Organic Chemistry I

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Open Textbook Collaborative

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Open Textbook Collaborative

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The courses align to career pathways in New Jersey's growth industries including health services, technology, energy, and global manufacturing and supply chain management as identified by the New Jersey Council of Community Colleges.

Organic Chemistry I

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Chapter 0

0.0 Carbon Atom

0.1 Objectives

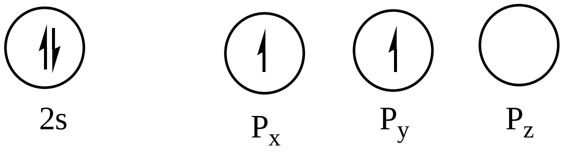
1. Identify the atomic structure of carbon
2. Explain the hybridization and bonding of carbon
3. Explain oxidation and reduction of organic compounds
4. Describe acidity and basicity of organic compounds

0.2 Atomic Structure

Carbon is the sixth element in the periodic table. Therefore, its atomic number is six. There are 6 protons (in the nucleus) and six electrons. Carbon has three isotopes. These carbons have 6, 7, and 8 neutrons (in the nucleus) in C^{12}, C^{13}, and C^{14} respectively. The electronic configuration of carbon is as follows:

$$1s^2, 2s^2\ 2p^4$$

The electrons in the last shell can be drawn as follows:



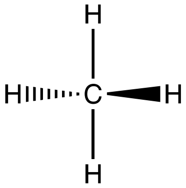
0.3 Bonding and Hybridization

The orbitals in the last shell can combine in three different forms to produce different types of bonds. The combination of these orbitals is known as hybridization.

The possible hybridizations and the resulting bonds are as follows:

- A sp^3 hybridization leads to four sigma (σ) bonds. The bond angle is 109^0. The geometry is tetrahedral.
  In this situation, one carbon atom is connected to four atoms by sigma bonds.

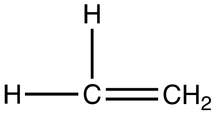
e.g. methane



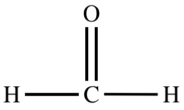
- A sp2 hybridization leads to three sigma bonds and one pi (π) bond. The bond angle is 120^0. The geometry is trigonal planar.

  In this situation, one carbon atom is connected to three atoms. Two of them are sigma bonds and one is a double bond (which has one sigma and one pi bond).

  e.g.



$H-\overset{H}{\overset{|}{C}}=CH_2$



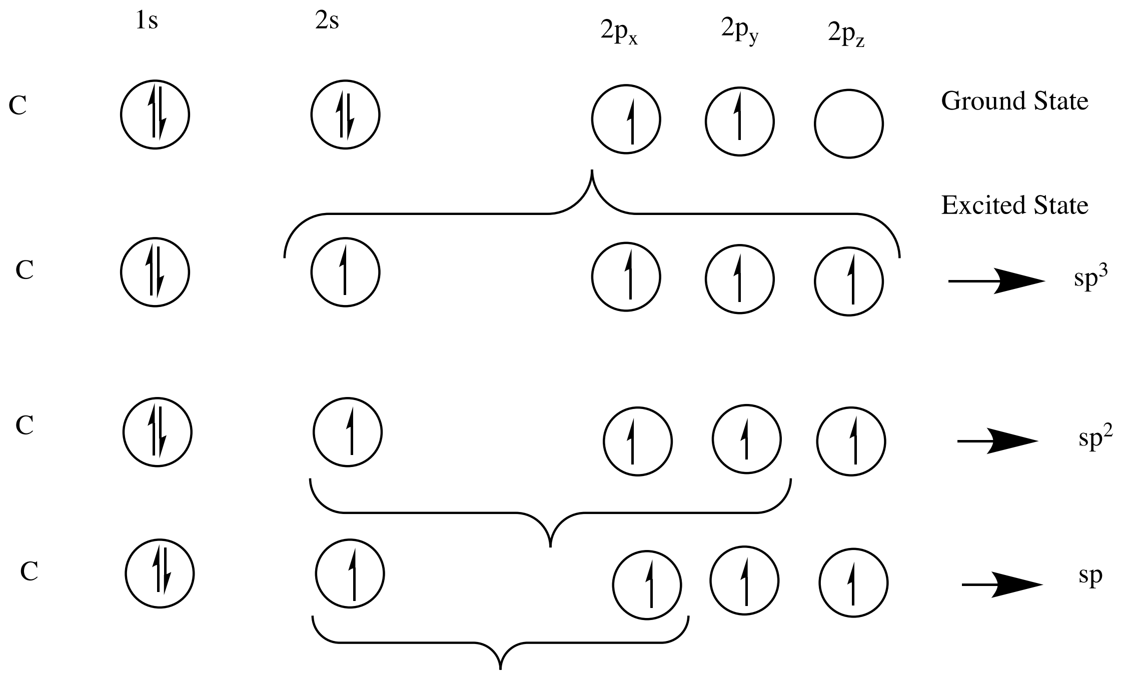
$H-\overset{O}{\overset{\|}{C}}-H$

- An sp hybridization leads to two sigma and two pi bonds. The bond angle here is 180^0. The geometry is linear.
  In this situation, one carbon atom is connected to two atoms, by one sigma and one triple bond (which has one sigma and two pi bonds).

$$H-C\equiv C-H$$

Another form is when carbon atom is connected to two atoms by two double (one sigma and one pi in each) bonds.

e.g. $O=C=O$



Hybridization of Carbon

The above hybridizations will contribute to the reactivity of a compound. The types of bonds in carbon atoms as a result of hybridization are single, double, and triple.

The strengths of these bonds are as follows:

Strength Decreases →

triple > double > single

The length of these bonds are as follows:

Length Decreases →

single > double > triple

The following table provides the bond lengths and bond energies. The higher the bond energy, the stronger the bond.

Bond Type	Bond Length Angstroms (Å) (10^{-10} m)	Bond Energy kJ/mol (approximate values)
C - H	1.09	413
C - C	1.54	345
C = C	1.34	610
C≡C	1.19	835
C – O	1.43	358
C = O	1.22	749
C – N	1.47	304
C = N	1.30	615
C ≡ N	1.16	889
O - H	0.96	490
C – F	1.35	480
C – Cl	1.66	339
C – Br	1.82	284
C – I	2.14	213
N – H	0.99	391
N – N	1.35	163
O - O	1.45	143

Please note when there are double bonds, the energy value is simply not the double of the value of a single bond energy. This is because of the difference of bond energies between sigma and pi bonds. In general, sigma is a stronger bond than a pi bond.

0.4 Oxidation and Reduction Reactions

In organic compounds, during an oxidation, carbon atoms make bonds with more electronegative atoms; oxygen is the most common in this case. Therefore, as the oxidation state increases, more bonds will be connected to the oxygen atom. e.g. alcohol has one bond between C and O. In a carbonyl compound, there are two bonds between C and O. Therefore, carbonyl bond has a higher oxidation state than an alcohol.

During a reduction, carbon atoms make bonds with less electronegative atoms; hydrogen is the most common in this case.

The oxidation of organic compounds follows one or more of the following:

1. An increase in the multiple bond order of carbon
2. An addition of an oxygen atom to a carbon atom
3. A replacement of a hydrogen atom by an oxygen atom

Similarly, the reduction of organic compounds follows one or more of the following:

1. A reduction in the multiple bond order of carbon
2. An addition of a hydrogen atom to a carbon atom
3. A replacement of an oxygen atom by a hydrogen atom

The following is a diagram of gradual oxidation and reduction from alkane to carbon dioxide.

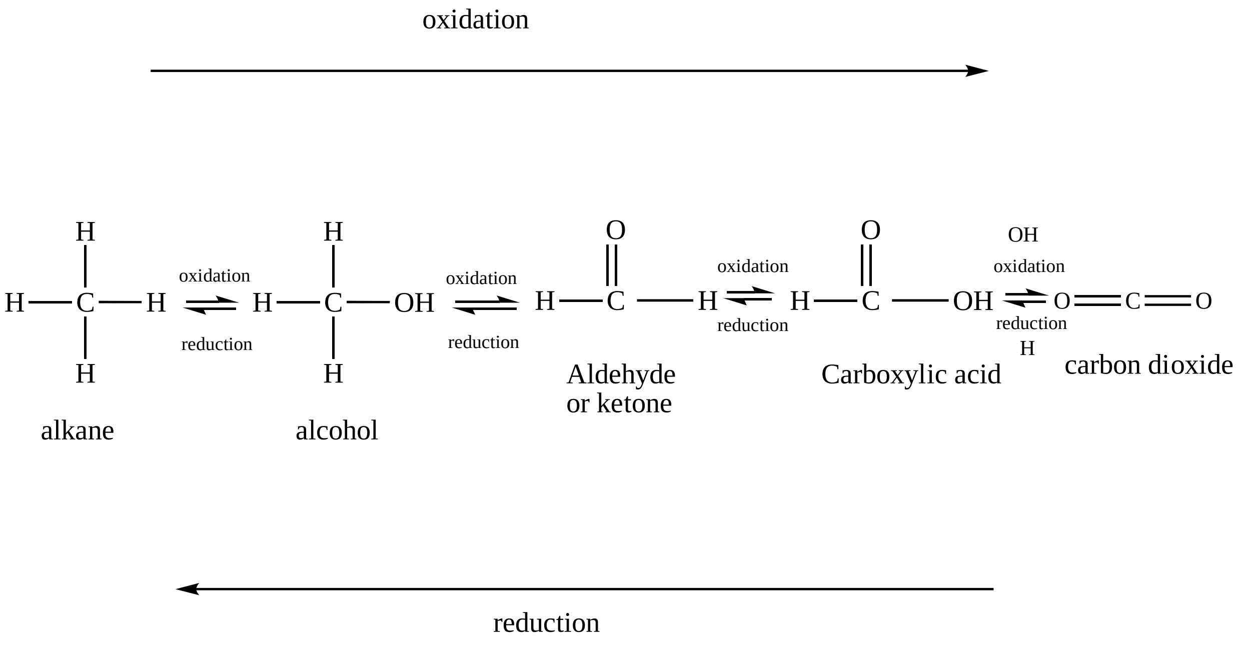
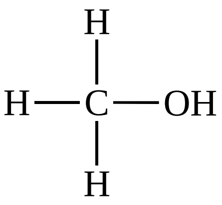


Figure 0.4.1: Gradual oxidation and reduction from alkane to carbon dioxide.

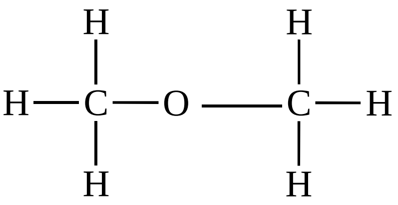
The above diagram shows how the carbon atom of a functional group goes from highly oxidized to highly reduced.

In some cases, certain organic compounds with different functional groups can have the same oxidation state.

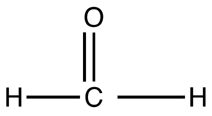
e.g.



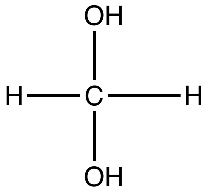
alcohol



Ether



Aldehyde



Aldehyde hydrate

It is important to recognize that above examples related to the oxidation and reduction of one carbon atom of the functional group where that carbon is not attached to any other carbon atom.

At instances where that carbon atom of the functional group is attached to another carbon atom/s, the oxidation and reduction changes. In such cases, the formation of carbon dioxide is not possible; therefore, the oxidation stops after reaching carboxylic acid state. This happens in primary, secondary, and tertiary forms of compounds with functional groups.

e.g.

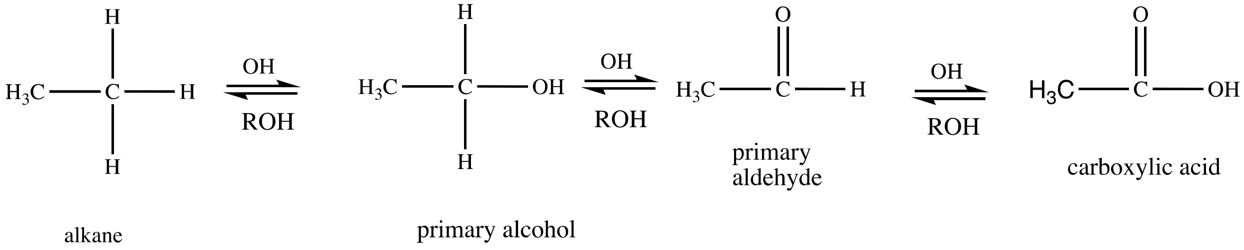


Figure 0.4.2: Carbon atom of the functional group is attached to another carbon atom

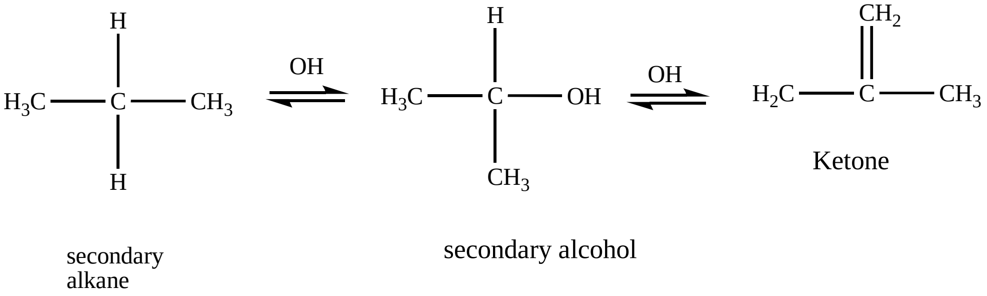


Figure 0.4.3: Carbon atom of the functional group is attached to two other carbon atoms

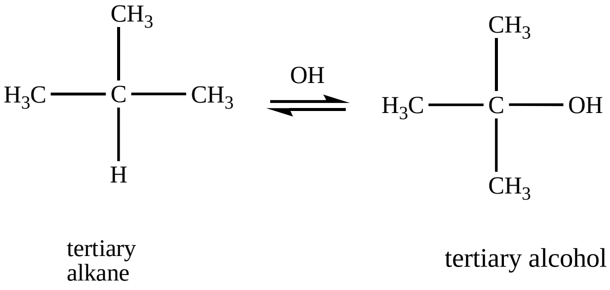


Figure 0.4.4: Carbon atom of the functional group is attached to three other carbon atoms

An oxidation or a reduction happens in the presence of certain chemicals also known as oxidizing or reducing agents.

Some oxidizing agents that promote oxidation of organic compounds are given below:

1. Chromates – Cr (VI) reagent. This is prepared by adding sodium or potassium dichromate or chromium trioxide to aqueous sulfuric or acetic acid. This is a very strong oxidizing agent. This reagent will oxidize a secondary alcohol to a ketone. But, when this reagent is used with a primary alcohol, the oxidation continues until it produces carboxylic acid. To control the oxidation of aldehydes to carboxylic acids, the aldehydes can be removed through distillation since the boiling points of aldehydes are lower than its original primary alcoholic form.
2. Manganese dioxide (MnO_2) – This reagent selectively oxidizes allylic and benzylic alcohols to ketones or aldehydes.
3. Sodium hypochlorite (NaOCl) – This reagent is commonly used in industrial conversion of secondary alcohols to ketones.
4. Percarboxylic acids – peroxytrifluoroacetic acid – Using this reagent, ketones can be converted to esters.
5. Sodium hydroxide (NaOH) – Using this reagent, aldehydes (since they have a hydrogen atom) can be converted to an equimolar mixture of carboxylic acid and alcohol.

Some reducing agents that promote reduction of organic compounds are given below:

1. Addition of hydrogen using metal catalysts such as Pt or Pd.
2. Lithium aluminum hydride ($LiAlH_4$)/THF/Acid or sodium borohydride ($NaBH_4$)/C_2H_5OH/Acid or diborane (B_2H_6)/THF/Acid - Using these reagents, aldehydes and ketones can be reduced to alcohols.
3. Aluminum triisopropoxide in isopropyl alcohol – Using this reagent, ketone and aldehydes can be reduced to alcohols.
4. Zinc amalgam in aqueous HCl = This reagent will convert the carbonyl group of a ketone or aldehyde to a CH_2 group

0.5 Acids and Bases in Organic Compounds

0.5.1 Definitions

It is important to refer to acids and bases you studied in general chemistry before you begin to read this chapter.

0.5.1.1 Bronsted - Lowry Definition

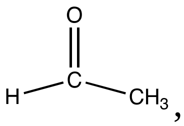
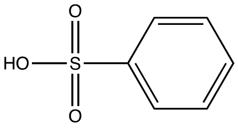
According to this definition, acids are proton donors while bases are proton acceptors.

When protium isotope of hydrogen (the other two types of isotopes of hydrogen are deuterium and tritium) loses an electron, it will have only one proton in its nucleus. Therefore, H^+ cation is also known as a proton.

Nevertheless, since free H^+ cannot exist in water, the existence of H^+ is denoted as H_3O^+; this is known as a hydronium ion indicating the acidic form.

A Bronsted-Lowry acid contains hydrogen atoms (a proton/H^+), where as a Bronsted-Lowery base contains an “available” electron pair. This electron pair should be available to be donated to form a new bond. The electron pair could be from a lone electron pair or a pair of electrons from π bonds.

Some examples of Bronsted-Lowry acids are,

HCl, H_2O, H_3O^+, H_2SO_4, HSO_4^-,  

Therefore, all Bronsted-Lowry acids contain a proton, and the net charge could be 0, +1, or -1.

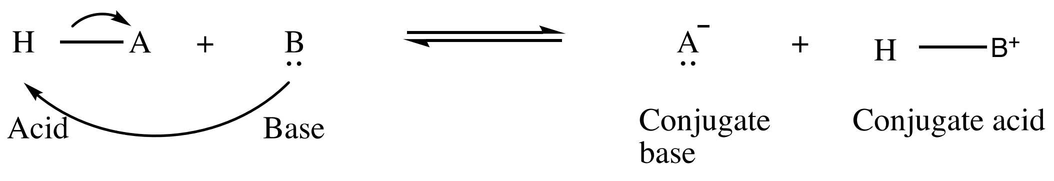
Some examples of Bronsted-Lowry bases are,

$H_2\ddot{O}:$ $\quad :\underset{\cdot\cdot}{\ddot{O}}H$ $\quad CH_3\underset{\cdot\cdot}{\ddot{O}}:$ $\quad :NH_3$ $\quad :\ddot{N}H_2$ $\quad CH_3\ddot{N}H_2$

Therefore, all Bronsted-Lowery bases have at least one lone pair or a π bond electrons. The possible net charges are 0 or -1.

From the examples above, it is clear that some compounds such as H_2O or CH_3OH can act as an acid or a base since they have hydrogen atoms and also lone pairs.

You may recall from general chemistry that Bronsted-Lowry acids or bases have conjugate bases and acids as shown below (**the curved arrows depict the movement of two electrons and double arrows show a reaction in equilibrium**):



In organic reactions,

- Common inorganic acids and bases such as HCl, H_2SO_4, HNO_3 act as strong acids while KOH and NaOH act as strong bases in organic reactions. (You may recall from your general chemistry learning that when you move from left to right and top to bottom in the periodic table, the acidity increases. When you move from right to left and bottom to top, the basicity increases)
- In general, when there are two starting materials, the one with a hydrogen is an acid, whereas the material with a lone pair or a π bond is a base.
- A starting material with a net positive charge is normally an acid and a material with a negative charge is a base.

In proton (H^+) transfer reactions, an electron-rich base donates an electron pair to the acid, which is electron-deficient (usually has a positive charge due to the polar nature of the bond).

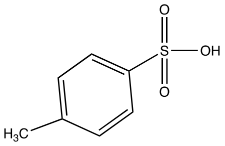
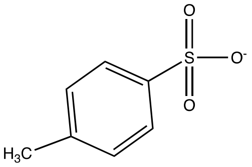
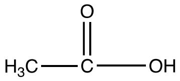
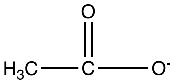
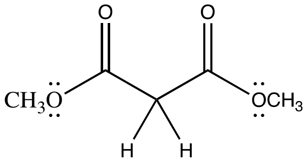
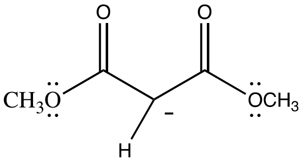
Please review the significance of K_a, pK_a, K_b, pK_b, and K_w from your general chemistry notes.

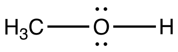
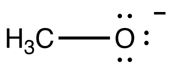
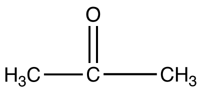
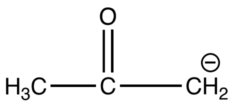
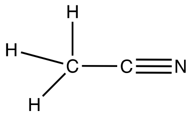
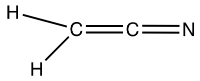
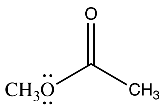
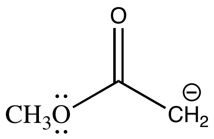
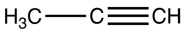
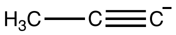
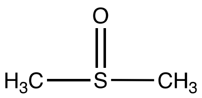
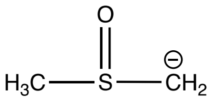
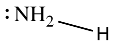
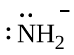
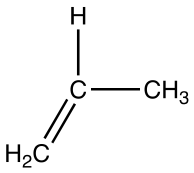
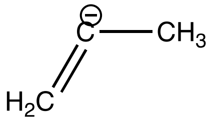
If K_a values is large, this means the acid is a stronger acid. Then the pK_a value (which is given as $-\log_{10}$ of K_a) will be smaller. A similar relationship exists for K_b and pK_b. Also, it is important to remember that the relationship between pK_a and pK_b as follows:

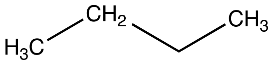
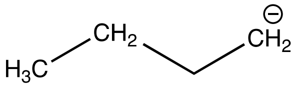
$$pK_b = 14 - pK_a$$

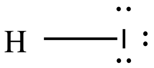
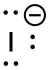
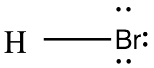
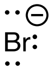
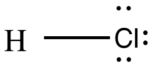
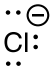
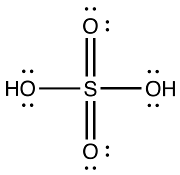
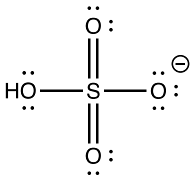
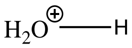
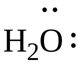
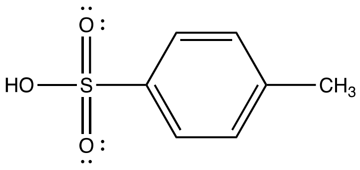
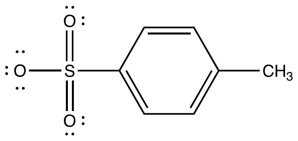
A strong acid can donate a proton easily and form a weak conjugate base. Similarly, a strong base accepts a proton easily and form a weak conjugate acid.

The following table provides the pK_a value range and conjugate bases of some selected organic compounds:

Name	Molecular Formula	pK_a	Conjugate Base
Sulfonic acid	 Tosic acid	-1	
Carboxylic acid		4	
Protonated amines	$H—NH_3^+ \, :\ddot{\underset{..}{Cl}}:^-$	9 - 11	$:NH_3$
Thiols	$CH_3\ddot{\underset{..}{S}}H$	13	$CH_3\ddot{\underset{..}{S}}:^-$
Malonates		13	

Alcohol		17	
Ketone/Aldehyde		20 - 24	
Nitrile		25	
Ester		25	
Alkyne		25	
Sulfoxide		31	
Amine		35	
Alkene		43	

Alkane		50	

Hydroiodic acid		-10	
Hydrobromic acid		-9	
Hydrochloric acid		-6	
Sulfuric acid		-3	
Hydronium ion		-1.7	
Sulfonic acids		-1	

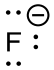
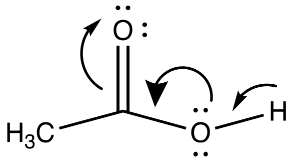
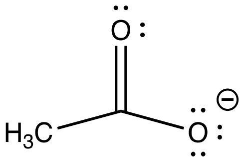
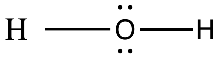
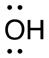
Hydrofluoric acid		3.2	
Carboxylic acids		4	
Protonated amines	$\text{H}-\overset{\oplus}{\text{N}}\text{H}_3\ :\overset{\ominus}{\text{Cl}}:$	9-11	$:NH_3$
Water		14	

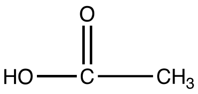
Table 0.5.1.1.1: pK_a value range and conjugate bases of some selected organic compounds:

0.5.1.2 Lewis Acids and Bases

A Lewis acid is an electron pair acceptor, and a base is an electron pair donor. All Lewis acids accept an electron pair. Therefore, all Bronsted-Lowry acids are Lewis acids. Yet, all Lewis acids are not Bronsted-Lowry acids since any molecule that is electron deficient and ready to accept an electron pair is considered a Lewis acid.

H_2O and CH_3OH are Examples of Lewis acids that are also Bronsted-Lowry acids.

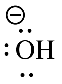
Lewis acids such as BF_3 and $AlCl_3$, which display electron deficiency, (these have unfilled valence shells) are not considered Bronsted-Lowry acids. Some other examples of Lewis acids are given below:

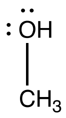
$FeBr_3$, HNO_3, HCl, 

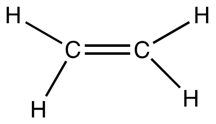
$$HO-\overset{\overset{\displaystyle O}{\|}}{C}-CH_3$$

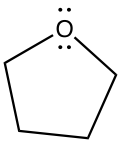
When it comes to Lewis bases, these are structurally the same as Bronsted-Lowry bases. Both have an available electron pair either from a lone pair or from an electron pair in a π bond. A Lewis base donates an electron pair to species that is electron deficient, while Bronsted-Lowry base donates and electron pair to a proton.

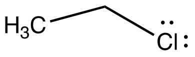
Examples of Lewis bases:

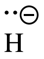


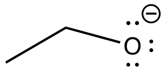












0.5.2 Factors affecting acid strength

Consider HA as an acid. The strength of this acid is dependent upon the stability of its conjugate base A^-.

$$\underset{\text{acid}}{HA} \longrightarrow H^+ \quad + \quad \underset{\text{conjugate base}}{A^-}$$

When comparing two acids, the pK_a values can be compared to determine the strengths of those two acids. The acid with a smaller pK_a value will be the stronger out of the two acids. The stronger acid will have a more stable conjugate base.

There are four factors that affect the acidity. They are,

1. The position in the periodic table

   The position of the element in the periodic table will determine the acidity. When comparing two chemical compounds, the more acidic compound will be the one with the element of concern more toward the right side and to the bottom of the periodic table.
   e.g. H_2O is more acidic than CH_4 (although the conjugate bases of the two compounds have only one negative charge, thereby charge wise they are both equal), since O will have a more stable conjugate base; O is more electronegative than C; O is more toward the right side of the periodic table than C.
   When HF and HBr are compared, HBr will show more acidity since Br is at a position lower in periodic table than F. Therefore, Br volume is larger than F volume; hence, electronegative charge is distributed across a larger volume in Br. This makes Br more stable.

2. Inductive effects

   The inductive effect can be seen when there are other atoms more electronegative than C in the compound.
   e.g.

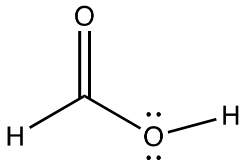
   Compare CH_3CH_2OH and CF_3CH_2OH

   Both of these compounds will generate a conjugate base with one negative charge on the oxygen. Since both compounds have an oxygen atom there is no difference in electronegativity or in the position in the periodic table. The only difference is that one compound has three Fs. Since these three Fs are electronegative, the three Fs will withdraw the electron density from the C atom to which they are attached. This will make this C atom electron deficient. As a result, C will in-turn pull electron density from the negatively charged oxygen through σ bond. The pull of electron density from an electronegative atom through σ bonds is known as the inductive effect (I effect). As a result, CF_3CH_2OH will be more acidic. What is observed in this situation is an electron withdrawing inductive effect which is also denoted as -I effect. This electron withdrawing effect stabilizes the negative charge of the conjugate base. The more electronegative the atom that is causing -I effect and closer this atom to the site of the negative charge, the greater the stability.

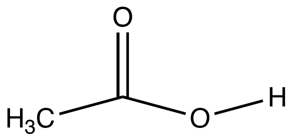
3. Resonance effects

   When two or more different Lewis structures exist for compounds with the same arrangement of atoms, they are known as resonance structures. When comparing two compounds, the compound whose conjugate base can undergo resonance will have a more stable conjugate base. Therefore, the acid of that compound will be a stronger acid. When resonance leads to the delocalization of the electron pairs, it makes the compound more acidic.

   e.g.

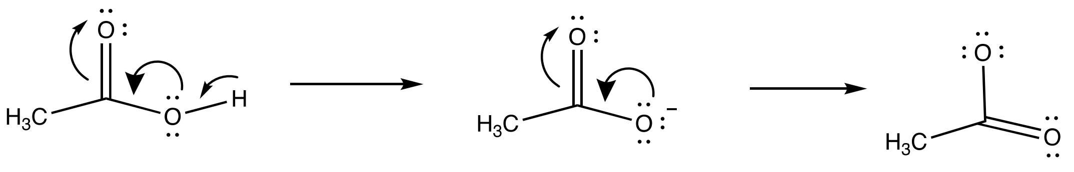


formic acid



acetic acid

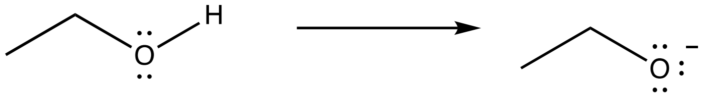
Out of the above two compounds, acetic acid will have a delocalized electron pair as shown below:



acetic acid

conjugate base

When acetic acid is compared with ethanol, as shown below, ethanol has only one structure.



Ethanol

Therefore, acetic acid is a stronger acid than ethanol.

4. Hybridization effects

It has been observed that when hybridization exists, the compound with a higher percent of s character in the hybrid orbital will be more acidic.

Ethane (CH_3-CH_3) has sp3 hybridization and 25% of s character.
Ethylene ($CH_2 = CH_2$) has sp3 hybridization and 33% of s character.

Acetylene ($HC\equiv CH$) has sp hybridization and 50% of s character.

Therefore, acetylene is more acidic.

Chapter 1

1.0 Classification of Organic Compounds

1.1 Objectives

1. Identify different functional groups
2. Classify organic compounds according to the functional groups
3. Identify formulas and structures according to the functional groups
4. Calculate the degree of unsaturation

1.2 Introduction

All organic compounds contain a skeleton of carbon atoms mainly bonded to hydrogen atoms. In addition, they also have groups that include other atoms (generally termed as heteroatoms) such as oxygen, nitrogen, phosphorous, halogens. These groups are known as functional groups. These functional groups are the sites of chemical reactivity. In unsaturated organic compounds (explained below), the double and triple bond sites are also considered the reactive sites. Therefore, organic compounds can be studied under different classes of functional groups since the reactions and the behavior of these compounds under each functional group tend to behave in a similar manner.

1.3 Drawing of organic compounds

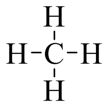
When drawing organic compounds, the following types are followed:

1. Molecular formula – e.g. Benzene – C_6H_6
2. Structural formula
    a) Displayed formula – shows all the bonds and atoms in the molecule
    e.g. Methane

Molecular formula

CH_4

Displayed formula



$$\begin{array}{c} H \\ | \\ H-C-H \\ | \\ H \end{array}$$

Please note the following line types when drawing structures:

a. Straight line: ——— indicates that the bond is on the plane of the paper.
b. Broken line: · · · · · · indicates that the bond is going into the paper.
c. Bold line: ▬ indicates the bond is coming out of the paper.

Displayed formula in three dimensions

Therefore, if CH_4 is drawn as a displayed formula in 3 dimensions, it will look as follows:

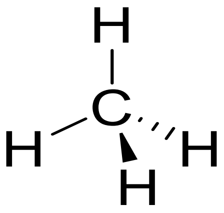


Figure 1.3.1: Methane drawn in three-dimensional form

3. Skeletal formula

In this case the, the carbon and hydrogen atoms are not drawn. Only the bonds are shown except if atoms other than carbon and hydrogen exists.

$CH_3 – CH_2 – CH_3$ is drawn as,

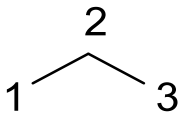


Figure 1.3.2: Skeletal formula of propane

The three carbons are at 1, 2, and 3. Since they are not double or triple bonds, it is assumed that all carbons have the correct number of hydrogens (1C has 3 Hs, 2C has 2Hs, and 3C has 3Hs).

e.g.

1. C_6H_6

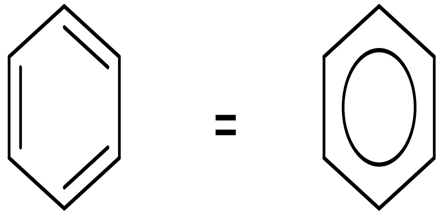


Figure 1.3.3: Displayed and skeletal formula of resonance structure of benzene

2. C_3H_8OH

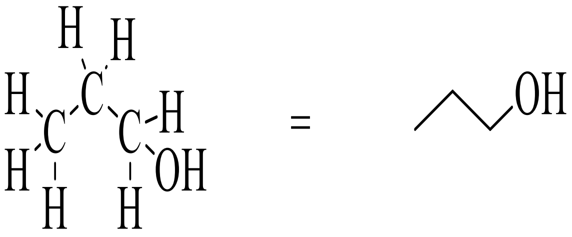


Figure 1.3.4: Displayed and skeletal formula of propanol

3 C_6H_{12}

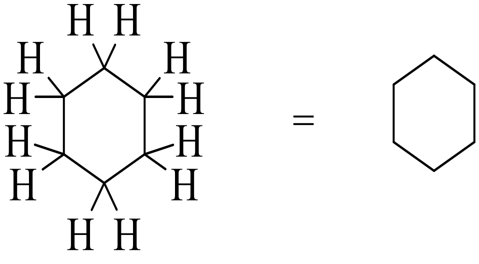


Figure 1.3.5: Displayed and skeletal formula of cyclohexane

1.4 Classification

Organic compounds can be broadly classified into three groups:

- Hydrocarbons – aliphatic (non-cyclic), alicyclic, and aromatic compounds
- Heterocyclic Compounds – one or more of carbon atoms in the ring have been replaced by heteroatoms
- Compounds with heteroatom functional groups – Studied under different functional groups

1.4.1 Aliphatic Hydrocarbons

This group of compounds only contain carbon and hydrogen atoms. As you already know, carbon can make four covalent bonds to satisfy the octet rule. Therefore, if one or more carbon atoms in a compound combines with another carbon or hydrogen to make four bonds, then such a compound is called a saturated compound. If a compound does not have a sufficient number of atoms to complete single bonds with each carbon atom, then those compounds will be known as unsaturated compounds and will have double or triple bonds. The formation of double or triple bonds is due to the hybridization of s and p orbitals of the outermost shell of the carbon atoms.

There are three groups of aliphatic hydrocarbons:

Alkanes – Saturated – All single bonds in the compound. e.g. methane CH_4, ethane C_2H_6

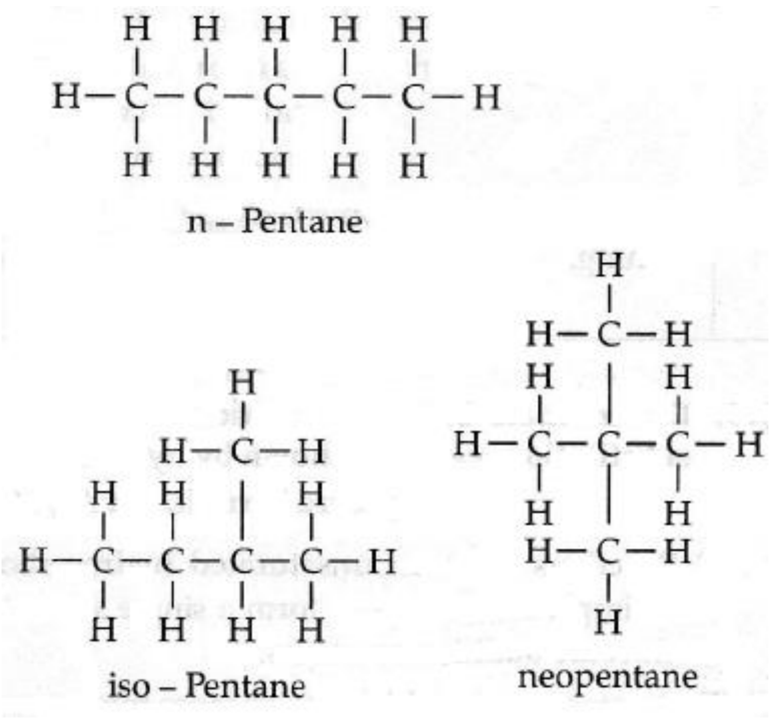


Figure 1.4.1.1: Isomers of pentane (we will be discussing about isomers in another chapter)

Alkenes – Unsaturated – At least one double bond in the compound. e.g. ethene C_2H_4

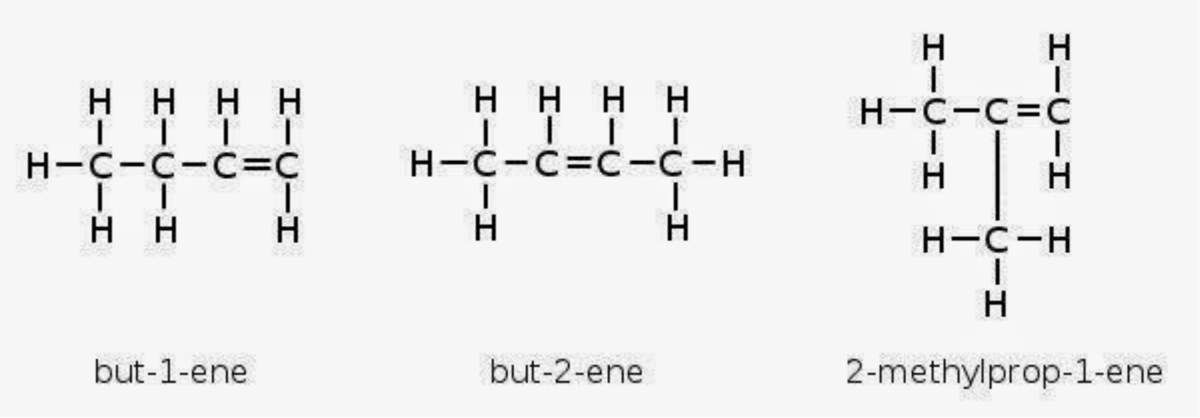


Figure 1.4.1.2: Isomers of butene

Alkynes – Unsaturated – At least one triple bond in the compound. e.g. ethyne C_2H_2

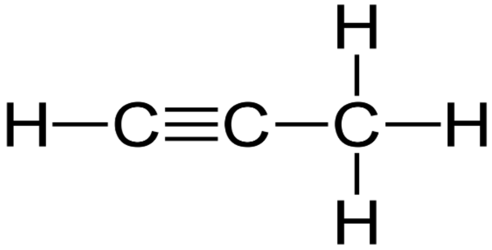


Figure 1.4.1.3.: Prop-1-yne

A compound with a single-bond carbon atoms displays sp^3 hybridization. A compound with a double-bond carbon atoms display sp^2 hybridization, and the ones with a triple-bond display sp hybridization. A compound with carbon having single bonds will have sigma bonds. A double bond compound will have one sigma and one pi bond. A triple bone will have one sigma and two pi bonds.

1.4.2 Alicyclic Hydrocarbons

The compounds of this class can be considered to have been formed by joining two aliphatic hydrocarbons together. These cyclic compounds are different to aromatic compounds.

e.g. Cylcopentane – C_5H_{10}

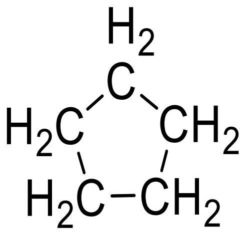


Figure: 1.4.2.1: Displayed formula of cyclopentane

1.4.3 Aromatic Compound

This group includes cyclic polyunsaturated compounds with unique physical and chemical properties. Benzene is the simplest aromatic hydrocarbon. It is a six-membered cyclic conjugated triene.

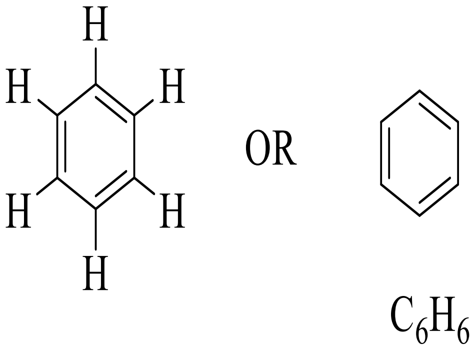


Figure 1.4.3.1: Displayed and skeletal formula of benzene

1.4.3.1 Benzene

Aromatic compounds have a special stability that is different to other unsaturated compounds. The trienes shown rotates among the carbon atoms. Therefore, the actual bonds between each carbon are a mixture of double and single bonds. These compounds show a resonance structure.

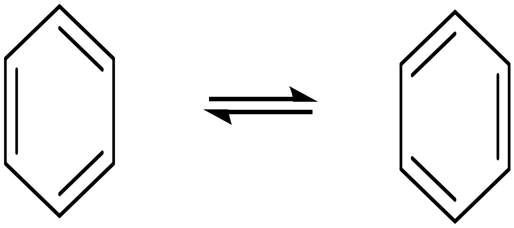


Figure 1.4.3.1.1: Resonance Structures of Benzene

The aromaticity of benzene has also been observed in other conjugated cyclic polyene systems. Therefore, the general formula that determines the aromaticity for a closed shell, fully conjugated cyclic polyene is 4n +2 number of π electrons.

n = number of closed, conjugated, polyene shells.

This is known as Huckel rule. This rule states that if a cyclic, planar molecule has (4n+2) πelectrons, it is aromatic.

Benzene has 6 π electrons (three double bonds). Therefore, benzene shows aromaticity. Applying the formular for benzene gives the following:

1 ring,   n = 1

4n + 2 = 6

Benzene has 6 π electrons.

1.4.3.2 Naphthalene

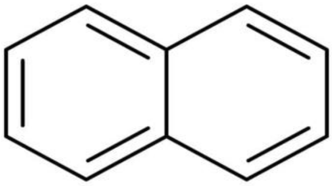


Figure 1.4.3.2.1: Skeletal formula of naphthalene – 10 pi electrons (4n+2, n=2)

There are 2 fused rings. Therefore, n = 2. The number of π electrons is 10. This matches the number of π electrons in naphthalene. Therefore, the compound exhibits aromaticity.

1.4.3.3 Annulene

Annulenes could be aromatic, non-aromatic, or anti-aromatic.

Annulenes are completely conjugated monocyclic hydrocarbons containing an even number of carbon atoms. They have the general formula C_nH_n (when n is an even number) or C_nH_{n+1} (when n is an odd number). Alternatively, they are represented by $(CH{=}CH)_{n.}$

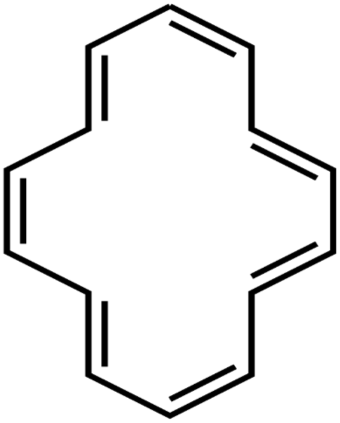


Figure 1.4.3.3.1: Skeletal formula of [14] annulene $C_{14}H_{14}$

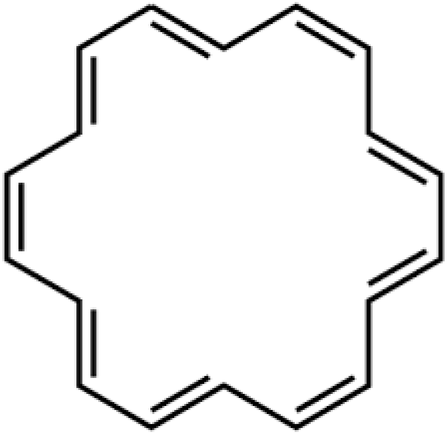
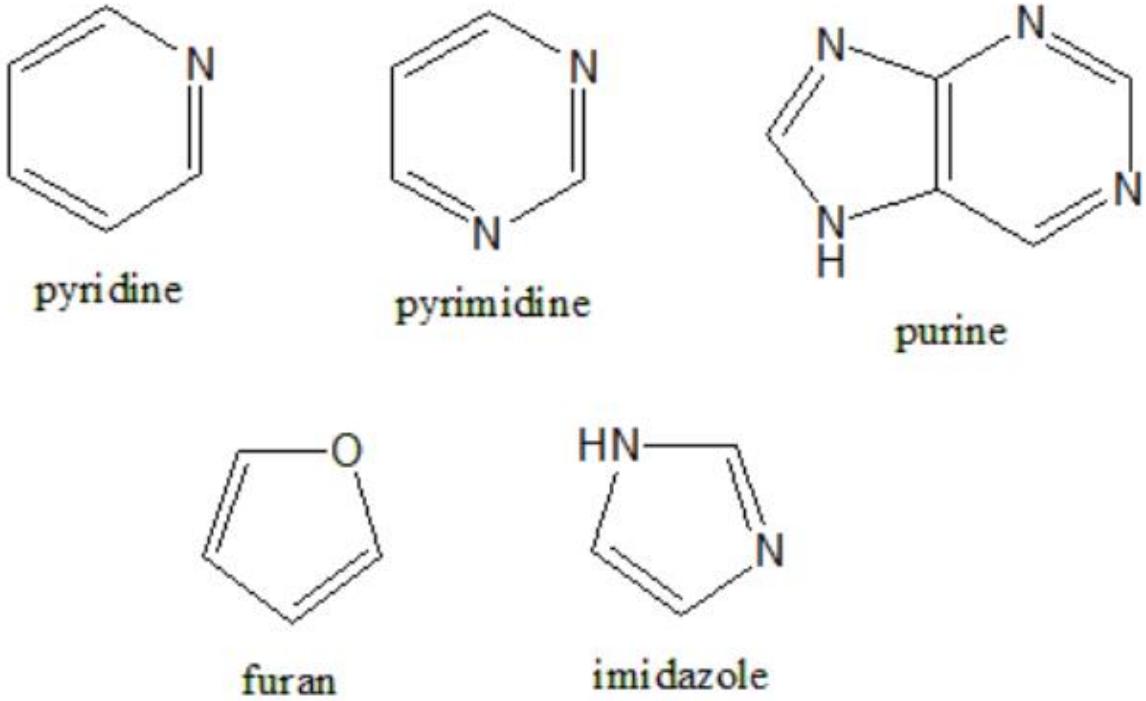


Figure 1.4.3.3.2: Skeletal formula of [18] annulene $C_{18}H_{18}$ selected annulenes

1.4.4 Heterocyclic Compounds

In this group, one or more carbon atoms in the ring have been replaced by heteroatoms. The physical and chemical properties of these groups differ from cyclic compounds with carbon atoms only (carbocyclic). Whilst the heteroatom in the cycle changes the physical and chemical nature of its corresponding carbocyclic compound, they can exhibit aromaticity if the heteroatom can provide sufficient electrons to the π system to satisfy the 4n+2 condition.

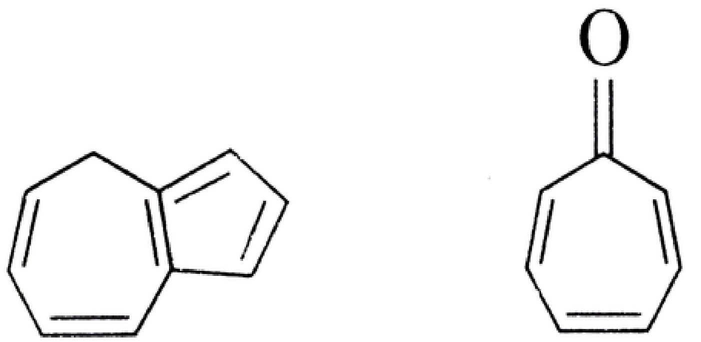


pyridine pyrimidine purine

furan imidazole

Figure 1.4.4.1: Some examples of aromatic, heterocyclic compounds

These heterocyclic groups also provide a basic skeleton for the attached functional groups as same as the corresponding aliphatic, alicyclic, or aromatic carbon group.



Azulene Tropone

Figure 1.4.4.2: Some examples of non-aromatic heterocyclic compounds

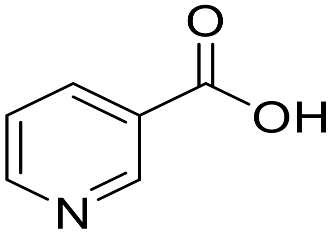


Figure 1.4.4.3: Heterocyclic carboxylic acid

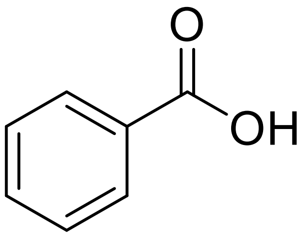


Figure 1.4.4.4: Aromatic carboxylic acid

The properties of heterocyclic compounds will be a combination of the characteristics of the parent heterocyclic group and the functional group. Therefore, these heterocyclic compounds make a separate category.

It is important to note that there are aromatic, non-aromatic, and anti-aromatic compounds. The following figure provides the classification and examples:

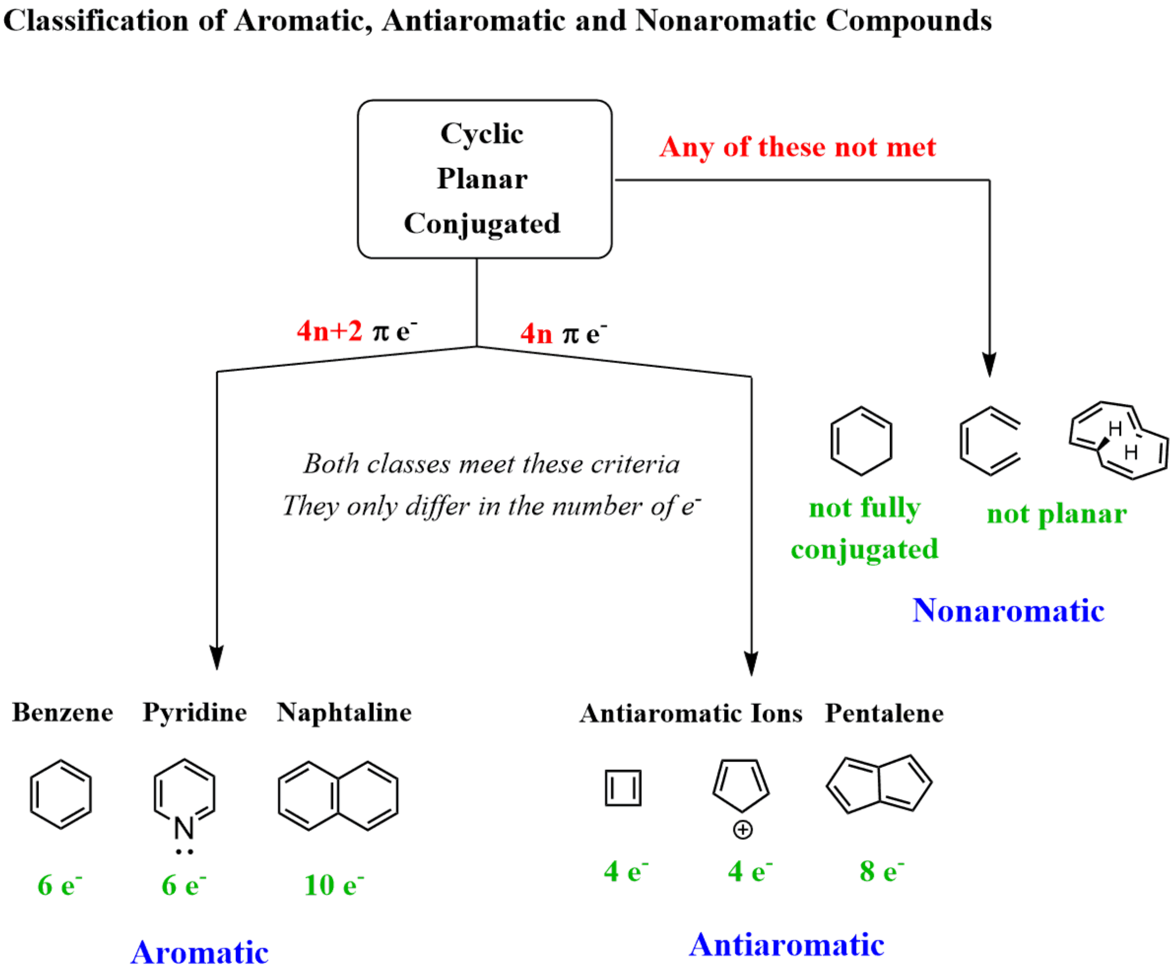


Figure 1.4.4.5: Classification of aromatic, anti-aromatic, and non-aromatic compounds

1.4.5 Compounds with heteroatom functional groups

These compounds are classified according to the reactive group. This group could be further classified as aliphatic, alicyclic, aromatic, or heterocyclic according to the principal skeleton.

Each functional group has a carbon atom that may be attached to the principal skeleton. Also, one or more heteroatoms in this function group have joined the carbon atom by replacing hydrogen atoms. This first carbon atom, which is a part of the functional group, plays a significant role in the naming of the compound (by numbering it as the first carbon)

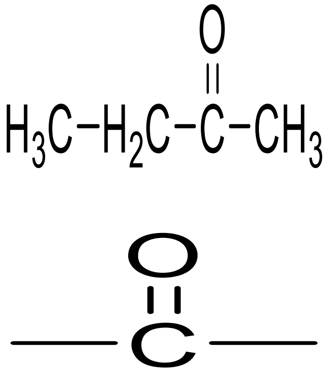


Figure 1.4.5.1: Carbonyl group as the functional group

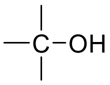
The classification of this group depends on the number of bonds formed between the heteroatom and the carbon (skeletal carbon) atom.

1.4.5.1 One bond between heteroatom and the carbon

Alcohols, ethers, organic halides, and nitro compounds belong to this group.

1.4.5.1.1 Alcohols

The general structure is R- C – OH.



$$-\overset{|}{\underset{|}{C}}-OH$$

These are further classified according to the nature of the Carbon atom attached to OH (hydroxy) group. The number of hydrogen atoms attached to the carbon will determine its nature.

If only two hydrogen atoms are attached to the carbon, it is called a primary alcohol.

$$CH_3\cdot CH_2\cdot CH_2\cdot CH_2OH$$

Figure 1.4.5.1.1.1: Butan-1-ol – aliphatic primary alcohol

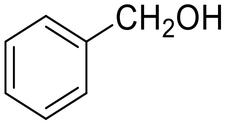
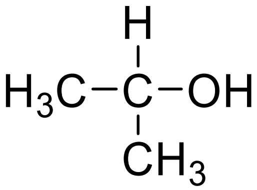


Figure 1.4.5.1.1.2: - Benzyl alcohol - aromatic primary alcohol

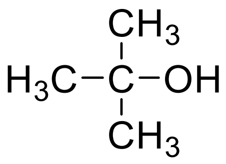
If only one hydrogen atom is attached to the carbon, it is called a secondary alcohol.



$$H_3C-\overset{\displaystyle H}{\underset{\displaystyle CH_3}{C}}-OH$$

Figure 1.4.5.1.1.3: - Isopropyl alcohol (propan-2-ol) secondary alcohol

If no hydrogens are attached to the carbon, it is called a tertiary alcohol.

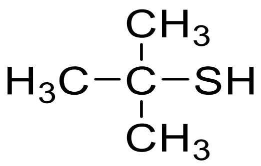


$$H_3C-\overset{\displaystyle CH_3}{\underset{\displaystyle CH_3}{C}}-OH$$

Figure 1.4.5.1.1.4: - Tertiary alcohol

1.4.5.1.2 Thioalcohols

If instead of -OH group, a -SH is attached to the carbon, it is called thioalcohols or mercaptans.



$$H_3C-\overset{\displaystyle CH_3}{\underset{\displaystyle CH_3}{C}}-SH$$

Figure 1.4.5.1.2.1: Thiol group

1.4.5.1.3 Phenol

If the C to which -OH is attached is from an aromatic system, then it is called a phenol.

These phenols are chemically and physically different to alcohols.

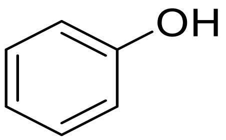
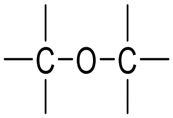


Figure 1.4.5.1.3.1: Phenol

1.4.5.1.4 Ether

The basic structure of ether is as follows:



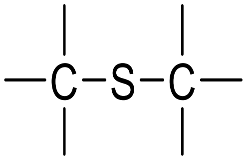
$$-\overset{|}{\underset{|}{C}}-O-\overset{|}{\underset{|}{C}}-$$

e.g.

$$CH_3-O-CH_3$$

Figure 1.4.5.1.4.1: Dimethyl Ether

When O is replaced with S, they are called, thioethers or sulfides. It is important to note that although ether and correspond alcohol have the same number of C, H, and O atoms, the physical and chemical properties are different.

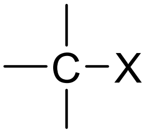


$$-\overset{|}{\underset{|}{C}}-S-\overset{|}{\underset{|}{C}}-$$

Figure 1.4.5.1.4.2: Thioether (sulfide)

1.4.5.1.5 Organic halides

These have the following basic structure:



X could be any halide. The name will depend on the type of halide.

If X is F – Fluoro - compound

If X is Cl – Chloro - compound

If X is Br – Bromo - compound

If X is I – Iodo – compound

Similar to alcohol classes, organic halides also have primary, secondary, and tertiary compounds.

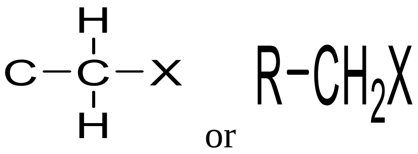


Figure 1.4.5.1.5.1: Primary halide basic structure

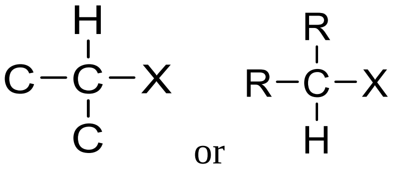


Figure 1.4.5.1.5.2: Secondary halide

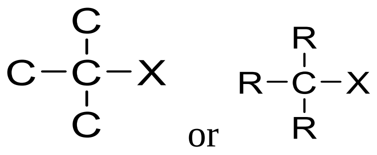


Figure 1.4.5.1.5.3: Tertiary halide

1.4.5.1.6 Amines

These can be considered as derivations of ammonia (NH_3). The hydrogen atoms attached to the heteroatom nitrogen (N) are replaced with carbon atoms.

These have the following structures:

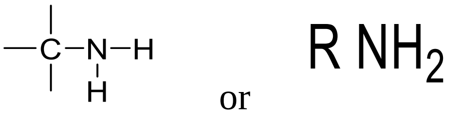


Figure 1.4.5.1.6.1: Primary amine

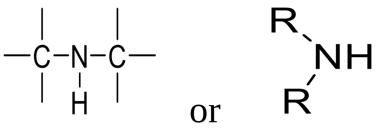


Figure 1.4.5.1.6.2: Secondary amine

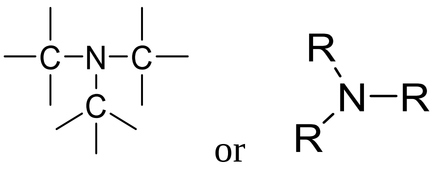
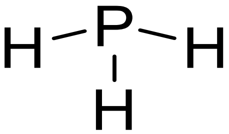


Figure 1.4.5.1.6.3: Tertiary amine

1.4.5.1.7 Phosphine

When N atom is replaced with phosphorous (P), phosphine group is created.



$$H-\underset{\displaystyle H}{\overset{}{\underset{|}{P}}}-H$$

Figure 1.4.5.1.7.1: Phosphine

1.4.5.1.8 Nitro compounds

In this group, the heteroatom is nitrogen attached to two oxygen atoms.

$$R-NO_2$$

Figure 1.4.5.1.8.1: Nitro structure

1.4.5.2 Two bonds between heteroatom and carbon

Aldehydes, ketones, and imines are included in this group. Aldehydes and ketones have a single oxygen atom attached to the carbon with two bonds (this C=O is known as carbonyl group); their corresponding compounds with two oxygen atoms attached to the carbon with one bond each are known as acetals and ketals respectively.

1.4.5.2.1 Aldehydes

In Aldehydes, in addition to the single oxygen attached (by double bond) to the carbon, there is one hydrogen atom attached to the carbon as well.

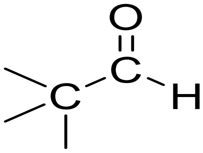


Figure 1.4.5.2.1.1 Aldehyde (R-CHO)

1.4.5.2.2 Ketones

In Ketones, in addition to the single oxygen attached (by double bond) to the carbon, there is one more carbon atom attached to it the carbon as well.

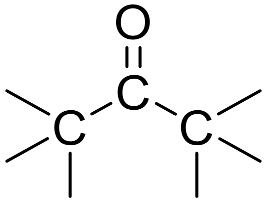


Figure 1.4.5.2.2.1 Ketone ($R_2C=O$)

Aldehydes and ketones are similar in their chemical reactions due to the common reactive group, carbonyl (– C=O). They also have a common general chemical formula.

1.4.5.2.3 Imines

Imines are a derivation from carbonyl compounds and primary amines. These have the following structure:

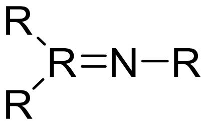


Figure 1.4.5.2.3.1: Imine structure

One of the R groups attached to the Carbon directly can be a hydrogen when it is a derivation from aldehydes.

1.4.5.3 Three bonds between heteroatom and carbon

In this group, the heteroatom is bonded to the carbon atom with three groups. Cyanides fall under this category.

1.4.5.3.1 Cyanides

Cyanides are also called nitriles. There is a difference between the two in the usage. Cyanide refers to an inorganic compound with a cyano- group. The organic compound containing cyano group is known as nitrile.

This group has the following structure:

$-C\equiv N$ or $R-C\equiv N$

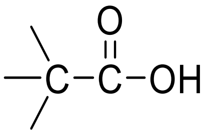
Figure 1.4.5.3.1.1 Possible two cyanide structures

1.4.5.4 Two heteroatoms and a carbon

In this group, a carbon atom forms two bonds with an oxygen atom and one bond with another oxygen, nitrogen, or halide.

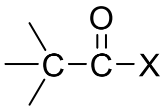
1.4.5.4.1 Carboxylic acids and derivatives

The following is a list of such compounds:



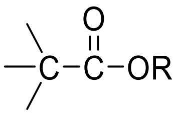
or RCOOH

Figure 1.4.5.4.1.1: Carboxylic acid



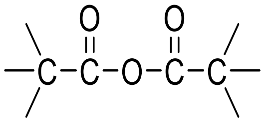
or $R-COX$

Figure 1.4.5.4.1.2 : Acid halide



or $R-CO_2R$

Figure 1.4.5.4.1.3 : Ester



or RCO.O.COR

Figure 1.4.5.4.1.4 : Acid anhydride

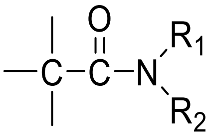


Figure 1.4.5.4.1. 5: Amide

When R_1 and R_2 are H atoms – it is a primary amide.

When are R is an alkyl group and the other is H – it is a secondary amide.

When both Rs are alkyl groups – it is a tertiary amide.

1.4.5.4.2 Sulphonic acids and derivatives

In this group, sulfur is bonded to the carbon (skeletal) and displays structures somewhat similar to carboxylic acids and their derivatives.

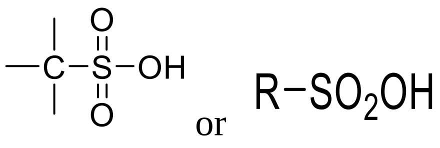


Figure 1.4.5.4.2.1: Sulfonic acid

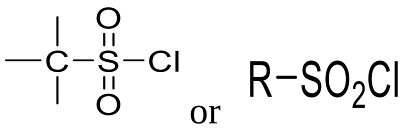


Figure 1.4.5.4.2.2: Sulfonyl chloride

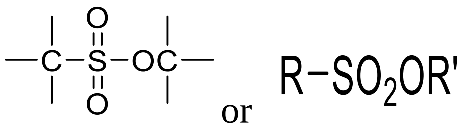


Figure 1.4.5.4.2.3: Sulfonate ester

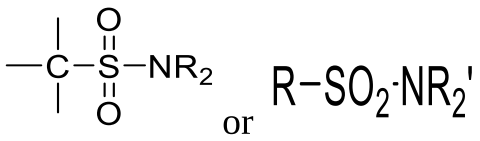
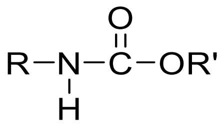


Figure 1.4.5.4.2.4: Sulfonamide

1.4.5.5 Four bonds between the heteroatom and carbon

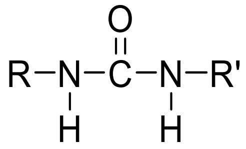
In this group, carbon is bonded to heteroatoms using all four bonds.

Some of the functional groups in this class are given below:



$$R-\underset{\displaystyle H}{\underset{|}{N}}-\overset{\displaystyle O}{\overset{\|}{C}}-OR'$$

Figure 1.4.5.5.1: Urethane



$$R-\underset{\displaystyle H}{\underset{|}{N}}-\overset{\displaystyle O}{\overset{\|}{C}}-\underset{\displaystyle H}{\underset{|}{N}}-R'$$

Figure 1.4.5.5.2: Urea

$$R-N=C=O$$

Figure 1.4.5.5.3: Isocyanate

$$R-N=C=S$$

Figure 1.4.5.5.4: Isothiocyanate

1.5 Calculation of the Degree of Unsaturation

In order to calculate the degree of unsaturation (DOU) also known as double bond equivalent, the following formula is used:

If the molecular formula is given, plug in the numbers into this formula:

$$DoU = 2C + 2 + N - X - H/2$$

C = Number of carbon atoms

N = Number of nitrogen atoms

X = Number of halides

H = Number of hydrogens

When there is one degree of unsaturation, it is equivalent to 1 double bond or 1 ring. If there are two degrees of unsaturation, it is equivalent to 2 double bonds, 2 rings, 1 ring and 1 double bond, or 1 triple bond. If there are three degrees of unsaturation, it is equivalent to 3 rings, 2 rings and1 double bond, 1 ring and 2 double bonds, 1 ring and1 triple bond, 1 double bond and 1 triple bond, or 3 double bonds.

N.B. Oxygen and other divalent atoms do not contribute to DoU.

Chapter 2

2.0 Nomenclature of Organic Compounds

2.1 Objectives

1. Identify the skeleton names of compounds
2. Identify the class names of compounds
3. Identify the substituent groups of compounds
4. Identify the priority order of functional groups
5. Name the compounds using IUPAC nomenclature

2.2 Introduction

In this section, the naming of compounds and rules are explained. The international Union of Pure and Applied Chemistry (IUPAC) developed a system that will clearly identify any compound.

There are three main parts in the systematic naming of organic compounds.

They are,

Substituent Name --- Skeleton Name --- Class Name

Prefix Suffix

Part 1 - Skeleton Name – This part of the name identifies the carbon skeleton of the compound

Part 2 – Class name (suffix) – This part of the name indicates the class of the compound based on the functional group present.

Part 3 – Substituent Group (prefix) – This part of the name indicates the substituents present in the compound.

Since many compounds contain two or more functional groups, the naming of the class (suffix) of these compounds is done after identifying the principal functional group within those compounds. In order to recognize the main functional group, a priority order of functional groups has been determined. So, if a compound has more than one functional group, the functional group with the highest priority is selected when providing the compound with a class name.

The table below provides the relevant class name for each functional group if added as a suffix, and a substituent name if considered as a prefix.

The halides (X) and nitro (NO_2) groups are always considered substituents and if a compound contains only these as functional groups, then they are named as derivative of hydrocarbons.

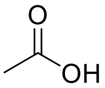
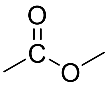
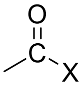
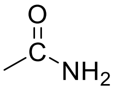
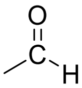
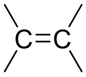
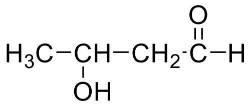
Priority Order	Functional Group	Class Name (Suffix)	Substituent Name (Prefix)
1		-oic acid	carboxy-
2	—SO_3H	-sulphonic acid	sulpho-
3		-oate	alkoxycarbonate-
4		-oyl halide	haloformyl-
5		-anamide	carbamoyl or carboxamido-
6		-al	formyl- or oxo-
7	—C≡N	-onitrile	cyano-
8	=O	-one	keto- or oxo-
9	—OH	-ol	hydroxy-
10	—NH_2	-amine	amino-
11	—O—	-ether	alkoxy-
12	—C≡C—	-yne	yne
13		-ene	ene
14	—X or —NO_2	alkane	halo-, nitro-

Table 2.2.1: Priority order of functional groups in IUPAC nomenclature

Step 1 – Determination of Class Name

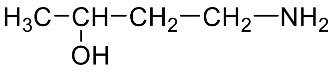
In naming compounds, step 1 is the selection of the class name according to the priority order given in the Table 2.2.1:

Two examples on selecting the correct class name:



$H_3C-\underset{OH}{\underset{|}{CH}}-CH_2-\overset{O}{\overset{\|}{C}}-H$

I



$H_3C-\underset{OH}{\underset{|}{CH}}-CH_2-CH_2-NH_2$

II

In the above compound I, there are two functional groups.

They are,

-OH

-COH

Out of the two groups, -COH has the priority over -OH. Therefore, the class name should follow COH suffix – AL.

In the above compound II, there are two functional groups.

They are,

-OH

-NH_2

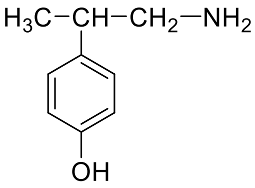
Out of the two groups, -OH has the priority over -NH_2. Therefore, the class name should follow -OH suffix – OL.

Step 2 – Determination of Skeleton Name

The next step is to determine if the compound is aliphatic, alicyclic, aromatic, or heterocyclic.

This is determined by identifying the carbon skeleton to which the main functional group is directly bonded.

e.g.



In the above compound, there are two functional groups – OH and NH_2.

Following the step 1, OH has the priority over NH_2 as a functional group. Therefore, the compound will have the class name of -ol. (Similarly, when you have a carbon chain with branches, and if one has a double bond and the other has a triple bond, you select the chain with a triple bond because triple bond has the priority over the double bond)

Once that is determined, the next step is to determine to which carbon skeleton. -OH is attached In this case, OH is attached to an aromatic carbon. Therefore, the naming now follows the aromatic system in this case (skeleton name).

Step 3 – Skeleton naming continued

After determining to which carbon skeleton, the functional group with the highest priority is attached, the naming follows the rules depending on aliphatic, aromatic, alicyclic, or heterocyclic.

2.3 Nomenclature of aliphatic compounds

- After the selection of the principal functional group, please follow the steps given below in the same order. At this stage, the class name (suffix) has already been determined.
- All other functional groups (if attached in addition to the principal functional group) are considered substituents.
- If the carbon skeleton has a double (alkene) or triple bond(alkyne) (not as a principal functional group), they are considered subsidiary group (not a substituent group). These double bonds or triple bonds necessitate an adjustment to the skeleton name to indicate what type of a bond exists in the carbon skeleton.

- When selecting the main chain (in situations of branched chains), it is important to select the chain that has only carbon atoms and the chain is continuous. The rules are given below **in the order** they must be applied.

  Rule 1 - The main chain must include the principal functional group – already discussed

  Rule 2 - The main chain must include the maximum possible number of **subsidiary groups** (double or triple bonds).

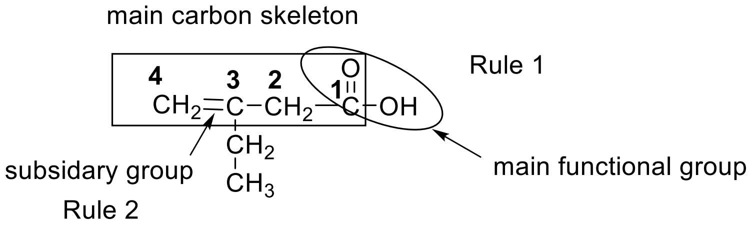
  Rule 3 - The main chain must include the maximum possible number of carbon atoms. **The first carbon should be the carbon from the principal functional group.**

  Rule 4 - The main chain must include the maximum number of **substituents**.

  Rule 5 – Name the main skeleton according to the number of C atoms.

N.B. The carbon atom of the main functional group is considered the first carbon and included in the carbon skeleton. If a functional group is not the main group, then it is not included in the counting of the carbon atoms in the carbon skeleton but considered a part of the substituent group.

e.g.



The correct name for the above compound is,

3-ethyl-but-3-enoic acid

(You will understand this naming of compound as you continue to read the rest of the rules given below including the isomerism.)

The principal functional group (in this case the only functional group) is a carboxylic acid (rule 1). The suffix would have **-oic acid. Note the numbering of the carbon atoms, starting with the carbon in the functional group.**

It is attached to a carbon chain with a **double bond**. Therefore, we need to consider this chain as the main carbon skeleton (rule 2).

Rule 3 is not necessary since rule 2 overrides it.

Rule 4 is not applicable since no substituent groups attached.

Rule 5 – Name the main skeleton according to the number of carbon atoms.

In the above example there are 4 carbon atoms since we consider the carbon from COOH. Therefore, the root name will be - but

Word roots for carbon chain depending on the number of carbon atoms:

1 carbon – meth-

2 carbons – eth-

3 carbons – prop-

4 carbons – but-

5 carbons – pent-

6 carbons – hex-

7 carbons - hept-

8 carbons – oct-

9 carbons – non-

10 carbons – dec-

11 carbons – undec-

12 carbons – dodec-

When naming the main carbon skeleton, the letters -an is added to the end of the word root, if no double or triple bonds (unsaturation) are present.

If there is a double bond a subsidiary group) is present, then -en is added to the end of the word root.

In the above example, there is a double bond. Therefore, the skeletal name will be modified to include – en in the word root making it, "but-en".

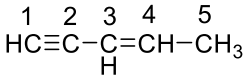
If there a triple bond (a subsidiary group) is present, then -yn is added to the end of the word root.

Now, if we add the suffix to the main skeleton name, we get but-en-oic acid.

Rule 6 – The numbering of carbon atoms is done according to several rules.

The numbering should indicate the correct position of the main functional group, subsidiary, and substituents.

- The numbering of carbon atoms in the main skeleton should be done in a manner to give the smallest number to the carbon of the principal functional group (already discussed).
  (In the previous example, 1-C was the carbon atom from COOH.)
- If the principal functional group of a compound has a triple and a double bond, then the naming should have -yne at the end of the name, and -ene part before -yne since alphabetically -ene comes before -yne.
- Now when numbering, -ene and -yne should get the lowest possible numbering combination (lowest set of locants).
  e.g.

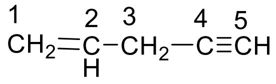


$\overset{1}{HC}\equiv\overset{2}{C}-\underset{H}{\overset{3}{C}}=\overset{4}{CH}-\overset{5}{CH_3}$

pent-3-en-1-yne

This is the correct name since both the double and triple bond get the lowest numbers. Also, note that yne is mentioned at the end of the name. This matches the priority for the class name according to the priority order table.

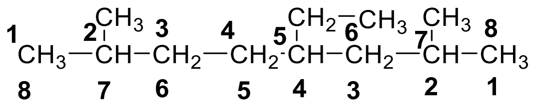
- **When there is a tie, then -ene should get the lowest numbering before -yne**



$\overset{1}{C}H_2=\underset{H}{\overset{2}{C}}-\overset{3}{C}H_2-\overset{4}{C}\equiv\overset{5}{C}H$

Pent-1-en-4-yne is the correct name since there is a tie between the numbers of triple and double bond, and the double bond has been given the lowest number. Note that -ene has been modified to -en in the name.

- For compounds without any functional groups (those with only alkyl, halo, and nitro groups), when there are two or possible numbering, the one that provides **the lowest possible numbering to substituent group at the first point of difference** is selected.



$CH_3-CH(CH_3)-CH_2-CH_2-CH(CH_2-CH_3)-CH_2-CH(CH_3)-CH_3$

OR

As shown above, there are two options. Therefore, it is necessary to consider the first point of difference, when numbered either way.

Top numbering provides, 2 (for CH_3) 5 (for CH_2-CH_3) 7 (for CH_3)

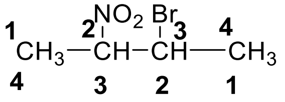
Bottom numbering provides, 2 (for CH_3) 4 (for CH_2-CH_3) 7 (for CH_3)

Therefore, the first point of difference is 5 and 4 for top numbering and bottom numbering. The bottom numbering provides the lowest number. Therefore, the bottom numbering is considered the correct numbering.

N.B. The selection is made by comparing the numbers individually at the first point of difference.

- In an instance similar to the above, if the numbering provides the same identical numbers, then the numbering that provides the lowest number to the substituent whose name comes first in the alphabetical order is chosen.

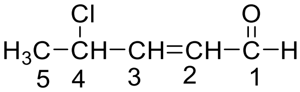
e.g.



$\underset{4}{\overset{1}{CH_3}}-\underset{3}{\overset{2}{\overset{NO_2}{CH}}}-\underset{2}{\overset{3}{\overset{Br}{CH}}}-\underset{1}{\overset{4}{CH_3}}$ OR

Since, bromo comes before nitro according to the alphabetical order, the bottom numbering is selected: 2-bromo 3-nitro.

- Upon completion of the numbering, following the rules given above for aliphatic skeleton compounds, for principal functional group, subsidiary group/s, and/or substituent group/s, relevant numbers are allocated and included in the name. The number is followed by a hyphen followed by its functional group, subsidiary group/s and/or substituent group according to the compound.
  e.g.



$\underset{5}{H_3C}-\underset{4}{\overset{Cl}{CH}}-\underset{3}{CH}=\underset{2}{CH}-\underset{1}{\overset{O}{\overset{\|}{C}}}-H$

Final Name: 4 – chloro – 2 – pentenal

4 – position of the substituent

2 – position of the subsidiary group

chloro – substituent name - **Prefix**

pent – carbon atom word root → **Skeleton Name**

en – substituent group modified (note – ene has become -en) al – principal group class name – **Suffix.**

Since the position of the principal group is in the first place, number 1 is not used in the name. If the principal group is non-terminal (therefore will not be attached to carbon 1), then its position is indicated by the number. Also, if there are more than one subgroup or substituent attached, the positions of those are given by the number followed by di, tri, etc.

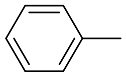
- Naming of the substituent groups such as alky and aryl can be done as a derivative of corresponding hydrocarbon
  e.g.

H_3C-

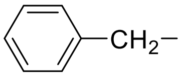
methyl

H_3C-CH_2-

ethyl



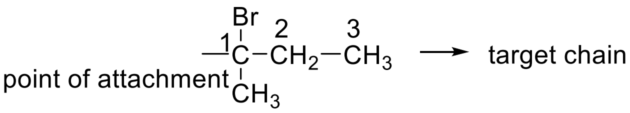
phenyl



benzyl

Any complex substituents are named systematically following the rules as before. This is done firstly by determining the longest continuous carbon chain **starting from the point of attachment** and then by following the rules of naming.

e.g.



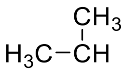
$$-\overset{Br}{\underset{CH_3}{\overset{1}{C}}}-\overset{2}{CH_2}-\overset{3}{CH_3} \longrightarrow \text{target chain}$$

1-bromo-1-methyl pentyl

Number the attached longest C chain to give the point of attachment number 1 and indicate all substituents on this chain with a number.

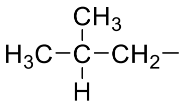
N.B. IUPAC has retained some common names for some substituent (which are unsubstituted) hydrocarbons. These also can be given the systematic IUPAC naming when necessary.

e.g.



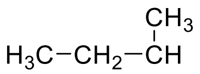
$H_3C-\overset{CH_3}{\overset{|}{CH}}$

Isopropyl



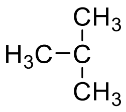
$H_3C-\underset{H}{\underset{|}{\overset{CH_3}{\overset{|}{C}}}}-CH_2-$

Isobutyl



$H_3C-CH_2-\overset{CH_3}{\overset{|}{CH}}$

Sec-butyl



$H_3C-\underset{CH_3}{\underset{|}{\overset{CH_3}{\overset{|}{C}}}}$

tert-butyl

$CH_2{=}CH—$ vinyl

$CH_2{=}CH-CH_2-$ allyl

- **Naming of ethers and amines**:

These two compounds are named in general terms using a non-IUPAC and IUPAC naming. Therefore, both types are explained.

Ethers have two alkyl groups connected to an oxygen atom. Therefore, they are named as radicofunctional names in non-IUPAC naming. This means the names of both groups (radicals) together with the functional group name is given.

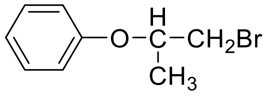
e.g. 1

$$H_3C-H_2C-O-CH_2-CH_3$$

Diethyl ether or Ethyl ether - common name

Ethoxyethane -IUPAC name

e.g. 2.



2-bromo-1-methylethyl phenyl ether – common name

(1-Bromo-2-propanyl) benzene -IUPAC name

According to the IUPAC naming, ethers are named as alkoxy or aryloxy derivatives of hydrocarbons of the groups attached to the oxygen atom. The longer chain is considered as the hydrocarbon part. Nevertheless, please note that IUPAC names are not used normally for ethers.

Similarly, amines are named in a non-IUPAC naming system as derivatives of ammonia.

The non-IUPAC naming of primary (R-NH_2), secondary (R'-NH-R'') and tertiary (R'R''R'''N)

- Select the largest group attached to N. The group is named accordingly, and the suffix amine is added. If two or three similar groups are present, the prefix di- or tri- is added.
- The other group names are added to the front of the amine name. Each of these names will have N in front to indicate that these groups are attached to a nitrogen atom and not a carbon atom.

When naming according to IUPAC, the NH_2 group is considered as a substituent and named as an amino. If it is the only functional group, the compound is named as a hydrocarbon with NH_2 as a substituent.

Naming of compounds with two or more identical principal groups

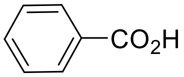
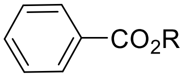
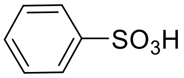
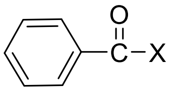
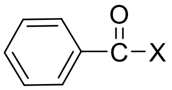
In this situation, the main chain is selected to include both these functional groups. The class name (suffix) is modified with a prefix di- (or tri- depending on the situation) and two (or three) carbon atom numbers are mentioned in the name.

If the functional groups are attached to the two terminal ends of a chain, then the numbers are not used, but di-prefix is mentioned.

2.4 Nomenclature of aromatic compounds

If the main carbon skeleton is an aromatic compound, then the following steps are followed:

- In the naming of all aromatic compounds, the principal functional group and the aromatic ring are considered the parent compound.
- Whilst the table given below only consider, benzene rings connected to a functional group, a similar extension can be made for other aromatic compounds.
- The following table shows the priority order similar to the naming of aliphatic compounds. Nitrobenzenes and halobenzenes are named as substituted benzenes and not as parent compounds.

Priority Order	Parent compound	Name
1		Benzoic acid
2		Alkyl benzoate
3		Benzene sulphonic acid
4		Benzoyl halide
5		Acetanilide

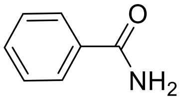
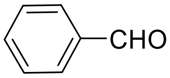
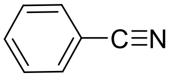
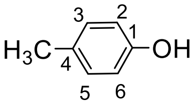
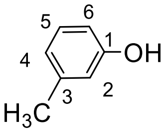
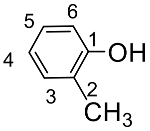
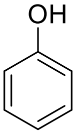
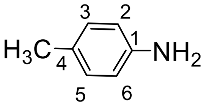
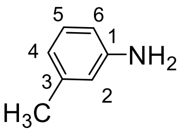
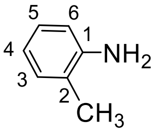
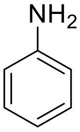
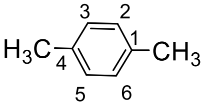
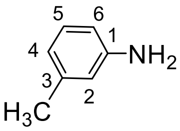
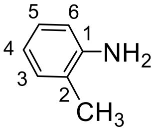
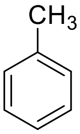
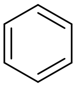
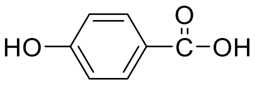
6		Benzamide
7		Benzaldehyde
8		Benzonitrile
9	  	p-Cresol, m-Cresol, o-Cresol
10		Phenol
11	  	p-Toluidine, m-Toluidine, 0-Toluidine
12		Aniline
13	  	p-Xylene, m-Xylene, o-Xylene
14		Toluene
15		Benzene

Table 2.4.1: Priority order of aromatic parent compounds (benzene-base) in IUPAC nomenclature

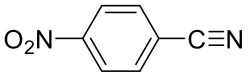
- Begin the naming by identifying the highest-priority parent structure within the compound

e.g.



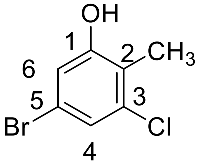
Parent group is benzoic acid, since it has the highest priority (not phenol).

e.g.



Benzonitrile is the parent group. NO_2 is considered a substituent.

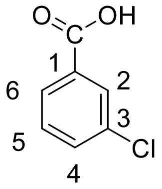
- Once the parent group is identified, all the other groups are considered substituents.
- The carbon atoms that make the aromatic ring are given numbers, so that substituent groups can be correctly named.
- In numbering, number 1 is given to the carbon that is attached to the principal functional group. If the parent structure carries two functional groups in cases like toluidines, cresols, then the direction of numbering are already determined.
  e.g.
  o-Cresol with Br attached to the ring. From the table above, you can see that the numbering is already given:



5-Bromo-o-cresol

- Bromide number is already determined.

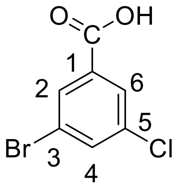
- In all other cases, the numbering is done in the direction that provides the lowest set of number to the substituents.
  e.g.



Cl is given number 3, and not number 5 (when numbered counterclockwise).

- From the two possible directions available (since when numbering a benzene ring, you can number them clockwise or counterclockwise), if both directions provide the same set of numbers, then the numbering is done in the direction that provides lower number to the group that comes first in the alphabetical order.

e.g.

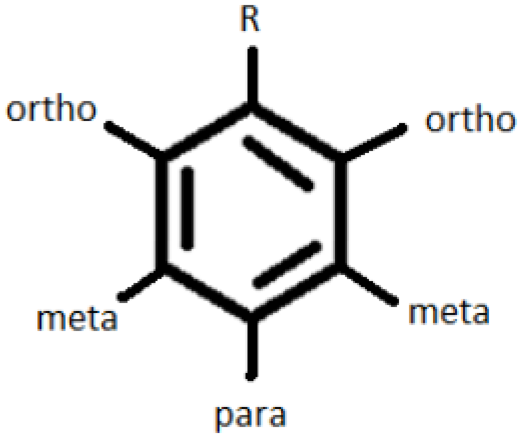


3-bromo-5-chlorobenzoic acid

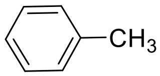
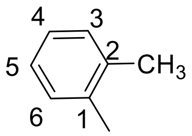
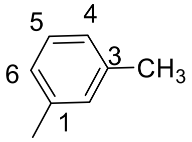
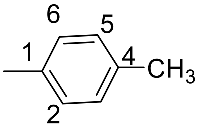
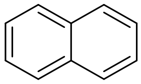
Bromine comes first in the alphabetical order before chloro; therefore, Br is given the lowest number.

- In a benzene ring, when the principal functional group is attached to the first carbon, the second carbon position is known as ortho-, third carbon position is known as meta-, and the fourth carbon position is known as para.

  e.g. ortho (o), meta (m), and para (p) positions of a benzene ring with an attachment at the first carbon position. Please note that numbering could be clockwise or anti-clockwise. Therefore, there are two ortho positions, two meta positions, and one para position.



- When an aromatic group becomes the substituent, a name is provided depending on the parent hydrocarbon. When the ring in addition to being a substituent group carries other substituents, names are given as per the table given below (only a few examples are given):

• Parent Compound	Substituent
Toluene 	o- Tolyl  m-Tolyl  p-Tolyl 
Naphthalene 	Naphthyl

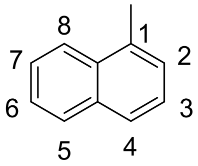
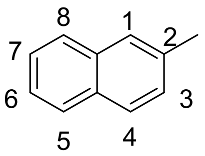
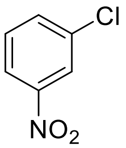
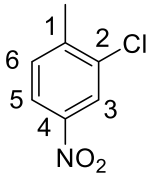
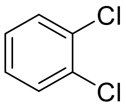
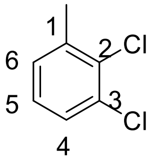
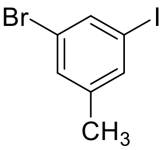
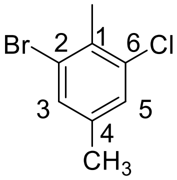
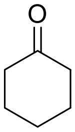
	 1-  2-
Chloro-nitrobenzene 	2-Chloro-4-nbitrophenyl 
Dichlorobenzene 	2,3-Dichlorophenyl 
Bromo-iodotoluene 	2-Bromo-6-iodo-p-tolyl 

Table 2.4.2: Names of aromatic as the parent compound and as a substituent

2.5 Nomenclature of alicyclic compounds

- In alicyclic compounds, the principal functional group determined according to the table 2.2.1 must be directly connected to the alicyclic compound.
- The word root to match the number of carbon atoms in the ring is combined with prefix cyclo. This indicates that the ring is a hydrocarbon.
- Similar to the naming of aliphatic compounds, a suffix is added to match the principal functional group.
  e.g.



Cylohexanone

(Note that the ring structure above has no double bonds or a ring to indicate the resonance structure due to conjugated double bonds. This has a cyclic alkane carbon skeleton.)

Cyclic system – cyclo

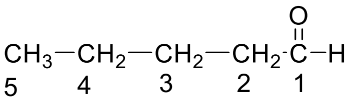
Hex – word root for six carbons

An – saturated alkane

One – class name/functional group - suffix

- A major difference in the numbering of alicyclic versus acyclic (non-cyclic) hydrocarbons is that the carbon atom of the main functional group is not counted in alicyclic unlike acyclic.

e.g. 1



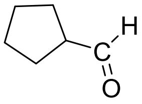
$$\underset{5}{CH_3}-\underset{4}{CH_2}-\underset{3}{CH_2}-\underset{2}{CH_2}\text{-}\underset{1}{\overset{\overset{O}{\|}}{C}}-H$$

Name: **Pentanal**

Pentan – skeleton name

al – class name - aliphatic

e.g. 2



Name: **Cyclopentanecarboxaldehyde**

Cyclopentane – skeleton name

Carboxaldehyde – class name - alicyclic

2.6 Nomenclature of heterocyclic compounds

- There are many rules in the naming of heterocyclic compounds. Since the number of common names used for basic unsubstituted heterocyclic ring systems are many, IUPAC has retained these names. This section covers only the important and widely used compounds.
- IUPAC rules allow three types of nomenclatures: Hantzsch-Widman Nomenclature, Common Names, Replacement Nomenclature.
- In naming these compounds, three aspects are considered: size of the ring, prefix that indicates the type heteroatom present, degree of unsaturation. This is Hantzsch-Widman Nomenclature.
- The following table provides common word roots:

Element	Prefix
Oxygen	Oxa-
Nitrogen	Aza-
Sulfur	Thia-
Phosphorous	Phospha-

Table 2.6.1: Word roots and significance in the naming of heterocyclic compounds.

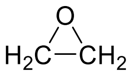
- The following table provide the ring size and indication of the unsaturation. Please note that an unsaturated name indicates that the compound has the maximum number of conjugated double bonds. When partial unsaturation exists, prefixes such as dihydro-, tetrahydro- are used.

	Nitrogen Present	Nitrogen Present	Nitrogen Absent	Nitrogen Absent
Number of atoms	Unsaturated	Saturated	Unsaturated	Saturated
3 -ir	-irine	-iridine	-irene	-irane
4 - et	-ete	-etidine	-ete	-etane
5 - ol	-ole	-olidine	-ole	-olane
6 - in	-ine	-*	-in	-inane
7 - ep	-epine	-*	-epin	-epane
8 - oc	-ocine	-*	-ocin	-ocane
9 - on	-onine	-*	-onin	-onane
10 - ec	-ecine	-*	-ecin	-ecane

*Perhydro is used as the prefix followed by the unsaturated name. When combining prefix and suffix together, drop the first vowel, if two vowels come together.

Table 2.6.2: Ring size and unsaturation are indicated the naming of heterocyclic compounds.

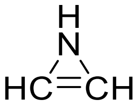
Some examples of heterocyclic compounds:

- 

Oxirane

Ox – Oxygen heteroatom

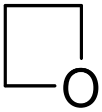
Irane – Saturated 3-membered ring with no nitrogen

- 

Azirine

Az – Nitrogen heteroatom

Irine – Unsaturated 3-membered ring with nitrogen

- 

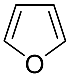
Oxetane

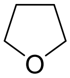
Ox – Oxygen heteroatom

Etane – Saturated 4-membered ring with no nitrogen

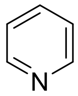
Two examples of heterocyclic compounds with standard (trivial) names.

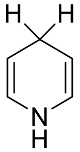
These names do not indicate any information about the ring size or their heteroatoms.





Furan → Derivative – Tetrahydrofuran – Losing two double, gaining H atoms.





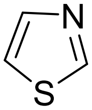
Pyridine → Derivative – Dihydropyridine – Losing one double bond, gaining H atoms

- When a compound has more than one heteroatom, the order of naming starts with the atom of from a high group number in the periodic table and low atomic number in that group.

  e.g.

  Priority order for N, P, O, S is,
  O> S> N> P

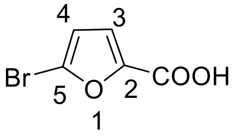
  e.g.



Thiazole

Thi – For S atom
Az – For N
Ole – For 5-membered ring

- In monocyclic compounds the numbering starts with the heteroatom and moves in the direction that provides the lowest numbers to substituents. e.g.



5-Bromofuran-2-carboxylic acid

Numbering has started at O, and COOH, which is the principal group gets the lower number.

- When there are more than one heteroatoms, the numbering starts at the carbon atom

In this chapter, important aspects of IUPAC nomenclature have been covered.

2.7 Drawing of structures according to the IUPAC nomenclature

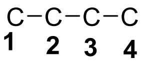
When an IUPAC name is given, you should be able to draw the correct structure. The systematic approach to drawing the structure is as follows:

1. Draw the number of carbon atoms according to the skeleton name and number them.
2. Introduce the principal functional group according to the suffix and the subsidiary groups according to the skeleton name modifier, at correct positions of the skeleton by following the given numbers.
3. Place substituents at the correct position.
4. Finally, add hydrogen atoms to complete the valency.

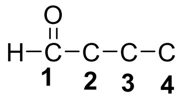
e.g. 2-methyl-2-butenal

Step 1:

But - 4 carbons – Carbon skeleton



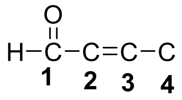
Step 2:



$\mathrm{H{-}C({=}O){-}C{-}C{-}C}$

Al – aldehyde group – Functional Group

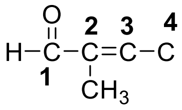
Step 3:



$\mathrm{H{-}C({=}O){-}C{=}C{-}C}$

2 - En – Double bond – subsidiary group

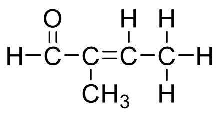
Step 4:



$\mathrm{H{-}C({=}O){-}C(CH_3){=}C{-}C}$

2 – Methyl – Substituent group

Step 5:



$\mathrm{H{-}C({=}O){-}C(CH_3){=}CH{-}CH_3}$

Add hydrogen

Chapter 3

Isomers of Organic Compounds

3.0 Objectives

1. Classify isomers
2. Identify different type of isomers
3. Draw structures of various isomers

3.1 Introduction

Isomerism exists when two or more compounds have the same chemical formula (same number of atoms of each element) but different structural or spatial arrangements of the atoms within those compounds. Isomerism is divided into two main groups: constitutional (structural) isomers and stereoisomers.

The following classification shows various types of isomers:

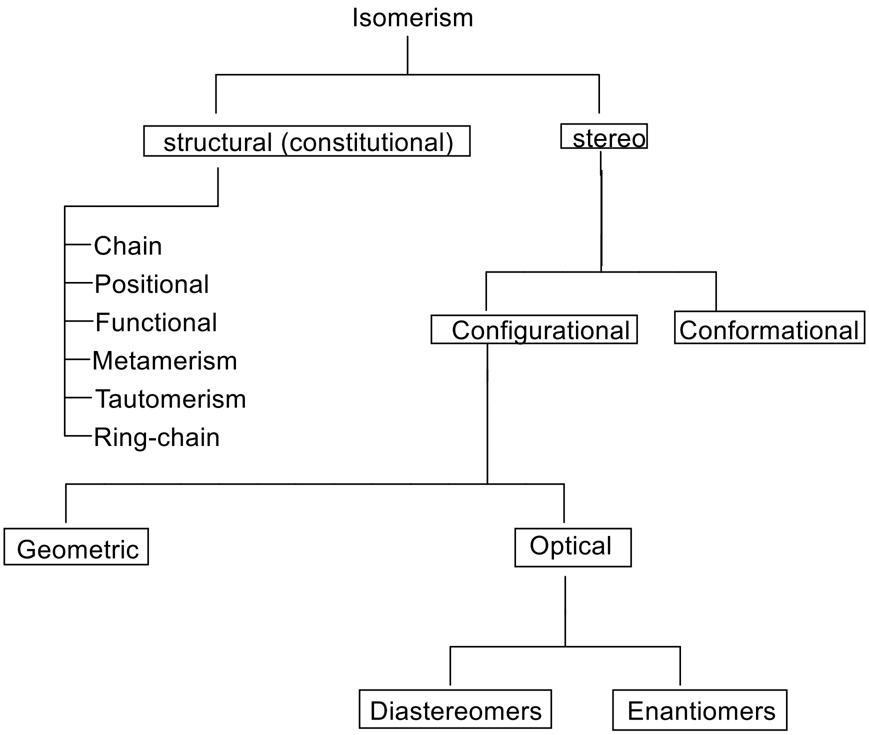


Figure 3.1.1: Classification of Isomers

The logical approach given below should help you determine the types of isomers of organic compounds:

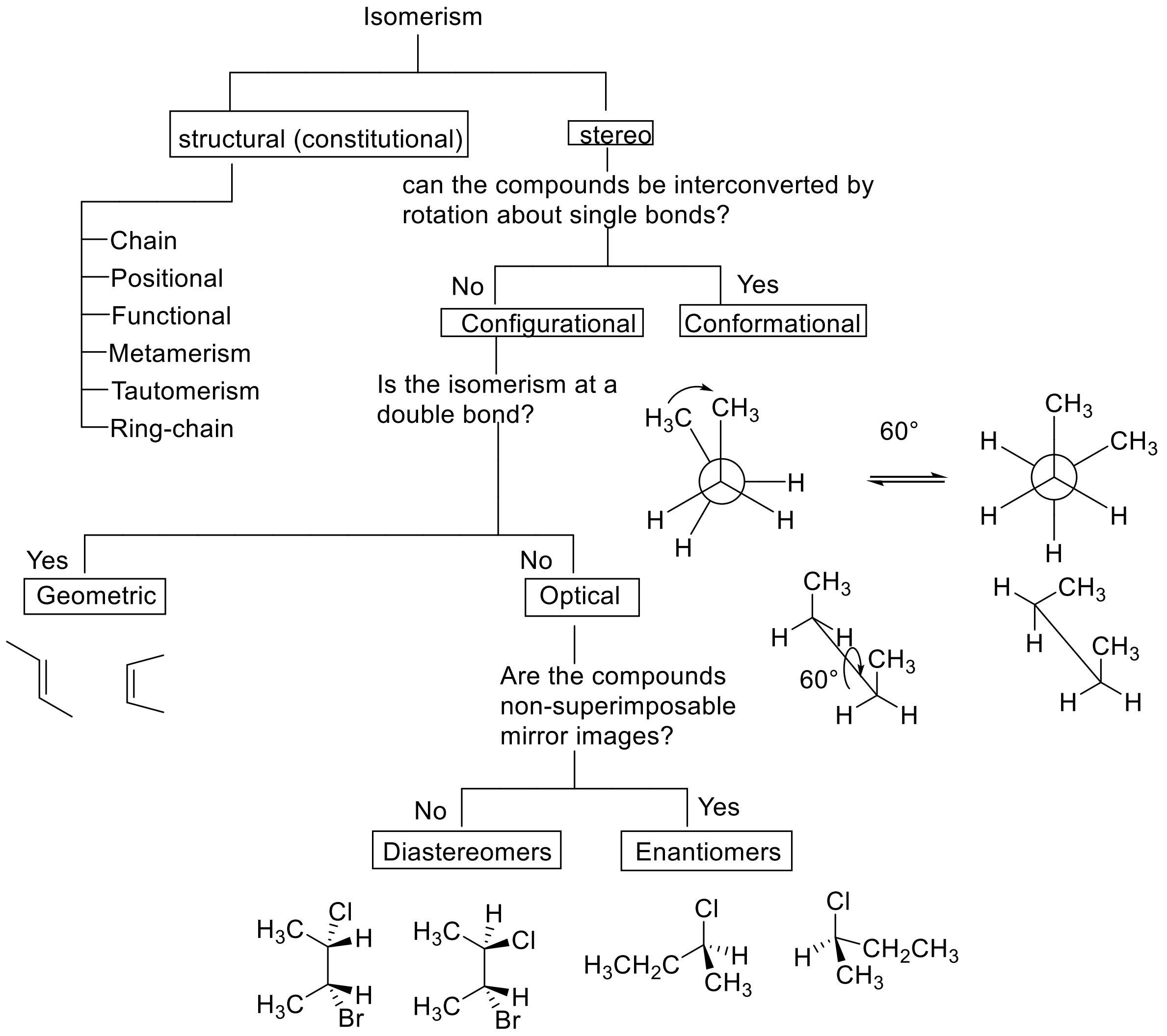


Figure 3.1.2: A logical approach to determining the type of isomer for any compound

3.2 Constitutional (Structural) Isomers

This group of isomers can be divided into five groups:

1. Chain isomers
2. Position isomers
3. Functional isomers
4. Metamerism
5. Tautomerism
6. Ring-chain

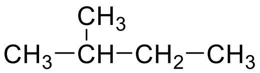
3.2.1Chain Isomers

These isomers have the same molecular formula but have different arrangements in the order in which atoms are connected.

e.g.

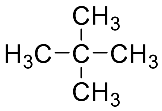
$CH_3CH_2CH_2CH_2CH_3$

pentane



$CH_3-\overset{\overset{CH_3}{|}}{C}H-CH_2-CH_3$

isopentane
(2-Methylbutane)



$H_3C-\overset{\overset{CH_3}{|}}{\underset{\underset{CH_3}{|}}{C}}-CH_3$

neopentane
(2,2-dimethylpropane)

Above compounds are all alkanes. Alkanes show chain isomers starting with butane (four carbon compounds).

3.2.2 Position Isomers

These isomers have the same molecular formula but their functional groups (including double or triple bond) or substituent atoms are in different positions.

e.g.

Alkenes

$CH_2=CH-CH_2-CH_3$

but-1-ene

$CH_3-CH=CH-CH_3$

but-2-ene

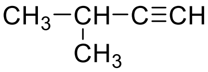
Alkynes

$CH_3-CH_2-CH_2-C\equiv CH$

pent-1-yne

$CH_3-CH_2-C\equiv C-CH_3$

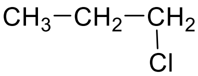
pent-2-yne



$$\begin{array}{l}CH_3-\underset{\displaystyle CH_3}{CH}-C\equiv CH\end{array}$$

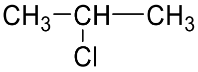
3-methyl-1-butyne

Functional Group



$$CH_3-CH_2-\underset{\displaystyle Cl}{CH_2}$$

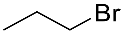
1-chloropropane



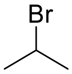
$$CH_3-\underset{\displaystyle Cl}{CH}-CH_3$$

2-chloropropane

Substituent atom



bromopropane

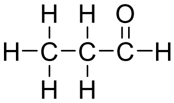


2-bromopropane

3.2.3 Functional Isomers

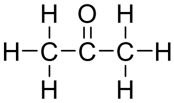
These isomers have the same molecular formula, but their functional groups are different.

e.g.



$$\begin{array}{ccccccc} & & H & & H & & O \\ & & | & & | & & \| \\ H & - & C & - & C & - & C & - & H \\ & & | & & | & & \\ & & H & & H & & \end{array}$$

propanal



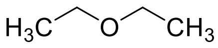
$$\begin{array}{ccccccc} & & H & & O & & H \\ & & | & & \| & & | \\ H & - & C & - & C & - & C & - & H \\ & & | & & & & | \\ & & H & & & & H \end{array}$$

propanone

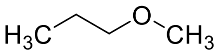
3.2.4 Metamerism

These isomers have the same molecular formula but the alkyl groups on each sides of the functional group are different.

e.g.



diethyl ether

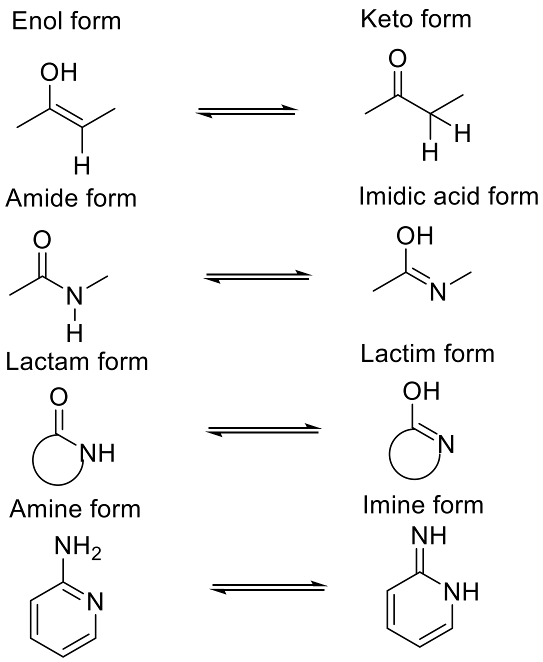


methyl propylether

3.2.5 Tautomerism

These isomers have the same molecular formula but differ only in the position of protons and electrons and they are interconvertible. This is not the same as functional isomerism, since in tautomerism there is a dynamic equilibrium process, which is not seen in functional isomers.

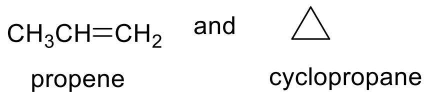
e.g.



3.2.6 Ring-chain Isomerism

These isomers have the same molecular formula but differ only by one structure being a ring structure and the other being an open-chain structure.

e.g.

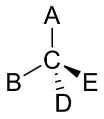


3.3 Stereoisomers

These compounds have the same formula, but they are arranged differently in a three-dimensional setting. Although structural isomers can be distinguished easily when displayed in a two-dimensional setting, stereoisomers need to be analyzed in a three-dimensional setting. Therefore, when drawing stereoisomers on a two-dimensional setting the following standard convention is followed:

- A broken line depicts an atom below the plane of the paper
- A normal line depicts an atom on the plane of the paper
- A thickened line depicts an atom above the plane of the paper

e.g.



C is the central atom. A and B atoms are on the plane of the paper. E atom exists above the plane of the paper. D atom exists below the plan of the paper.

This group of isomers can be divided into two groups:

1. Conformational isomers
2. Configurational isomers

3.3.1 Conformational Isomers

In understanding conformational isomers, it is important to understand the role played by single bonds. These single bonds consist of axially symmetrical σ orbitals; they are capable of free rotations. These free rotations will allow the atoms attached to these bonds to assume different positions in a three-dimensional space.

e.g.

(A) (B)

Figure 3.3.1.1: A and B are separated only by the rotation about C -2 atom

The above example shows how butane can exist as conformational isomers. If you consider a rotation of 120° degrees at carbon 2 in the case of A compound, the final product will look like B. These two are conformers or rotational isomers and can inter-convert at room temperatures. This is because the energy difference between the two is small. At low temperatures (-200 ^{0}C), the existence of two conformers have been observed since there is no sufficient energy to convert from A to B.

Some possible rotations of acyclic alkane (acyclic) are given below:

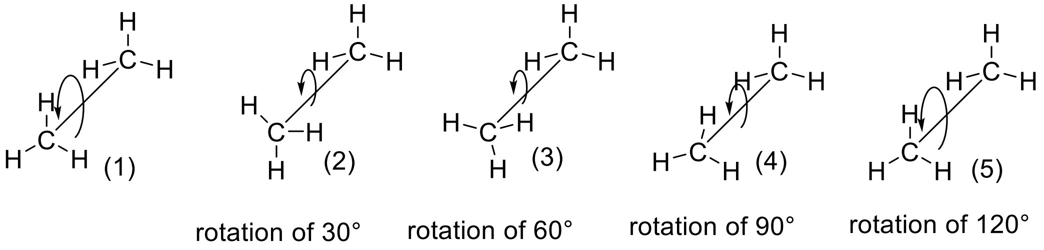


Figure 3.3.1.2: Some possible rotations of ethane

During the free rotations between the two C atoms, the compound ethane may attain a position where H atoms of the two C atoms may be near to each other. This is a high energy and less stable state. When H atoms are near to each other repulsions will be higher. The images 1 and 5 show two such situations. These two situations are known as “eclipsed conformation” since H atoms shadow or eclipse each other. The image 3 is a situation where H atoms are farthest apart. Therefore, this is a very stable form and is known as “Staggered Conformation.”

The following graph shows the potential energy of different structures at different rotations between the two C atoms. Low energy level indicates the stability of those structures.

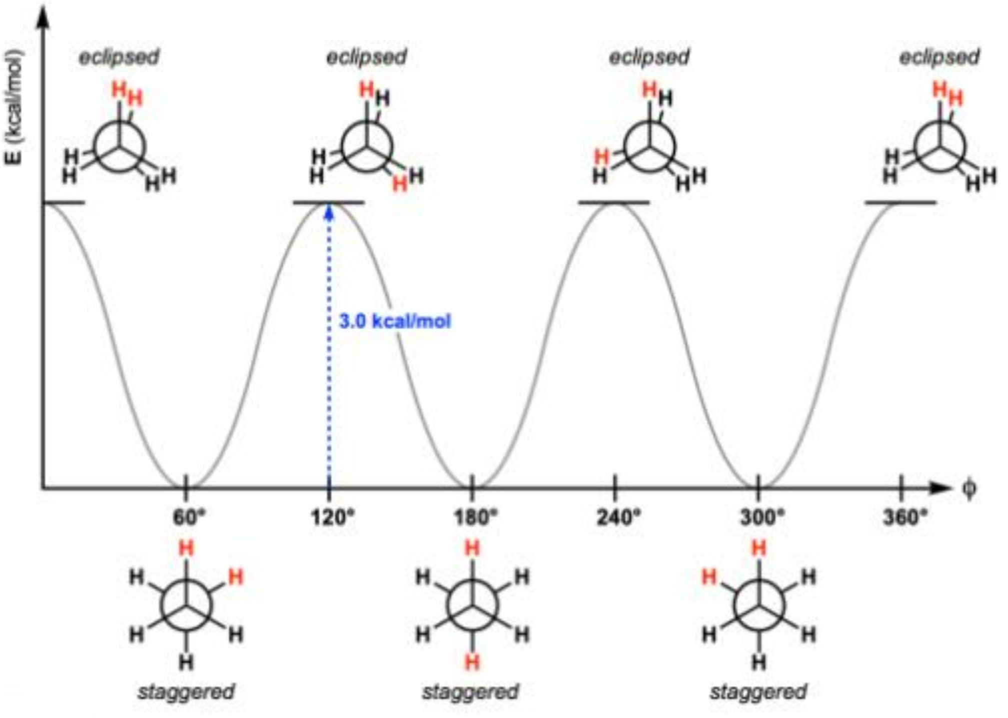


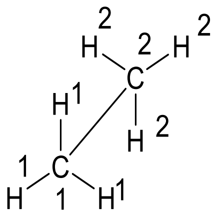
Figure 3.3.1.3: The potential energy changes during rotations about C-C bond in ethane

The representation of conformational isomers on paper (two dimensions) in three-dimensional form is done in two ways:

1. **Sawhorse structure**

In this structural drawing, the bond between the two carbon atoms is oriented diagonally backwards and exaggerated in length and the entire molecule is displayed in three dimensions.

e.g. Ethane C_2H_6

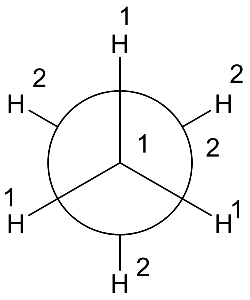


Sawhorse structure

2. Newman Projection

In this structural drawing, carbon-carbon bond is viewed from one end and the nearer carbon is displayed by a point (a dot) with the three bonds attached to it radiating outward. The carbon atom further away is represented by a circle with the three bonds of that carbon radiating outward from the circle.

e.g. Butane C_4H_{10}



Newman Projection

Different forms of Newman projections depending on the angles with their names are given below:

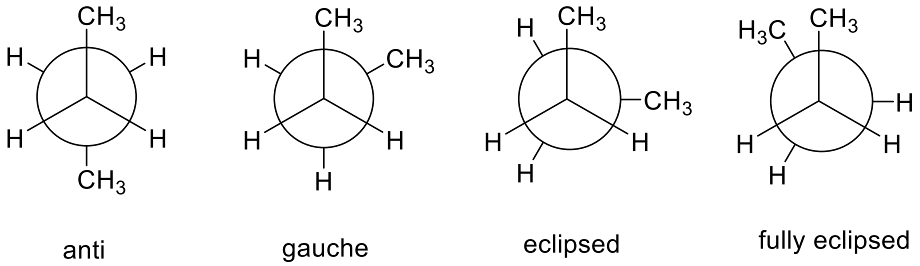


Figure 3.3.1.4: Different forms of Newman projections of butane

The most stable compound out of the above 4 types is anti, since the large groups are farther apart.

The energy diagram of the several forms of butane is given below:

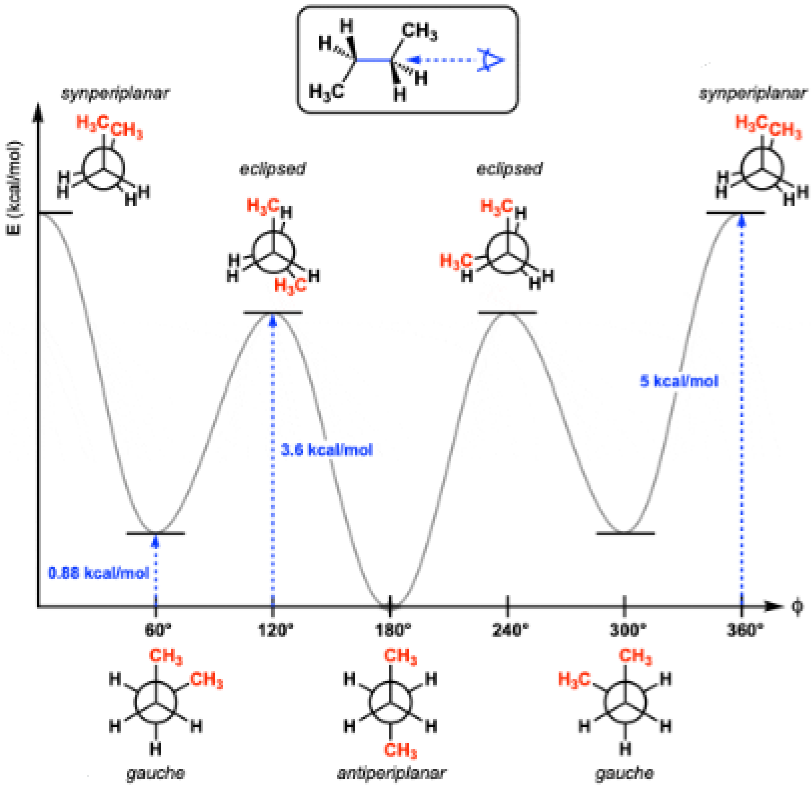


Figure 3.3.1.5: The potential energy changes during rotations about C-C bond in butane

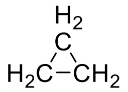
At normal temperatures it is difficult to separate a mixture of these optical isomers since they can interchange due low energy barriers. The most stable form out of the mixture is the staggered form where all large groups are arranged farthest apart.

At low temperatures, these different forms of isomers cannot easily cross the energy barrier and attain another form; therefore, the separation of the mixture becomes easier.

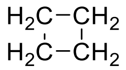
When it comes to the conformation in cyclic systems, it is important to understand that although a ring cannot show free rotation without breaking the bonds, the ring can assume different forms. The energy of cyclic conformation is dependent on the spatial relationship among ring substituents in the given conformation. In the formation of bonds, a stronger bond will emit more energy. A bond is considered stronger if the overlap of bonding orbitals is greater.

A carbon with sp3 hybridization connected to four other atoms will display tetrahedral structure with a bond angle of 109.5 ^{0}. When such a carbon bonds with another carbon to form (both under sp^3 hybridization), depending on the type of the ring, the compound will be under strain. Smaller rings will be under additional strain since the bonds have to bend deviating from the standard 109.5 ^{0}. Another factor to consider is the substituents in the ring.

The ring strain can be understood by considering the angles of compounds like cyclopropane or cyclobutane. The angle of cyclopropane is 60 ^{0} and that of cyclobutene is 90 ^{0}. The bond formations of these compounds do not produce high exothermic energy values. This means these bonds are under strain.



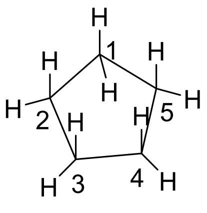
cyclopropane



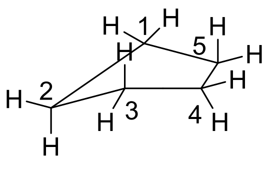
cyclobutane

The table below shows the heat of formation values of cycloalkanes and their corresponding alkanes. Cyclopentane and cyclohexane show less strain and more stability of bonds. This is because the bond angles between two carbons come closer to 109.5^0. Further, in cyclopentane and cyclohexane due to the presence of eclipsed hydrogen atoms, the structure is strained. As a result, the conformation is a non-planar, puckered form also known as envelope conformation in cyclopentane and cyclohexane.

e.g.



Planar Structure



Puckered structure

No. of carbon atoms	Cycloalkane	Heat of Formation kJ/mol	Corresponding Alkane	Heat of Formation kJ/Mol
3	Cyclopropane	+52.3	Propane	-63
4	Cyclobutane	+27.5	Butane	-84
5	Cyclopentane	-77.8	Pentane	-105
6	Cyclohexane	-123.9	Hexane	-126

Table 3.3.1.1: Heat of formation values for cyclic and corresponding acyclic alkanes

Due to the configuration of cyclohexane, although its bond angle nears 120^0 surpassing the ideal angle of 109.5^0, it shows relative stability. Cyclohexane shows the following non-planar conformations that help the compound to show relative stability:

3. Chair and Boat Conformations

In the chair conformation, all C atoms have tetrahedral confirmation. The tetrahedral form leads to stability. In Chair conformation all H atoms are staggered as shown below using Newman Projection:

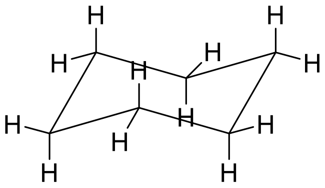


Figure 3.3.1.6: **Cyclohexane - Chair Conformation**

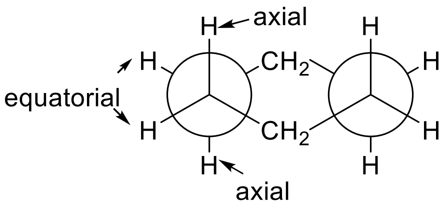


Figure 3.3.1.7: Cyclohexane - Newman Projection

As shown above, the bonds that attach H atoms to C atoms are of two types: Axial and Equatorial. Therefore, the H atoms attached to each carbon will occupy either equatorial or axial space.

Axial atoms are perpendicular to the plane of the paper and equatorial are on the plane of the ring.

As a result, at each C atom, one H atom will be equatorial and the other will be axial and the two H atoms in the same carbon will face opposite directions.

While at room temperature, 99% of the isomers is in the chair form, the others exist in the boat form. This form is high energy, and unstable at room temperature. The H atoms are not completely staggered in the boat form. The eclipsing of some H atoms by the adjacent H atoms happens. The H atoms at the two ends of the boat form of the ring are close enough to create some repulsion. This is the reason that boat form, which is less stable than the chair form exists in small amounts at room temperature.

The chair form and the boat form are normally in equilibrium. The conversion of one form to the other is done by pushing one end of the ring upwards.

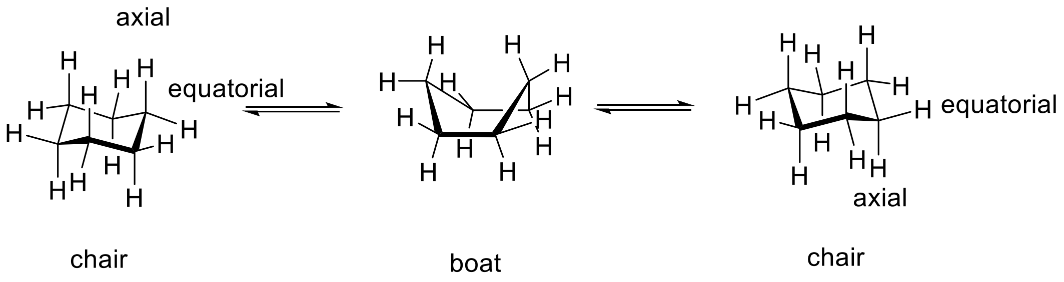
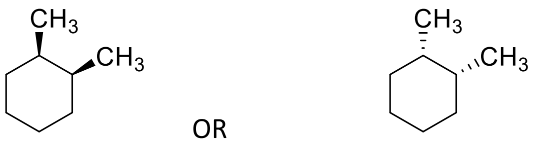


Figure 3.3.1.8: Interchangeable forms of chair and boat of cyclohexane

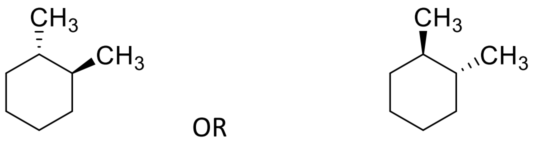
The two chair forms are identical in the above image, although the two H atoms have interchanged from axial to equatorial. This interchange known as inversion or flipping enables cyclohexane ring to attain lower forms of energy and be stable. This logical understanding is true for substituted (mono or di) cyclohexanes.

Disubstituted cyclohexanes can exist in cis-trans form of isomerism. If the two substituted groups are on the same side (out of plane or below the plane), then such an arrangement is known as cis. If the substituted groups are in opposite planes, then they are known as trans form.

e.g.



cis – 1,2-dimethyl cyclohexane



Trans – 1,2-dimethyl cyclohexane

3.3.2 Configurational Isomers

In compounds where rotation is not possible under normal conditions and normal temperatures, the inability to rotate leads to configurational isomers. Such compounds have multiples bonds between two carbon atoms. This is the case in alkenes. The existence of double bonds makes it impossible to rotate without breaking the bond. The breaking of the bond requires higher energy. Therefore, such cleavage does not occur at room temperatures due to low energy.

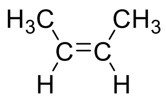
There are two types of configurational isomers:

1. Geometric isomers
2. Optical isomers

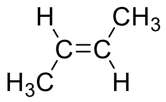
3.3.2.1 Geometric isomers

These isomers are also known as cis-trans isomers are displayed by alkenes and some cyclic compounds. Due to the π bond that exists in a double bond the rotation is restricted.

e.g.



cis-but-2-ene



trans-but-2-ene

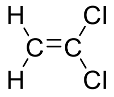
Cis- isomer shows that both CH_3 groups are on the same side. Please note the way the name is written – cis in front of the IUPAC name to indicate that two identical groups are on the same side.

In trans- isomer, the CH_3 groups are on opposite side. Please note the way the name is written – trans in front of the IUPAC name to indicate that two identical groups are on the opposite side.

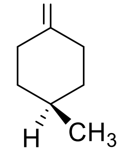
Any rotation about C=C requires about 200 kJ/mol. Therefore, the two isomers would exist as cis and trans. A rotation about C-C would require only 20kJ/mol. As a result, geometrical isomers are stable at room temperatures. Since π bonds are formed by parallel overlapping, any rotation of one carbon by 90^0 degrees will break the bonds.

Cis and trans isomers cannot exist when identical groups are attached to one of the double-bond forming carbon atoms.

e.g.



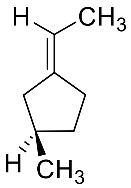
1,1-dichloroethene



(R, Z)-1-ethylidene-4-methylcyclohexane

There are no cis-trans isomerism in any of the above compounds. In the ring compound, the symmetry of the ring makes it a non-cis-trans isomer.

Alternatively, the above compound has cis-trans isomer due to the asymmetry of the ring.



(R, E)-1-ethylidene-3-methylcyclohexane

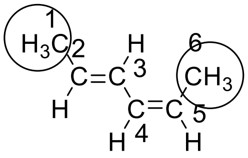
The number of possible stereoisomers increases when a compound has more than one double bond. The general formula to calculate the number of isomers is,

$$\mathbf{2^n.}$$

n = number of restricted rotational points (such as double bonds)

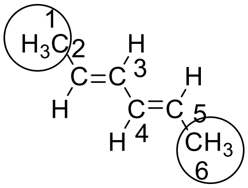
While the above equation provides all possible isomers, when applied to symmetric compounds, some of the isomers will be the same. Therefore, in the case of symmetric compounds the number will be less than 2^n.

e.g. hexa-2,4-diene isomers

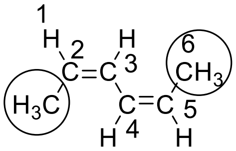


(1)

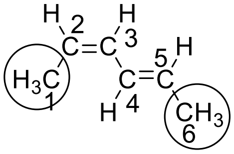
In the above structure, there are two double bonds. Therefore, the number of possible cis-trans isomers are $2^2 = 4$. Nevertheless, because of the symmetry, two of the possible isomers will be the same. Therefore, this compound will only have three possible structures as shown below:



(2)



(3)



(4)

In the above cis-trans possibilities, 1 and 4 compounds are the same. Therefore, the total number of possible isomers in this symmetrical compound is 3.

Naming of cis-trans isomers:

1. E – Z Nomenclature

As explained previously, cis isomer is a compound with two identical groups on the same side of the double bond. A trans isomer is when the two identical groups are on the opposite sides.

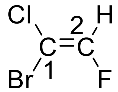
There are situations when the two groups are not identical but separated by a double bond. In such situations, E-Z nomenclature is used. This naming is based on sequence rules that determine the priority of the attached groups to the two carbon atoms that form the double bond. The priorities of the groups attached to each carbon are determined separately. If the group with the highest priorities in each carbon is on the same side, then it is known as Z (Zusammen in German meaning together). If the groups with the highest priorities in each carbon are opposite to each other then, it is known as E (Entgegen in German meaning across).

The sequence rules

The following rules are applied to the atoms or groups that are attached to the carbon making the double bond to find the priority order:

1) An atom with the largest atomic number will have the highest priority. Therefore, H has the lowest priority.

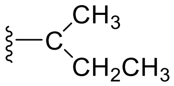
e.g.



(Z) - 1-bromo, 1-chloro, 2-fluoroethene

In the above example, for C_1, Br has the highest priority. For C_2, F has the highest priority. Both, Br and F are on the same side. Therefore, this is a Z configuration.

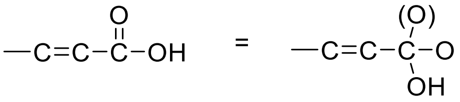
2) If two groups are attached to the carbon by identical atoms, then other atoms attached to these groups are considered until there is a difference in the priority at the first point of difference.



It the above example, the ethyl group has a higher priority than the methyl group since ethyl has an extra carbon (the first point of difference) and two more hydrogen atoms than the methyl group.

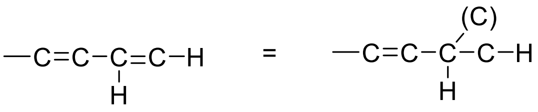
3) When there are multiple bonds, each bond is considered to be attached to the same atom to match the number of multiple bonds.

e.g. 1



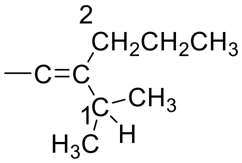
The extra O atom is drawn in parenthesis.

e.g. 2



The extra C atom is drawn in parenthesis.

3. If the groups attached have identical and the same number of atoms, then the atoms immediately attached to the atom that is directly attached to the carbon with a double bond are considered to determine the priority.
   e.g.



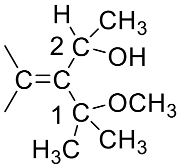
Both groups in the above example have the same atoms and the same number.

i.e. 3 Cs and 7Hs.

Yet, for group 2, carbon of the group is immediately attached to one carbon and two hydrogen group.

For group 1, carbon of the group is immediately attached to two carbons and one hydrogen. This has the higher priority.

e.g.



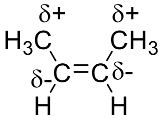
As same as the previous example, group 1 and 2 have a difference in the atoms attached to the carbon atoms connected to the double-bonded carbon. Group 1 has higher priority.

The Differences of Cis-Trans Isomers

Diploe Moment

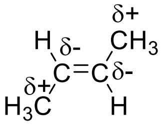
All alkyl groups have positive inductive effect (+I). As a result, when a methyl group is attached to each carbon atom that share a double bond, due to the differences in partial negative charge at those two carbon atoms, a dipole is the created. Therefore, in a cis compound this dipole effect is observed while in a trans compound, the dipole effects are cancelled leading to a zero resultant dipole charge.

e.g. Isomers of but-2-ene



(z)-but-2-ene

Cis (or Z) form showing a resultant charge



(E)-but-2-ene

Trans (or E) form showing a zero resultant charge.

N.B. Z and E forms do not always correspond to Cis and Trans forms.

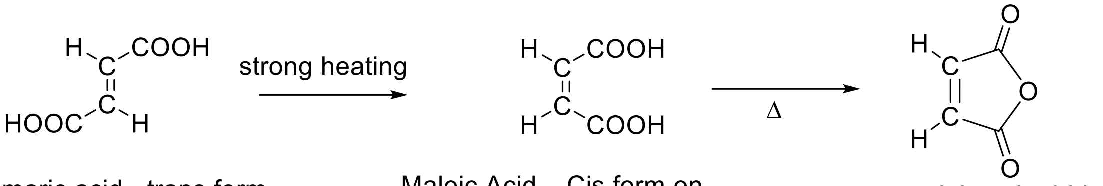
Please note that in the case of identical molecules as in the example given above, the existence of dipole charge is an indication that the molecule is in cis or Z form.

Stability

Trans compounds are more stable than cis compounds. The heat of formation values are high in trans than cis compounds. In cis compounds, the two large groups are on the same side leading to more repulsions of each other. Therefore, trans compounds are more stable.

Expanding on the stability, it is also important to recognize that cis compounds will form its cyclic molecule more easily than the trans compounds. Having both groups on the same side makes it easier to create its cyclic form.

e.g.



fumaric acid - trans form

Maleic Acid – Cis form on heating produces its cyclic form.

maleic anhydride

For fumaric acid to form its cyclic compound strong heating is necessary.

3.3.2.2 Optical Isomerism

When a carbon atom has four different atoms or groups attached to it, such a carbon is known as a chiral carbon. Such compounds are known as chiral compounds (the compounds that are not chiral are known as achiral compounds). A mirror image form of a chiral compound cannot be superimposed with the original. Such compounds are known as optical isomers. The two optical isomers will have identical densities, solubilities, boiling points, and melting points. Nevertheless, they have different chemical reactivity.

The optical isomers are optically active, and they have an effect on plane polarized light. When there are two optical isomers, both are known as enantiomers. One enantiomer will rotate the plane polarized light clockwise (also known as + or **d** for dextrorotatory form) and the other enantiomer will rotate plane polarized light count-clockwise (also known as – or **l** for levorotatory form). If a solution consists of 50/50 mixture of the two types of enantiomers, such a solution is known as a racemic mixture. It will have no effect on plane polarized light.

Nearly, all amino acids are chiral compounds. Therefore, enzymes, hormones, and proteins that are derived from these amino acids are also chiral compounds.

The following diagram shows the optical activity of two alanine isomers:

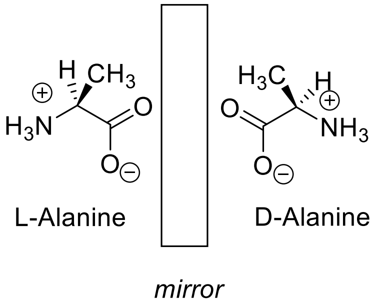


Figure 3.3.2.2.1: L and D forms of alanine

The rotation of the plane polarized light is measured using a polarimeter. In this case, monochromatic (single wavelength) light is passed through the polarimeter to convert into plane polarized light. The plane polarized light is directed through the sample. The sample is dissolved in a solution of achiral solvent. The light that emanates, after passing through the sample would have undergone rotation. Therefore, to see the light, the analyzer has to be rotated until the maximum intensity of the light is seen. This rotation corresponds to the rotation of the plane polarized light.

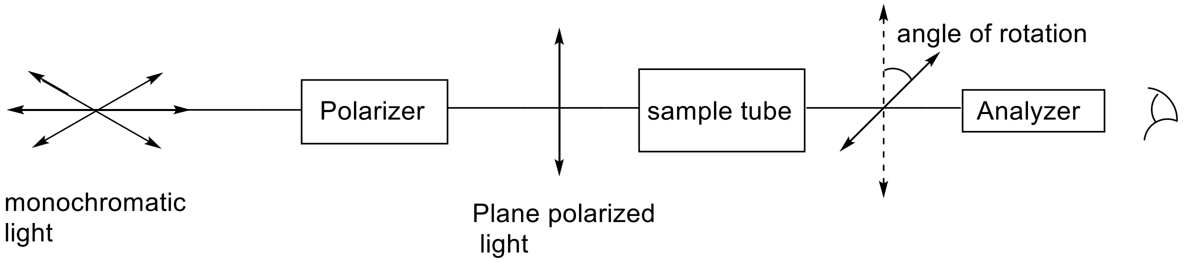


Figure 3.3.2.2.2: Schematic diagram of a polarimeter

The rotation of plane polarized light is dependent on the number of chiral molecules that interact with polarized light. The factors that determine the interaction are the concentration of the sample and the length of the sample tube.

The specific rotation ([α]) is defined as the rotation per length of sample tube (in dm) per concentration at 25 ^{0}C at a wavelength of 589 nm (the D line emitted by a sodium lamp).

$$\text{Specific Rotation } [\alpha] = \frac{\alpha}{l \text{ x } c}$$

$[\alpha\ ]$ = Observed rotation

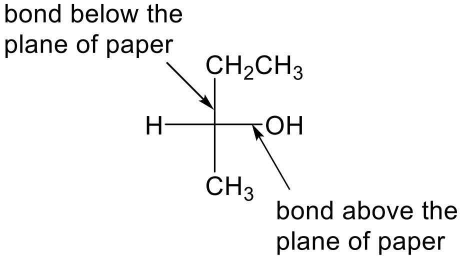
l = Length of the sample tube (dm)

c = Concentration (g/ml)

Fischer Projections

It is important to understand that when there are several chiral centers in one molecule, the three-dimensional drawings become difficult. In an earlier form of drawing, we have used darkened and broken lines to show above the plane and below the plane atoms respectively. We also used Newman projections and sawhorse forms to display acyclic compounds. In Fischer projection, horizontal lines indicate bonds coming out of the plane of the paper and vertical lines indicate bonds below the plane of the paper. This is known as the Fisher projection formulae.

e.g.



butan-2-ol

All equivalent structures that match the above are given below in different drawing formats:

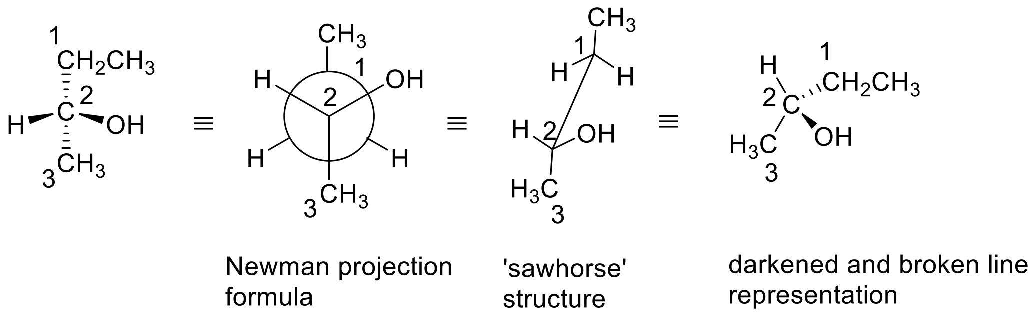
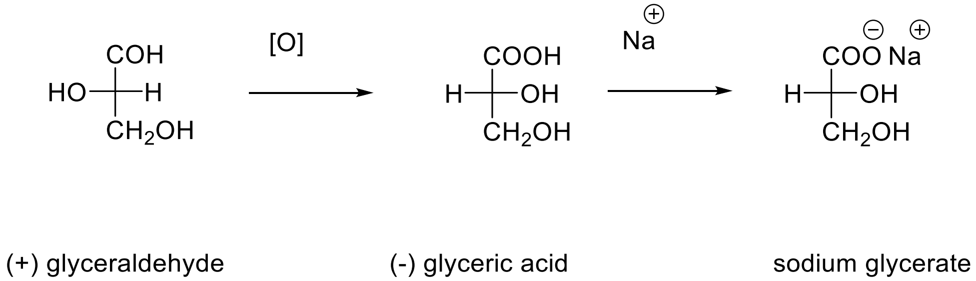


Figure 3.3.2.2.3: Comparison of Fisher drawing with other different drawing types for butan-2-ol

It is important to note that when Fischer projection is used, any even number of interchanges of any two groups provide a structure of the same configuration but the groups will be differently oriented in space. Similarly any odd number of interchanges will provide the opposite configuration or mirror image. Also, when using Fischer projection, a rotation of 180^0 along the plane of the paper is allowed without a change of configuration. But a rotation out of the paper is not allowed since this will change the configuration.

The nomenclature of optically active compounds is done by adding + or – to show the direction of the rotation. Nevertheless, consider the following situation:

e.g.



The three-dimensional images of the above three will look as follows:

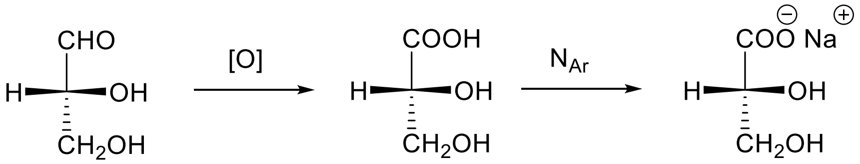
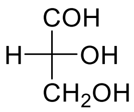


Figure 3.3.2.2.4: Three dimensional images of (+) glyceraldehyde, (-) glyceric acid, and sodium glycerate

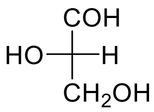
There is no change in the configuration. Yet, they differ in the signs indicating the direction of the rotation. Therefore, a better naming of such compounds were attempted using the Fischer projection formula.

According to the Fischer projection, the following naming can be done easily:

e.g.



D – (+) - glyceraldehyde

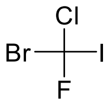


L – (-) - glyceraldehyde

N.B. Upper case D and L are used in the naming of carbohydrates and amino acids in the conventional format. Nevertheless, they mean d as + and l as – rotations.

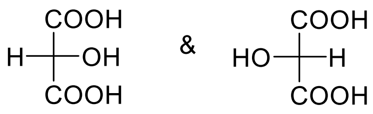
Fischer projection can also be used to name many amino acids and sugars. Yet, this is not effective in naming the following compounds:

e.g.



Tetrahalomethane

or in naming the following 2-hydoxy malonic acids in two forms:



The above two compounds cannot be determined as + or – due to the configuration.

Therefore, R and S nomenclature was introduced.

R and S Naming

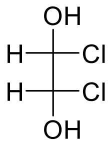
In this method, the priority rule, which was used in E-Z method is followed.

Following the same priority rules, the four atoms or compounds attached to the chiral carbon are numbered. Then the compound is oriented in a way for the atom or the group with the lowest priority to face away from the observer. The other three atoms/groups will face the observer. Then if the priority order of the three groups is clockwise, then it is considered to have R configuration, and if the priority order is counterclockwise, then it is known as S configuration. This method is not elaborated here since it is beyond the scope of the level of this book.

Meso Isomers

When there is more than one chiral center in a compound, meso isomerism can exist. Meso compounds can be superimposed with each other, and they are optically inactive, although there are chiral centers. This happens because the compound has two symmetrical sides (an internal plane of symmetry). There are cyclic compounds that are meso isomers, too. The stereochemistry of these compounds is a mixture of R and S, thus cancelling the optical activity.

e.g.



trans-1,2-dichloro-1,2-ethanediol

Finally, meso compounds should have two or more stereocenters, an internal plane and the stereochemistry should be R and S.

Recemic mixture

When two enantiomers (d and l or R and S forms) are mixed together in equal amounts, plane polarized light will not rotate because the two rotations opposite to each other (d and l) get cancelled. The is called the racemic mixture and it is indicated by the symbol (±)

e.g. (±) 2-chlorobutane

Chapter 4

4.0 Reaction Mechanism of Organic Compounds

4.1 Objectives

1. Classify reactions
2. Explain mechanisms
3. Predict final products following mechanisms

4.2 Introduction

Organic reactions can be classified into seven types (although the last three may be classified under previous four types):

1. Substitution
2. Elimination
3. Addition
4. Radical
5. Condensation
6. Rearrangement
7. Oxidation-reduction

An understanding of organic reaction mechanisms will provide the information about the steps of a reaction, an understanding of the slowest step (which is the rate determining step) which atoms get removed or joined first, what bonds are broken and formed, etc.

There are two basic principles of chemical reactions that need to be reviewed at this stage:

1. The feasibility and spontaneity of a reaction

Thermodynamically, for a reaction to move forward spontaneously, the Gibbs' free energy (ΔG) should have a negative value. Gibbs free energy is the amount of usable energy. This is the energy that can do work.

If a reaction is in equilibrium and the equilibrium constant is K_{eq}, the relationship between K_{eq} and ΔG is given as follows:

$$\Delta G^0 = -RT \ln K_{eq}$$

The value of ΔG, also indicates the extent to which a reaction will proceed or the current stage of the reaction

2. The speed of a reaction

The speed of a reaction is determined by the slowest step reaction, when there are several steps in a reaction. Also, the speed is dependent on the energy barrier the reactants must cross to make products. Therefore, the arrangements of reactants at the intermediate transition state will determine how fast or slow a reaction will move. The lower the ΔG value at transition state, the higher the rate of a reaction. If the molecular arrangement at the transition state is more stable, it will be positioned at a low energy level. Therefore, if there is more than one step in a reaction, the transition state with the highest ΔG will be the rate determining step, since it will be the slowest step.

4.3 Substitution Reactions (S)

In this type of a reaction, an atom or a group in a molecule is substituted by a different atom or a group.

e.g.

$$A{-}B \quad + \quad C \longrightarrow A{-}C \quad + \quad B$$

In the above example, A-B is the substrate that undergoes a substitution reaction. C is the incoming, attacking group that replaces B from A. B will be the leaving group.

If C is a nucleophile (an atom or a group with affinity for a positive center. Normally, it is a donor of a pair of electrons [Lewis bases]) and B is connected to a saturated carbon atom, then this substitution is a nucleophilic substitution denoted as $\mathbf{S_N}$.

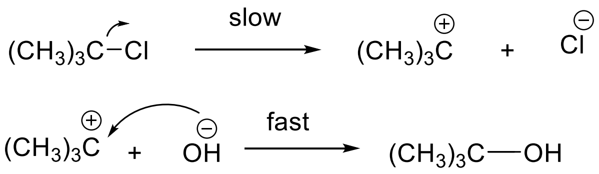
S_N reactions are further categorized as S_N1 and S_N2.

This further categorization of reactions is dependent on the following:

1. The way the bonds break and make.
2. The type of the substrate i.e. tertiary, secondary, or primary.
3. The concentration of the substrate and/or the nucleophile, depending on the rate equation.
4. The stereochemistry of the product when compared to the reactant.

4.3.1 S_N1 reactions – Substitution Nucleophilic Unimolecular

In substitution reactions, the bond of the leaving group has to break and then the substituent group has to make a bond.



In S_N1 reactions, the first step is the formation of planar carbenium ion. This step is also the rate determining step. Therefore, this is a unimolecular reaction. This is the reason this reaction is known as an S_N1 reaction. The rate determining step is the slowest step. Therefore, the rate of this reaction is dependent on the concentration of the $(CH_3)_3$-Cl, since it is the substrate involved in the rate determining step. The nucleophile concentration will not affect the rate of the reaction. (Cl is the leaving group).

(Note: Carbenium and carbonium ions are both carbocations with a positive charge at the carbon. In carbenium, it is a trivalent carbon with +1 formal charge, while in carbonium, it is pentavalent. In S_N1 reactions you would find a carbenium ion, while in S_N2 reactions you will notice a carbonium ion.)

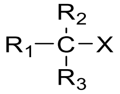
Step 1 – slowest step reaction, which is also the rate determining step.

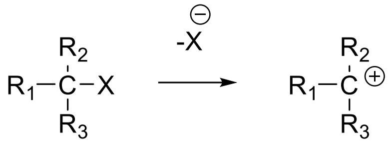
Therefore, the rate equation is written as

$$\text{Rate} = \text{k. Concentration of } [R_1R_2R_3CX]$$

k is the rate constant.

$R_1R_2R_3CX$ =

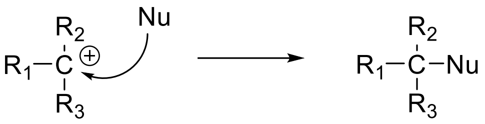




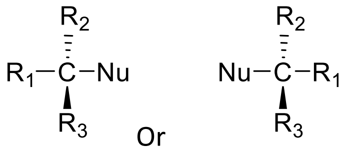
In the second step, the reaction with the nucleophile (Nu:) happens.

Step 2

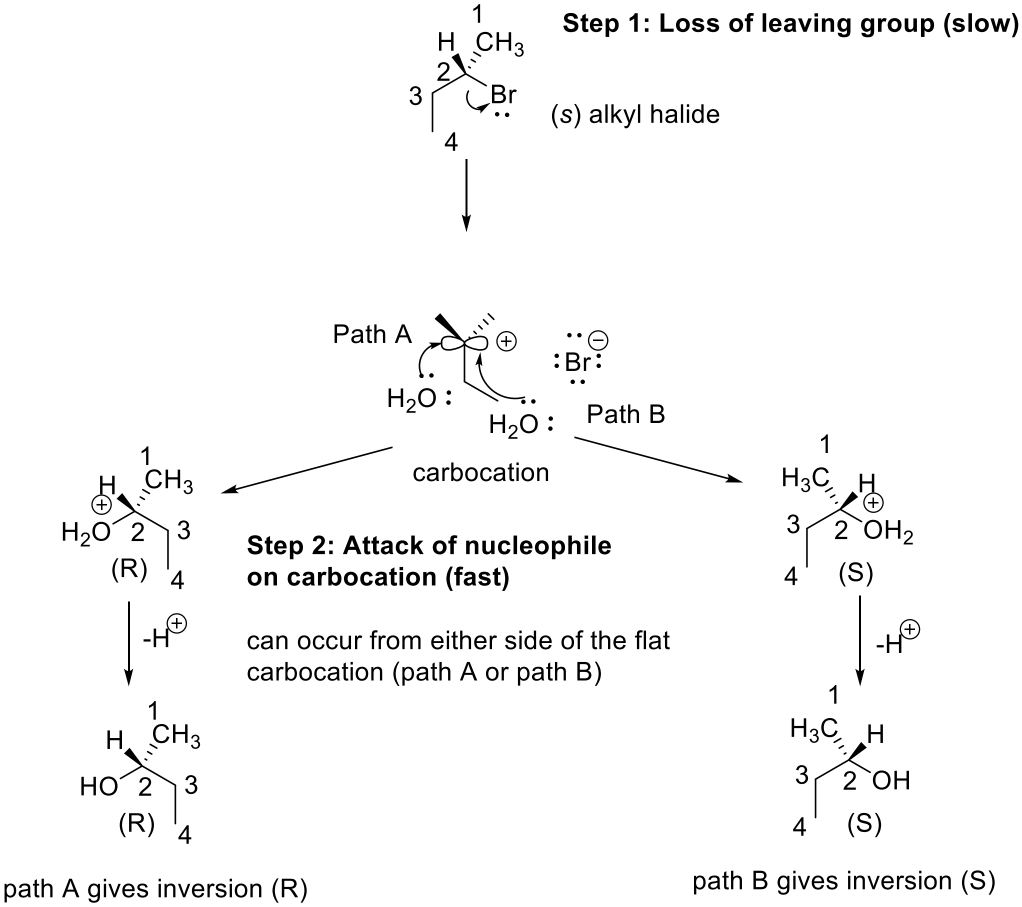
This is a fast step. Therefore, this is not included in the rate equation.



Please note that the attack by the nucleophile can happen from both sides at the carbenium providing two possible optical isomers leading to racemization. This means if the nucleophile connects from one end, the product will have the stereochemistry exactly as the reactant. This is known as retention. If the nucleophile connects from the opposite end, then the stereochemistry of the product will be opposite to the reactant. This is known as inversion.



Stepwise mechanism of S_N1:



S_N1 reactions are preferred by tertiary alkyl groups.

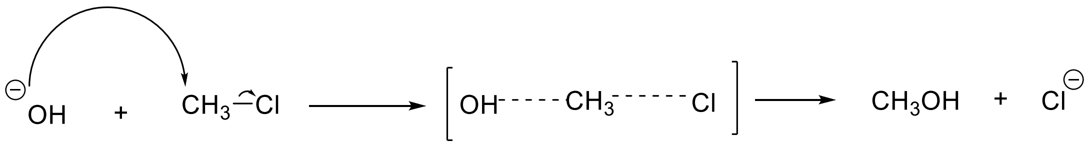
4.3.2 S_N2 reactions – Substitution Nucleophilic Bimolecular

In this reaction the removal of the leaving group and the addition of the nucleophile happens at the same time. Therefore, the rate equation is written as,

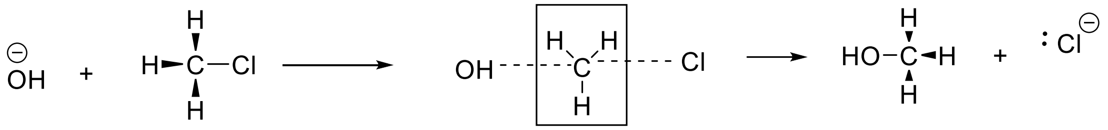
$$\text{Rate} = \text{k. (substrate) (nucleophile)}$$

The incoming nucleophile attacks from a direction opposite to the leaving group. This approach reduces steric repulsions. The leaving group takes with it the two electrons in the bond that connected it to the C atom.

e.g.



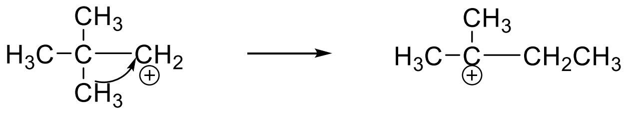
The following diagram shows its transition state:



As a result of the stereochemistry of the carbon atom at which the reaction takes place, the product is the inverted version of the reactant.

4.3.3 Rearrangement in SN reactions

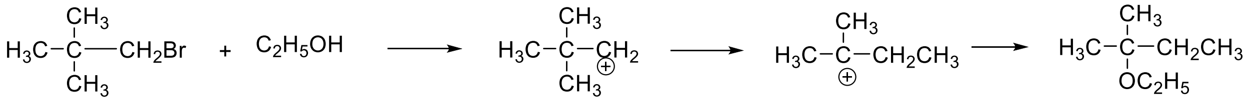
One of the characteristics of a carbocation is that it can undergo rearrangement to become more stable.



neo pentyl carbocation III^{ry} pentyl carbocation

This is a 1,2 shift of a methyl group. As a result, when neopentyl bromide is reacted with ethanol, the product is ethyl tert-pentyl ether and not ethyl neo-pentyl ether.

Nevertheless, in S_N2 reactions such a rearrangement is not observed since there are no intermediates in the reaction to undergo rearrangement.



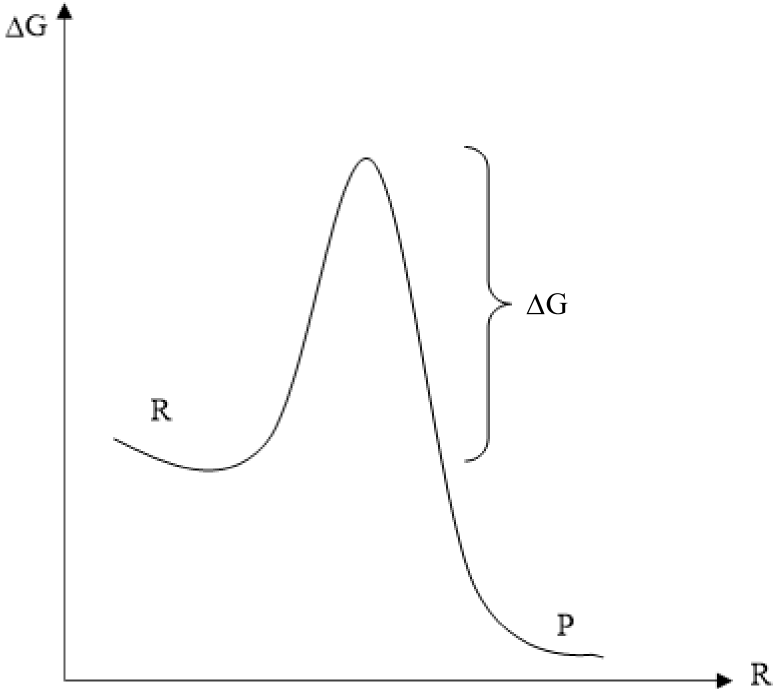
Therefore, when rearrangement is present, it could be inferred that the reaction has followed S_N1 pathway.

4.3.4 Important Points

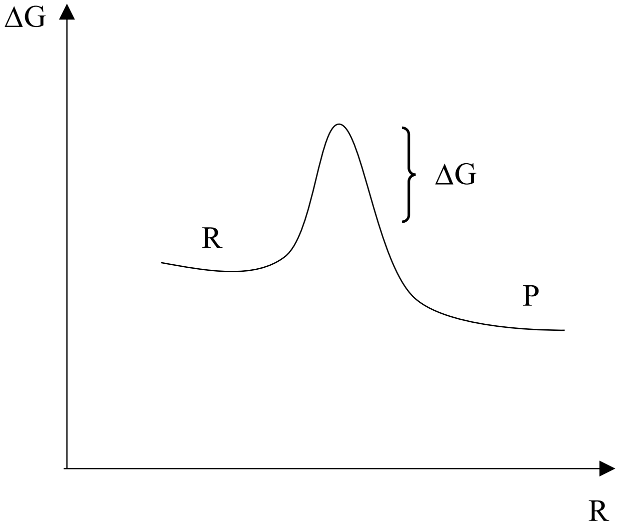
When a reaction undergoes S_N1 or S_N2, the pathway is determined by the following factors:

1. Change in Gibbs free energy (ΔG)

The preferred pathway is the one that has a lower ΔG. Also, the stability of the transition state plays an important role.

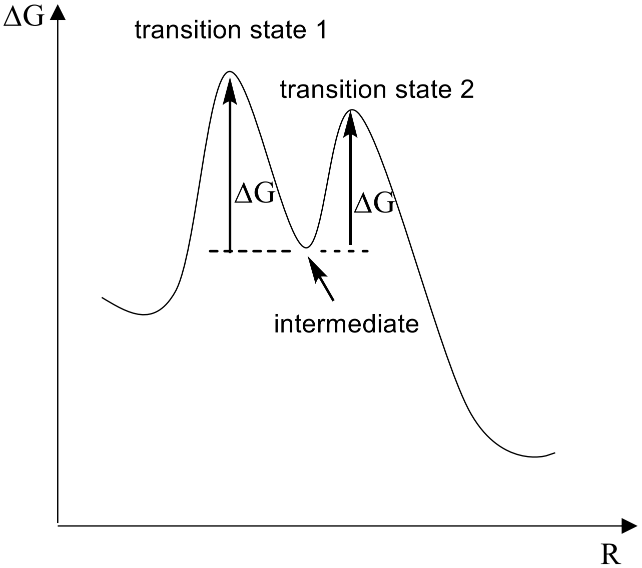


Graph 4.3.4.1: High ΔG Value



Graph 4.3.4.2: Low ΔG Value

Graph 4.3.4.2 shows lower ΔG. Therefore, this pathway is preferred.

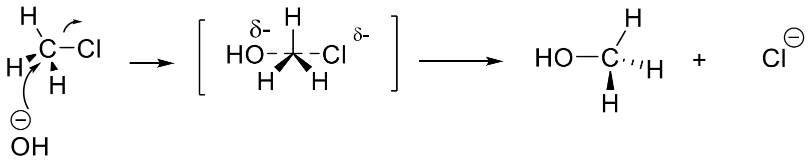


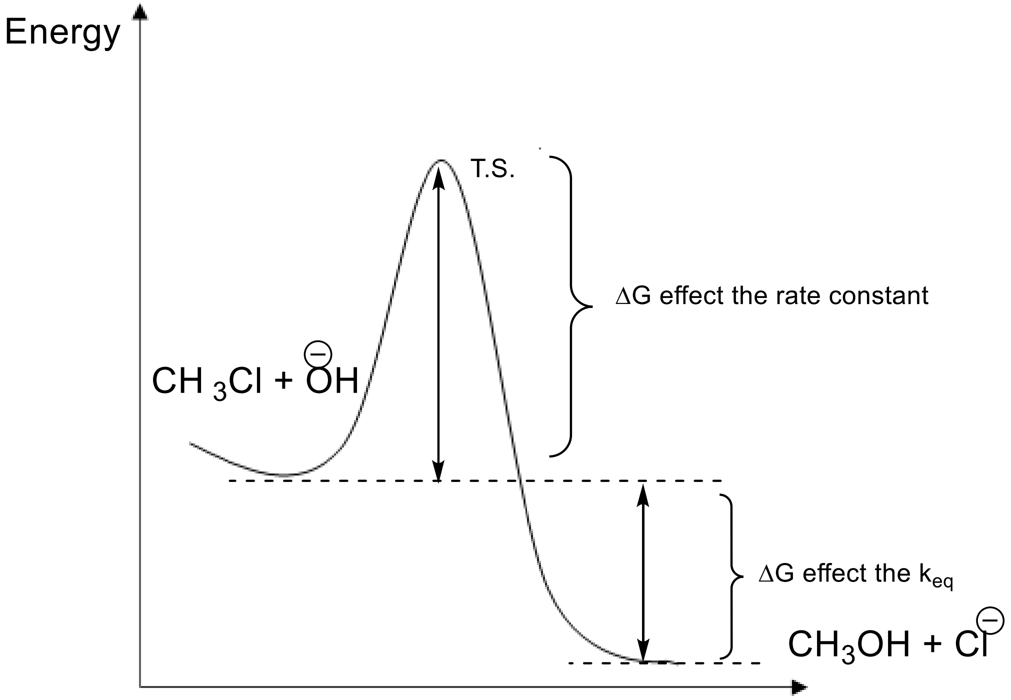
Graph 4.3.4.3: A two-step reaction showing low and high ΔG values

According to the above energy diagram (Graph 4.3.4.3), state 1 has a higher ΔG than state 2. Therefore, the slowest step is state 1. This will be the rate determining step.

This understanding of the nature of the transition state enables us to determine the path of reactions. In S_N1 reactions, the carbocation plays an important role, and its stability is shown by the low energy intermediate state. Therefore, this reaction undergoes two step reaction. The carbocation is formed as a result of a leaving group in S_N1. The first step which is the slowest step is the rate determining step and the substrate concentration is the only part in the rate equation, making it a unimolecular reaction – S_N1, as described earlier.

The reaction profile for S_N2 is as follows:





Graph 4.3.4.4: Energy diagram for an S_N2 reaction

In an S_N2 reaction, steric hindrance of the intermediate plays an important role. Make a note of the structure of the intermediate in S_N2 reactions (Graph 4.3.4.4).

The rate constant of a reaction varies with the difference in standard Gibbs free energy values between the reactant and the transition state. This relationship is given in the following equation:

$$k_r = \frac{(kT)}{h} e^{-\frac{\Delta G^{\neq}}{RT}}$$

k_r = rate constant
k = Boltzmann constant
T= absolute temperature
h= Plank constant
$\Delta G^{\neq} = G^{\neq}$ (transition state) - $G^{\neq}$ (reactants)
R = k x Avogadro constant

According to this above equation, K_r increases as ΔG decreases.

ΔG is important in determining the equilibriums constant (Keq) and the rate constant (K_r).

2.The stability of the carbocation

Any factor that affects the stability of carbocation will also affect the stability of the transition state since the structure of the transition state molecule is closer to carbocation in an S_N1 reaction.

Due to steric and electronic effects, the stability of carbocation decreases in the following order of reactivity for S_N1:

benzyl > tertiary > secondary > primary > CH_3

As a result, ΔG will increase in the above order

* The rate constant for the S_N1 reaction of RX (X denotes the leaving group) will decrease in the above order.

As mentioned previously, an S_N2 transition state has five groups attached to the carbon at which the reaction happens. Therefore, S_N2 experiences more strain. If larger groups are attached, then this strain will be higher. As a result, ΔG value will be higher, and the rate constant will be lower.

The order of reactivity for S_N2 reactions is opposite to S_N1 order of reactivity:

CH_3 > primary > secondary > tertiary > benzyl

It has been observed that tertiary halides react fast via S_N1 path.

CH_3 or primary halides will react fast via S_N2 path.

Secondary halides will react either via S_N1 or S_N2 slowly.

3. Solvent effect

The polarity of a solvent in which the reaction takes place will affect the stability of charged species. The more polar the solvents, the charged species will be more stable. Therefore, the solvent affects the mechanism pathway of a reaction and its rate.

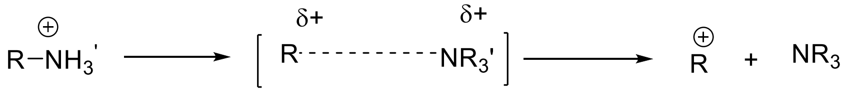
In an S_N1 reaction, transition state is more polar than the reactant. Therefore, when the solvent polarity is increased from less polar to more polar, the transition state will be stabilized. As a result, ΔG will decrease, and the rate constant will increase. The polarity can be changed either by using a more polar solvent or by increasing the percentage of the polar solvent used in the reaction.

When it comes to S_N2, the charge of the nucleophile (negative charge) is spread within the transition state. Therefore, when the polarity is increased, it will lead to the stabilization of reactants than the transition state. This means ΔG is increased, and the rate constant is reduced.

Therefore, high polarity leads to S_N1 reactions than S_N2 reactions.

Nevertheless, when it comes to different types of charged substrates such as a reaction involving tetra alkyl ammonium ion, the polarity of a solvent affects differently to the above studied pattern. The reason for this deviation is that in the transition state the charge is more dispersed. Therefore, it is important to consider the charge dispersion in the transition state, when considering the effect of a polar solvent.

e.g.



In the above reaction, the polarity of the solvent will increase ΔG and decrease the rate constant. Although the reactant is in quaternary form (similar to the tertiary form), there is an N atom instead of a C atom that leads to the dispersion of the charge in the transition state.

The following table provides a list of nucleophiles and the final products. R could be an alkyl or an aryl group.

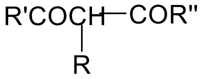
Nucleophile	Product	
$\overset{\ominus}{O}H$	$R-OH$	Alcohol
H_2O	$R-OH$	Alcohol
$R'O^{\ominus}$	$R-OR'$	Ether
$I^{\ominus}$	$R-I$	Alkyl iodide
$R'SH$	$R-SR'$	Sulfide
H_2NR'	$R-NHR'$	Secondary amine
$[R'COCHCOR'']^{\ominus}$	 $R'CO\underset{R}{\underset{\mid}{C}}H-COR''$	Diketone

Table 4.3.4.1: A list of nucleophiles and the final products

The following table provides a list of leaving groups and their original reactant.

Leaving group	Reactant	
$Cl^{\ominus}$	$R-Cl$	Alkyl chloride
H_2O	$R-\overset{\oplus}{O}H_2$	Conjugate acid of alcohol
$:NR'_3$	$R-\overset{\oplus}{N}R_3'$	Tetraalkyl ammonium ion
$^{\ominus}OSO_2R'$	$R-OSO_2R'$	Alkyl sulphonate

Table 4.3.4.2 : A list of leaving groups and the original reactants

4. Leaving Group

In S_N reactions, if the leaving group can leave fast the rate will increase in both S_N1 and S_N2. The stability of the leaving group will determine if it is a good leaving group or not.

Since in an S_N1 reaction, the rate determining step is the leaving of the group, a better leaving group will increase the speed.

When you consider the atom that is leaving, the ability to leave fast will depend on the type of the atom. The ability to leave easily increases as you move from left to right in the periodic table (electronegativity increases from left to right in the periodic table). This means the leaving group can leave with a pair of electrons (a negative charge) since it attracts electrons better.

Yet, the size of an atom also plays a role in determining if it is a good leaving group or not. As you go down a group in the periodic table, the size increase leading to reduced basicity. Iodine is a better leaving group than F, because of its large size. As a result of the large size of an atom, the bonding interaction becomes weak; therefore, the bond could be broken easily for iodine to leave as an iodide.

Resonance also plays an important role in the ability to leave. A group that undergoes resonance upon leaving, is a good leaving group.

e.g.

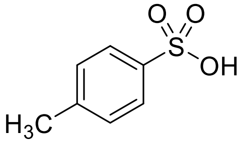
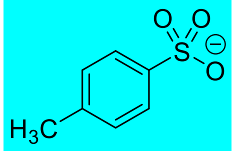
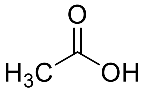
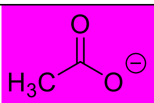
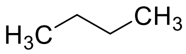
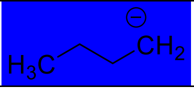
Leaving ability in a decreasing order:

NH_3, sulphonate esters > I^-, H_2O > Br > Cl > F > OH^-, NH_2^-

When it comes to acids, the stronger the acid, the higher the separation of ions, meaning they will have a stable conjugate base (a weak base) which is a good leaving group. Therefore, pKa values will indicate if the leaving group is a good or weak group. The lower the pKa value, the stronger the acid and more stable the weak conjugate base that is produced as a result of the separation.

Therefore, weak basicity makes a group a good leaving group.

When it comes to S_N2 also, a good leaving group will speed up the reaction.

Functional group	Example	pKa	Conjugate base (Leaving group)
Hydroiodic acid	HI	-10	$I^{\ominus}$
Hydrobromic acid	HBr	-9	$Br^{\ominus}$
Hydrochloric acid	HCl	-6	$Cl^{\ominus}$
Sulfuric acid	H_2SO_4	-3	$HSO_4^{\ominus}$
Sulfonic acid		-3	
Hydronium ion	$H_3O^{\oplus}$	-1.7	H_2O
Hydrofluoric acid	HF	3.2	$F^{\ominus}$
Carboxylic acid		4	
Protonated amines	$NH_4^{\oplus}\ Cl^{\ominus}$	9-11	NH_3
Water	HO−H	14	$^{\ominus}OH$
Alcohols	$H_3CO{-}H$	16-18	$H_3C{-}O^{\ominus}$
Amine	NH_3	~35	$^{\ominus}NH_2$
Hydrogen	H−H	42	$H^{\ominus}$
Alkane		~50	

▭ Excellent leaving groups (extremely weak bases)

F^- ▸ is typically an extremely poor leaving group (forms strong bond to carbon)

🟪 Moderate leaving groups (weak bases)

🟩 Poor leaving groups (strong bases)

🟦 Extremely poor leaving groups (very strong bases)

Table 4.3.4.3: A list of leaving groups and pK_a values

5. Nucleophile

In the case of S_N1, the addition of a nucleophile is the second step, and it is a fast reaction. This step is not the rate determining step. Therefore, the nucleophilicity does not play a major role in the rate. The concentration of the nucleophile has an effect on the product formed. When the nucleophile is also the solvent, it is called solvolysis. If water is the solvent, then it is called hydrolysis.

When it comes to S_N2, since the nucleophile is a part of the rate determining step, a stronger nucleophile will react faster.

The strength of a nucleophile depends on the following factors:

- Charge

  The nucleophilicity increases with increasing electron density on an atom. Therefore, strong conjugate bases are strong nucleophiles.

- Electronegativity

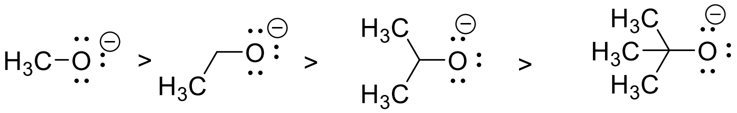
  The nucleophilicity increases with decreasing electronegativity across the periodic table.

- Solvent

  A polar protic solvent (e.g. water, ethanol, methanol, ammonia) will increase the hydrogen bonding of a nucleophile. When this happens, the nucleophile will be less available for the reaction. The ability to form hydrogen bonding decreases from top to bottom of a group in the periodic table. Therefore, iodine will be a better nucleophile than bromine and bromine will be better than chlorine. This trend follows up to the top of the group.
  When it comes to polar aprotic solvents (e.g. acetone, dimethyl sulfoxide, dimethylformamide, etc. – no hydrogen atom connected directly to an electronegative atom), the opposite happens since they do not form hydrogen bonds with nucleophiles. Therefore, F will be a stronger nucleophile than Cl and Cl will be better than Br, etc.

6. Steric Hindrance

The nucleophilicity decreases with increasing steric hindrance. Therefore, when a nucleophile with large groups react the reaction rate goes down.



<u>Strong Nucleophiles</u>

$Br^{\ominus}$ $I^{\ominus}$ $R{-}S^{\ominus}$ $H{-}S^{\ominus}$ $N{\equiv}C^{\ominus}$ $N_3^{\ominus}$

$R{-}C{\equiv}C^{\ominus}$ $R{-}O^{\ominus}$ $H{-}O^{\ominus}$

strong bases

<u>Medium Nucleophiles</u>

$R{-}CO_2^{\ominus}$ $R{-}S{-}H$ R_2S

NH_3 RNH_2 R_2NH NR_3

<u>Weak Nucleophiles</u>

$R{-}CO_2H$ $R{-}O{-}H$ H_2O

very weak bases

Special case

Tert-Butoxide ($tBuO^{\ominus}$) is a strong base, but is not a nucleophile due to non-bonded interaction strain.

8. Two Special Cases

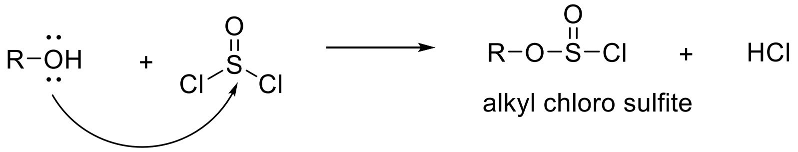
While we have studied S_N1 or S_N2, where inversion or racemization happens, there are two instances when retention happens. This means the nucleophile attaches to the substrate in the same orientation as the leaving group.

The two types are as follows:

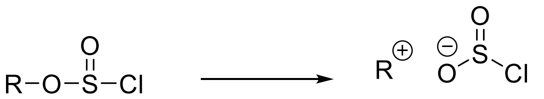
1. S_Ni – Substitution Nucleophilic Internal Mechanism

$$R-OH \quad + \quad SOCl_2 \longrightarrow R-Cl \quad + \quad SO_2 \quad + \quad HCl$$

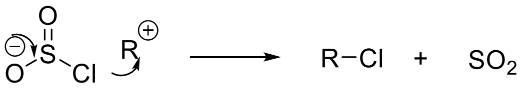
step 1



Ionization of the alkyl chlorosulfite yields a pair of intimate ions. These ions are held close to each other.



Soon after this pair is formed, before the two ions dissociate, Cl will attack R+ from the same side where the original oxygen was connected. This will produce a product that has retained the configuration.

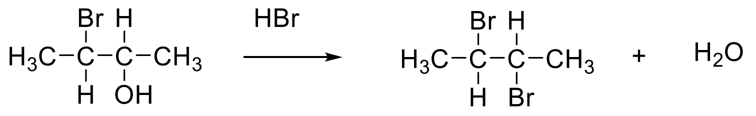


This is an internal substitution - S_Ni.

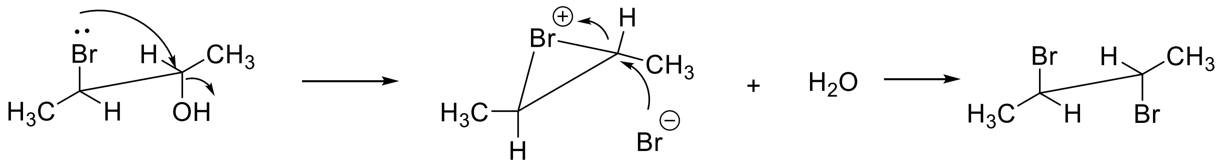
2. Neighboring Group Mechanism

When there is a non-bonded pair (this could be a lone-pair or a covalent bond pair) of electrons in a group, which is placed at β position to the reacting carbon center, this group will initiate the reaction by attacking the carbon from a position opposite to the leaving group. As a result, the incoming nucleophile will get attached only from the same side as the leaving group, because the group in the β position blocks the other entrance. Since the initial attacking group is an internal group already attached to the substrate and is close to the reaction center, the reaction happens faster than a normal S_N reaction. This support by the neighboring group is known as anchimeric assistance. The original configuration is retained as a result.

e.g.,



$H_3C-CH(Br)-CH(OH)-CH_3 \xrightarrow{HBr} H_3C-CH(Br)-CH(Br)-CH_3 + H_2O$

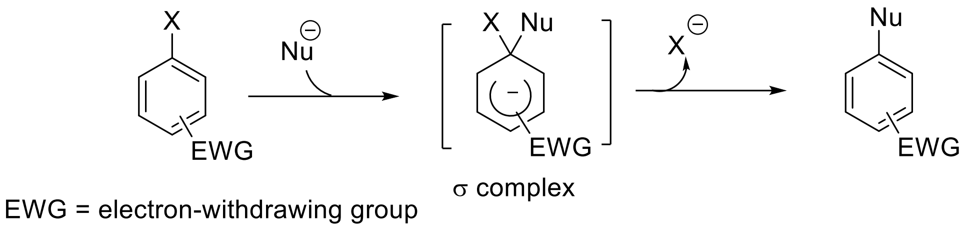


All of the above nucleophilic substitutions we discussed were related to aliphatic compounds. When it comes to aromatic compounds, only some compounds undergo nucleophilic substitution, since aromatic rings themselves are nucleophiles. Nevertheless, some aromatic compounds can undergo S_N2 type substitution, as long as the aromatic ring is attached to a good electron-withdrawing substituent. When such a substituent is attached, the aromatic ring becomes electrophilic.

Yet, the S_N2 reaction that happens in an aromatic ring is different to the type that happens in an aliphatic compound. Due to the steric hindrance created by the ring in aromatic compounds, the substitution cannot happen at a trigonal carbon. Therefore, the nucleophile approaches the active carbon from the back but in line with the leaving group.

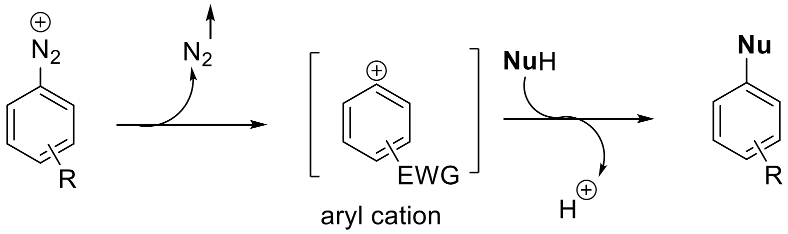
There are six nucleophilic substitution reactions known in aromatic systems:

1. S_NAr (addition-elimination) mechanism - S_N2 type

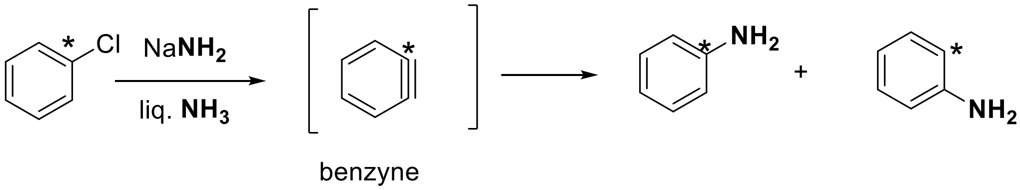


2. In aromatic compounds, S_N1 reaction is not favorable. This could happen only if there is an exceptionally good leaving group. Once the group leaves, an aryl cation will be formed.

   e.g. S_N1 mechanism with diazonium salts

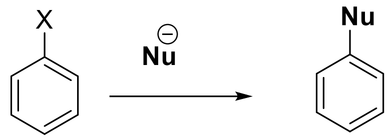


3. The benzyne mechanism (E1cb-Ad_N)

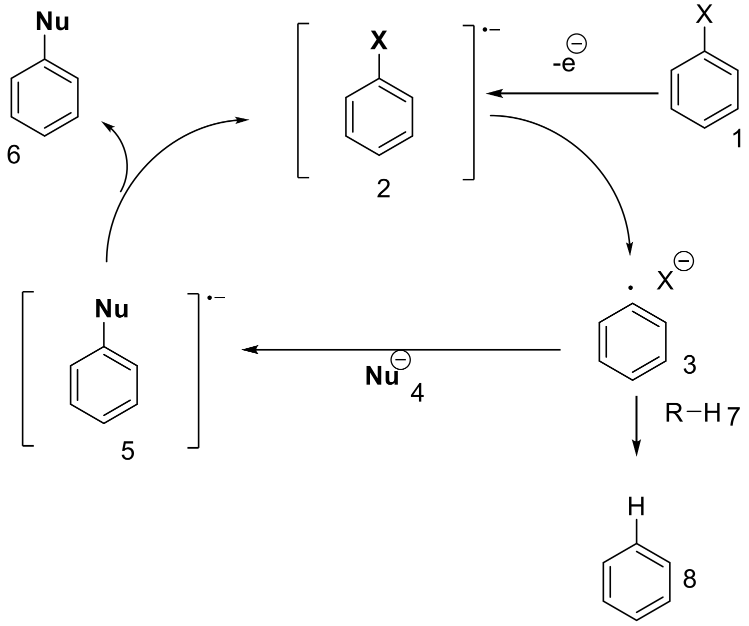


4. Radical-nucleophilic aromatic substitution – $S_{RN}1$

In a radical-nucelophilic aromatic substitution, a substituent attached to an aromatic compound is replaced by a nucleophile through an intermediary free radical species:



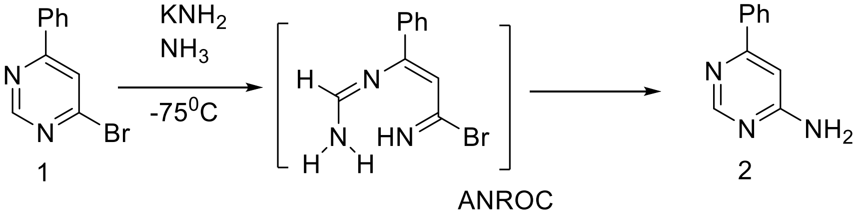
Mechanism



5. Addition of the Nucleophilic, Ring Opening, and Ring Closure - ANRORC

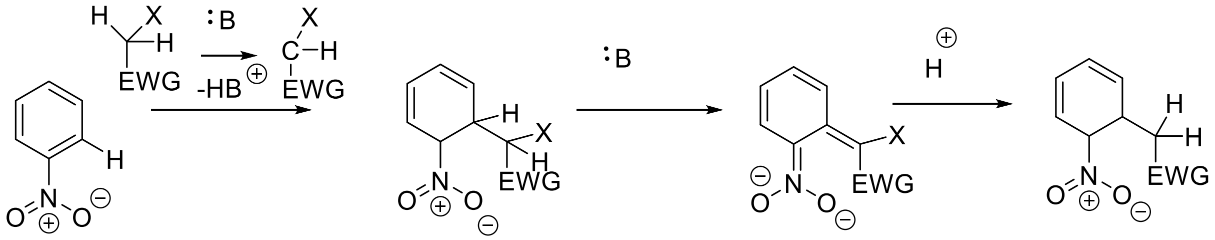
This is a special type of substitution. This reaction has been observed in reactions between metal amide nucleophiles (e.g. potassium amide) and substituted pyrimidines (e.g. 4-phenyl-6-bromopyrimidine) in ammonia at low temperatures. The main product is 4-pheny-6-aminopyrimidine.
The bromine is replaced by amine group.

Mechanism



6. Vicarious nucleophilic substitution

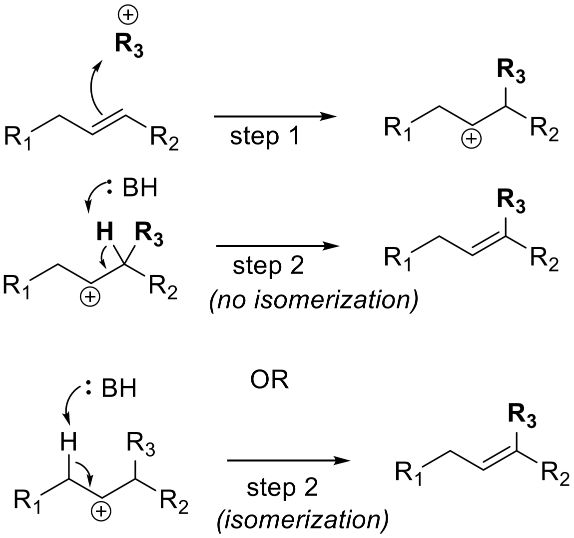
This is mainly observed in nitroarenes. In this reaction, a hydrogen in an aromatic ring is substituted by a nucleophile.



4.3.5 Electrophilic Substitution (S_E)

In an aliphatic, electrophilic, substitution reactions, an electrophile replaces the functional group in an aliphatic compound. The resulting product could be an inversed configuration if the electrophile attack happens at an angle 180^0 to the leaving group.

In the electrophilic substitution shown below, a pair of π bonded electrons attack an electrophile. An electrophile is generally a carbocation.

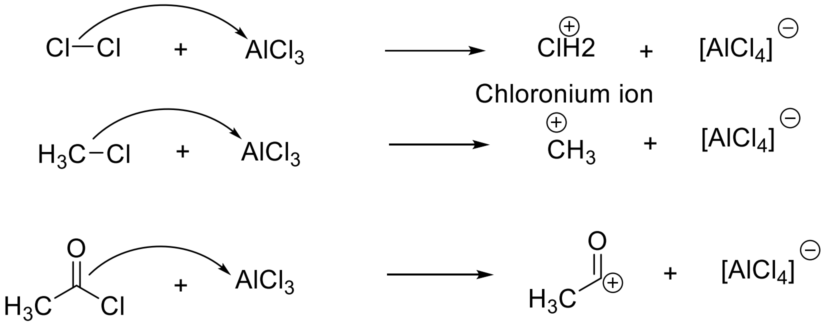


The mechanism of electrophilic substitution:

The first step is the generation of an electrophile.

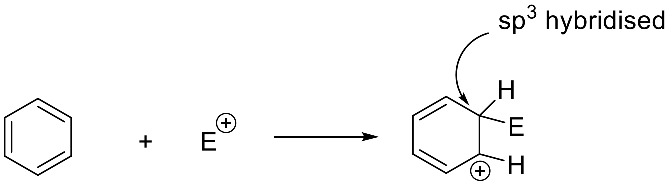
Lewis acids such as aluminum chloride (anhydrous) are useful in generating electrophiles from chlorination, alkylation, and acylation of an aromatic ring.

e.g.



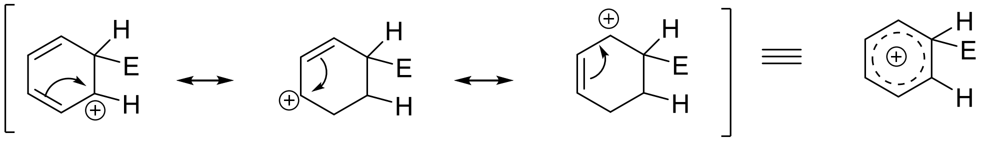
The second step is the formation of carbocation.

The electrophile will attack the aromatic ring. This leads to the formation of sigma complex (arenium ion).



Sigma complex (arenium ion)

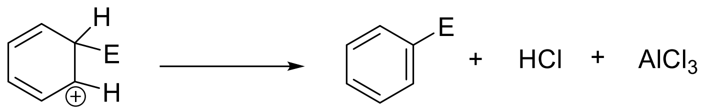
The above arenium ion will undergo resonance as follows:



The carbon at the point of attack shows sp^3 hybridization that leads to the loss of aromaticity.

Final step is the removal of proton.

The sp^3 hybridized carbon will release a proton when [AlCl]- produced earlier gets attached to this carbon.



4.3.5.1. Aliphatic electrophilic substitution

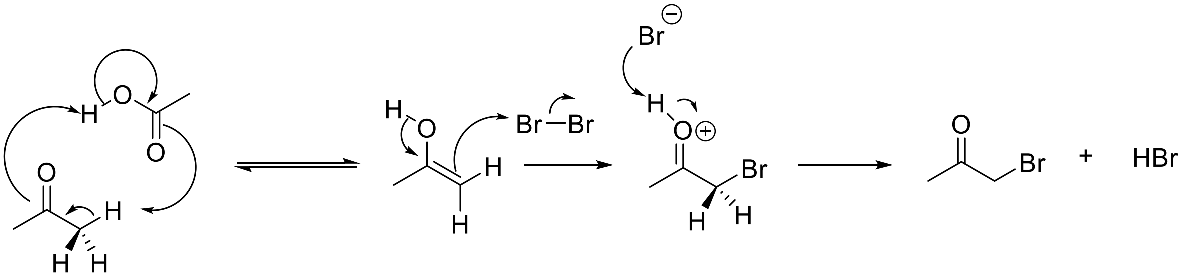
There are five such types:

1. Halogenation of ketones

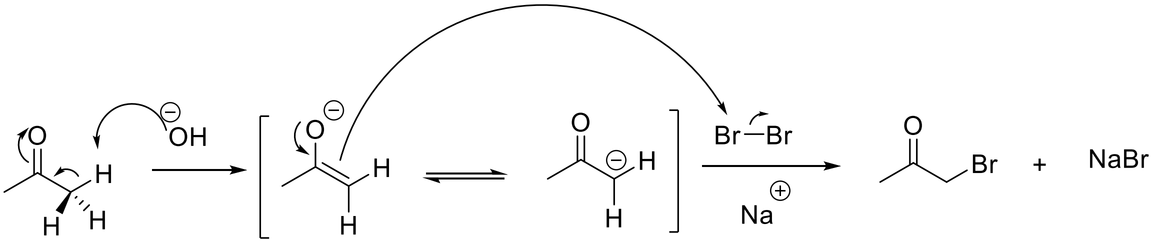
This is a α keto halogenation. The reaction is usually carried out in acidic or basic conditions in an aqueous medium. The typical halogens that undergo this reaction are Cl, Br, and I.

The α position to the carbonyl group in a ketone can be easily halogenated since the compound forms an enolate (in a basic solution) or an enol (in an acidic solution).

e.g. In acidic solution



In basic solution:



2. Nitrosation

This is a process of converting organic compounds into nitroso (R-NO) derivatives.

C-Nitroso Compounds:

$$RNHOH + [O] \longrightarrow RNO + H_2O$$

S-Nitroso compounds

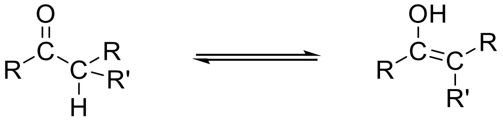
$$RSH + HONO \longrightarrow RSNO + H_2O$$

O-Nitroso Compounds

$$ROH + HONO \longrightarrow RONO + H_2O$$

3. Keto-Enol tautomerism

The presence of α hydrogen in organic esters, ketones, and aldehydes could form enols. This reaction involves the migration of a proton from a carbon to oxygen.



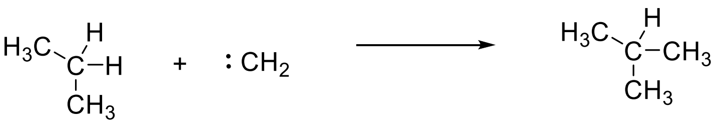
The existence of above state in ketones is called keto-enol tautomerism.

4. Insertion of a carbene into a carbon-hydrogen bond

A carbene is a carbon atom with two bonds (two shared electrons) and two free electrons.

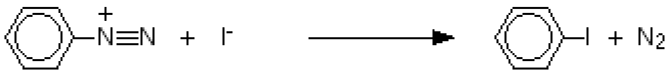
R -:C – R or R=C:

e.g.

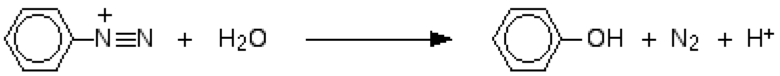


5. Aliphatic Diazonium coupling

e.g. 1



e.g. 2

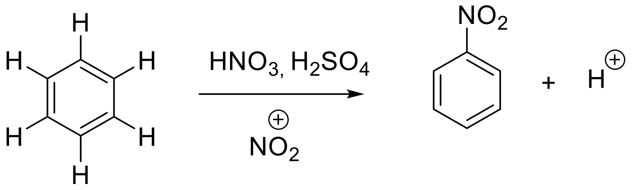


4.3.5.2. Aromatic Electrophilic Substitution

An aromatic ring has high electron density. Therefore, aromatic compounds would easily undergo electrophilic substitution.

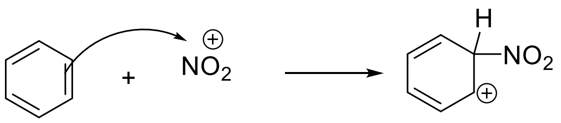
e.g.

Nitration of benzene in the presence of a mixture of concentrated nitric and sulfuric acids.

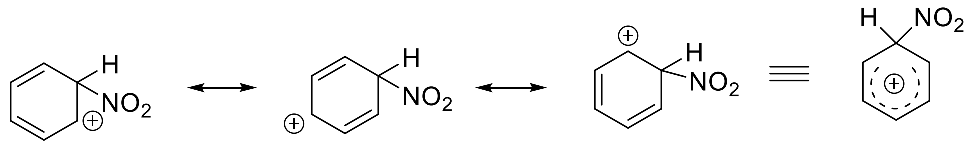


The mechanism shown below matches the one already described for electrophilic substitution reactions.

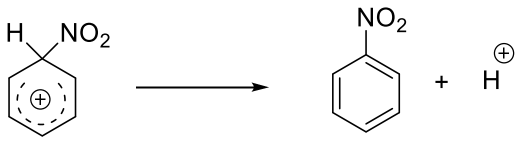
Once an electrophile is formed (or available), it will attack the aromatic substrate to form an arenium ion.



This arenium ion will undergo resonance as follows. As a result, the arenium ion attains stability.

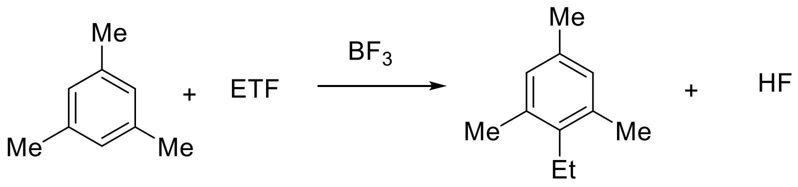


The formation of a sigma complex is the slowest step or the rate determining step of this electrophilic substitution. The second step is the removal of a proton and it happens fast.



The evidence for the existence of arenium ion is shown by the following reaction:

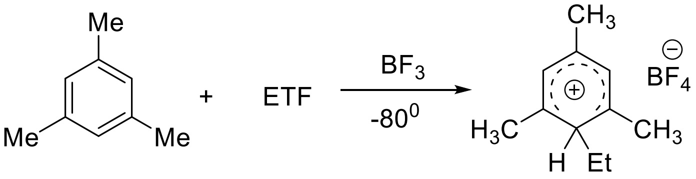
Mesitylene is reacted with ethyl fluoride (EtF) using boron trifluoride as the catalyst.



A hydrogen in the ring is replaced by ethyl. In this reaction, ehtyl cation acts as the electrophile.

$$\mathrm{ETF} + \mathrm{BF_3} \rightleftharpoons \mathrm{Et}^{\oplus}\ \mathrm{BF_4}^{\ominus}$$

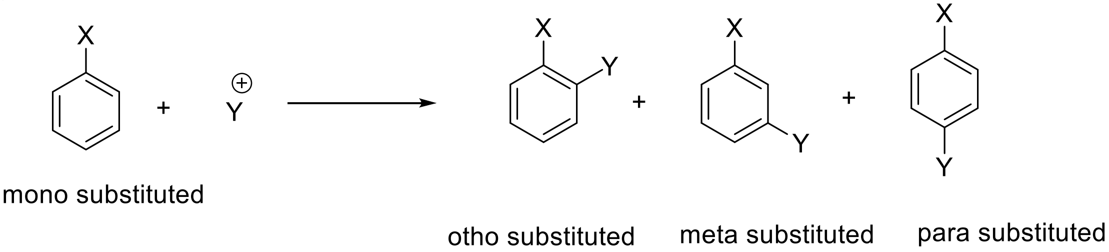
When this reaction is carried out at -80 0 C, arenium ion can be isolated.



Once this product is heated, the substitued final product is formed.

The rate of mono substituted benezens undergoing electrophilic substitution is dependent on the subsituent attached to the benzene.

e.g.,



The substituents that increase the reaction rate are called activating groups.

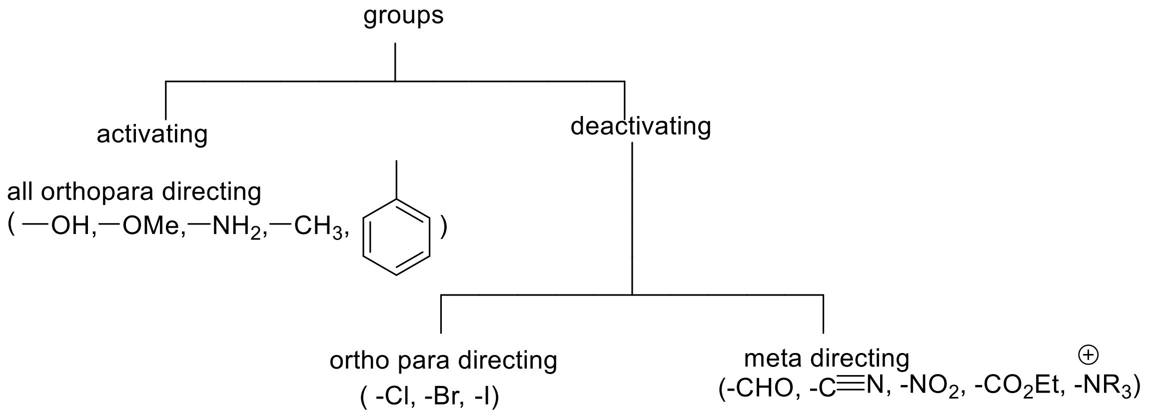
The substituents that decrease the reaction rate are called deactivating groups.

The incoming group has three possible attacking positions. They are ortho, para, and meta. As a result, there are three possible products as shown above.

Experimentally, the products obtained are metadisubstituted product or a mixture of ortho and para distributed products. The final product combination is dependent on the substitutent group attached to the benzene. Accordingly, substitutents attached to benzene can be classified as meta-directing or ortho/para – directing groups. Meta-directing groups are deactivating groups while ortho/para-directing groups are activating groups. There are a few exceptions to this rule. A better understanding is given by considering arenium ion as the transition state.

As mentioned earlier, the substituent group attached to the benzene ring will affect the reactivity of the ring. This influence is created through σ electrons (inductive effect or I effect) or through π electrons (resonance effect).

The substituent groups can be divided into two groups:



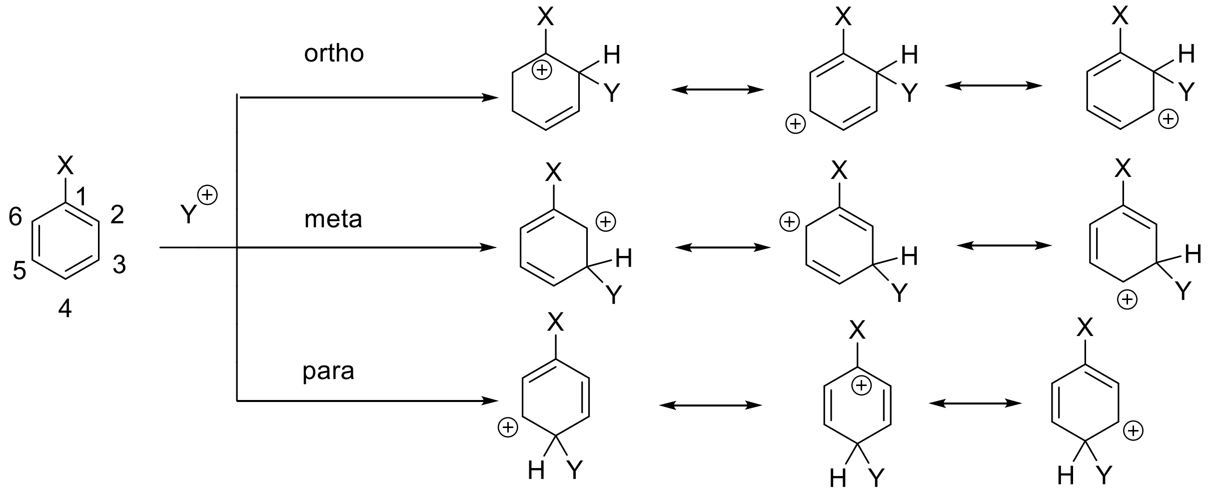
1. Substituent groups without a non bonded electron pair create inductive effect

-CH3, -CN

These groups influence the reaction by two types of inductive effects:

- +I effect (e.g. -CH3) stabilise the charge in the arenium and will activate the ring.
- -I effect (e.g. -CN) will deactivate the ring.

This + or – of I effect is strongest at the carbon atom (C-1) to which the original group (denoted as X) is connected.

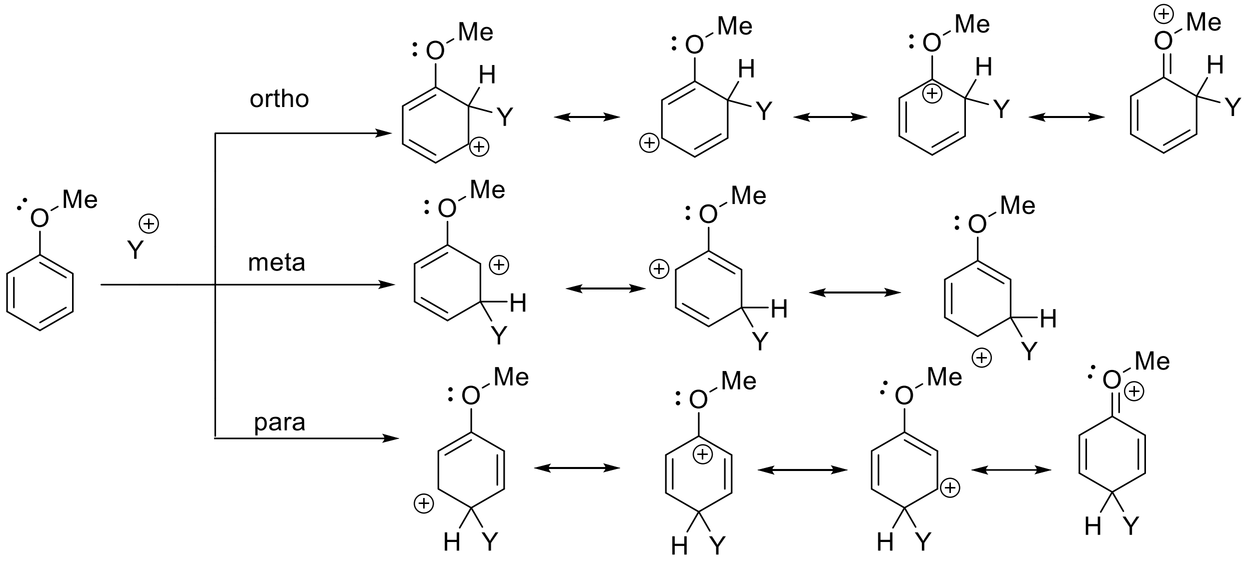


The above digram shows that + charge on the carbon (C-1) joined to the group (denoted as X) is established only in ortho and para substitution This establishes the fact that + I or – I effect is important in the case of ortho and para than in meta substitution. As a result, +I groups will activate ortho and meta positions and they are ortho and para directing. Similarly, -I groups will deactivate ortho and para positions, and they are meta directing.

2. Substitutent groups with a non bonded electron pair create resonance.

-OMe, - Cl

When it comes to groups with a non bonded electron pair that are connected to the benzene ring, the delocalizing of the charge on the arenium ion happens.



The above diagram once again shows the same pattern as before where ortho and para positions are the only ones showing a + charge at the C-1 position. Therefore, these groups are ortho and para directing. When it comes to understanding if they are activating or deactivating, that effect depends on the relative importance of +R and -I effect of each group. In the case of -OMe, +R effect dominates. This group is activating and ortho and para directing. In the case of -Cl, the electronegativity plays a greater role to make -I effect to dominate and it is deactivating. Yet, non-bonded pair plays an important role thus making it ortho and para directing.

When a benzene ring is disubstituted, the two groups may jointly reinforce or oppose each other of their orienting effects and activating/deactivating effects. If they oppose each other then a mixture of products can be expected.
The above discussed patterns are not limited to substituted benzenes, but also to aromatic substrates such as naphthalene and pyridine.
Apart from nitration, there are other synthetically important reactions such as Friedel Crafts acylation, Reimer-Tiemnna reactions, which will be discussed under relevant functional groups.

4.3.6 Radical Substitution Reactions

Free radical is an atom or a group of atoms possessing an upaired electron. Alkanes which are non-polar are inert to electrophiles or nucleophiles. Therefore, they undergo free radical reactions. These will be discussed under alkanes.

$$4Cl_2 \quad + \quad CH_4 \longrightarrow CCl_4 \quad + \quad 4HCl$$

There are three majore steps in a free radical reaction:

1. Formation of free radicals.

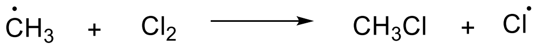
This happens via homolytic cleavage. The homolytic cleavage is brough about by heat or light in general.

$$Cl_2 \xrightarrow{h\nu} Cl^\bullet \quad + \quad Cl^\bullet$$

This is also known as the initiation reaction. The free radicals formed are highly reactive. They can remove a hydrogen from an alkane or get attracted to each other.

$$Cl^\bullet \quad + \quad CH_4 \longrightarrow \dot{C}H_3 \quad + \quad HCl$$

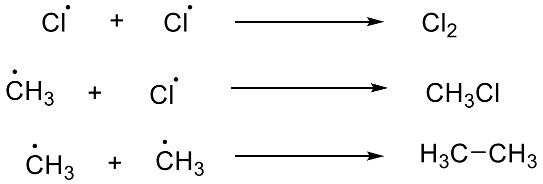
Now the methyl radical can remove a chlorine atom from a chlorine molecule and create a chloring free radical.



$$\dot{C}H_3 + Cl_2 \longrightarrow CH_3Cl + Cl^{\bullet}$$

This process can continue until there is no more chlorine free radicals or alkanes to be substituted. This steps is called propagation and is a chain reaction.

The final steps is the reverse of the initiation step. The free radicals will combine with each other or complete the substitution to end the chain reaction. This step is called the termination reaction.



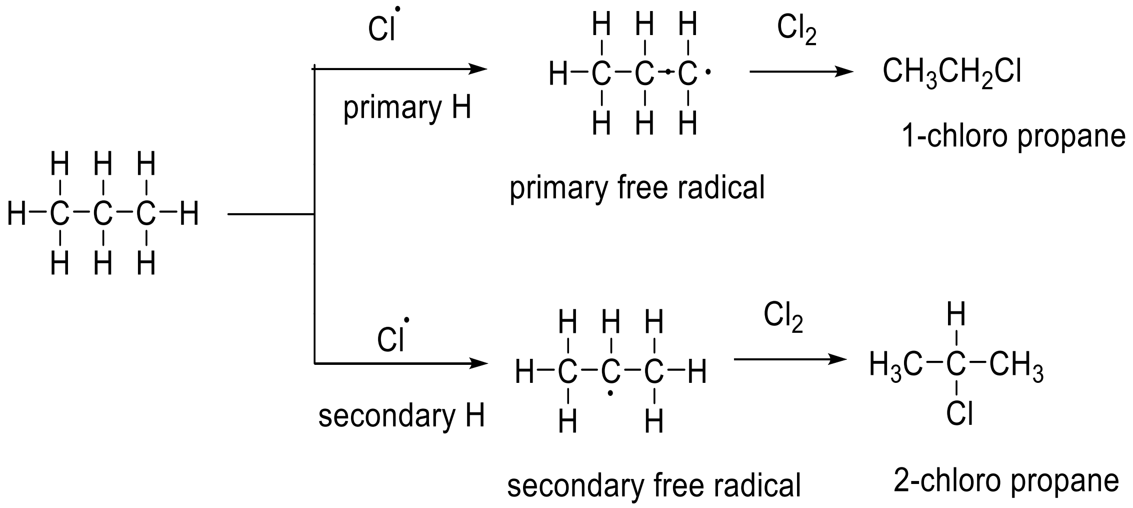
$$Cl^{\bullet} + Cl^{\bullet} \longrightarrow Cl_2$$
$$\dot{C}H_3 + Cl^{\bullet} \longrightarrow CH_3Cl$$
$$\dot{C}H_3 + \dot{C}H_3 \longrightarrow H_3C{-}CH_3$$

The free radical substitution also has a preference order as same as other substitution reactions where carbocation stabilty plays (S_N1) a preference role. It has been shown that the free radical preference order is same as the carbocation formation preference order:

Tertiary> secondary> primary

Therefore, the stability depends on how effectively the radical can disperse its odd electron.

e.g. The following chlorination of propane shows that the formation of secondary free radical or primary free radical as options. Although, the formation of primary free radicals to secondary free radicals is 3:1 (6 primary hydrognes to 2 secondary hydrognes), experimentally the product ratio is 1:1. This means the formation of secondary free radical product is easier or faster than that of primary free radical. This confirms the preference order mentioned above.



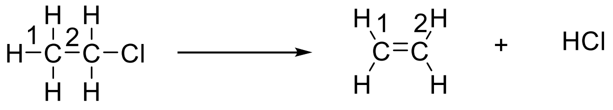
4.4 Elimination Reactions

The following reactions are examples of elimination reactions.

1. Formation of a double bond

When two adjacent groups are removed, the resulting compound will have a double bond.

e.g.



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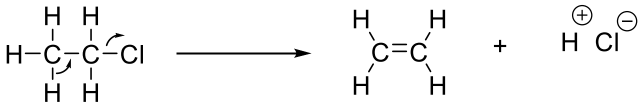
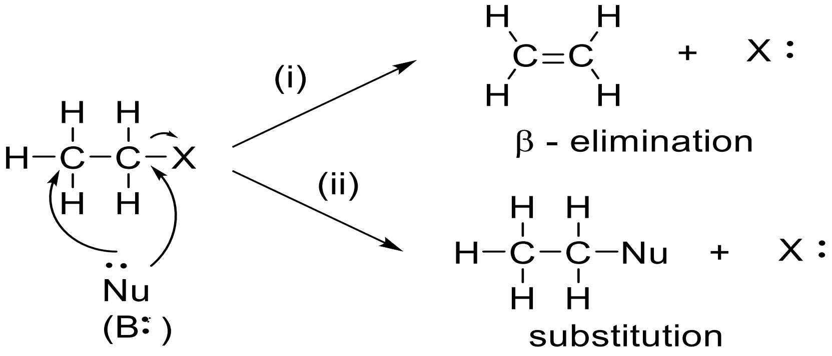
Two two adjacent groups removed in the above reaction are, H from C-1 and Cl from C-2. Since the two groups attached to each other are β to each other, this is known as β elimination.

Mechanism of β elimination:



Since the leaving group Cl^- is a leaving group similar to the ones seen in S_N reactions, β eliminations and S_N reactions are competing reactions. Therefore, whether elimination or substitution is preferred can be determined by the nature of the substrate and the reaction conditions.



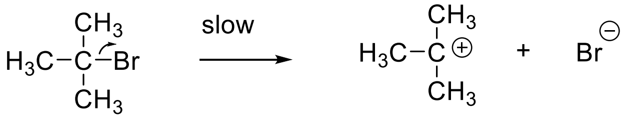
Elimination has two paths as E_1 – unimolecular or E_2 – bimolecular.

4.4.1 Mechanism of E_1 Reactions

E_1 reaction, similar to S_N1 mechanism, goes through the formation of a carbocation.

Step 1

Leaving group takes away the pair of electrons that formed the bond

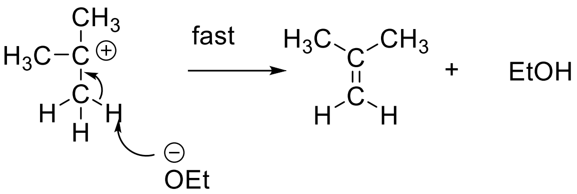


This is the rate determining step. In an alkyl halide, the elemination by E1 is favored in the following order:

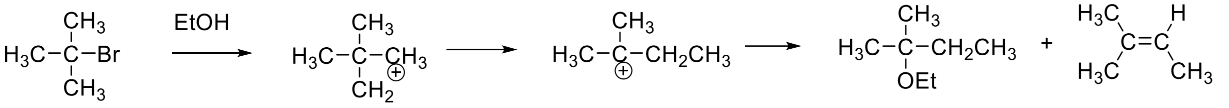
Tertiary > Secondary > Primary.

Step 2

This is the fast reaction where the other group leaves from the adjacent carbon.



In addition, once the carbocation is formed, rearrangments are possible. Therefore, similar to the S_N1 rearrangements, the following products can be seen too.

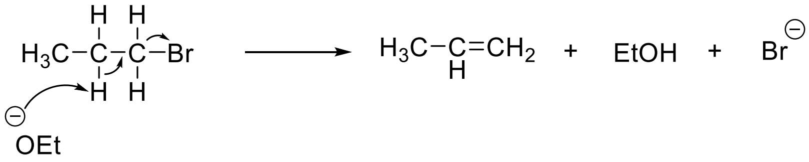


2-methyl-2-butene

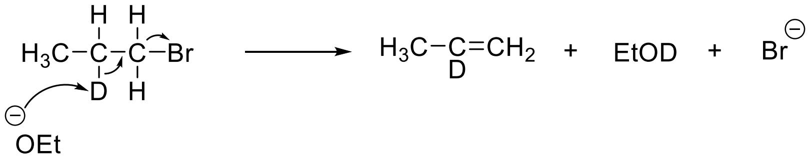
4.4.2 E 2 Mechanism

Similar to S_N2, E_2 reacion is a one step reaction.

The elimination of both groups happens simultaneously.



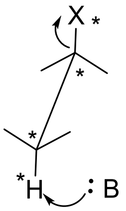
There are no rearrangments during this pathway. An important aspect of this reaction is when the leaving H is replaced with a deuterium (D), the reaction slows down considerably. Therefore, this reaction is known to have an isotope effect. The isotope effect happens because C-D bond breaks slower than the C-H bond.



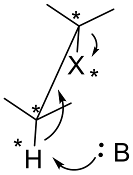
In E_1 reactions, in the formation of carbocation, there is no C-H bond breaking, therefore, this isotope effect is not seen.

The transition state of an E_2 reaction requires that all five atoms involved be on the same plane. This is achieved in two ways:

1. Anti periplanar transition state



2. Syn periplanar transition state

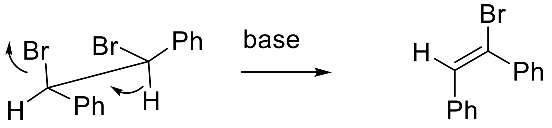


In reactions, the preferred transition state is antiperiplanar. E_2 reactions also, similar to S_N2 exhibit stereospecificity.

4.4.3 Stereospecific elimination

$$\mathrm{PhCHBr{-}CHBrPh} \xrightarrow{\text{base}} \mathrm{HCPh{=}CBrPh}$$

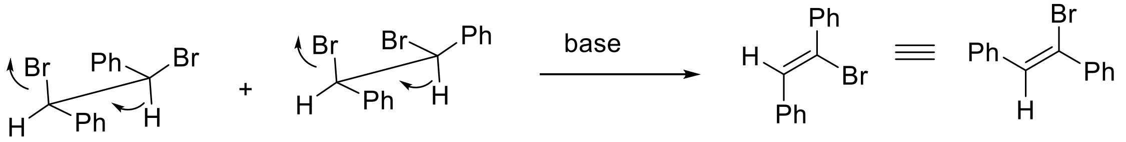
The above 1, 2- dibromo-1, 2 – diphenyl ethane has two optical centers. When this reaction is carried out on the meso compound the product is cis-bromostilbene.



meso compound

cis bromostilbene
(1-bromo-cis-1,2 diphenylethane)

The racemic mixture of the above compound will produce trans- bromostilbene.



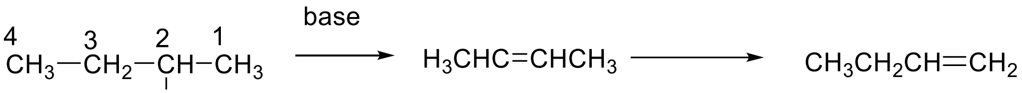
racemic mixture

trans bromostilbene

(1-bromo-trans-1,2 diphenyl ethane)

4.4.4 Regiospecific elimination

When HX is removed from a 2-substituted butane, two products are possible depending on whether a hydrogen atom is eliminated from C-1 or C-3.



$$\overset{4}{CH_3}-\overset{3}{CH_2}-\underset{X}{\overset{2}{CH}}-\overset{1}{CH_3} \xrightarrow{\text{base}} H_3CHC=CHCH_3 \longrightarrow CH_3CH_2CH=CH_2$$

2-butene

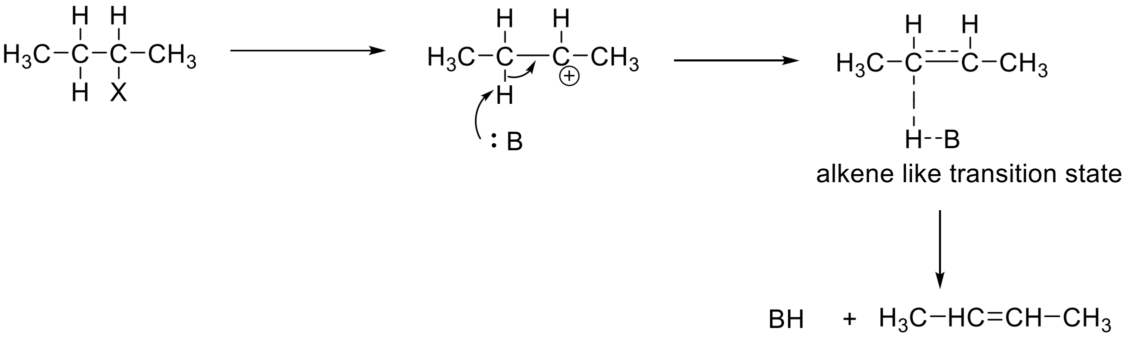
1-butene

Out of the two products, 2-butene with more substituted double bonds is the most stable product. This is called the Zaitsev rule for dehydrohalogenation reactions.

Nevertheless, the leaving group X and if the reaction takes E_1 or E_2 path determine which product is more favored.

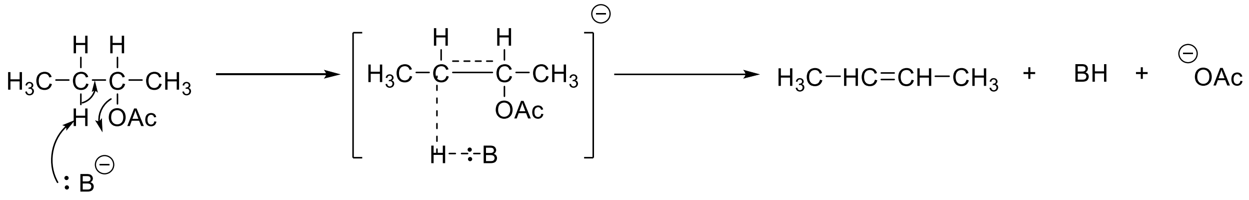
- In E_1 reactions, irrespective of the leaving group, the final product is always the most stable one. This is clear since the transition state has an alkene like structure. Therefore, the transition state with a more stable alkene (more substituted one) is preferred than a less stable (less substituted one) alkene. As a result, the product will be the more stable alkene.

A reaction of this nature, where out of the two possible structural isomers the more preferential form is generated, is known as regio-specific reactions.

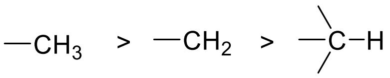


In E2 reactions also, when a leaving group such as Cl, OAc leaves as an anion (having stayed connected to the original carbon as a neutral atom without a charge at that point), more stable alkene is produced. Same as the reason given before, the transition state will have considerable alkene character.

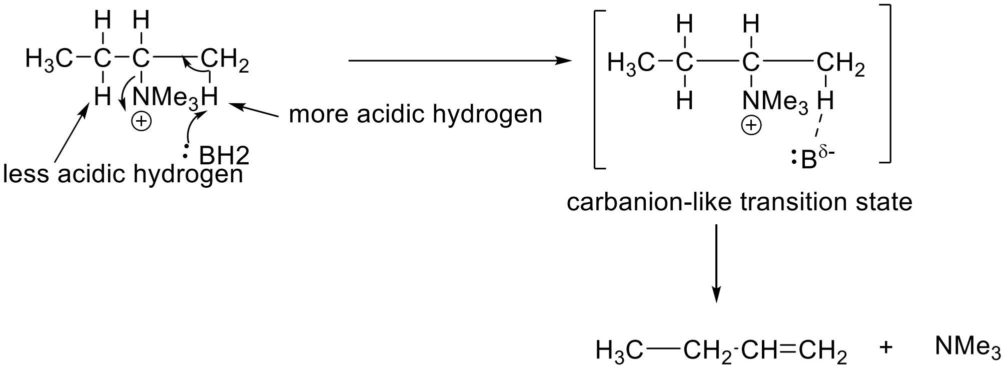
e.g.



- In cases where the leaving group is a positively charged one such as $^{+}\mathrm{NMe}_3$ (the positive charge is shown at the connection point), and then leaves as a neutral group, then the product formed is a less stable alkene. In such cases, the transition state is more carbanion in nature than alkene in nature. This is known as the Hoffmann rule.
- When there is more alkene nature at the transition state, the breaking of C-H and C-X occur to the same extent. When the transition state is in carbanion state, the breaking of C-H bond happens to a larger extent than the breaking of C-X bond.
- The more stable carbanion nature in the transition state happens when C-H bond being broken is more acidic in nature. This happens due to +I effect of alkyl groups. The order in which the acidic nature of C-H exists is given below:



The following reaction obeys the Hoffmann rule due to the high acidic hydrogen in CH_3.



All Lewis bases are nucleophiles. Therefore, elimination and nucleophilic substitution are competing reactions. Therefore, when a reagent acts as a nucleophile and attack carbon, the substitution happens. If the same reagent acts as a base and abstracts a proton, then elimination occurs. In general, S_N1 pathway predominates over E_1 pathway.

In order to establish unimolecular conditions in a reaction, high polar solvents are used. The polar solvent will promote the ionization to create a carbocation. The use of low concentration bases will also reduce the number of bimolecular collisions between the substrate and the reagent.

The percentage of elimination reaction happening increases with the branching of carbon to which the leaving group is attached. Therefore, the ratio of elimination to substitution will increase as follows:

primary < secondary < tertiary

This means more branched substrate (such as tertiary) will provide more substituted alkene.

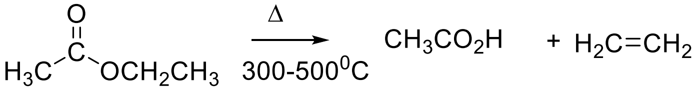
When it comes to bimolecular conditions (low solvent polarity and a high concentration of reagent) elimination (E_2) predominates substitution (S_N2). In this case also the ratio of elimination to substitution increases as follows:

primary < secondary < tertiary

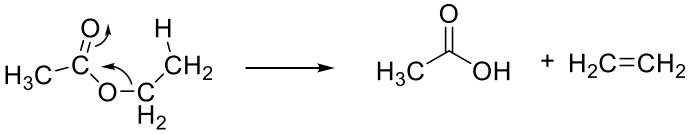
This means tertiary halides provide only a smaller proportion of the substituted products. The tertiary halide will favor a more stable alkene. Also, the steric hindrance in tertiary halide favors elimination to substitution.

4.4.5 Pyrolytic eliminations – Elimination internal - E_i

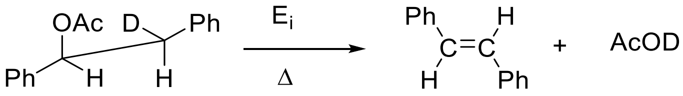
Carboxylic acid esters of alcohols with a β hydrogen atoms undergo elimination reaction on heating in the absence of any reagent.



In the above reaction, a molecule of acetic acid has been eliminated from the ester. These types of reactions are called E_i or elimination internal. This is a one-step reaction with a cyclic transition state of 4, 5, or 6 atoms. The breakage of leaving groups and bonding to each other happen simultaneously.



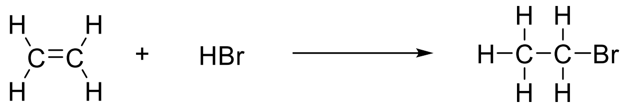
As per the mechanism, Ei reactions show first order kinetics and also predict that the two eliminated groups as syn to each other in the transition state. This is because a cyclic transition state with 6 atoms is otherwise not possible.



Some elimination reactions are dehydration of alcohols, Chugaev reaction, dehydrohalogenation of alkyl halides, and cleavage of quaternary ammonium hydroxide.

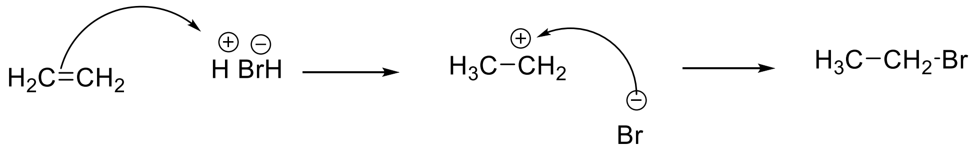
4.5 Addition Reactions

In these types of reactions, two molecules combine to form a single product. Unsaturated compounds such as alkenes and alkynes undergo addition reactions.



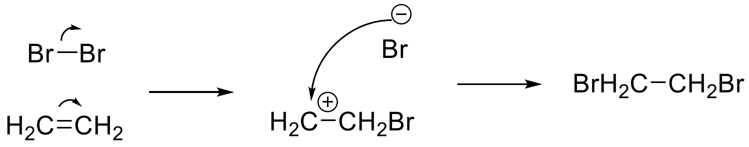
1. Addition to C = C bonds

These additions mostly take place in two steps:



Since the first step of the above reaction is the addition of an electrophile, this is known as electrophilic addition. The electrophile can be a completely free positive ion or a positive end of a dipole or a positive end of an induced dipole where the negative end will break during the addition.

e.g.

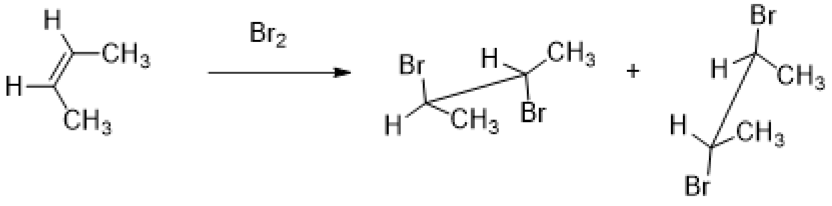


In addition-reactions, carbon-carbon double bond is a planar system. The adding of the groups could be syn, anti, or non-stereospecific.

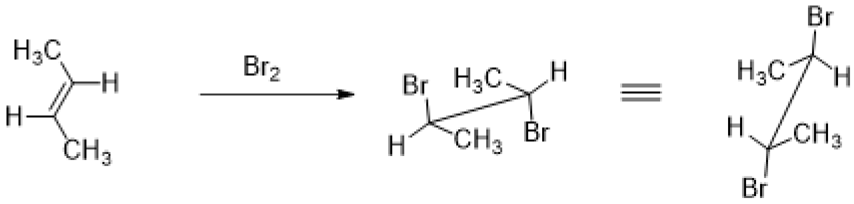
The addition at double bonds follows different stereochemical modes.

e.g.

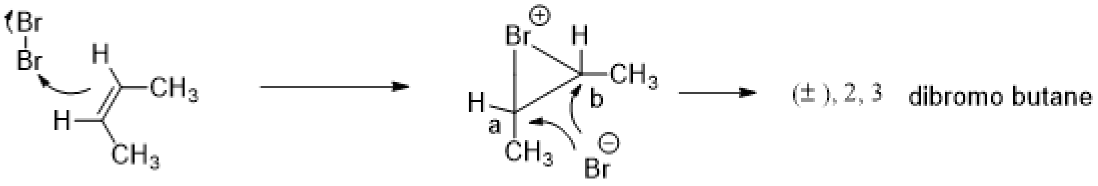
The addition of bromine to alkenes follows anti addition. The intermediate of this reaction is a bromonium ion.



(±), 2, 3 dibromo butane



meso 2,3 dibromo butane



intermediate bromonium ion
(Br^- can attack either a or b)

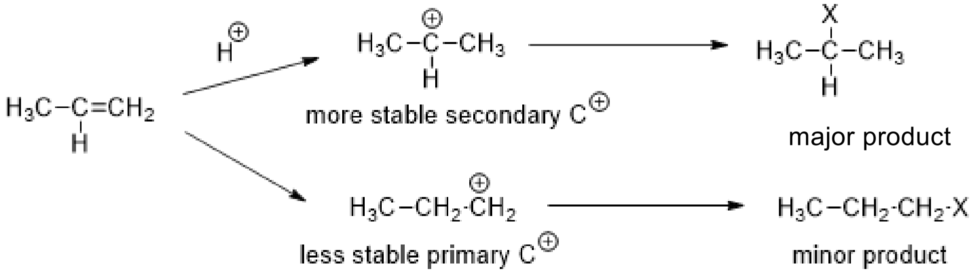
According to the above reaction, the bromine atom is bonded covalently to two carbon atoms. It also has a positive charge. Since this atom blocks one side of the molecule, the other incoming bromide ion (Br^-) will have to approach from the opposite side. This second step is similar to S_N2 reactions. After the first step of the addition reaction, any nucleophile present in the medium can compete during the second step to connect with the carbon atom.

When H^+ is the electrophile in an addition reaction, depending on the reacting molecules and the reaction conditions, the products could be syn, anti, or non-stereoselective products.

2. Addition of HX type molecule

When an HX type molecule (X is a halide) undergoes an addition reaction with an asymmetrical alkene there could be two products.

The product that is produced is the one that favors the most stable carbocation intermediate.



Markovnikov's rule

According to this rule, when HX is added to a double bond, H joins the carbon atom holding more hydrogens. X joins the carbon with less hydrogen meaning more substituted carbon. This rule predicts the regioselectivity of this addition reaction. This rule also follows the creation of more stable carbocation.

The exception to this rule happens in the presence of peroxide. The reason for this change is due to the ability of peroxides to dissociate as free radicals. As a result, the peroxide free radicals will dissociate HX to H and Br free radicals. Now, Br free radical will first join (not as a negatively charged atom but as a free radical) to the carbon (out of the two carbon atoms sharing a double bond) with more hydrogen atoms. This is a free radical reaction and follow the initiation, propagation, and finally termination steps. This reaction does not generate a carbocation. As a result, in the presence of a peroxide, HX addition is not an electrophilic addition, but a free radical reaction. Although there is no formation of carbocation, the stability of free radicals follow pattern below:

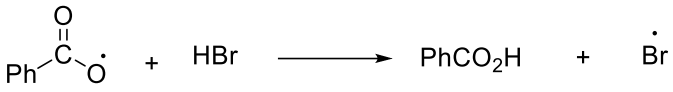
Tertiary > Secondary > Primary

Tertiary is the most stable form.

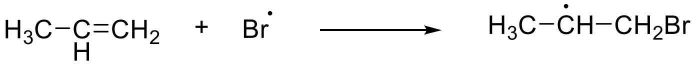
Addition in the presence of peroxides:

Benzoyl peroxide dissociating to two free radicals:

The above free radicals remove H from HBr.

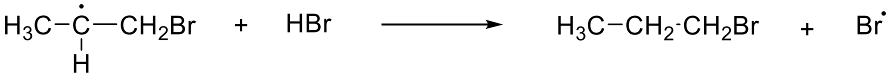


Br radical adding to an alkene



$$H_3C-\underset{H}{C}=CH_2 + Br^{\bullet} \longrightarrow H_3C-\dot{C}H-CH_2Br$$

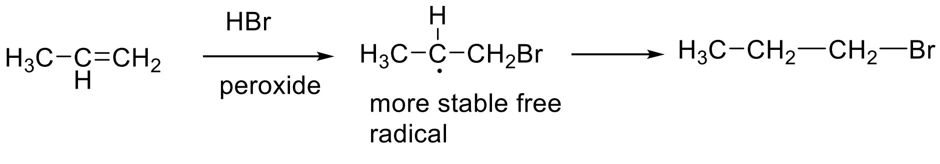
Continuation of the free radical reaction – propagation step



$$H_3C-\underset{H}{\overset{\bullet}{C}}-CH_2Br + HBr \longrightarrow H_3C-CH_2\cdot CH_2Br + Br^{\bullet}$$

The reaction continues until all free radicals are consumed.

Overall reaction could be written as follows:



$$H_3C-\underset{H}{C}=CH_2 \xrightarrow[\text{peroxide}]{HBr} H_3C-\underset{\bullet}{\overset{H}{C}}-CH_2Br \longrightarrow H_3C-CH_2-CH_2-Br$$

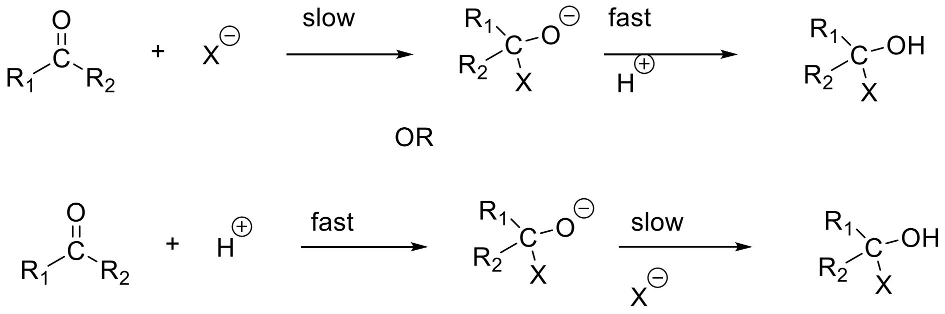
The above reaction is said to have followed anti-Markovnikov rule. The reversal of orientation noticed here is known as peroxide effect.

It is important to note that peroxide effect is not exhibited by HCl, HI, HOH, H_2SO_4. This is because the reactions involving this HX forms are endothermic; thus, these types of reactions are unfavorable.

3. Addition of C=O

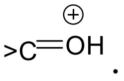
The bond between C and O are polar. This is different to a bond between C and C.

If an addition reaction of HX (X could be CN, OR, NHR) is considered, the more electrophilic H connects with the oxygen, while more nucleophilic X connects with the carbon. Also, depending on the nature of alkyl groups and X, the product can reacts further. Since oxygen atom cannot be asymmetric, it is not possible to confirm if the addition is syn or anti. As a result, these reactions are known as nucleophilic addition reactions. This is because it is the nucleophile that bonds to the carbon atom in C=O bond. This is also the rate determining step and could happen before or after the bonding of H to O.



4. Addition of >C=O in the presence of an acid of base catalyst

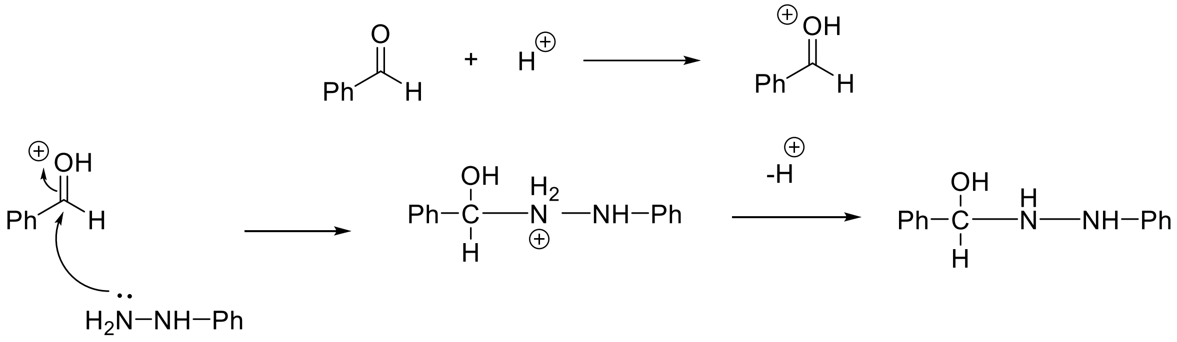
In the presence of an acid catalyst the double bond gets protonated on the oxygen atom as,


$>C=\overset{\oplus}{O}H$.

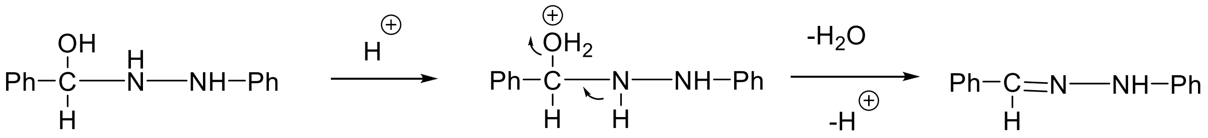
This increases the polarity of the bond. An increase in the polarity increases the preference for nucleophilic addition.

In the presence of a base catalyst, X of HX will be converted to a stronger X^- making it a stronger nucleophile.

e.g. Acid catalyzed addition reaction:



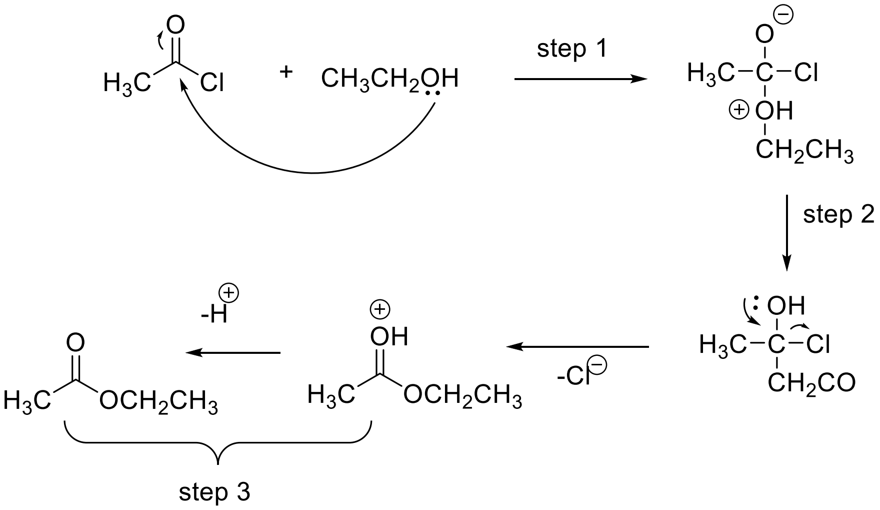
Most of the times, in aldehydes and ketones, when X has an ideally placed H, an elimination of a water molecule can happen. This will lead to the generation of a double bond.



Nevertheless, if C=O is attached to an acid derivative, then C=O is reformed with the elimination of a leaving group.

e.g. Reaction of acetyl chloride with ethanol.

Step 1 – ethanol adds across C=O.



Step 2 – C=O is reformed. Step 3 – elimination of Cl^- and H^+

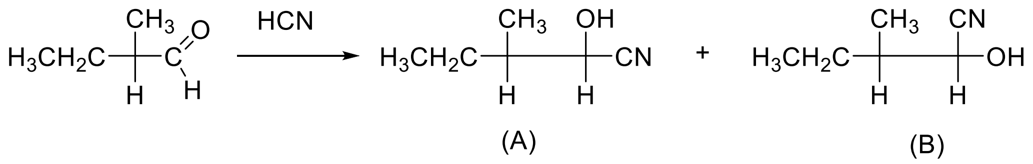
The overall effect of this addition-elimination reaction is substitution of -OCH_2CH_3 for Cl^-.

The above mechanism is known as tetrahedral mechanism of substitution at a carbonyl carbon.

In situations where one of the groups attached to carbonyl carbon has an asymmetric center, the stereochemistry becomes important. The carbon atom here is a trigonal planar and face a nucleophilic addition.

e.g.

Addition of HCN to an optically active 2 methyl butanol. The result is two diastereoisomers.

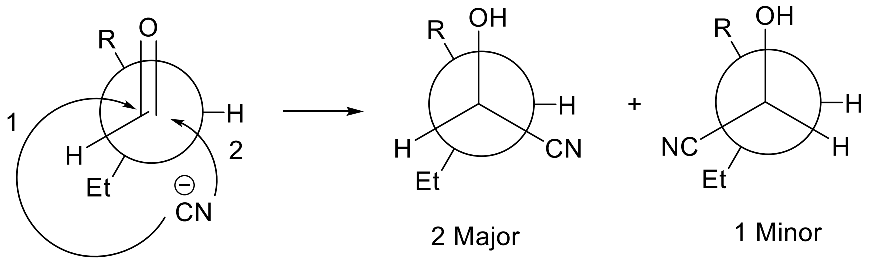


Out of A and B products, B will be the major isomer. The major product given out by this type of a reaction can be predicted using Cram's rule.

Cram rule states that,

- The oxygen atom of the C=O will orient itself to lie between the smallest and the medium size group joined to the asymmetric atom.
- The nucleophile will attack predominantly from the side containing the small group. This is because this path is the least hindered path.

e.g.

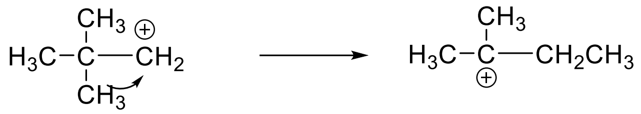


4.5 Rearrangement reactions

4.5.1 Nucleophilic rearrangements

In a rearrangement reaction, a molecule or ionic compound rearranges for a different compound, which is a structural isomer of the original compound. Most of the time, the rearrangement happens at the intermediate state. When a reaction has undergone rearrangement, the product's skeleton structure will be different to that of the reactant.

e.g.,



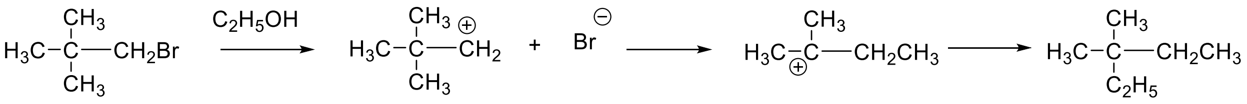
Neo pentyl carbocation tertiary pentyl carbocation

This rearrangement has provided more stability to the tertiary form of the product. This kind of rearrangement usually involves 1, 2 shift of a H atom or alkyl group. In the above reaction, it was 1, 2 shift of a methyl group.

A rearrangement can be seen in S_N1 and not in S_N2. This is because, S_N2 has no intermediate that can undergo rearrangement.

e.g

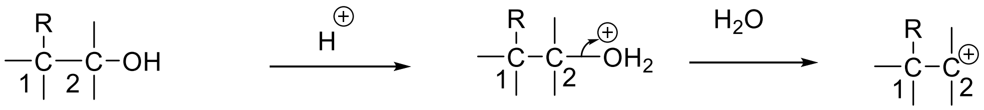
Neopentyl bromide reaction with ethanol



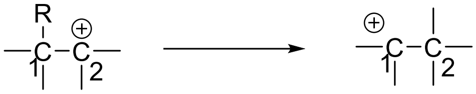
There are three processes involving nucleophilic rearrangement:

1. Creation of a carbocation – this is an electron deficient center

e.g. Reaction of an alcohol with an acid:

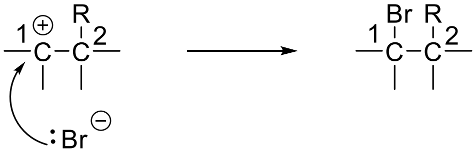


2. Migration of a group from an adjacent atom with a pair of bonding electrons:



As a result of this rearrangement, the original electron deficient (carbocation site) now has a complete octet. The need to gain stability is the driving force of this rearrangement.

3. Combination with a nucleophile in the medium:



The above three processes can happen simultaneously or consecutively. An understanding of the timing of these steps helps to understand the mechanism of nucleophilic rearrangement.

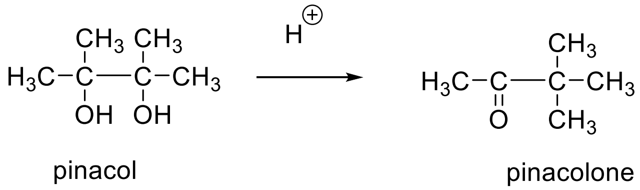
The rearrangement above is similar to an S_N reaction. If the leaving group leaves first and then R group migrates, it is an S_N1 type of a reaction. If the leaving of the group and the migration of R happens simultaneously, it is an S_N2 type of a reaction.

The atom to which the migrating group is originally attached is known as the migration origin and the atom to which the migrating group finally joins is known as the migration terminus.

The following are some important rearrangements:

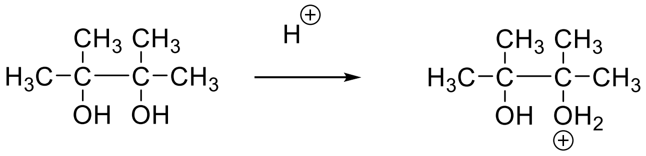
4.5.2. Pinacol-Pinacolone Rearrangement

In this reaction, vicinal diols in the presence of mineral acids eliminate water and rearrange to produce ketones of aldehydes. i.e. pinacol to pinacolone.

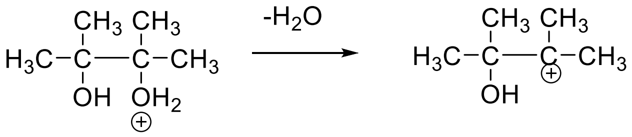


Mechanism:

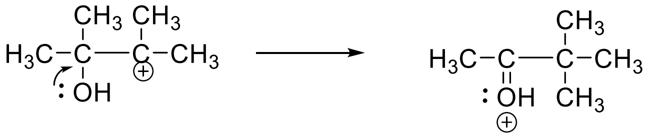
Step 1



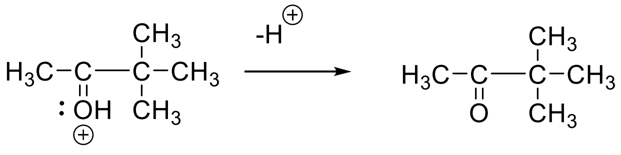
Step 2



Step 3



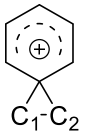
Step 4



The above mechanism clearly indicates how a tertiary carbocation is formed as a result of the elimination of water (step 2). Although, a tertiary carbocation is a stable form, as a result of the migration of CH_3, the positive charge created at the migration origin is better stabilized due the lone pairs of oxygen in step 3. Therefore, in this reaction, the driving forces are the stabilization of the positive charge (tertiary carbocation) and the stability gained as a result of the formation of C and O double bond.

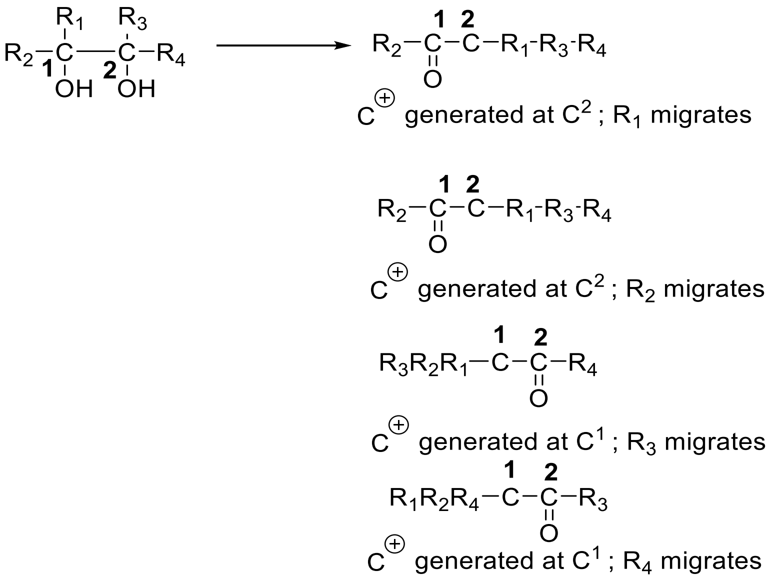
There are other vicinal glycols that undergo similar rearrangements. The migrating group could be hydrogen, alkyl, or aryl. The migratory aptitude is higher in aryl than alkyl. The hydrogen migratory aptitude is dependent on the substrate and the reaction condition.

The higher migratory aptitude of aryl is due to the stability of the transition state (or intermediate) as shown below:



Aryl groups can bond simultaneously to the migration origin and the migration terminus. It can also disperse the positive charge within the ring as shown above. Accordingly, an electron donating substituent group on the aryl ring will increase the migratory aptitude, while an electron withdrawing group will decrease migratory aptitude. This type of stabilization is not possible in alkyl groups.

In the event the vicinal glycol is not symmetrical, several products can be expected.



C⊕ generated at C^2; R_1 migrates

C⊕ generated at C^2; R_2 migrates

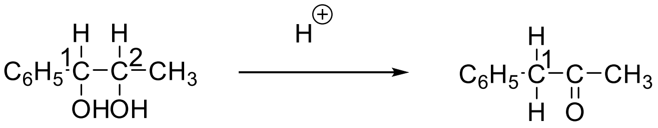
C⊕ generated at C^1; R_3 migrates

C⊕ generated at C^1; R_4 migrates

The products obtained here are dependent on two factors:

1. The atom at which the electron deficient center is created (i.e. which hydroxyl group is lost)
2. Which group migrates

The general rule is that the most stable carbocation is formed and the group with the higher migratory aptitude migrates.

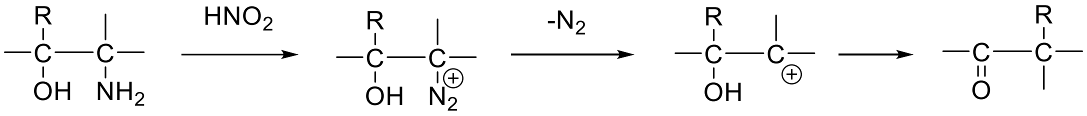


In the above reaction, C1 has produced the most stable carbocation and H has migrated in preference to methyl.

4.5.3. Semipinacol Rearrangement or Pinacolic Deamination

Any carbocation that has a hydroxy group on the carbon atom adjacent to the carbon atom bearing the positive charge can undergo pinacol-pinacolone rearrangement.

Therefore, similar rearrangement can be generated by treating β amino alcohols with nitrous acid.



The above reaction is known as semipinacol rearrangement or pinacolic deamination.

The above reaction is an S_N1 type reaction. Therefore, a 23% racemization and 77% inversion are observed. If the reaction was an S_N2 type, there would be 100% inversion.

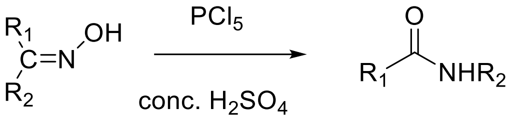
Factors that determine the migratory groups:

1. Electronic factors
2. Conformational factors

Experimentally, it has been shown that in pinacolic deamination reactions, the higher migratory aptitude is not the determining factor of what optical isomer is given as the product. In this reaction, an S_N1 type of a rearrangement happens. This happens via the most stable conformation of the molecule. Also, the migration happens before the bond rotation takes place along the central C – C bond.

4.5.4 Beckmann Rearrangement

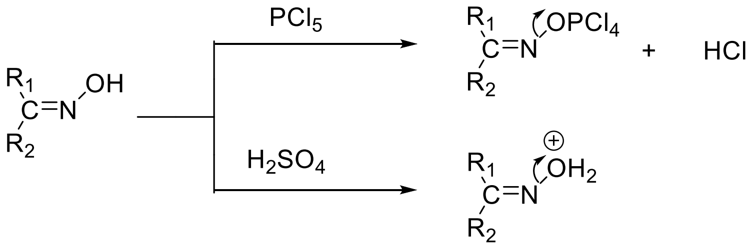
When an oxime is treated with phosphorous pentachloride or concentrated sulfuric acid, the product rearranges to produce amides.



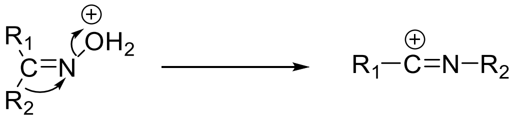
In this reaction, the migration terminus is N. In pinacol-pinacolone reaction the migration origin and migration terminus is C. Similar to pinacol=pinacolone, the migrating group could be aryl, alkyl, or rarely hydrogen.

Steps of Beckmann rearrangement:

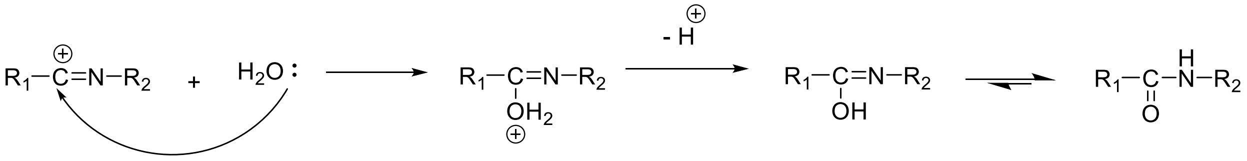
Step 1: Conversion of -OH group of oxime to a leaving group.



Step 2: The migration of the R group and the departure of the leaving group happens simultaneously. Therefore, the rearrangement is S_N2 type. Due to electronic and steric reasons, the R group anti to OH group can easily displace the leaving group from N atom.

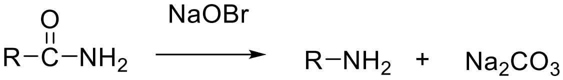


Step 3: The reaction with a water molecule satisfies the electron deficiency. This is followed by the loss of a proton and tautomerization of the amide.



4.5.5 Hoffmann Rearrangement or Hoffmann Degradation

This is another rearrangement where C to N migration of a group happens. In this case, an amide is reacted with sodium hypobromite. The resulting product is a primary amine containing one carbon less than the amide.



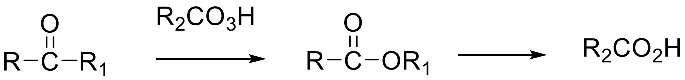
$$R-\overset{\overset{\displaystyle O}{\|}}{C}-NH_2 \xrightarrow{NaOBr} R-NH_2 + Na_2CO_3$$

R could be an alkyl or an aryl group. This rearrangement is an intramolecular reaction.

4.5.6 Baeyer Villiger Rearrangement or Baeyer Villiger Oxidation

In this reaction, a group migrates from C to O.

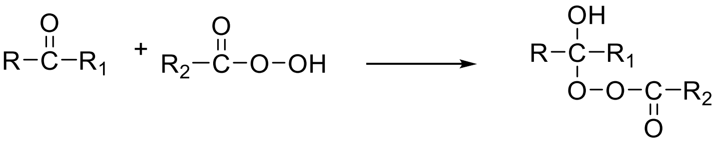
When ketones are treated with peracids, the reaction will produce esters. Perbenzoic acid and peracetic are the most common peracids used in this reaction.



$$R-\overset{\overset{\displaystyle O}{\|}}{C}-R_1 \xrightarrow{R_2CO_3H} R-\overset{\overset{\displaystyle O}{\|}}{C}-OR_1 \longrightarrow R_2CO_2H$$

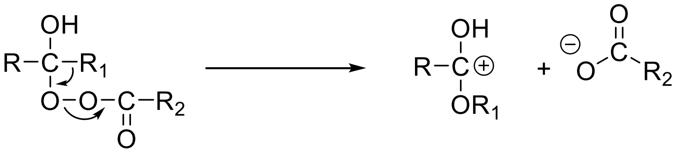
The steps of the reaction:

1. The first step is the addition of peracid across the carbonyl group of the ketone.



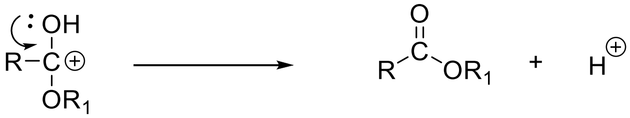
$$R-\overset{\overset{\displaystyle O}{\|}}{C}-R_1 + R_2-\overset{\overset{\displaystyle O}{\|}}{C}-O-OH \longrightarrow R-\underset{\underset{\displaystyle O-O-\underset{\underset{\displaystyle O}{\|}}{C}-R_2}{|}}{\overset{\overset{\displaystyle OH}{|}}{C}}-R_1$$

2. In the second step, the migration of R^1 to oxygen happens while the departure of $R^2CO_2^-$ happens



$$R-\underset{\underset{\displaystyle O-O-\underset{\underset{\displaystyle O}{\|}}{C}-R_2}{|}}{\overset{\overset{\displaystyle OH}{|}}{C}}-R_1 \longrightarrow R-\underset{\underset{\displaystyle OR_1}{|}}{\overset{\overset{\displaystyle OH}{|}}{C}}{}^{\oplus} + {}^{\ominus}O-\overset{\overset{\displaystyle O}{\|}}{C}-R_2$$

3. In the third step, the carbon at the migration origin is neutralized by the reformation of carbonyl group.



In this reaction, both R_1 and R_2 are capable of migrating. The order of migratory aptitude is as follows:

Tertiary alkyl > secondary alkyl, aryl > primary alkyl > methyl.

Chapter 5

5.0 Alkanes

5.1 Objectives

1. Draw and interpret Lewis structures, line-bond structures and functional groups of alkanes using IUPAC system of nomenclature.
2. Draw reaction mechanisms.
3. Describe reactions, predicting reactivity, and reaction products.
4. Devise syntheses including steps, reagents, and products including regiochemistry and stereochemistry.

5.2 Introduction

Alkanes are hydrocarbons that have C – C bonds and C – H bonds only. There are no double or triple bonds in alkanes. Therefore, alkanes that are aliphatic (open chain) have the highest number of hydrogen atoms connected to carbon atoms than any other hydrocarbons. These alkane compounds are known as saturated compounds. These aliphatic, saturated compounds have the following empirical formula:

$$\mathbf{C_n\ H_{2n+2}}$$

n = Any positive integer

Alkanes occur naturally in the animal and plant world. They are also known as paraffins. The fossil deposits of crude oil and natural gas are the primary source of alkanes. These natural alkane resources are used as fuel for heating, electricity generating electricity, in the production of lubricants, in transportation, and as a source of hydrocarbons in chemical industry.

Crude oil is a complex mixture of hydrocarbons. In crude oil, there are three main series of hydrocarbons are present. They are alkanes (aliphatic), cycloalkanes, and aromatics. At a particular boiling point, aromatic compounds will have the highest density. The density values of cycloalkanes will be lower than the aromatic compounds but will be higher than aliphatic alkanes.

A fractional distillation column can be used to separate crude oil according to the boiling points of constituent compounds. The separation of crude oil provides the following major compounds:

1. Refinery gases – simple alkanes with up to four carbons. These compounds are used as fuel or to build other compounds.
2. Gasoline – contains alkanes with five to ten carbon atoms. These compounds are used as fuel. Naphtha is one of such important compounds used in chemical industry.
3. Kerosene – used in aviation fuels and domestic heating.
4. Diesel – used as a vehicle fuel.
5. Bitumen – mixed with crushed stones is the tarmac used for roads.

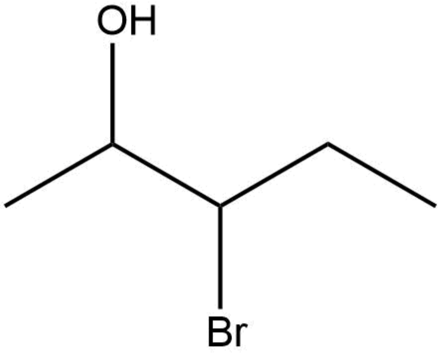
After fractional distillation, the separated compounds are subject to different separation methods such as vacuum distillation (separation of less volatile compounds), desulphurization (remove sulfur), and cracking (to create more gasoline and alkenes).

5.3 Nomenclature and Isomerism

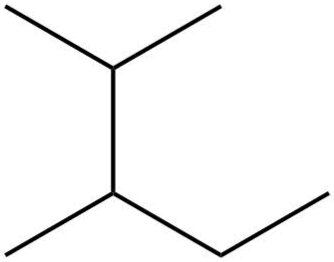
Please refer to the chapter on nomenclature and isomerism and answer the following questions:

1. **Naming Compounds**

   A) Are the following structures properly named, and if they are not, what is the correct naming?

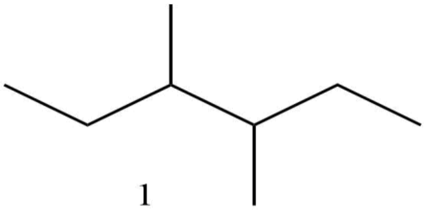


3-bromo-4-hydroxypentane

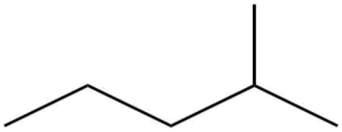


2-isopropylbutane

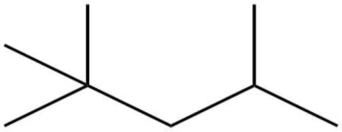
B) Give the names of the following molecules:



1



2



3

2. **Draw the structures of the following compounds**
A. 2-methylpentane
B. 3-methyl hexane
C. 3,4-dimethyl hexane

3. Questions on isomers

A. Draw all possible isomers for C_6H_{14}

B. Draw all possible isomers for C_3H_8

Solutions:

1. **Naming Compounds**

A)

1. They are both labeled incorrectly:
2. 3-bromo-2-hydroxypentane
3. 2, 3-dimethylpentane

B)

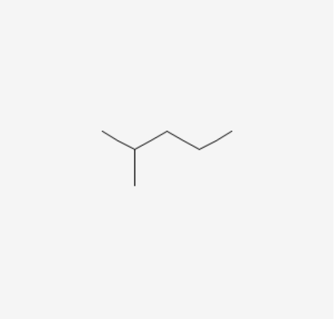
1. 3,4-Dimethyl hexane

2. 2-methyl pentane

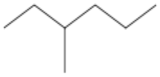
3. 2,2,4-trimethyl pentane

2. Drawing of Compounds

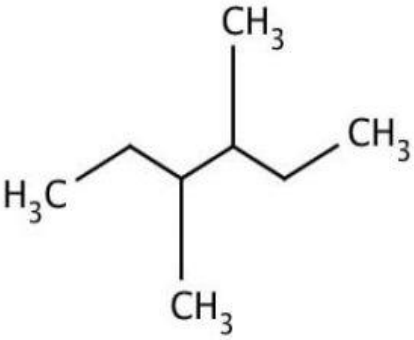
A)



B)

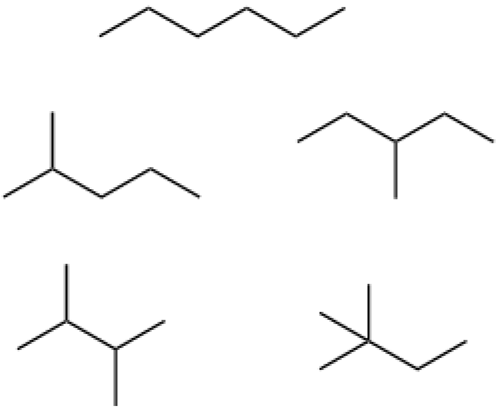


C)



4. Answers to Isomers Questions

A.



The top structure is when it is a 6-carbon chain. The middle row contains the 5 carbon chained isomers with branching at the 2nd and 3rd carbon. The bottom row contains the two 4 carbon chain isomers that can be drawn.

B. No possible isomers.

5.4 Physical Properties

Alkanes are nonpolar compounds. Therefore, they are insoluble in water. Alkanes are widely used as solvents for organic compounds. The densities of most of the alkanes are less than water. The boiling points, melting points, and densities of alkanes vary in a normal manner. Alkanes are less reactive compounds. They are all colorless and odorless compounds.

Methane to butane are gases at room temperature. Pentane boils just above room temperature. All other alkanes show a normal increase in boiling point with each increase of methylene unit. The longer the alkane chain, the higher the boiling point values. Branched chain alkanes display lower boiling points than unbranched alkane compounds with the same number of carbon atoms due to greater surface area. Unbranched chain alkane compounds have greater van der Walls forces between molecules than that of the unbranched alkanes. These intermolecular forces (IMF) can be dipole-dipole, dipole-induced dipole, or induced dipole – induced dipole.

Molecular Name – n-alkane	Formula	Melting Point (^{0}C)	Boiling Point (^{0}C)	Density (20^{0}C) at 1atm	Physical State (at 20^{0}C)
Methane	CH_4	-183	-162	0.668 g/l	gas
Ethane	C_2H_6	-183	-89	1.265 g/l	gas
Propane	C_3H_8	-190	-42	1.867 g/l	gas
Butane	C_4H_{12}	-138	-1	2.493 g/l	gas
Pentane	C_5H_{12}	-130	36	0.626 g/ml	liquid
Hexane	C_6H_{14}	-95	69	0.659 g/ml	liquid
Heptane	C_7H_{16}	-91	98	0.684 g/ml	liquid
Octane	C_8H_{18}	-57	125	0.703 g/ml	liquid

Nonane	C_9H_{20}	-54	151	0.719 g/ml	liquid
Decane	$C_{10}H_{22}$	-30	174	0.730 g/ml	liquid

Table 5.4.1 A selected list of physical properties of alkanes

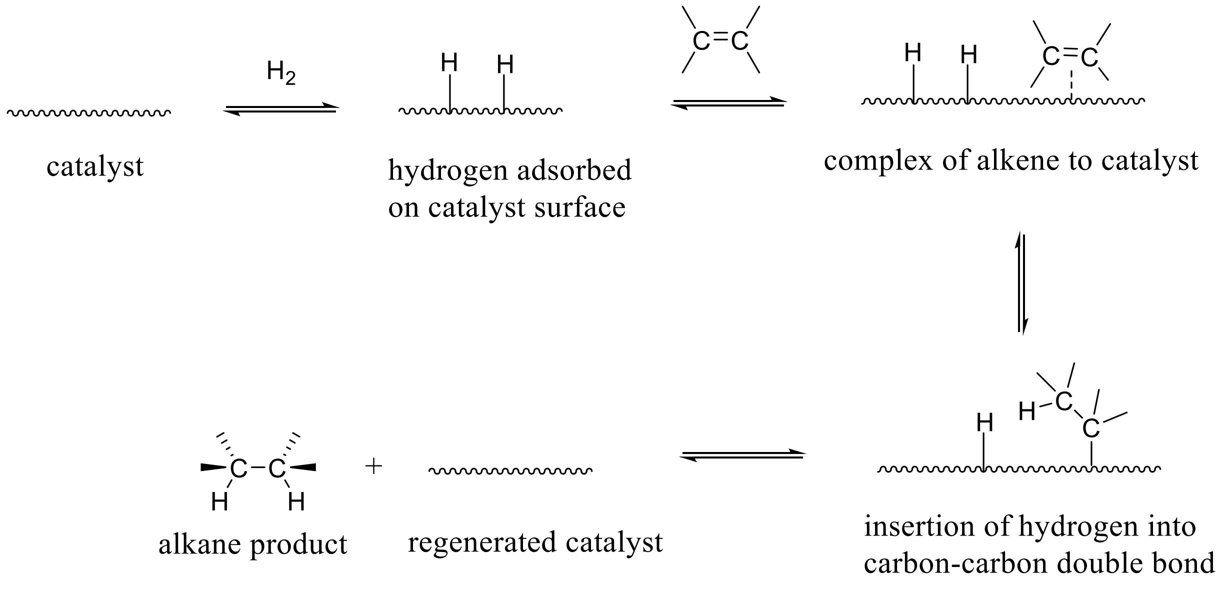
5.5 Preparation of Alkanes

1. Preparation of alkanes from unsaturated hydrocarbons - Catalytic hydrogenation

The catalytic hydrogenation of unsaturated hydrocarbons is a very common method to synthesize alkanes.

Palladium (5-10%) on carbon is generally used as the catalyst for the reduction of unsaturated hydrocarbons at room temperature and at atmospheric pressure. Another two catalysts used are Platinum as PtO_2 (also known as Adam's catalyst) and Raney Ni (prepared by treating Ni/Al alloy with sodium hydroxide).

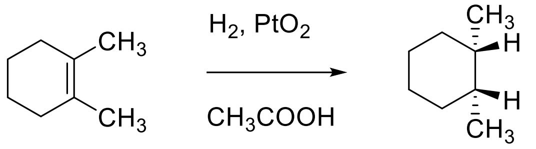
In this reaction, hydrogen is trapped in the porous material.



In the synthesis of alkanes using a catalyst, the first step is the adsorption of hydrogen onto the catalyst surface, The alkene also gets adsorbed onto the surface of the catalyst. The next step is the movement of hydrogen atoms from the catalyst surface to the double bond in the alkene. Once the alkane is formed, the compound leaves the catalyst.

$$\text{Catalyst} + H_2 + \text{ethene } (C_2H_4) \rightarrow \text{Catalyst} + C_2H_6 \text{ (ethane)}$$

e.g.



1,2 dimethylcyclohexene

cis - 1,2 dimethylcyclohexane

2. **Preparation of alkanes from alkyl halides**

a) Reduction of alkyl halide using dissolving metals. The dissolving metal could be introduced as,

* Zn/acetic acid

* Zn/sodium hydroxide

* Zn/Cu and ethanol

An example of the mechanism (the reduction of alkyl halide) is given below:

$$Zn \longrightarrow Zn^{2+} + 2e$$

$$RX + e \longrightarrow X^- + R \xrightarrow{e} R^-$$

$$R^- + C_2H_5OH \longrightarrow RH + {}^-OC_2H_5$$

*Reduction of secondary or primary alkyl halides using lithium aluminum hydride ($LiAlH_4$)

$$R\text{-}X \xrightarrow{LiAlH_4} R\text{-}H$$

3. **Preparation of alkanes from organometallic reagents**

$$\text{Grignard Reagents} + \text{Water (or dilute acid)} \rightarrow RH + M\text{-}OH$$

Grignard reagent is prepared by getting Magnesium to react with alkyl halides in ether. Grignard reagent is also known as alkylmagnesium halide (RMgX).

$$\mathrm{R^{\delta-}{-}M^{\delta+} + H_2O \longrightarrow RH + M{-}OH}$$

$$\mathrm{CH_3Br \xrightarrow[\text{dry ether}]{Mg} \underset{\textbf{Grignard reagent}}{CH_3MgBr} \xrightarrow{H_2O} CH_4 + Mg(OH)Br}$$

4.**Wurtz reaction**

In this reaction, a solution of alkyl halide in diethyl ether is mixed with sodium to obtain alkane due to coupling of two alky groups.

$$\mathrm{R^1X + 2Na + XR^2 \longrightarrow R^1{-}R^2 + 2NaX}$$

e.g. $$\mathrm{2CH_3I + 2Na \longrightarrow \underset{\text{Ethane}}{H_3C{-}CH_3} + 2NaI}$$

There are two mechanisms suggested for the above two reactions:

1. This involves the formation of an organometallic compound.
   e.g.

$$\mathrm{C_2H_5Br + 2Na \longrightarrow C_2H_5^{-}\,Na^{+} + NaBr}$$

$$\mathrm{C_2H_5^{-}\,Na^{+} + C_2H_5Br \longrightarrow C_2H_5{-}C_2H_5 + NaBr}$$

2. This involves the intermediate formation of free radicals

e.g. $$C_2H_5Br + Na^{\bullet} \longrightarrow C_2H_5^{\bullet} + NaBr$$

$$C_2H_5^{\bullet} + C_2H_5^{\bullet} \longrightarrow C_2H_5{-}C_2H_5$$

4. Kolbe’s electrolysis method

This method involves the electrolysis of a concentrated solution of sodium or potassium salt of carboxylic acid or a mixture of carboxylic acids.

$$2\,R'CO_2K + 2H_2O \xrightarrow{\text{electrolysis}} R'{-}R' + 2CO_2 + H_2 + 2KOH$$

The by-products of this reaction are,

At the anode

e.g. $$C_2H_5COO^{-} \longrightarrow C_2H_5COO^{\bullet} + e$$

$$C_2H_5COO^{\bullet} \longrightarrow C_2H_5^{\bullet} + CO_2$$

decarboxylation step

(a) $$2C_2H_5^{\bullet} \longrightarrow C_4H_{10} \quad \text{butane}$$

(b) $$C_2H_5^{\bullet} + C_2H_5^{\bullet} \longrightarrow \underset{\text{ethane}}{C_2H_6} + \underset{\text{ethylene}}{C_2H_4}$$

dispropotionation step

(c) $$C_2H_5^{\bullet} + C_2H_5COO^{\bullet} \longrightarrow C_2H_5CO_2C_2H_5 \quad \text{ester}$$

ethyl propionate

5. Addition of water on aluminum carbide to form methane

$$Al_4C_3 + 12H_2O \longrightarrow 3CH_4\uparrow + 4Al(OH)_3$$

5.6 Reactions of Alkanes

Since C-H bond is very strong, the alkane series is resistant to acids, alkalis, and reducing or oxidizing agents. Also, alkanes do not have a functional group or any unsaturation; therefore, they are less reactive than other organic compounds. Nevertheless, alkanes react under certain conditions.

1. Halogenation

Chlorination of alkanes can happen under light, heat, or catalysts. This is a radical process. The process is a substitution of hydrogen atoms by chlorine atoms.

In this reaction, the first step is the formation of a free radicals. This happens through homolytic cleavage initiated by heat or light.

e.g. Chlorination of methane reaction

The reaction is carried out by irradiating a mixture of chlorine and methane with ultraviolet light.

Step 1 – Generation of chlorine free radicals – this is known as the “initiation step of the reaction.”

$$\mathrm{Cl_2} \xrightarrow{\text{UV light}} \mathrm{Cl}^{\bullet} + \mathrm{Cl}^{\bullet}$$

These highly reactive chlorine free radicals can remove a hydrogen (they can also get attracted to each other) from a methane molecule. This process will generate a methyl free radical.

$$\mathrm{Cl}^{\bullet} + \mathrm{CH_4} \longrightarrow {}^{\bullet}\mathrm{CH_3} + \mathrm{HCl}$$

Now, this methyl free radical can remove a chlorine atom from a chlorine molecule to generate another chlorine free radical.

$${}^{\bullet}\mathrm{CH_3} + \mathrm{Cl_2} \longrightarrow \mathrm{CH_3Cl} + \mathrm{Cl}^{\bullet}$$

This process will continue as follows

$$\mathrm{CH_3Cl} + \mathrm{Cl}^{\bullet} \longrightarrow {}^{\bullet}\mathrm{CH_2Cl} + \mathrm{HCl}$$

$$ {}^{\bullet}CH_2Cl \quad + \quad Cl_2 \longrightarrow CH_2Cl_2 \quad + \quad Cl^{\bullet} $$

$$ CH_2Cl_2 \quad + \quad Cl^{\bullet} \longrightarrow {}^{\bullet}CHCl_2 \quad + \quad HCl $$

$$ {}^{\bullet}CHCl_2 \quad + \quad Cl_2 \longrightarrow CHCl_3 \quad + \quad Cl^{\bullet} $$

$$ CHCl_3 \quad + \quad Cl^{\bullet} \longrightarrow {}^{\bullet}CCl_3 \quad + \quad HCl $$

The above reactions are chain reactions. Therefore, this part of the free radical reaction is known as the propagation.

Finally, the following reaction happens. This reaction ends the chain reaction. Therefore, it is known as the termination reaction.

$$ {}^{\bullet}CCl_3 \quad + \quad Cl^{\bullet} \longrightarrow CCl_4 $$

Depending on the amount of chlorine present, the reaction can proceed to replace all hydrogen atoms in the carbon, thus generating carbon tetrachloride. Otherwise, the termination can happen in any of the following ways:

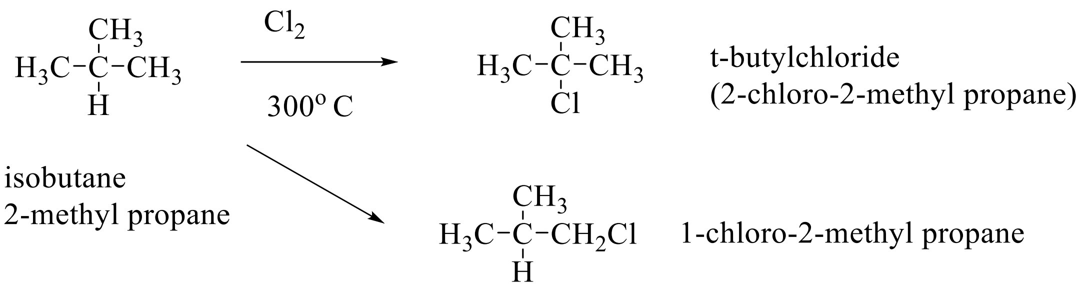
$$ Cl^{\bullet} \quad + \quad Cl^{\bullet} \longrightarrow Cl_2 $$

$$ \overset{\bullet}{C}H_3 \quad + \quad Cl^{\bullet} \longrightarrow CH_3Cl $$

$$ {}^{\bullet}CH_3 \quad + \quad {}^{\bullet}CH_3 \longrightarrow H_3C{-}CH_3 $$

The chlorine substitutes the hydrogen of the C-H bond with the highest electron availability in the cases of alkane isomers.

e.g. Tertiary hydrogen of isobutane is replaced about 4 or 5 times faster than its primary hydrogens. Therefore, tertiary butyl chloride is favored.



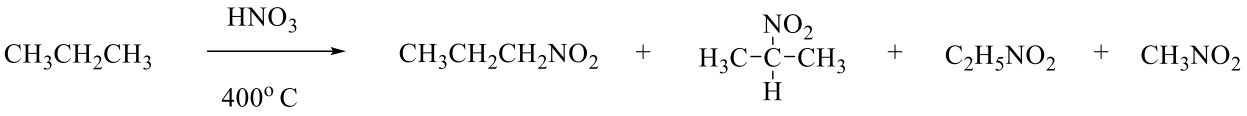
The substitution of hydrogens happens easily in tertiary than secondary, and in secondary than primary alkanes.

In addition to chlorination, the substitution of other atoms from group 7 can happen as well, but at different reaction rates. Direct fluorination is a very explosive reaction and need special conditions. Bromination is not as vigorous as chlorination. Iodination is a reversible reaction.

$$\text{e.g.} \quad CH_4 + I_2 \rightleftharpoons CH_3I + HI$$

2. Nitration

Under special conditions (at temp. of 425^0C), alkanes react with nitric acid.



$$CH_3CH_2CH_3 \xrightarrow[400^\circ C]{HNO_3} CH_3CH_2CH_2NO_2 + H_3C-\overset{NO_2}{\underset{H}{C}}-CH_3 + C_2H_5NO_2 + CH_3NO_2$$

The above reaction of propane generates a mixture of mononitro derivates:

Nitropropane – 25%, 2- Nitropropane – 40%,

Nitroethane – 10%, Nitromethane – 25%

3. Sulfonation

For this reaction to happen, sulfur trioxide in sulfuric acid known as fuming sulfuric acid is used. When this reagent is mixed with isobutane that has a tertiary hydrogen atom, that hydrogen atom is sulfonated to give tertiary butyl sulfonic acid.

$$\underset{\text{isobutane}}{(CH_3)_3CH} + SO_3 \xrightarrow{H_2SO_4} \underset{\text{t-butyl sulphonic acid}}{(CH_3)_3CSO_3H}$$

4. Combustion

Alkane burns in oxygen to produce carbon dioxide and water.

$$CH_4 + 2O_2 \longrightarrow CO_2 + 2H_2O$$

Methane above explodes when mixed with air or oxygen.

Reaction with oxygen in the presence of an oxidizing agent (e.g. potassium permanganate – $KMnO_4$)

$$\underset{\text{isobutane}}{(CH_3)_3CH} + [O] \xrightarrow{KMnO_4} CO_2 + \underset{\text{t-butanol}}{(CH_3)_3COH}$$

5. Isomerization

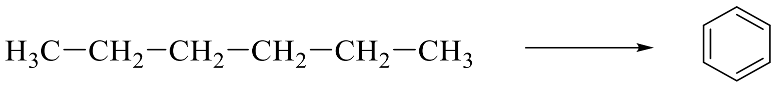
Normal alkanes (n-alkanes) when heated with aluminum chloride undergoes isomerization.

Therefore, only those n-alkanes with isomers react with anhydrous aluminum chloride/HCl to produce its isomer.

N – hexane $\xrightarrow{AlCl_3/HCl}$ 2-methylpentane + 3-methylpentane + minor products

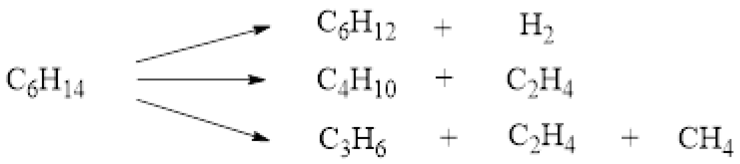
6. Aromatization

When straight chain alkenes with six or more carbon atoms are heated to 773K and 10-20 atm with the addition of oxides of chromium/vanadium/molybdenum, the chain gets dehydrogenated and converted to benzene and its homologues products.



7. Pyrolysis/Cracking

In this process, higher alkanes at higher temperatures will decompose into lower hydrocarbons (saturated or unsaturated).



Chapter 6

6.0 Alkenes

6.1 Objectives

1. Draw and interpret Lewis structures, line-bond structures and functional groups of alkenes using IUPAC system of nomenclature.
2. Draw reaction mechanisms.
3. Describe reactions, predicting reactivity, and reaction products.
4. Devise syntheses including steps, reagents, and products including regiochemistry and stereochemistry.

6.2 Introduction

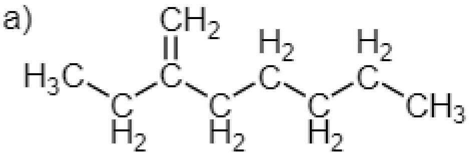
Alkenes are compounds with at least one carbon-carbon double bond. This double bond is made out of one sigma bond and one pi bond. The two carbon atoms that share the double bond are sp^2 hybridized atoms. The rigidity of π bond in alkenes leads to a different kind of isomerism in these compounds (please refer to isomerism). The existence of a double bond makes alkenes unsaturated compounds. If there are two double bonds, then they are called dienes. If there are three bonds, they are called trienes. Compounds with multiple double bonds are called polyenes. Alkenes are also called olefins (etymology - oil producing). Alkene has the common formula of C_nH_{2n}.

6.3 Nomenclature and Isomerism

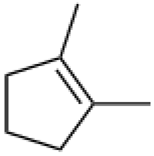
Please refer to the chapter on nomenclature and isomerism and answer the following questions:

1. **Name the following compounds:**

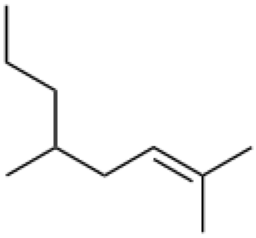
a)



b)



c)



2. **Draw structures for the following compounds from the given names:**

   a) 3-butylhept-2-ene (3-butyl-2-heptene)

   b) 1,4-pentadiene (penta-1,4-diene)

   c) 3-vinyl-1,4-cyclohexadiene (cyclohexa-1,4-diene)

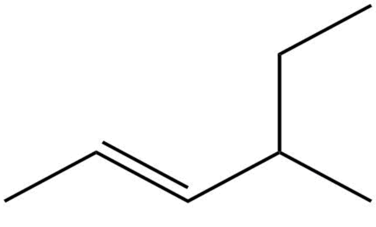
3. **Questions on isomers:**

   A) There are two geometric isomers of 2-butene, C_4H_8. There are two other alkenes with the formula C_4H_8. Draw their structures and determine whether they too can exist in *cis* and *trans* forms.

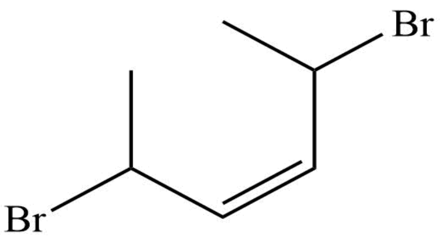
   B) Which of the following can have cis/trans isomers? Draw their isomers.

   (CH3CH2)CH=CH2, (CH3CH2)2C=CHCH3, (CH3CH2)CH=CHCH3

   C) Name the following compounds, with cis/trans nomenclature.



A

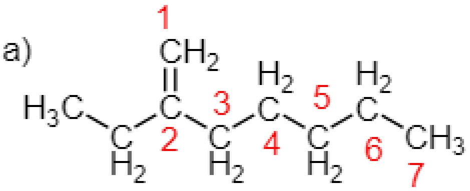


B

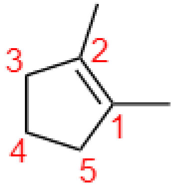
Solutions:

1. **Answers to Naming Compounds**

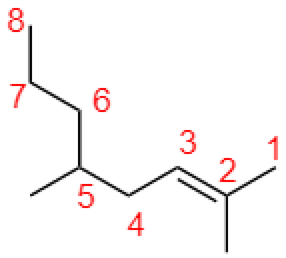
a)



b)



c)



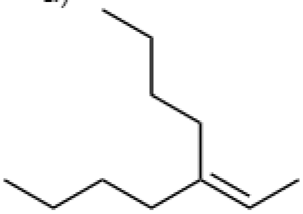
c) 2-ethylhept-1-ene or 2-ethyl-1-heptene

b) 1,2-dimethylcycloheptene

c) 2,5-dimethyloct-2-ene or 2,5-dimethyl-1-octene

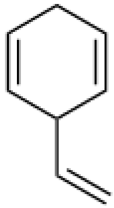
2. Answers to Drawing of Compounds

a)



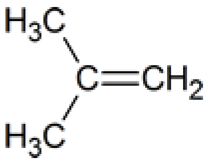
b)

c)



3. Answers to Isomers Questions

A)



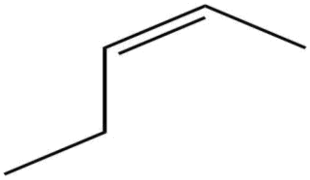
$$(H_3C)_2C{=}CH_2$$

There are no cis and trans forms for 2-methylpropene

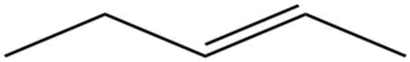
$H_3C{-}CH_2{-}CH{=}CH_2$

There are no cis and trans forms for 1-butene

B) The last compound in the list can be a cis/trans isomer.



cis



trans

C)
A – trans-4-methyl-2-hexene

B – cis-2,5-dibromo-3-hexene

6.4 Physical Properties

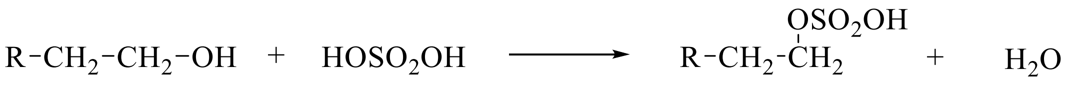
Alkenes below 5 carbon atoms are gases. The ones above 5 carbon atoms are volatile liquids. The isomers of alkenes are separated by fractional distillation since the boiling points are closer together.

6.5 Preparation of Alkenes

1.Dehydration of alcohols

Alcohol + Excess concentrated H_2SO_4 at 170°C → Alkyl hydrogensulfate + H_2O

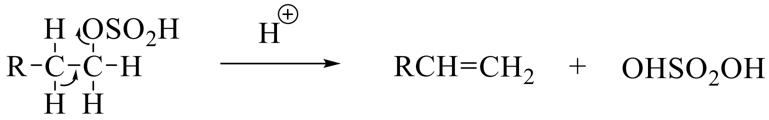
This alky hydrogen sulfate will decompose to form an alkene and generate H_2SO_4.



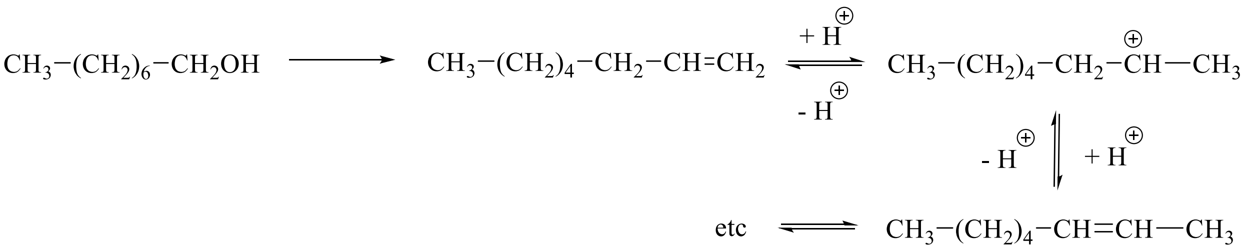
$$R-CH_2-CH_2-OH \quad + \quad HOSO_2OH \longrightarrow R-CH_2-\overset{\overset{OSO_2OH}{|}}{C}H_2 \quad + \quad H_2O$$

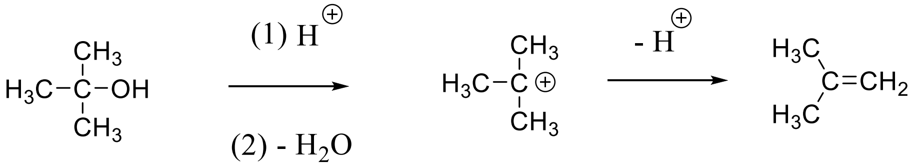
alkyl hydrogen sulphate

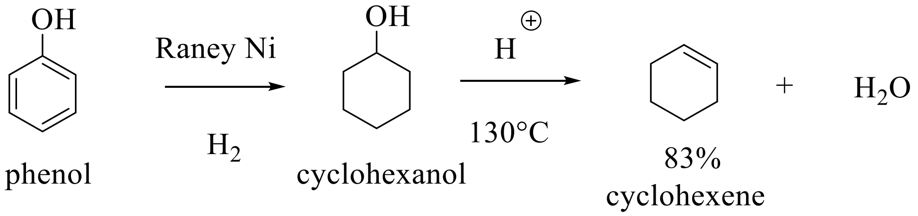
This is not the best method to produce ethylene, since some of the ethyl alcohol is converted to ether. Also, sulfuric acid as an oxidizing agent which will lead to the formation of carbon dioxide and sulfur dioxide. When use primary alcohols above propyl for this reaction, a mixture of alkenes results.

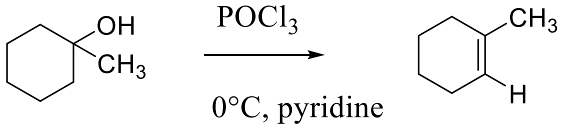


$$CH_3-(CH_2)_6-CH_2OH \xrightarrow[\Delta]{H_3PO_4} CH_3-(CH_2)_4-CH=CH-CH_3 + CH_3-(CH_2)_3-CH=CH-CH_2-CH_3$$









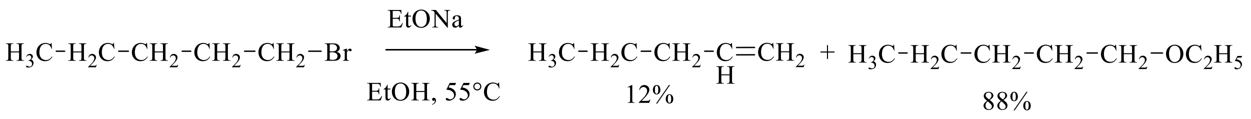
1- methyl cyclohexanol 1- methyl cyclohexene

2.Dehydrohalogenation of alkyl halides.

When an alkyl halide is treated with a base, a hydrogen halide will be eliminated, and an alkene will be produced. This reaction can easily be completed using compounds where halogen is attached to a tertiary or secondary carbon. For primary reactions, S_N2 reactions may happen (depending on the conditions) to produce ethers or alcohols as primary products.

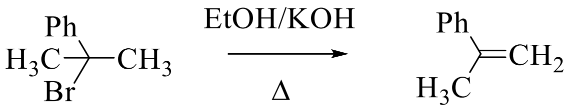
Ethanoic potassium hydroxide or sodium ethoxide are commonly used as in these reactions.

e.g.

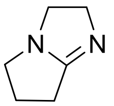


$$H_3C-H_2C-CH_2-CH_2-CH_2-Br \xrightarrow[\text{EtOH, 55°C}]{\text{EtONa}} \underset{12\%}{H_3C-H_2C-CH_2-\underset{H}{C}=CH_2} + \underset{88\%}{H_3C-H_2C-CH_2-CH_2-CH_2-OC_2H_5}$$

e.g.



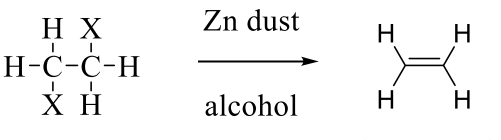
- Dehydration of alcohols and alkyl halides would in general produce highly substituted products. These reactions which are elimination reactions follow Saytzeff rule.
- Different bases effect dehydrohalogenation reactions. Hydroxides (OH-) and alkoxide (OR-), which are strong oxygen bases, do not provide strong yields. Diazabicyclononene (DBN) is a very effective base in this type of a reaction.



DBN

3.Dehydrohalogenation of vicinal halides

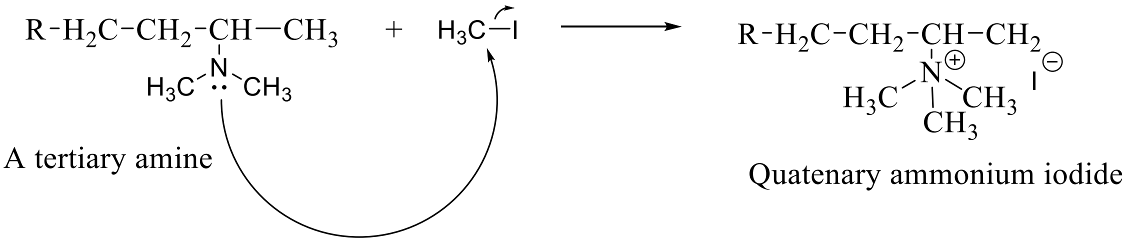
In this reaction, an alkyl halide is reacted with alcohol in the presence of Zn (or mg or iodide). The advantage of this reaction is that one can easily find where the double bonds are because the two leaving halide groups are near to each other.



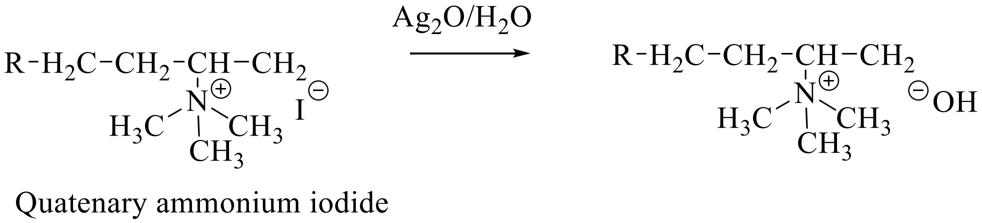
trans planar E_2 elimination

4. Hoffmann Elimination (also known as Hoffmann degradation or Hoffmann exhaustive methylation)

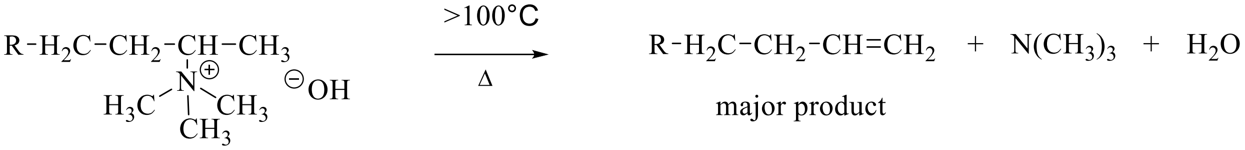
In this reaction, an amine is first converted to a quaternary ammonium halide. The amine could be in primary, secondary, or tertiary form and it is treated with excess methyl halide.



Next the halide is converted to the hydroxide when treated with silver oxide/water.

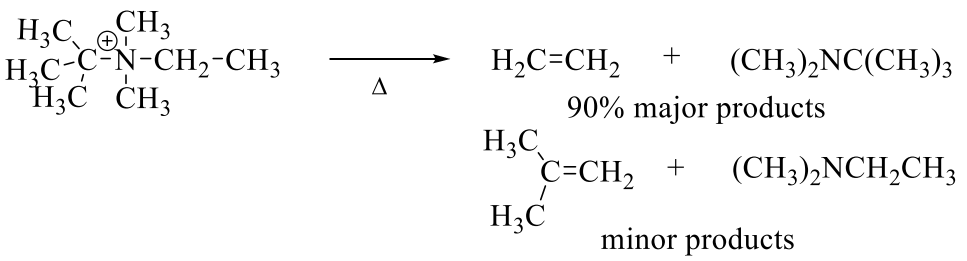


Finally, the quaternary ammonium hydroxide when heated above 100^0C will produce an alkene.

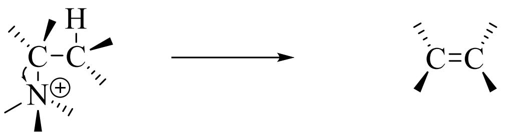


The least substitute alkene is the predominant product when there are several possible routes of elimination in this type of reaction. This is known as the Hoffmann's rule.

e.g.

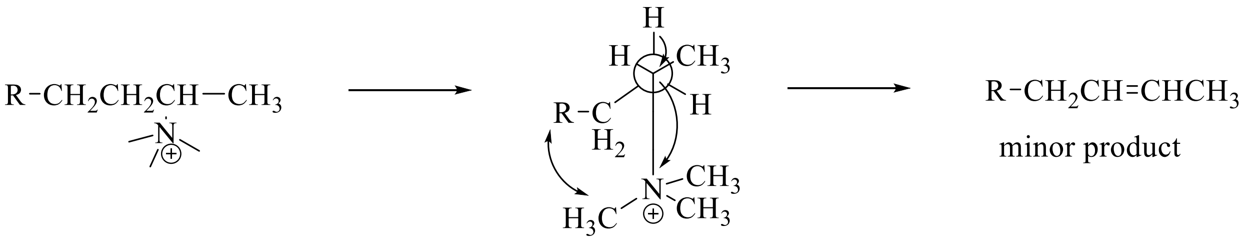


This is an E_2, β-elimination reaction



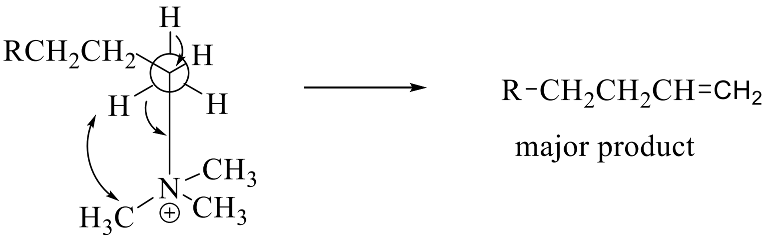
The reason for the selectivity in the elimination is dependent on two factors:

1. Steric effect on the stability of the transition state

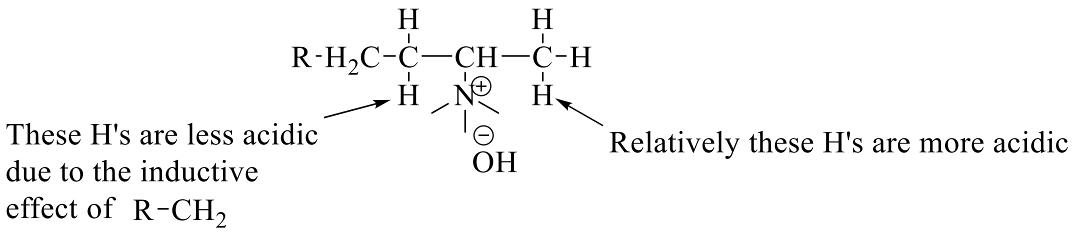


The more substituted alkene is created by a transition state with high energy and less stable. This is because the interaction between N atom with R groups and RCH_2 is sterically strained.

Nevertheless, in the reaction given below, the interchange with an H is easier than with an R as in the previous reaction. Therefore, this transition state is more stable and produce the least substitute alkene.



2. Relative acidities of alternative β-hydrogen that could influence the formation of the product

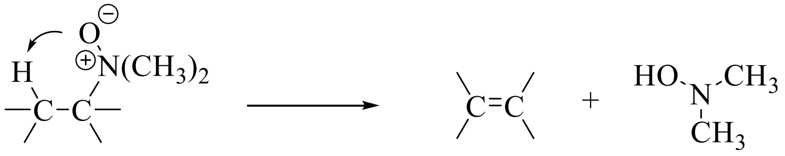


These H's are less acidic due to the inductive effect of R-CH$_2$

Relatively these H's are more acidic

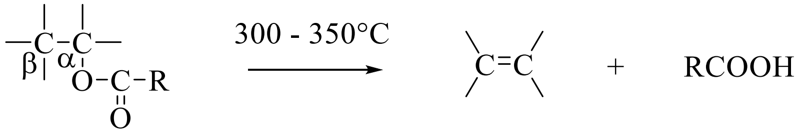
5.Cope Elimination

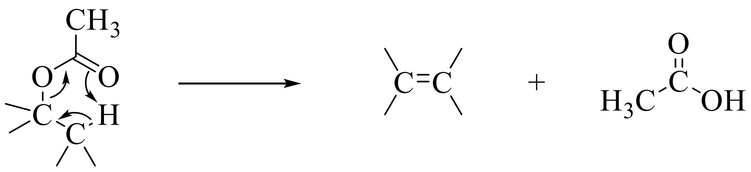
In this reaction, alkenes are prepared by thermal elimination of amine oxides. When heated to 150 – 200 ^{0}C, amine oxides undergo elimination, provided there is at least one β-hydrogen to the nitrogen. This reaction is performed in general with a mixture of amine and an oxidizing agent. In the presence of dry di methyl sulfoxide or tetrahydrofuran, this reaction can be carried out at room temperature.



6. Pyrolysis of Esters

Esters with a β-hydrogen can be pyrolyzed to give an acid and an alkene in the absence of any other solvent. This reaction is carried out in gaseous phase. The yield of this reaction is very high. Also, there are only a very few rearrangements and any side reactions. Therefore, this is a synthetically very useful reaction. The mechanism is E_i meaning elimination is internal/intermolecular. The transition state in this reaction is a six-membered group.

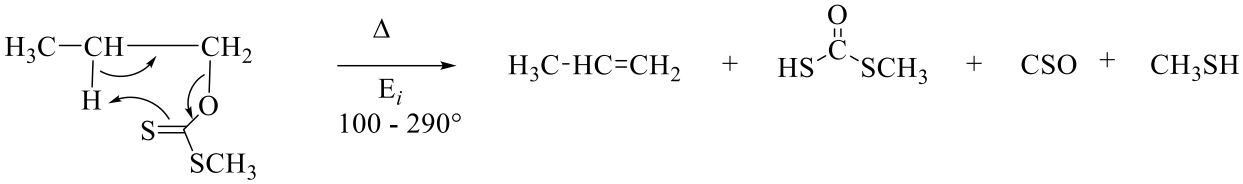




7. Chugaev Reaction

Pyrolysis of methyl xanthate to produce alkene is known as Chugaev reaction.

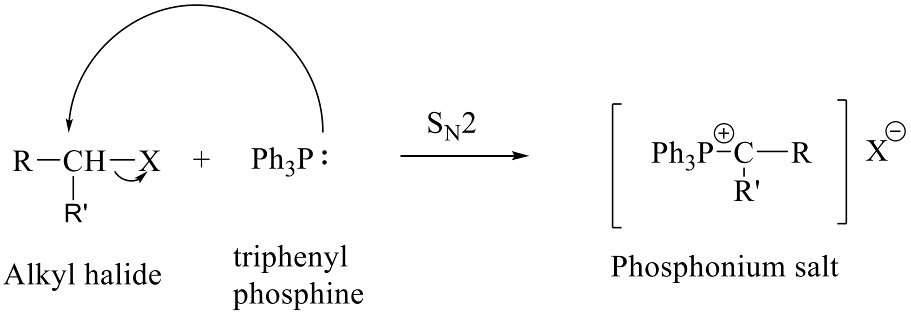
In this reaction, the pyrolytic elimination of xanthate is at lower temperature than esters. This is a widely used technique to dehydrate alcohols.



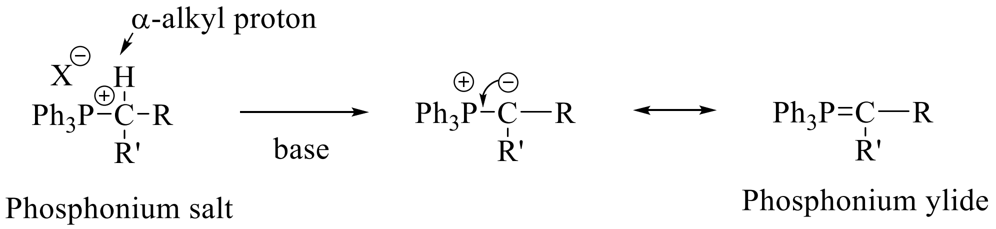
8.The Wittig Reaction

In this reaction, an aldehyde or ketone is heated with a phosphonium ylide to produce an alkene.

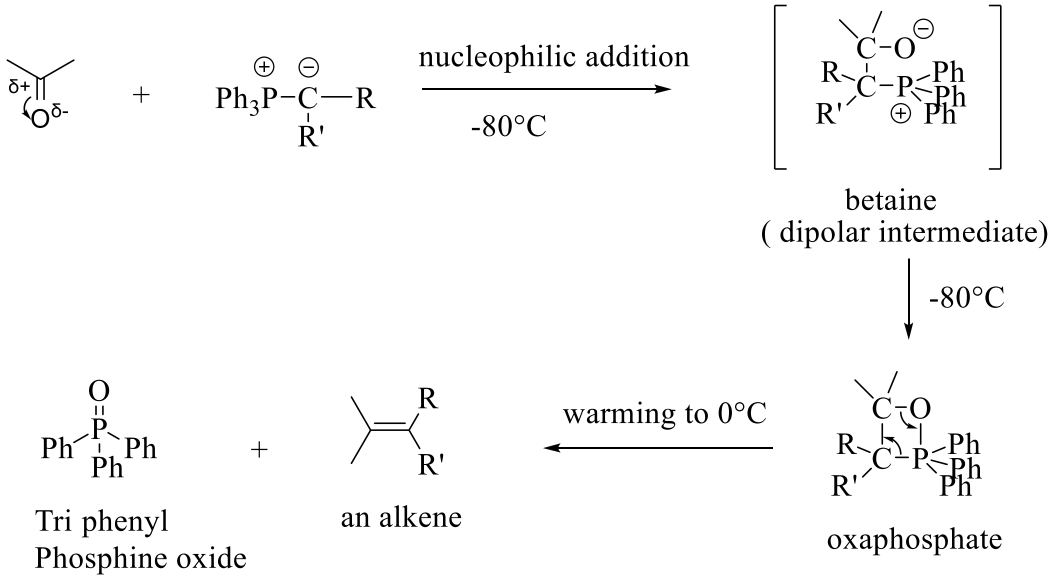
Phosphonium ylides are hybrids of two canonical forms (two resonance structures each of which contribute to the real structure). This is prepared as follows:



Phosphine are good nucleophiles and weak bases. Therefore, most primary and secondary alkyl halides produce good yield of phosphonium salt. The alkyl proton α to the positive phosphorous is removed by a strong base (e.g. butyllithium or sodium hydride). This reaction will produce a neutral phosphorous ylide known as phosphorane.

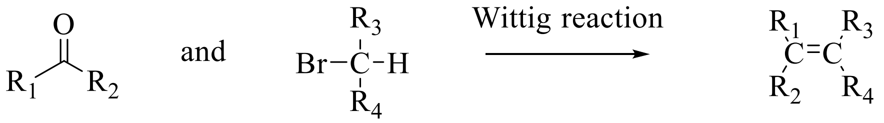


Ylides react quickly with aldehydes and ketones at -80 ^{0}C. This reaction produces a neutral oxaphosphatanes which in turn upon warming decomposes to produce alkene and triphenyl phosphine oxide.

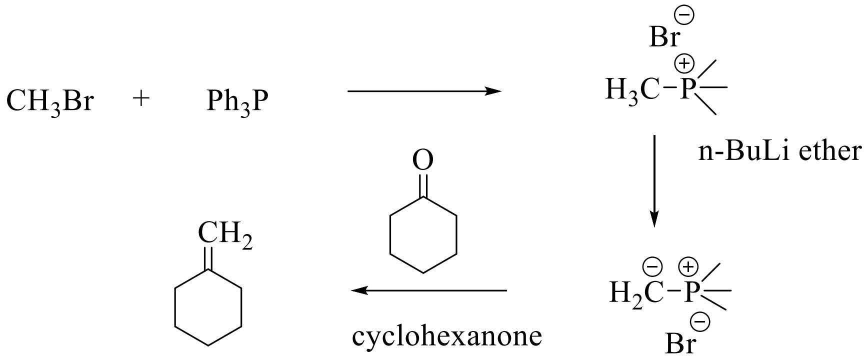


A mixture of cis and trans isomers are produced mostly; yet, only a single positional isomer is produced. The aldehyde or ketone used can be aliphatic, alicyclic or aromatic.

Whilst ylide can contain functional groups such as -OH, -OR, -NR_2, -NO_2, Halo or even -COOR, the position of the new double bond also can be predicted easily.



Further, Wittig reaction is useful for the introduction of exocyclic bonds:



9.Thermal Cracking of Hydrocarbons

Thermal cracking is used in industrial preparation of alkenes and in refining petroleum.

$$H_3C-CH_3 \xrightarrow[\text{1 atm}]{\text{700 - 900°C}} H_2C{=}CH_2 \quad + \quad H_2$$

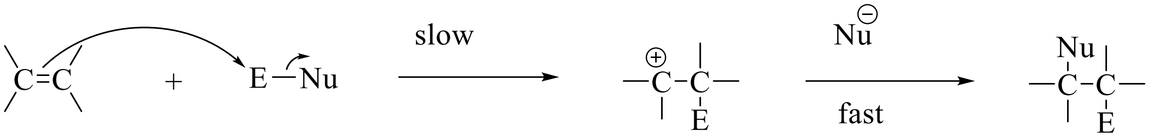
Cracking of higher hydrocarbons will produce significant amounts of propene.

$$n\text{-}C_6H_{14} \xrightarrow[\text{1 atm}]{\text{700 - 900°C}} \underset{15\%}{CH_4} \quad + \quad \underset{40\%}{H_2C{=}CH_2} \quad + \quad \underset{20\%}{H_3C\text{-}HC{=}CH_2} \quad + \quad \underset{25\%}{\text{others}}$$

6.6 Reactions of Alkenes

Alkenes undergo addition reactions. This is mainly due to the existence of unsaturated double bonds. Nevertheless, alkenes also undergo substitution reactions under special conditions.

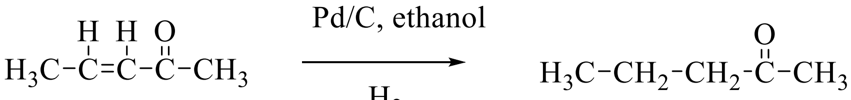
The addition reaction has two steps. The slow step, which is the first step, is the addition of an electrophile to one of the carbon atoms with a double bond. The next fast step is the addition of a nucleophile. The slowest step produces a carbonium ion intermedium. Therefore, the stability of the carbonium ion plays a significant role in this reaction.



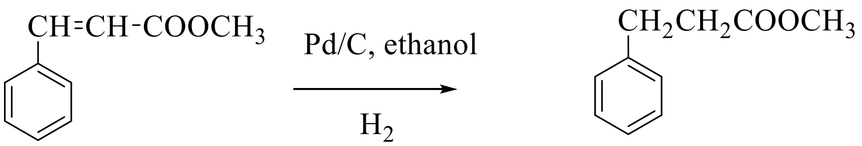
6.61 Addition Reactions

1. Addition of H_2

This is a reduction reaction. Platinum or palladium is used as a catalyst in this reaction.



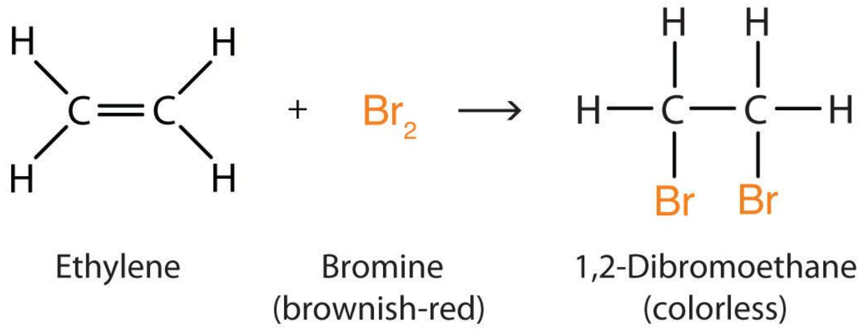
ketone not reduced



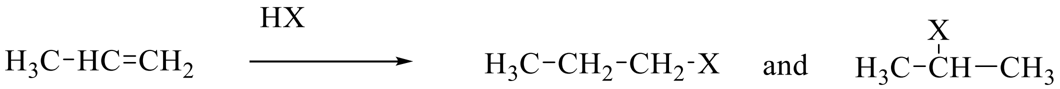
benzene ring and ester ($COOCH_3$)
not reduced

2. Addition of Halogens

The addition of halogens follows either electrophilic path or free radical process depending on the conditions.



3. **Addition of HX (haloacids/Bronsted acids)**



$$H_3C-HC=CH_2 \xrightarrow{HX} H_3C-CH_2-CH_2-X \quad \text{and} \quad H_3C-\overset{X}{\overset{|}{C}}H-CH_3$$

The addition reaction of HX with alkene is an electrophilic reaction that follows Markovnikov rule.

Markovnikov rule states that the proton (H$^+$) will add to the less substituted carbon (carbon with more hydrogen atoms) and the halogen will add to the more substituted carbon (more R groups). This rule shows that the stability of the intermediate determines the progress of the reaction. This is a two- step reaction. In the first step a carbo cation (C$^+$) is produced. The second step is the addition of nucleophile (halide). The rate of the reaction increases as the number of R groups attached to the C with triple bond increases. This is due to the ability of R groups to push electrons toward the double bond also known as positive inductive effect (+I). As a result, the addition of halide becomes easier. The +I effect of R also helps to stabilize the carbo cation in the intermediate stage. This effect is clear when asymmetric alkynes react with HX. Therefore, according to Markovnikov's rule the preferred regioselectivity is the combination of halide to the carbon with more R groups.

Also, when X is large (such as iodide (I) instead of fluoride(F)) the reaction happens faster since the bond between H and I is weaker than the bond between H and F. So, the size of the X determines the speed of the reaction.

The rate increases in the following order:

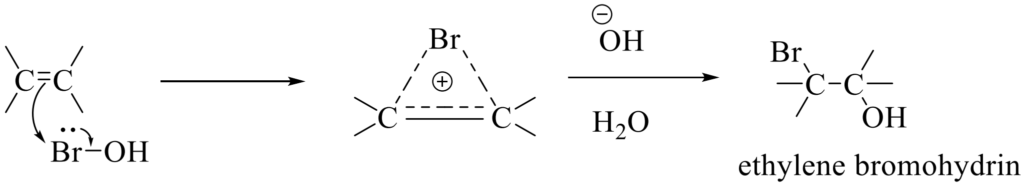
$$F < Cl < Br < I$$

Anti-Markovnikov rule produces the product where halide is connected to the carbon with more hydrogen atoms. This reaction happens in the presence of peroxides (H_2O_2) via a radical mechanism.

4. Addition of HOX (hypohalous acids)

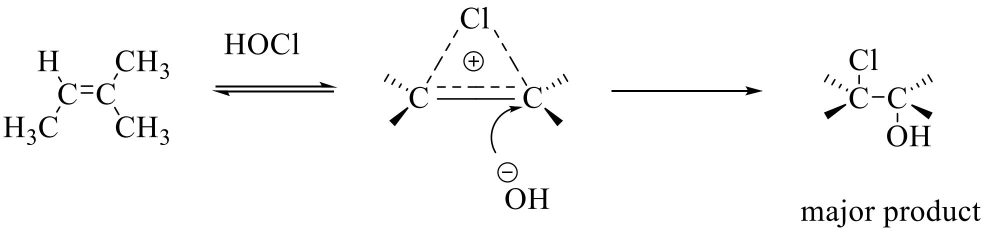
When alkenes are reacted with hypochlorous (HOCl), hypobromous (HOBr), and hypoiodous (HOI), halohydrins are produced.

e.g.



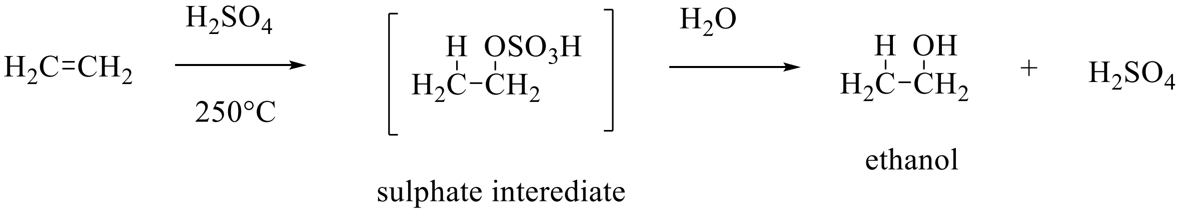
Bromine acts as the positive end of the dipole and becomes the attacking electrophile. This addition also follows, Markovnikov’s rule.

e.g.

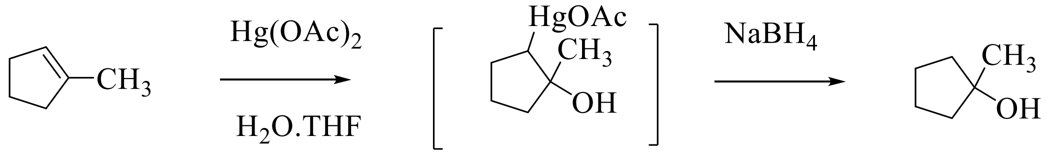


5. Addition of Water - Hydration

When alkenes react with water, alcohol is produced. In industrial production, alkenes are hydrated using sulfuric acid.



In labs, alkenes are hydrated by oxymercuration. This is done by treating an alkene with mercuric acetate in the presence of aqueous tetrahydrofuran as a solvent. The intermediate organomercury is treated with $NaBH_4$, which yields an alcohol. The reaction follows anti Markovnikov addition of water (anti-addition rule– hydroxyl becomes attached to the more substituted carbon atom).



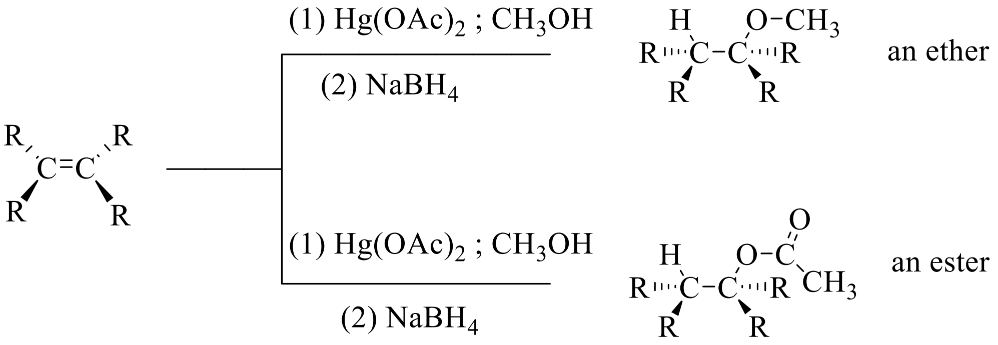
1- methyl cyclopentane

organo mercury intermediate

90%

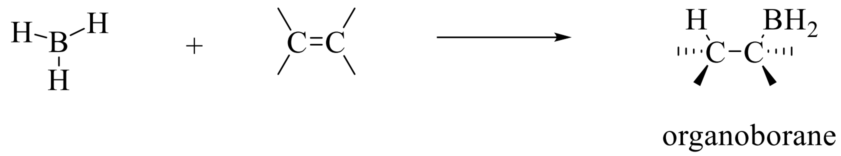
1-methyl cyclopentanol

If the oxymercuration-demercuration sequence happens in methanol instead of water, methyl ether is formed. If the reaction happens in acetic acid an acetate ester is formed.

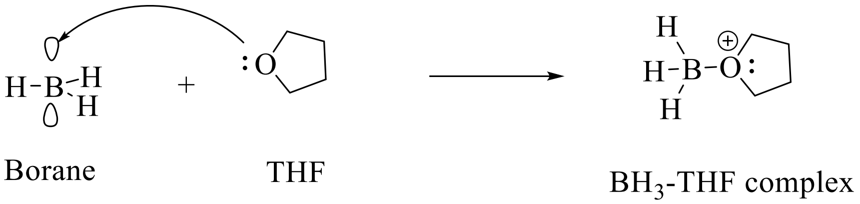


6. Addition of BH_3 - Hydroboration

When alkene is reacted with borane, an organoborane is produced due to the addition.

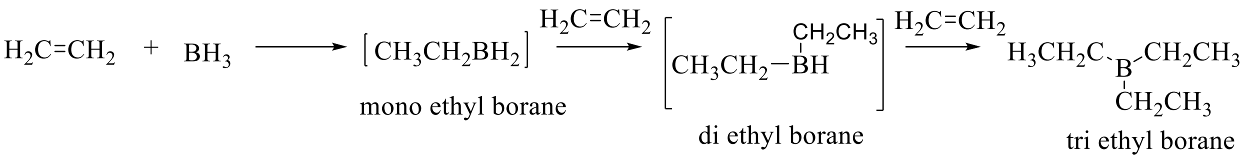


The reaction of BH_3 with THF (tetrahydrofuran also known as oxolane):

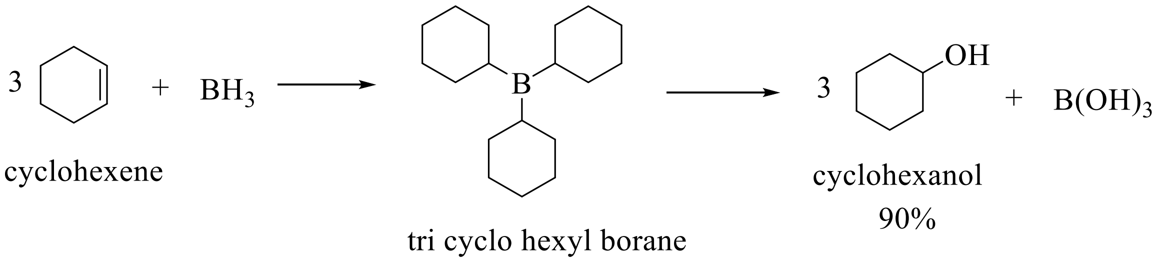


This complex behaves chemically in the same way as BH_3.

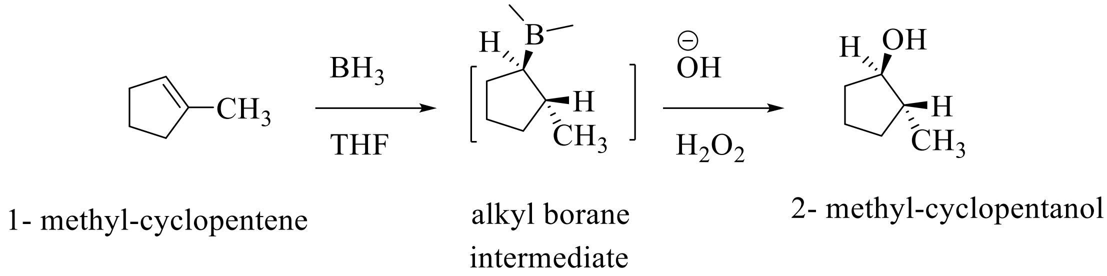
Addition of BH_3 to a double bond of an alkene will continue until all three Hs are replaced.



Trialkyl boranes are useful since they can undergo further reactions.

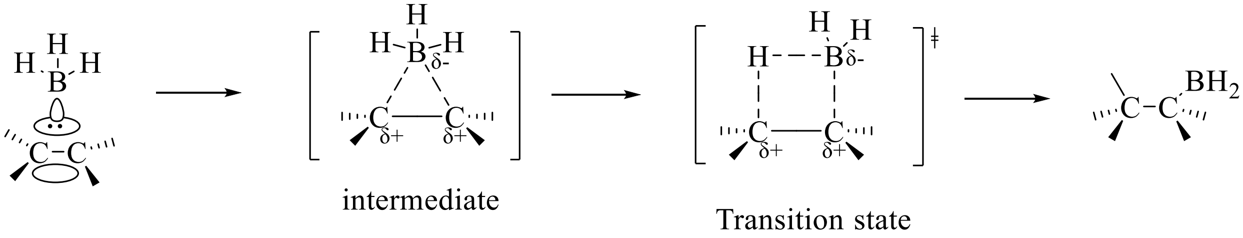


Hydroboration is useful because of the regiochemistry of the product.

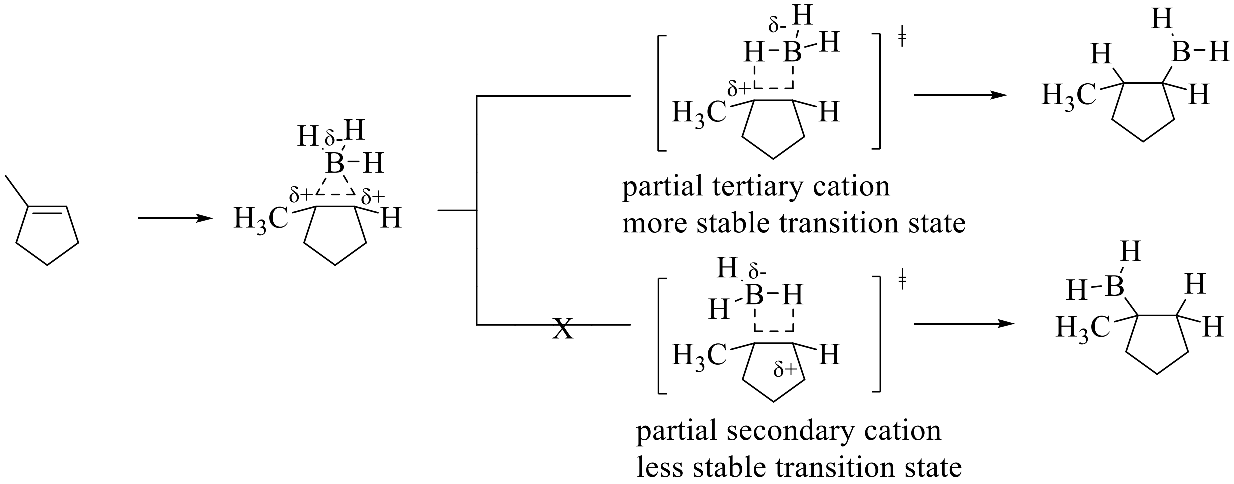


Boron-hydrogen bond adds to alkene in a syn manner. The boron will be attached to the less substituted carbon. During the oxidation step boron is replaced by hydroxy with the same stereochemistry. Therefore, the final product is an anti-Markovnikov syn addition of water. This is both regio specific (syn addition) and stereo specific (anit-markovinikov) reaction.

Mechanism is given below for the addition of BH_3 to an alkene.

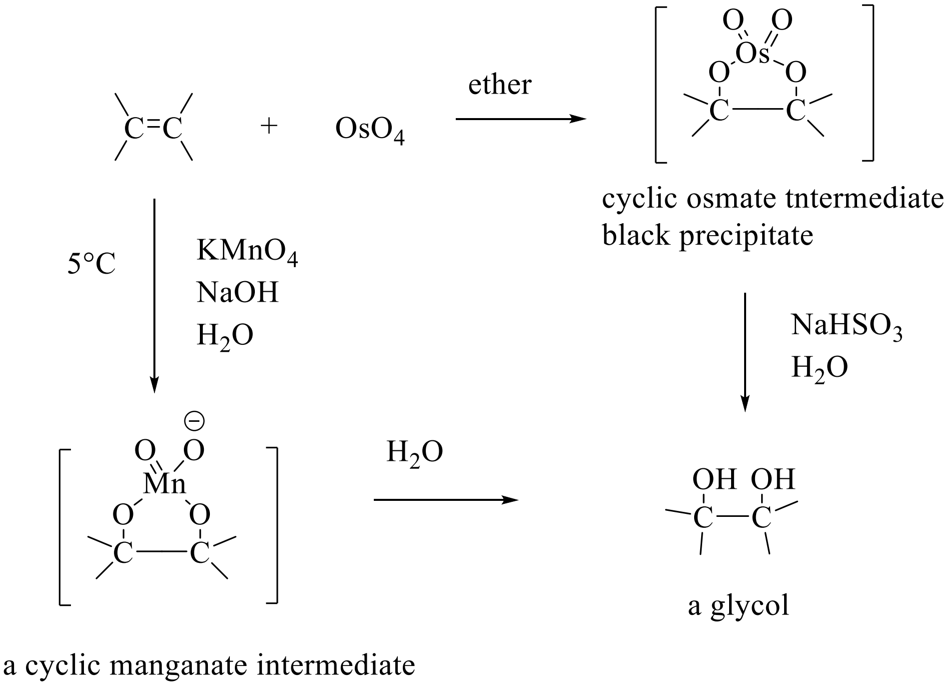


The formation of C-H and C-B bond at the same time indicates syn-addition indicating regio specificity. Boron attaches to the less substituted C.



7. Addition of OH - Hydroxylation

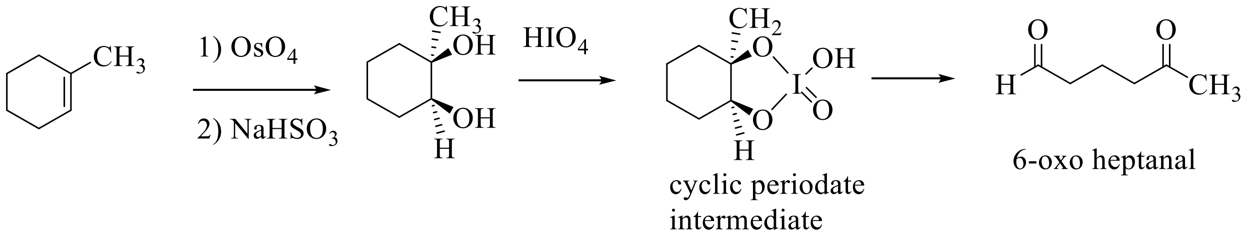
When alkene is reacted with osmium tetroxide (OsO_4) (or cold alkaline potassium permanganate) in the presence of ether, NaHSO3, and water, two OH groups can be added to the double bond producing sys 1, 2 -dialcohols (diols).

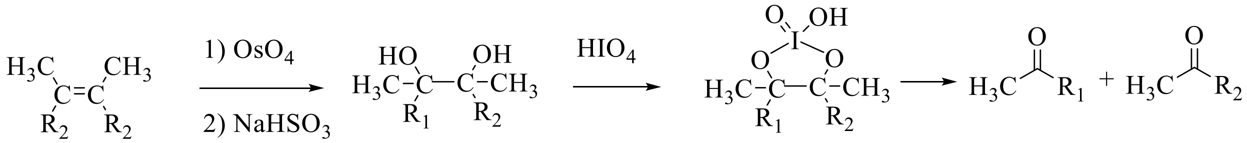


OsO_4 is used in the lab for preparation of diols.

1,2 -diols can be cleaved to carbonyl compounds when periodic acid is used. Therefore, combination of periodic acid with OsO_4 hydroxylation will provide a good alternative to ozonolysis.

If 2 hydroxyls are on a ring, dicarbonyl compounds can be formed. If the two hydroxyls compounds are on an open chain, then two separate carbonyl compounds are formed.

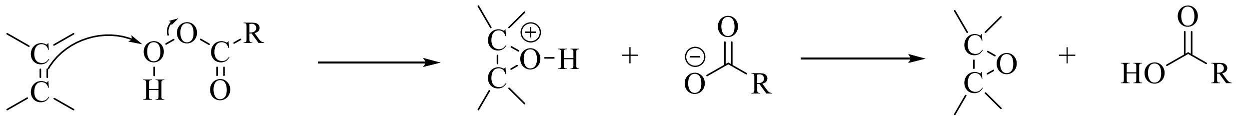




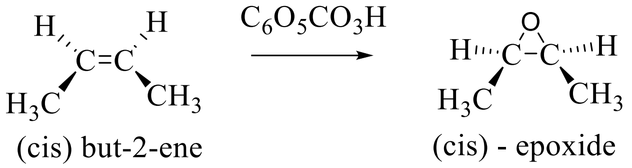
8. Addition of O - Epoxidation

When an alkene is reacted with peroxy acids (RCO_3H, peroxybenzoic acid), an epoxide can be produced.

The mechanism of the reaction is a displacement reaction on an electrophilic O by a nucleophilic alkene.



This reaction is stereospecific. Trans alkene will produce a trans epoxide and a cis alkene will produce a cis epoxide. The reaction is a displacement of an electrophilic oxygen by a nucleophilic alkene.



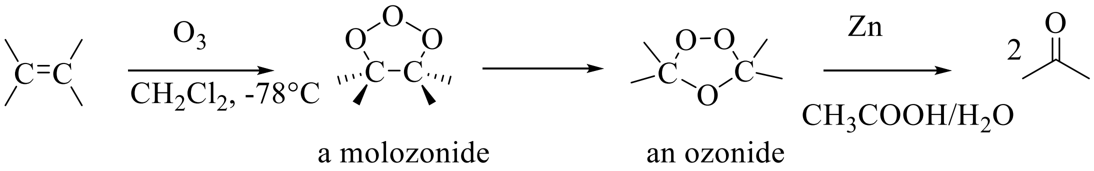
Epoxide can be prepared by the ring closure of halo hydrins (halo alcohols) in the presence of a base.

6.62 Cleavage Reactions

1. Ozonolysis

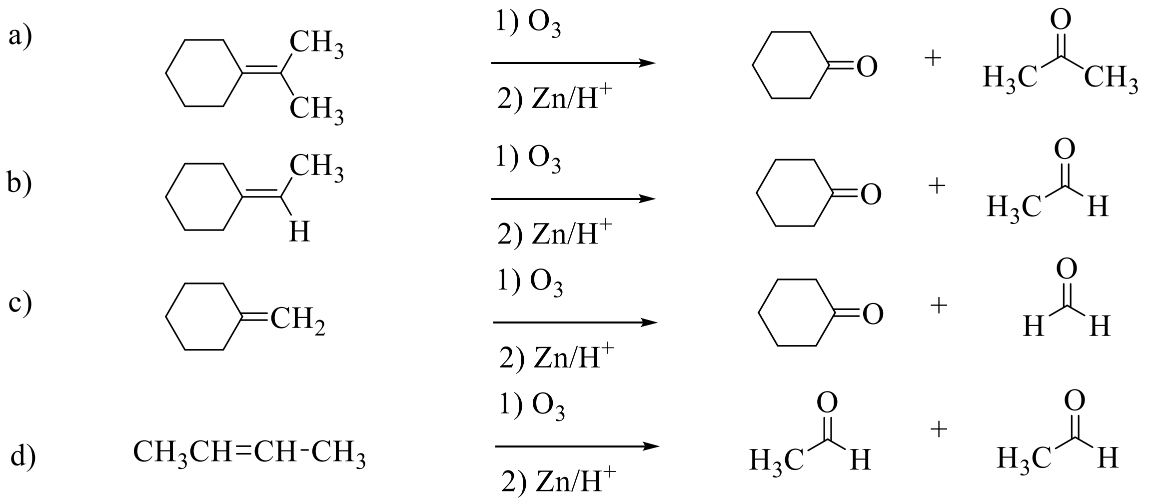
In this this reaction, the double bond is broken to produce two fragments of alkene. Ozone is a useful cleavage reagent.

$$3O_2 \xrightarrow[\text{discharge}]{\text{electric}} 2O_3$$

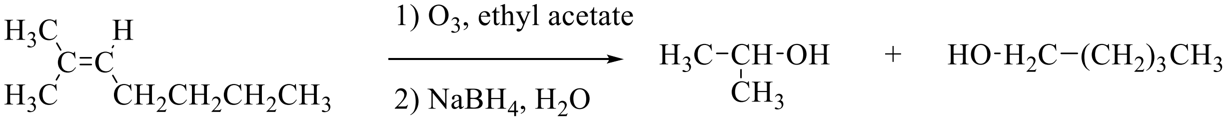


The following is a list of alkenes and their products when undergo ozonolysis:

Alkene		Product
a) Tetra substituted double bond	→	2 ketone fragments
b) Tri substituted double bond	→	1 ketone fragment + 1 aldehyde
c) Di substituted double bond (both substituents on one carbon)	→	1 ketone + formaldehyde
d) Di substituted double bond (one substituent on each carbon)	→	2 aldehydes



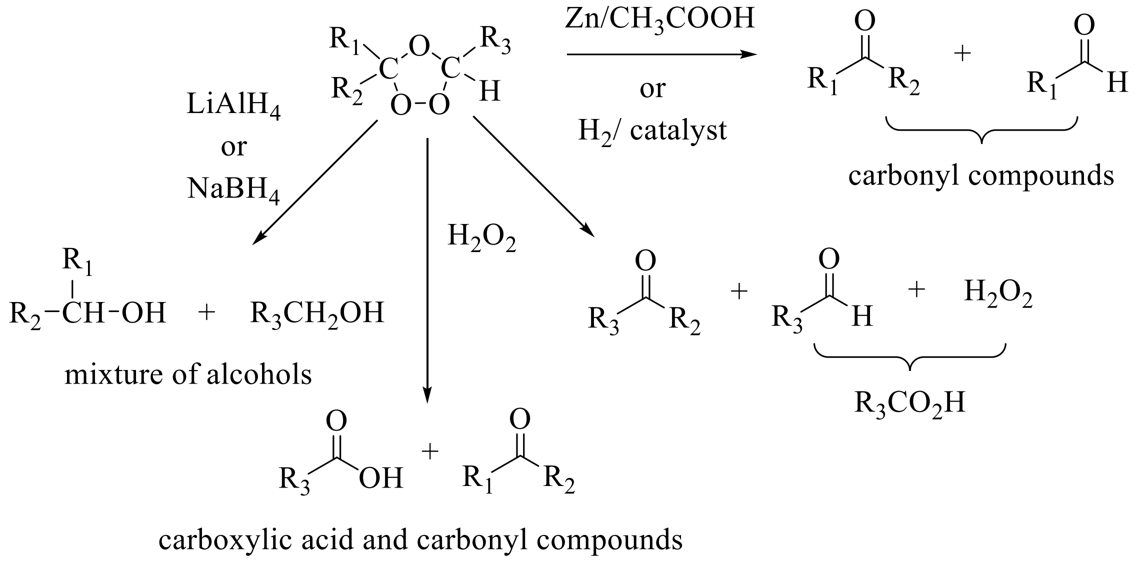
In the following reaction, an alkene is converted to ozonide and then to alcohols by treating with NaBH$_4$.



2-methyl-2-heptane

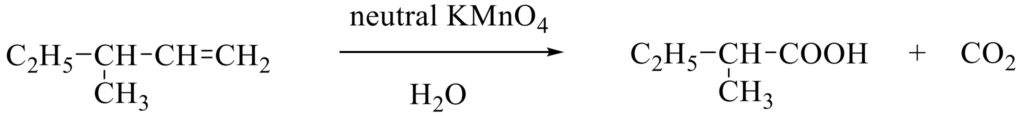
2.Ozonides in other ring cleavage products

Ozonides also react with different reagents to produce ring cleavage products:



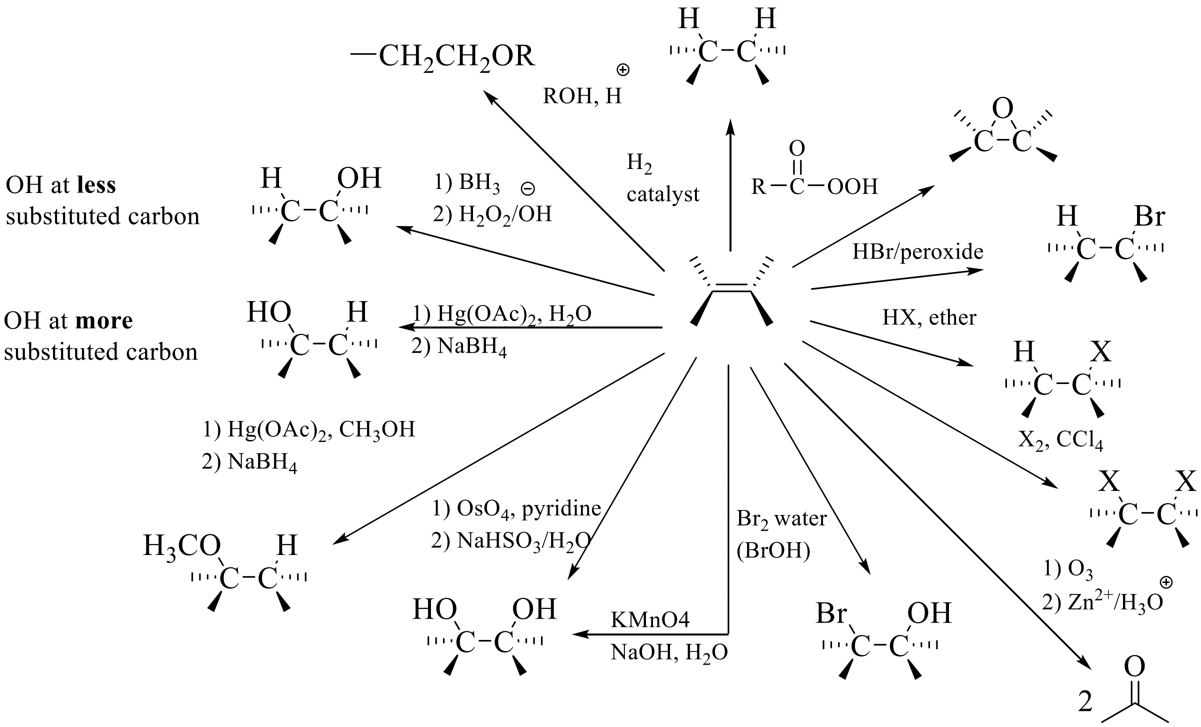
3.Cleavage using permanganate

Alkenes can also be cleavaged using neutral or acidic permanganate. If Hs are present on the double bond, carboxylic acid is produced. If the two Hs are on the same carbon, CO_2 is formed.



$$C_2H_5-\underset{CH_3}{\underset{|}{CH}}-CH=CH_2 \xrightarrow[H_2O]{\text{neutral } KMnO_4} C_2H_5-\underset{CH_3}{\underset{|}{CH}}-COOH + CO_2$$

6.7 Summary of Reactions



Chapter 7

7.0 Alkynes

7.1 Objectives

1. Draw and interpret Lewis structures, line-bond structures and functional groups of alkynes using IUPAC system of nomenclature.
2. Draw reaction mechanisms.
3. Describe reactions, predicting reactivity, and reaction products.
4. Devise syntheses including steps, reagents, and products including regiochemistry and stereochemistry.

7.2 Introduction

Alkynes are a group of hydrocarbons with one or more carbon-carbon triple bond. Two of the three bonds are π bonds and the other is a σ bond. The two carbon atoms forming the triple bond have undergone sp hybridization and the shape is linear. Therefore, no geometrical isomerism is seen in these compounds. The triple bond is known as acetylenic bond. Alkyne group has the common formula of C_nH_{2n-2}.

In this series of alkynes, acetylene (also known as ethyne) is considered the most important member. This compound has a high content of carbon. Therefore, when ethyne is burnt, it emits luminous smoky flame. The compound is used in oxy-acetylene blow pipe when the flame reaches a temperature of 2000 ^{0}C.

Ethyne's reaction with oxygen:

$$C_2H_2 \quad + \quad 5/2\,O_2 \quad \longrightarrow \quad 2CO_2 \quad + \quad H_2O$$

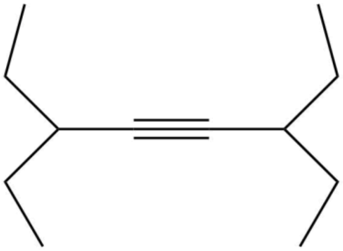
Ethyne is used in the synthesis of acetaldehyde, ethanol, and acetic acid. Ethyne is a colorless gas with a boiling point of -84 ^{0}C and is sparingly soluble in water. Ethyne could be explosive when compressed or liquified. Ethyne is called acetylene.

7.3 Nomenclature and Isomerism

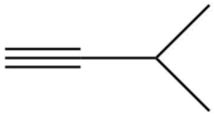
Please refer to the chapter on nomenclature and isomerism and answer the following questions:

1. **Name the following compounds**:

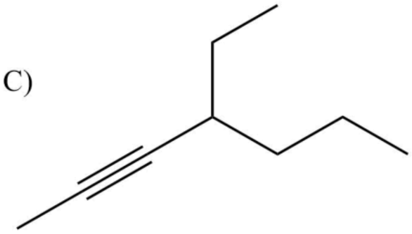
A)



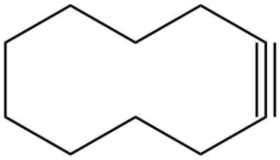
B)



C)



D)



2. **How many isomers are possible for C_5H_8? Draw them.**

3. Draw the following compounds:

A) 4,4-dimethyl-2-pentyne

B) 3-octyne

C) 3-methyl-1-hexyne

D) *trans* 3-hepten-1-yne

4. **Do alkynes show cis-trans isomerism? Explain.**

Solutions:

1. **Answers to Naming Compounds**

A – 3,6-diethyl-4-octyne

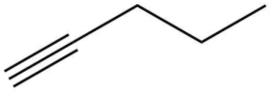
B – 3-methylbutyne

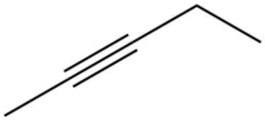
C – 4-ethyl-2-heptyne

D – cyclodecyne

2. Answers to Possible Isomers

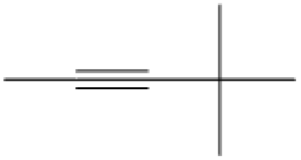
2 possible isomers



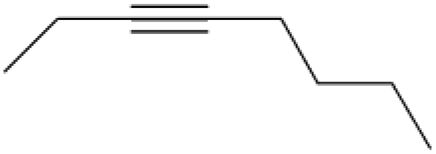


3. Answers to Drawing of Compounds

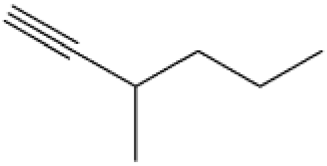
A)



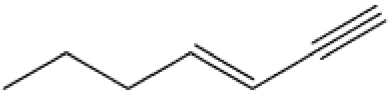
B)



C)



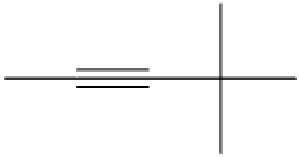
D)



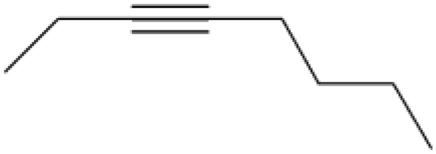
4. Answer to Cis-Trans Isomer Question

No. A triply bonded carbon atom can form only one other bond and has linear electron geometry so there are no "sides". Alkenes have two groups attached to each inyl carbon with a trigonal planar electron geometry that creates the possibility of cis-trans isomerism.

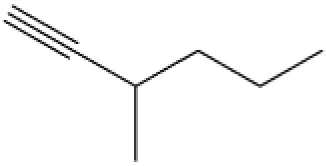
A)



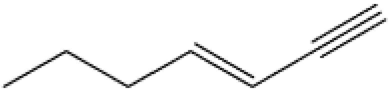
B)



C)



D)



7.4 Physical Properties

The physical properties are similar to alkenes. Terminal alkynes have lower boiling points. Internal alkynes can be separated only by fractional distillation. All terminal alkynes are weakly acidic. Lower compounds in this series are gases with boiling points slightly higher than the alkenes.

$$R-C\equiv C-H$$

terminal alkyne

$$R-C\equiv C-R$$

internal alkyne

7.5 Preparation

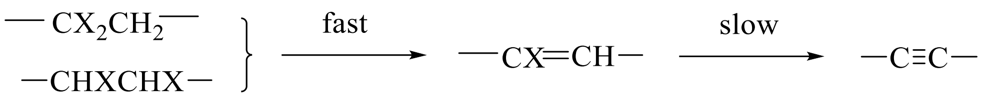
1. Elimination from dihalides

For this elimination reaction, two molecules of HX (hydrogen halides) are removed from a compound with twin (geminal) or a near (vicinal) dihalide.

$$-CBr_2\text{-}CH_2 \xrightarrow{-2HBr} -C\equiv C-$$

a geminal bromide

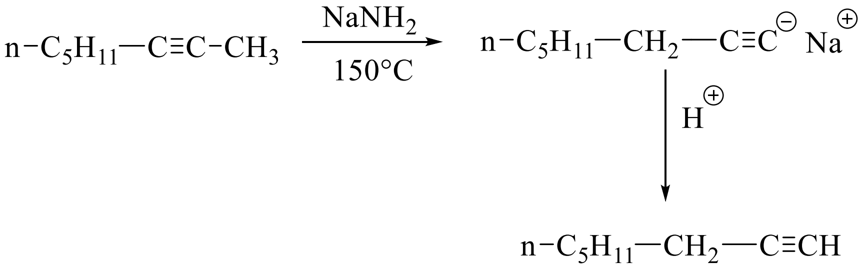
This reaction happens in two stages. The second elimination of HX is more difficult than the first elimination of HX.



The reaction conditions used are molten KOH or concentrated alcoholic KOH at a temperature of 100 – 200 ^{0}C.

$$CH_3CH_2C\equiv CH \underset{\Delta}{\overset{\text{alcoholic KOH}}{\rightleftharpoons}} CH_3C\equiv CCH_3$$

Internal alkynes can be isomerized to terminal alkynes by reacting with sodium amide ($NaNH_2$) at 150^{0}C. Sodium amide is an effective strong base to prepare 1-alkynes.



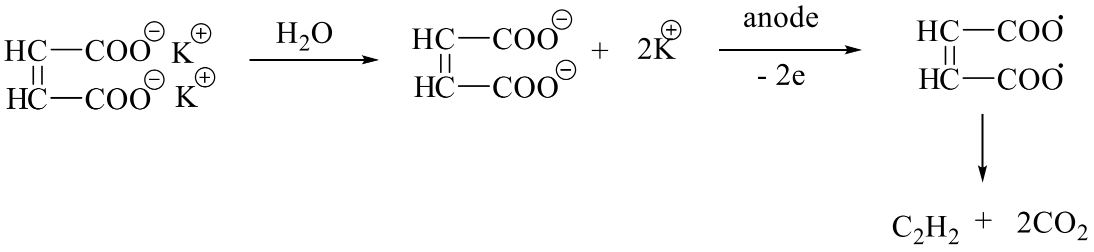
2. From cuprous acetylide

Pure ethyne can be obtained by dissolving cuprous acetylide in a warm aqueous solute of potassium cyanide.

$$CuC_2 + 4\,KCN + 2\,H_2O \longrightarrow C_2H_2\uparrow + K_2[Cu(CN)_4] + 2KOH$$

3. Kolbe Method

Electrolysis of a concentrated solution of sodium or potassium salt of fumaric or maleic acid will generate ethyne at the anode.



4. From calcium carbide

Ethyne is prepared industrially by mixing calcium carbide with water.

$$CaC_2 + H_2O \longrightarrow C_2H_2\uparrow + Ca(OH)_2$$

7.6 Reactions of Alkynes

The reactions of alkynes can be categorized into three types:

1. Addition Reactions
2. Substitution Reactions
3. Oxidation Cleavage Reactions

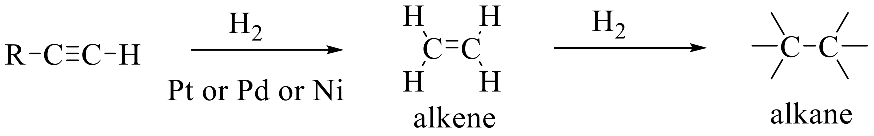
7.61 Addition Reactions

Since π bond electrons in alkynes are easily accessible to incoming electrophiles, the reactions proceed in a manner similar to alkenes. The chemistry of alkynes is similar to alkenes, but there are some differences.

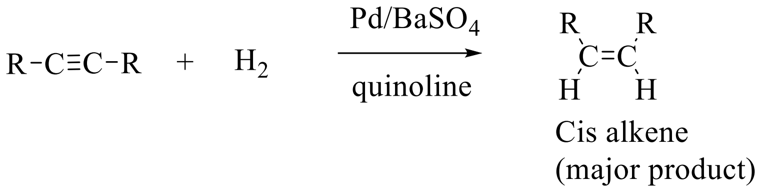
A) Hydrogenation

1. Catalytic Hydrogenation

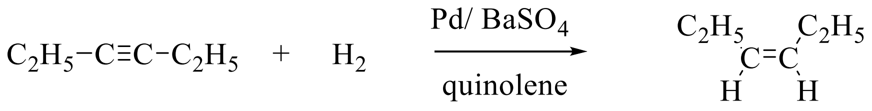
Ethyne reacts with hydrogen in the presence of a catalyst such as Pt (or Ni or Pd) to produce its corresponding alkane.



Since this reaction moves from alkyne to alkene and then finally alkane, with the use of Lindlar's catalyst (Pd on $CaCO_3$ or $BaSO_4$ mixed with quinoline, sulfur or lead), the reaction can be stopped after the conversion to an alkene. In this reaction, the hydrogen is attached to the triple bond to produce cis alkene.

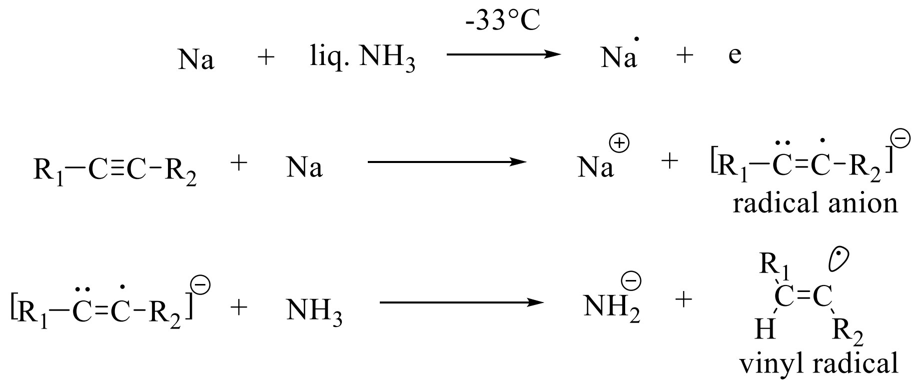


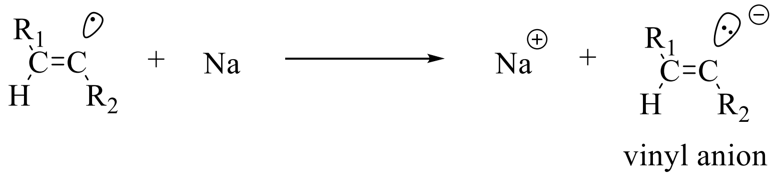
Another way to convert a triple bond to a double bond is to supply only one mole of hydrogen to the reaction mixture.

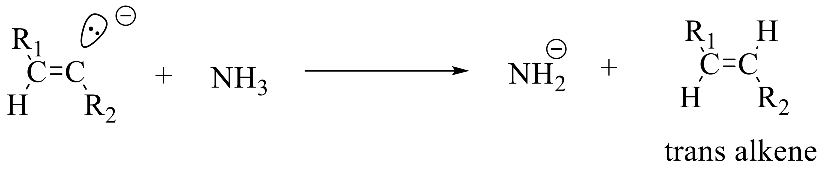


2. Birch Reduction

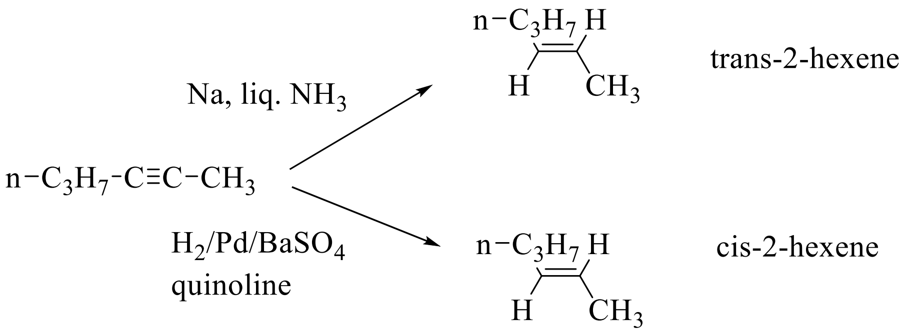
In this reaction, alkyne is reacted with fine pieces of an alkali metal such as sodium in liquid ammonia at a low temperature (about -33^{0}C). This is also known as dissolving metal reduction.





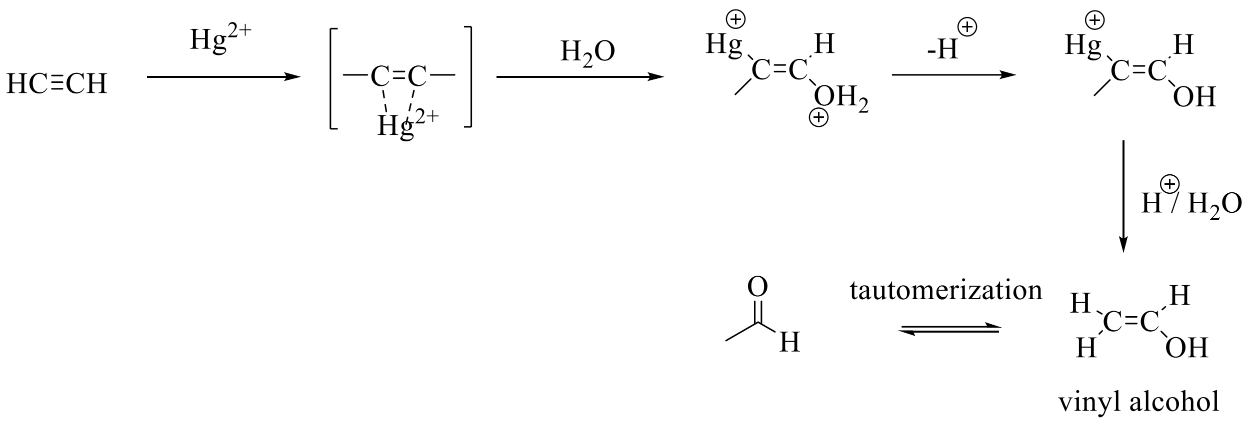


In this reaction, trans alkene is produced completely. Since simple alkenes are not reduced by sodium in liquid ammonia, the reaction produces alkenes. It is important to note the difference of sodium in liquid ammonia, which has sodium ions and solvated electrons from $NaNH_2$ in liquid ammonia, which has sodium ions and NH_2^- ions. $NaNH_2$ in liquid ammonia will not reduce alkynes but deprotonate to produce terminal alkynes. Therefore, this reaction can be used to produce larger chains from small ones, with specific cis or trans structure of compounds.

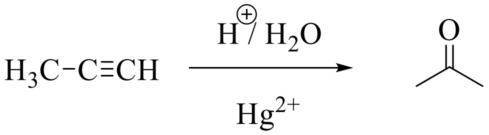


B. Hydration

In this reaction, ethyne is mixed with dilute sulfuric acid containing a catalytic amount of mercuric sulfate and one molecule of water is added to the triple bond to form a vinyl alcohol. Since this is unstable, it will rearrange to produce an acetaldehyde. The alcohol and aldehyde formed will exist in tautomerization.

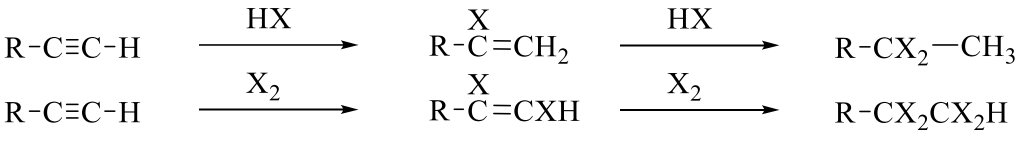


When the same reaction is carried out with propyne, the product is acetone.



C. Addition of HX, X_2, and HOX

Alkyne triple bond will react with HX or X_2 in the same manner as an alkene. The reaction happens in steps and Markovnikov's rule is followed.

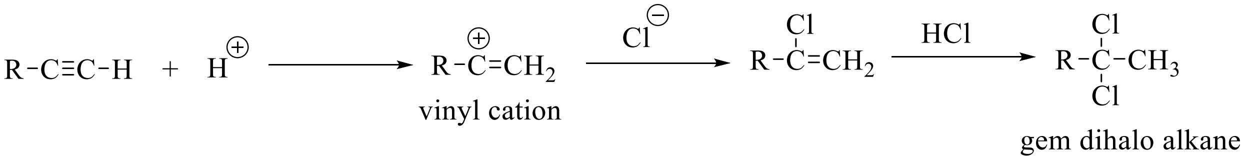


$$R-C\equiv C-H \xrightarrow{HX} R-\overset{X}{C}=CH_2 \xrightarrow{HX} R-CX_2-CH_3$$

$$R-C\equiv C-H \xrightarrow{X_2} R-\overset{X}{C}=CXH \xrightarrow{X_2} R-CX_2CX_2H$$

Alkynes are less reactive than alkenes toward electrophilic reagents.

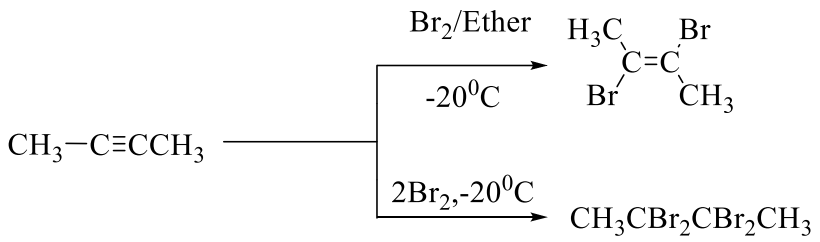
The overall reaction with HCl involves the initial formation of vinyl cation followed by its reaction with Cl^-.

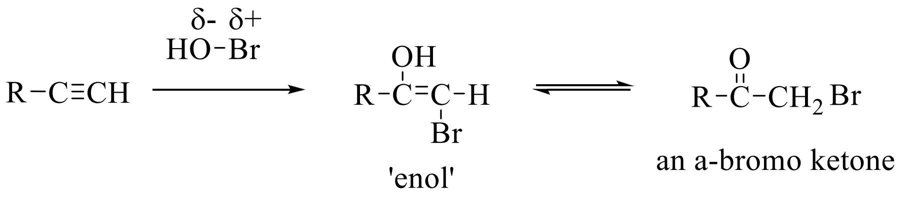


$$R-C\equiv C-H \;+\; \overset{\oplus}{H} \longrightarrow R-\overset{\oplus}{C}=CH_2 \xrightarrow{Cl^{\ominus}} R-\overset{Cl}{C}=CH_2 \xrightarrow{HCl} R-\underset{Cl}{\overset{Cl}{C}}-CH_3$$

The vinyl halide undergoes electrophilic addition to give a gem-dihaloalkane. The addition can be stopped at the alkenyl halide stage.

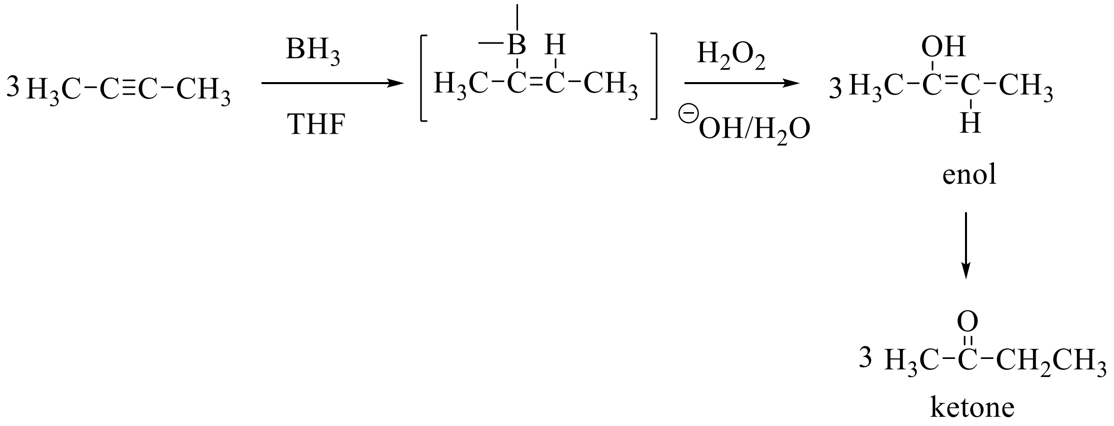
Similarly, the addition of X_2 to a triple bond can be stopped after the addition of one mole equivalent. The dihaloalkane mostly have the trans structure.



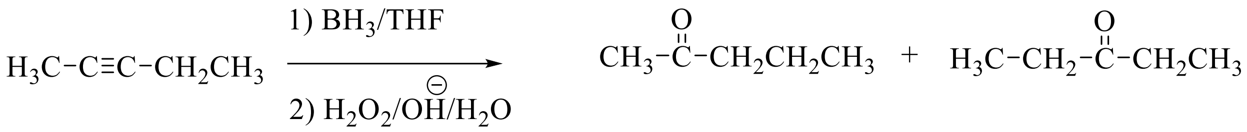


D. Hydroboration

When symmetrical internal alkynes are reacted with hydroboration, they will produce vinylic boranes that in turn can be converted to ketones in the presence of basic H_2O_2.

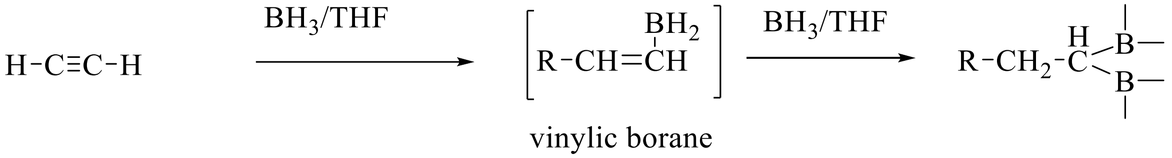


If this reaction is performed with unsymmetrical internal alkynes, it will produce a mixture of both possible ketones.



$$H_3C{-}C{\equiv}C{-}CH_2CH_3 \xrightarrow[2)\ H_2O_2/\overset{\ominus}{OH}/H_2O]{1)\ BH_3/THF} CH_3{-}\overset{O}{\overset{\|}{C}}{-}CH_2CH_2CH_3 + H_3C{-}CH_2{-}\overset{O}{\overset{\|}{C}}{-}CH_2CH_3$$

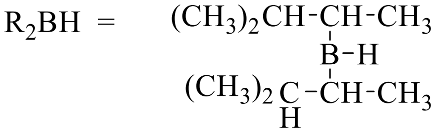
When terminal alkynes are reacted with borane, the reaction cannot be stopped at vinylic borane. The reaction will proceed to the second addition of borane.



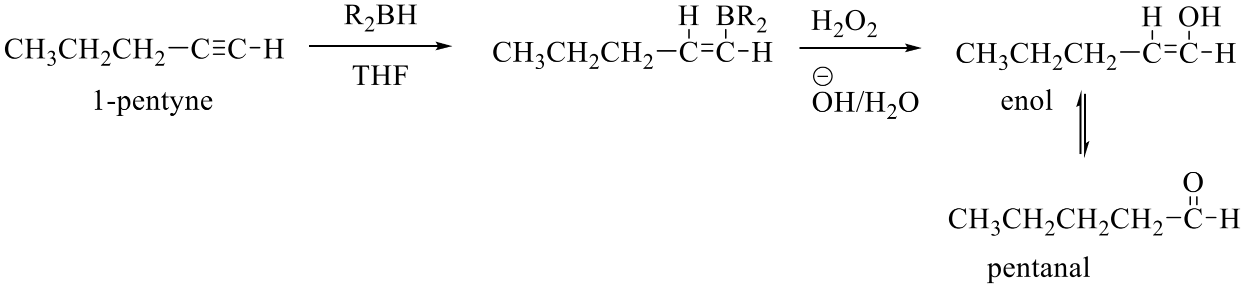
$$H{-}C{\equiv}C{-}H \xrightarrow{BH_3/THF} \left[R{-}CH{=}\overset{BH_2}{\overset{|}{C}H}\right] \xrightarrow{BH_3/THF} R{-}CH_2{-}\overset{H}{C}{<}\begin{matrix}B{-}\\B{-}\end{matrix}$$

vinylic borane

Therefore, to prevent this, a bulky, sterically hindered borane such as bis (1, 2 – dimethyl propyl) borane can be used.



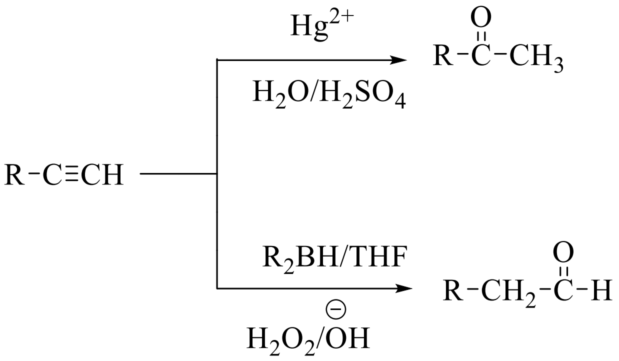
$$R_2BH = \begin{matrix}(CH_3)_2CH{-}CH{-}CH_3\\ \quad\;\; | \\ \quad\;\; B{-}H \\ \quad\;\; | \\ (CH_3)_2\underset{H}{C}{-}CH{-}CH_3\end{matrix}$$



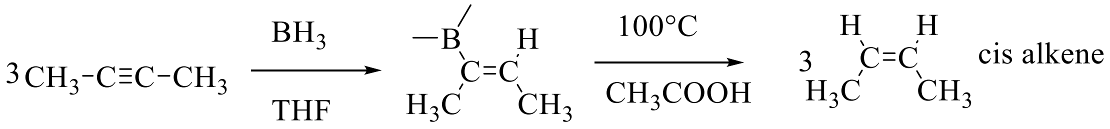
$$CH_3CH_2CH_2{-}C{\equiv}C{-}H \xrightarrow[THF]{R_2BH} CH_3CH_2CH_2{-}\overset{H}{\overset{|}{C}}{=}\overset{BR_2}{\overset{|}{C}}{-}H \xrightarrow[\overset{\ominus}{OH}/H_2O]{H_2O_2} CH_3CH_2CH_2{-}\overset{H}{\overset{|}{C}}{=}\overset{OH}{\overset{|}{C}}{-}H \rightleftharpoons CH_3CH_2CH_2CH_2{-}\overset{O}{\overset{\|}{C}}{-}H$$

1-pentyne; enol; pentanal

The hydroboration-oxidation steps are similar to the direct hydration of alkynes. Direct hydration of a terminal alkyne will produce a methyl ketone. Similarly, hydroboration-oxidation of the same alkyne will produce an aldehyde.



Protonolysis of boranes happens when organo borane is heated with carboxylic acid. The boron is replaced by a hydrogen atom. This will lead to a reduction of alkynes. The result would be a cis alkene. This is a good method to produce cis alkenes.



7.62 Substitution Reactions

A. Metallic Derivatives of Alkynes

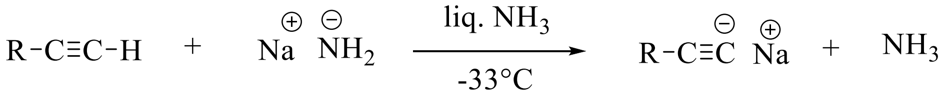
Terminal alkynes show weak acidity. This is because the hydrogen in the terminal triple bond can leave the molecule. Although the acidity of terminal alkynes is weaker than water or alcohol, they are more acidic than ammonia.

Therefore, when an alkyne is treated with a base, the acidic hydrogen can be replaced by an electropositive metal ion. e.g. Na^+, K^+, Ba^{2+}, Li^+. The resultant is an ionic acetylides.

Acetylide ion

Acetylide anions participate in S_N2 reactions since they are highly nucleophilic.

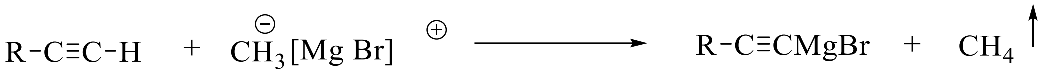
The reaction is carried out in a liquid NH_3 solution or hexamethyl phosphoric triamide (polar aprotic solvent) with sodium amide or n-butyl lithium.



$$R{-}C{\equiv}C{-}H + \overset{\oplus}{Na}\ \overset{\ominus}{NH_2} \xrightarrow[-33°C]{liq.\ NH_3} R{-}C{\equiv}\overset{\ominus}{C}\ \overset{\oplus}{Na} + NH_3$$

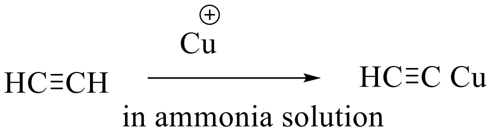
$$CH_3(CH_2)_3C{\equiv}CH + n\text{-}C_4H_9Li \xrightarrow{HMPT} C_4H_{10} + CH_3(CH_2)_3C{\equiv}\overset{\ominus}{C}\ \overset{\oplus}{Li}$$

There is another reaction in this category that can be performed using Grignard's reagent. When methylmagnesium bromide (Grignard's reagent) is reacted with acetylene the corresponding acetylenyl-1- magnesium bromide is formed (and an alkane is given out).

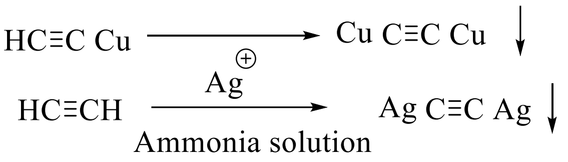


$$R{-}C{\equiv}C{-}H + \overset{\ominus}{CH_3}[Mg\ Br]^{\oplus} \longrightarrow R{-}C{\equiv}CMgBr + CH_4\uparrow$$

When Ag or Cu, in ammonia solution is reacted with acetylene, Cu compound (reddish solid) or Ag compound (gray/white solid) is formed. The color difference can be used to identify alkynes.



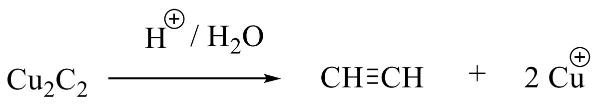
$$HC{\equiv}CH \xrightarrow[\text{in ammonia solution}]{\overset{\oplus}{Cu}} HC{\equiv}C\ Cu$$



$$HC{\equiv}C\ Cu \longrightarrow Cu\ C{\equiv}C\ Cu\downarrow$$

$$HC{\equiv}CH \xrightarrow[\text{Ammonia solution}]{\overset{\oplus}{Ag}} Ag\ C{\equiv}C\ Ag\downarrow$$

These compounds when treated with diluted mineral acid, the pure compound will be released. Therefore, this method also could be used as a purification method.



$$Cu_2C_2 \xrightarrow{H^{\oplus} / H_2O} CH{\equiv}CH + 2\ Cu^{\oplus}$$

B. Extension of Carbon Chains – Reaction of the Acetylide Ion

1. Alkylation

When acetylide salt is reacted with alkyl bromide an alkyl group can be introduced.

$$R{-}C{\equiv}\overset{\ominus}{C}\,Na^{\oplus}\quad \text{or}\quad R{-}C{\equiv}CMgBr \xrightarrow{R'\,Br} R{-}C{\equiv}C{-}R'$$

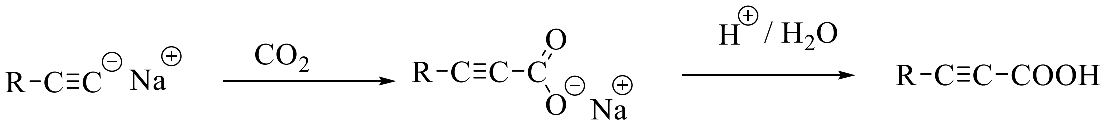
Acetylene can be alkylated once to produce alkyne or can be alkylated twice to produce an internal alkyne. Make a note of the reagents used in these reactions.

$$HC{\equiv}CH \quad + \quad NaNH_2 \xrightarrow{\text{liq. } NH_3} HC{\equiv}C^{\ominus}\ Na^{\oplus} \xrightarrow{n\text{-}C_4H_9Br} CH_3(CH_2)_3C{\equiv}CH$$

$$HC{\equiv}CH \xrightarrow[\text{liq. } NH_3]{2NaNH_2} HC{\equiv}C^{\ominus}\ Na^{\oplus} \xrightarrow{2(n\text{-}C_3H_7Br)} CH_3CH_2CH_2C{\equiv}CCH_2CH_2CH_3$$

2. Carboxylation

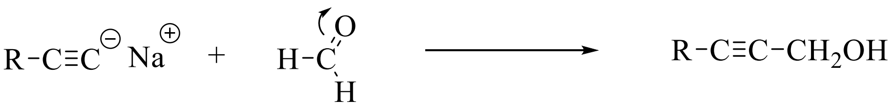
The salt of acetylide when reacted with carbon dioxide followed by hydrolysis will lead to the introduction of carboxylic acid.



$$R{-}C{\equiv}C^{\ominus}\ Na^{\oplus} \xrightarrow{CO_2} R{-}C{\equiv}C{-}C(=O)O^{\ominus}\ Na^{\oplus} \xrightarrow{H^{\oplus} / H_2O} R{-}C{\equiv}C{-}COOH$$

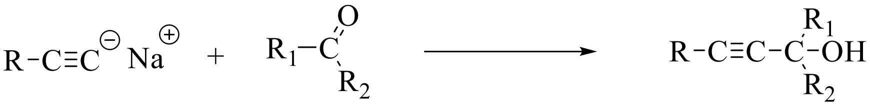
3. Hydroxyalkylation

When an acetylide is treated with formaldehyde the corresponding hydroxymethyl derivative is formed.



$$R{-}C{\equiv}C^{\ominus}\ Na^{\oplus} \quad + \quad H{-}C(=O){-}H \longrightarrow R{-}C{\equiv}C{-}CH_2OH$$

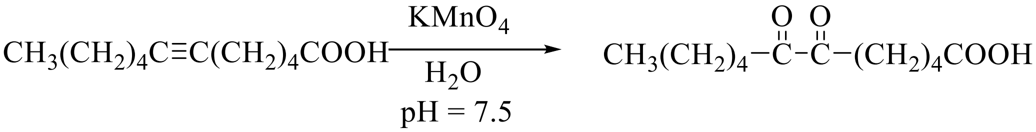
When the same reaction is carried out with other aldehydes and ketones, it will provide their corresponding hydroxy derivatives.



$$R-C\equiv C^{\ominus}\ Na^{\oplus} + R_1-\overset{O}{\overset{\|}{C}}-R_2 \longrightarrow R-C\equiv C-\underset{R_2}{\overset{R_1}{C}}-OH$$

7.63 Oxidation

Di-substituted ethynes undergo oxidation by MnO_4^- to produce 1,2 – diketones and/or cleavaged products. This is used as an important synthetic method to prepare 1,2 – diketones.



$$CH_3(CH_2)_4C\equiv C(CH_2)_4COOH \xrightarrow[\substack{H_2O \\ pH = 7.5}]{KMnO_4} CH_3(CH_2)_4-\overset{O}{\overset{\|}{C}}-\overset{O}{\overset{\|}{C}}-(CH_2)_4COOH$$

When more vigorous conditions are used a mixture of carboxylic acids are formed.

$$R-C\equiv C-R' \xrightarrow[\text{or } O_3]{\text{aq. } KMnO_4} RCOOH + R'COOH$$

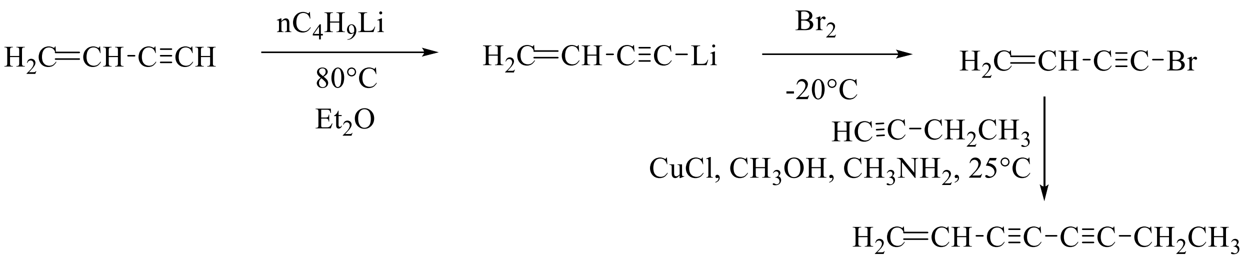
When a terminal alkyne is oxidized, CO_2 is formed.

$$R-C\equiv C-H \xrightarrow[\text{or } O_3]{\text{aq. } KMnO_4} RCOOH + CO_2$$

In the presence of pyridine at 60^0C and CuCl, terminal alkenes will undergo an oxidation coupling reaction called Eglintan reaction.

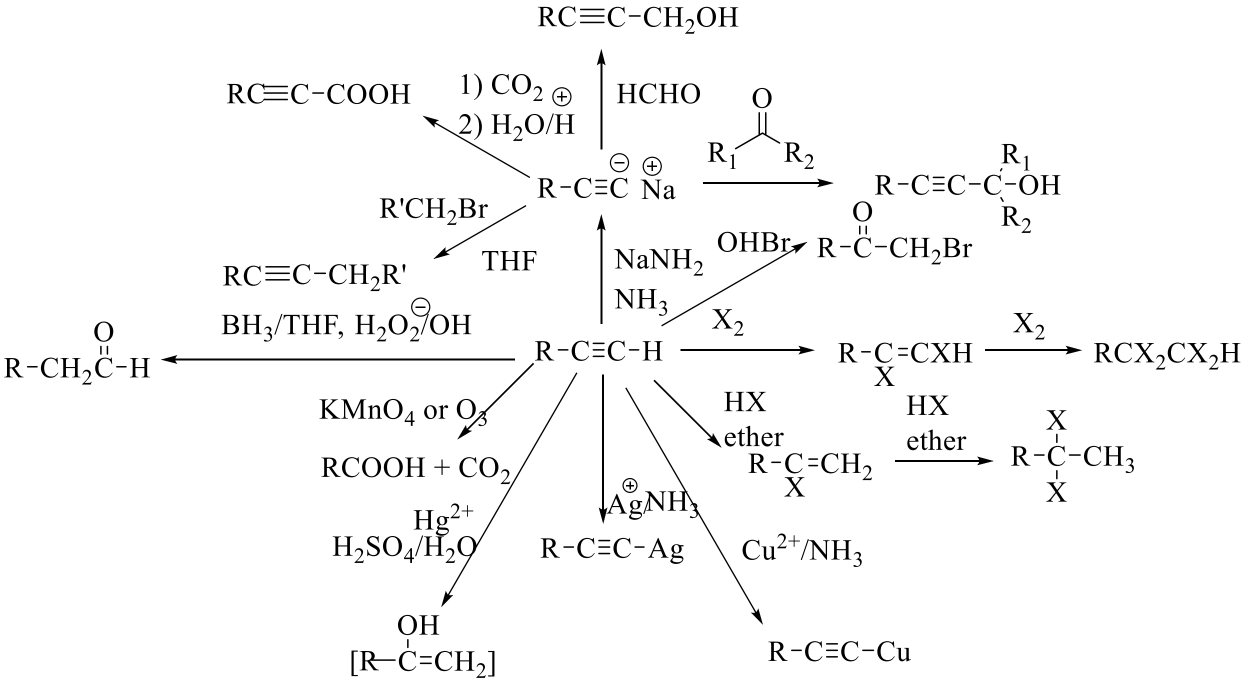
$$\text{n-}C_4H_9-C\equiv C-H \xrightarrow[\substack{O_{2,}\ \text{pyridine} \\ 60°C}]{CuCl} \text{n-}C_4H_9-C\equiv C-C\equiv C-C_4H_9$$

Unsymmetrical diynes can be prepared by using cadiot-chodkeivicz coupling. A bromo or chloro alkyne is treated with cuprous salt.

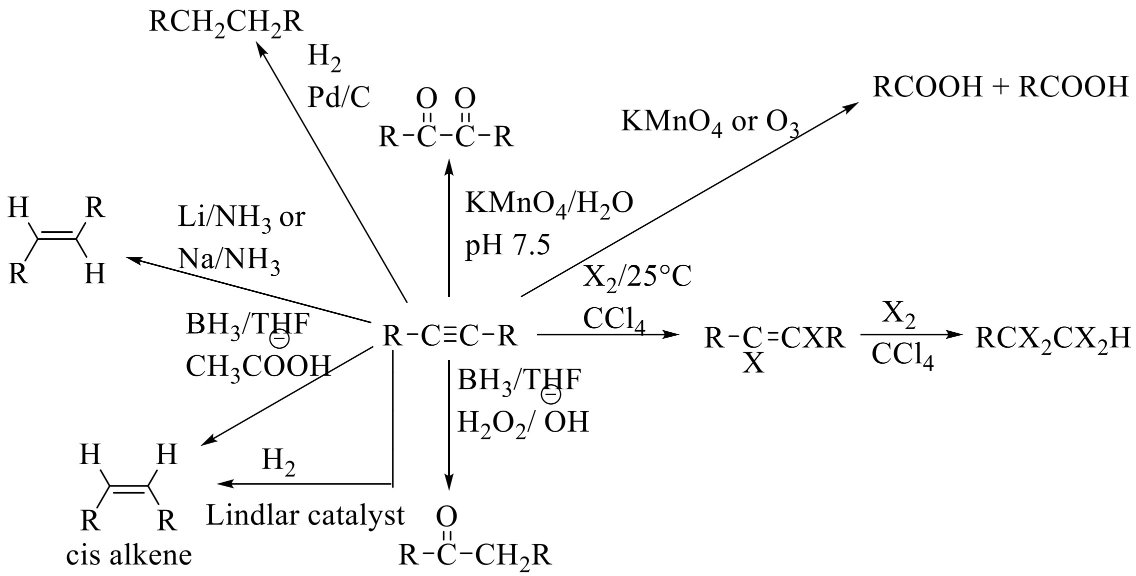


7.7 Summary of Alkyne Reactions

7.71 Terminal Alkyne Reactions



7.72 Internal Alkyne Reactions



Chapter 8

8.0 Alkyl Halides

8.1 Objectives

1. Draw and interpret Lewis structures, line-bond structures and functional groups of alkyl halides using IUPAC system of nomenclature.
2. Draw reaction mechanisms.
3. Describe reactions, predicting reactivity, and reaction products.
4. Devise syntheses including steps, reagents, and products including regiochemistry and stereochemistry

8.2 Introduction

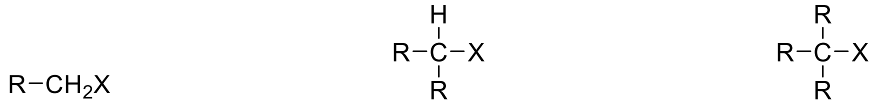
This group of compounds are also known as halogen alkanes or halo alkanes. The occurrence of alkyl halides is mostly in marine than terrestrial grounds. Depending on the number of halogen atoms in the compound, they are named as mono, di, tri, etc.

Monohalogen derivatives of alkanes

The monohalogen derivatives of alkanes (mono alkyl halides) are the simplest type of this class of compounds.

Alkyl halides have the following general formula, $C_nH_{2n+1}X$.

X is any halide (Cl, Br, I) except fluoride (F). This is because F behave differently to other halides. The halides are classified as primary, secondary, or tertiary.



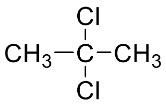
Primary Secondary Tertiary

Figure 8.2.1: Primary, Secondary, Tertiary Alkyl Halides

Dihalogen derivatives of alkanes

The dihalogen derivatives of alkanes are of four types:

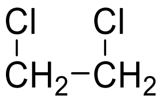
a) Both halogens are attached to the same carbon. These compounds are said to be in the geminal position.
Gem-dihalides are named as the alkylidene dihalides. Nevertheless, IUPAC naming is the more accepted method to naming these compounds.



$$CH_3-\underset{\displaystyle Cl}{\overset{\displaystyle Cl}{C}}-CH_3$$

Figure 8.2.2: Isopropylidene dicholorde or IUPAC name 2,2-dichloropropane

b) Two halogen atoms are on adjacent carbon atoms. These compounds are said to be in the vicinal position.
Vic-dihalides are named as the dihalide of the alkene from which they can be prepared.
e.g.



$$\overset{\displaystyle Cl}{C}H_2-\overset{\displaystyle Cl}{C}H_2$$

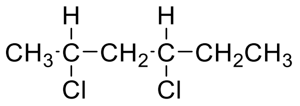
Figure 8.2.3: Ethylene dichloride or IUPAC name – 1,2 - dichlorethane

c) Two halogen atoms are attached to the two terminal carbon atoms of the compound. They are named as polymethylene dihalide.
e.g.

$$Cl-CH_2-CH_2-CH_2-CH_2-Cl$$

Figure 8.2.3: Tetramethylene dichloride or IUPAC name – 1, 4 - dichlorobutane

d) When two halogens occupy positions other than the three types mentioned above. These compounds are named as dihalogen derivatives of the parent hydrocarbon. The positions of the halogen atoms are indicated by a numbering system.
e.g



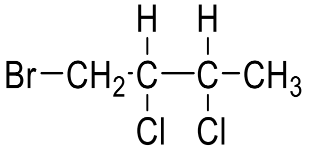
$CH_3\text{-}\underset{Cl}{\overset{H}{C}}-CH_2\text{-}\underset{Cl}{\overset{H}{C}}-CH_2CH_3$

Figure 8.2.4: 2,4-dichlorohexane – IUPAC name

Polyhalogen derivatives

These compounds are named using the IUPAC naming.

e.g.



$Br-CH_2\text{-}\underset{Cl}{\overset{H}{C}}-\underset{Cl}{\overset{H}{C}}-CH_3$

Figure 8.2.5: **5-Bromo-1-chloro-2-iodo-3-methylpentane**

8.3 Nomenclature and Isomerism

Please refer to the chapter on nomenclature and isomerism and answer the following questions:

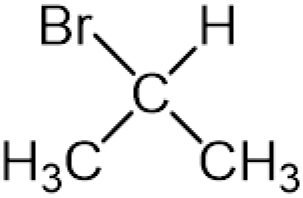
Naming Compounds

1.Name the following compounds as methyl, ethyl, primary (1^0), secondary (2^0) or tertiary (3^0)

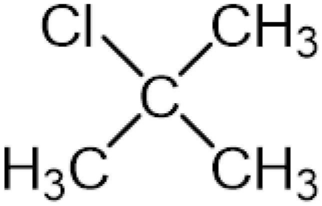
a. CH_3I

b. CH_3CH_2Br

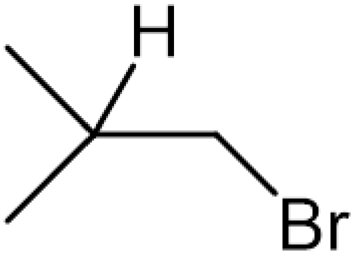
c.



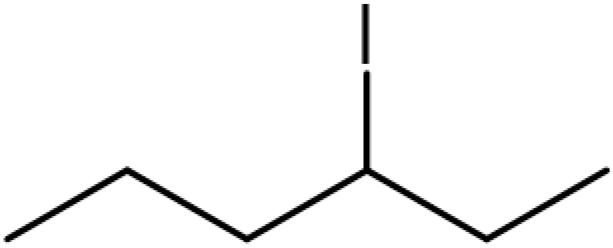
d.



e.



f.



2. Give the IUPAC names of the following compounds:

a. $CH_3CH_2CH_2Br$

b. $(CH_3)_2CHCl$

c. CH_3CH_2I

d. $CH_3CH_2CH_2CH_2F$

3. Draw the structures of the following compounds

a. 2-bromopentane
b. 3-bromo-5-methylhexane
c. 2-chloro-3-methylbutane
d. 1-bromo-2-chloro-4-methylpentane

4.Questions on isomers

a) What are the possible **types** of isomers for alkyl halides?

Solutions:

1.Naming Compounds

a. Methyl and 1^0
b. Ethyl and 1^0
c. 2^0
d. 3^0
e. 1^0
f. 2^0

2. Give the IUPAC names of the following compounds

a. 1-bromopropane

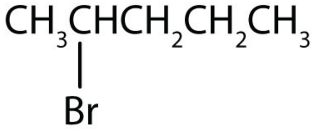
b. 2-chloropropane

c. 1-iodoethane

d. 1-fluorobutane

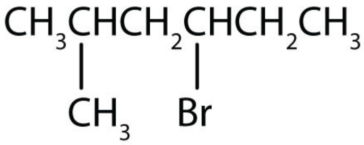
3. Draw the structures of the following compounds

a.



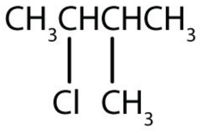
$CH_3\underset{\underset{Br}{|}}{C}HCH_2CH_2CH_3$

b.



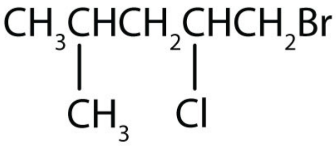
$CH_3\underset{\underset{CH_3}{|}}{C}HCH_2\underset{\underset{Br}{|}}{C}HCH_2CH_3$

c.



$CH_3\underset{\underset{Cl}{|}}{C}H\underset{\underset{CH_3}{|}}{C}HCH_3$

d.



$CH_3\underset{\underset{CH_3}{|}}{C}HCH_2\underset{\underset{Cl}{|}}{C}HCH_2Br$

4. **Questions on isomers**

1. The structural isomers – chain and positional.

8.4 Physical Properties

Ethyl bromide and ethyl iodide are liquids at room temperature. Lower molecular weight alkyl halides are gases at room temperature. As the alkyl chain increases, the boiling point increases. Branched alkyl chains have lower boiling points. Alkyl halides are insoluble in water. They are soluble in most of the organic solvents. Alkyl halides lose HX when heated. Chloroform undergoes decomposition when exposed to sunlight, but this reaction can be reduced by adding some alcohol. Bromides and iodides react with light and emanate free halogens.

Alkyl halides are used as industrial chemicals. Freons (e.g. dichloro difluoromethane) are refrigerants and aerosol propellants. Another useful material is Teflon polymer, which is polytetrafluoroethylene.

The bond length of R-X increases in the following order:

$$R\text{-}F < R\text{-}Cl < R\text{-}Br < R\text{-}I$$

The bond dissociation energy is highest in R-F and the lowest is R-I

8.5 Preparation of Alkyl Halides

8.5.1 Preparation of Mono Alkyl Halides

1. **From Alcohols**
   This is the most valuable method.

   a) Treat alcohol with HX (X = Cl, Br, I)

$$R{-}OH \xrightarrow{HX} R{-}X + H_2O$$

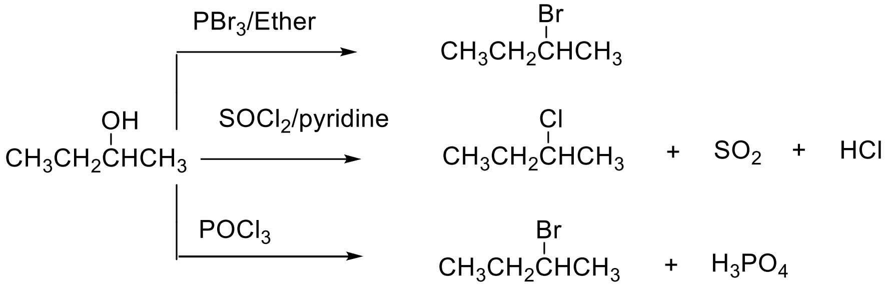
The reactivity order of alcohols are as follows:

$$R_3COH > R_2CHOH > R_1CH_2OH$$

Tertiary > Secondary > Primary alcohols

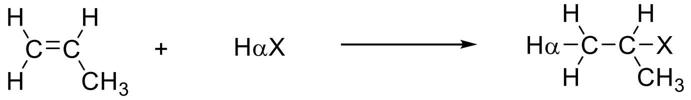
Although, tertiary alcohol reacts easily, secondary and primary alcohols also can be converted to R-X by adding $ZnCl_2$ as a catalyst.

b) Primary and secondary alcohols to halides
This reaction is carried out by using different reagents.



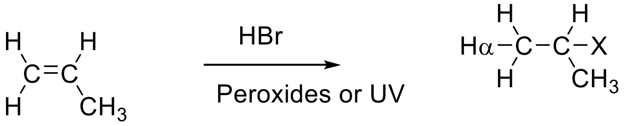
2. From Alkenes

a) Reaction with HX (X = Cl, Br, I)



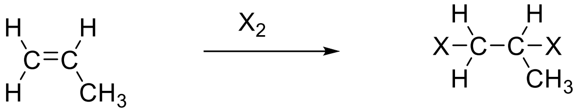
Markovnikov Addition

b) Reaction with HBr in the presence of peroxides or UV light

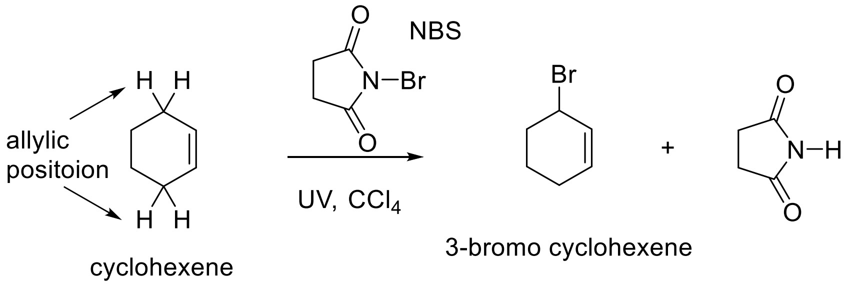


Anti Markovnikov Addition

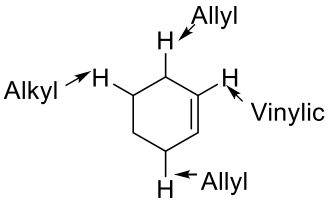
c) Reaction with halogens



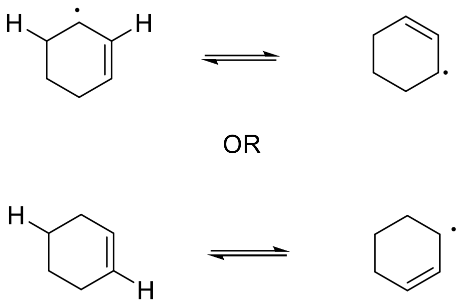
Allylic bromination of alkenes



Alkenes react with N-bromosuccinimide (NBS) to give products formed by the substitution of hydrogen by bromine at the carbon atoms after the ones with the double bonds, which are known as allylic positions. This allylic bromination in the presence of NBS is similar to the bromination of alkanes, because C – H bond in a saturated carbon is broken and H is replaced with Br. Both reactions follow a radical pathway. The reason for the replacement of allylic H atoms, but not any other H atoms can be explained by understanding the stability of the intermediate of this reaction. In free radical halogenation reactions, it is the stability of the intermediate that determines the final product.



The bond energy requires to break allylic bond is 87 kCal/mol. This is lower than alkyl (95 kCal/mol) and vinylic (108 kCal/mol). Therefore, once this hydrogen leaves, the molecule will undergo resonance. The more resonance a compound has, the more stable it will be. Therefore, in a free radical reaction, replacing allylic H will lead to a more stable intermediate.



Both forms lead to identical products.

3. From Alkanes

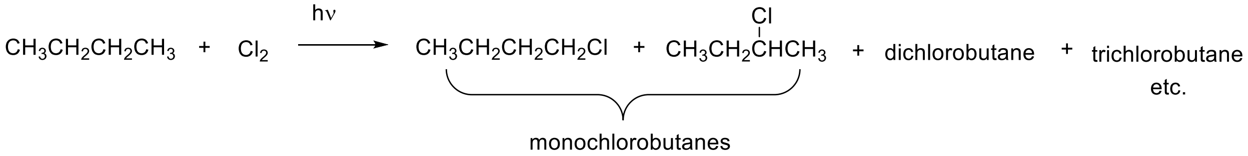
Chlorination or bromination of alkanes lead a to a mixture alkyl chlorides or bromides.

$$CH_4 + Cl_2 \xrightarrow{UV} CH_4 + CH_3Cl + CH_2Cl_2 + CHCl_3 + CCl_4 + HCl$$

The above reaction follows a free radical reaction initiated by heat or UV light.

When halogenation takes place with alkanes with more than one carbon (i.e. several types of replaceable hydrogens), the mixture will lead to mono, di, and tri forms of alkyl halides.

e.g.



$$CH_3CH_2CH_2CH_3 + Cl_2 \xrightarrow{h\nu} \underbrace{CH_3CH_2CH_2CH_2Cl + CH_3CH_2\overset{Cl}{C}HCH_3}_{\text{monochlorobutanes}} + \text{dichlorobutane} + \text{trichlorobutane etc.}$$

4. From carboxylic acid salts

$$RCOOAg + X_2 \xrightarrow[\Delta]{} RX + CO_2 + AgX$$

In this reaction, thermal decarboxylation of silver salts of carboxylic acids takes place. The compound RCOOAg is heated in the presence of halogens.

8.5.2 Preparation of Dihalogen Alkyl Halides

8.5.2.1 Gem-Dihalides

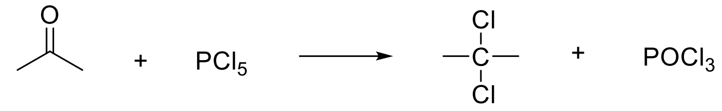
1. **Reaction of alkynes with halogen acids**

$$HC \equiv CH + HBr \longrightarrow CH_2{=}CHBr \xrightarrow{HBr} CH_3CHBr$$

vinyl bromide

1,1-dibromoethane

2. **Reactions of aldehydes and ketones with phosphorous pentahalide**

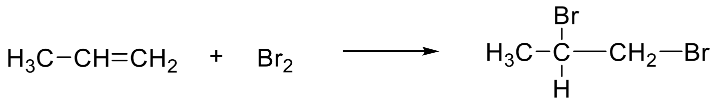


Acetone

2,2-dichloropropane

8.5.2.2 Vic-Dihalides

1) **Addition of Halogens to alkenes**

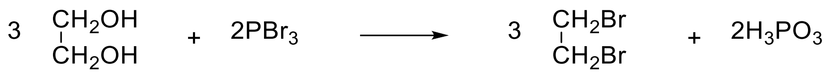


$$H_3C{-}CH{=}CH_2 + Br_2 \longrightarrow H_3C{-}CHBr{-}CH_2{-}Br$$

propene

1,2 -dibromopropene

2) **Reaction between phosphorous tribromide and glycols**



$$3\ \begin{matrix} CH_2OH \\ | \\ CH_2OH \end{matrix} + 2PBr_3 \longrightarrow 3\ \begin{matrix} CH_2Br \\ | \\ CH_2Br \end{matrix} + 2H_3PO_3$$

3) Specific dihalides preparation

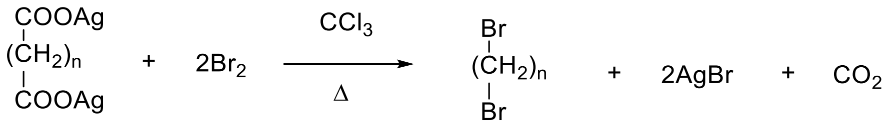
The preparation of these dihalides is specific to each particular dihalide being produced.

e.g.

- Preparation of 1, 3- dibromopropane using HBr and allyl bromide at low temperature

$$H_2C{=}CH{-}CH_2Br + HBr \longrightarrow BrCH_2CH_2CH_2Br$$

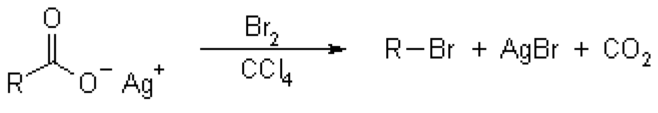
- Use of Hunsdiecker reaction to prepare dihalides where the number of carbon atoms (n) is less than 5.



$$\begin{matrix} COOAg \\ | \\ (CH_2)_n \\ | \\ COOAg \end{matrix} + 2Br_2 \xrightarrow[\Delta]{CCl_3} \begin{matrix} Br \\ | \\ (CH_2)_n \\ | \\ Br \end{matrix} + 2AgBr + CO_2$$

- Hunsdiecker Reaction

In this reaction, the silver(I) salts of carboxylic acids react with halogens to produce unstable intermediates which decarboxylate thermally to produce alkyl halides.



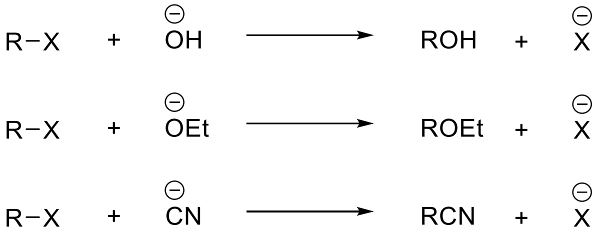
8.6 Reactions of Alkyl Halides

8.6.1 Reactions of Mono Halogen Alkyl Halides

1. Substitution reactions of alkyl halides

a) Substitution by -OH, -OEt, CN^-

In alkyl halide the bond between C and X (halide) is polarized due to the high electronegativity of halogen. As a result, nucleophilic substitution takes place in the presence of alcohol (-OH), ether (-OEt), and -CN. The reaction takes place either by S_N1 or S_N2 pathway (Please refer to the chapter on reactions).



$$R{-}X + \overset{\ominus}{OH} \longrightarrow ROH + \overset{\ominus}{X}$$

$$R{-}X + \overset{\ominus}{OEt} \longrightarrow ROEt + \overset{\ominus}{X}$$

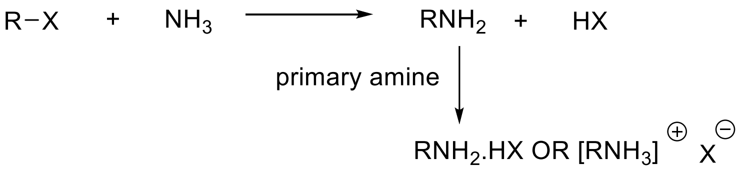
$$R{-}X + \overset{\ominus}{CN} \longrightarrow RCN + \overset{\ominus}{X}$$

-OH, -OEt, and -CN are all nucleophiles.

b) Substitution by ammonia

When alkyl halides are heated, under pressure in the presence of ethanolic ammonia, a mixture of amines is produced. Alkylation of amines happens well with primary and secondary alkyl halides.

This is an S_N2 reaction.



$$R{-}X + NH_3 \longrightarrow RNH_2 + HX$$

primary amine

$$RNH_2.HX \text{ OR } [RNH_3]^{\oplus} X^{\ominus}$$

If there is excess ammonia (base), then the following path occurs:

$$CH_3CH_2X \quad + \quad 2NH_3 \longrightarrow CH_3CH_2NH_2 \quad + \quad CH_3CH_2NH_2$$

amine

If there is excess RX, then the product could be a secondary amine, because the primary amine itself acts as a nucleophile.

$$CH_3CH_2Br \quad + \quad 2CH_3CH_2NH_2 \longrightarrow (CH_3CH_2)_2NH \quad + \quad CH_3CH_2\overset{\oplus}{N}H_3\,\overset{\ominus}{Br}$$

Since secondary amine is also nucleophile, the final product will be a tertiary amine.

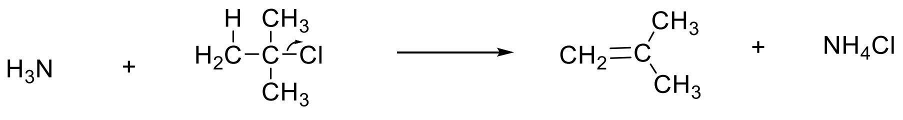
$$CH_3CH_2Br \quad + \quad 2(CH_3CH_2)_2NH \longrightarrow (CH_3CH_2)_3N \quad + \quad (CH_3CH_2)_2\overset{\oplus}{N}H_2\,\overset{\ominus}{Br}$$

Finally, this will lead to a quaternary salt:

$$CH_3CH_2Br \quad + \quad (CH_3CH_2)_3N \longrightarrow (CH_3CH_2)_4\overset{\oplus}{N}\,\overset{\ominus}{Br}$$

These products can be controlled by changing the concentration of RX.

- When this reaction is carried out with tertiary halides, it gives out alkenes.



The order of reactivity of halides is.

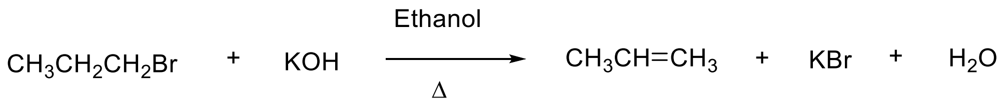
$$RI > RBr > RCl$$

The mechanism is $S_N{}^2$ in a primary alkyl halide, and $S_N{}^1$in a tertiary alkyl halide, and S_N1 or S_N2 in secondary.

2. Elimination Reactions of Alkyl Halides

In this reaction, alkyl halides are boiled with ethanolic potassium hydroxide. The product is the corresponding alkene. i.e. 1- bromopropane giving propene.

e.g.

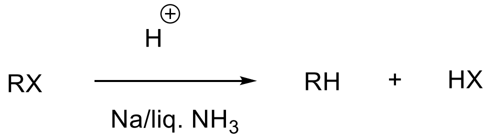


$$CH_3CH_2CH_2Br + KOH \xrightarrow[\Delta]{\text{Ethanol}} CH_3CH{=}CH_3 + KBr + H_2O$$

In this reaction, 1, 2 or β elimination happens. Secondary and tertiary halides usually react with alkoxides and hydroxides leading to alkenes. As a result, they will not produce ethers or alcohols. This is because alkoxides and hydroxides act as bases and not as nucleophiles. These reactions undergo E_1 or E_2 type reactions.

3. Reduction of Alkyl Halides

a) Alkyl halides can be reduced to alkanes by reacting in the presence of dissolving metals (e.g. sodium in liquid ammonia).



$$RX \xrightarrow[\text{Na/liq. } NH_3]{H^{\oplus}} RH + HX$$

b) Hydrogenolysis using a catalyst

Palladium on carbon is considered the most suitable catalyst. Another useful catalyst is Raney nickel.

$$RX + H_2 \xrightarrow{\text{Pd/C}} RH + HX$$

c) Hydride ion reduction using lithium aluminium hydride

Alkyl halides undergoes hydride ion reduction when reacted with lithium aluminimum hydride. This is a nucleophilic substitution where hydride ions (H^-) replace halides from primary and secondary alkyl halides. Another effective reducing agent is triethyl borohydride.

$$RX \quad + \quad LiAlH_4 \xrightarrow{Pd/C} RH$$

$$RX \quad + \quad (CH_3CH_2)_3BH \xrightarrow{ether} RH$$

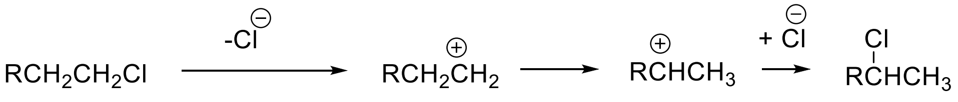
4. Coupling of Alkyl groups - Wurtz Reaction

In this reaction, alkyl halide in diethyl ether with sodium gives alkane. This is through the combination of alkyl groups.

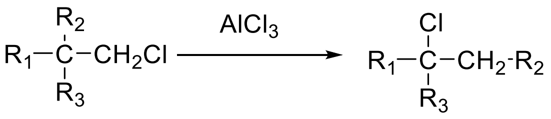
$$R_1X \quad + \quad R_2X \quad + \quad 2Na \xrightarrow{ether} R_1—R_2 \quad + \quad 2NaX$$

5. Rearrangement of Alkyl halides

Alkyl halides can undergo rearrangements in the presence of aluminum chloride at 300^{0}C. At times in tertiary alkyl halides, an alkyl group can move when there are no alpha hydrogen atoms.



$$RCH_2CH_2Cl \xrightarrow{-\overset{\ominus}{Cl}} RCH_2\overset{\oplus}{C}H_2 \longrightarrow R\overset{\oplus}{C}HCH_3 \xrightarrow{+\overset{\ominus}{Cl}} R\overset{Cl}{\overset{|}{C}}HCH_3$$



$$R_1-\underset{R_3}{\underset{|}{\overset{R_2}{\overset{|}{C}}}}-CH_2Cl \xrightarrow{AlCl_3} R_1-\underset{R_3}{\underset{|}{\overset{Cl}{\overset{|}{C}}}}-CH_2\text{-}R_2$$

6. Alkyl halides forming Grignard reagent

Reactions between certain metals and alkyl halides lead to the formation of a carbon-metal. When the metal is Mg, it is called Grignard reagent.

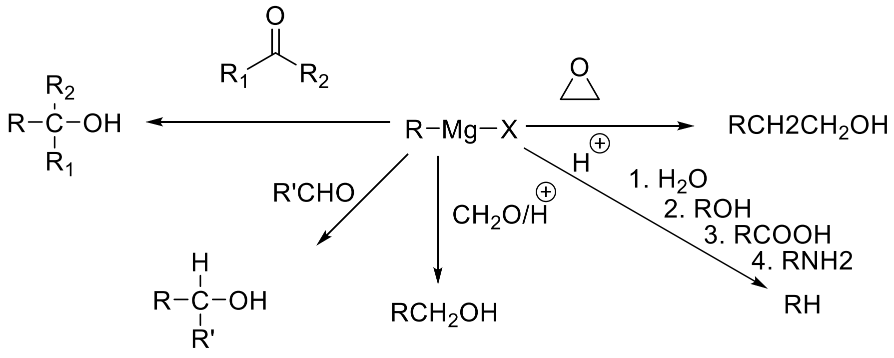
$$RX + Mg \xrightarrow[\text{or tetrahydrofuran (THF)}]{\text{anhydrous ether}} R{-}Mg{-}X$$

R could be a primary, secondary or tertiary alkyl or aryl or vinylic.

X could be Cl^-, Br^- or I^-

The bond between C-metal (in this case Mg) is highly polarized. Therefore, the compound acts as a nucleophile and a base.

The following is a list of possible reactions:



There are limitations to the preparation of Grignard reagent. It cannot be prepared from an alkyl halide, if there are other reactive functional groups in the molecule.

e.g. A compound that is an alkyl halide and a ketone will not form Grignard reagent. Similarly, a compound that is an alkyl halide and carboxylic acid, alcohol, or amine will not form a Grignard reagent. This is because the acidic protons of carboxylic acid, alcohol, or amine present in the same molecule react with the basic Grignard reagent while it is forming.

- The presence of the following functional groups will **stop** the formation of Grignard reagent:

Br – R – Functional Group

Functional Groups: -OH, -NH, -SH, -COOH, $-NO_2$, -CHO, -COR, -CN, $-CONH_2$, $-SO_2R$, -F

- The presence of the following functional groups will **enable** the formation of Grignard reagent:

Functional Groups: Alkyl, Aryl, Vinylic, ether (-OR), $-NR_2$, -SR,

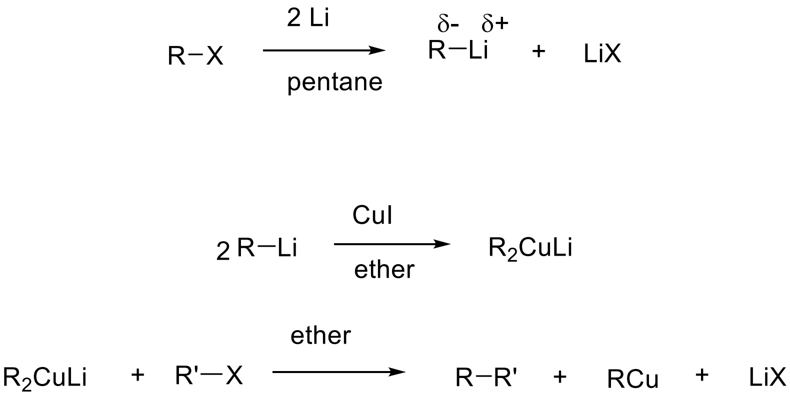
7. Alkyl halide coupling reaction through organometallic formation

A reaction between alkyl halides and Li will produce alkyl lithium reagents.

The alklyl lithium is a nucleophile and a base. This compound is produced in a similar manner to the formation of Grignard reagent and the reactions are also similar.

When alkyl lithium is reacted with cuprous iodide, it will produce lithium diorganocoppers, also known as Gilman reagent.

The Gilman reagent undergoes organometallic coupling in the presence of alkyl chloride, alkyl bromide, or alkyl iodides (bromides and iodides react easily). Alkyl fluorides do not undergo coupling reactions.



$$R-X \xrightarrow[\text{pentane}]{\text{2 Li}} \overset{\delta-}{R}-\overset{\delta+}{Li} + LiX$$

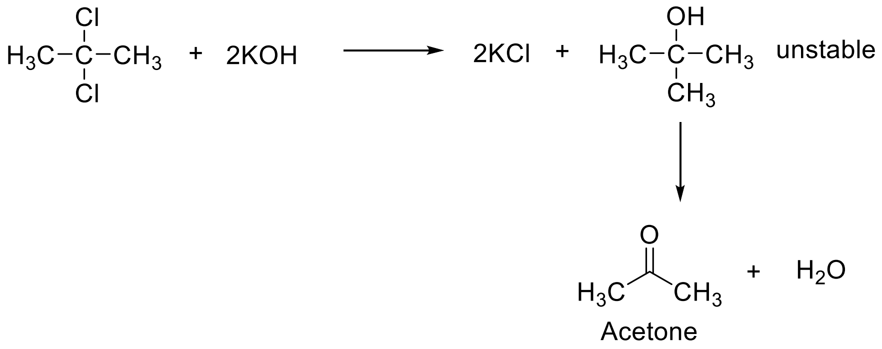
$$2\,R-Li \xrightarrow[\text{ether}]{\text{CuI}} R_2CuLi$$

$$R_2CuLi + R'-X \xrightarrow{\text{ether}} R-R' + RCu + LiX$$

8.6.2 Reactions of Dihalogen Alkyl Halides

1. Hydrolysis

Gem-dihalides are hydrolyzed using aqueous alkali to produce the corresponding carbonyl (aldehyde or ketone) compound.



2. Dehalogenation

1. Gem-dihalides

Gem-dihalides will produce alkenes when treated with Zn dust and methanol.

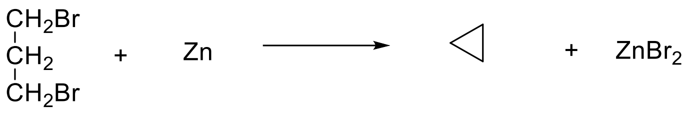
$$CH_3CH_2CHBr_2 + Zn \longrightarrow CH_3CH{=}CH_2 + ZnBr_2$$

2. Vic-dihalides

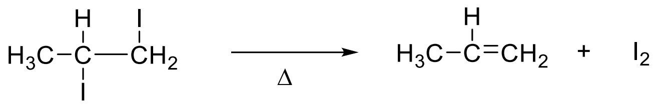
Vic-dihalides will produce alkenes when treated with Zn dust and methanol.

$$CH_3CHBrCH_2Br + Zn \longrightarrow CH_3CH{=}CH_2 + ZnBr_2$$

3. Trimethylene dibromides produce cyclopropane



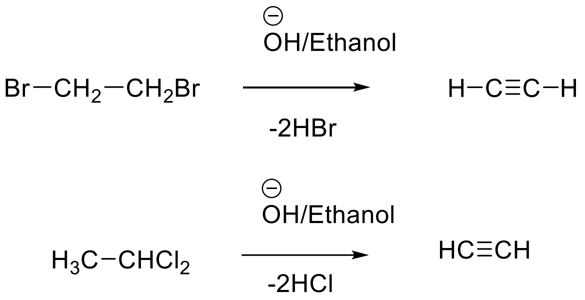
4. Vic di-iodides eliminate iodine at high temperatures



$$H_3C-CHI-CH_2I \xrightarrow[\Delta]{} H_3C-CH=CH_2 + I_2$$

3. Dehydrohalogenation

Gem dihalides produce alkynes on treatment with ethanolic KOH.



$$Br-CH_2-CH_2Br \xrightarrow[-2HBr]{\ominus OH/Ethanol} H-C\equiv C-H$$

$$H_3C-CHCl_2 \xrightarrow[-2HCl]{\ominus OH/Ethanol} HC\equiv CH$$

8.7 Summary of Reactions

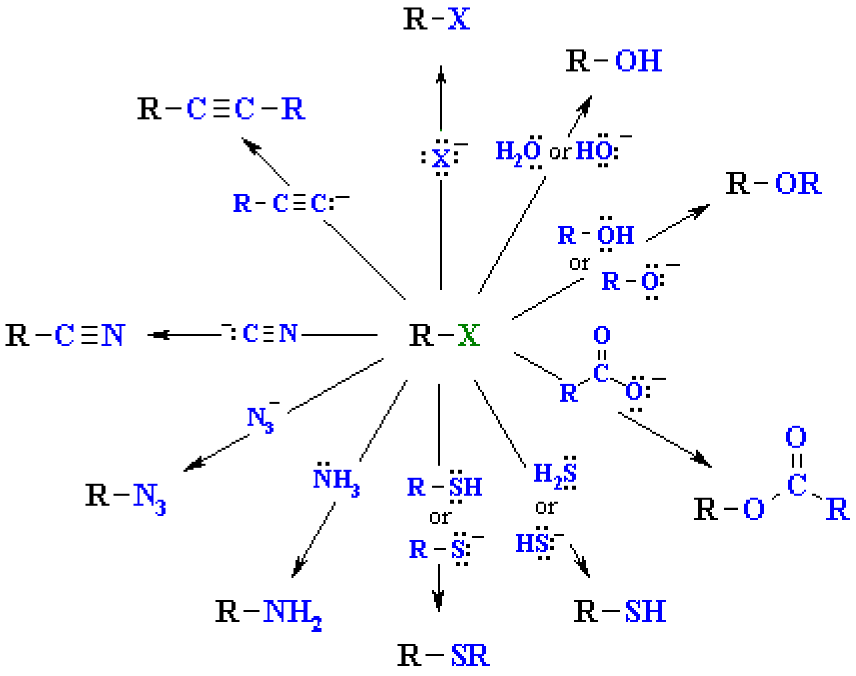
Reactions of alkyl halides follow the pathways given below:

Primary RX ---------------------- S_N2
E2 (with bulky base only)

Secondary RX ------------------ S_N2
E2 with strong base
S_N1/E1 with weak base/nucleophile

Tertiary RX -------------------- E2 with strong base
S_N1/E1 with weak base/nucleophile

Summary of RX reactions S_N1 and S_N2



Chapter 9

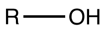
9.0 Alcohols and Thiols

9.1 Objectives

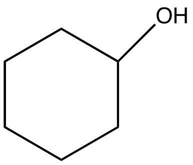
1. Draw and interpret Lewis structures, line-bond structures and functional groups of alcohols and thiols using IUPAC system of nomenclature.
2. Draw reaction mechanisms.
3. Describe reactions, predicting reactivity, and reaction products.
4. Devise syntheses including steps, reagents, and products including regiochemistry and stereochemistry

9.2 Introduction

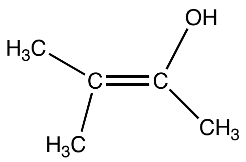
Alcohols have the functional group -OH (hydroxyl) attached to sp^3 hybridized (saturated) atoms. In this chapter, we are not discussing phenols (OH bonded to an aromatic ring) and enols (OH bonded to a vinyl carbon). The chemistry of phenols and enols are different to saturated alcohols.



Alcohol



Phenol



Enol

Alcohols are hydroxy derivatives of alkanes. The alcohols are classified according to the number of hydroxyl groups.

One -OH group = Monohydric alcohols

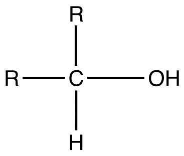
Two -OH groups = Dihydric alcohols

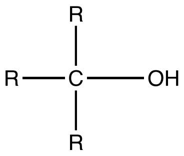
Three -OH groups = Trihydric alcohols

Four or more -OH groups = Polyhydric alcohols

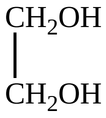
Monohydric alcohols can be primary, secondary, or tertiary alcohols.


Alcohol


secondary alcohol

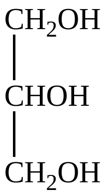

tertiary alcohol

Ethylene glycol (ethane 1,2 -diol) and glycerol (Propane-1,2,3- triol) are the simplest members of diols and triols. Both of these compounds have high boiling points and they are colorless, viscous liquids. They have a sweet taste. The hydrogen bonding in these two compounds cause higher boiling points and the solubility in water. Both of these compounds are used as anti-freezing agents. Glycol is also used as a solvent. Glycerol is used in the manufacture of explosives. Trinitroglycerine is used in dynamites and other explosives after mixing with other chemicals.



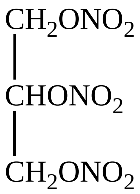
$$\begin{array}{l} CH_2OH \\ | \\ CH_2OH \end{array}$$

ethylene glycol



$$\begin{array}{l} CH_2OH \\ | \\ CHOH \\ | \\ CH_2OH \end{array}$$

glycerol



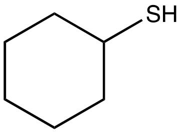
$$\begin{array}{l} CH_2ONO_2 \\ | \\ CHONO_2 \\ | \\ CH_2ONO_2 \end{array}$$

trinitroglycerine

Thiols are R-SH type compounds. They are sulfur analogous of alcohols. The naming of thiols is done by removing -ol suffix and adding -thiol suffix.

CH_3CH_2SH

Ethane thiol



Cyclohexane thiol

$HS\text{-}CH_2\text{-}CH_2\text{-}COOH$

3-mercapto propanoic acid

The -SH group is known as a mercapto group.

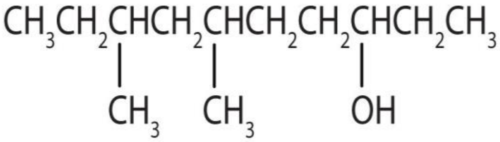
They have a pungent odor. Small amounts of thiols are added to natural gases to be able to detect a leaking gas by the smell.

9.3 Nomenclature and Isomerism

Please refer to the chapter on nomenclature and isomerism and answer the following questions:

1. **Naming Compounds – Give the IUPAC names for the following compounds.**

a)

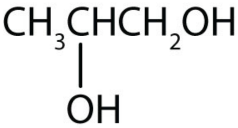


$$CH_3CH_2\underset{CH_3}{\underset{|}{C}H}CH_2\underset{CH_3}{\underset{|}{C}H}CH_2CH_2\underset{OH}{\underset{|}{C}H}CH_2CH_3$$

b) $HOCH_2CH_2CH_2CH_2CH_2OH$

2. **Give the IUPAC names of the following compounds:**

a)



$$\mathrm{CH_3\underset{\displaystyle OH}{\underset{|}{C}}HCH_2OH}$$

b)

3.Draw the structures of the following compounds

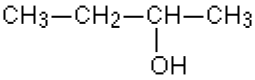
a) 2-hexanol
b) 3-methyl-2-pentanol

4.Questions on Isomers

a) Identify the two isomers given below:

$\mathrm{CH_3{-}CH_2{-}CH_2{-}CH_2{-}OH}$

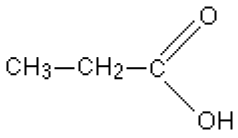
butan-1-ol



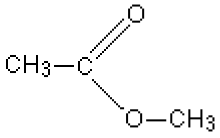
$$\mathrm{CH_3{-}CH_2{-}\underset{\displaystyle OH}{\underset{|}{C}}H{-}CH_3}$$

butan-2-ol

b)



propanoic acid

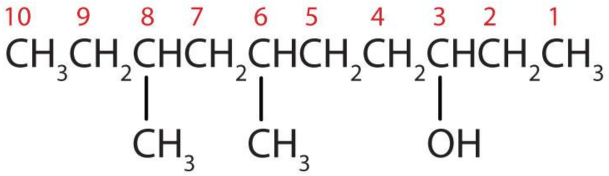


methyl ethanoate

Solutions:

1.Naming Compounds – Give the IUPAC names for the following compounds.

a) The longest carbon chain has 10 Cs. This makes it a decane derivative. The -OH on the 3rd carbon makes it 3-decanol.



$$\mathrm{CH_3CH_2CH(CH_3)CH_2CH(CH_3)CH_2CH_2CH(OH)CH_2CH_3}$$

The carbon atoms are numbered from the end closest to the OH group. That fixes the two methyl (CH3) groups at the sixth and eighth positions. The name is 6,8-dimethyl-3-decanol (not 3,5-dimethyl-8-decanol).

b) Five carbon atoms in the longest carbon chain make the compound a pentane derivative. Two OH groups on the first and fifth carbon atoms make the compound a diol and give the name 1,5-pentandiol.

2. Give the IUPAC names of the following compounds:

a) Propan-1,2-diol

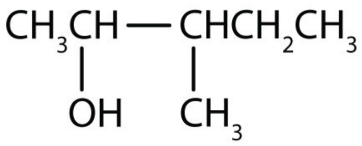
b) 1-methylcyclopentan-1-ol

3. Draw the structures of the following compounds

a)

$CH_3\underset{\substack{|\\ OH}}{CH}CH_2CH_2CH_2CH_3$

b)



$CH_3\underset{\substack{|\\ OH}}{CH}-\underset{\substack{|\\ CH_3}}{CH}CH_2CH_3$

4. Questions on isomers

a) Positional isomers
b) Functional isomers

9.4 Physical Properties

Alcohols have a higher boiling point than their corresponding hydrocarbons or alkyl halides. This is due to hydrogen bonding.

Lower alcohols are soluble in water. The solubility decreases with increasing molecular weight. Lower members of alcohol group have a distinctive smell, burning taste, and inflammable liquids.

Some of the common alcohols are,

Methanol – used as a solvent, used in the production of formaldehyde (HCHO), and acetic acid (CH_3COOH). This is a toxic solvent that will lead to blindness in low doses and death in large doses.

Ethanol – used in drinking alcohol.

Cholesterol – produced in the body and known to cause heart diseases. This is a steroidal alcohol.

t-butyl alcohol – used to increase the octane rating in gasoline. This is a clean octane booster. The use of $Pb(C_2H_5)_4$ as a converter leads to toxic lead oxide emanation on combustion.

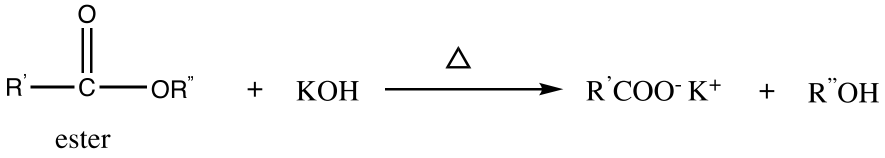
Menthol – 10 carbon alcohol - used for flavoring, used in colognes.

9.5 Preparation of Alcohols and Thiols

Alcohols can be synthesized using alkenes, alkyl halides, ketones, esters, and aldehydes.

9.5.1 Hydrolysis

1. An ester in the presence of an alkaline undergoes hydrolysis to produce alcohol.



$$R'COOR'' + KOH \xrightarrow{\Delta} R'COO^- K^+ + R''OH$$

This is a useful method in industrial preparation of alcohols. Naturally occurring esters are converted to alcohols.

2. Diethyl ether in the presence of diluted sulfuric acid and under pressure produces alcohol.

$$C_2H_5 - O - C_2H_5 \quad + \quad H_2O \xrightarrow{H^+} 2\,C_2H_5OH$$

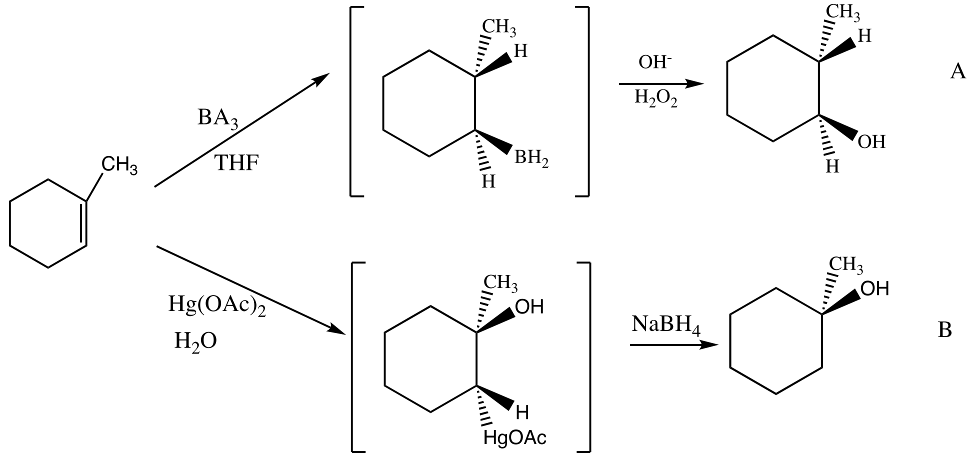
3. Alkyl halides on treatment with mild alkali give alcohols

$$RX \;+\; Ag_2O/H_2O \longrightarrow ROH \;+\; AgX\downarrow$$

9.5.2 Hydration of Alkenes

The direct hydration of alkenes with aqueous acid is not an effective path to produce alcohol.

Therefore, the two common methods used are hydroboration-oxidation and oxymercuration-reduction.



A = trans-2-methyl cyclohexanol

B = 1-methyl cyclo hexanol Markownikoff hydration

9.5.3 Reductions

1. Bouveault-Blanc Reduction

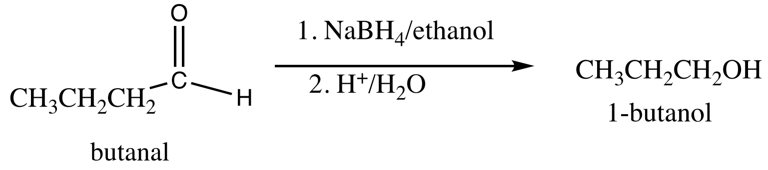
Esters can be reduced by Na in ethanol. This is a useful method for the production of large-scale reductions.

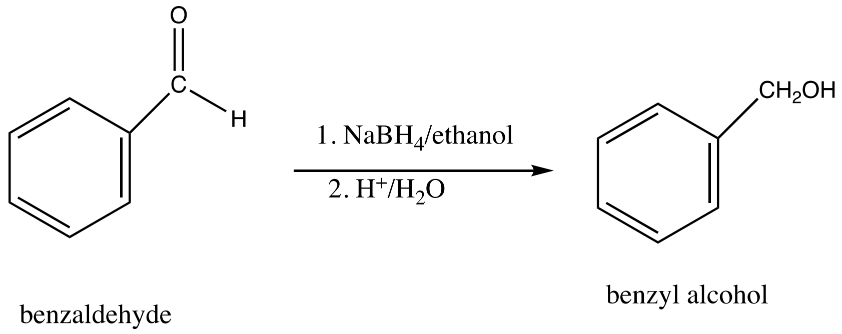
$$CH_3(CH_2)_8COOC_2H_5 + Na \xrightarrow[C_2H_5OH]{\Delta} CH_3(CH_2)_8CH_2OH + C_2H_5OH$$

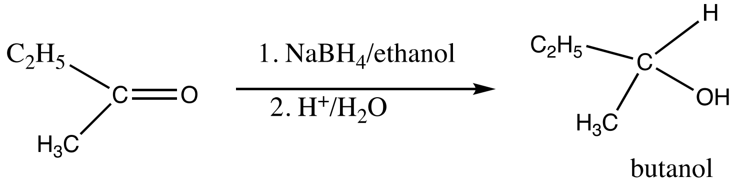
2. Reductions with metallic hydrides

a) Reduction using $NaBH_4$

This is a safe and a convenient reaction to be carried out in a laboratory. This is the reduction of ketones and aldehydes using sodium borohydride ($NaBH_4$); aldehydes are reduced to primary alcohols and ketones are reduced to secondary alcohols.







b) Reduction using $LiAlH_4$

$LiAlH_4$ is a reagent that reacts violently with water. This reagent reduces carbonyl group in the presence of a double bond. $LiAlH_4$ is used in tetrahydrofuran (THF) or ether.

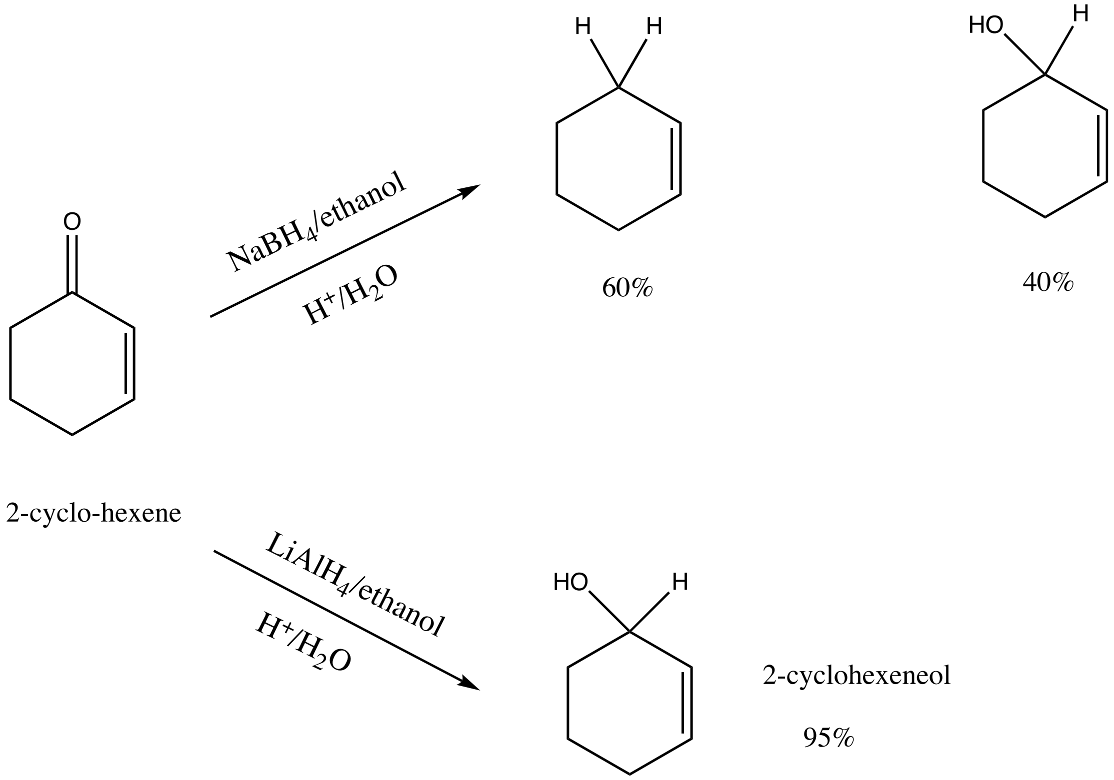
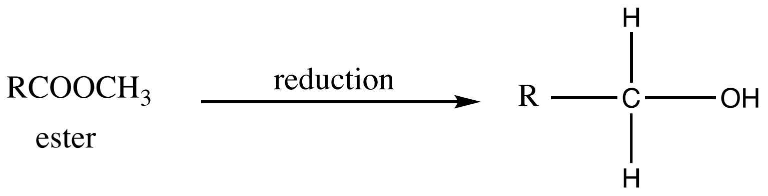
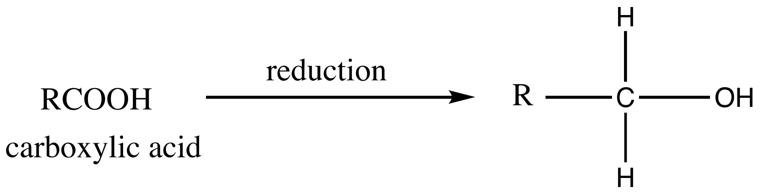


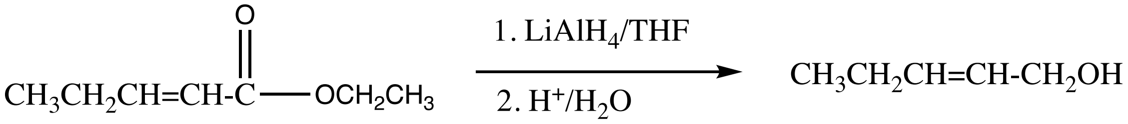
Figure 9.5.3.1: $LiAlH_4$ and $NaBH_4$ reactions compared. 95% yield of 2-cyclohexenol is given when $LiAlH_4$ is used as the reducing agent.

The reduction of esters and carboxylic acids to primary alcohols are difficult than the reduction of aldehydes and ketones. When $NaBH_4$ is used, the reduction happens slowly. Nevertheless, in the presence of $LiAlH_4$, the reduction of esters and carboxylic acids leads to high yields.





$$CH_3(CH_2)CH{=}CHCH_2COOH \xrightarrow[2.\ H^+/H_2O]{1.\ LiAlH_4/THF} CH_3(CH_2)CH{=}CHCH_2CH_2OH$$



$$CH_3CH_2CH{=}CH\text{-}C(=O)\text{—}OCH_2CH_3 \xrightarrow[2.\ H^+/H_2O]{1.\ LiAlH_4/THF} CH_3CH_2CH{=}CH\text{-}CH_2OH$$

3. Catalytic Hydrogenation

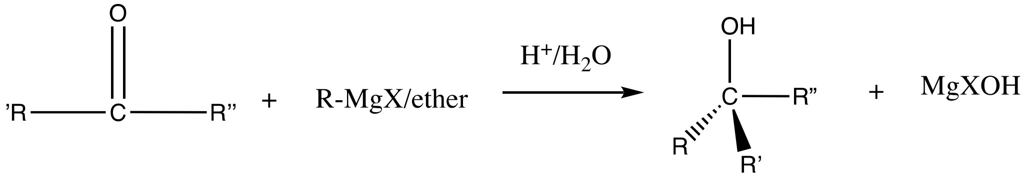
In this conversion, functional groups are reduced using catalysts. Only certain catalysts are active toward certain substrates. Some of the common catalysts are given below:

Ni, Pt, Pd, Rh, Ru, copper chromite, copper-barium-chromium oxide.

In catalytic hydrogenation, aldehydes, ketones, esters, and anhydrides are converted to alcohols.

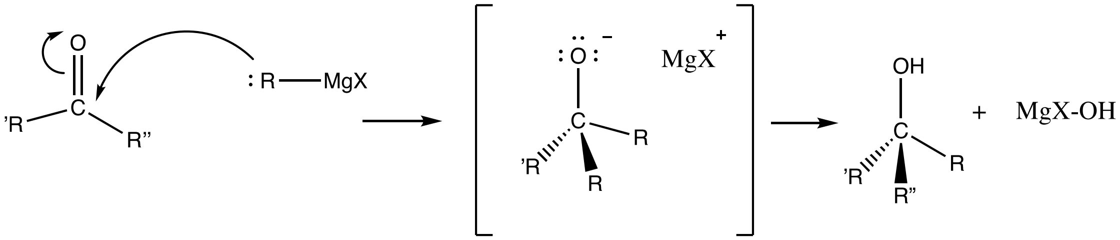
4. Using Grignard reaction

RMgX (Grignard) reacts with carbonyl compounds to produce alcohols.



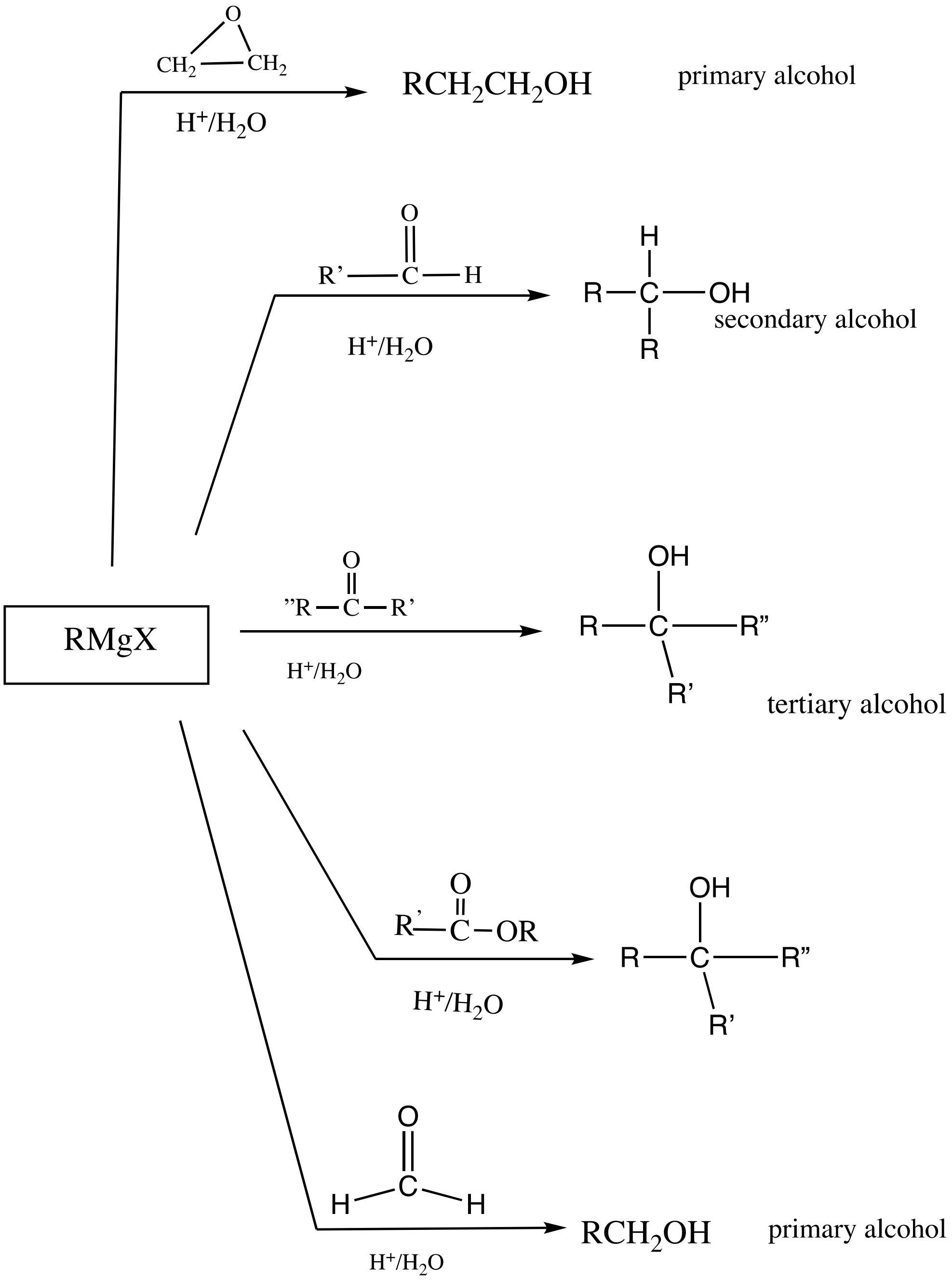
ketone

This is a very useful experiment. Carbonyl carbon acts as a nucleophile and a strong base. This is due to the bond between Mg and C being strongly polarized. As a result, the R group in Grignard reagent acts as a carbanion ($R:^-$) and undergoes nucleophilic, addition reactions.



alcohol

Depending on the reagents used, different types of alcohols can be produced.


RMgX
H+/H2O
RCH2CH2OH
primary alcohol
R'—C—H
R—C—OH
secondary alcohol
"R—C—R'
R—C—R"
tertiary alcohol
R'—C—OR
H—C—H
RCH2OH
primary alcohol

- **Protection of -OH group**

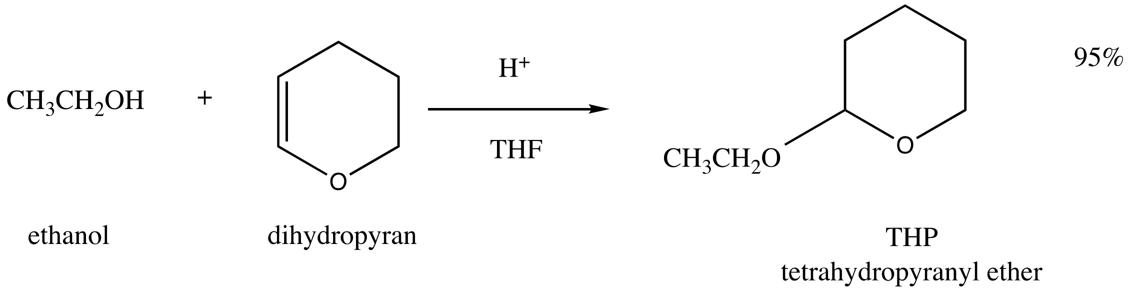
The protection of -OH group is necessary at times during a reaction. This is because in the formation of a complex molecule, two functional groups in the same molecule can interfere with each other.

e.g. Haloalcohol cannot be used to prepare Grignard regent since C-Mg bond is not compatible with an acidic OH group in the same molecule.

Therefore, the interfering group can be protected. This is done in the following order:

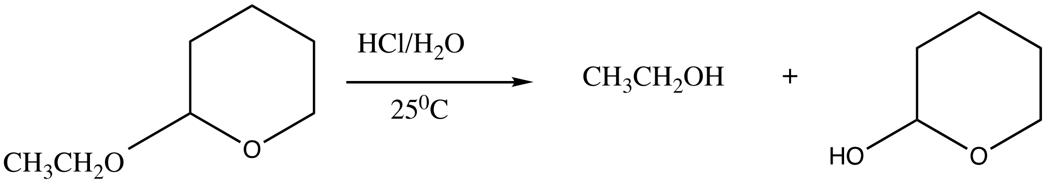
1. Form an inert derivative
2. Then, proceed with the desired reaction
3. Remove the protecting group

e.g. Formation of ether by reacting with dihydropyran.



THP ether here is inert. They are protected from nucleophiles, reducing agents, oxidizing agents, Grignard reagents, etc.

THP ethers (unlike other ethers) can be cleaved with acids to regenerate alcohol using aqueous mineral acid. Therefore, using this shielding, haloalcohols can be used to form Grignard reagent.



tetrahydropyranyl-1-ol

9.5.4 Industrial Preparation

Methanol is prepared by catalytic reduction of carbonmonoxide with H_2 gas.

$$CO \quad + \quad 2H_2 \xrightarrow[\text{ZnO/carbonmonoxide}]{400^{o}C} CH_3OH$$

Methanol can also be prepared in a crude form by heating wood in the absence of air.

Ethanol can be prepared using potatoes or grain or from fruit. The molasses (molasses is made by refining sugarcane or sugar beets into sugar) contain about 50% of fermentable sugar. This sugar is acidified with sulfuric acid and treated with yeast. The enzyme invertase and xymase in yeast will decompose sucrose to alcohol.

$$C_{12}H_{22}O_{16} + H_2O \xrightarrow{\text{invertase}} \underset{\text{glucose}}{C_6H_{12}O_6} \quad + \quad \underset{\text{fructose}}{C_6H_{12}O_8}$$

$$C_{12}H_{22}O_{16} + H_2O \xrightarrow{\text{Xymase}} 2C_2H_5OH \quad + \quad 2CO_2$$

9.5.5 Thiols Preparation

Thiols are synthesized using their corresponding alkyl halide by a S_N2 reaction with a sulfur nucleophile.

$$CH_3(CH_2)_3CH_2Br + Na^+ SH^- \longrightarrow CH_3(CH_2)_3CH_2SH + NaBr$$

2 – bromopentane

sodium hydrosulphide

1-pentanethiol

Since yields are poor in this reaction, an excess hydrosulfide is added. Otherwise, the above product will undergo further reaction with alkyl halide giving a symmetrical disulfide as a byproduct.

The following table shows the types of alcohol produced depending on the reagents/reactants and the reaction type:

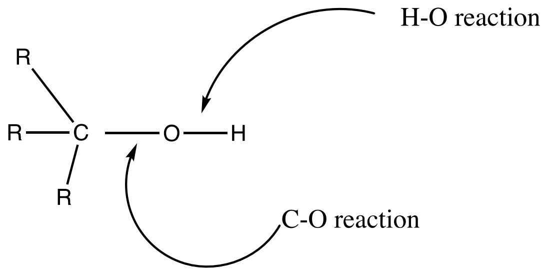
Reactants	**Reaction Type**	**Alcohol Type Produced**
Carboxylic Acid/$LiAlH_4$	Hydride Reduction	Primary
Ester/$LiAlH_4$	Hydride Reduction	Primary
Aldehyde/$NaBH_4$ or $LiAlH_4$	Hydride Reduction	Primary
Ketone/$NaBH_4$ or $LiAlH_4$	Hydride Reduction	Secondary
Formaldehyde/Grignard Reagent	Grignard Addition	Primary
Aldehyde/Grignard Reagent	Grignard Addition	Secondary
Ketone/Grignard Reagent	Grignard Addition	Tertiary

Table 9.5.5.1: Preparation of different types of alcohols using various reactants

9.6 Reactions of Alcohols and Thiols

There are two kinds of reactions:

1. C-O bond reactions
2. H-O bond reactions

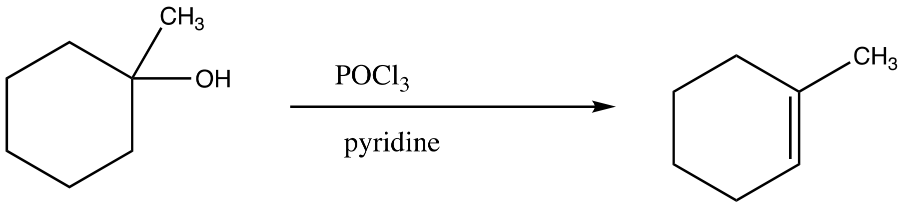


9.6.1 C-O Bond Reactions

1. Dehydration

Alcohol dehydration is a reaction at C-O bond. The resulting product is an alkene. This reaction is easier with tertiary alcohols when reacted with mineral acid under mild conditions. The loss of water produces an alkene. Nevertheless, primary and secondary alcohols need more rigorous conditions.

The dehydration of secondary or tertiary alcohols with $POCl_3$ in pyridine solvent is a useful reaction.



1-methyl cyclo hexanol

1-methyl cyclo hexene

2.Formation of alkyl halides

This is the a very valuable method.

a) Treat alcohol with HX (X = Cl, Br, I)

$$R\text{-}OH \xrightarrow{HX} R\text{-}X + H_2O$$

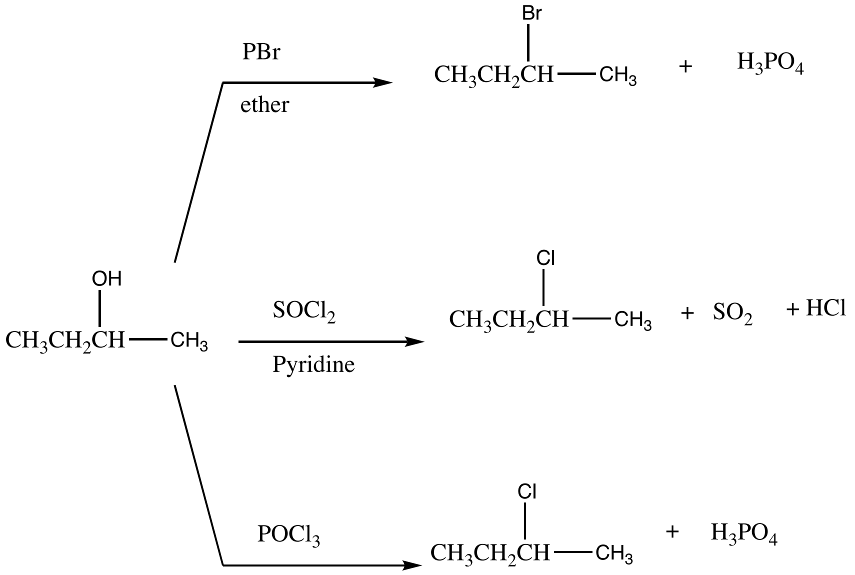
The reactivity order of alcohols are as follows:

$R_3COH > R_2CHOH > RCH_2OH$

Tertiary > Secondary > Primary alcohols

Although, tertiary alcohol reacts easily, secondary and primary alcohols also can be converted to R-X by adding $ZnCl_2$ as a catalyst.

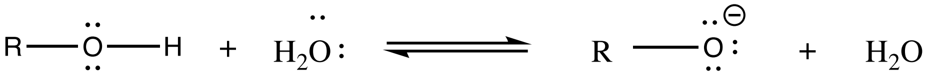
b) Primary and secondary alcohols to halides
This reaction is carried out by using different reagents.



9.6.2 O-H Bond Reactions

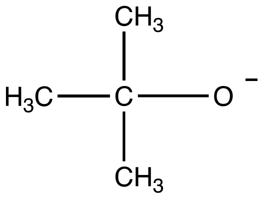
1. Acidity of alcohols

Alcohols behave as weak acids in dilute, aqueous forms. Alcohols dissociate in these conditions by donating a proton to the base, water.

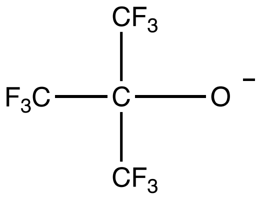


The pKa of methanol is 15.5 and that of ethanol is 16.0. (pKa indicates the acidity of a solution. If pKa is small, then the acidity is high.) pKa of an alcoholic compound with electron-withdrawing groups (such as CF_3) attached will have a much lower pKa. This is because the electron-withdrawing groups stabilize the alkoxide ion thereby increasing the acidity.

e.g.



pKa = 18



pKa = 5.4

tert- butyl alcohol

Since alcohols are weaker acids in general (mineral and carboxylic acids are stronger acids), they do not react with weak bases such as ammonia or bicarbonate ion. Yet, these react with strong bases such as sodium amide ($NaNH_2$), sodium hydride (NaH), Grignard reagents, and alkyl lithium reagents.

$$2\,CH_3OH + 2\,Na \longrightarrow 2\,CH_3O^-\,Na^+ + H_2$$

$$CH_3OH + NaH \longrightarrow CH_3ONa + H_2$$

$$2\,(CH_3)_3COH + 2\,K^{+\cdot} \longrightarrow 2\,(CH_3)_3CO^-K^+ + H_2$$

2) Formation of ether

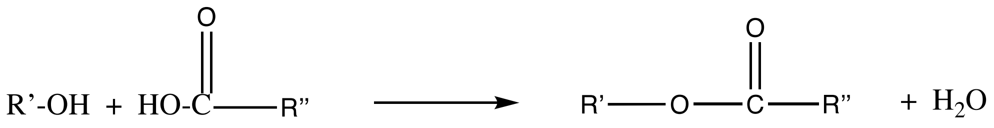
An S_N2 reaction between alkoxide anion and a primary halide is known as the Williamson ether synthesis.

$$CH_3CH_2\overset{-}{O}Na^{+} + CH_3CH_2CH_2Cl \longrightarrow CH_3CH_2OCH_2CH_2CH_3 + NaCl$$

3) Ester formation

Alcohols react with organic carboxylic acids and produce esters.

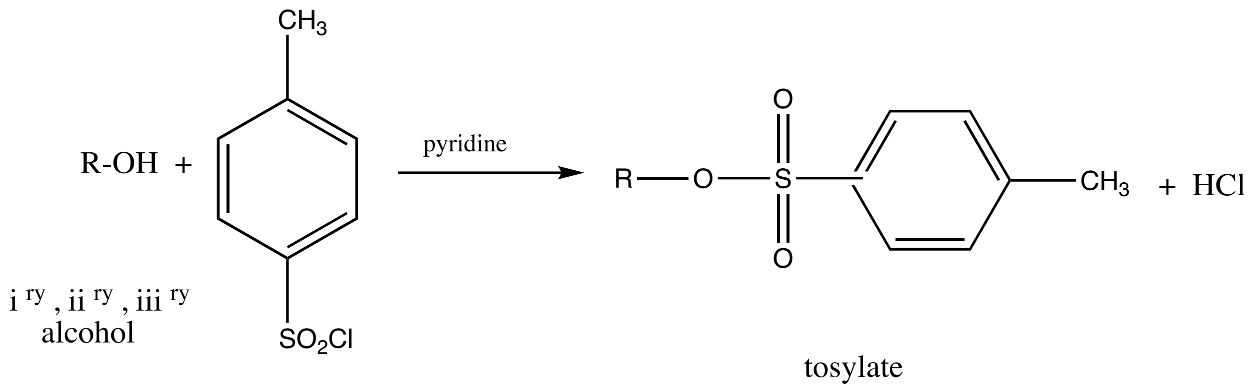
Alcohol + Carboxylic Acid → Ester and water



$$R'\text{-}OH + HO\text{-}\overset{\overset{\displaystyle O}{\|}}{C}\text{—}R'' \longrightarrow R'\text{—}O\text{—}\overset{\overset{\displaystyle O}{\|}}{C}\text{—}R'' + H_2O$$

4) Tosylate (p-toluene sulphonate) formation

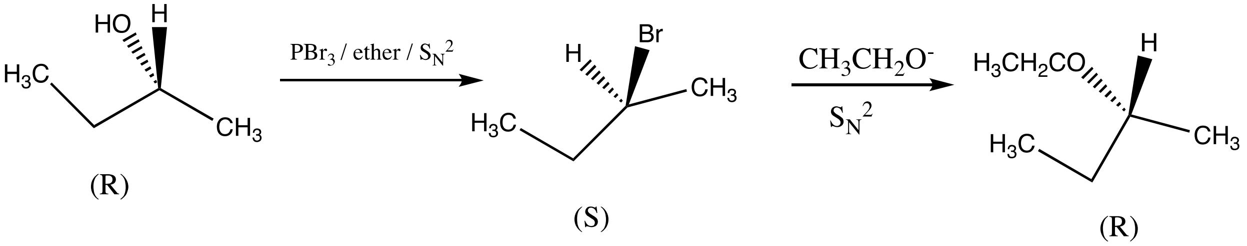
Alcohol can be converted to a tosylate using the following reaction:

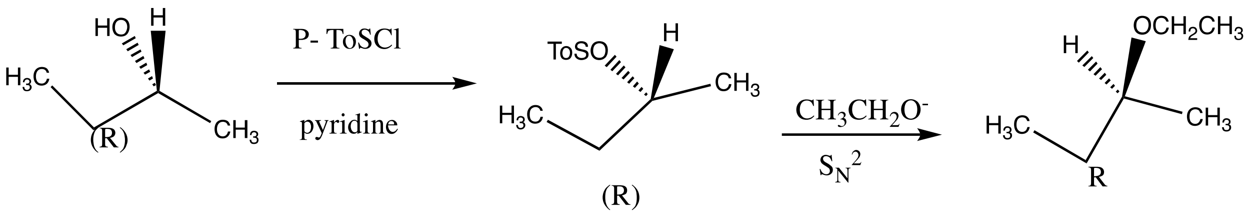


This conversion is important because alcohols normally do not undergo S_N2 displacement by nucleophiles (OH- is a poor leaving group in displacement).

Therefore, the conversion of alcohol into a tosylate makes it easier to undergo S_N1 or S_N2 displacement.

- Use of a tosylate is easier than converting alcohol to a halide and then proceeding with other reactions. Also, the use of tosylate instead of halides produce a product with stereochemistry opposite to the starting material. Tosylate pathway undergoes one inversion. When halide route is used, the pathway includes two inversions, and the stereochemistry of the product will match the starting material. Both pathways lead to S_N2 mechanisms.





9.6.3 Oxidation

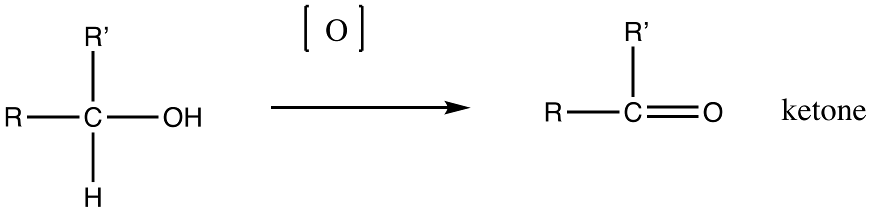
9.6.3.1 Alcohol Oxidation

The oxidation of alcohols depends on the type of alcohol:

Primary alcohols produce aldehydes and carboxylic acids.

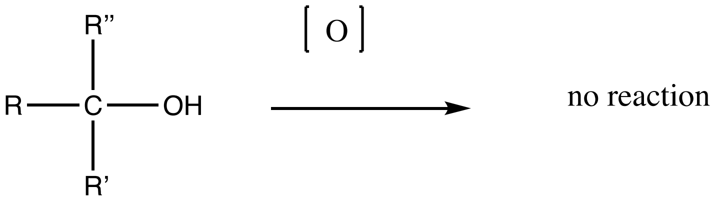
$$RCH_2OH \xrightarrow{[O]} \underset{\text{aldehyde}}{RCHO} \xrightarrow{[O]} \underset{\text{carboxylic acid}}{RCOOH}$$

Secondary alcohols produce ketones.



$$R-\overset{R'}{\underset{H}{C}}-OH \xrightarrow{[O]} R-\overset{R'}{C}=O \quad \text{ketone}$$

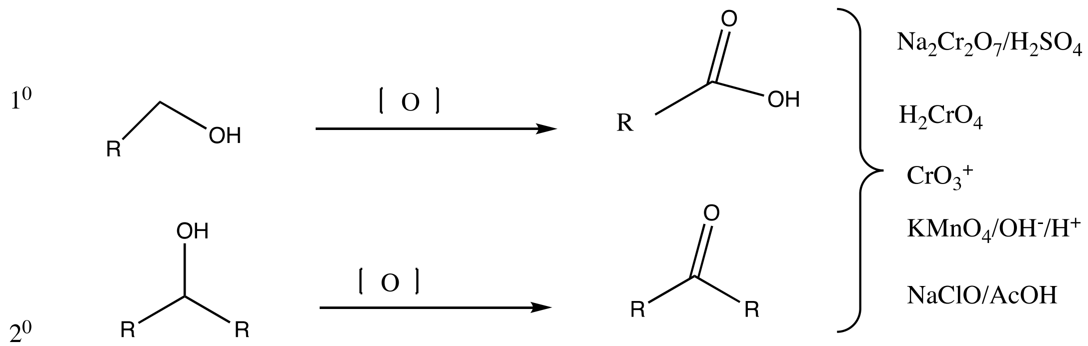
Tertiary alcohols do not react with most oxidizing agents, except under vigorous conditions.



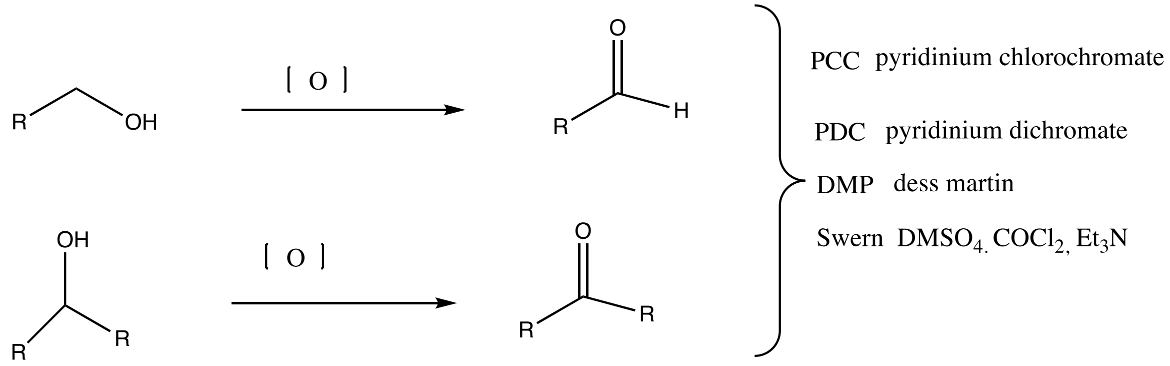
$$R-\overset{R''}{\underset{R'}{C}}-OH \xrightarrow{[O]} \text{no reaction}$$

The following table shows how alcoholic oxidation varies depending on the type of alcohol and the type of reagents used:

strong oxidizing agen ts oxidize primary alcohol to carboxylic acids and secondary alcohols to ketones



Some oxidizing agents can selectively oxidize primary alcohol to aldehyde



tertiary alcohol cannot be oxidized

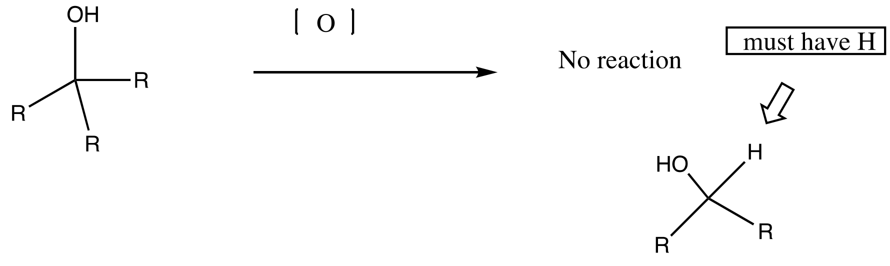
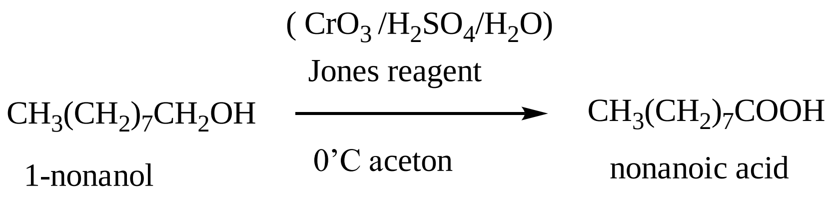


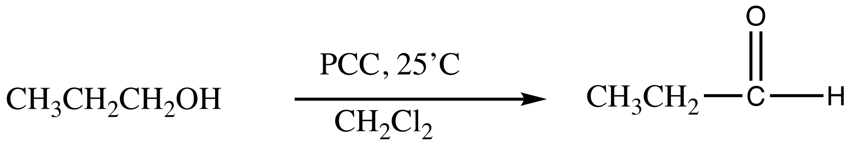
Table 9.6.3.1.1.: Alcoholic oxidation varies depending on the type of alcohol and the type of reagents used

NB: Where carboxylic acid is shown as the final product, it means the reaction cannot be stopped after alcohol turns to aldehyde due to continuous oxidation.

9.6.3.2 Oxidation using different Reagents

- 

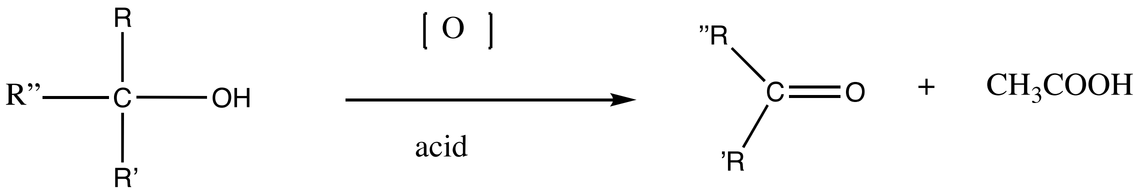
$$\underset{\text{1-nonanol}}{CH_3(CH_2)_7CH_2OH} \xrightarrow[\text{0'C aceton}]{(CrO_3/H_2SO_4/H_2O)\ \text{Jones reagent}} \underset{\text{nonanoic acid}}{CH_3(CH_2)_7COOH}$$

- $CrO_3/H_2SO_4.H_2O$ is known as Jones reagent
- The conversion of alcohol to an acid is carried out at 0^0C in the presence of Jones reagent.
- The conversion of primary alcohol to an aldehyde in the presence of PCC and CH_2Cl_2 is carried out at a temperature of 25^0C.
- 

$$CH_3CH_2CH_2OH \xrightarrow[CH_2Cl_2]{\text{PCC, 25'C}} CH_3CH_2-\overset{\overset{\large O}{\|}}{C}-H$$

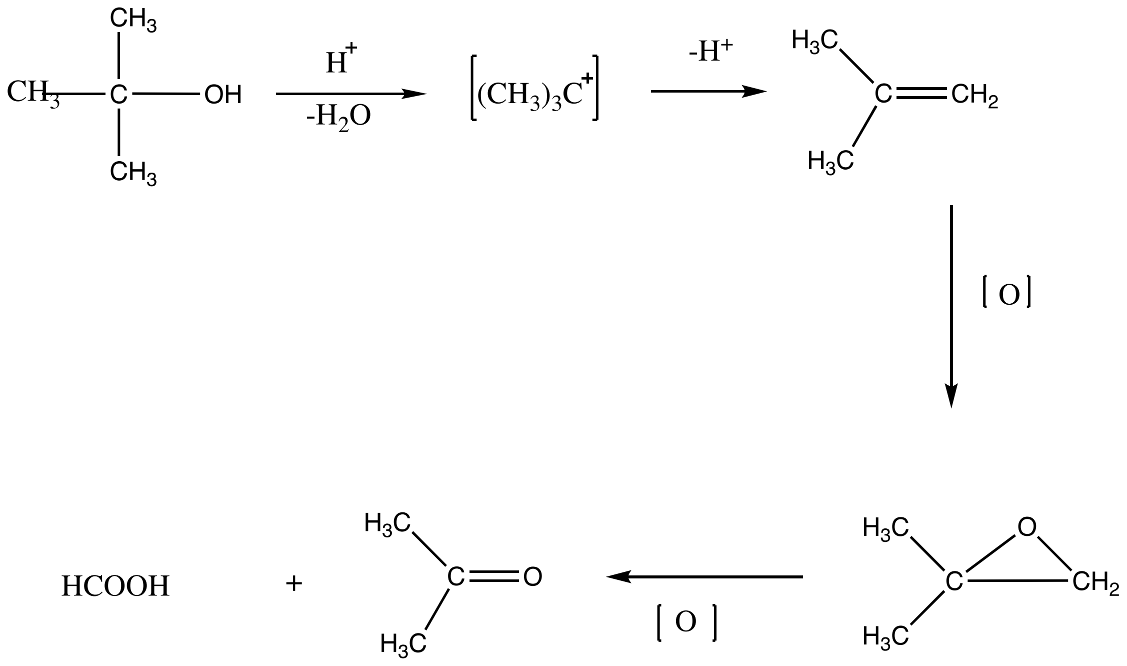
- More sensitive alcohols are oxidized using PCC or Jones reagent since the conditions are mild and the reactions are carried out at a low temperature.
- Large scale oxidations are carried out using sodium dichromate in aqueous acetic acid due to low cost.
- All the oxidation reactions happen via E2 reactions.
- Tertiary alcohols do not get oxidized under mild conditions (basic or neutral conditions), but they form ketones and carboxylic acids when oxidized in acidic medium.

e.g. 1



R
R''
C
OH
R'
[O]
acid
''R
C
O
'R
+
CH_3COOH

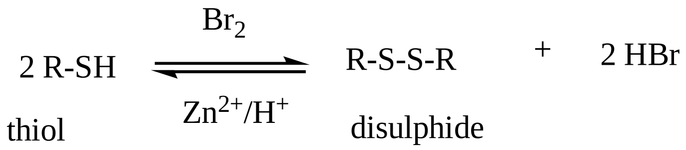
e.g. 2



CH_3
CH_3
C
OH
CH_3
H^+
$-H_2O$
$[(CH_3)_3C^+]$
$-H^+$
H_3C
C
CH_2
H_3C
[O]
H_3C
O
C
CH_2
H_3C
[O]
HCOOH
+
H_3C
C
O
H_3C

9.6.3.3 Thiols Oxidation

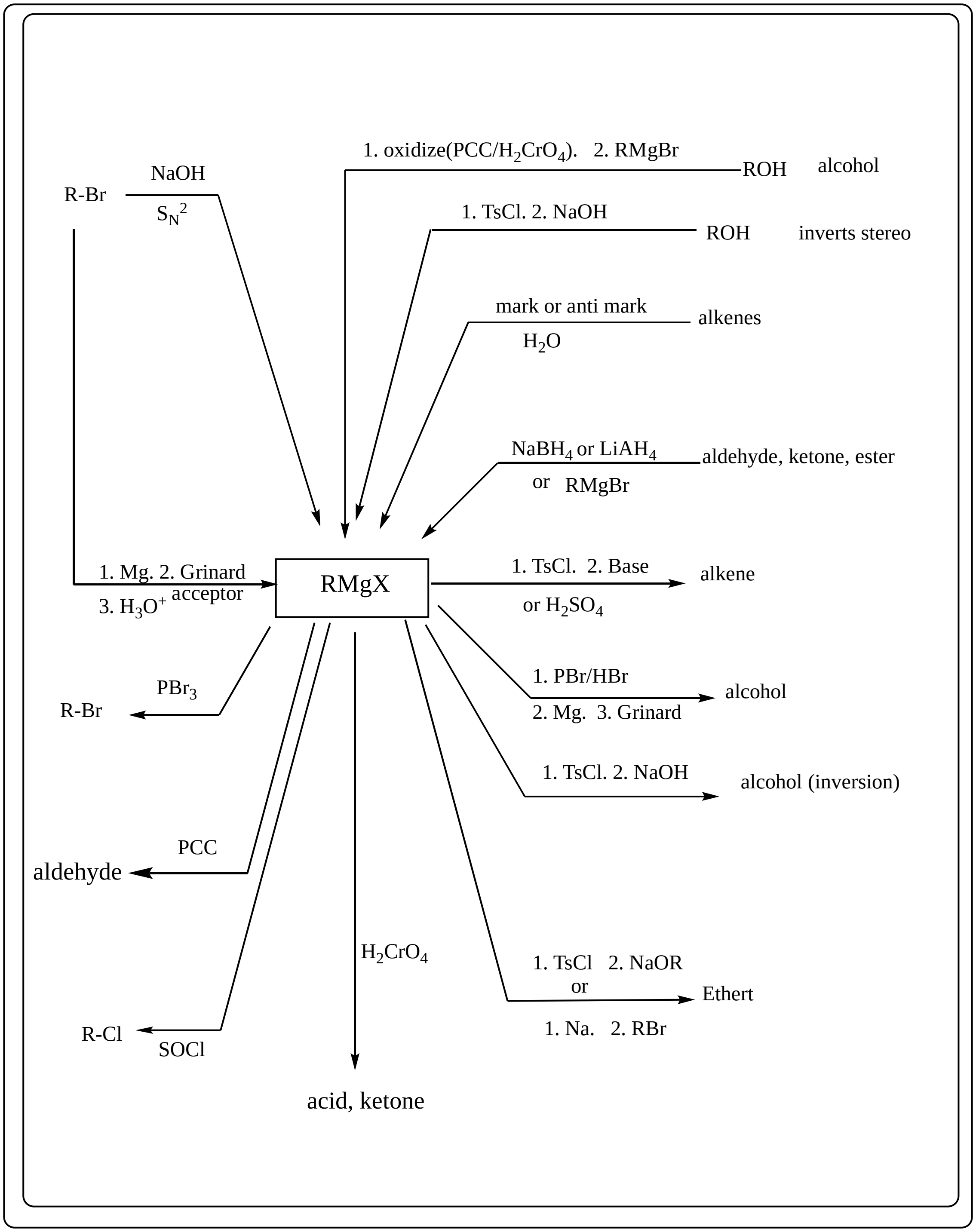
Thiols are oxidized by mild reagents such as Br_2 and I_2 to produce disulfides. This is a reversible reaction since thiols can be reproduced using Zn and acid.



$$\underset{\text{thiol}}{2\ \text{R-SH}} \xrightleftharpoons[Zn^{2+}/H^{+}]{Br_2} \underset{\text{disulphide}}{\text{R-S-S-R}} + 2\ \text{HBr}$$

These disulfide bridges play an important role in protein synthesis.

9.7 Summary of Reactions



Chapter 10

10.0 Ethers

10.1 Objectives

1. Draw and interpret Lewis structures, line-bond structures and functional groups of ethers using IUPAC system of nomenclature.
2. Draw reaction mechanisms.
3. Describe reactions, predicting reactivity, and reaction products.
4. Devise syntheses including steps, reagents, and products including regiochemistry and stereochemistry

10.2 Introduction

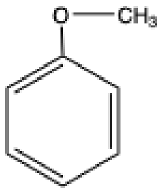
Ether contains two alkyl or aryl, or any combination of such groups joined by an oxygen atom of an open or closed chain.

e.g.

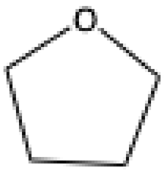
- Diethyl ether

$$CH_3CH_2—O—CH_2CH_3$$

- Methyl phenyl ether (anisole)



- A cyclic ether - Tetrahydrofuran (THF)



The general formula for ether is $C_nH_{2n+2}O$. This formula is the same as monohydric alcohols. Therefore, if you compare ether with alcohol, you will notice that ether is derived by substituting an alkyl or aryl group to the H atom of -OH of an alcohol.

e.g.

CH_3CH_2-OH

n = 2 in this alcohol.

$CH_3CH_2-O-CH_2CH_3$

n = 4 in this ether.

H atom of ethanol has been replaced with CH_2CH_3. The ethyl is called diethyl ether. The common formula $C_nH_{2n+2}O$ can be applied to both compounds.

Since both R groups are the same in this example, such an ether is known as symmetrical ether. When the two R groups are different, such an ether is called an unsymmetrical or mixed ether.

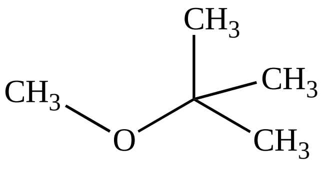
10.3 Nomenclature and Isomerism

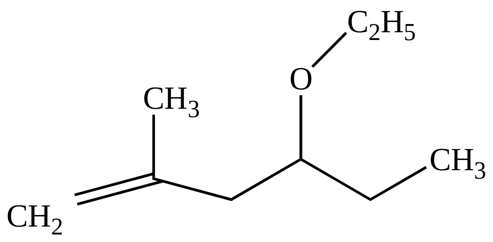
Please refer to the chapter on nomenclature and isomerism and answer the following questions:

1. **Naming Compounds – Give the IUPAC names for the following compounds.**
   a. $CH_3CH_2CH_2CH_2CH_2\text{-}O\text{-}CH_2CH_2CH_3$
   b. $CH_3\text{-}CH_2\text{-}O\text{-}CH_2\text{-}CH_3$

2. **Draw the structure of the following compounds**

a)



b) 

3. **Question on Isomers**

Name the class of isomers of the following two compounds.

R-CH_2-CH_2-OH

R-CH_2 O-CH_3

Solutions:

1. **Naming Compounds – Give the IUPAC names for the following compounds:**

a. 1-propoxypentane
b. 1-ethoxyethane

2. **Draw the structures of the following compounds:**
   a. 2-methoxy-2-methylpropane
   b. 4-ethoxy-2-methyl-1-hexene

3. **Questions on Isomers**

a. Functional isomers

10.4 Physical Properties

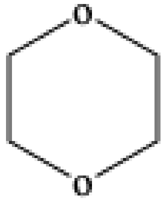
The lower molecular weight ethers are gases or easily evaporating (volatile) liquids. These compounds produce highly flammable vapors. The boiling points of these compounds are lower than that of their corresponding alcohols due to the absence of hydrogen bonding. Ethers are less dense than water (float on water) and are mostly insoluble (the solubility in water and H bonding are dependent on the structure of the ether).

Ethers have lower boiling points than their corresponding alcohols. They do not react with mild acids, active metals, strong bases, nucleophiles, reducing or oxidizing agents. As a result, ethers are good solvents for many reactions. THF is more soluble in water due to the lone pair of O atom being available because of the cyclic structure. When there are acyclic R groups attached to the O atom, they will interfere with H bonding. When a cyclic R group is attached to ether, the interference is less; therefore, H bonding is favored leading to higher boiling points and solubility in water.

The angle between the two R groups at the center of O atom is about 110^0. As a result, ethers display significant dipole moments, because the angle does not allow the cancellation of diploe moments.

The presence of an alkyl group, the possible cleavage between C-O, and the lone pair of electrons on O atom affect the chemical properties of ethers.

Although most ethers are stable, the following compounds react slowly with air to produce peroxides (compounds with O-O bonds). They are highly explosive and dangerous compounds.



Dioxane

CH_3-O-CH_2-CH_2-O-CH_3

1,2 dimethoxy ethane (DME, Glyme)

CH_3-O-CH_2-CH_2-O-CH_2-CH_2-O-CH_3

Bis-β -methoxyethyl ether (diglyme)

10.5 Preparation of Ethers

Ethers are prepared from nucleophilic displacement reactions.

10.51 From alcohols in acid

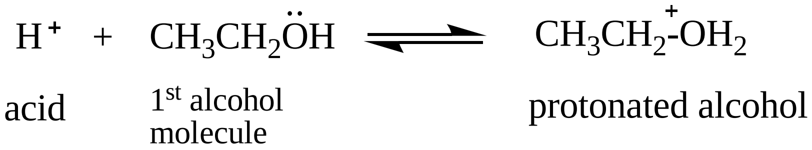
This method is used to form symmetrical or simple ethers in industries.

Dehydration of alcohols is carried out using sulfuric acid.

$$2\ CH_3\text{-}CH_2\text{-}OH \xrightarrow{H_2SO_4} CH_3\text{-}CH_2\text{-}O\text{-}CH_2\text{-}CH_3 + H_2O$$

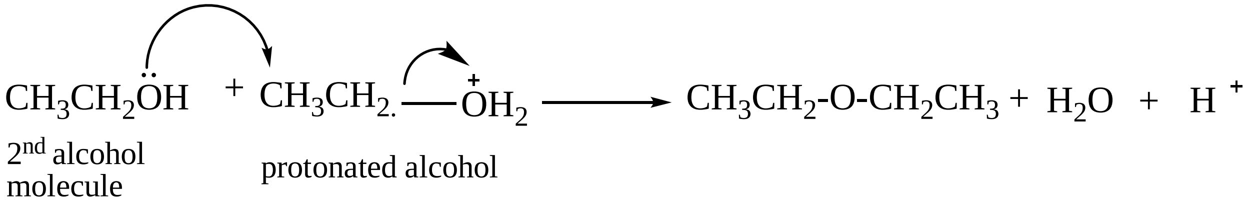
Reaction Mechanism:

Step 1: Fast reaction



$$H^+ + CH_3CH_2\ddot{O}H \rightleftharpoons CH_3CH_2\text{-}\overset{+}{O}H_2$$

Step 2: S_N2 path:

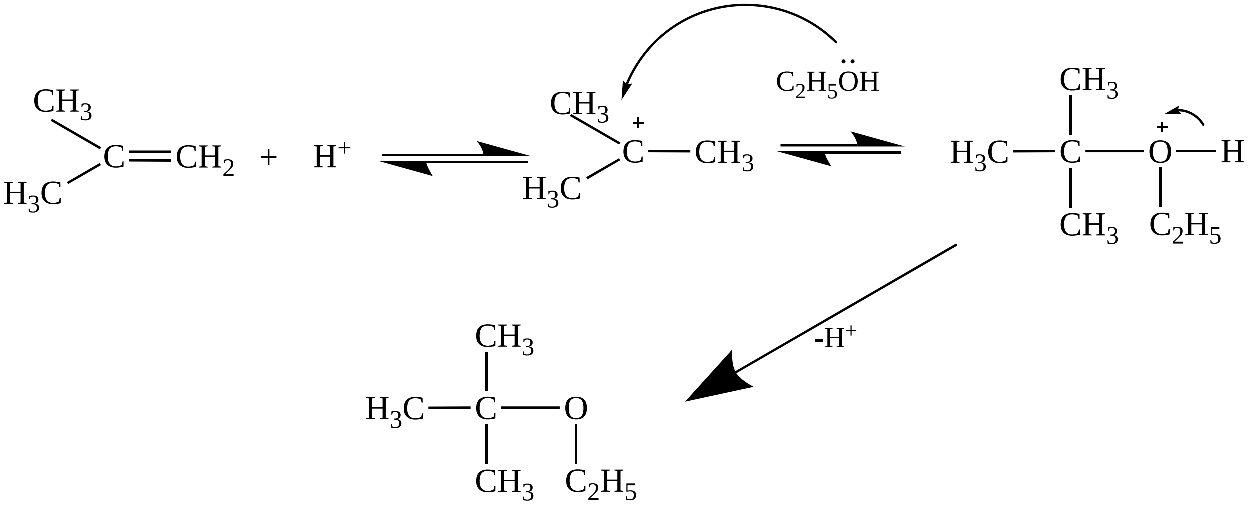


$$CH_3CH_2\ddot{O}H + CH_3CH_2\text{—}\overset{+}{O}H_2 \longrightarrow CH_3CH_2\text{-}O\text{-}CH_2CH_3 + H_2O + H^+$$

The limitation of this reaction is that ether can be prepared only with primary alcohols. When this reaction is carried out with secondary or tertiary alcohols, the result would be alkenes.

10.52 Alkenes in acid

In this reaction, a tertiary cation is produced through protonation of an alkene, which in turn reacts with a primary or secondary alcohol to produce an ether molecule. This reaction produces a mixture of ethers.



t-butyle ethyle ether

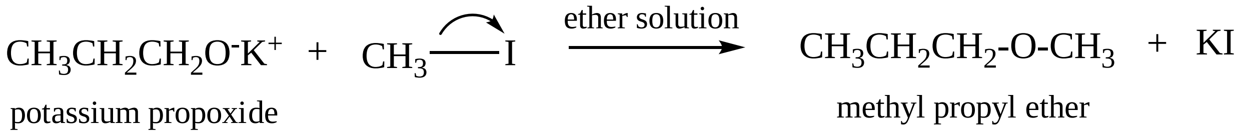
10.53 Williamson synthesis

This is a popular form of synthesis of ethers in a laboratory. This method provides symmetrical and asymmetrical ethers.

$$R\text{-}OH + NaH \longrightarrow RO^- Na^+ + H_2$$

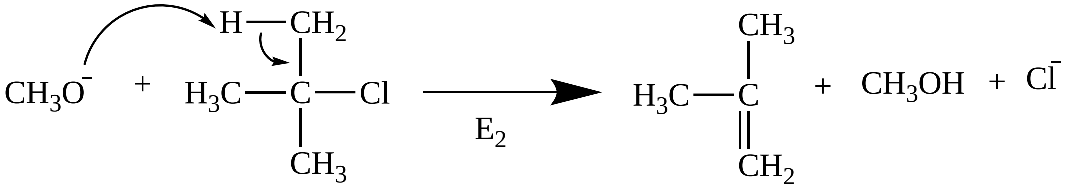
Sodium alkoxide is produced by reacting alcohol with a strong base such as sodium hydride.

In the reaction below, potassium propoxide is reacted with an alkyl halide.



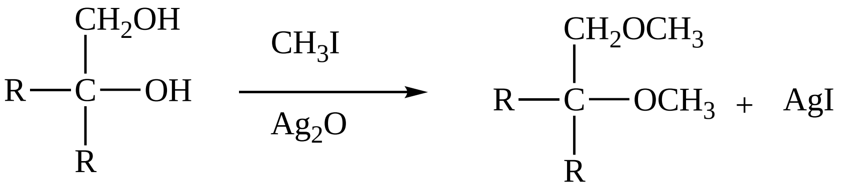
This is an S_N2 reaction where alkyl halides and alkoxide react to produce ethers. In general, primary alkyl halides are used in this reaction.

When secondary or tertiary alkyl halides are used, the reaction will follow E2 path in the presence of a base. The resultant is an alkene.



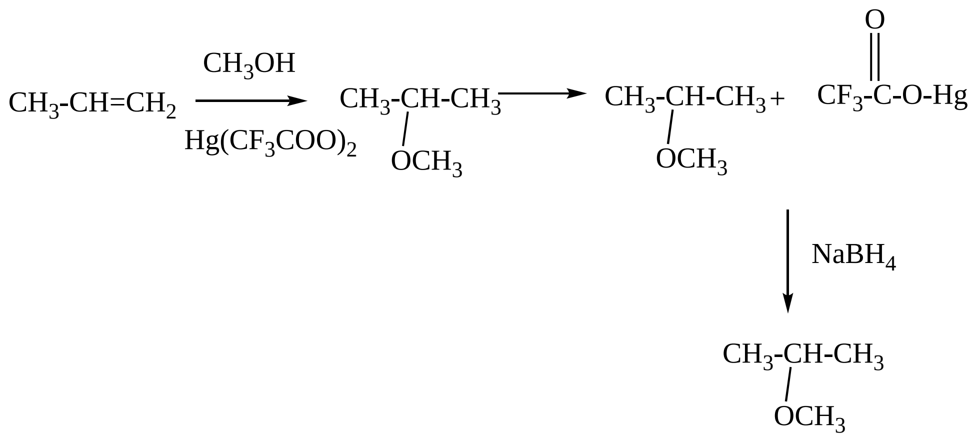
Therefore, in the preparation of mixed ethers, the less hindered alkyl halide (primary) is made to react with more hindered alkoxide, or more hindered alkyl halide (secondary or tertiary) is made to react with less hindered alkoxide.

A variation of Williamson reaction is the use of silver oxide. In this reaction, the free alcohol directly reacts with alkyl halide without forming metal alkoxide.



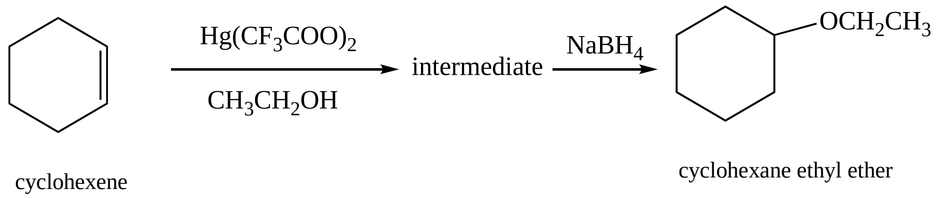
10.54 Demercuration of alkenes (alkoxymercuration)

1.



$$CH_3\text{-}CH{=}CH_2 \xrightarrow[Hg(CF_3COO)_2]{CH_3OH} CH_3\text{-}\underset{OCH_3}{CH}\text{-}CH_3 \longrightarrow CH_3\text{-}\underset{OCH_3}{CH}\text{-}CH_3 + CF_3\text{-}\overset{O}{\overset{\|}{C}}\text{-}O\text{-}Hg \xrightarrow{NaBH_4} CH_3\text{-}\underset{OCH_3}{CH}\text{-}CH_3$$

2.



In the above reactions, an alkene reacts with alcohol in the presence of mercuric trifluoracetate. When the produced oxymercuration compound is reacted with $NaBH_4$, the C-Hg bond breaks (demercuration) to produce an ether. The overall reaction is the Markovnikov addition of alcohol to an alkene.

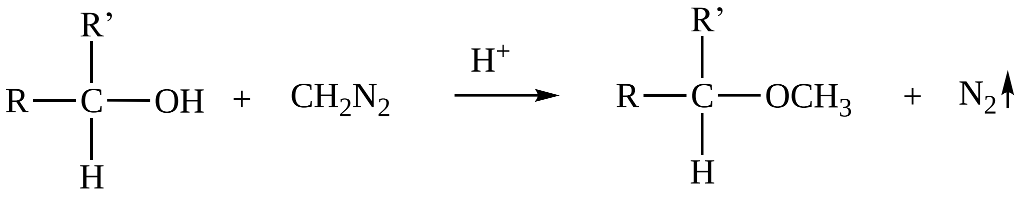
10.55 Grignard reagent

When Grignard reagent is reacted with a monochloro ether, the chloro atom is removed to form the ether. This method is used to increase the alkyl carbon chain of ether.

$$R'O\text{—}CH_2\text{—}Cl + R''MgX \longrightarrow R'\text{——}O\text{——}CH_2R'' + MgXCl$$

10.56 Diazomethane reaction

When alcohols are treated with diazomethane in the presence of a catalyst such as aluminum alkoxide or fluoroboric acid, ethers are formed.



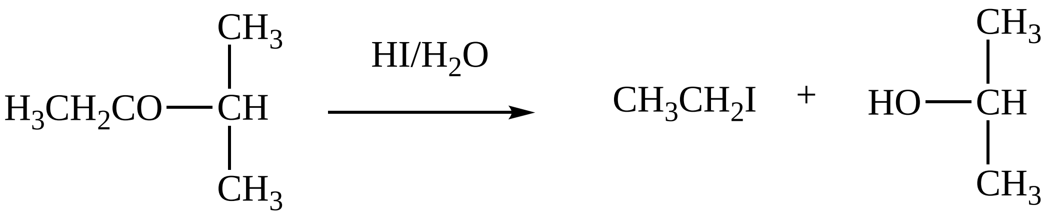
$$R-\overset{R'}{\underset{H}{C}}-OH + CH_2N_2 \xrightarrow{H^+} R-\overset{R'}{\underset{H}{C}}-OCH_3 + N_2\uparrow$$

10.6 Reactions of Ethers

10.6.1 Reactions with acids

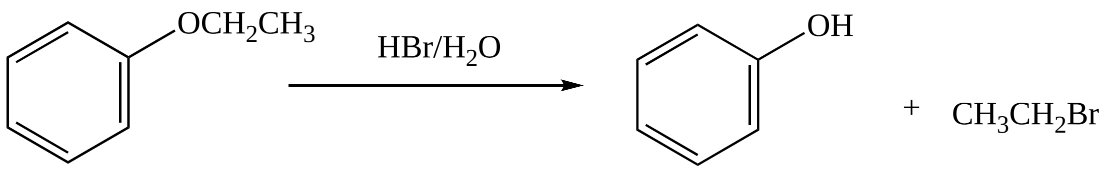
- The reactions with strong acids lead to acidic cleavage.

e.g.



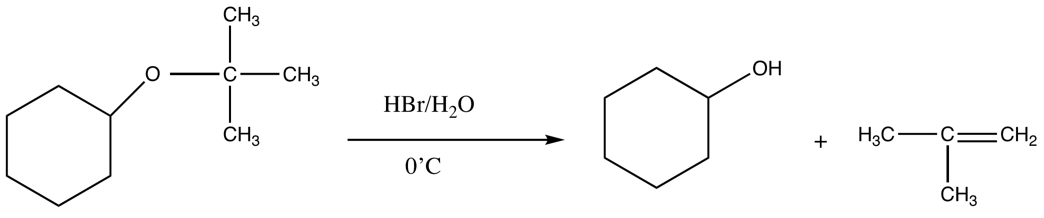
$$H_3CH_2CO-\overset{CH_3}{\underset{CH_3}{CH}} \xrightarrow{HI/H_2O} CH_3CH_2I + HO-\overset{CH_3}{\underset{CH_3}{CH}}$$

ethyl isopropyl ether



ethyl phenyl ether

phenol

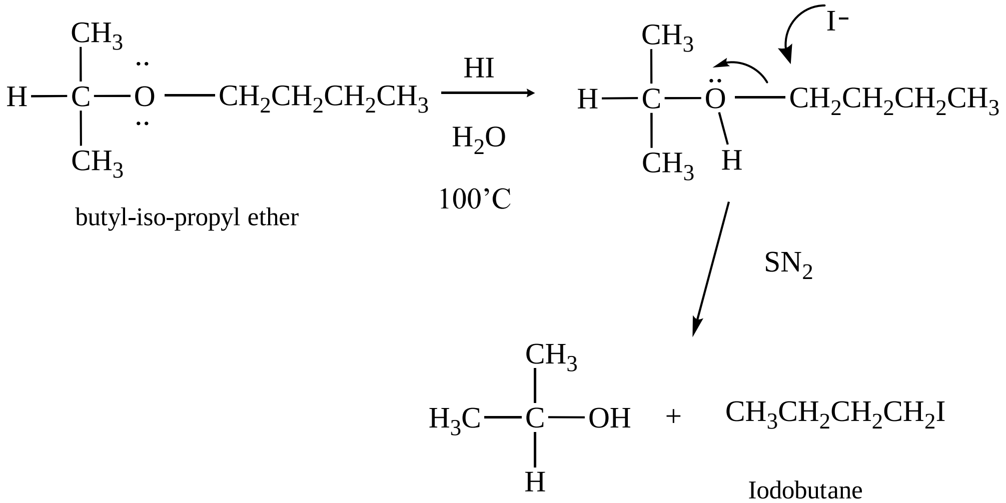


t-butyl cyclohexyl ether

2-methyl propene

- Aqueous HI and HBr are used to cleave ethers. Yet, aqueous HCl does not break ether bonds.
- Another cleaving agent is BCl_3. This is a mild reagent that reacts at 0^0C. This reagent is useful to cleave sensitive ethers that may be destroyed when refluxed with HI.

The above reactions happen under S_N1 or S_N2.



butyl-iso-propyl ether

Isopropyl alcohol

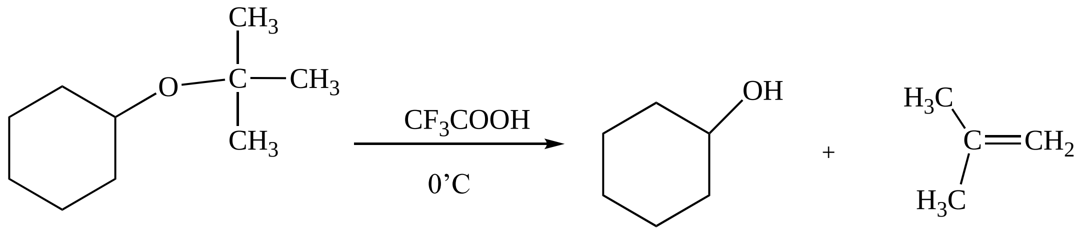
Iodobutane

The produced alcohol can react with excess HI at high temperature to provide the corresponding iodide.

$$\text{R-OH} + \text{HI} \longrightarrow \text{RI} + H_2O$$

- When ether undergoes cleavage after reacting with primary or secondary alkyl halides, they undergo S_N2 pathway. The result is a selective attack by an iodide or a bromide ion at a less substitute (less hindered) site. This leads to a single alcohol and a single alkyl halide instead of a mixture. The O atom of ether stays with the more hindered alkyl group.
- Tertiary, benzylic, and allylic ethers follow S_N1 path, because intermediate carbocations are stable.

e.g.



t-butyl cyclohexyl ether

cyclo hexanol (90%)

Note the use of CF_3COOH instead of HI or HBr.

- When ethers react with concentrated inorganic acids, they form oxonium salts.

  e.g.

$$C_2H_5\text{-}O\text{-}C_2H_5 + H_2SO_4 \rightleftharpoons [(C_2H_5)_2OH]^+ HSO_4^-$$

- When ethers are warmed with concentrated sulfuric acid, they produce alkyl hydrogen sulfates.

  e.g.

$$C_2H_5\text{-}O\text{-}C_2H_5 + H_2SO_4 \rightleftharpoons [(C_2H_5)_2OH]^+ HSO_4^- \longrightarrow C_2H_5OH + C_2H_5HSO_4$$

- When ethers are heated with dilute sulfuric acid under pressure, they produce their corresponding alcohol.

e.g.

$$C_2H_5\text{-}O\text{-}C_2H_5 + H_2O \xrightarrow{H_2SO_4} 2\ C_2H_5OH$$

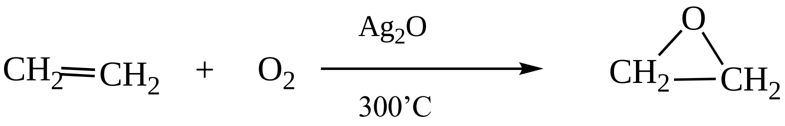
10.6.2. Reactions of epoxides - ring opening

Whilst acyclic and cyclic ethers behave the same way, epoxides or oxiranes behave differently.

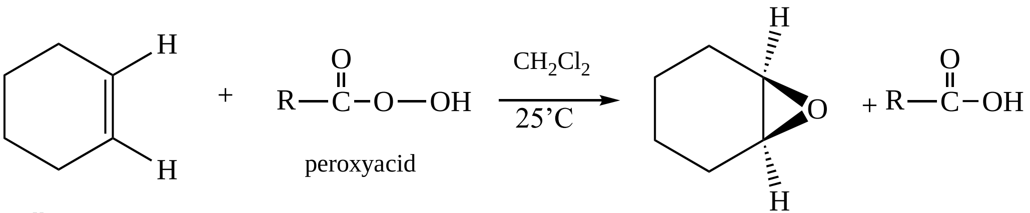
Epoxides or oxiranes are three-membered rings containing oxygen.

- Formation of epoxide

1.



2. Laboratory preparation of epoxides are prepared by mixing alkene with peroxy acid.



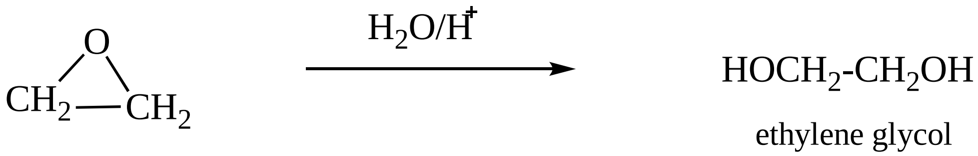
peroxyacid

alkene

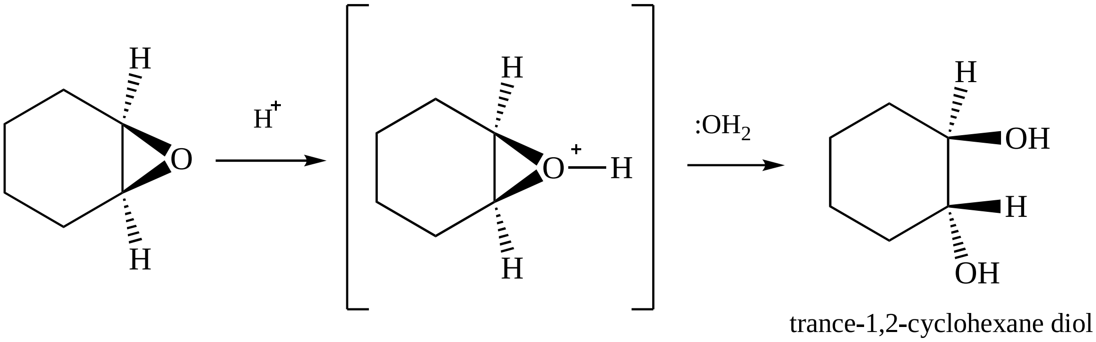
cyclohexene epoxide
1,2-epoxycyclohexene

- Ring Opening

Ring opening of epoxides can be done with acids at mild conditions, because of the existence of ring strain. Generally, an aqueous mineral acid will cause hydrolysis producing 1, 2-diols.

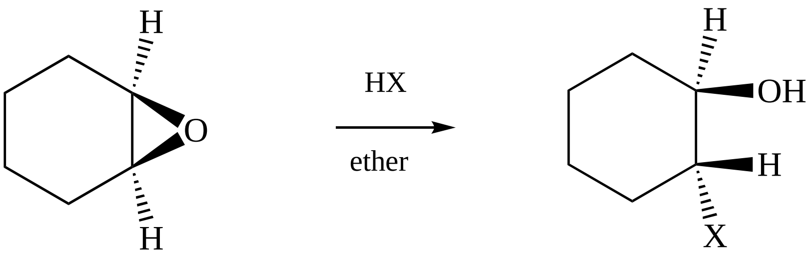


The ring opening follows S_N2 path when a nucleophile attacks on the protonated epoxide similar to the reaction given below:

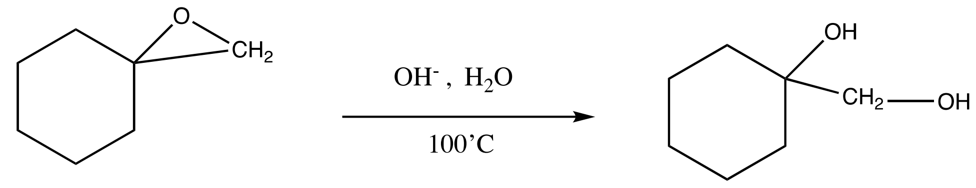


There are several nucleophiles such as HX can be used to open epoxides as well.

e.g.



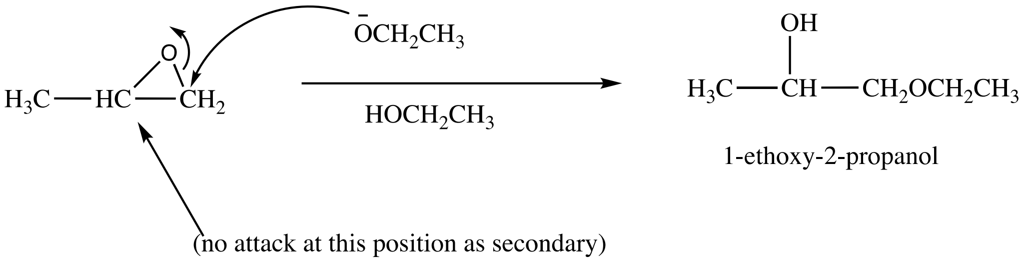
Unlike ethers, epoxides can be cleaved by a base. The reactivity of the three-membered ring makes it possible to react with hydroxide ion at high temperature (compare this with O atom of ether, which is a poor leaving group in S_N2 reactions.)



methylene cyclohexane oxide

1-hydroxy methyl cyclohexanol 70%

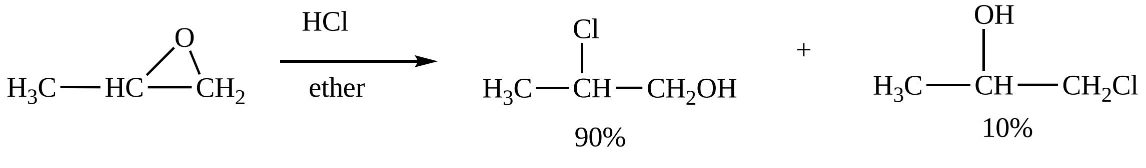
- The direction of ring opening of unsymmetrical epoxides depends on the conditions used. If a base is used, then the reaction follows S_N2 path and the attack happens at the less hindered epoxide carbon.



1-ethoxy-2-propanol

(no attack at this position as secondary)

- When an acid is used the attack takes place at the more substituted carbon.



90%

10%

1,2 epoxy propane

2-chloro-1-propanol

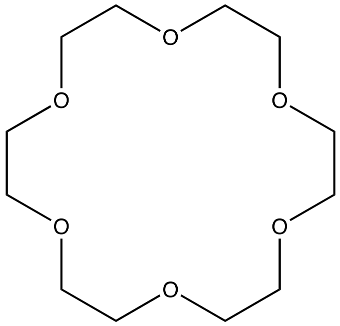
This difference in regiochemistry is explained as follows:

The transition state of an acid induced opening has a high degree of carbocationic character. Therefore, attack of the nucleophile occurs at the more stabilized (highly substituted) cationic site.

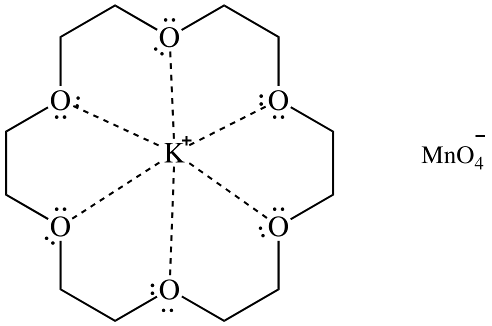
- **Crown ethers**

Crown ethers are a class within ether group. These are cyclic polymers of ethylene glycol and are named according to the x- crown-y-ether system. X is the total number of atoms in the ring and y is the number of oxygen atoms.

e.g.



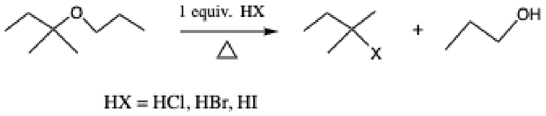
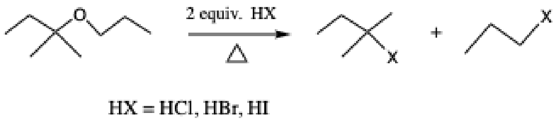
18-crown-6-ether



KMnO4 solvated by 18-crown-6-ether

The crown ethers can solvate metal cations by trapping metals in the polyether cavity. Different crown ethers solvate different metals, which are dependent on the ion size and the cavity size. These compounds are soluble in nonpolar organic solvents.

10.7 Summary of Ether Reactions

Reaction	Regiochemistry	Stereoselectivity	
Williamson ether synthesis	No rearrangement	Inversion, S_N2	
Dehydration of alcohol	No differentiate ether formation from alkene formation	N/A	
Acid catalyzed addition to the alkene	Rearrangements possible	None	 Carbocation intermediate
Acid cleavage of ethers	With 1 equivalent, x will go to more substituted if 3^0,2^0/3^0 benzylic 2^0 still undergo S_N^2 so 1^0 will get x	None	 Carbocation intermediate
Acid cleavage of ethers	Both atoms connected to the ether oxygen have halogen	None	 Carbocation intermediate

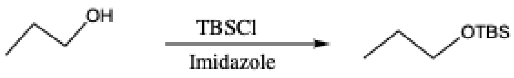
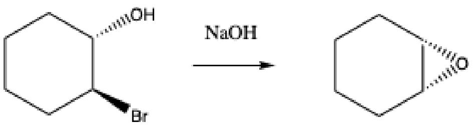
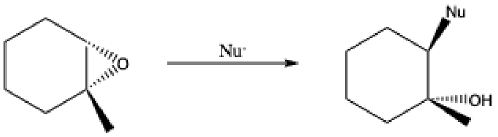
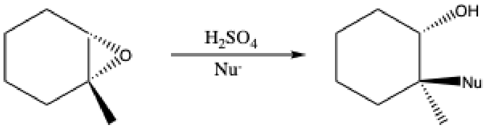
Making silyl ether	N/A	N/A	
Removing silyl ether	N/A	N/A	
Halohydrin to epoxide	N/A	Stereochemistry of -OH becomes stereochemistry of epoxide	
Peroxyacid	No rearrangement	Syn-addition	
Nucleophilic ring opening of epoxide	Nu adds to least substituted side of epoxide	Inversion	
Acid catalyzed ring opening of peroxide	Nu adds to most substituted side of epoxide	Inversion	

Table 10.7.1 Summary of all ether reactions including synthesis

- **A Summary of Tosylate (Toluenesulfonate) Reactions**

R — OTs + OH → R — OH + OTs	alcohol
R — OTs + C≡N → R — C≡N + OTs	nitrile
R — OTs + Br → R — Br + OTs	alkyl halide
R — OTs + R’— O → R — O — R + OTs	ether
R — OTs + :$NH_{3.}$ → R — NH_3^+ OTs^-	Amine
R — OTs + $LiAlH_4$ → R — H + OTs	Alkane

- **A Summary of Ring Opening Reactions**