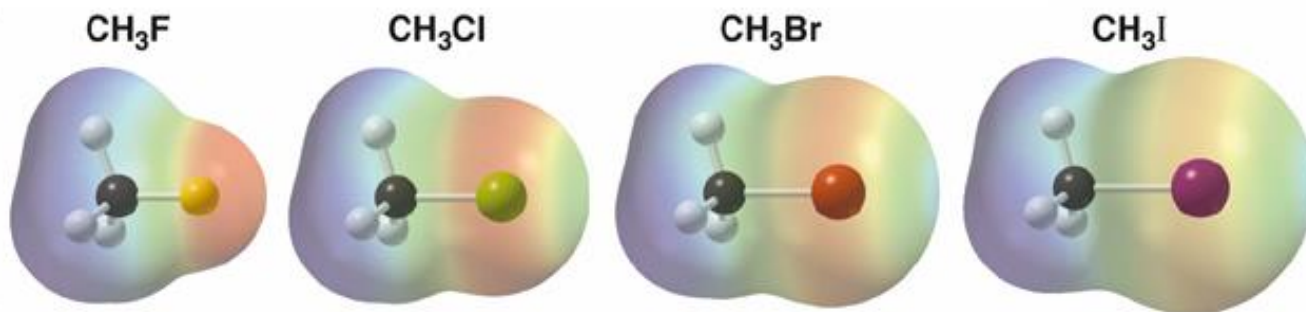
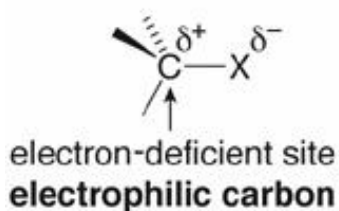


- The carbon-halogen bond of alkyl halides is **polarized**.
- The **carbon** atom bears a partial **positive** charge, the **halogen** atom a partial **negative** charge.
- They exhibit **dipole-dipole** interactions because of their polar C–X bond, but because the rest of the molecule contains only C–C and C–H bonds, they are **incapable of intermolecular hydrogen bonding**.

- 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.

Electrostatic potential maps of four halomethanes (CH_3X)

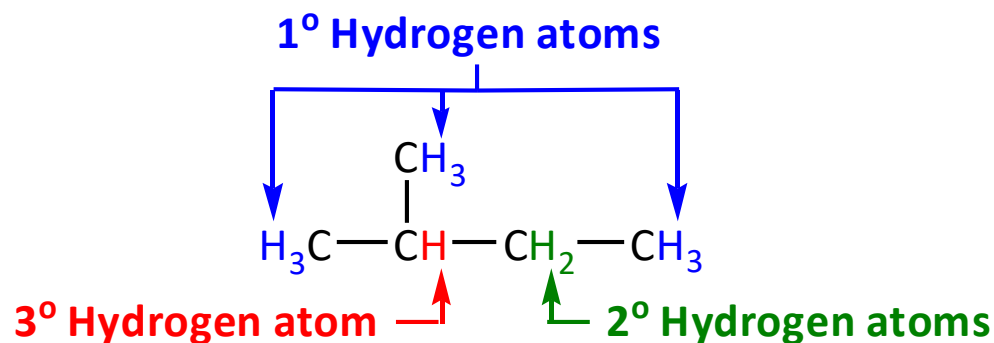
General structure



- The polar C—X bond makes the carbon atom *electron deficient* in each CH_3X molecule.

NOMENCLATURE OF ALKYL HALIDES

Halogen atoms are classified on the basis of the carbon atom to which they are attached as may be primary 1° , secondary 2° or tertiary 3° exactly as the hydrogen atom:

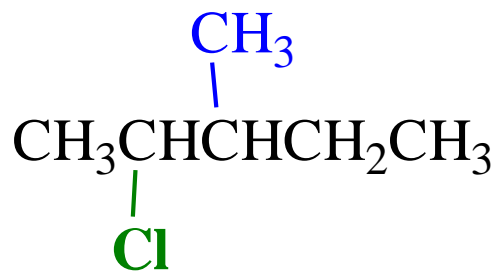


1- Haloalkanes:

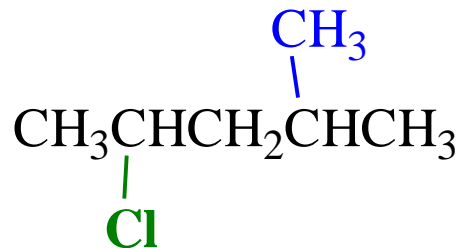
1. Find longest chain, name it as parent chain (Contains double or triple bond if present)
2. Number from end nearest any substituent (alkyl or halogen)

	$\text{CH}_3\text{CH}_2\text{Cl}$	$\text{CH}_3\text{CH}_2\text{CH}_2\text{F}$	$\text{CH}_3\text{CHBrCH}_3$
IUPAC name	Chloroethane	1-Fluoropropane	2-Bromopropane
Common name	Ethyl chloride	<i>n</i>-Propyl fluoride	Isopropyl bromide
Class of carbon	1°	1°	2°

When the parent chain has both a halo and an alkyl substituent attached to it, **number the chain from the end nearer the first substituent.**

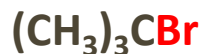


2-Chloro-3-methylpentane



2-Chloro-methylpentane

Common names for simple haloalkanes are accepted by the IUPAC \Rightarrow alkyl halides (*radicofunctional nomenclature*).



2-Bromo-
2methylpropane

tert-Butyl bromide



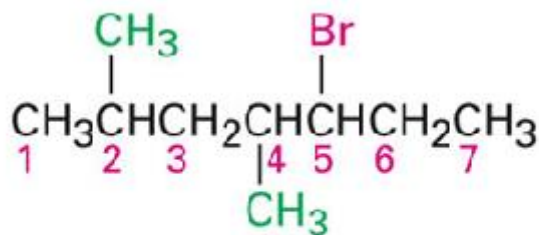
1-Chloro-2-methylpropane

Isobutyl chloride

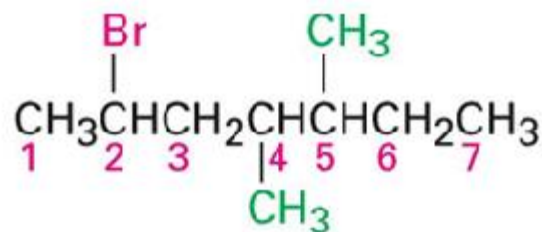


1-Bromo-2,2-dimethylpropane

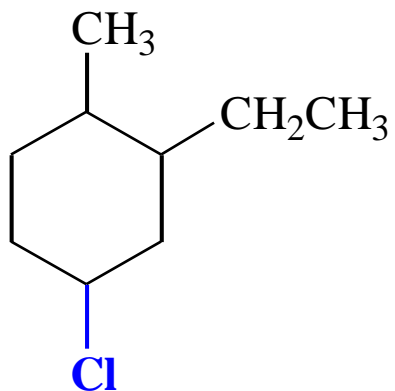
Neopentyl bromide



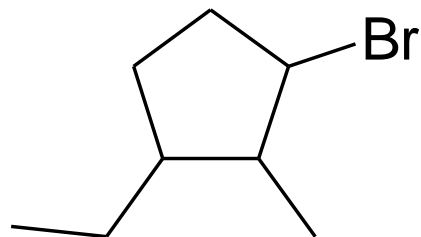
5-Bromo-2,4-dimethylheptane



2-Bromo-4,5-dimethylheptane



4-Chloro-2-ethyl-1-methylcyclohexane
(not **1-Chloro-3-ethyl-4-methylcyclohexane**)



1-Bromo-3-ethyl-2-methylcyclopentane
not **1-bromo-2-methyl-3-ethylcyclopentane**

Preparation of Organic Halogen Compounds

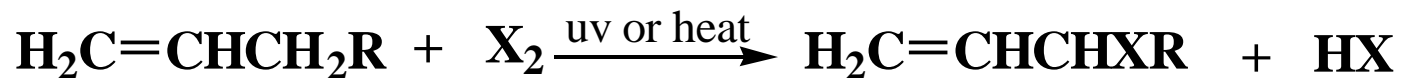
Chloro, Bromo, and Iodo Compounds

Direct halogenation of hydrocarbons.

a) Halogenation of alkanes: **Alkyl halides**



b) Halogenation of alkenes: **Allyl halides**



c) Halogenation of alkyl benzenes: **Benzyl halides**



d) Halogenation of aromatic ring: **Aryl halides**

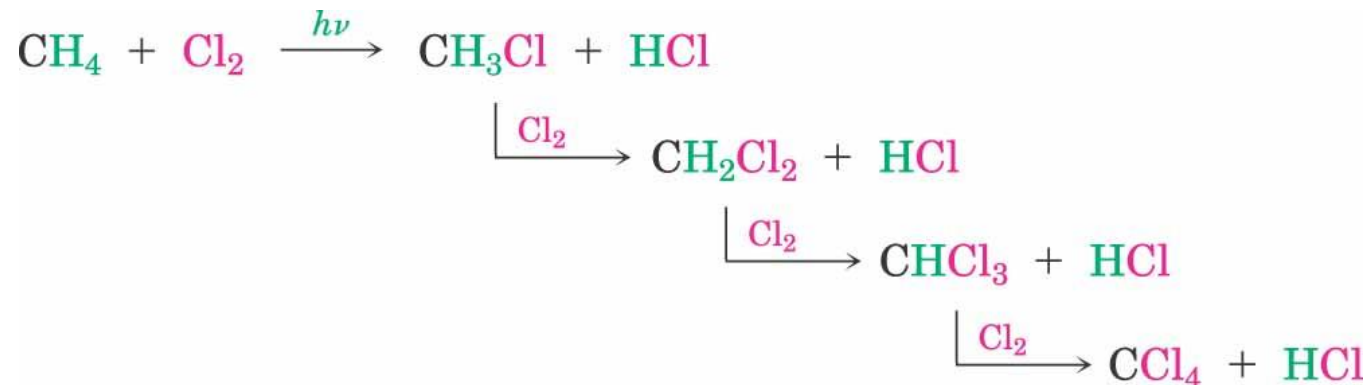


Halogenation of Alkanes



Reactivity: $\text{F}_2 \gg \text{Cl}_2 > \text{Br}_2 \gg \text{I}_2$

Chlorination of Methane

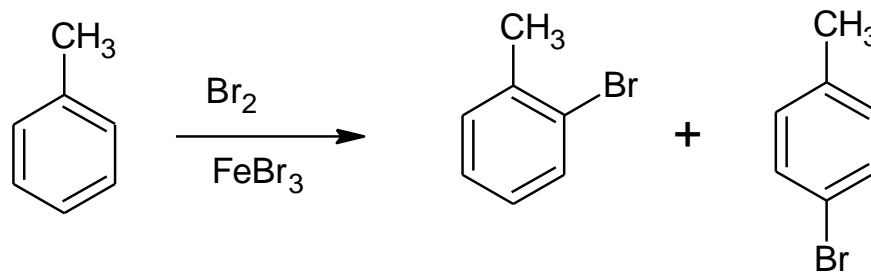
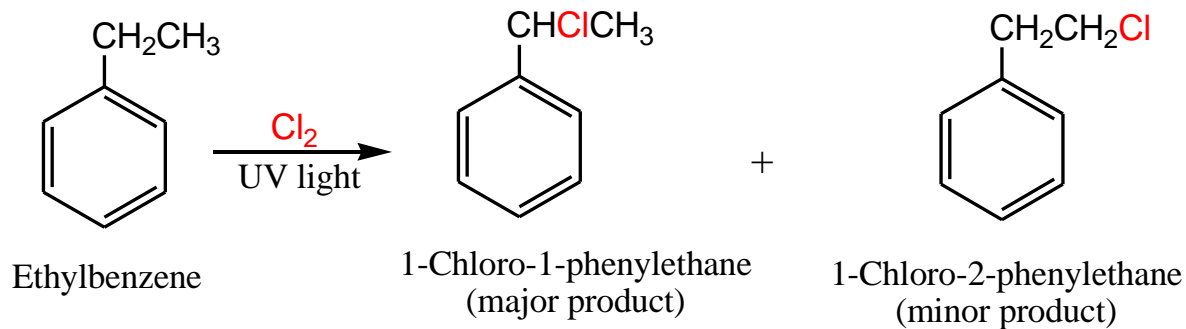
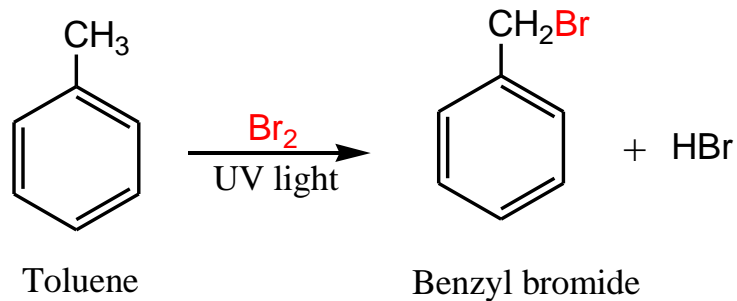


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Mechanism of free radical halogenation has three distinct steps

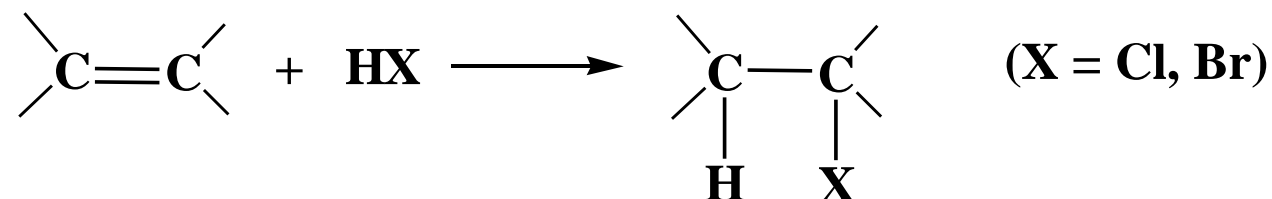
1. Initiation
2. Propagation
3. Termination

Free radical chlorination is not very useful for making alkyl chlorides: polychlorination, non-specific chlorination

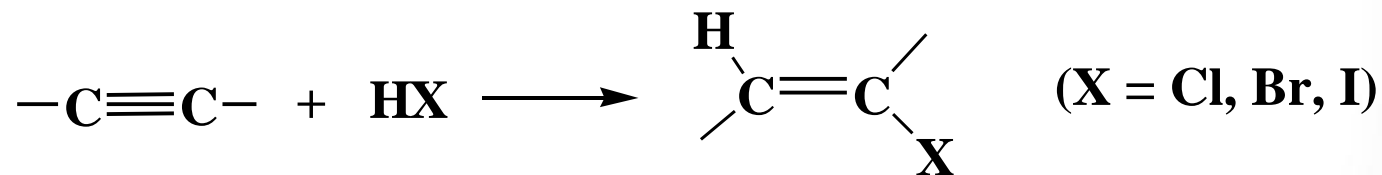


Addition of HX to unsaturated hydrocarbons

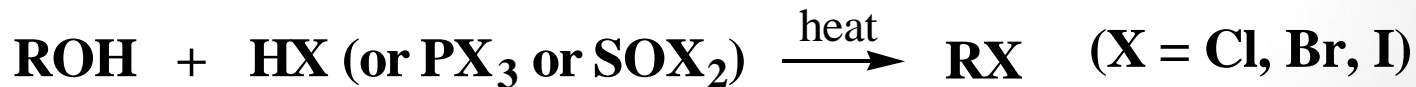
a) Addition of HX to alkenes: **Alkyl halides**



b) Addition of HX to alkynes: **Vinyl halides**



Conversion of alcohols: Alkyl halides



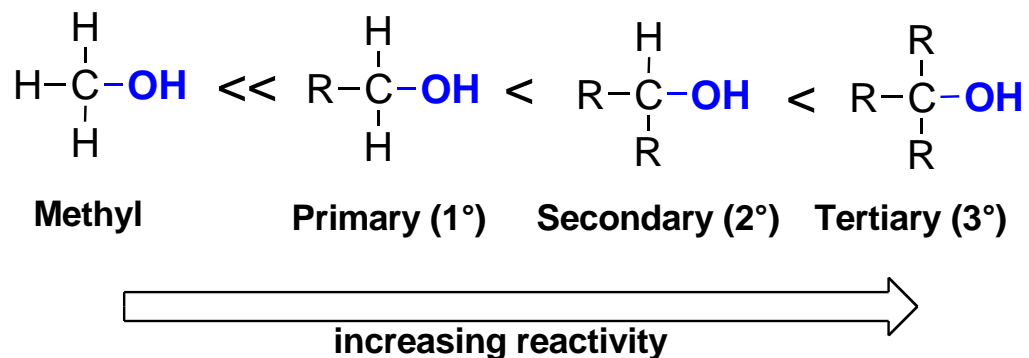
Reaction of Primary Alcohols with Hydrogen Halides:

The S_N2 Mechanism:

Methyl and primary carbocations are the least stable, and they are not likely to be intermediates in reaction mechanism



Reactivity of the alcohol:



Reactivity of the H-X : parallels the acidity of HX

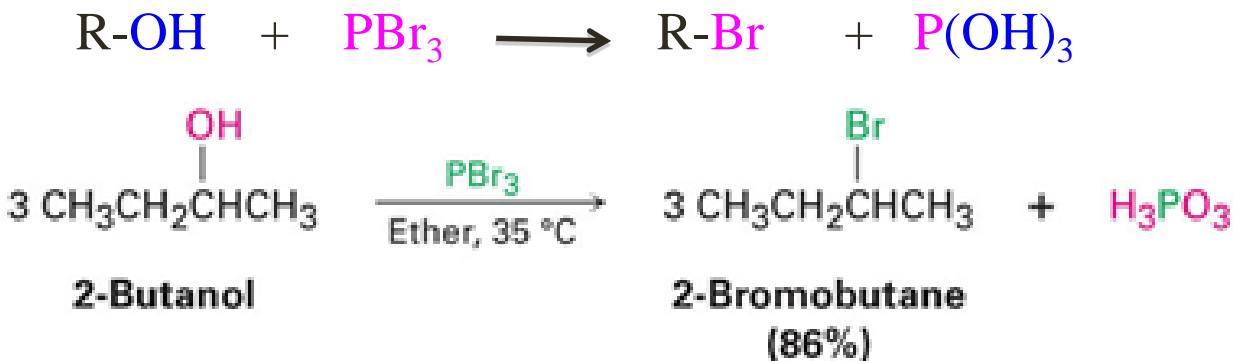


Other Methods for Converting Alcohols to Alkyl Halides

Preparation of alkyl chlorides by the treatment of alcohols with *thionyl chloride* (SOCl_2)



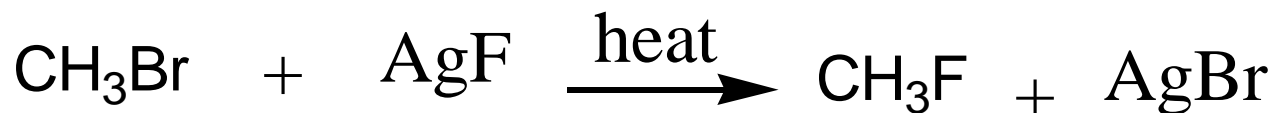
Preparation of alkyl bromides by the treatment of alcohols with *phosphorous tribromide* (PBr_3)



These methods work best on primary and secondary alcohols. They do not work at all for tertiary alcohols

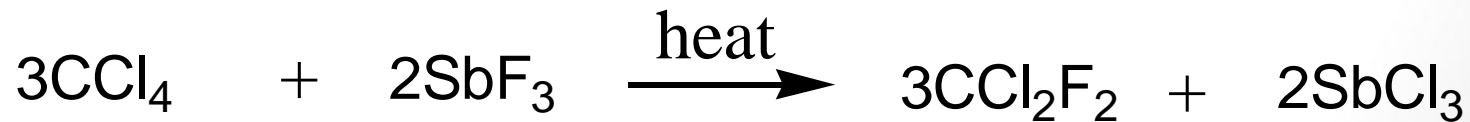
Halogen Exchange: A Way to Alkyl Fluorides

➔ An alkyl chloride or bromide is heated in the presence of a metallic fluoride such as AgF, Hg₂F₂, or SbF₃.



➔ The manufacture of chlorofluoro compounds, known as Freons.

The simplest Freon, CCl₂F₂, is made as follows.



Chemical Properties of Organic Halogen Compounds

There are three main classes of reactions for the organic halogen compounds; these are :

Nucleophilic Substitution,

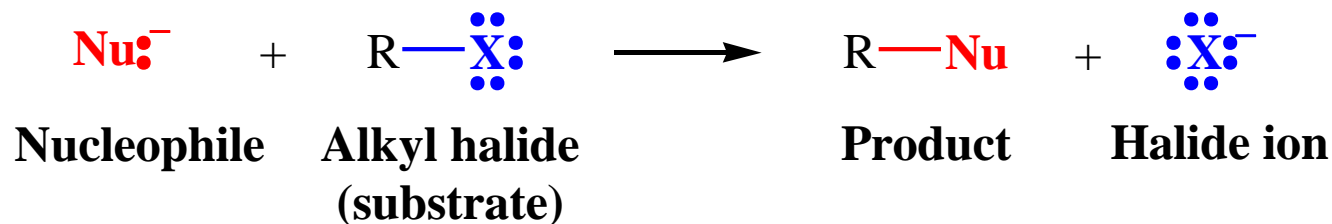
Elimination reaction

and

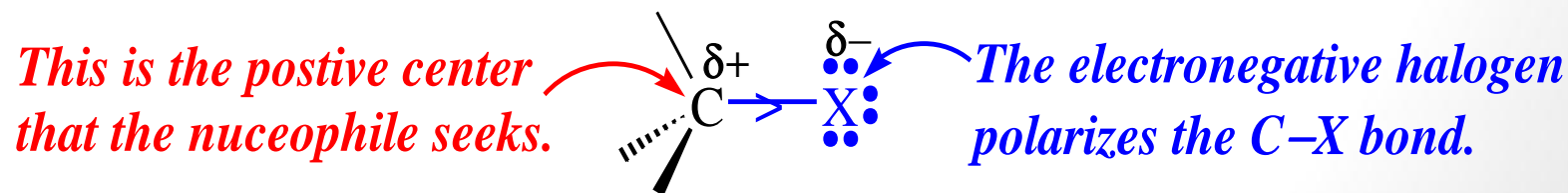
Organometallic formation.

Nucleophilic Substitution Reactions:

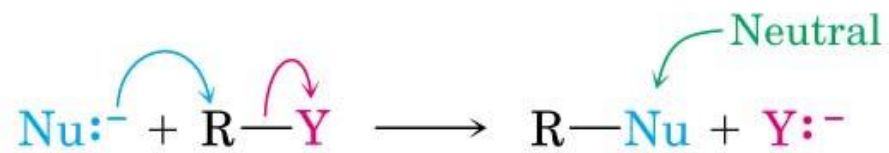
The electron -deficient carbon atom in alkyl halides renders these compounds susceptible to reaction with electron -rich reagents:



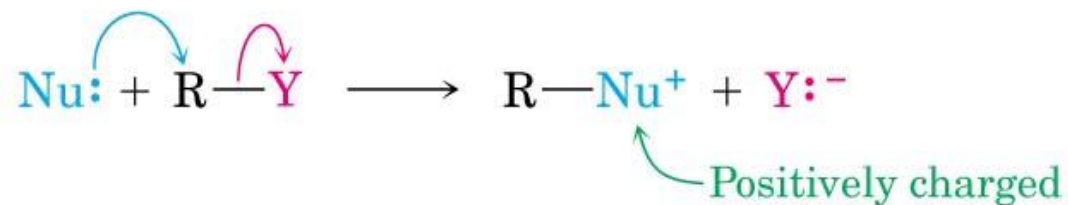
A **nucleophile**, is a species with an **unshared electron pair (lone-pair electrons)**, reacts with an **alkyl halide (substrate)** by replacing the halogen substituent (**leaving group**).



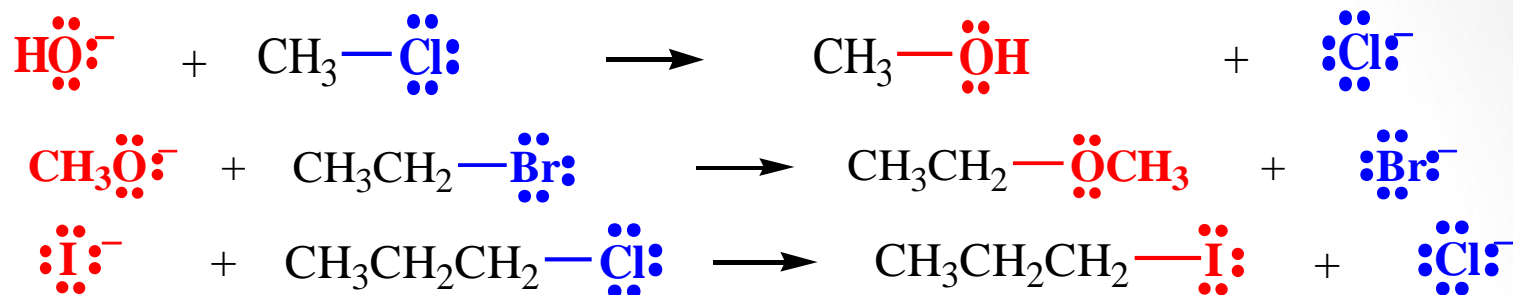
**Negatively charged
Nu:⁻**



Neutral Nu:



Examples:



Nucleophilic Reagents

Being electron-pair donor, nucleophilic reagents must necessarily possess unshared electrons, they include:

Negative ions

e.g. $\text{H}\ddot{\text{O}}\text{:}^-$ Hydroxide ion, $\text{H}\ddot{\text{S}}\text{:}^-$ Hydrosulphide ion, $\text{R}\ddot{\text{O}}\text{:}^-$ Alkoxide ions,

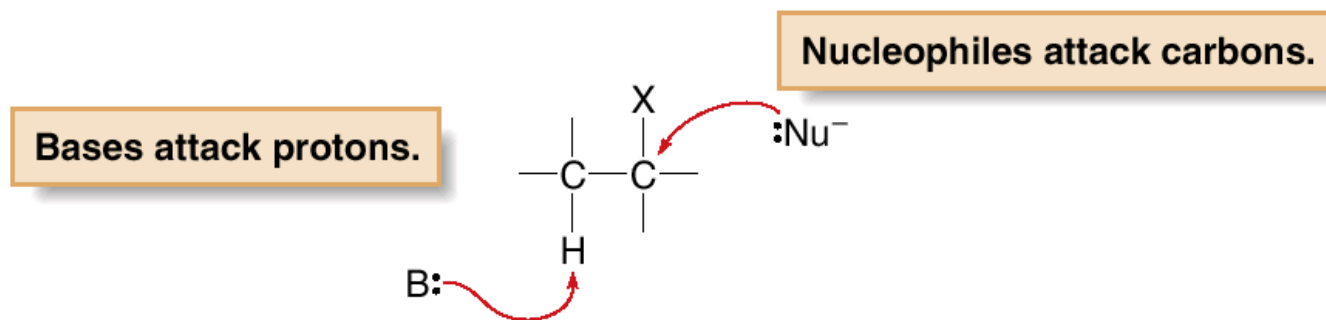
$\text{:}\text{N}\equiv\text{C}\text{:}^-$ Cyanide ion, $\text{:}\ddot{\text{X}}\text{:}^-$ Halide ions, ...etc.

Neutral molecules

e.g. $\text{H}_2\ddot{\text{O}}$, $\text{R---}\ddot{\text{O}}\text{---H}$, $\text{R---}\ddot{\text{O}}\text{---R}$, $\text{H}_3\ddot{\text{N}}$, $\text{R}_3\ddot{\text{N}}$, ...etc.

Nucleophiles and bases are structurally similar: both have a lone pair or a π bond. They differ in what they attack.

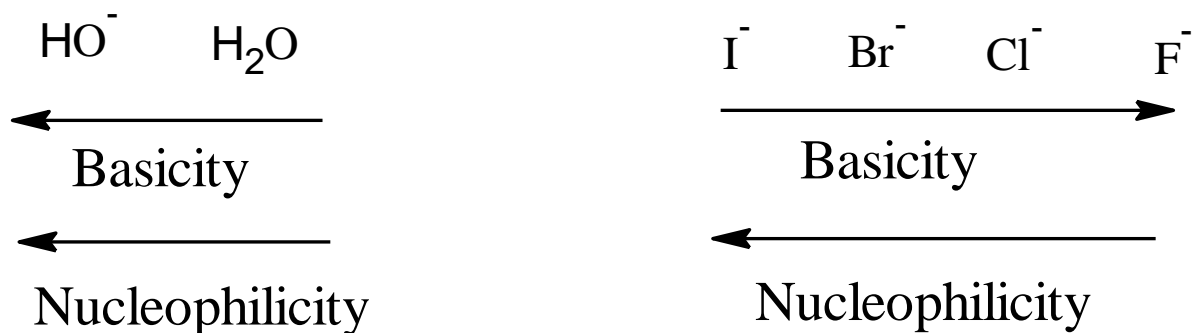
- Bases attack protons. Nucleophiles attack other electron-deficient atoms (usually carbons).



- Although nucleophilicity and basicity are interrelated, they are fundamentally different.
 - ➔ **Basicity** is a measure of how readily an atom donates its electron pair to a proton at the moment of nucleophilic substitution. It is characterized by an equilibrium constant, K_a in an acid-base reaction, making it a thermodynamic property.
 - ➔ **Nucleophilicity** is a measure of how readily an atom donates its electron pair to other atoms. It is characterized by a rate constant, k , making it a kinetic property.

Nucleophilicity depends on the ability of the nucleophile to donate a pair of electrons to H^+ (basicity) and on the influence on such ability from the substrate (usually polarizability).

Polarizability is characteristic for large atoms and greatly increases nucleophilicity.

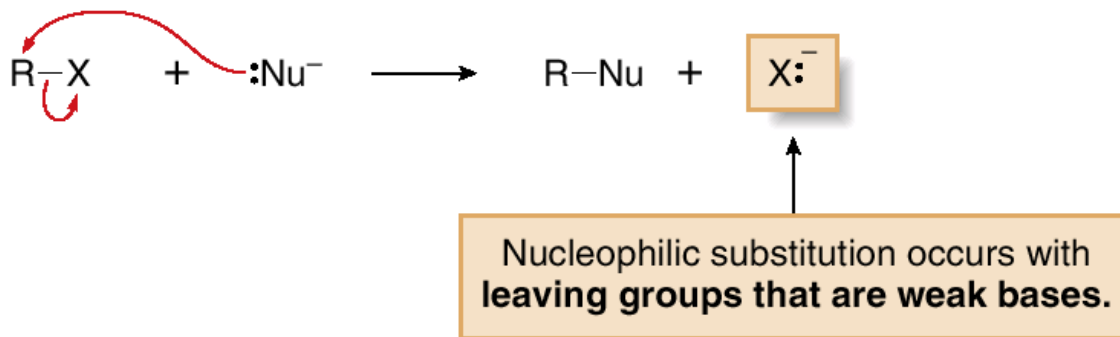


Weaker bases make better leaving groups.

The Leaving Group

In a nucleophilic substitution reaction of R—X, the C—X bond is heterolytically cleaved, and the leaving group departs with the electron pair in that bond, forming X:⁻. The more stable the leaving group X:⁻, the better able it is to accept an electron pair.

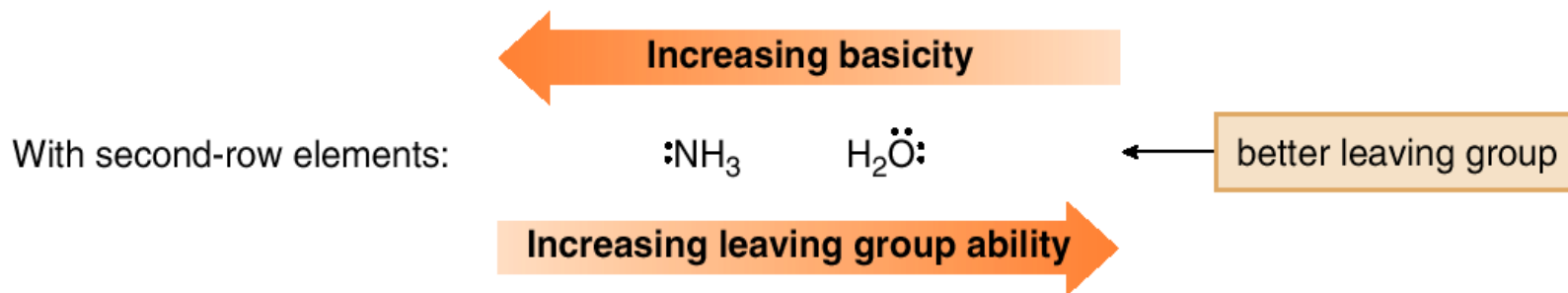
- In comparing two leaving groups, the better leaving group is the weaker base.



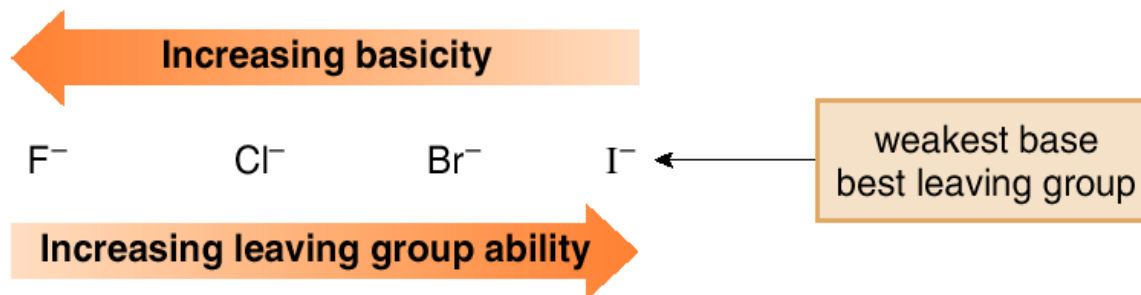
- For example, H₂O is a better leaving group than HO⁻ because H₂O is a weaker base.

- There are periodic trends in leaving group ability:

- Left-to-right across a row of the periodic table, basicity *decreases* so leaving group ability *increases*.



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




Good leaving group for nucleophilic substitution			
Starting material	Leaving group	Conjugate acid	pK_a
R-Cl	Cl ⁻	H-Cl	-7
R-Br	Br ⁻	H-Br	-9
R-I	I ⁻	H-I	-10
R-OH ₂ ⁺	H ₂ O	H ₃ ⁺ O	-1.7
Molecules under undergo nucleophilic substitution	Good leaving group		

Poor leaving group for nucleophilic substitution

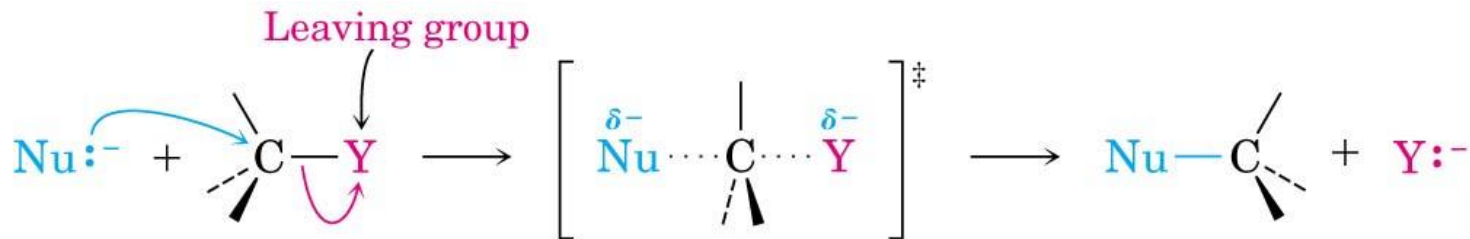
Starting material	Leaving group	Conjugate acid	pK_a
R-F	F ⁻	H-F	3.2
R-OH	⁻ OH	H ₂ O	15.7
R-NH ₂	⁻ NH ₂	NH ₃	38
R-H	H	H ₂	35
R-R	R ⁻	R-H	50
Molecules do not undergo nucleophilic substitution	Poor leaving group		

The Leaving Group

- Stable anions that are **weak bases** are usually excellent leaving groups and can delocalize charge

Relative reactivity	$\text{OH}^-, \text{NH}_2^-, \text{OR}^-$	F^-	Cl^-	Br^-	I^-	TosO^-
	$\ll 1$	1	200	10,000	30,000	60,000
	Less reactive	Leaving group reactivity 				More reactive

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Transition state
(Negative charge is delocalized over both Nu: and Y)

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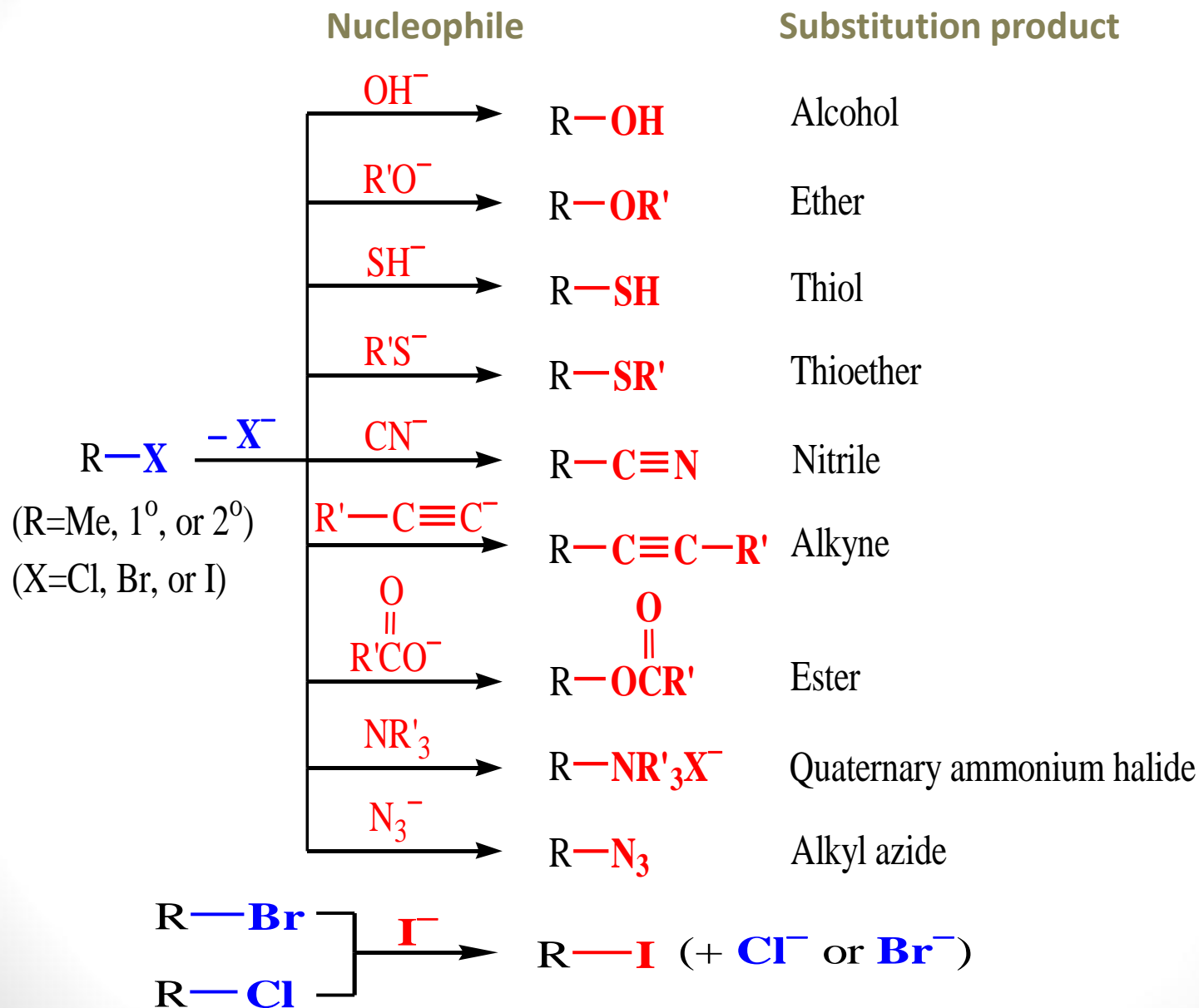
Poor Leaving Groups

- If a group is very basic or very small, it prevents reaction



These compounds do not undergo $\text{S}_{\text{N}}2$ reactions.

Nucleophilic substitution (S_N) Reactions



Reaction kinetics

- The study of rates of reactions is called *kinetics*
- Rates decrease as concentrations decrease but the rate constant does not
- The *rate law* depends on the mechanism
- The *order* of a reaction is sum of the exponents of the concentrations in the rate law – the example below is second order

Experiments show that for the reaction



$$\text{Rate} = k[\text{OH}^-][\text{CH}_3\text{Br}]$$

- **Rate** is change in concentration with time
- Depends on concentration(s), temperature, inherent nature of reaction (activation energy)
- A **rate law** describes relationship between the concentration of reactants and rate of conversion to products – determined by experiment.
- A **rate constant (k)** is the proportionality factor between concentration and rate

Example: for $S \rightarrow P$

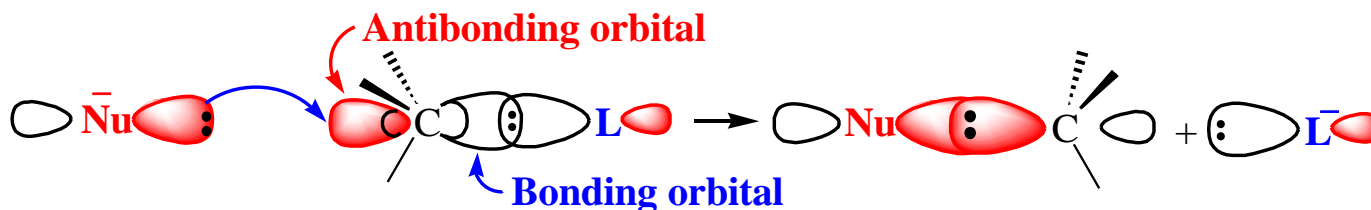
an experiment might find

Rate = $k [S]$ (first order)

MECHANISM FOR THE S_N2 REACTION:

The **nucleophile** attacks the carbon bearing the **leaving group** from the **back side**.

- ❑ The orbital that contains the **electron pair** of the **nucleophile** begins to **overlap** with an **empty (antibonding) orbital** of the carbon bearing the **leaving group**.
- ❑ The bond between the **nucleophile** and the carbon atom is **forming**, and the bond between the carbon atom and the **leaving group** is **breaking**.
- ❑ The formation of the bond between the **nucleophile** and the carbon atom provides most of the energy necessary to break the bond between the carbon atom and the **leaving group**.



Stereochemistry of S_N2

The **configuration** of the carbon atom becomes **inverted** during S_N2 reaction

In a nucleophilic substitution:

Overall reaction

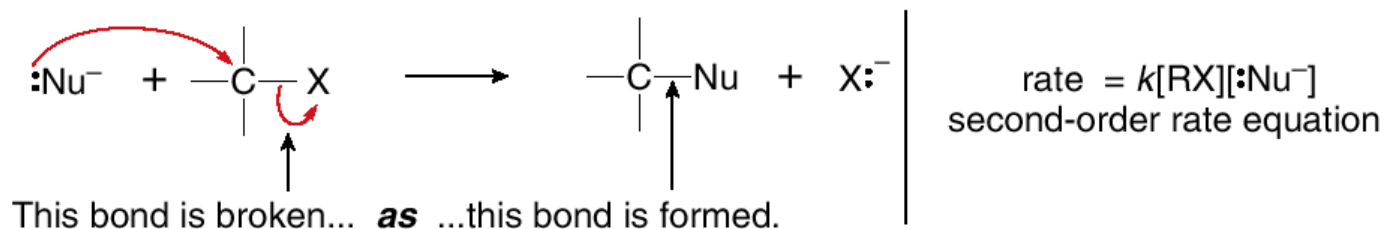


This σ bond is broken.

This σ bond is formed.

Bond making and bond breaking occur at the same time.

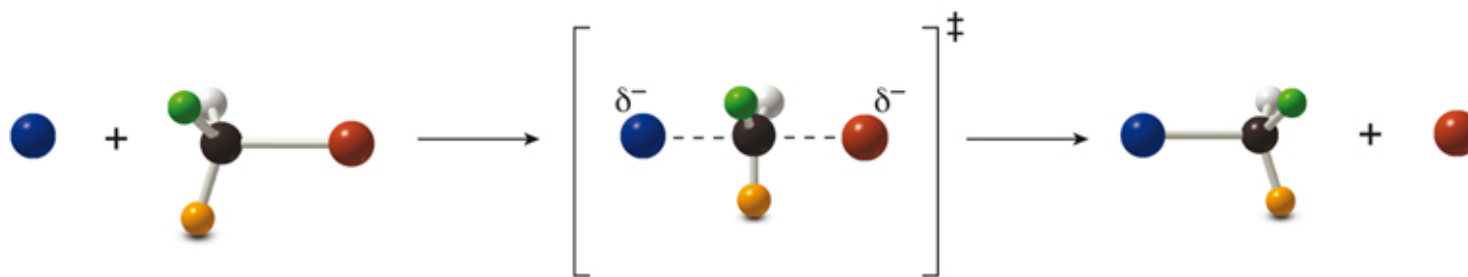
One-step mechanism



The mechanism is comprised of one step. In such a bimolecular reaction, the rate depends upon the concentration of both reactants, that is, the rate equation is second order.

Stereochemistry of S_N2 Reaction

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



:Nu⁻ and Br⁻ are 180° away from each other, on either side of a plane containing R, H, and D.

One-Step Mechanism: S_N² Reactions

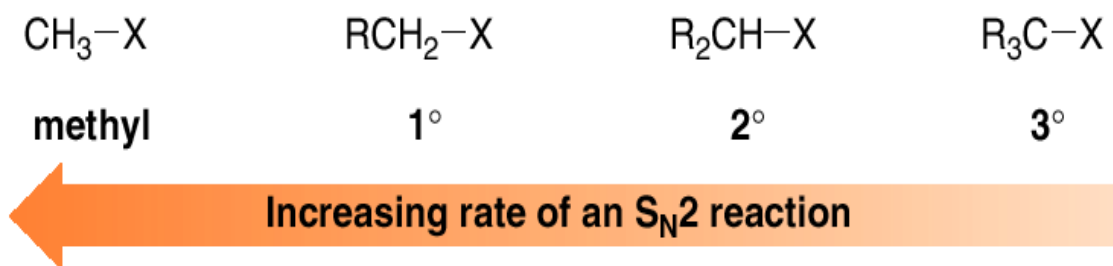
Summary;

1. The S_N² reaction is a single, concerted process.
2. The rate of S_N² reaction depends on the concentrations of both the alkyl halide and the nucleophile.
3. The reaction is fastest for primary halides and slowest for tertiary halides.
4. All S_N² reactions proceed with complete inversion of configuration.

Characteristics of the S_N2 Mechanism

Characteristic	Result
Kinetics	<ul style="list-style-type: none">• Second-order kinetics, rate = $k[\text{RX}][\text{:Nu}^-]$
Mechanism	<ul style="list-style-type: none">• One step
Stereochemistry	<ul style="list-style-type: none">• Backside attack of the nucleophile• Inversion of configuration at a stereogenic center
Identity of R	<ul style="list-style-type: none">• Unhindered halides react fastest• Rate: $\text{CH}_3\text{X} > \text{RCH}_2\text{X} > \text{R}_2\text{CHX} > \text{R}_3\text{CX}$

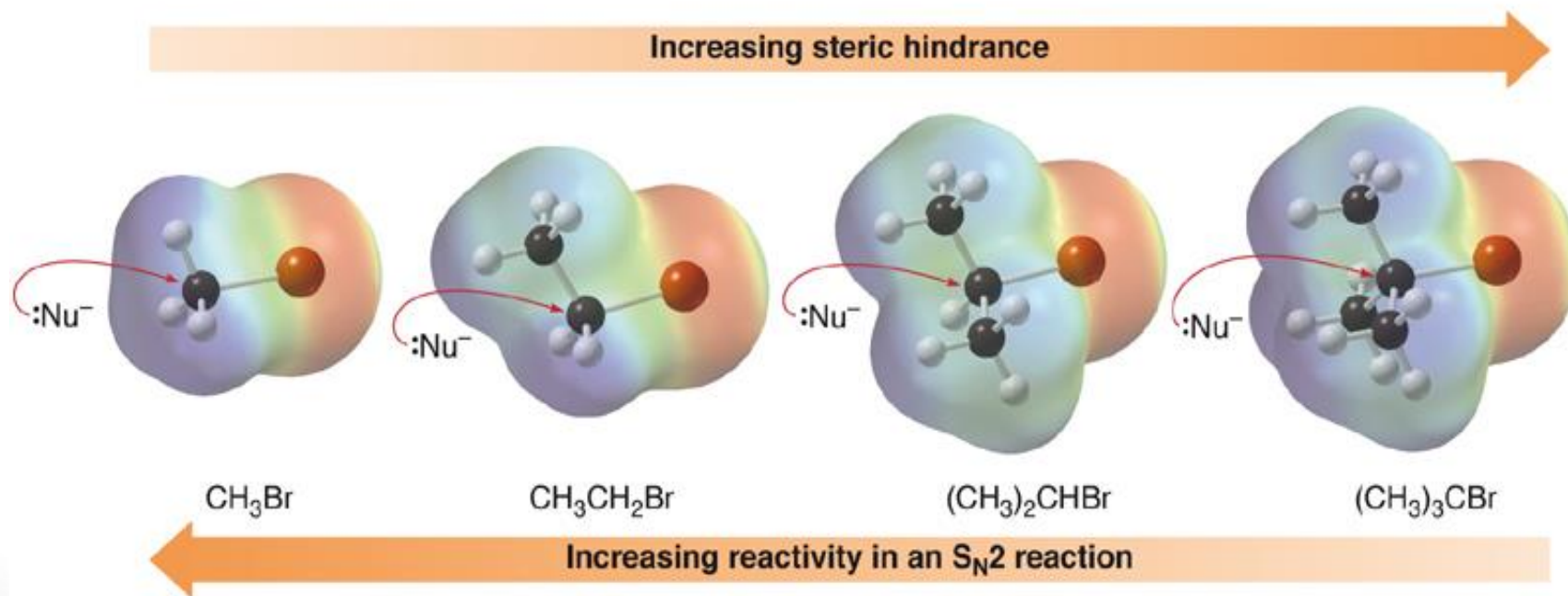
- As the number of R groups on the carbon with the leaving group *increases*, the rate of an S_N2 reaction *decreases*.



- 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. This order of reactivity can be explained by steric effects. Steric hindrance caused by bulky R groups makes nucleophilic attack from the backside more difficult, slowing the reaction rate.

Electrostatic potential maps illustrate the effects of steric hindrance around the carbon bearing the leaving group in a series of alkyl halides.

Steric effects in the S_N2 reaction



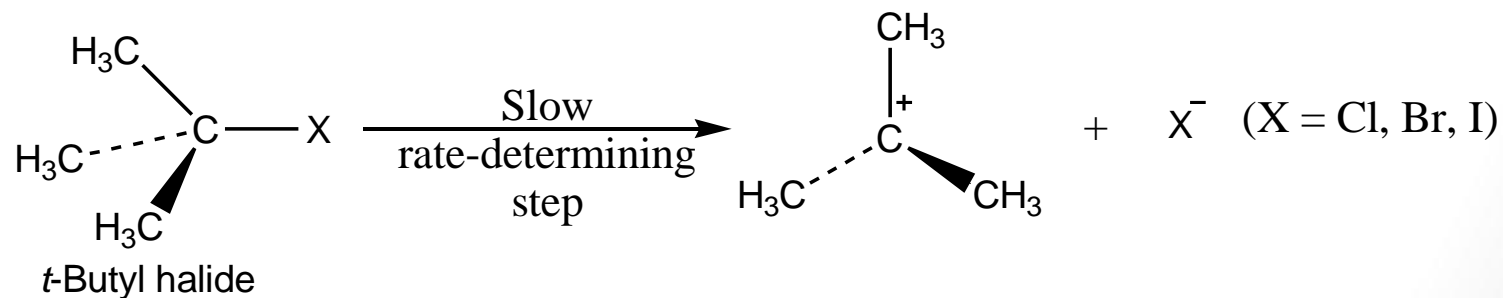
Two-Step Mechanism: S_N¹ Reactions

S_N¹ reactions take place with both *inversion* and *retention* of configuration.

A mechanism that accounts for these facts involves two steps.

Step 1. The tertiary alkyl halide ionizes to form a carbocation.

This is the slow, *rate-determining step*.



Step 2. A covalent bond forms between the carbocation and the OH⁻ nucleophile.

This step occurs rapidly.

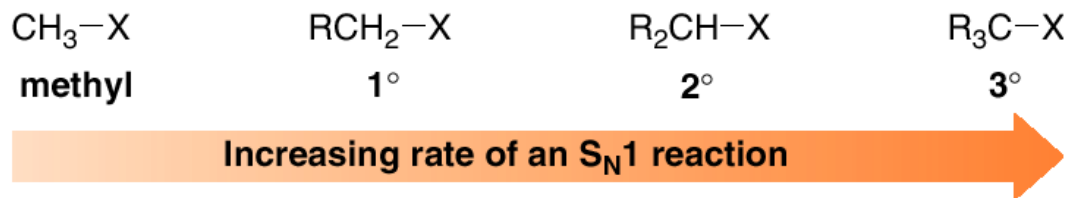
The **nucleophile** has as much chance to **bond with the positively charged carbon on the same side as the departed leaving group** (giving *retention* of configuration) **as on the back side** (leading to *inversion*).

If the starting alkyl halide were optically active, the product would be a racemic mixture.

Mechanisms of Nucleophilic Substitution:

- 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*.



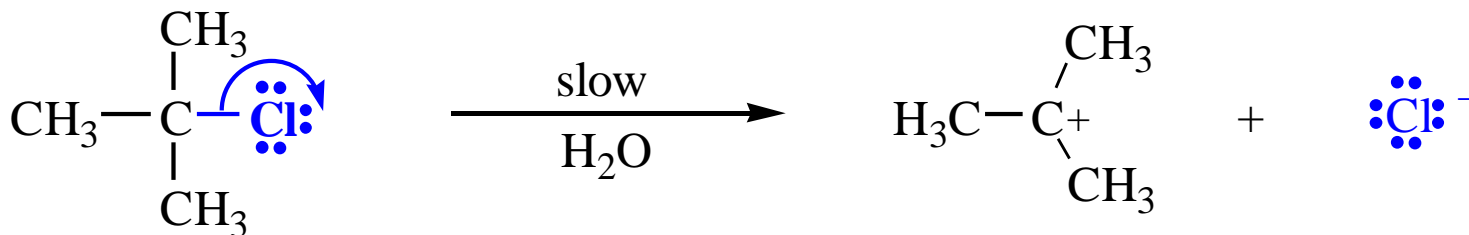
- 3° Alkyl halides undergo S_N1 reactions rapidly.
 - 2° Alkyl halides react more slowly.
 - Methyl and 1° alkyl halides do *not* undergo S_N1 reactions.
- This trend is exactly opposite to that observed in S_N2 reactions.

Reaction:



Mechanism of S_N1

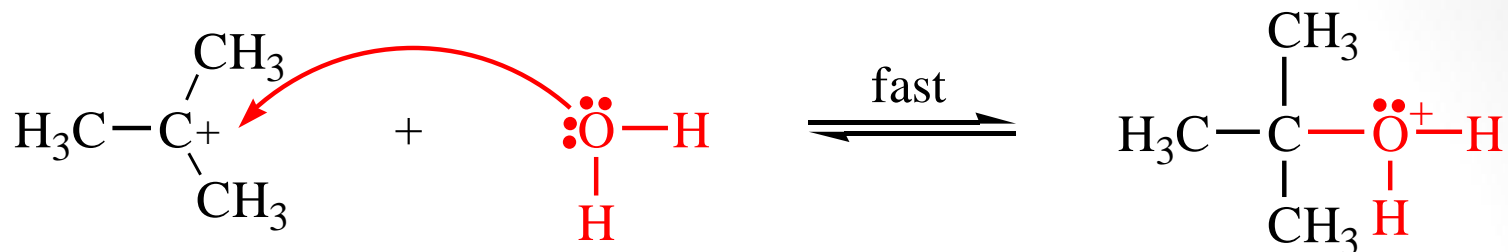
Step 1



Aided by the polar solvent a chlorine departs with the electron pair that bonded it to the carbon.

This slow step produces the relatively stable 3^o carbocation and a chloride ion. Although not shown here, the ions are solvated (and stabilized) by water molecules.

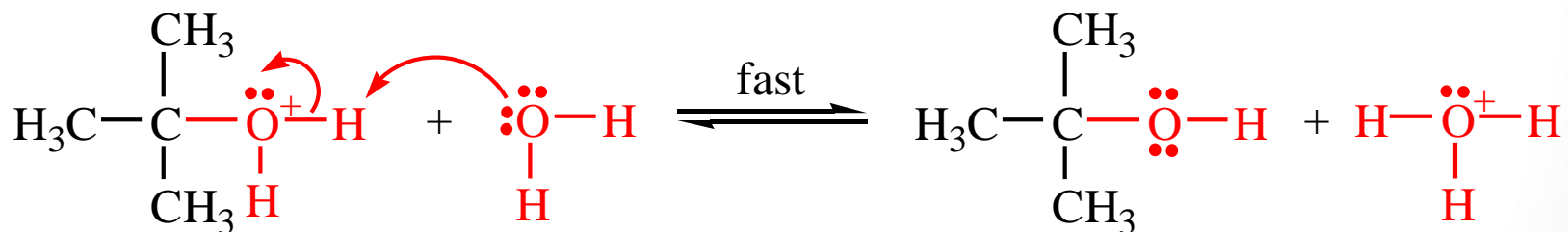
Step 2



A water molecule acting as a Lewis base donates an electron pair to the carbocation (a Lewis acid). This gives the cationic carbon eight electrons.

The product is a *tert*-butyloxonium ion (or protonated *tert*-butyl alcohol).

Step 3

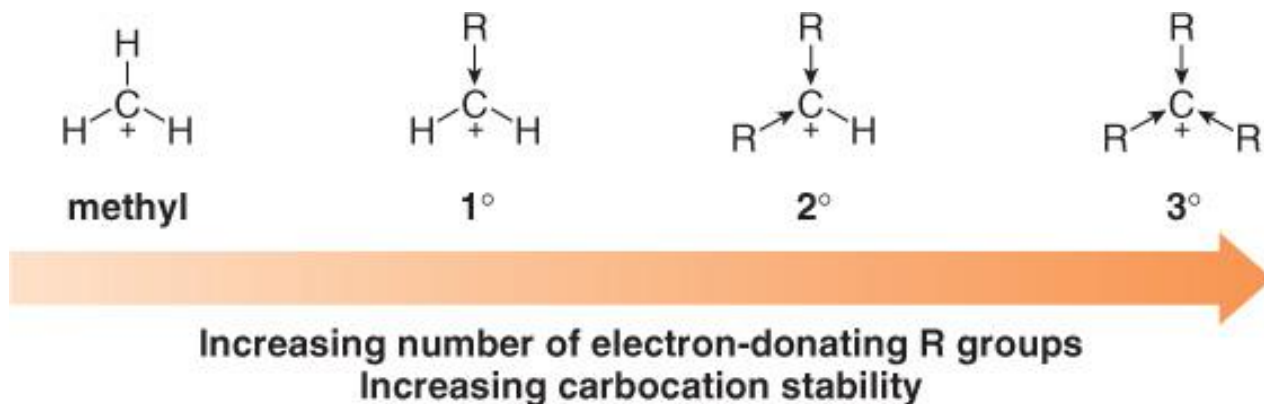


A water molecule acting as a Brønsted base accepts a proton from the *tert*-butyloxonium ion.

The products are *tert*-butyl alcohol and a hydronium ion.

Carbocation formation and stability

- Key features of the S_N1 mechanism are that it has two steps, and carbocations are formed as reactive intermediates
- The effect of the type of alkyl halide on S_N1 reaction rates can be explained by considering carbocation stability.
- Carbocations are classified as **primary (1°)**, **secondary (2°)**, or **tertiary (3°)**, based on the number of R groups bonded to the charged carbon atom. As the number of R groups increases, carbocation stability increases.

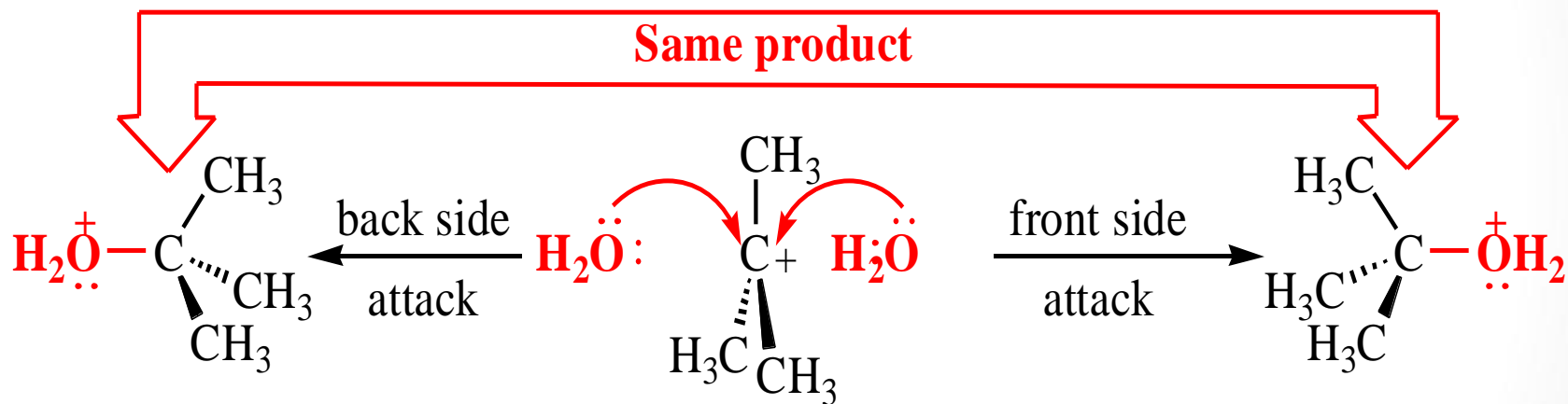


Alkyl groups are **electron donating** groups that stabilize a positive charge.

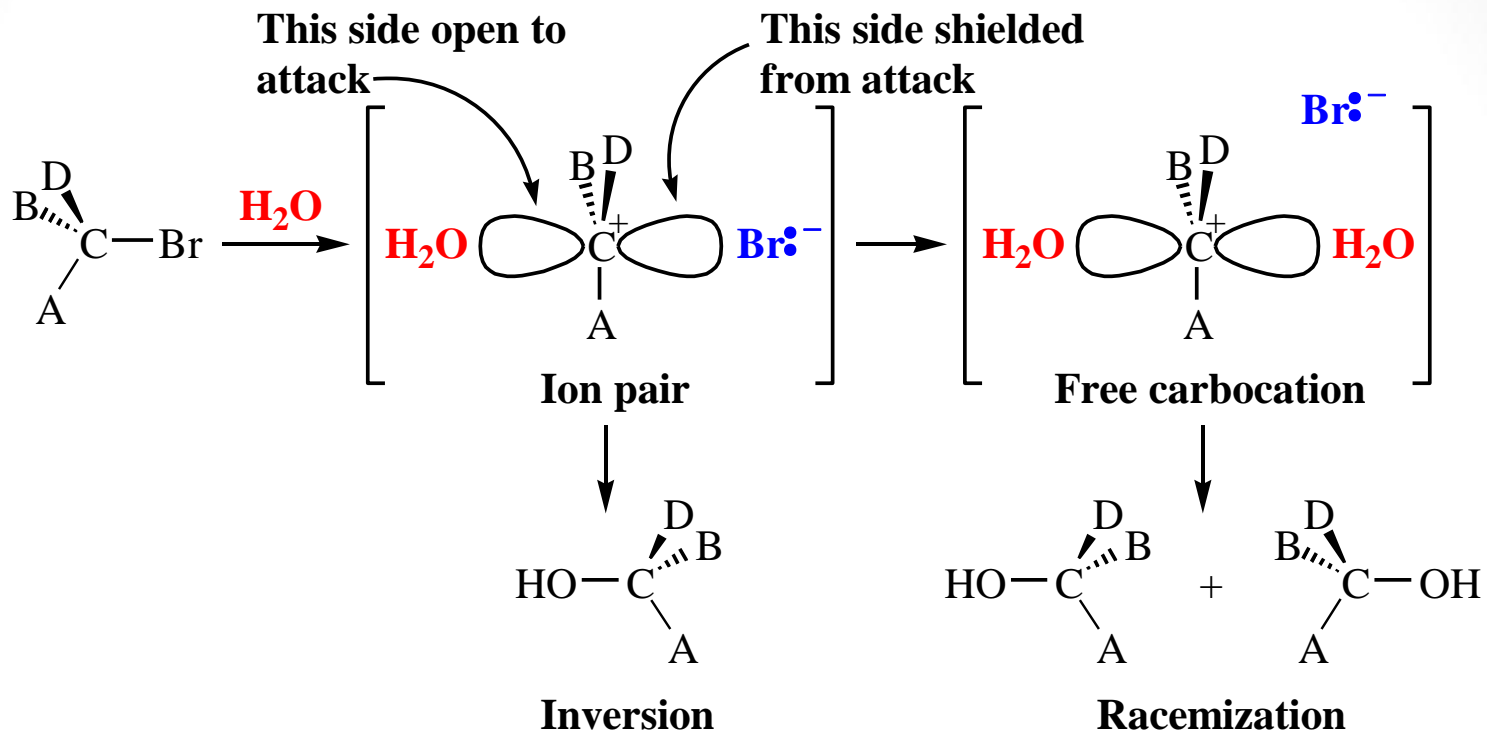
The relative stabilities of carbocations is $3^\circ > 2^\circ > 1^\circ > \text{methyl}$

THE STEREOCHEMISTRY OF S_N1 REACTIONS

The carbocation has a **trigonal planar structure** \Rightarrow It may react with a **nucleophile** from either the **front side** or the **back side** so that a **racemic mixture** is obtained :



Racemic mixture : is two equal parts of oppositely **optically active** compounds



Factors Favoring S_N1 versus S_N2 Reactions

Factor	S_N1	S_N2
Substrate	3° (requires formation of a relatively stable carbocation)	Methyl > 1° > 2° (requires unhindered substrate)
Nucleophile	Weak Lewis base, neutral molecule, nucleophile may be the solvent (solvolysis)	Strong Lewis base, rate favored by high concentration of nucleophile
Solvent	Polar protic (e.g. alcohols, water)	Polar aprotic (e.g. DMF, DMSO)
Leaving group	Good LG important to form C ⁺	Not as important but enhances reaction
Kinetics:	rate = k[RX]	rate = k[RX][Nu:]
Stereochemistry	both inversion and retention (racemic)	inversion only
Rearrangement	rearrangements common	rearrangements not possible