

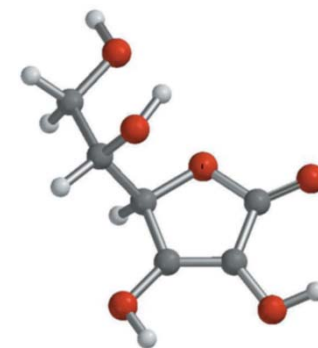
CHEM 244

PRINCIPLES OF ORGANIC CHEMISTRY I

FOR CHEMICAL ENGINEERING' STUDENTS, COLLEGE OF ENGINEERING

PRE-REQUISITES COURSE; CHEM 101

CREDIT HOURS; 2 (2+0)



Dr. Mohamed El-Newehy

Chemistry Department, College of Science, King Saud University

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

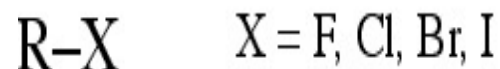
CHAPTER 5

ORGANIC HALOGEN COMPOUNDS

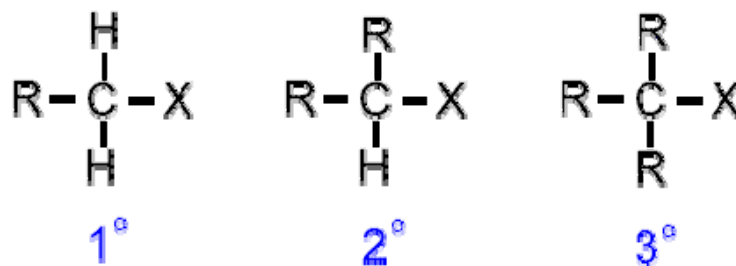
CLASSES AND NOMENCLATURE OF HALOGEN COMPOUNDS



- *Alkyl halides*, R-X.

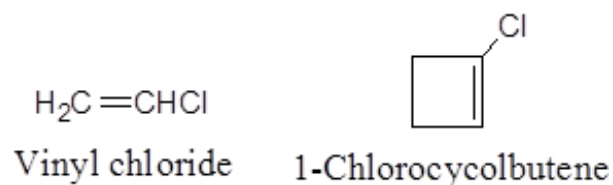


- Depending on the type of carbon to which the halogen is attached, *Alkyl halides* are subdivided into; *primary* (1°), *secondary* (2°), or *tertiary* (3°).

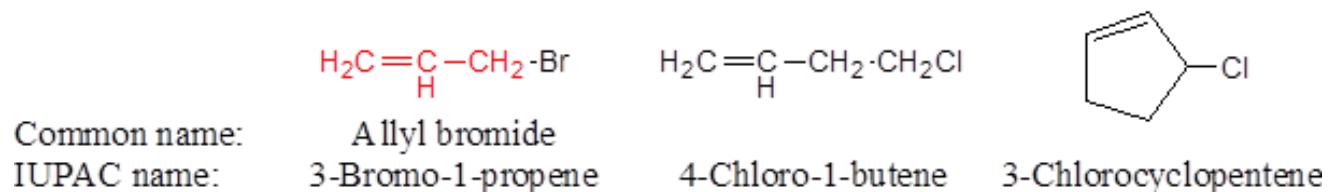


CLASSES AND NOMENCLATURE OF HALOGEN COMPOUNDS

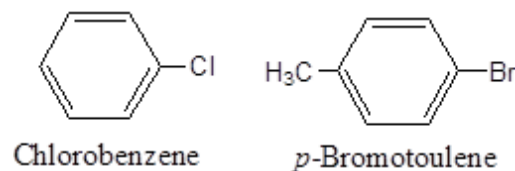
- **Vinylic halides;** A halogen attached directly to a doubly bonded carbon.



- **Allylic halides;** The halogen attached to a carbon next to a doubly bonded carbon.

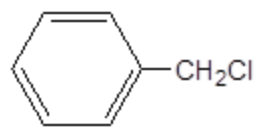


- **Aryl halides, Ar-X;** The halogen is directly attached to an aromatic ring.

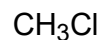


CLASSES AND NOMENCLATURE OF HALOGEN COMPOUNDS

- **Benzylic halides, $Ar-C-X$** ; The halogen one carbon away from an aromatic ring.



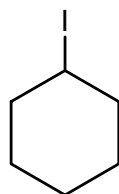
Benzyl chloride



Common name: Methyl chloride

IUPAC name: Chloromethane

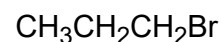
Class: 1°



Common name: Cyclohexyl iodide

IUPAC name: Iodocyclohexane

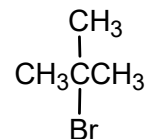
Class: 2°



n-Propyl bromide

1-Bromopropane

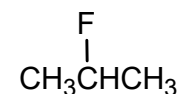
1°



t-Butyl bromide

2-Bromo-2-methylpropane

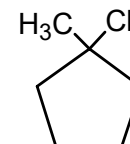
3°



Isopropyl fluoride

2-Fluoropropane

2°



Methylcyclopentyl chloride

1-Chloro-1-methylcyclopentane

3°

PHYSICAL PROPERTIES OF HALOGEN COMPOUNDS

○ Solubility

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

○ Boiling points

- *Within a series of halides, the boiling points increase with increasing molecular weights.*

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

	CH_3F	CH_3Cl	CH_3Br	CH_3I
Mol Wt =	34	50.5	95	142
bp =	$-78^{\circ}C$	$-24^{\circ}C$	$4^{\circ}C$	$42^{\circ}C$

- *Within a homologous series, the boiling points also increase regularly with molecular weights.*

CH_3Cl	CH_3CH_2Cl	$CH_3CH_2CH_2Cl$
(bp = $-24^{\circ}C$)	(bp = $12^{\circ}C$)	(bp = $47^{\circ}C$)

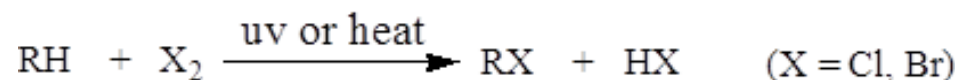
- *Within a series of isomers, the straight-chain compound has the highest boiling point, and the most branched isomer the lowest boiling point.*

$CH_3CH_2CH_2CH_2Br$	$\begin{array}{c} CH_3 \\ \\ H_3C-C-CH_2Br \\ \\ CH_3 \end{array}$
(bp = $101^{\circ}C$)	(bp = $73^{\circ}C$)

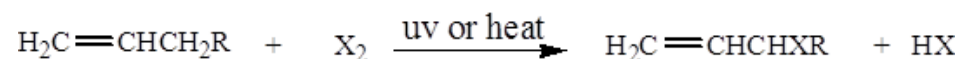
PREPARATION OF HALOGEN COMPOUNDS

1) Direct halogenation of hydrocarbons.

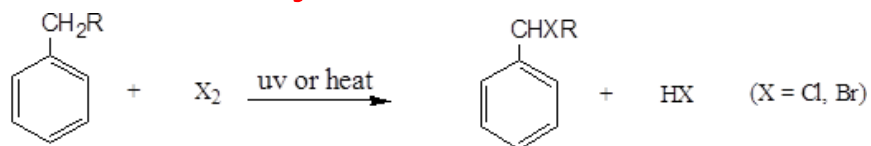
a) Halogenation of alkanes: Alkyl halides



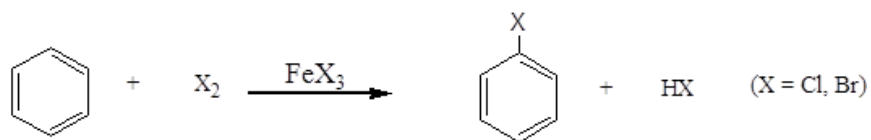
b) Halogenation of alkenes: Allyl halides



c) Halogenation of alkyl benzenes: Benzyl halides



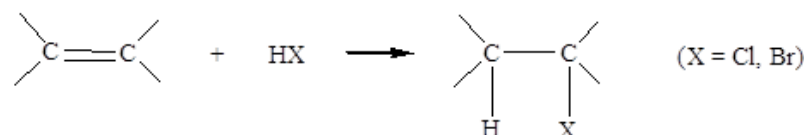
d) Halogenation of aromatic ring: Aryl halides



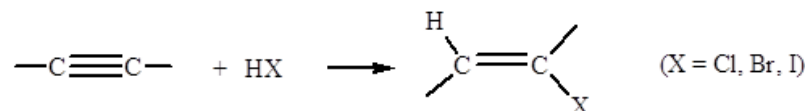
PREPARATION OF HALOGEN COMPOUNDS

2) Addition of HX to unsaturated hydrocarbons

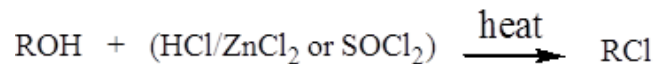
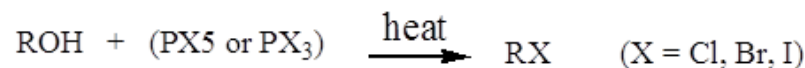
a) Addition of HX to alkenes: Alkyl halides



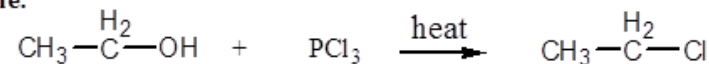
b) Addition of HX to alkynes: Vinyl halides



3) Conversion of alcohols: Alkyl halides



Example:



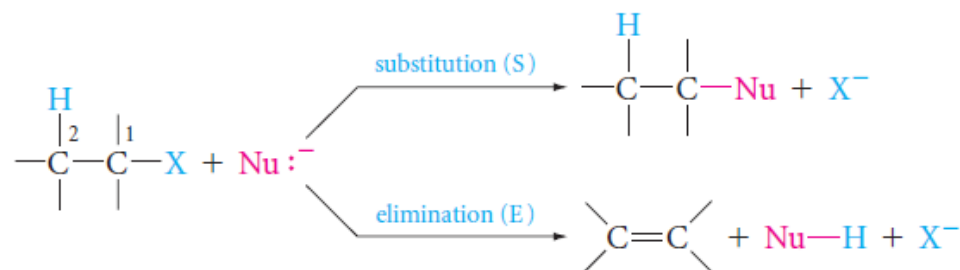
REACTIONS OF ALKYL COMPOUNDS

A) Nucleophilic substitution, or S_N , reactions.

Alkyl halides undergo **nucleophilic substitution reactions**, in which a nucleophile displaces the halide **leaving group** from the alkyl halide **substrate**.

B) Elimination, or E, reactions.

Those that involve the loss of HX from the halide.



C) Formation of organometallic compounds.

Those that involve reaction with certain metals.

A) NUCLEOPHILIC SUBSTITUTION (S_N) REACTIONS

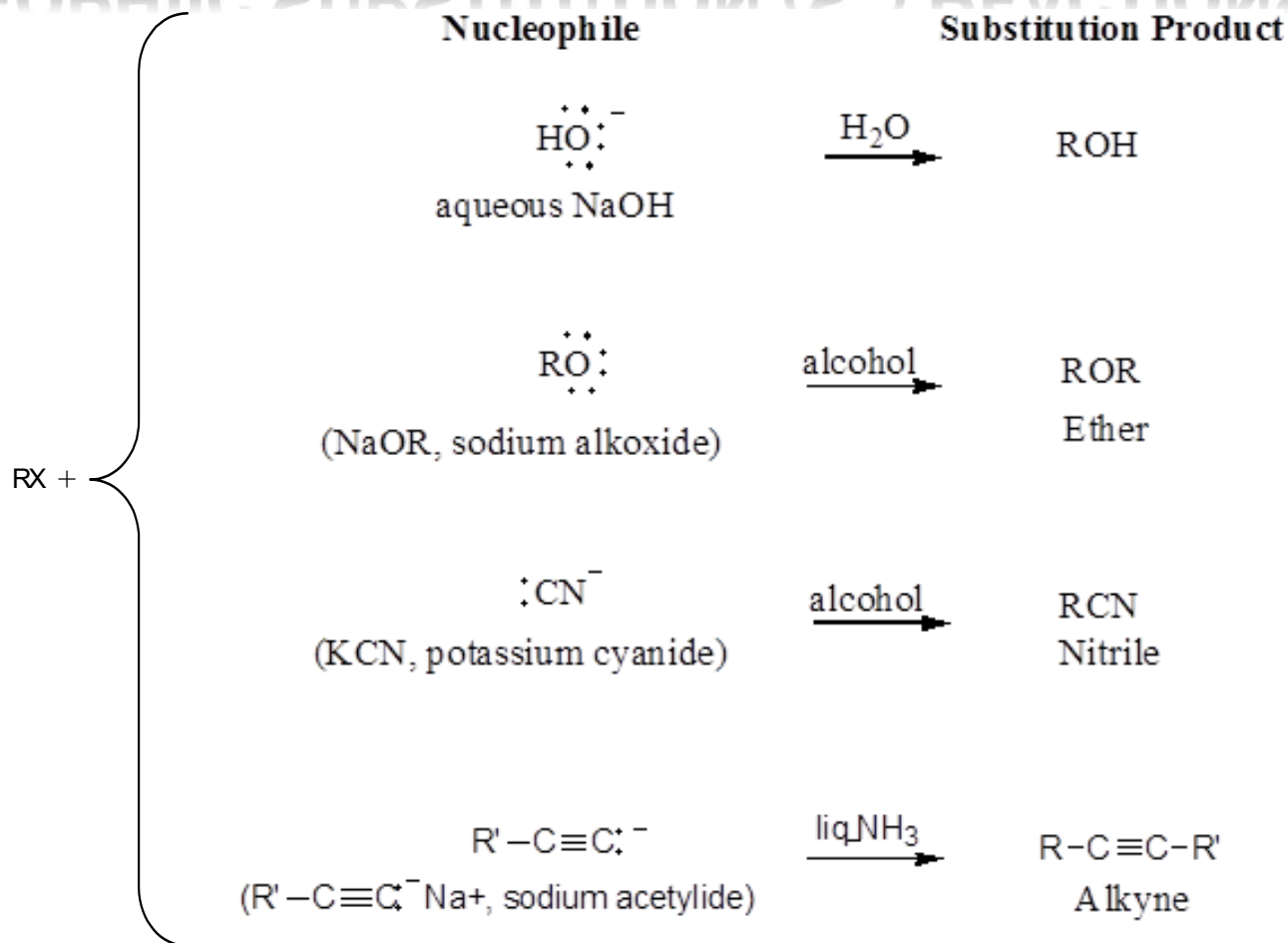
- $$\text{HO}^- + \underset{\text{ethyl bromide}}{\text{CH}_3\text{CH}_2-\text{Br}} \xrightarrow{\text{H}_2\text{O}} \underset{\text{ethanol}}{\text{CH}_3\text{CH}_2-\text{OH}} + \text{Br}^-$$

- In general



REACTIONS OF ALKYL COMPOUNDS

A) NUCLEOPHILIC SUBSTITUTION (S_N) REACTIONS



REACTIONS OF ALKYL COMPOUNDS

A) NUCLEOPHIIC SUBSTITUTION (S_N) REACTIONS

Reactions of Common Nucleophiles with Alkyl Halides				
Nu		R—Nu		Comments
Formula	Name	Formula	Name	
<i>Oxygen nucleophiles</i>				
1. HO^-	hydroxide	$\text{R}-\text{OH}$	alcohol	<div><div></div><div>These ions lose a proton and the products are alcohols and ethers.</div><div>$\xrightarrow{-\text{H}^+} \text{ROH}$ (alcohol)</div><div>$\xrightarrow{-\text{H}^+} \text{ROR}$ (ether)</div></div>
2. RO^-	alkoxide	$\text{R}-\text{OR}$	ether	
3. HOH	water	$\text{R}-\overset{+}{\text{O}}\begin{matrix} \text{H} \\ \text{H} \end{matrix}$	alkyloxonium ion	
4. ROH	alcohol	$\text{R}-\overset{+}{\text{O}}\begin{matrix} \text{R} \\ \text{H} \end{matrix}$	dialkyloxonium ion	
5. $\text{R}-\text{C}\begin{matrix} \text{O} \\ \parallel \\ \text{O}^- \end{matrix}$	carboxylate	$\text{R}-\overset{\text{O}}{\parallel}\text{O}-\text{R}$	ester	

REACTIONS OF ALKYL COMPOUNDS

A) NUCLEOPHIIC SUBSTITUTION (S_N) REACTIONS

Reactions of Common Nucleophiles with Alkyl Halides				
Nu		R—Nu		Comments
Formula	Name	Formula	Name	
<i>Nitrogen nucleophiles</i>				
6. $\ddot{\text{N}}\text{H}_3$	ammonia	$\text{R}-\overset{+}{\text{N}}\text{H}_3$	alkylammonium ion	} With a base, these ions readily lose a proton to give amines. <div>$\xrightarrow{-\text{H}^+} \ddot{\text{N}}\text{H}_2$ $\xrightarrow{-\text{H}^+} \text{R}_2\ddot{\text{N}}\text{H}$ $\xrightarrow{-\text{H}^+} \text{R}_3\ddot{\text{N}}:$</div>
7. RNH_2	primary amine	$\text{R}-\overset{+}{\text{N}}\text{H}_2\text{R}$	dialkylammonium ion	
8. $\text{R}_2\ddot{\text{N}}\text{H}$	secondary amine	$\text{R}-\overset{+}{\text{N}}\text{HR}_2$	trialkylammonium ion	
9. $\text{R}_3\ddot{\text{N}}$	tertiary amine	$\text{R}-\overset{+}{\text{N}}\text{R}_3$	tetraalkylammonium ion	

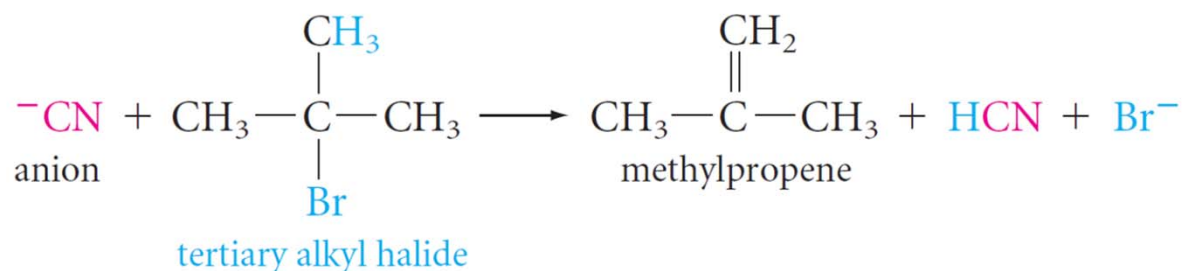
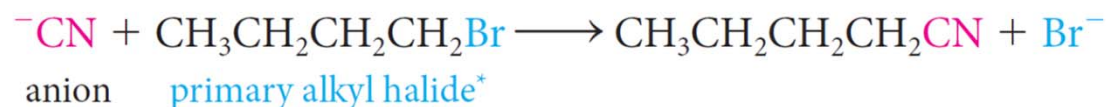
REACTIONS OF ALKYL COMPOUNDS

A) NUCLEOPHIIC SUBSTITUTION (S_N) REACTIONS

Reactions of Common Nucleophiles with Alkyl Halides				
Nu		R—Nu		Comments
Formula	Name	Formula	Name	
Sulfur nucleophiles				
10. HS^-	hydrosulfide	$\text{R}-\ddot{\text{S}}\text{H}$	thiol	
11. RS^-	mercaptide	$\text{R}-\ddot{\text{S}}\text{R}$	thioether (sulfide)	
12. $\text{R}_2\ddot{\text{S}}:$	thioether	$\text{R}-\overset{+}{\text{S}}\text{R}_2$	trialkylsulfonium ion	
Halogen nucleophiles				
13. $:\ddot{\text{I}}^-$	iodide	$\text{R}-\ddot{\text{I}}:$	alkyl iodide	The usual solvent is acetone. Sodium iodide is soluble in acetone, but sodium bromide and sodium chloride are not.
Carbon nucleophiles				
14. $^-:\text{C}\equiv\text{N}:$	cyanide	$\text{R}-\text{C}\equiv\text{N}:$	alkyl cyanide (nitrile)	Sometimes the isonitrile, $\text{R}-\overset{+}{\text{N}}\equiv\text{C}^-:$, is formed.
15. $^-:\text{C}\equiv\text{CR}$	acetylide	$\text{R}-\text{C}\equiv\text{CR}$	alkyne	

REACTIONS OF ALKYL COMPOUNDS

A) NUCLEOPHIIC SUBSTITUTION (S_N) REACTIONS



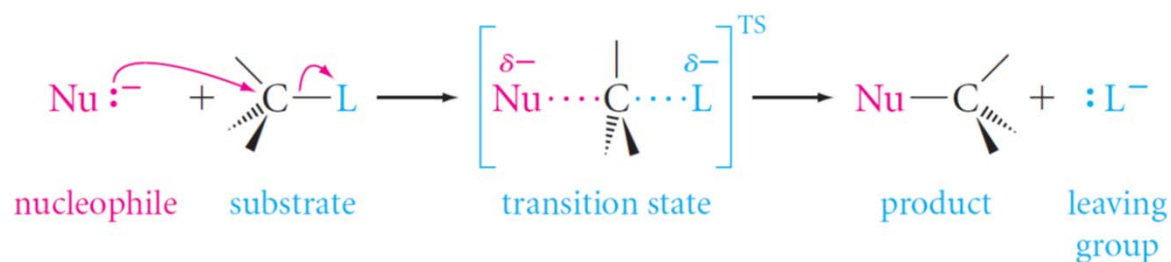
Nucleophilic Substitution (S_N) Mechanisms

- There are two main nucleophilic substitution mechanisms; S_N2 and S_N1.
 - The S_N part of each symbol stands for “substitution, nucleophilic”.
 - The meaning of the numbers 2 (*bimolecular*) and 1 (*unimolecular*).

NUCLEOPHILIC SUBSTITUTION (S_N) REACTIONS

THE S_N2 MECHANISM

The S_N2 mechanism is a **one-step process**; the bond to the leaving group begins to break as the bond to the nucleophile begins to form.



- The nucleophile attacks from the **backside of the C - L bond** (**inversion of configuration**).
- At the **transition state**; the nucleophile *and* the leaving group are *both* partly bonded to the carbon at which substitution occurs.
- The **number 2** (**bimolecular**); The **rate of the reaction** depends on both the *nucleophile and the substrate concentrations*.

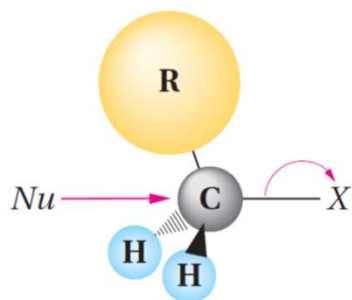
NUCLEOPHILIC SUBSTITUTION (S_N) REACTIONS

THE S_N2 MECHANISM

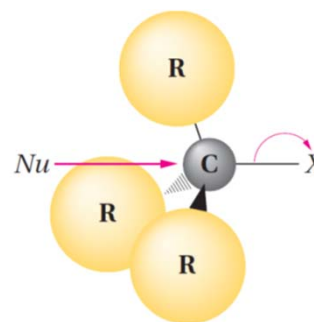
Class of Alkyl Halide

- The reaction is **fastest** when the alkyl group of the substrate is **methyl or primary alkyl halides**.
- The reaction is **slowest** when it is **tertiary alkyl halides**.
- **Secondary alkyl halides** react at an **intermediate rate**.

The rear side of the carbon, where displacement occurs, is more crowded if more alkyl groups are attached to it, thus slowing down the reaction rate.



primary alkyl halide
(rear side not crowded; S_N2 fast)



tertiary alkyl halide
(rear side crowded; S_N2 slow or impossible)

NUCLEOPHILIC SUBSTITUTION (S_N) REACTIONS

THE S_N2 MECHANISM

Summary,

- The S_N2 mechanism is a **one-step process** favored for methyl and primary halides.
- It occurs more slowly with secondary halides and usually not at all with tertiary halides.
- An S_N2 reaction occurs with **inversion of configuration**, and its rate depends on the concentration of *both* the nucleophile and the substrate (the alkyl halide).

NUCLEOPHILIC SUBSTITUTION (S_N) REACTIONS

THE S_N1 MECHANISM

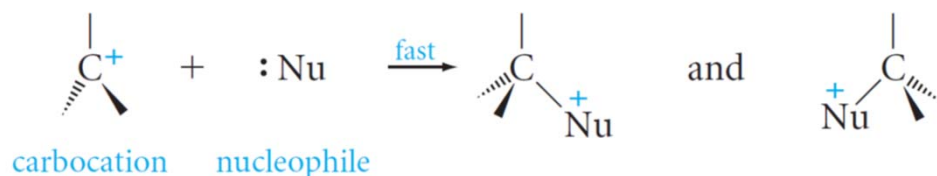
The S_N1 mechanism is a two-step process;

- In the **first step**, which is **slow**, the bond between the carbon and the leaving group breaks as the substrate dissociates (ionizes).



The electrons of the C - L bond go with the leaving group, and a carbocation is formed.

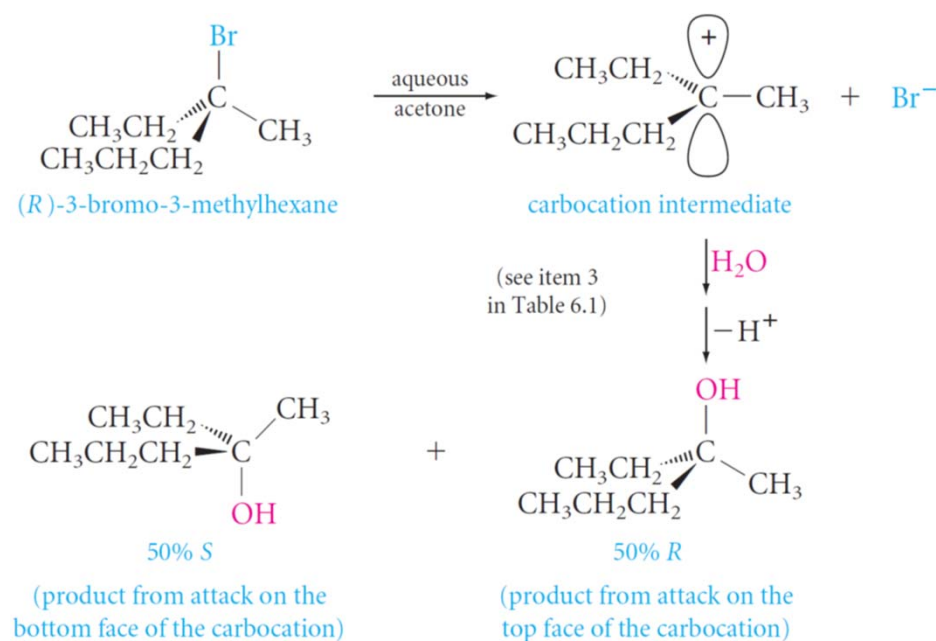
- In the **second step**, which is **fast**, the carbocation combines with the nucleophile to give the product.



NUCLEOPHILIC SUBSTITUTION (S_N) REACTIONS

THE S_N1 MECHANISM

- The number **1** (*unimolecular*);
 - Rate determining, step involves *only one* of the two reactants: the substrate.
 - It does *not* involve the nucleophile at all.
 - That is, the first step is *unimolecular*.
- **Primary halides normally do not react by this mechanism.**
- The S_N1 process occurs with racemization, and its rate is independent of the nucleophile's concentration.



NUCLEOPHILIC SUBSTITUTION (S_N) REACTIONS

THE S_N1 AND S_N2 MECHANISMS COMPARED

○ Class of Alkyl halide;

- **Primary halides** almost always react by the S_N2 mechanism
- **Tertiary halides** react by the S_N1 mechanism.
- Only with **secondary halides** are we likely to encounter **both possibilities**.

○ Solvent polarity.

- **Polar protic solvents** (Water and alcohols) (proton-donating).
 - The rate of S_N1 processes is **enhanced** by polar solvents.
The first step of the S_N1 mechanism involves the formation of ions and polar solvents can solvate ions.
 - S_N2 reactions, are usually **retarded** by polar protic solvents.
solvation of nucleophiles ties up their unshared electron pairs.
- **Polar but aprotic solvents** (acetone, dimethyl sulfoxide, $(CH_3)_2S=O$, DMF)
 - These solvents **accelerate** S_N2 reactions because, by solvating the cation (say, K^+ in K^+CN^-), they leave the anion more “naked” or unsolvated, thus improving its nucleophilicity.

NUCLEOPHILIC SUBSTITUTION (S_N) REACTIONS

THE S_N1 AND S_N2 MECHANISMS COMPARED

The S_N1 and S_N2 Mechanisms Compared

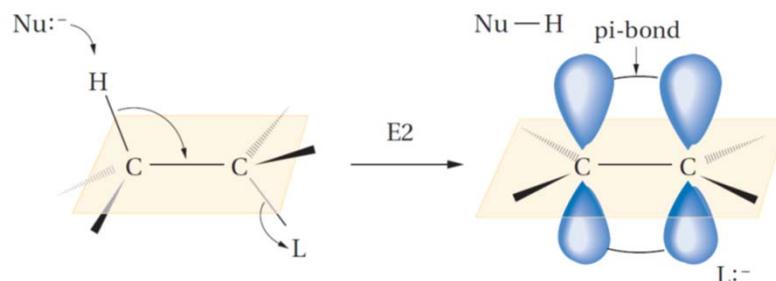
Comparison of S_N2 and S_N1 Substitutions		
Variables	S_N2	S_N1
Halide structure		
Primary or CH_3	Common	Rarely*
Secondary	Sometimes	Sometimes
Tertiary	Rarely	Common
Stereochemistry	Inversion	Racemization
Solvent	Rate is retarded by polar protic solvents and increased by polar aprotic solvents	Because the intermediates are ions, the rate is increased by polar solvents
Nucleophile	Rate depends on nucleophile concentration; mechanism is favored when the nucleophile is an anion	Rate is independent of nucleophile concentration; mechanism is more likely with neutral nucleophiles

ELIMINATION (E) REACTIONS

E2 MECHANISM

There are two main mechanisms for elimination reactions, designated E2 and E1.

The **E2 mechanism** is a process in which HX is eliminated and a C=C bond is formed in the same step.



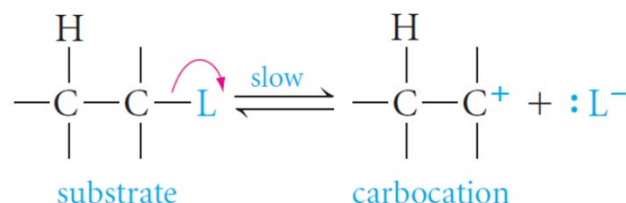
- Like the $\text{S}_{\text{N}}2$ mechanism, the **E2 mechanism** is a **one-step process**.
- The **nucleophile, acting as a base**, removes the proton (hydrogen) on a carbon atom adjacent to the one that bears the leaving group.

ELIMINATION (E) REACTIONS

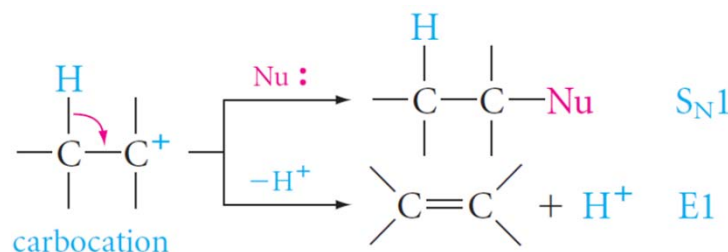
E1 MECHANISM

Like the S_N2 mechanism, the **E1 mechanism** is a **two-step process**.

- The **first step** as the S_N1 mechanism, the slow and rate-determining ionization of the substrate to give a carbocation



- The **second step**; Two reactions are then possible for the carbocation.
 - It may **combine with a nucleophile** (the S_N1 process).
 - or it may **lose a proton** from a carbon atom adjacent to the positive carbon, to give an alkene (the **E1** process).



REACTIONS OF ALKYL COMPOUNDS

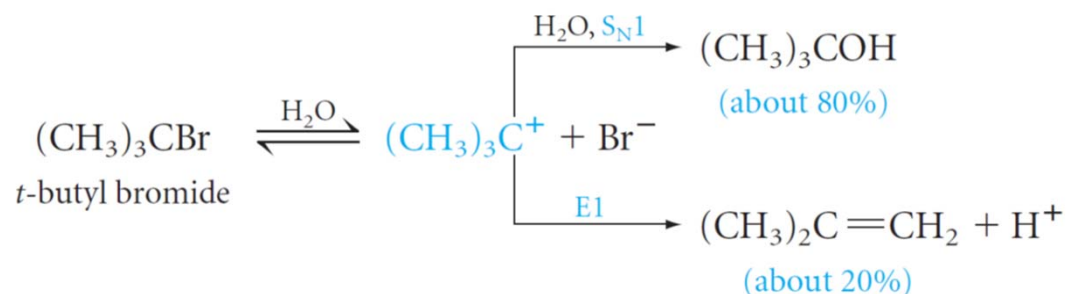
ELIMINATION VERSUS SUBSTITUTION

How substitution and elimination reactions compete with one another.

Let us consider the options for each class of alkyl halide.

Tertiary Halides

- Substitution can only occur by the S_N1 mechanism.
- Elimination can occur by either the E1 or the E2 mechanism.
 - With weak nucleophiles and polar solvents, the S_N1 and E1 mechanisms compete with each other.

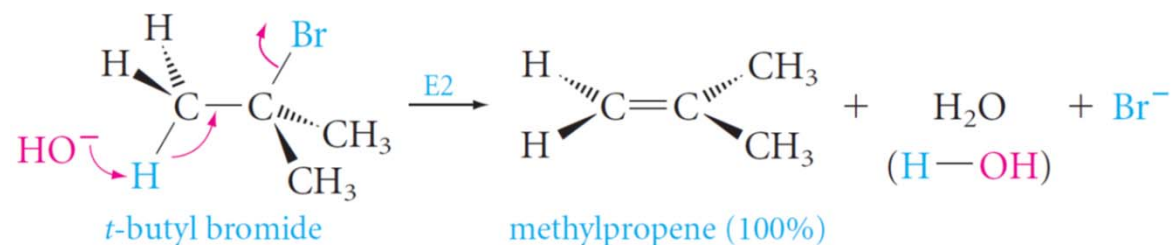


REACTIONS OF ALKYL COMPOUNDS

ELIMINATION VERSUS SUBSTITUTION

Tertiary Halides

- If we use a **strong nucleophile** (which can act as a base) instead of a weak one, and if we use a **less polar solvent**, we favor elimination by the E2 mechanism.



- Because the tertiary carbon is too hindered sterically for $\text{S}_{\text{N}}2$ attack, substitution does not compete with elimination.

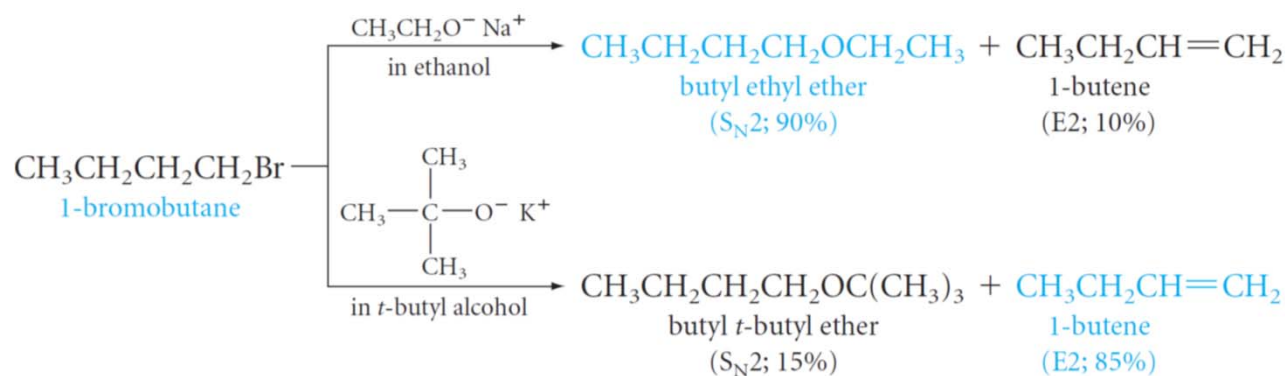
REACTIONS OF ALKYL COMPOUNDS

ELIMINATION VERSUS SUBSTITUTION

Primary Halides

Only the S_N2 and E2 mechanisms are possible, because ionization to a primary carbocation, the first step required for the S_N1 or E1 mechanisms, does not occur.

- With **most nucleophiles**, primary halides give mainly substitution products (S_N2).
- Only with **very bulky, strongly basic nucleophiles**, the E2 process is favored.

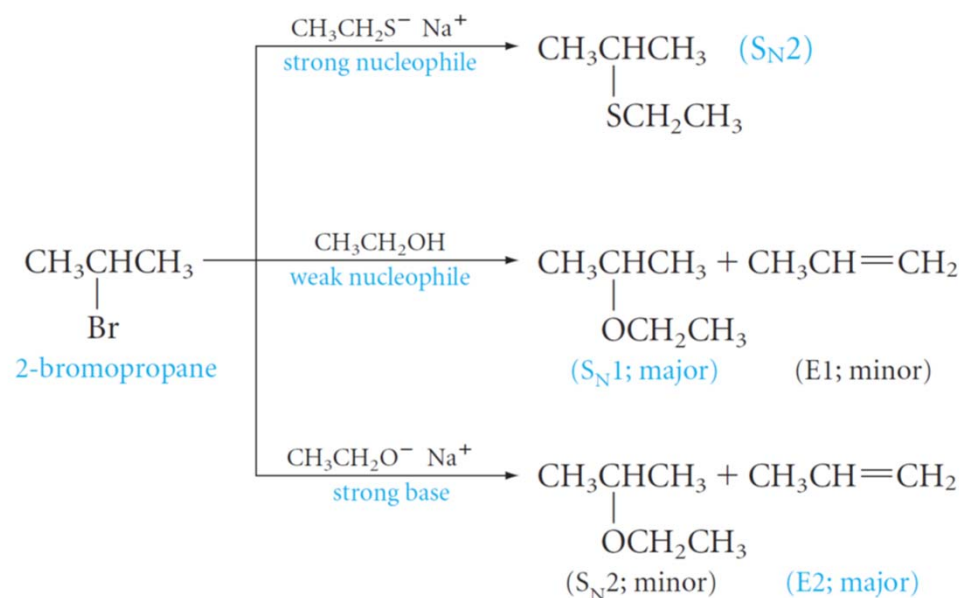


REACTIONS OF ALKYL COMPOUNDS

ELIMINATION VERSUS SUBSTITUTION

Secondary Halides

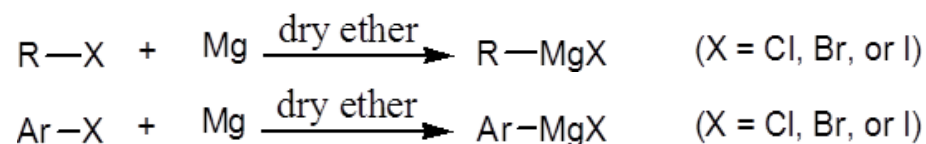
- All four mechanisms, S_N2 and E2 as well as S_N1 and E1, are possible.
- The product composition is sensitive to the nucleophile (its strength as a nucleophile and as a base) and to the reaction conditions (solvent, temperature).
- S_N2 is favored with **stronger nucleophiles** that are **not strong bases**.
- S_N1 is favored with **weaker nucleophiles** in **polar solvents**.
- E2 is favored by **strong bases**.



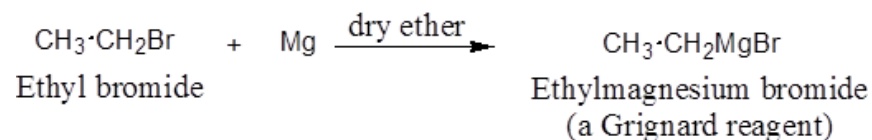
REACTIONS OF ALKYL COMPOUNDS

C) FORMATION OF ORGANOMETALLIC COMPOUNDS

- Most organic chlorides, bromides, and iodides react with certain metals to give **organometallic 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.
- General reaction**



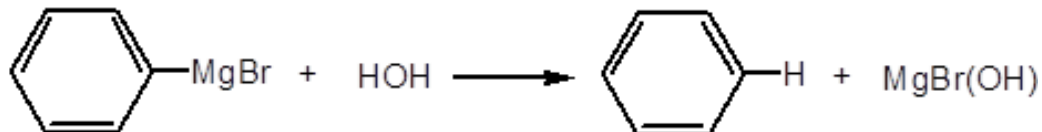
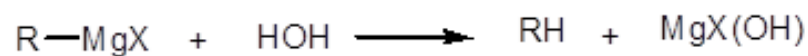
Specific example



REACTIONS OF ALKYL COMPOUNDS

C) FORMATION OF ORGANOMETALLIC COMPOUNDS

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



GENERAL QUESTIONS

EXAMPLE 6.1

Use Table 6.1 to write an equation for the reaction of sodium ethoxide with bromoethane.

EXAMPLE 6.3

Show how 1-butyne could be converted to 3-hexyne using a nucleophilic substitution reaction.