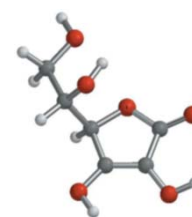جامعة الملك سعود
King Saud University

CHEM 241

Organic Chemistry II

FOR CHEMISTRY' STUDENTS, COLLEGE OF SCIENCE

PRE-REQUISITES COURSE; CHEM 240

CREDIT HOURS; 2 (2+0)

Prof. Mohamed El-Newehy

Chemistry Department, College of Science, King Saud University

http://fac.ksu.edu.sa/melnewehy/home

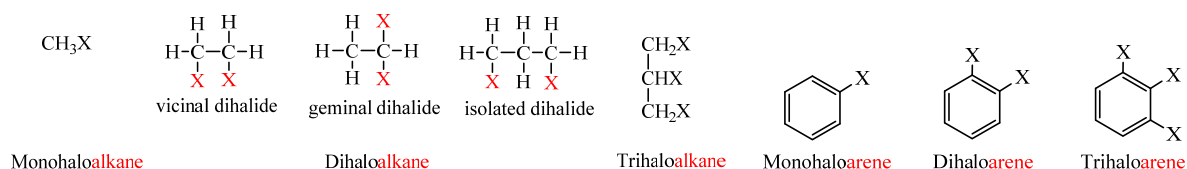**Organo-halogen Compounds**   *Based on NCERT*

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, 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.*

| CH₃X | vicinal dihalide | geminal dihalide | isolated dihalide | CH₂X CHX CH₂X | Monohaloarene | Dihaloarene | Trihaloarene |

Monohaloalkane   Dihaloalkane   Trihaloalkane

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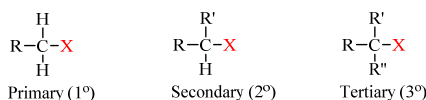
⇓

Classification of Haloalkanes and Haloarenes

Compounds Containing sp^3 C—X Bond (X= F, Cl, Br, I)
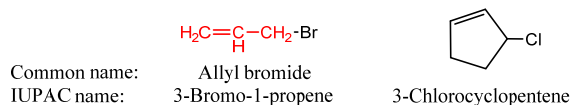
(a) *Alkyl halides or haloalkanes* (R—X)

- o The halogen atom is bonded to an alkyl group (R) & the *general formula* is $C_nH_{2n+1}X$.
- o They are classified as *primary*, *secondary* or *tertiary* according to the nature of carbon to which halogen is attached.
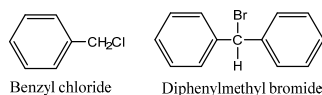
$$\underset{\substack{| \\ H \\ \text{Primary (1°)}}}{\overset{\substack{H \\ |}}{R-C-X}} \qquad \underset{\substack{| \\ H \\ \text{Secondary (2°)}}}{\overset{\substack{R' \\ |}}{R-C-X}} \qquad \underset{\substack{| \\ R'' \\ \text{Tertiary (3°)}}}{\overset{\substack{R' \\ |}}{R-C-X}}$$

(b) *Allylic halides*

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

$$H_2C=\underset{\overset{|}{H}}{C}-CH_2\text{-Br}$$

Common name: Allyl bromide
IUPAC name: 3-Bromo-1-propene

3-Chlorocyclopentene

(c) *Benzylic halides*

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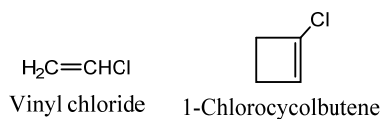
Benzyl chloride

Diphenylmethyl bromide

Classification of Haloalkanes and Haloarenes

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

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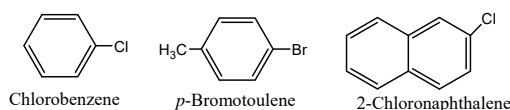
- o These are the compounds in which the halogen atom is bonded to an sp^2-hybridized carbon atom of a carbon-carbon double bond (C = C).

$$H_2C=CHCl$$

Vinyl chloride

1-Chlorocyclobutene

(b) *Aryl halides*

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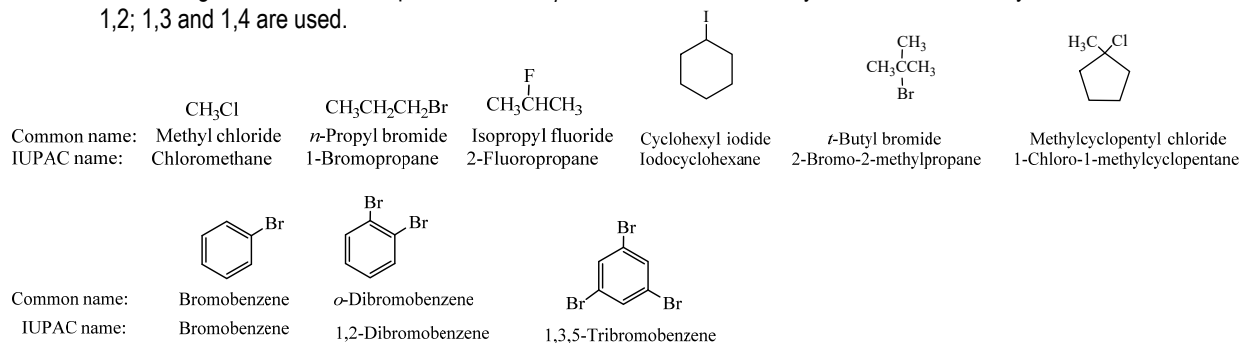
Chlorobenzene

p-Bromotoulene

2-Chloronaphthalene

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.

	CH_3Cl	$CH_3CH_2CH_2Br$	$CH_3\overset{F}{\underset{}{CH}}CH_3$	Cyclohexyl iodide	$CH_3\overset{CH_3}{\underset{Br}{CCH_3}}$	$H_3C\;Cl$
Common name:	Methyl chloride	*n*-Propyl bromide	Isopropyl fluoride	Cyclohexyl iodide	*t*-Butyl bromide	Methylcyclopentyl chloride
IUPAC name:	Chloromethane	1-Bromopropane	2-Fluoropropane	Iodocyclohexane	2-Bromo-2-methylpropane	1-Chloro-1-methylcyclopentane

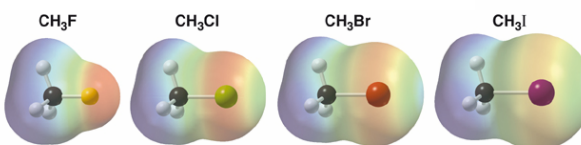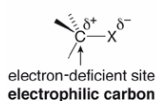|	Bromobenzene	*o*-Dibromobenzene	1,3,5-Tribromobenzene
Common name:	Bromobenzene	*o*-Dibromobenzene	
IUPAC name:	Bromobenzene	1,2-Dibromobenzene	

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*.

$$\overset{\delta+}{C} \longrightarrow \overset{\delta-}{X}$$
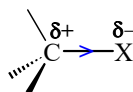
Carbon-Halogen (C—X) Bond Lengths, Bond Strength and Dipole Moments

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

General structure CH_3F CH_3Cl CH_3Br CH_3I

$\overset{\delta+}{C}—\overset{\delta-}{X}$

electron-deficient site
electrophilic carbon

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

Importance of Organohalogen Compounds

a) **Solvents:** Alkyl halides are used as solvents for relatively **non-polar** compounds: CCl_4, $CHCl_3$, CCl_3CH_3, CH_2Cl_2, ….*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.*
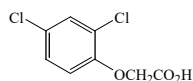
c) Refrigerants: Freons (ChloroFluoroCarbon)

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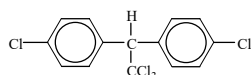
DDT: [1,1,1-trichloro-2,2-bis(*p*-chlorophenyl)ethane]

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}
CH₂=CH−	−72	0.68^{26}	−13.9	0.91^{20}	16	1.52^{14}	56	2.04^{20}
CH₂=CHCH₂−	−3		45	0.94^{20}	70	1.40^{20}	102-103	1.84^{22}
C₆H₅−	85	1.02^{20}	132	1.10^{20}	155	1.52^{20}	189	1.82^{20}
C₆H₅CH₂−	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 polarizabilty 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

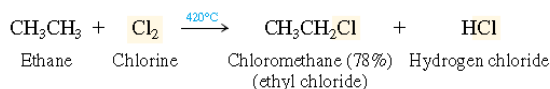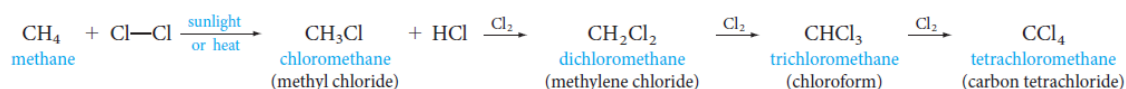| Size of hydrocarbon part		Type of halogen		# of halogen atoms	
Compound	bp [°C]	Compound	bp [°C]	Compound	bp [°C]
$CH_3 - Cl$	- 24	$CH_3CH_2 - F$	- 38	CH_3Cl	- 24
$CH_3CH_2 - Cl$	12	$CH_3CH_2 - Cl$	12	CH_2Cl_2	40
$CH_3CH_2CH_2 - Cl$	47	$CH_3CH_2 - Br$	38	$CHCl_3$	61
$CH_3CH_2CH_2CH_2 - Cl$	78	$CH_3CH_2 - I$	72	CCl_4	77

For comparison: $CH_3 - CH_3$ bp – 89 °C

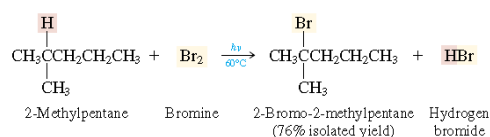# Preparation of Halogen Compounds

From Hydrocarbons

(a) *By free radical halogenation; Alkyl halide*

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

$$CH_4 + Cl-Cl \xrightarrow{sunlight \ or \ heat} CH_3Cl + HCl \xrightarrow{Cl_2} CH_2Cl_2 \xrightarrow{Cl_2} CHCl_3 \xrightarrow{Cl_2} CCl_4$$

methane   chloromethane   dichloromethane   trichloromethane   tetrachloromethane
                        (methyl chloride)   (methylene chloride) (chloroform)   (carbon tetrachloride)

$$CH_3CH_3 + Cl_2 \xrightarrow{420°C} CH_3CH_2Cl + HCl$$

Ethane   Chlorine   Chloromethane (78%) Hydrogen chloride
                      (ethyl chloride)

$$CH_3CH_2CH_3 + Cl_2 \xrightarrow{light \ or \ heat} CH_3CH_2CH_2Cl + CH_3CHCH_3 + HCl$$
                                                                                 |
                                                                                 Cl

propane   1-chloropropane   2-chloropropane
                                          (*n*-propyl chloride) (isopropyl chloride)

○ **Rate of halogenation:** $R_3CH > R_2CH_2 > RCH_3$

(tertiary)   (secondary)   (primary)

$$CH_3\overset{H}{C}CH_2CH_2CH_3 + Br_2 \xrightarrow[60°C]{hv} CH_3\overset{Br}{C}CH_2CH_2CH_3 + HBr$$
           | |
           CH_3 CH_3

2-Methylpentane   Bromine   2-Bromo-2-methylpentane   Hydrogen
                              (76% isolated yield)   bromide
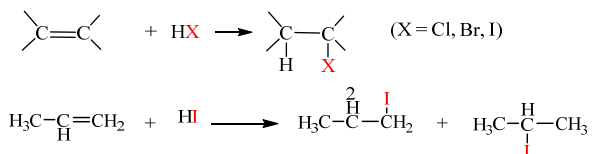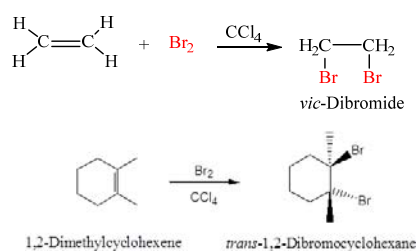
Preparation of Halogen Compounds

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.
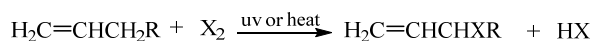
$$\text{C}=\text{C} \quad + \quad \text{HX} \quad \longrightarrow \quad \underset{\underset{\text{H} \quad \text{X}}{|} }{\text{C}}-\text{C} \qquad (\text{X} = \text{Cl, Br, I})$$

$$\text{H}_3\text{C}-\underset{\text{H}}{\text{C}}=\text{CH}_2 \quad + \quad \text{HI} \quad \longrightarrow \quad \text{H}_3\text{C}-\overset{\text{H}}{\underset{}{\text{C}}}-\text{CH}_2 \quad + \quad \text{H}_3\text{C}-\underset{\text{I}}{\overset{\text{H}}{\text{C}}}-\text{CH}_3$$

(ii) *Addition of halogens:* addition of bromine in CCl$_4$ to an alkene resulting in the synthesis of *vic*-dibromides.
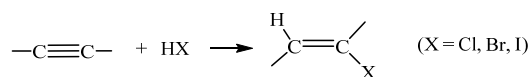
$$\underset{\text{H}}{\overset{\text{H}}{\text{C}}}=\underset{\text{H}}{\overset{\text{H}}{\text{C}}} \quad + \quad \text{Br}_2 \quad \xrightarrow{\text{CCl}_4} \quad \text{H}_2\text{C}-\text{CH}_2$$
$$\underset{\text{Br} \quad \text{Br}}{}$$
vic-Dibromide

1,2-Dimethylcyclohexene $\xrightarrow[\text{CCl}_4]{\text{Br}_2}$ *trans*-1,2-Dibromocyclohexane

Preparation of Halogen Compounds

From Hydrocarbons

(iii) *Halogenation of alkenes: Allyl halides*

$$\text{H}_2\text{C}=\text{CHCH}_2\text{R} \quad + \quad \text{X}_2 \quad \xrightarrow{\text{uv or heat}} \quad \text{H}_2\text{C}=\text{CHCHXR} \quad + \quad \text{HX}$$

(c) *From Alkynes*

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

$$-\text{C}\equiv\text{C}- \quad + \quad \text{HX} \quad \longrightarrow \quad \underset{\text{X}}{\overset{\text{H}}{\text{C}}}=\text{C} \qquad (\text{X} = \text{Cl, Br, I})$$

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

$$\text{H}-\text{C}\equiv\text{C}-\text{H} \xrightarrow{\text{Br}_2} \underset{\text{Br}}{\overset{\text{H}}{\text{C}}}=\underset{\text{H}}{\overset{\text{Br}}{\text{C}}} \xrightarrow{\text{Br}_2} \text{H}-\underset{\underset{\text{Br}}{|}}{\overset{\overset{\text{Br}}{|}}{\text{C}}}-\underset{\underset{\text{Br}}{|}}{\overset{\overset{\text{Br}}{|}}{\text{C}}}-\text{H}$$

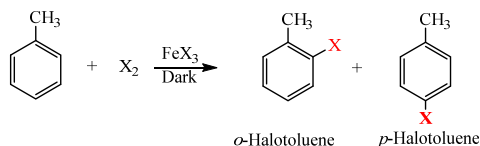ethyne   *trans*-1,2-dibromoethene   1,1,2,2-tetrabromoethane
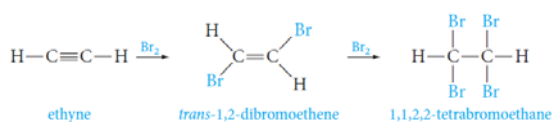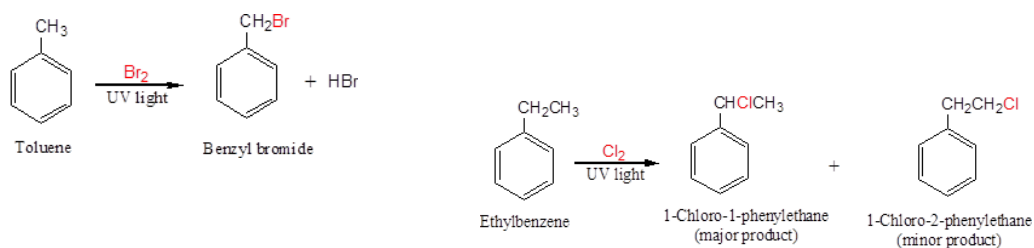
Preparation of Halogen Compounds

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.

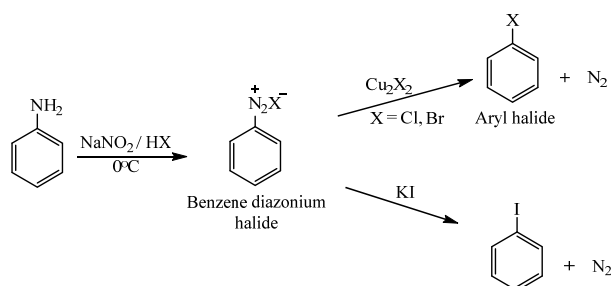(ii) *Halogenation of an Alkyl Side Chain of Benzene derivatives; Benzyl halides*

Preparation of Halogen Compounds

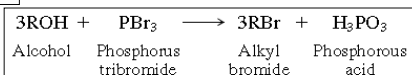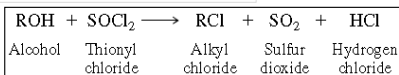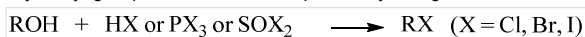## From Hydrocarbons

(e) Sandmeyer's reaction; Aryl halide

o 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.
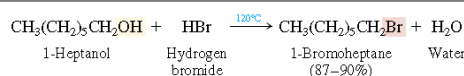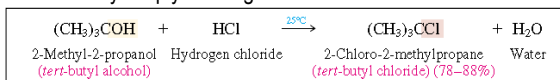
Preparation of Halogen Compounds

From Alcohols

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

$$ROH \ + \ HX \ or \ PX_3 \ or \ SOX_2 \ \longrightarrow \ RX \ \ (X = Cl, Br, I)$$

$$ROH \ + \ SOCl_2 \longrightarrow \ RCl \ + \ SO_2 \ + \ HCl$$

| Alcohol | Thionyl chloride | Alkyl chloride | Sulfur dioxide | Hydrogen chloride |

$$3ROH \ + \ PBr_3 \ \longrightarrow \ 3RBr \ + \ H_3PO_3$$

| Alcohol | Phosphorus tribromide | Alkyl bromide | Phosphorous acid |

o The reactions of *primary* and *secondary alcohols* with HCl require the presence of a catalyst, $ZnCl_2$.

$$CH_3(CH_2)_5CH_2OH \ + \ HBr \ \xrightarrow{120^\circ C} \ CH_3(CH_2)_5CH_2Br \ + \ H_2O$$

| 1-Heptanol | Hydrogen bromide | 1-Bromoheptane (87–90%) | Water |

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

$$(CH_3)_3COH \ + \ HCl \ \xrightarrow{25^\circ C} \ (CH_3)_3CCl \ + \ H_2O$$

| 2-Methyl-2-propanol (*tert*-butyl alcohol) | Hydrogen chloride | 2-Chloro-2-methylpropane (*tert*-butyl chloride) (78–88%) | Water |

o The order of reactivity of alcohols is 3°>2°>1°.

o *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.*
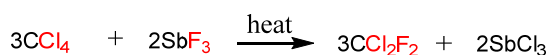
Preparation of Halogen Compounds

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.

$$R-X \ + \ NaI \ \longrightarrow \ R-I \ \ (X = Cl, Br)$$

(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, Hg_2F_2, CoF_2 or SbF_3. The reaction is termed as Swarts reaction.

$$CH_3Br \ + \ AgF \ \xrightarrow{heat} \ CH_3F \ + \ AgBr$$
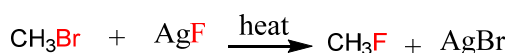
The manufacture of chlorofluoro compounds, known as Freons.

$$3CCl_4 \ + \ 2SbF_3 \ \xrightarrow{heat} \ 3CCl_2F_2 \ + \ 2SbCl_3$$

Reactions of Haloalkanes

The reactions of organic halides fall into three categories

(i) Nucleophiic 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

$$\text{Nu:} \; + \; \overset{+}{\text{C}}-\text{X}^- \longrightarrow \text{C}-\text{Nu} \; + \; \text{X}^-$$
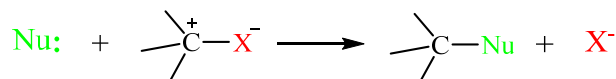
Nu:, is the nucleophile.
The nucleophile has an unshared electron pair available for bonding.

X, is the leaving group.
The leaving group is also a nucleophile.

Reactions of Haloalkanes

Nucleophilic Substitution (S_N) Reactions

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

  ✓ Good leaving groups include H_2O and *anions* (the conjugate bases) of strong acids, such as Cl, Br, I, and HSO_4.

  ✓ 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)

$$Nu: \;+\; R{-}X \longrightarrow R{-}Nu \;+\; X^-$$
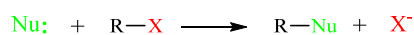
| Reagent	Nucleophile (Nu⁻)	Substitution product R–Nu	Class of main product
NaOH (KOH)	HO⁻	ROH	Alcohol
H₂O	H₂O	ROH	Alcohol
NaOR′	R′O⁻	ROR′	Ether
NaI	I⁻	R—I	Alkyl iodide
NH₃	NH₃	RNH₂	Primary amine
R′NH₂	R′NH₂	RNHR′	Sec. amine
R′R″NH	R′R″NH	RNR′R″	Tert. amine
KCN	C≡N:	RCN	Nitrile (cyanide)
AgCN	Ag-CN:	RNC (isocyanide)	Isonitrile
KNO₂	O=N—O	R—O—N=O	Alkyl nitrite
AgNO₂	Ag—Ö—N=O	R—NO₂	Nitroalkane
R′COOAg	R′COO⁻	R′COOR	Ester
LiAlH₄	H	RH	Hydrocarbon
R⁻M⁺	R⁻	RR′	Alkane

Reactions of Haloalkanes

Mechanism of Nucleophilic Substitution (S_N) Reactions

o Alkyl halides may undergo nucleophilic substitutions in two different ways:
  (i) by a one-step mechanism.
  (ii) by a two-step mechanism.

o Which route is taken depends on
  (i) The structure of the halide.
  (ii) The nature of the solvent.
  (iii) The strength of the nucleophile, Nu:.

o 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.

o Let us consider the conversion of an alkyl halide to an alcohol by hydroxide.

$$R{-}X \;+\; {}^-OH \longrightarrow R{-}OH \;+\; X^-$$
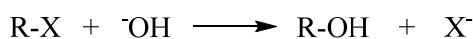
Reactions of Haloalkanes
One-Step Mechanism: S_N2 Reactions
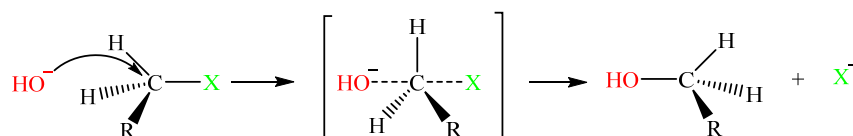
- o The incoming nucleophile interacts with alkyl halide causing; *the carbon-halide bond to break while forming a new carbon-OH bond*.

- o These two processes take place in a single step and no intermediate is formed.

- o The nucleophile attacks the halogen-bearing carbon from the side opposite the leaving group; *a so-called backside attack.*

- o 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").*

- o This flipping of the bonds, known as the Walden inversion.

Reactions of Haloalkanes
One-Step Mechanism: S_N2 Reactions
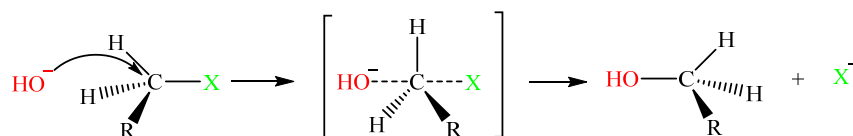
- o Bimolecular Nucleophilic Substitution (S_N2) reaction.

- o The reaction rate depends on the concentrations of both reactants, the alkyl halide and the nucleophile.

- o 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
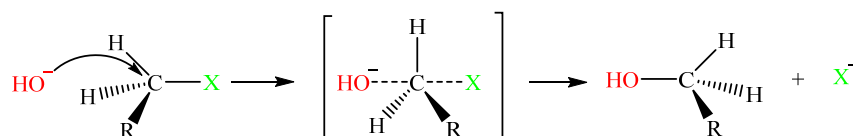
o The rates of hydrolysis follow the order; 1° RX > 2° RX > 3° RX

o Tertiary alkyl halides react slowest by the S_N2 mechanism because the three alkyl groups on the carbon that bears the halogen binder the backside approach of the attacking nucleophile.
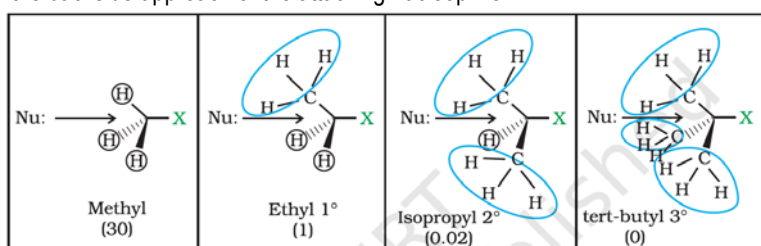
Steric effects in S_N2 reaction.

Reactions of Haloalkanes

One-Step Mechanism: S_N2 Reactions
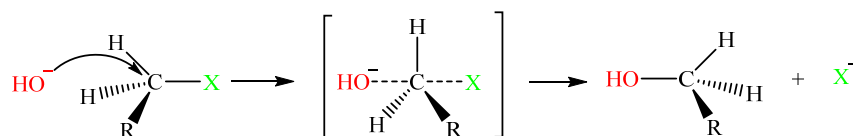
Summary;

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

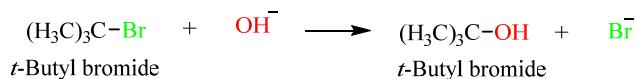➢ The reaction between *tert*-butyl bromide and hydroxide ion yields *tert*-butyl alcohol and follows the first order kinetics, *i.e., the rate of reaction depends upon the concentration of only one reactant*, which is *tert- butyl bromide*.

$$(H_3C)_3C-Br \quad + \quad OH^- \longrightarrow (H_3C)_3C-OH \quad + \quad Br^-$$

t-Butyl bromide   *t*-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.*

t-Butyl bromide   Carbocation
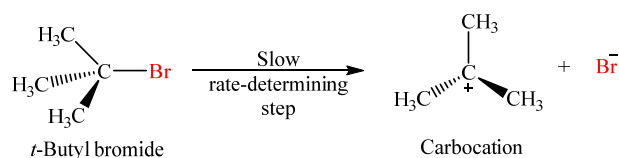
Reactions of Haloalkanes

Two-Step Mechanism: S_N1 Reactions

 Step 2. The carbocation thus formed is then attacked by nucleophile to complete the substitution reaction. *This step occurs rapidly.*

  o 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)

Retained configuration
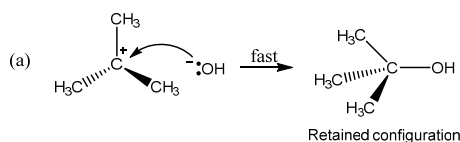
   ▪ on *the back side* (leading to *inversion).*

Inverted configuration
(Walden inversion)
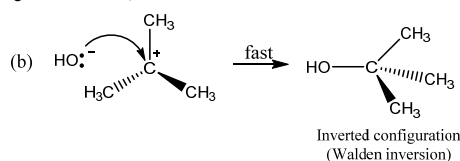
  o If the starting alkyl halide were optically active, the product would be a *racemic mixture.*

Reactions of Haloalkanes

Two-Step Mechanism: S_N1 Reactions

o The rate of substitution is _independent of the OH⁻ ion concentration_ and _depends only on the concentration of the alkyl halide_.

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

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

o S_N1 reactions are generally carried out in polar protic solvents (like water, alcohol, acetic acid, etc.).

▪ _Polar protic solvents have a hydrogen atom attached to an electronegative atom so the hydrogen is highly polarized and help to stabilize the transition state._

▪ Sometimes in an S_N1 reaction is called a solvolysis reaction if the solvent acts as the nucleophile.

o Weak bases are good leaving groups as they can leave with both electrons and in order for the leaving group to leave, it needs to be able to accept electrons.

o Strong bases can't be good leaving groups as they donate electrons.

o Halides are an example of a good leaving group.

|	
Excellent	• TsO⁻ • NH₃
Very Good	• I⁻ • H₂O
Good	• Br⁻
Fair	• Cl⁻
Poor	• F⁻
Very Poor	• OH⁻ • NH₂⁻

I⁻ > Br⁻ > Cl⁻ > F⁻

Best   Worst

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

o *General consideration*

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

B=Base ; X=Leaving group
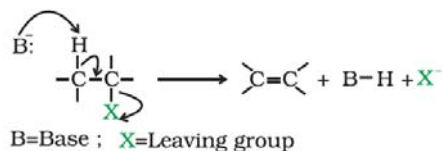
o Mechanism of Eliminations are of two types:

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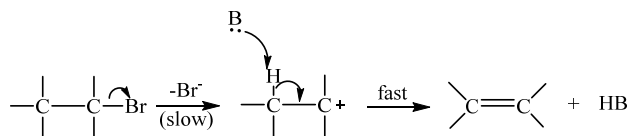- The E2 (elimination bimolecular) reaction.

o *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

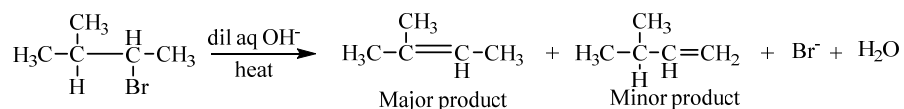o The E1, involves the *formation of a carbocation* in the rate-determining step.

o The order of reactivity of E1 reactions is

Benzyl > allyl = 3° > 2° > 1° halide

o The product of an E1 reaction is an alkene.

Major product   Minor product

Reactions of Haloalkanes

E2 Mechanism

- o **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 /3 hydrogen).

- o 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.*

- o *The single-step E2 elimination.*

- o The order of reactivity of E2 elimination is

    1° RX > 2° RX > 3° RX

Reactions of Haloalkanes

Elimination versus Substitution

- o 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.

- o 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.

Elimination   *vs*   Substitution

Reactions of Haloalkanes

Elimination versus Substitution

o The most important being the structure of the alkyl group and the nature of the nucleophilic reactant.

o Strong nucleophile favor substitution, and strong bases, especially strong hindered bases (such as *tert*-butoxide) favor elimination.

o It is assumed that the alkyl halides have one or more beta-hydrogens, making elimination possible.

o The nature of the halogen substituent on the alkyl halide is usually not very significant if it is Cl, Br or I.

- In cases where both S_N2 and E2 reactions compete;
  - chlorides generally give more elimination than do iodides, since the greater electronegativity of chlorine increases the acidity of beta-hydrogens.
  - Indeed, although alkyl fluorides are relatively unreactive, when reactions with basic nucleophiles are forced, elimination occurs (note the high electronegativity of fluorine).
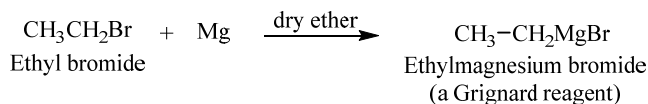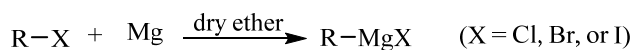

Reactions of Haloalkanes

Elimination versus Substitution

| Nucleophile		Anionic Nucleophiles (Weak Bases: I⁻, Br⁻, SCN⁻, N₃⁻, CH₃CO₂⁻ , RS⁻, CN⁻ etc.) pK$_a$'s from -9 to 10 (left to right)	Anionic Nucleophiles (Strong Bases: HO⁻, RO⁻) pK$_a$'s > 15	Neutral Nucleophiles (H₂O, ROH, RSH, R₃N) pK$_a$'s ranging from -2 to 11
Alkyl Group				
	Primary RCH₂–	Rapid S$_N$2 substitution. The rate may be reduced by substitution of β-carbons, as in the case of neopentyl.	Rapid S$_N$2 substitution. E2 elimination may also occur. *e.g.* ClCH₂CH₂Cl + KOH ——> CH₂=CHCl	S$_N$2 substitution. (N ≈ S >>O)
	Secondary R₂CH–	S$_N$2 substitution and / or E2 elimination (depending on the basicity of the nucleophile). Bases weaker than acetate (pK$_a$ = 4.8) give less elimination. The rate of substitution may be reduced by branching at the β-carbons, and this will increase elimination.	E2 elimination will dominate.	S$_N$2 substitution. (N ≈ S >>O) In high dielectric ionizing solvents, such as water, dimethyl sulfoxide & acetonitrile, S$_N$1 and E1 products may be formed slowly.
	Tertiary R₃C–	E2 elimination will dominate with most nucleophiles (even if they are weak bases). No S$_N$2 substitution due to steric hindrance. In high dielectric ionizing solvents, such as water, dimethyl sulfoxide & acetonitrile, S$_N$1 and E1 products may be expected.	E2 elimination will dominate. No S$_N$2 substitution will occur. In high dielectric ionizing solvents S$_N$1 and E1 products may be formed.	E2 elimination with nitrogen nucleophiles (they are bases). No S$_N$2 substitution. In high dielectric ionizing solvents S$_N$1 and E1 products may be formed.

Reactions of Haloalkanes

Reaction with Metals

o Most organic chlorides, bromides, and iodides react with certain metals to give organo-metallic compounds, molecules with carbon-metal bonds.

o *Grignard reagents* are obtained by the reaction of alkyl or aryl halides with metallic magnesium in dry ether as the solvent.

$$R-X \ + \ Mg \ \xrightarrow{\text{dry ether}} \ R-MgX \qquad (X = Cl, Br, or I)$$

$$CH_3CH_2Br \ + \ Mg \ \xrightarrow{\text{dry ether}} \ CH_3-CH_2MgBr$$
Ethyl bromide
Ethylmagnesium bromide
(a Grignard reagent)

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

$$R-MgX \ + \ HOH \longrightarrow \ RH \ + \ MgX(OH)$$
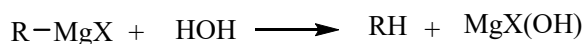
o Wurtz reaction; Alkyl halides react with sodium in dry ether to give hydrocarbons containing double the number of carbon atoms present in the halide.

$$2RX \ + \ 2Na \longrightarrow \ R-R \ + \ 2NaX$$
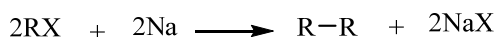
Reactions of Haloarenes

Replacement by hydroxyl group

o Chlorobenzene can be converted into phenol by heating in aqueous sodium hydroxide solution at a temperature of 623K and a pressure of 300 atmospheres.
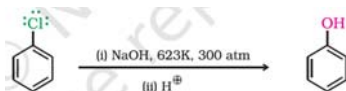
o *Electrophilic substitution reactions;* Haloarenes undergo the usual electrophilic reactions of the benzene ring such as halogenation, nitration, sulphonation and Friedel-Crafts reactions.
o Halogen atom besides being slightly deactivating is *o-*, *p*-directing; .
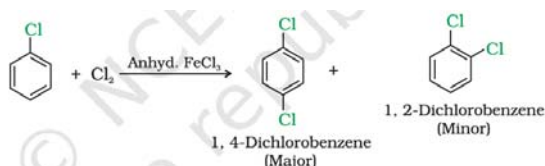
o Wurtz reaction; a mixture of an alkyl halide and aryl halide gives an alkylarene when treated with sodium in dry ether