

ORGANIC CHEMISTRY 2

CHEM 340

2 Credit hrs

*Chemistry Department
College of Science
King Saud University*

By

Prof. Mohamed El-Newehy

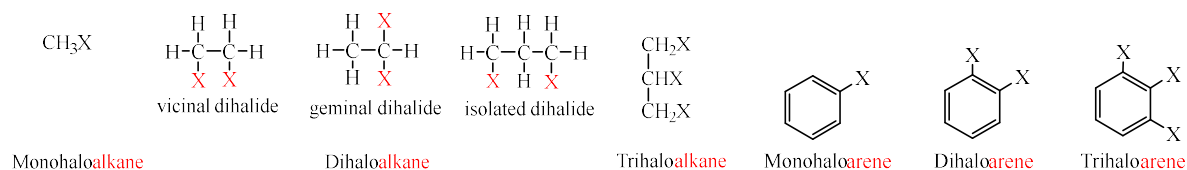
Organo-halogen Compounds

Classification of Haloalkanes and Haloarenes

➤ The replacement of hydrogen atom(s) in a hydrocarbon, aliphatic or aromatic, by halogen atom(s) ($X = F, Cl, Br, \text{ or } I$; fluoro, chloro, bromo, and iodo compounds) results in the formation of alkyl halide (**haloalkane**) and aryl halide (**haloarene**)

➤ On the basis of number of halogen atoms; **Haloalkanes** and **haloarenes** may be classified as follows:

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



➤ **Monohalocompounds** may further be classified according to the hybridization of the carbon atom to which the halogen is bonded, as following:

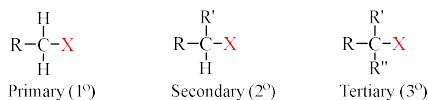


Classification of Haloalkanes and Haloarenes

Compounds Containing sp^3 C—X Bond ($X = F, Cl, Br, I$)

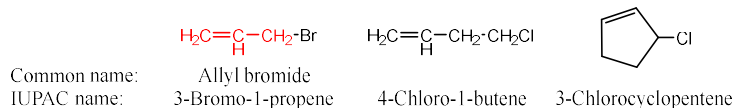
(a) Alkyl halides or haloalkanes (R—X)

- The halogen atom is bonded to an alkyl group (R) & the *general formula* is $C_nH_{2n+1}X$.
- They are classified as *primary, secondary* or *tertiary* according to the nature of carbon to which halogen is attached.



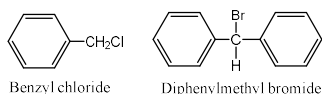
(b) Allylic halides

- The halogen atom is bonded to an sp^3 -hybridized carbon atom next to carbon-carbon double bond (C=C).



(c) Benzylic halides

- The halogen atom is bonded to an sp^3 -hybridized carbon atom next to an aromatic ring.

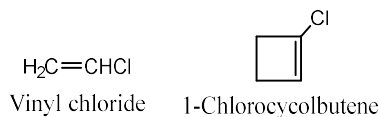


Classification of Haloalkanes and Haloarenes

Compounds Containing sp^2 C—X Bond (X= F, Cl, Br, I)

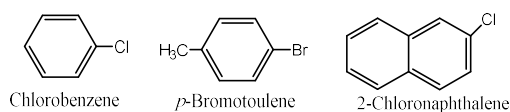
(a) Vinylic halides

- These are the compounds in which the halogen atom is bonded to an sp^2 -hybridized carbon atom of a carbon-carbon double bond (C = C).



(b) Aryl halides

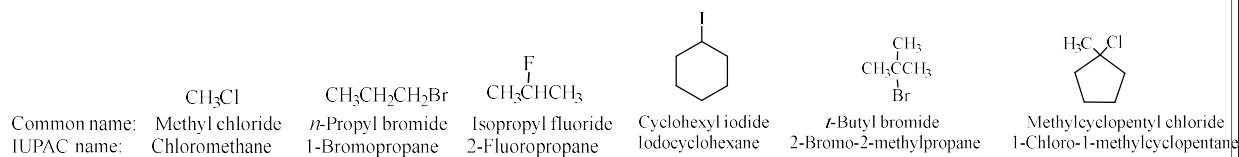
- These are the compounds in which the halogen atom is bonded to the sp^2 -hybridized carbon atom of an aromatic ring.



Nomenclature of Haloalkanes and Haloarenes

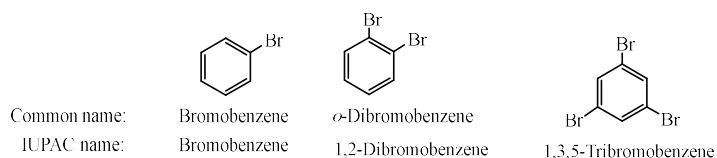
Haloalkanes

- **Common names;** alkyl halides are derived by naming the alkyl group followed by the halide. *Alkyl halide*
- **IUPAC system;** alkyl halides are named as *halosubstituted hydrocarbons*.



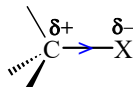
Haloarenes

- Haloarenes are the common as well as IUPAC names of *aryl halides*.
- For dihalogen derivatives, the prefixes *o*-, *m*-, *p*- are used in common system but in IUPAC system, the numerals 1,2; 1,3 and 1,4 are used.



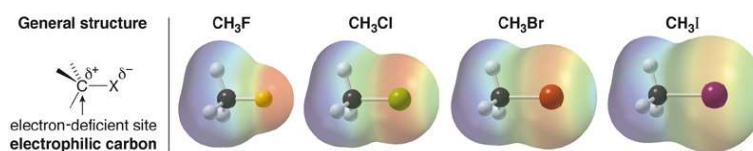
Nature of C-X Bond C-X Bond

- Since halogen atoms are more electronegative than carbon, the **carbon-halogen bond of alkyl halide is polarized**; the **carbon atom bears a partial positive charge** whereas the **halogen atom bears a partial negative charge**.



Carbon-Halogen (C—X) Bond Lengths, Bond Strength and Dipole Moments

Bond	Bond Length (Å)	Bond Strength (kJ/mol)	Dipole moment (Debye)
CH ₃ —F	1.39	452	1.847
CH ₃ —Cl	1.78	351	1.860
CH ₃ —Br	1.93	293	1.830
CH ₃ —I	2.14	234	1.636



• The polar C—X bond makes the carbon atom *electron deficient* in each CH₃X molecule.

Importance of Organohalogen Compounds

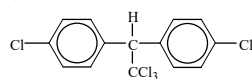
- a) Solvents:** Alkyl halides are used as **solvents** for relatively non-polar compounds: CCl₄, CHCl₃, CCl₃CH₃, CH₂Cl₂,etc.
They are good solvents for fats and oils.
Polychloro compounds, such as trichloroethylene and tetrachloroethylene, are widely used as solvents for dry cleaning.

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.*

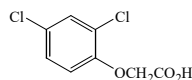
c) Refrigerants: Freons (ChloroFluoroCarbon)

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

f) Chlorine containing antibiotic, chloramphenicol: is very effective for the treatment of typhoid fever.

g) Our body produces iodine containing hormone, thyroxine: the deficiency of which causes a disease called goiter.

Physical Properties of Organic Halides

Solubility

- All organic halides are insoluble in water.
- All organic halides are soluble in common organic solvents (benzene, ether, etc.).

Density

- The simple monofluoro and monochloro compounds are less dense than water,
- The monobromo and monoiodo derivatives have densities greater than water.
- As the number of halogen atoms increases, the density increases.

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

Physical Properties of Organic Halides

Boiling points

- Within a series of halides, the boiling points increase with increasing molecular weights.
This is due to the increase in van der Waals forces when the size and mass of the halogen atom increases.
- Within a homologous series, the boiling points also increase regularly with molecular weights.
- Within a series of isomers, the straight-chain compound has the highest boiling point, and the most branched isomer the lowest boiling point.
- Haloalkanes generally have a boiling point that is higher than the alkane they are derived from due to
 - The increased molecular weight due to the large halogen atoms
 - The increased intermolecular forces due to the polar bonds, and the increasing polarizability of the halogen.

	Flouride	Chloride	Bromide	Iodine
Group	bp	bp	bp	bp
Methyl	-78.4	-28.8	-3.6	42.5
Ethyl	-37.7	13.1	38.4	72
Propyl	-2.5	46.6	70.8	102
Isopropyl	-9.4	34	59.4	89.4
Butyl	32	78.4	101	130
Sec-butyl		68	91.2	120
Tert-butyl		51	73.3	100

BOILING POINT TRENDS

Size of hydrocarbon part		Type of halogen		# of halogen atoms	
Compound	bp [°C]	Compound	bp [°C]	Compound	bp [°C]
CH ₃ -Cl	-24	CH ₃ CH ₂ -F	-38	CH ₃ Cl	-24
CH ₃ CH ₂ -Cl	12	CH ₃ CH ₂ -Cl	12	CH ₂ Cl ₂	40
CH ₃ CH ₂ CH ₂ -Cl	47	CH ₃ CH ₂ -Br	38	CHCl ₃	61
CH ₃ CH ₂ CH ₂ CH ₂ -Cl	78	CH ₃ CH ₂ -I	72	CCl ₄	77

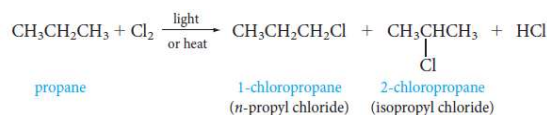
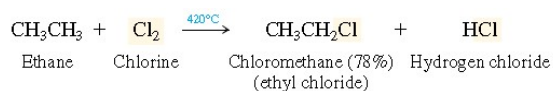
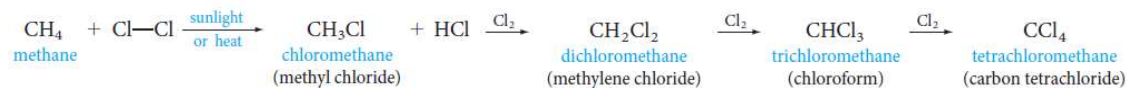
For comparison: CH₃-CH₃ bp - 89 °C

Preparation of Halogen Compounds

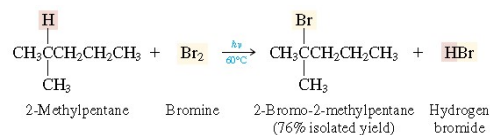
From Hydrocarbons

(a) By free radical halogenation; Alkyl halide

Free radical chlorination or bromination of alkanes gives a complex mixture of isomeric mono- and polyhaloalkanes,



- **Rate of halogenation:** $\text{R}_3\text{CH} > \text{R}_2\text{CH}_2 > \text{RCH}_3$
 (tertiary) (secondary) (primary)

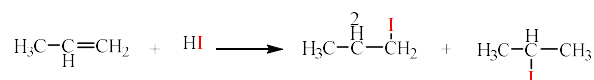
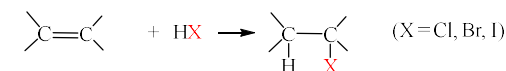


Preparation of Halogen Compounds

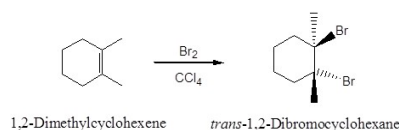
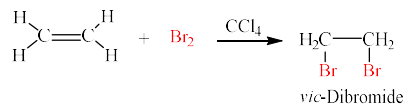
From Hydrocarbons

(b) From alkenes

- (i) **Addition of hydrogen halides:** an alkene is converted to corresponding **alkyl halide** by reaction with hydrogen chloride, hydrogen bromide or hydrogen iodide.



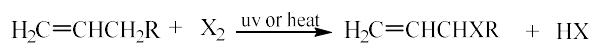
- (ii) **Addition of halogens:** addition of bromine in CCl_4 to an alkene resulting in the synthesis of **vic-dibromides**.



Preparation of Halogen Compounds

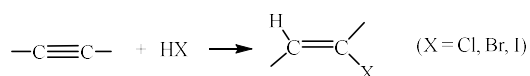
From Hydrocarbons

(iii) **Halogenation of alkenes: Allyl halides**

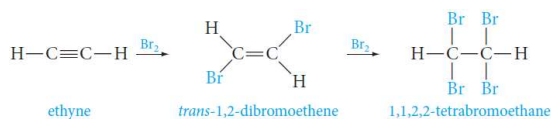


(c) **From Alkynes**

(i) **Addition of HX to alkynes: Vinyl halides**



(ii) **Addition of Halogen:** Bromine adds to alkynes and the addition occurs mainly trans.

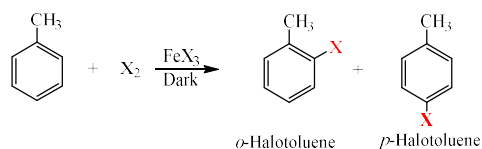


Preparation of Halogen Compounds

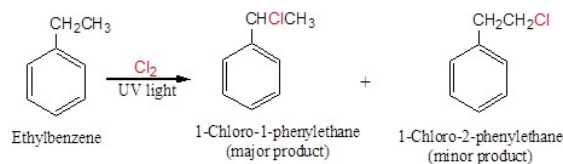
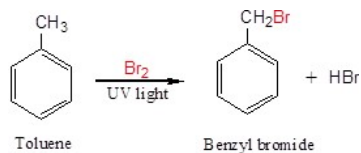
From Hydrocarbons

(d) **By electrophilic substitution; Aryl halide**

(i) **Aryl chlorides and bromides** can be easily prepared by electrophilic substitution of arenes with chlorine and bromine, respectively in the presence of Lewis acid catalysts like iron or iron(III) chloride.



(ii) **Halogenation of an Alkyl Side Chain of Benzene derivatives; Benzyl halides**

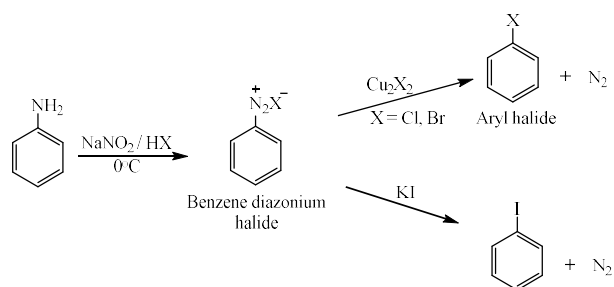


Preparation of Halogen Compounds

From Hydrocarbons

(e) Sandmeyer's reaction; Aryl halide

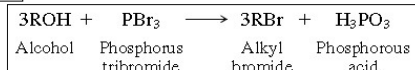
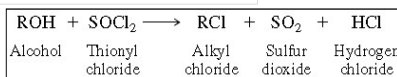
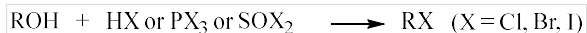
- Mixing the solution of freshly prepared diazonium salt with cuprous chloride or cuprous bromide or potassium iodide results in the replacement of the diazonium group by -Cl or -Br or -I.



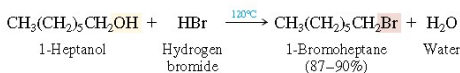
Preparation of Halogen Compounds

From Alcohols

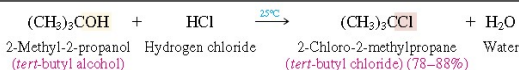
The hydroxyl group of an alcohol is replaced by halogen on reaction with concentrated halogen acids, phosphorus halides or thionyl chloride.



- The reactions of **primary** and **secondary alcohols** with HCl require the presence of a catalyst, ZnCl₂.



- With **tertiary alcohols**, the reaction is conducted by simply shaking with concentrated HCl at room temperature.

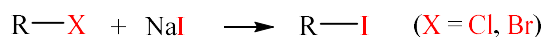


- The **order of reactivity of alcohols** is 3° > 2° > 1°.
- The above methods are not applicable for the preparation of **aryl halides** because the carbon-oxygen bond in phenols has a partial double bond character and is difficult to break being stronger than a single bond.

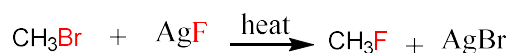
Preparation of Halogen Compounds

Halogen Exchange

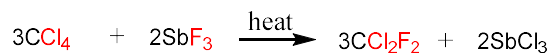
- (i) **Alkyl iodides** are often prepared by the reaction of alkyl chlorides/bromides with NaI in dry acetone. This reaction is known as **Finkelstein reaction**.



- (ii) The synthesis of **alkyl fluorides** is best accomplished by heating an alkyl chloride/bromide in the presence of a metallic fluoride such as AgF, Hg₂F₂, CoF₂ or SbF₃. The reaction is termed as **Swarts reaction**.



The manufacture of chlorofluoro compounds, known as Freons.



Reactions of Haloalkanes

The reactions of organic halides fall into three categories

- (i) **Nucleophilic substitution, or S_N, reactions.**

Those in which the halogen is replaced by some other atom or group.

- (ii) **Elimination, or E, reactions.**

Those that involve the loss of HX from the halide.

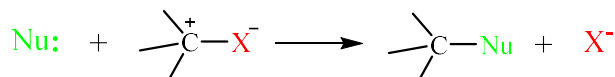
- (iii) **Reaction with metals (Formation of organometallic compounds).**

Those that involve reaction with certain metals.

Reactions of Haloalkanes

Nucleophilic Substitution (S_N) Reactions

- A nucleophile reacts with haloalkane (the substrate) having a partial positive charge on the carbon atom bonded to halogen.
- The overall process describing any S_N reaction is



Nu:, is the nucleophile.

The nucleophile has an unshared electron pair available for bonding.

X, is the leaving group.

The leaving group is also a nucleophile.

Reactions of Haloalkanes

Nucleophilic Substitution (S_N) Reactions

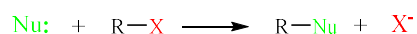
- The incoming nucleophile must be stronger than the leaving one.

- ✓ Good leaving groups include H₂O and anions (the conjugate bases) of strong acids, such as Cl, Br, I, and HSO₄.
- ✓ Strong nucleophiles, but poor leaving groups conjugate bases of weak acids; HO, RO, and CN.
- ✓ The iodide ion is both a good nucleophilic reagent and a good leaving group.

- The rates of S_N reactions for a series of halides always follow the order .

C-X bond dissociation energy (kcal/mole):	R-I	>	R-Br	>	R-Cl	>>	R-F
	55		67		80		107

Nucleophilic Substitution of Alkyl Halides (R-X)



Reagent	Nucleophile (Nu ⁻)	Substitution product R-Nu	Class of main product
NaOH (KOH)	HO ⁻	ROH	Alcohol
H ₂ O	H ₂ O	ROH	Alcohol
NaOR'	R'O ⁻	ROK	Ether
NaI	I ⁻	R-I	Alkyl iodide
NH ₃	NH ₃	RNH ₂	Primary amine
R'NH ₂	R'NH ₂	RNHR'	Sec. amine
R'R''NH	R'R''NH	RNR'R''	Tert. amine
KCN	$\overset{-}{\text{C}}\equiv\text{N:}$	RCN	Nitrile (cyanide)
AgCN	Ag-CN:	RNC (isocyanide)	Isonitrile
KNO ₂	O=N-O ⁻	R-O-N=O	Alkyl nitrite
AgNO ₂	Ag-O-N=O	R-NO ₂	Nitroalkane
R'COOAg	R'COO ⁻	R'COOR	Ester
LiAlH ₄	H ⁻	RH	Hydrocarbon
R'-M ⁺	R ⁻	RR	Alkane

Reactions of Haloalkanes

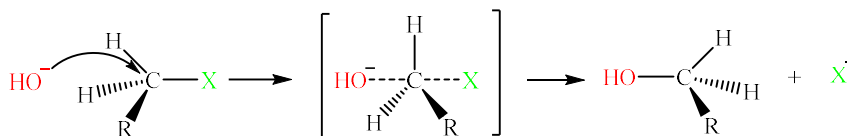
Mechanism of Nucleophilic Substitution (S_N) Reactions

- Alkyl halides may undergo nucleophilic substitutions in two different ways:
 - by a one-step mechanism.
 - by a two-step mechanism.
- Which route is taken depends on
 - The structure of the halide.
 - The nature of the solvent.
 - The strength of the nucleophile, Nu⁻.
- In general;
 - ✓ Primary alkyl halides undergo nucleophilic substitutions by the *one-step mechanism*.
 - ✓ Tertiary alkyl halides undergo nucleophilic substitutions by the *two-step mechanism*.
 - ✓ Secondary halides react by *either mechanism*.
- Let us consider the conversion of an alkyl halide to an alcohol by hydroxide.



Reactions of Haloalkanes

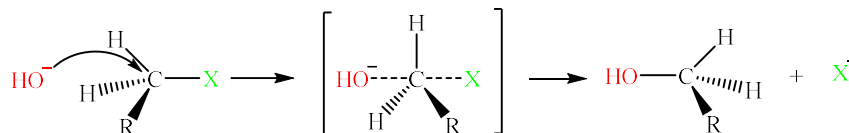
One-Step Mechanism: S_N² Reactions



- The incoming nucleophile interacts with alkyl halide causing; *the carbon-halide bond to break while forming a new carbon-OH bond.*
- These two processes take place in a *single step* and *no intermediate* is formed.
- The nucleophile attacks the halogen-bearing carbon from the *side opposite the leaving group*; a so-called *backside attack*.
- At the same time* that the nucleophile attacks from the back side and the leaving group departs, *the other bonds to the carbon invert (or "flip over")*.
- This flipping of the bonds, known as the *Walden inversion*.

Reactions of Haloalkanes

One-Step Mechanism: S_N² Reactions



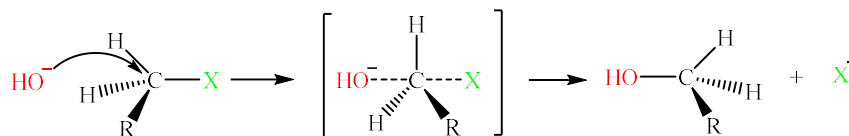
- Bimolecular Nucleophilic Substitution (S_N²) reaction.
- The **reaction rate** depends on the concentrations of both reactants, the **alkyl halide** and the **nucleophile**.
- For a given concentration of alkyl halide,

The rate of the reaction increases proportionally with the concentration of hydroxide ion.

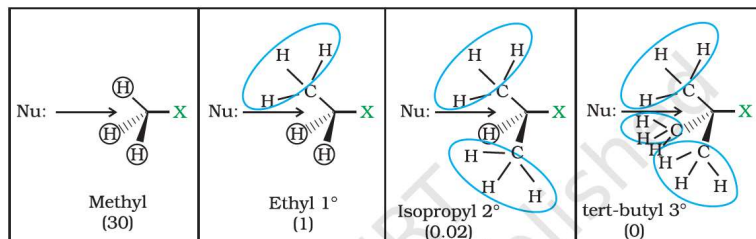
i.e. This means that if we double the concentration of hydroxide ion, but maintain the same concentration of alkyl halide, the S_N reaction proceeds twice as fast.

Reactions of Haloalkanes

One-Step Mechanism: S_N² Reactions



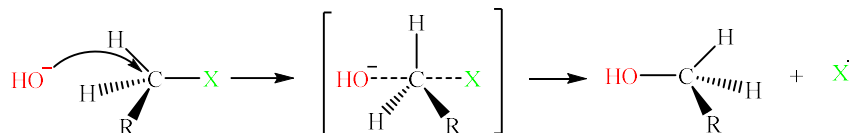
- The rates of hydrolysis follow the order; 1° RX > 2° RX > 3° RX
- Tertiary alkyl halides react slowest by the S_N² mechanism because the three alkyl groups on the carbon that bears the halogen hinder the backside approach of the attacking nucleophile.



Steric effects in S_N² reaction.

Reactions of Haloalkanes

One-Step Mechanism: S_N² Reactions



Summary;

1) S_N² reaction

S = substitution;

N = nucleophilic;

2 = bimolecular.

2) The S_N² reaction is a single, concerted process.

3) The rate of S_N² reaction depends on the concentrations of both the alkyl halide and the nucleophile.

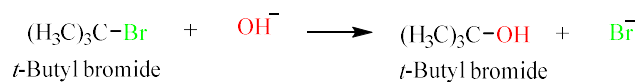
4) The reaction is fastest for primary halides and slowest for tertiary halides.

5) All S_N² reactions proceed with complete inversion of configuration.

Reactions of Haloalkanes

Two-Step Mechanism: S_N¹ Reactions

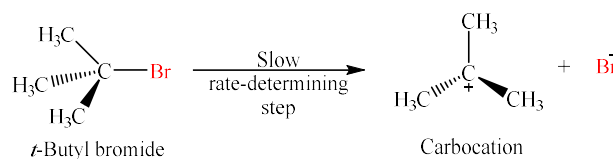
- The reaction between *tert*-butyl bromide and hydroxide ion yields *tert*-butyl alcohol and follows the first order kinetics, *i.e.*, the rate of reaction depends upon the concentration of only one reactant, which is *tert*-butyl bromide.



- A mechanism that accounts for these facts involves two steps.

Step 1. The polarized C—Br bond undergoes slow cleavage to produce a carbocation and a bromide ion.

This is the slow, rate-determining step.



Reactions of Haloalkanes

Two-Step Mechanism: S_N¹ Reactions

Summary;

1) S_N¹ reaction

S = substitution; N = nucleophilic; 1 = unimolecular.

2) The S_N¹ reaction is a two-step process.

3) The rate-determining step is the formation of a carbocation.

4) The rates of S_N¹ reactions follow the order of stability of carbocation.

Benzylic > allylic = 3° > 2° > 1° halide

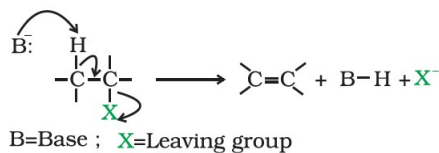
5) S_N¹ reactions proceed with racemization.

Reactions of Haloalkanes

Elimination Reactions

○ **General consideration**

Alkyl halides can lose H and X from adjacent carbons to form alkenes by an elimination process.



○ **Mechanism of Eliminations are of two types:**

- The E1 (elimination unimolecular) reaction.
- The E2 (elimination bimolecular) reaction.

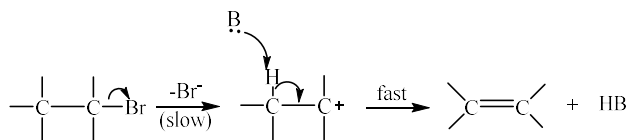
○ **Generally**

- The E1 process accompanies the S_N¹ reaction.
- The E2 reaction accompanies the S_N² reaction.
- E1 and E2 eliminations follow Saytzeff's rule.

Reactions of Haloalkanes

E1 Mechanism

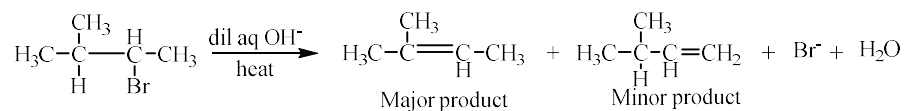
- The **E1**, involves the *formation of a carbocation* in the rate-determining step.



- The order of reactivity of **E1 reactions** is



- The product of an **E1 reaction** is an alkene.



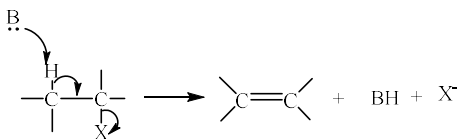
Reactions of Haloalkanes

E2 Mechanism

- In eliminations;**

The attack by the nucleophile (acting as a base, B:) is on the hydrogen atom attached to the carbon next to the one bearing the halogen (the β hydrogen).

- The **E2 mechanism** involves simultaneous bond breaking and bond formation and *occurs most readily when the β hydrogen and the halogen atom are trans to one another.*
- The single-step **E2 elimination**.



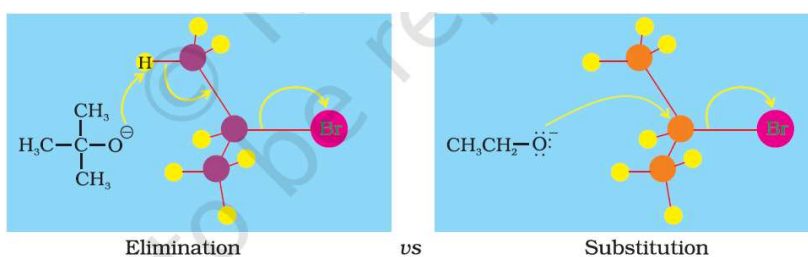
- The order of reactivity of **E2 elimination** is



Reactions of Haloalkanes

Elimination versus Substitution

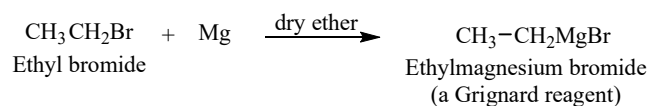
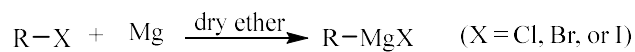
- When an alkyl halide with β -hydrogen atoms reacted with a base or a nucleophile, two competing routes: substitution (S_N^1 and S_N^2) and elimination.
- Which route will be taken up depends upon the *nature of alkyl halide, strength and size of base/nucleophile* and *reaction conditions*.
 - a **bulkier nucleophile** will prefer to act as a base and abstracts a proton rather than approach a tetravalent carbon atom (steric reasons) and vice versa.
 - a **primary alkyl halide** will prefer a S_N^2 reaction,
 - a **secondary halide- S_N^2 or elimination** depending upon the strength of base/nucleophile.
 - a **tertiary halide- S_N^1 or elimination** depending upon the stability of carbocation or the more substituted alkene.



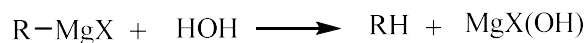
Reactions of Haloalkanes

Reaction with Metals

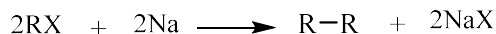
- Most organic chlorides, bromides, and iodides react with certain metals to give **organo-metallic compounds**, molecules with **carbon-metal bonds**.
- Grignard reagents** are obtained by the reaction of alkyl or aryl halides with metallic magnesium in dry ether as the solvent.



- Grignard reagents** react readily with any source of protons to give hydrocarbons.



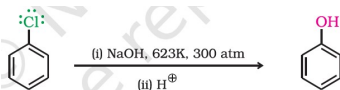
- Wurtz reaction**; Alkyl halides react with sodium in dry ether to give hydrocarbons containing double the number of carbon atoms present in the halide.



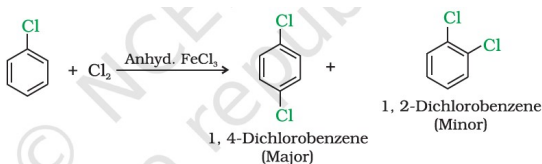
Reactions of Haloarenes

Replacement by hydroxyl group

- Chlorobenzene can be converted into phenol by heating in aqueous sodium hydroxide solution at a temperature of 623K and a pressure of 300 atmospheres.



- Electrophilic substitution reactions;** Haloarenes undergo the usual electrophilic reactions of the benzene ring such as halogenation, nitration, sulphonation and Friedel-Crafts reactions.
- Halogen atom besides being slightly deactivating is *o*-, *p*-directing; .



- Wurtz reaction;** a mixture of an alkyl halide and aryl halide gives an alkylarene when treated with sodium in dry ether

