SOUTH VALLY UNIVERSITY

FACULTY OF SCIENCE

# INTRODUCTION TO THE CHEMISTRY OF ALICYCLIC COMPOUNDS

**By**
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**For 3rd Science Students**

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# *Author's preface*

The chemistry of *alicyclic* compounds is important class of organic chemistry that studies the aliphatic cyclic compounds in their physical and chemical behavior because they react and behave in ways highly dependent on their stereochemistry.

The chemical reactions of *alicyclic* compounds require an understanding of their reaction mechanism and the stereochemistry of the molecules.

This book discussed the nomenclature of the different types of *alicyclic* compounds, physical properties, stereochemistry and methods of preparation and reactions of *alicyclic* compounds.

This book is designed to understanding of basic conceptual of the chemistry of *alicyclic* compounds in separated units and chapters with questions and exercises. Answers are given at the end of each chapter.

When this study has been completed the reader should be able to:

1. Demonstrate a scientific framework of organic chemistry knowledge in the chemistry of *alicyclic* compounds.
2. Demonstrate a working knowledge of the fundamental concepts of the chemistry of aliphatic cyclic compounds to allow further study of chemistry.
3. Define various kinds of *alicyclic* isomers.
4. Demonstrate the ability to name and draw structures of several types of *alicyclic* compounds.

I acknowledge the help I have from many sources during the preparation of this book.

Author
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# INTRODUCTION

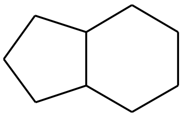
This course presents a brief introduction to the chemistry of alicyclic compounds, it is necessary to understand some of the language used to describe the stereochemistry of alicyclic compounds.

cyclic compound any one of a class of compounds whose molecules contain a number of atoms bonded together to form a closed chain or ring. If all of the atoms that form the ring are carbon, the compound is said to be carbocyclic; if not, the compound is called heterocyclic.

Alicyclic compounds behave chemically like the open-chain aliphatic compounds.

This course is aimed at providing the students with theoretical, usable knowledge that will allow them to carry out research and development in alicyclic chemistry. The course improves the student's ability to solve synthetic problems in alicyclic chemistry.

The author will discuss in this course some important topics Include types of aliphatic cyclic compounds, nomenclature, the physical properties, the stereochemistry and the methods of preparation of different types of alicyclic compounds.



# GENERAL OBJECTIVES OF THIS COURSE

**1-The student will be able to demonstrate a scientific framework of organic chemistry knowledge in the chemistry of alicyclic compounds.**

**2-The student will be able to demonstrate a working knowledge of the fundamental concepts of the chemistry of aliphatic cyclic compounds to allow further study of chemistry.**

**3-The student will be able to define various kinds of alicyclic isomers.**

**4-The student will be able to demonstrate the ability to name and draw structures of several types of alicyclic compounds.**

## ASSESSMENT OF LEARNER OUTCOMES

**The student will be evaluated by means of classroom participation, homework problems, exams, quizzes, and the final exam.**

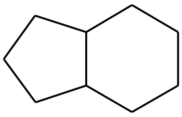
# OBJECTIVES OF EACH LESSON

**Lesson 1:**

- **a- The student will be able to identify and define the several types of aliphatic rings.**
- **b- The student will be able to name and draw structures of several types of alicyclic compounds.**

**Lesson 2:**

- **a- The student will be able to identify the naturally occurrence of many common rings.**



b- The student will be able to identify the physical properties of many common rings.

c- The student will be able to know the classification of momocyclic system.

d- The student will be able to know the different theories that discuss the stability of alicyclic compounds.

**Lesson 3:**

a- The student will be able to demonstrate the ability to name and draw structures of several kinds of alicyclic isomers.

b- The student will be able to know how to designate the geometrical isomers as *cis*- or *trans* in the substituted rings.

**Lesson 4:**

a- The student will be able to identify the different conformations of cycloalkanes.

b- The student will be able to draw the different shapes of the common rings.

c- The student will be able to identify the different conformations of cyclohexane.

**Lesson 5:**

a- The student will be able to know the different methods of preparation of alicyclic compounds.

b- The student will be able to identify the mechanisms of some reactions.

**Lesson 6:**

a- The student will be follow the different methods of preparation of alicyclic compounds with explanation the mechanisms of some reactions.

**Lesson 7:**

a- The student will be able to know the physical properties of cyclopropane and its derivatives.

b- The student will be able to know the different methods of preparation of cyclopropane and its derivatives.

**Lesson 8:**

a- The student will be able to know the physical properties of cyclobutane and its derivatives.

b- The student will be able to know the different methods of preparation of cyclobutane and its derivatives.

**Lesson 9:**

a- The student will be able to know the physical properties of cyclopentane and its derivatives.

b- The student will be able to know the different methods of preparation of cyclopentane and its derivatives.

**Lesson 10:**

a- The student will be able to know the physical properties of cyclohexane and its derivatives.

b- The student will be able to know the different methods of preparation of cyclohexane and its derivatives.

**Lesson 11:**

a- The student will be able to know the physical properties of cycloheptane and its derivatives.

b- The student will be able to know the different methods of preparation of cycloheptane and its derivatives.

**Lesson 12:**

a- The student will be able to know the different methods of preparation of bicyclic compounds, spirans and fused rings.

## Unit 1

# Lesson 1: Basic Concepts

## 1.1 Introduction

Alicyclic compounds are class of organic compounds whose molecules contain one or more rings and all of the atoms that form the ring are carbon.

The term "Alicyclic compound" means that "An organic compound that is both aliphatic and cyclic". Also, these compounds called *closed chain compounds, carbocyclic compounds and/or cycloalkanes.*

Alicyclic compounds behave chemically like the open-chain aliphatic compounds, but many cyclic compounds exhibit the special properties characteristic of the aromatic compounds. The saturated Alicyclic hydrocarbons have the general formula $C_nH_{2n}$ (the same as that of the alkenes); they do not contain a double bond but possess a ring structure, and when the molecular formula of a saturated hydrocarbon corresponds to the general formula $C_nH_{2n-2}$ , then the compound contains two rings; if to $C_nH_{2n-4}$, three rings, etc.

Simple Alicyclic compounds are cyclopropane, cyclobutane, cyclopentane and cyclohexane. A polycyclic cycloalkane is decalin. Bicyclic alkanes are norbornene and norbornadiene. Spiro compounds have bicyclic connected through one carbon atom is spiro[5.5]undecane (Fig. 1.1).

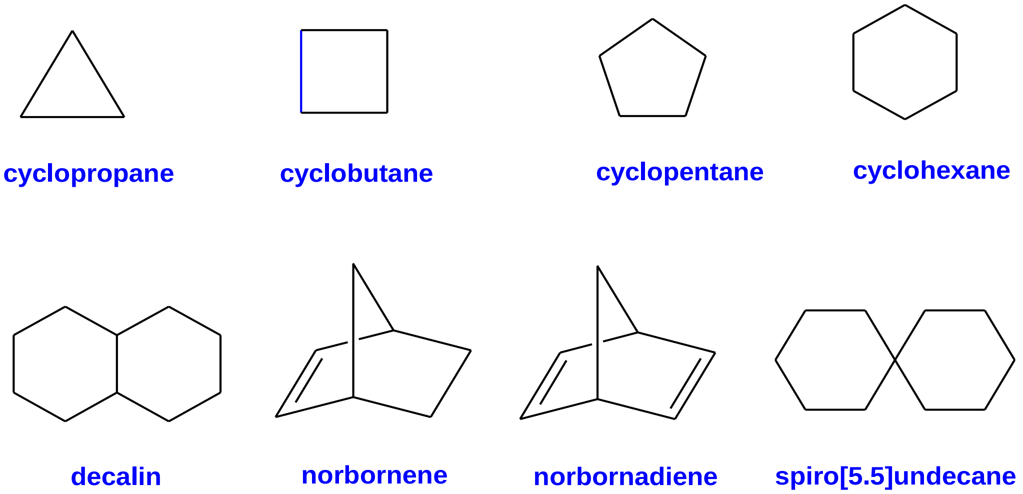


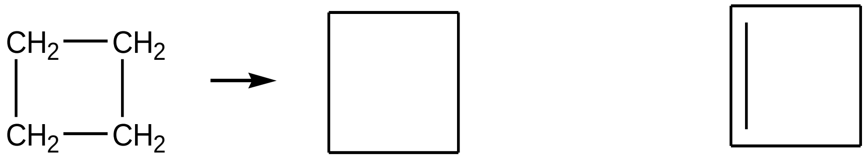
Fig. 1.1

## 1.2 Nomenclature

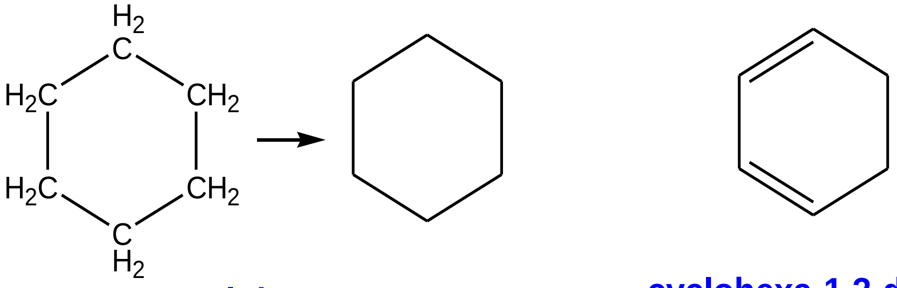
There are many rules used in the nomenclature of alicyclic compounds according to the I.U.P.A.C system are listed as follows:

### A- Monocyclic compounds:

The saturated monocyclic hydrocarbons take the name of the corresponding open chain saturated paraffins, preceded by the prefix ***cyclo-***, such as cyclobutane and cyclohexane, and if the cyclic hydrocarbon is unsaturated, the prefix ***cyclo-*** is followed by the name of the corresponding alkene, such as cyclopentene and 1,3-cyclohexadiene (Fig. 1.2).



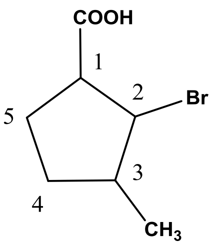
**cyclobutane** **cyclobutene**



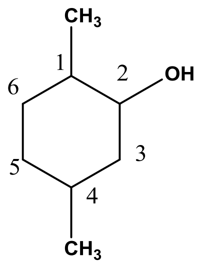
**cyclohexane** **cyclohexa-1,3-diene**

**Fig. 1.2**

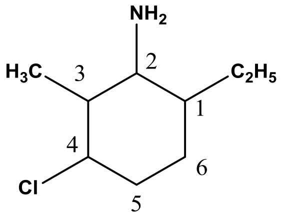
When a monocyclic hydrocarbon has a long and complex side chain, the open chain is named according to the I.U.P.A.C system, and the ring is regarded as a substituent, see examples in (Fig. 1.3).



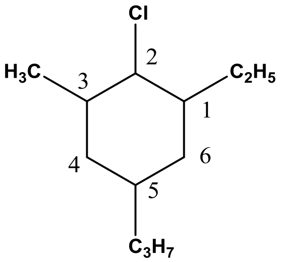
**2-bromo-3-methyl-cyclopentane carboxylic acid**



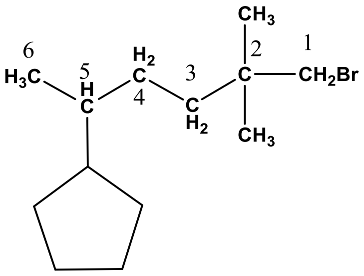
**1,4-dimethyl-2-cyclohexanol**



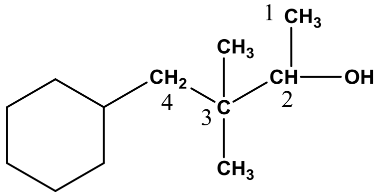
**4-chloro-1-ethyl-3-methyl-2-cyclohexylamine**



**2-chloro-1-ethyl-3-methyl-5-propyl-cyclohexane**



**1-bromo-5-cyclopentyl-2,2-dimethyl-hexane**



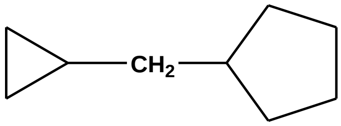
**4-cyclohexyl-3,3-dimethyl-2-butanol**

**Fig. 1.3**

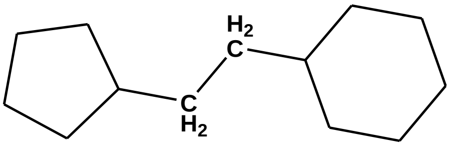
## B- Bicyclic system:

Bicyclic system may be divided into the following types:

**1- Bicyclic compounds with isolated rings separated by a chain of carbons:** The naming of this type is as the following examples;

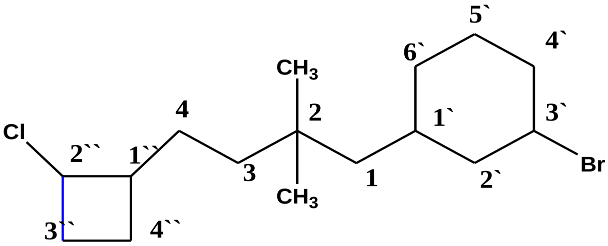


**cyclopropylcyclopentylmethane**

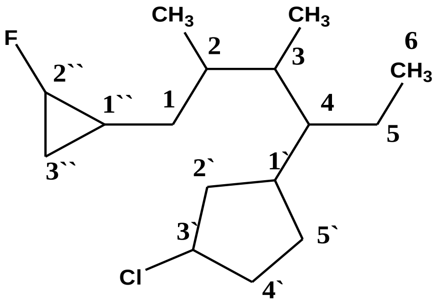


**cyclopentylcyclohexylethane**

If the carbon chain in between the two rings was more complicated, then the main chain is numbered as usual and the two rings being substituents and the carbon atoms in each ring are given primed numbered (Fig. 1.4).



**2,2-dimethyl-1-(3`-bromocyclohexyl)-4-(2``-chlorocyclobutyl)-butane**

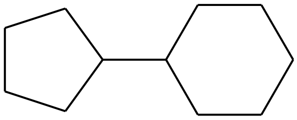


**2,3-dimethyl-4-(3`-chlorocyclopentyl)-1-(2``-flourocyclopropyl)-hexane**

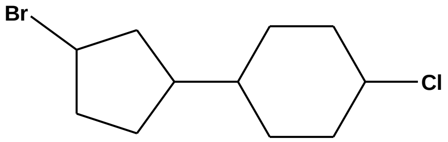
**Fig. 1.4**

## 2- Bicyclic compounds with rings connected by singly carbon-carbon bond:

In this type, the name of the smaller ring will be the first followed by the larger ring, e.g.,



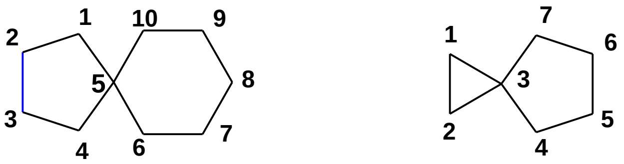
cyclopentyl-cyclohexane



1-(3`-bromocyclopentyl)-4-chloro-cyclohexane

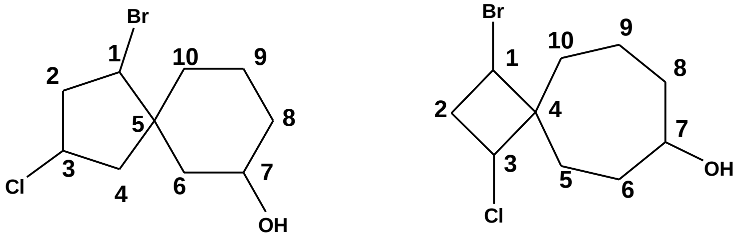
## 3- Bicyclic compounds with rings having one common atom (Spirans):

A spiro compound is a bicyclic organic compound with rings connected through one atom called a quaternary carbon "**spiro carbon**". The rings can be different in nature or identical. All spiro compounds have the prefix ***spiro*** followed by square brackets containing the number of atoms in the smaller ring and the number of atoms in the larger ring excluding the spiro atom itself, then the name of alkane corresponding to the total number of carbon atoms, sees examples in (Fig.1.5).



Spiro[4.5]decane

Spiro[2.4]heptane



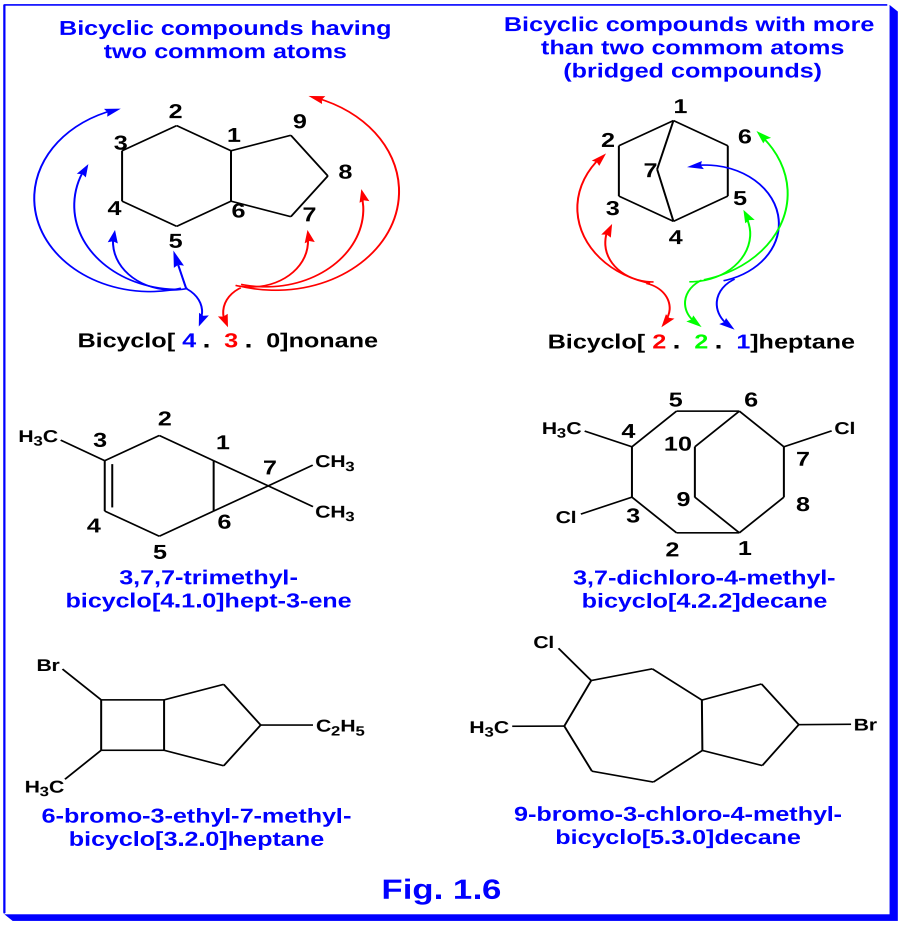
1-Bromo-3-chloro-spiro[4.5]decan-7-ol

1-Bromo-3-chloro-spiro[3.6]decan-7-ol

Fig. 1.5

## 4- Bicyclic compounds with rings having two or more common atoms:

According to the I.U.P.A.C system, the naming of these compounds is by taken the prefix "***bicyclo***" followed by the name of the alkane containing the same total number of carbon atoms, in between them square brackets containing three numbers, the first and the second indicate the number of atoms in the larger ring and the number of atoms in the smaller ring respectively excluding the common atoms, and the third is to express the number of carbons (**bridge atoms**) in between the two tertiary carbon atoms (**bridgeheads**) which connect the two rings (Fig.1.6).



Bicyclic compounds having two commom atoms

Bicyclic compounds with more than two commom atoms (bridged compounds)

Bicyclo[ 4 . 3 . 0]nonane

Bicyclo[ 2 . 2 . 1]heptane

3,7,7-trimethyl-bicyclo[4.1.0]hept-3-ene

3,7-dichloro-4-methyl-bicyclo[4.2.2]decane

6-bromo-3-ethyl-7-methyl-bicyclo[3.2.0]heptane

9-bromo-3-chloro-4-methyl-bicyclo[5.3.0]decane

Fig. 1.6

## Unit 1

# Lesson 2: General properties of alicyclic compounds

### 2.1 Occurrence and physical properties

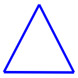
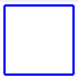
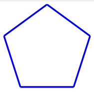
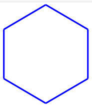
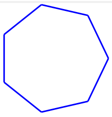
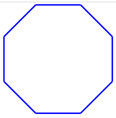
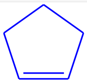
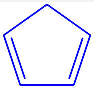
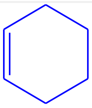
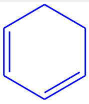
Five and six membered paraffins occur in petroleum (The naphthenes); three, four and five membered rings occur in terpenes which are the most important class of alicyclic compounds.

Many cyclic acids also occur in petroleum; these are known as the naphthenic acids and are mainly cyclopentane derivatives. Some cyclopentene derivatives of the fatty acids occur naturally, and are important in medicine.

Alicyclic hydrocarbons are light liquids (cyclopropane and cyclobutene are gases) which are immiscible with water and miscible in all proportions with the nonpolar solvents.

Some of physical properties of the lower and medium-sized alicyclic hydrocarbons are listed in (Table. 2.1).

## Table 2.1

| S | Name | Formula | Melting point °C | Boiling point °C | Density g/cm$^3$ |
|---|---|---|---|---|---|
| 1. | Cyclopropane |  | -126.6 | -34.4 | 0.72 |
| 2. | Cyclobutane |  | -91 | 12.5 | 0.703 |
| 3. | Cyclopentane |  | -93.3 | 49.5 | 0.751 |
| 4. | Cyclohexane |  | 6.5 | 81.4 | 0.779 |
| 5. | Cycloheptane |  | -12 | 118.1 | 0.809 |
| 6. | Cyclo octane |  | 14.3 | 148 | 0.835 |
| 7. | Cyclopentene |  | -93.3 | 44.2 | 0.772 |
| 8. | 1,3-cyclopentadiene |  | -8.5 | 42.5 | 0.802 |
| 9. | Cyclohexene |  | -103.7 | 83 | 0.810 |
| 10. | 1,3-cyclohexadiene |  | -98 | 80.5 | 0.84 |

## 2.2 Classification of monocyclic system

Monocyclic systems can be classified according to the number of carbon atoms in the ring into four main types, the first is the small rings as three and four-membered rings. The second is the common rings which refer to the five-, six-, and seven-membered rings.  The rings contains eight to eleven carbon atoms called the medium rings, and the rings have more than eleven carbons is the large rings. These types shown in the following (Diagram 2.2):

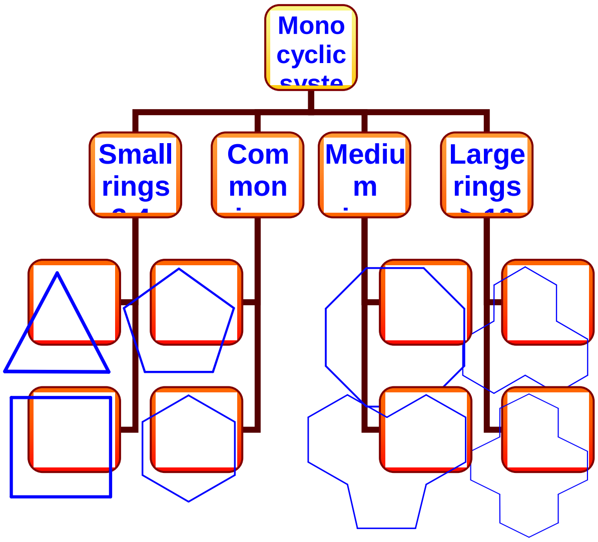


**Diagram 2.2**

Many chemical properties depend on the class of cycloalkane, and the difference in behavior has been explained largely in terms of steric strain.

## 2.3 Baeyer's strain theory (1885):

Baeyer point out that in cycloalkanes the valency angle can be altered from the normal tetrahedral value (109º 28`) of the carbon atom, and this cause a strain (α) in the molecule, consequently the greater deviation from the normal angle, the greater strain. Thus, according to Baeyer, five- and six-membered rings are the most stable because they have the least strain (or distortion) from the normal tetrahedron value. Also, Baeyer assumed that all the rings are planar, so the stain for each ring-size can be calculated, e.g., in cyclopropane, the angles of an equilateral triangle are 60º (Fig. 2.3), the stain in cyclopropane can be calculated as follows:

**(α) = 1/2 (109º 28` - 60) = + 24º 44`**

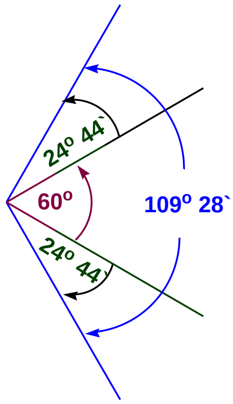


Fig. 2.3

A list of strains (distortions) can be explained in (Table 2.4).

**Table 2.4**

| *S* | *No. of carbon atoms in the ring* | *Angle between valency bonds* | *Distortion (Strain)* | *Heat of combustion in kJ/CH2* | *Total strain (kJ)* |
|---|---|---|---|---|---|
| **1.** | **3** | **60°** | **24° 44`** | **697** | **120** |
| **2.** | **4** | **90°** | **9° 44`** | **685** | **112** |
| **3.** | **5** | **108°** | **0° 44`** | **664** | **35** |
| **4.** | **6** | **120°** | **-5° 16`** | **659** | **12** |
| **5.** | **7** | **128° 34`** | **-9° 33`** | **662** | **35** |
| **6.** | **8-11** | **135°-147° 16`** | **-12° 46`-- 18° 54`** | **661-665** | **32-88** |

When the carbon valences are forced together, the stain is said to be positive (+), when forced apart it is negative (-).

**From the list of strains, it can be conclude that according to Baeyer's strain theory:**

- Because the deviation of the bond angles in cyclopropane is greater than in cyclobutane, the strain in cyclopropane is greater than in cyclobutane, so cyclopropane is less stable than cyclobutane.
- Due to the bond angle in cyclopentane is (108°), which is very similar to the tetrahedral angle (109° 28`), cyclopentane should be free of angle strain, where the

stain in cyclopentane (α) = 0º 44`. Hence, cyclopentane must posses the lowest energy and the highest stability.

- The bond angle in the planar cyclohexane is (120º), which is larger than the tetrahedral angle, so, the strain (α) = - 5º 16`. Also the stain in cycloheptane will be (α) = - 9º 33`.
- From the results shown in (Table 2.4), the stability increase up from the three- to six-membered ring, then decreases from seven to the eleven-membered rings, according to the values of heats of combustion.

## 2.4 The analysis of Baeyer's strain theory

- Baeyer's strain theory is based on a mechanical concept of valence, and this led to wrong conclusions on the assumption that all the rings are planar, where the physical methods and the quantum mechanical calculations shown that all rings (except cyclopropane) are not planar (See pages 30 and 31) and also do not permit very large distortion of bond angles.
- If cyclopropane was an equilateral triangle, the bond angle would be (60º). This value is impossible, since, the carbon valency angle never be less than (90º). Furthermore, according to Coulson *et al.* calculation has shown that the smallest carbon valency angle is (104º), and in cyclopropane, the carbon hybridized orbitals are not pointing towards one another in the same straight line, and

linked together with (bent) bonds. Hence, cyclopropane molecule being in the state of strain.

# Unit 1

## Lesson 3: Stereochemistry of Alicyclic compounds

### 3.1 Types of isomers in alicyclic compounds

There are many types of isomerism are known for alicyclic compounds as shown in the following diagram (3.1):

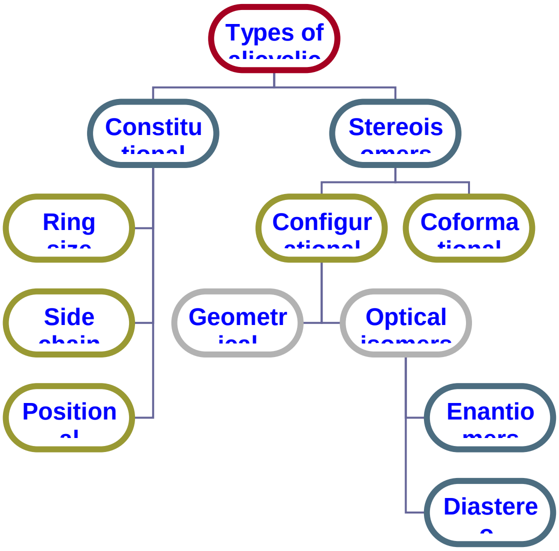


Diagram 3.1

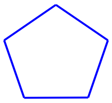
### 3.2 Constitutional isomers:

Constitutional isomers are isomers that differ because their atoms are connected in a different order.

**Types of constitutional isomers in alicyclic compounds:**

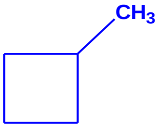
**I- Ring size isomers:**

Ring size isomers are compounds have the same molecular formula but differ in the ring size, e.g.,



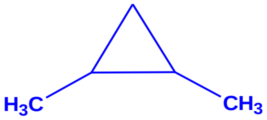
**Cyclopentane**

MF: $C_5H_{10}$



**Methyl-cyclobutane**

$C_5H_{10}$

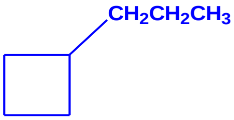


**1,2-Dimethyl-cyclopropane**

$C_5H_{10}$

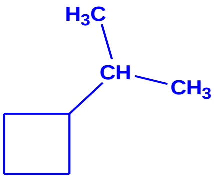
## II- Side chain isomers:

Side chain isomers are compounds have the same molecular formula but differ in the side chain structure, e.g.,



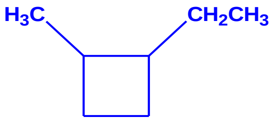
**Propyl-cyclobutane**

MF: $C_7H_{14}$



**Isopropyl-cyclobutane**

$C_7H_{14}$

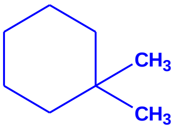


**1-Ethyl-2-methyl-cyclobutane**

$C_7H_{14}$

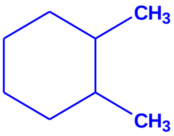
## III- Positional isomers:

Positional isomers are compounds have the same molecular formula but differ in the relative arrangement of the substituents connected to the ring, e.g.,



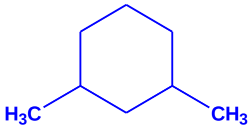
**1,1-Dimethyl-cyclohexane**

MF: $C_8H_{16}$



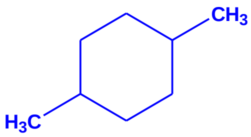
**1,2-Dimethyl-cyclohexane**

$C_8H_{16}$



**1,3-Dimethyl-cyclohexane**

$C_8H_{16}$



**1,4-Dimethyl-cyclohexane**

$C_8H_{16}$

**3.3 Stereoisomers:** Stereoisomers are isomers that have same formula and connectivity but differ in the position of the atoms in space.

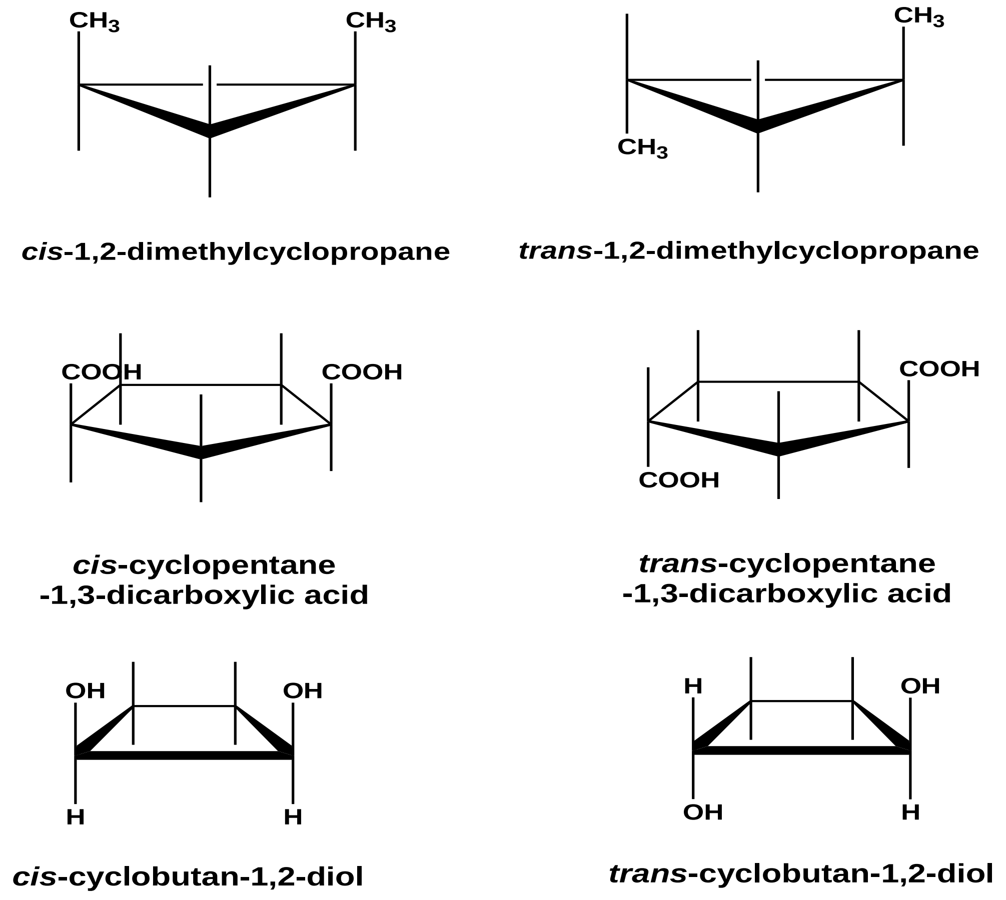
Stereoisomer can be divided into two categories configurational and conformational isomers.

**3.4 Configurational isomers:** Configurational isomers are divided into two types optical and geometrical isomers.

**3.4a Geometrical or *cis-trans* isomers:** Geometrical isomers are a type of stereoisomers resulting from difference in the special arrangement of the atoms or groups attached to the bonds around which rotation is largely restricted.

In Alicyclic compounds, the rigidity of atoms in rings to rotate completely about their bonds leads to ***cis- trans***- isomerism as shown in the next examples (Fig. 3.2).

**Ex:** *cis- trans*- isomers of 1,2-dimethylcyclopropane, cyclopentane-1,3-dicarboxylic acid and cyclopentane-1,2-diol. The ***cis***- isomer has both methyls on the same side of the ring; the ***trans-*** isomer has them on opposite sides.



*cis*-1,2-dimethylcyclopropane

*trans*-1,2-dimethylcyclopropane

*cis*-cyclopentane -1,3-dicarboxylic acid

*trans*-cyclopentane -1,3-dicarboxylic acid

*cis*-cyclobutan-1,2-diol

*trans*-cyclobutan-1,2-diol

Fig. 3.2

## 3.4b Optical isomers:

Optical isomers are isomers that resulting from presence of one or more chiral centers within a molecule.

- **Optical Activity:** The ability of some compounds to rotate plane polarized light.
- **Chirality:**

Chirality refers to objects which are related as non–superimposable mirror images.

### ❖ Chiral carbon atom:

Chiral carbon atom is a carbon atom attached to four different atoms or groups.

**Optical isomers can be divided into two general categories:**

### I- Enantiomers:

Enantiomers are stereoisomeric pair have the same chemical and physical properties but differ in the rotation of plane polarized light, one of them is mirror image of the other, and both enantiomers are non- superimposable.

### II- Diastereoisomers:

Diastereoisomers stereoisomers that are not mirror images.

### III- Racemic mixture:

Racemic mixture is an equimolar mixture (1:1) of two enantiomers.

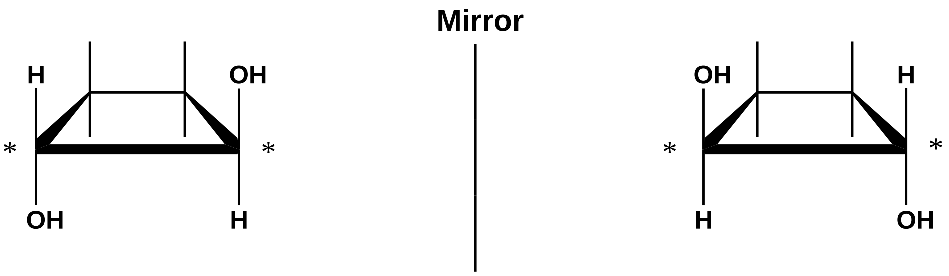
### IV- Meso-form:

The Meso-form is optically inactive compound with at least 2 stereocenters that is achiral due to the presence of a plane of symmetry, and is superimposable.

**V-** Molecules with **n** different chiral centers exist in $\mathbf{2^n}$ enantiomeric forms, and number ($\mathbf{2^{n-1}}$) of racemic mixtures.

**An example**, if we examine models of ***cis***- and ***trans***-cyclobutane-1,2-diol, it can be found two types of isomerism, geometrical and optical isomerism.

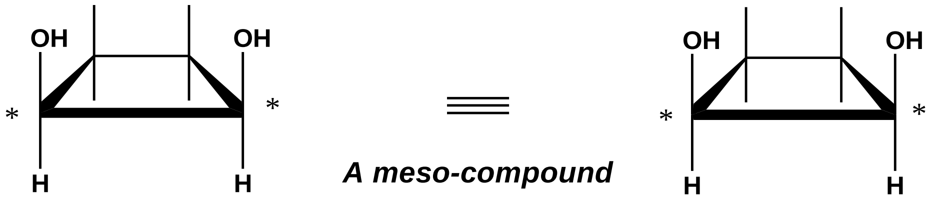
The ***trans***-isomer exists in two optically active enantiomers, whereas, the ***cis***-isomer has a plane of symmetry and is therefore optically inactive Meso-form.



***2 enantiomers***

***non-superimposable***

***trans*-cyclobutane-1,2-diol**



***A meso-compound***

***superimposable***

***cis-cyclobutane-1,2-diol***

*** - chiral carbon atom**

**Fig. 3.3**

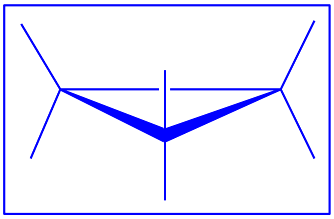
## Unit 1

# Lesson 4: Conformations of cycloalkanes

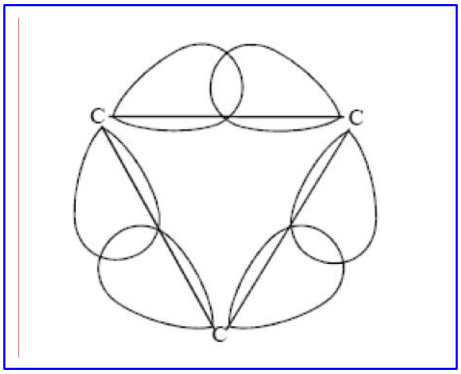
### 4.1 Geometrical shape of the rings

**A- Cyclopropane:** must be geometrically planar, three carbons into a plane. The hydrogen atoms in cyclopropane necessarily are eclipsed (Fig. 4.1).

On the other hand, according to the modern conceptions, the σ bonds in cyclopropane differ from ordinary σ bonds and their hybridization is different from ordinary *sp3* hybridization, in fact, it occupies an intermediate position between the ordinary σ- and π-bond. This bond is known as "**banana-(or bent) bond**" (Fig. 4.1). Now, the angle between the bonds in cyclopropane is $106^{O}$ instead of $60^{O}$ according to the classical conceptions, and the bond **H-C-H** angle is about ~ $120^{O}$.



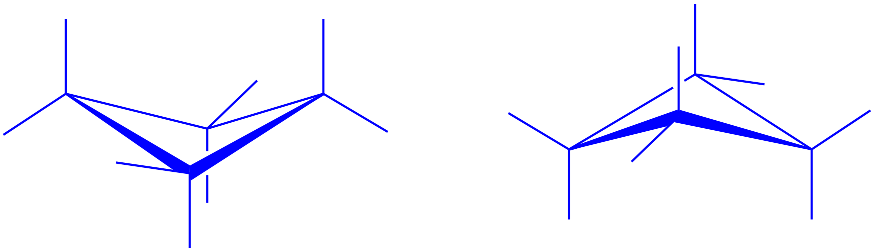
Propane molecule



Banana-bond of cyclopropane

Fig. 4.1

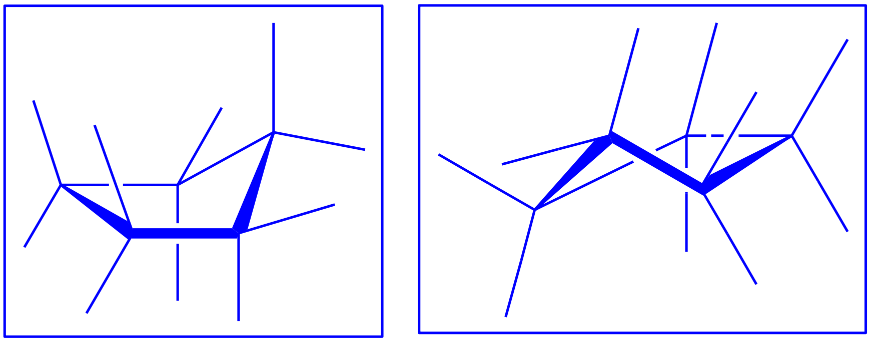
**B- Cyclobutane:** (Flat bond angles will be = $90^{O}$) is puckered, even through the puckered causes more-strained bond angles (Fig. 4.2).



Puckered conformation of cyclobutane

Fig. 4.2

**C- Cyclopentane** has near-optimal bond angle ($109^{O}28$`) if it was flat, but cyclopentane also is slightly puckered, so that the hydrogen atoms attached to the ring carbons are staggered as in envelop and half-chair conformers. Envelope and half-chair are of similar stability and interconvert rapidly.(Fig. 4.3).

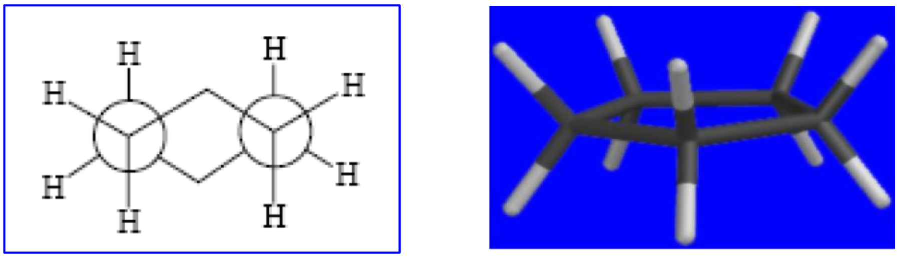


**Envelop-form** **Half chair-form**

**Envelop-, and half-chair conformations of cyclopentane**
**Fig. 4.3**

## D- Cyclohexane

If the cyclohexane ring was flat, all the hydrogen atoms on the ring carbons would be eclipsed. So, the planar conformation destabilized by torsional strain, but in puckered conformation (Fig. 4.4) that all the hydrogen atoms are staggered and the energy of this puckered conformer is lower than the energy of flat cyclohexane, due to the more-favorable *sp3* bond angle and fewer hydrogen-hydrogen repulsions.



Puckered conformation of cyclohexane

The hydrogen atoms are staggered

Planar conformation of cyclohexane

The hydrogen atoms are eclipsed

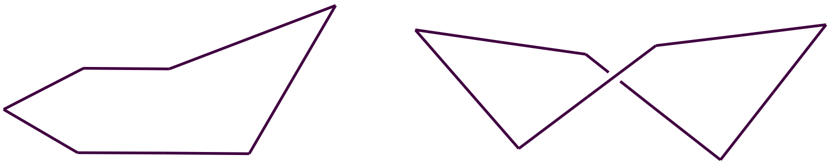
Fig. 4.4

## 4.2 Flexible conformers of cyclohexane

Cyclohexane is the most important of all the ring systems, it can be exists in a number of flexible forms in all of which angle strain is largely eliminated. These forms are known as chair, half-chair, boat, and twist-boat (Fig 4.5).

The chair-form of cyclohexane

The boat-form of cyclohexane

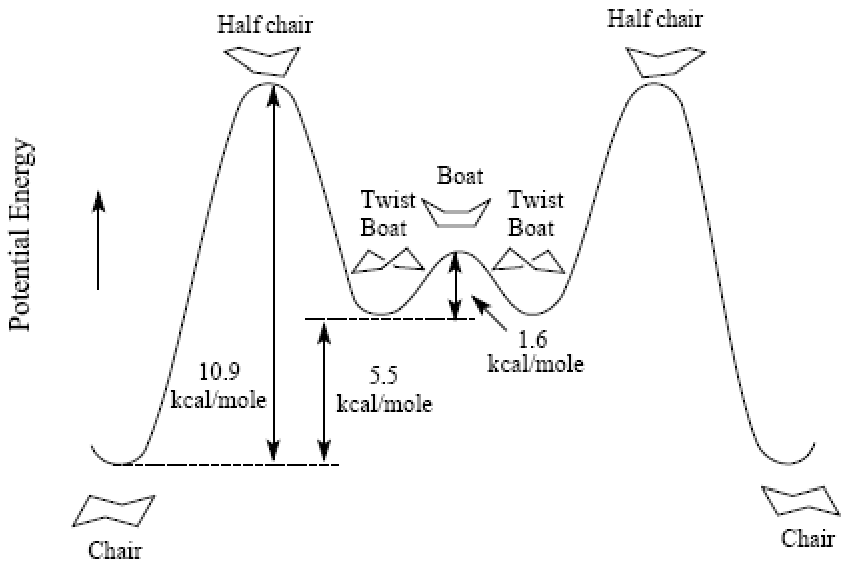


The half-chair form
of cyclohexane

The twist-boat form of
of cyclohexane

Fig. 4.5

The relative energies of the different forms of cyclohexane are shown in the following energy diagram (4.6).

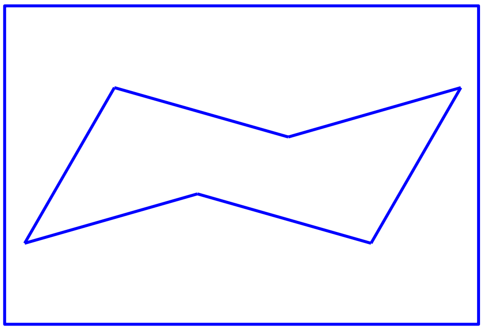


The energy diagram for the ring inversion of cyclohexane.

**Diagram 4.6**

From the above diagram, it can be concluding that:

1- The chair-form is the most stable conformation of cyclohexane (about 99.9% of cyclohexane molecules are in the chair-form at any time) (Fig. 4.7).



The chair-form of cyclohexane

Fig. 4.7

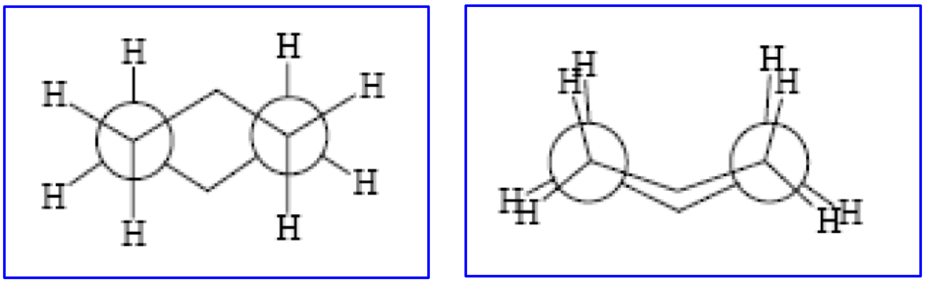
The stability of the chair-form is due to the following reasons:

(i) The chair-form is the less energy one.

(ii) The chair-form is free of angle stain (α), and torsional strain.

(iii) All hydrogen atoms in the chair-form are staggered in four of its carbon atoms as shown in (Fig. 4.8).

2- The boat-form of cyclohexane has eclipsed bonds in four of its carbon atoms, this eclipsing produces a significant amount of torsional. This torsional strain increases the energy of the boat-form and destabilizes it (Fig. 4.8).

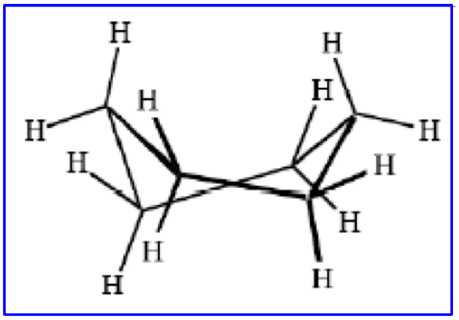


**Newman projection of the chair-form**

**Newman projection of the boat-form**

**Fig. 4.8**

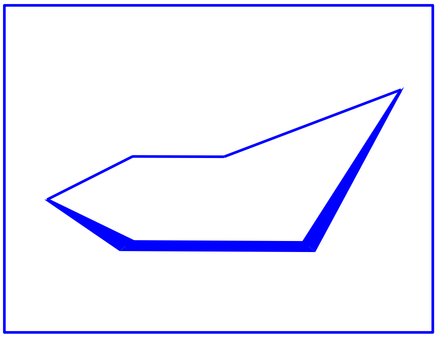
3- A third conformation of cyclohexane is the twist-boat (Fig. 4.9), there is a relieving in this form minimizes the torsional strain and make the twist-boat is lower in energy than the boat-conformation.



**The twist-boat form of cyclohexane**

**Fig. 4.9**

4- The last conformation is called half-chair, which has an almost-planar structure. So, it has the highest energy and the less stability (Fig. 4.10).

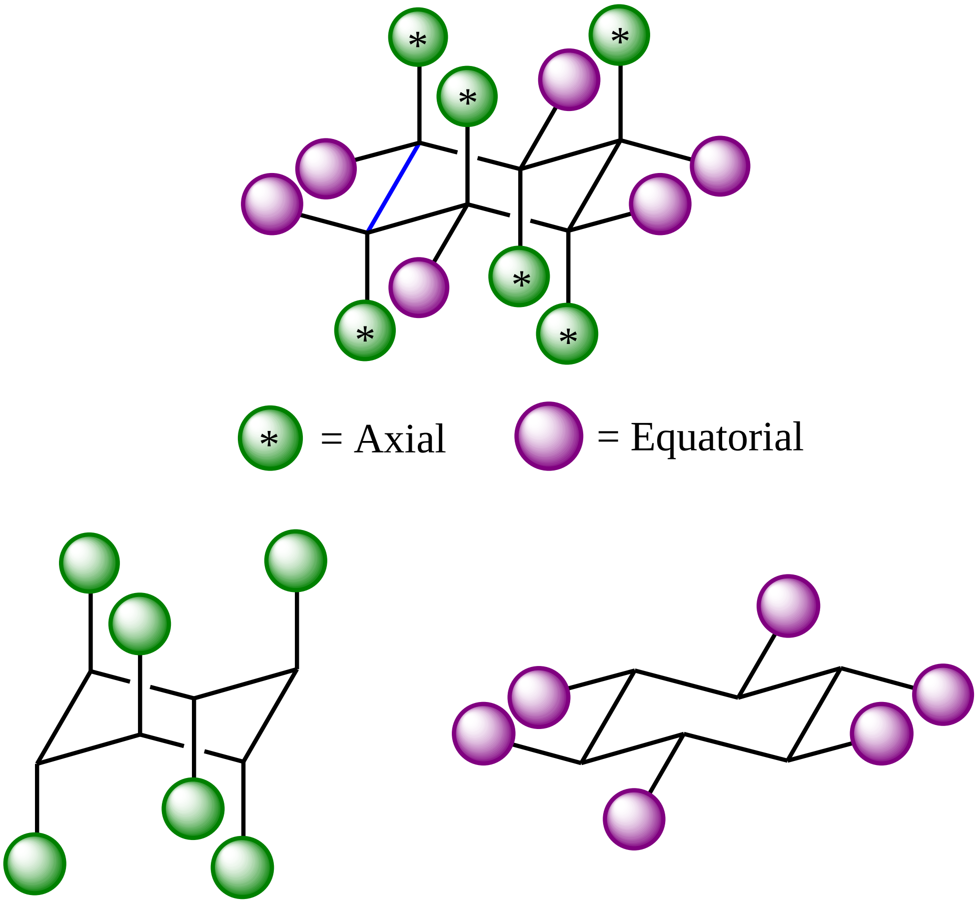


The half-chair form of cyclohexane

Fig. 4.10

## 4.3 Axial and equatorial hydrogens of cyclohexane

The chair conformation of cyclohexane has two distinct types of carbon—hydrogen bonds: **axial** and **equatorial**. Six of these bonds are **axial** and the other six **equatorial**, with one axial and one equatorial bond on each carbon (Fig. 4.11).



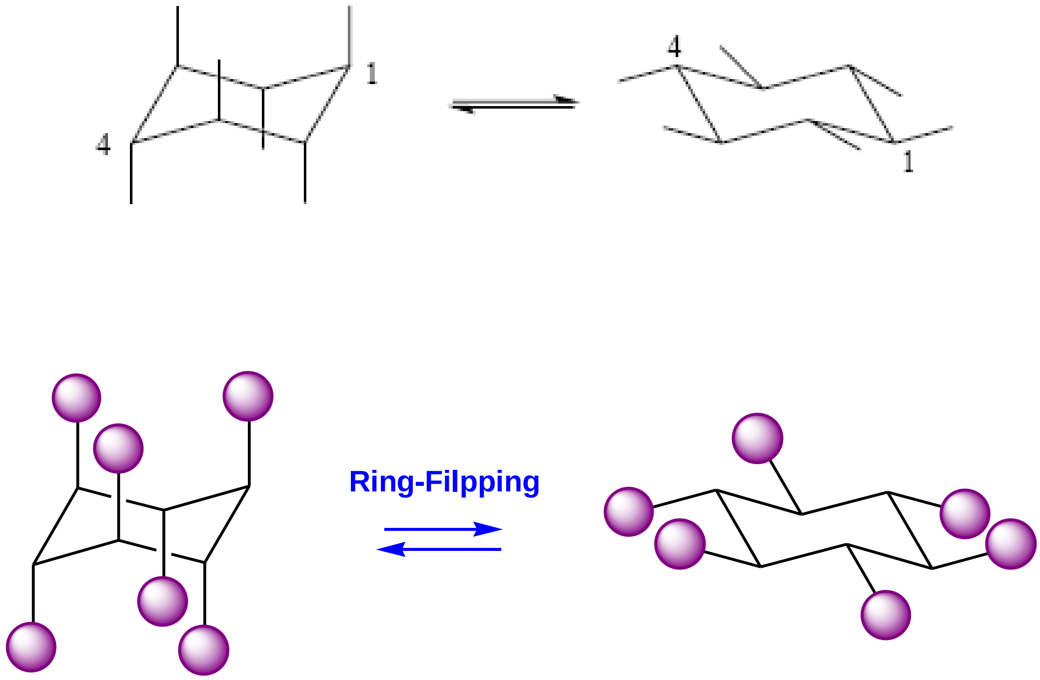
Axial hydrogens of cyclohexane

Equatorial hydrogens of cyclohexane

Fig. 4.11

## 4.4 Conformational inversion of cyclohexane

**A ring flipping**: is a chair-chair interconversion, one chair form of cyclohexane converts to another chair form of cyclohexane. In this process of ring flipping, the equatorial substituents become axial, and the axial substituents become equatorial (Fig. 4.12).



**Axial hydrogens of cyclohexane   Euatorial hydrogens of cyclohexane**

**Fig. 4.12**

***Activities:***

Try to draw well each puckered conformer of the cycloalkanes in this lesson.

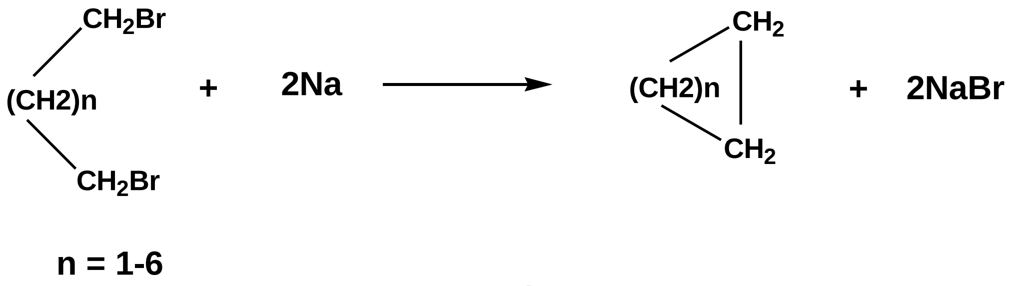
## Unit 2

# Lesson 5: General methods for the preparation of alicyclic compounds

Many methods have been introduced to prepare various-sized rings as follows:

### 1. Freund method (1882):

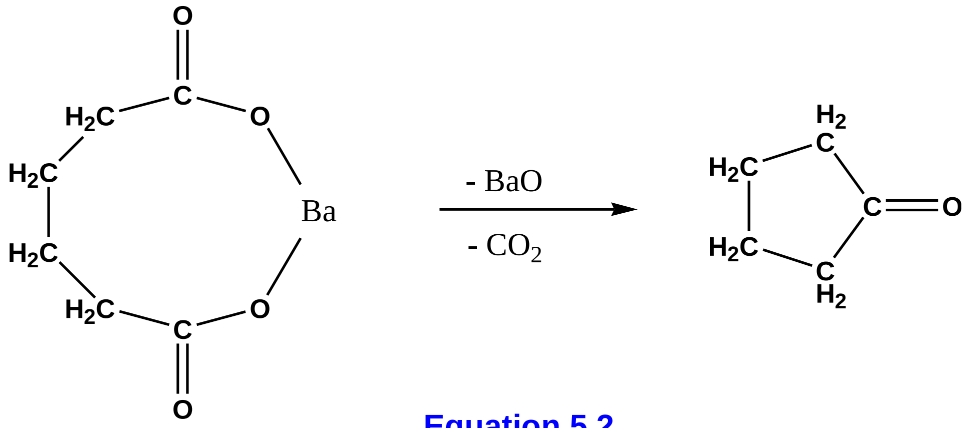
Treatment of an alkyl dihalide with sodium or zinc gives the corresponding cycloalkane (Equation 5.1).



Equation 5.1

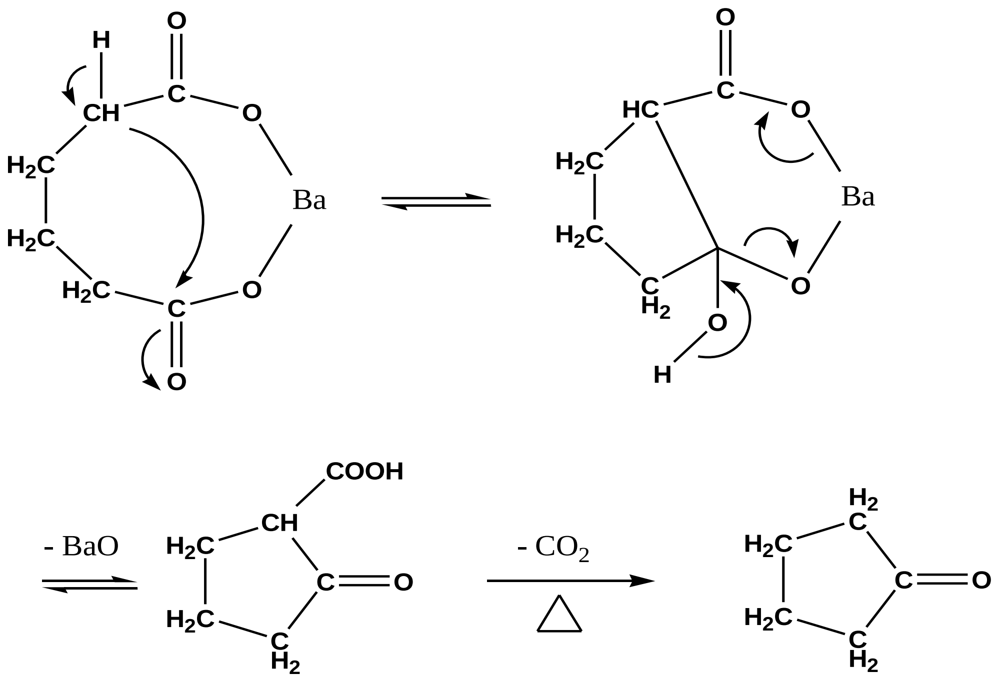
### 2. Pyrolysis of the salts of dibasic acid:

A cyclic ketone is formed, when the calcium or barium salts of a dicarboxylic acid is distilled, e.g., barium adipate gives cyclopentanone (Equation 5.2).



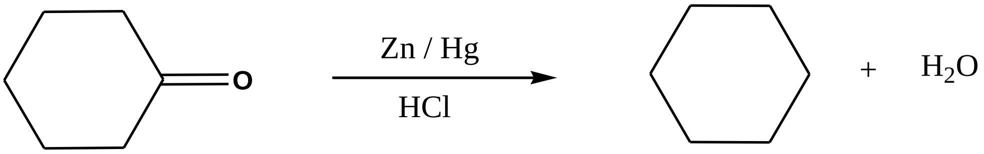
Equation 5.2

The reaction mechanism;



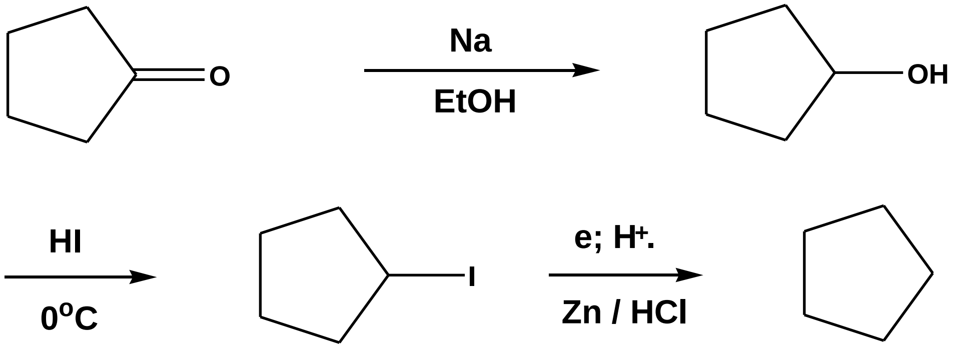
## 3. Reduction of cyclic ketones:

Cyclic ketones may be converted into the corresponding cycloalkanes by means of the **Clemmensen** reduction (Equation 5.3).

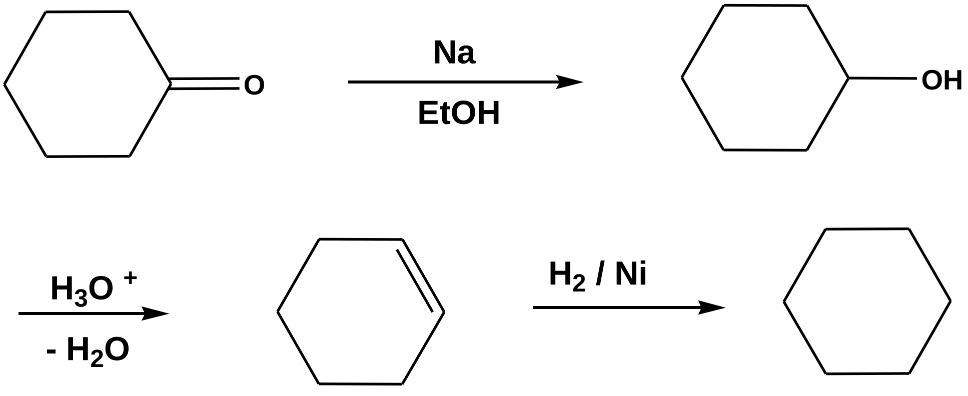


Equation 5.3

There are another two methods for this conversion as follows (Equations 5.4 and 5.5):



Equation 5.4



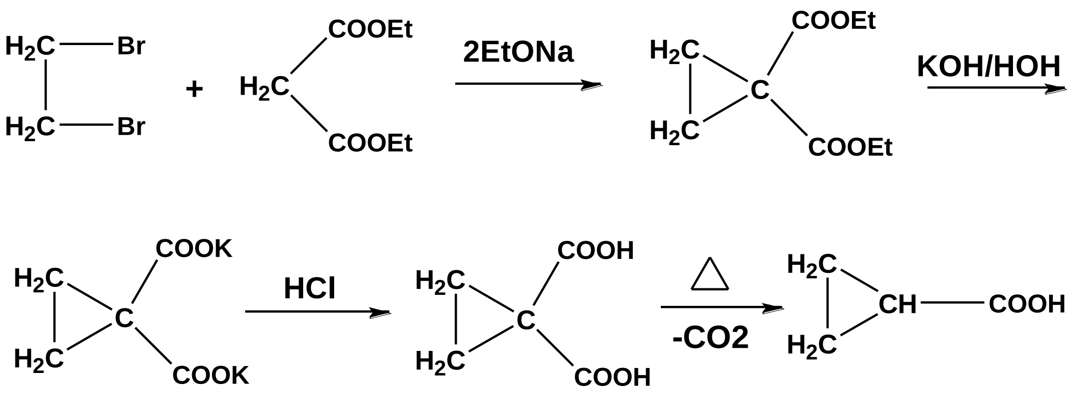
Equation 5.5

## 4. Perkin's methods (1883):

Condensation of certain alkyl dihalide ( **$Br(CH_2)_nBr$; n= 2-5** ) with either malonic ester or ethylacetoacetate in presence of sodium ethoxide gives the corresponding cyclic ester, which upon hydrolysis followed by decarboxylation turns to the cycloalkane derivative.

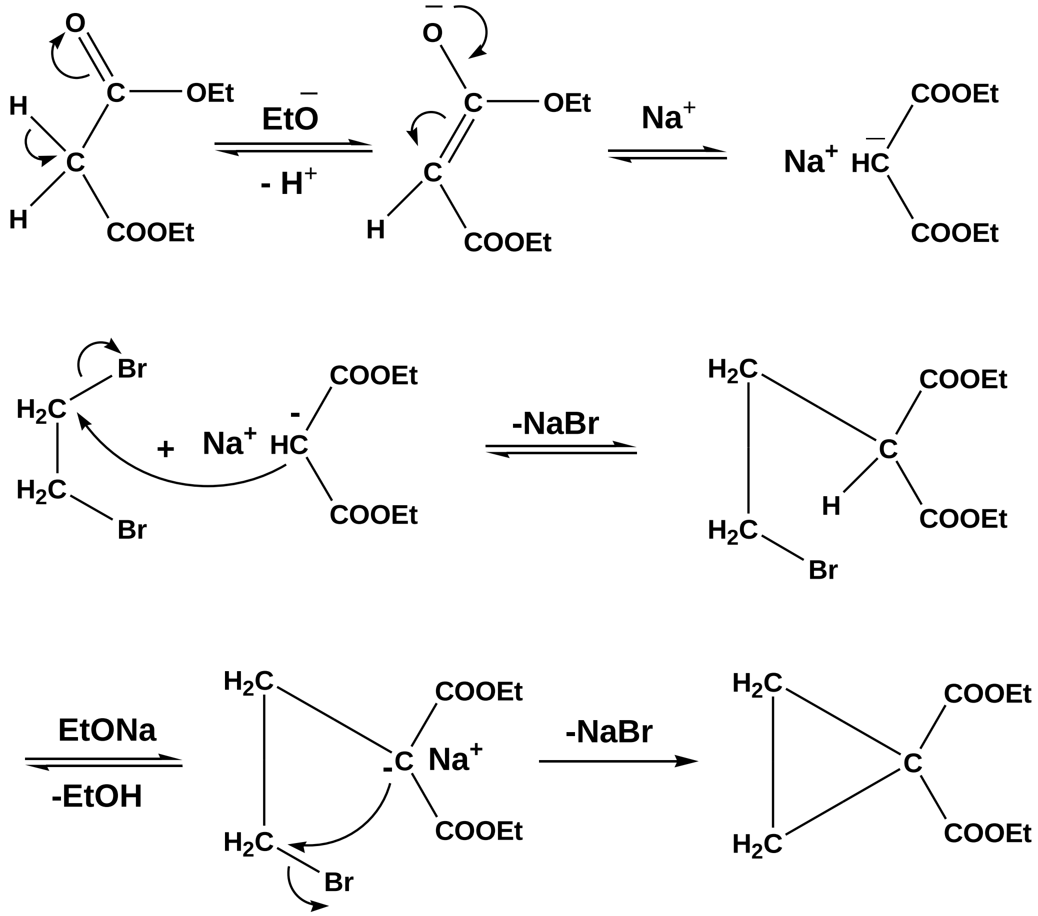
### I- Condensation with malonic ester:

One molecule of malonic ester condenses with an alkyl dihalide in presence of two molecules of sodium ethoxide to form cycloalkane-dicarboxylic ester, which may be converted into the monocarboxylic acid by hydrolysis then decarboxylation (Equations 5.6).



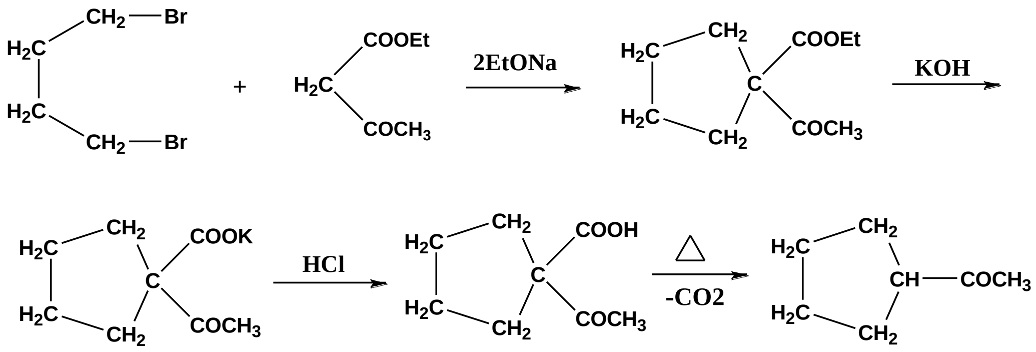
Equation 5.6

**The reaction mechanism;**



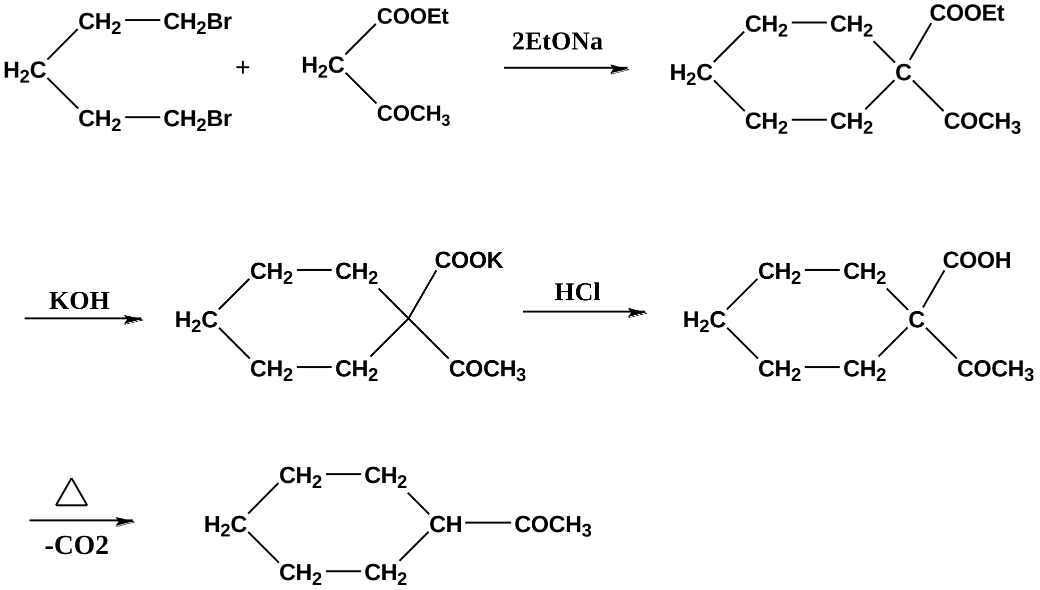
## I- Condensation with ethylacetoacetate:

On treatment of ethylacetoacetate with appropriate alkyldihalide; three, five, six and seven-membered rings are obtained ((Equations 5.7 and 5.8).



cyclopentylmethylketone

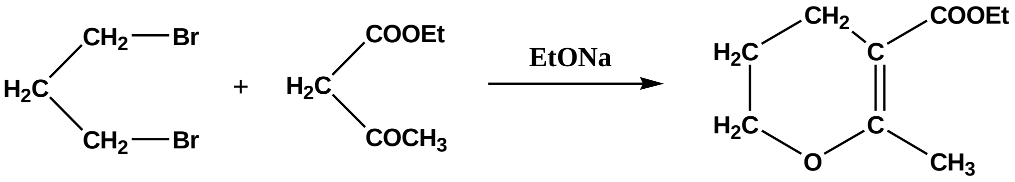
Equation 5.7



cyclohexylmethylketone

Equation 5.8

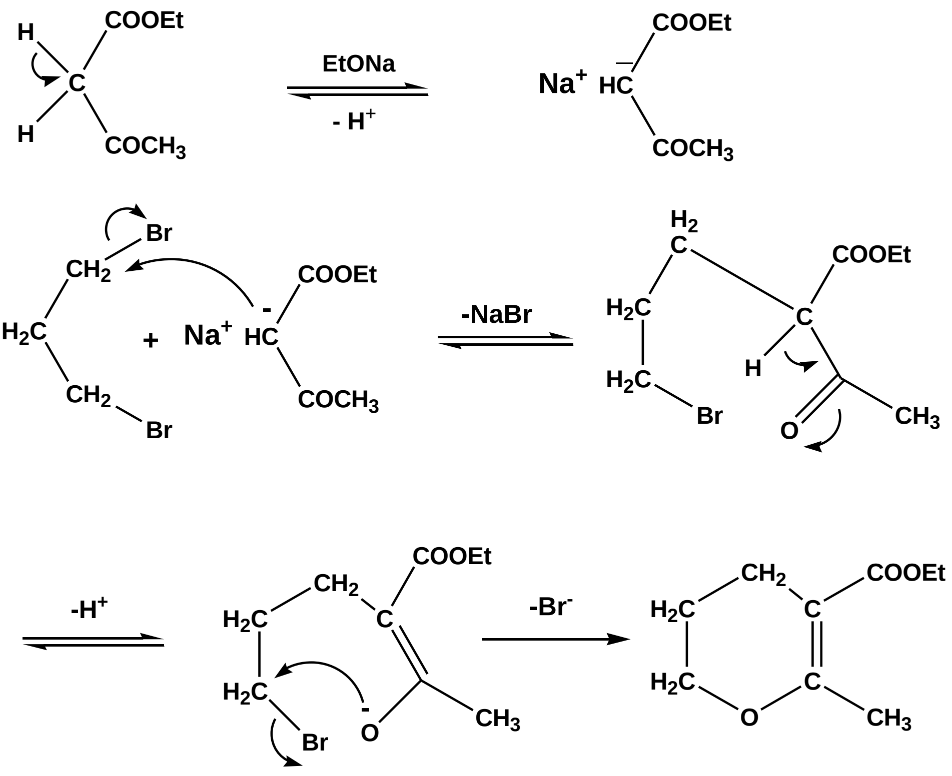
All attempts to prepare a four-membered ring result in the formation of a dihydropyran derivative (Equations 5.9).



2-methyl-5,6-dihydro-4*H*-pyran-3-ethylcarboxylate

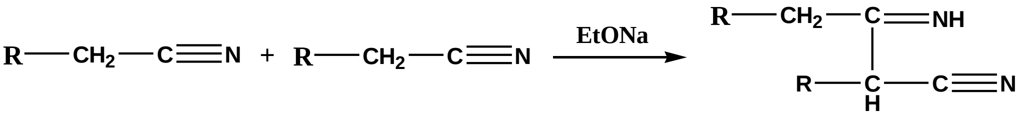
**Equation 5.9**

**The reaction mechanism;**



## 5. Ziegler-Thorpe reaction:

**Thorpe** nitrile reaction is a base catalyzed condensation of two nitrile molecules to yield a **β-iminonitrile** (Equation 5.10).

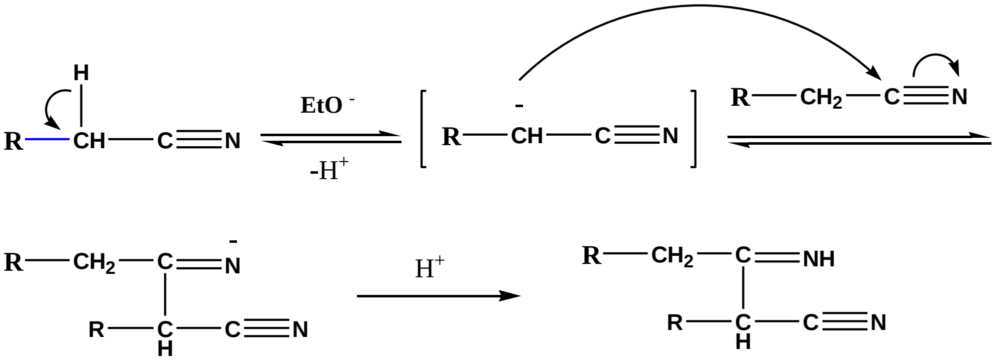


**β – iminonitrile**

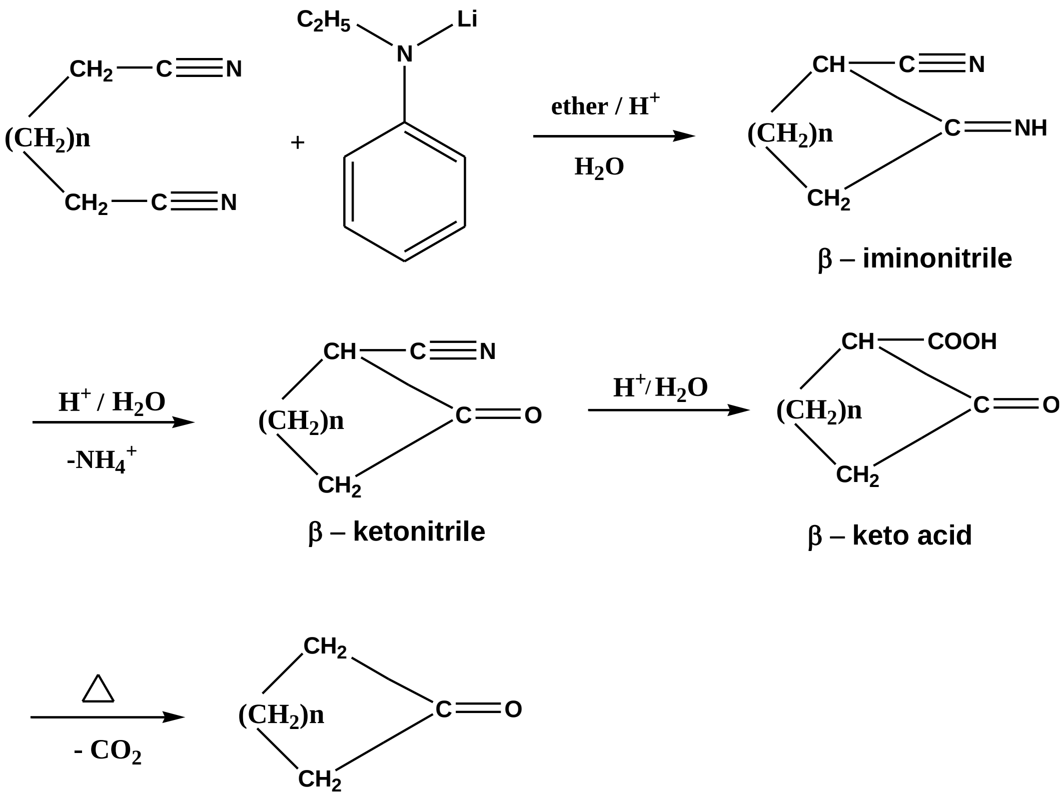
**Equation 5.10**

The Mechanism of this reaction shown as follows:

**The reaction Mechanism;**



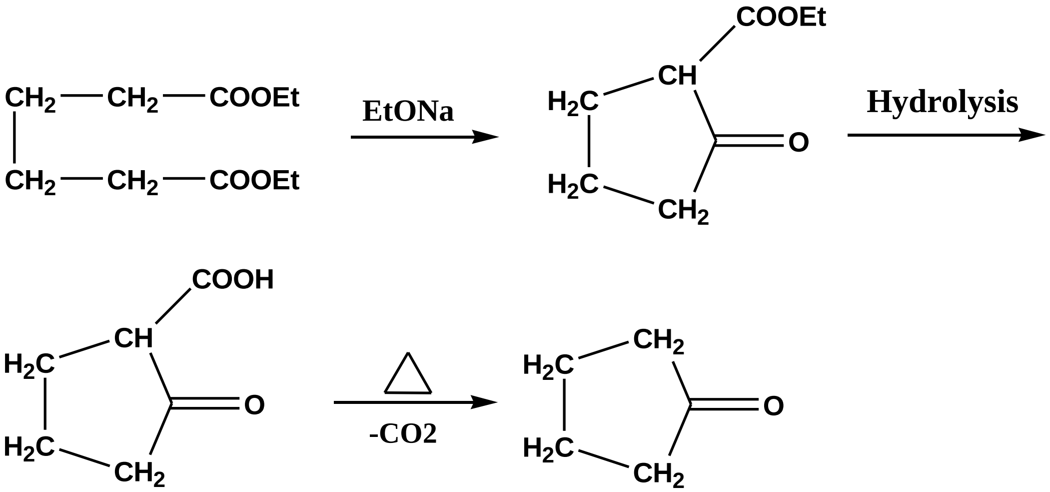
**Ziegler** used **Thorpe** reaction to yield a **cyclic iminonitrile** using Lithium n-ethylaniline as a basic catalyst, then the product hydrolyzed with aqueous acid to yield the **cyclic ketonitrile**. Boiling the later with aqueous acid converts the nitrile group to a carboxylic acid to yield **β-ketoacid**, which on decarboxylation gives the **cyclic ketone** (Equation 5.11).



Equation 5.11

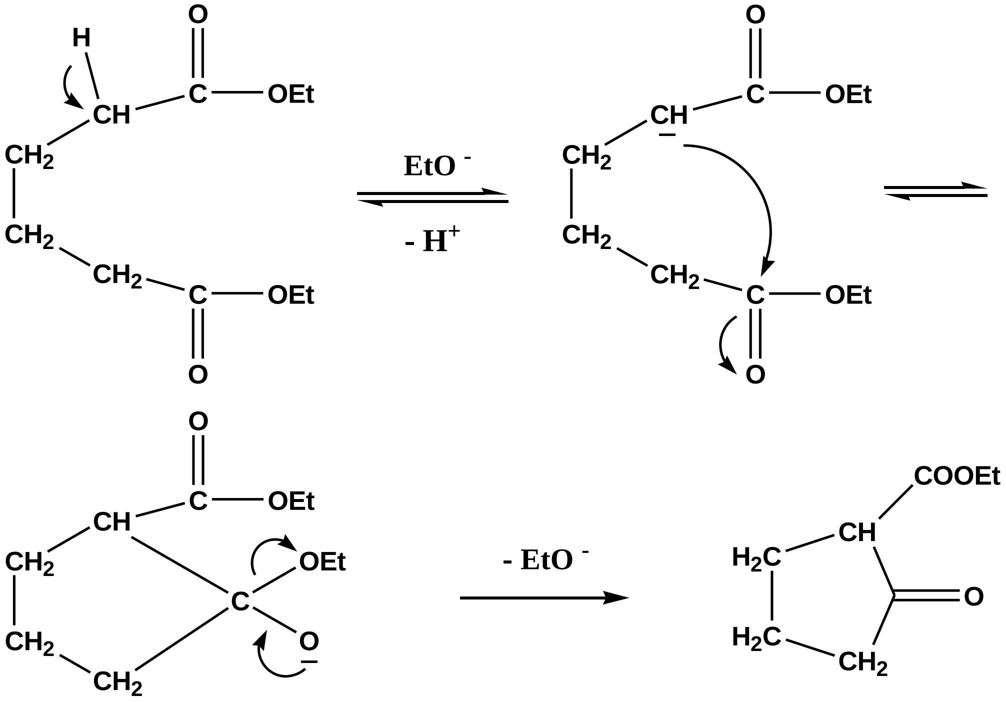
## 6. Dieckmann condensation:

This reaction is an intramolecular Claisen condensation, many cycloalkanes (five-, six- and seven-membered rings) can be obtained by treating the esters of adipic, pimelic or suberic acids with sodium ethoxide (Equation 6.1).

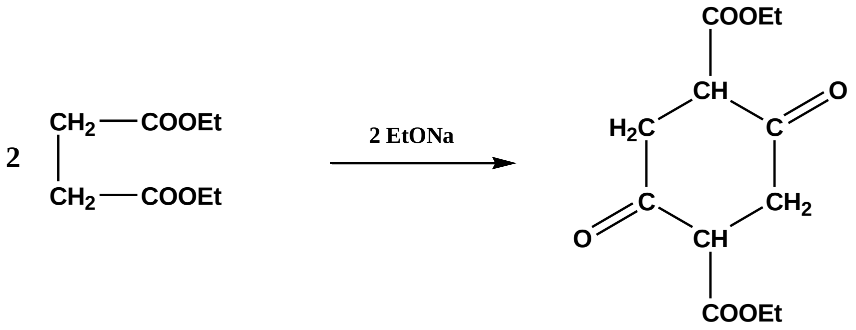


Equation 6.1

### The reaction mechanism;



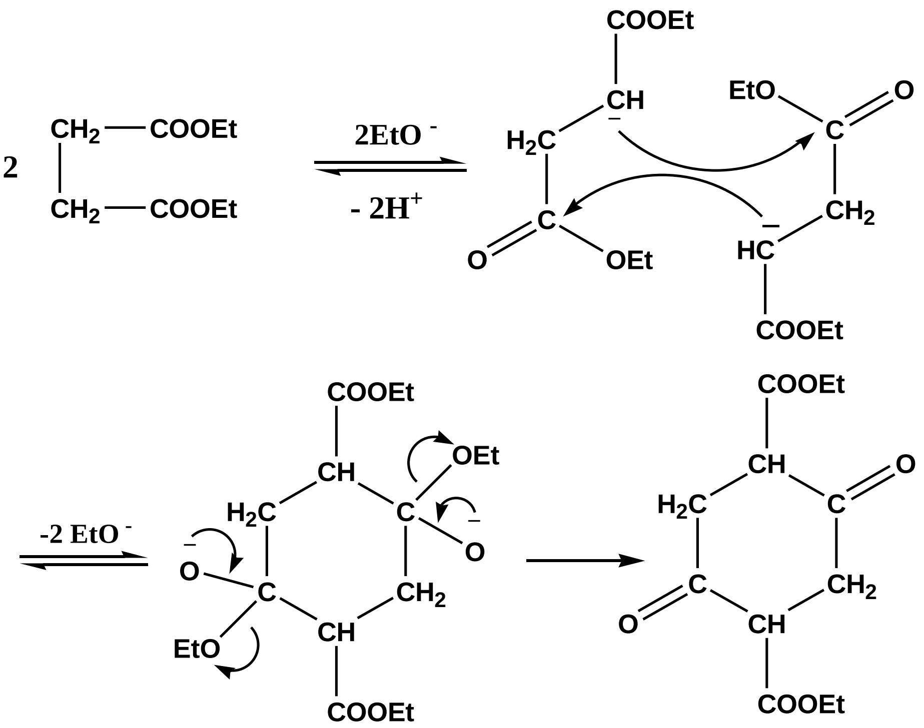
Esters lower than adipic ester may form cyclic products through the intermolecular condensation and cyclization, e. g., treatment of ethyl succinate in presence of sodium ethoxide forms succino-succinic ester (cycohexane-2,5-dione-1,4-carboxylic ester) (Equation 6.2).



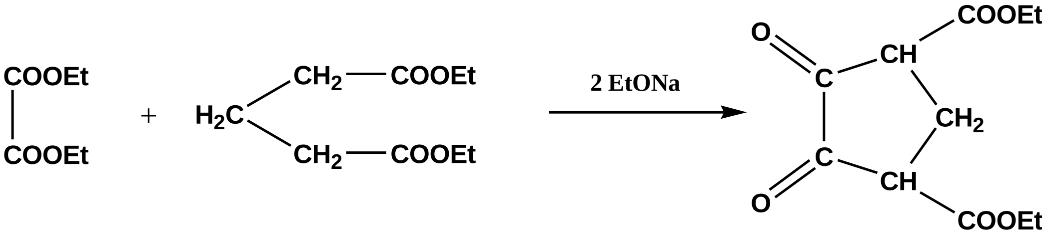
succino-succinic ester

**Equation 6.2**

## The reaction mechanism;



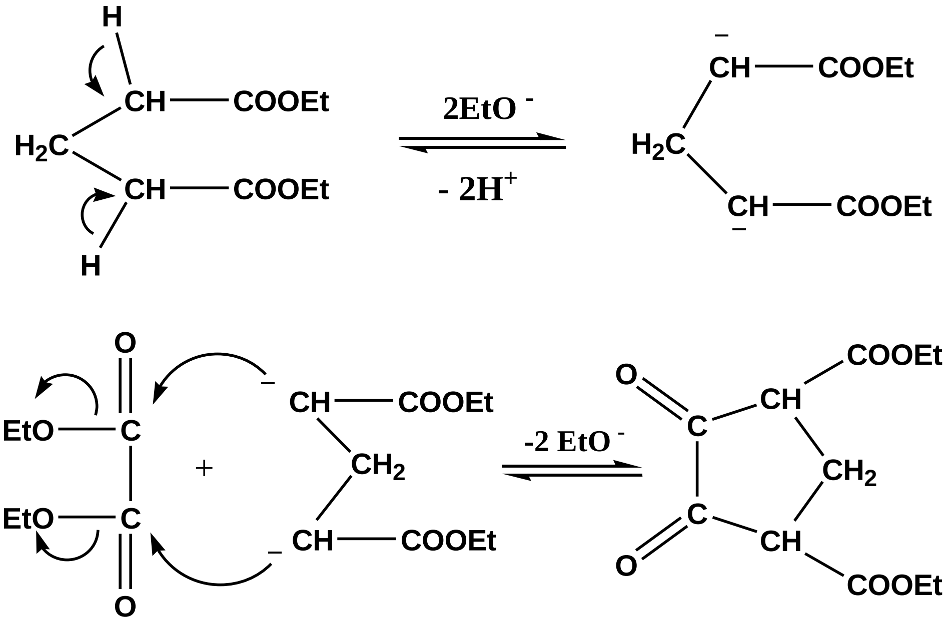
Also, five-membered ring cycloalkanes may be obtained through the intermolecular condensation between two different esters, such as, ethyl oxalate and ethyl glutarate (Equation 6.3).



**cyclopentane-4,5-dione-1,3-diethylcarboxylate**

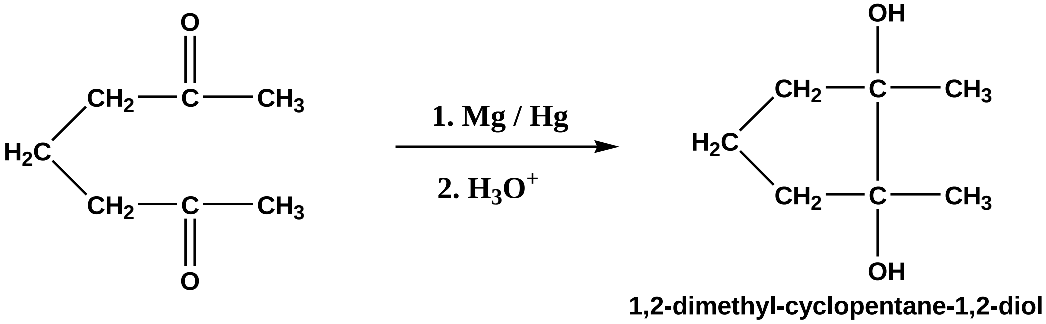
**Equation 6.3**

### The reaction mechanism;



## 7. Reduction of diketones:

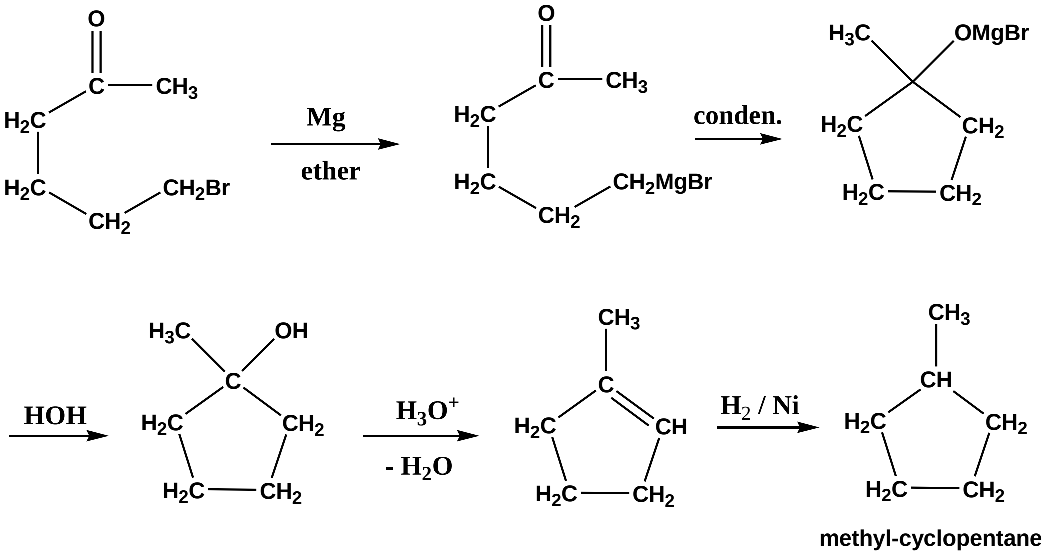
Five- or six-membered ring can be obtained through an intramolecular cyclization of certain diketones with magnesium amalgam, e. g., reduction of heptane-2,6-dione to form 1,2-dimethylcyclopentane-1,2-diol (Equation 6.4).



Equation 6.4

## 8. The Grignard method:

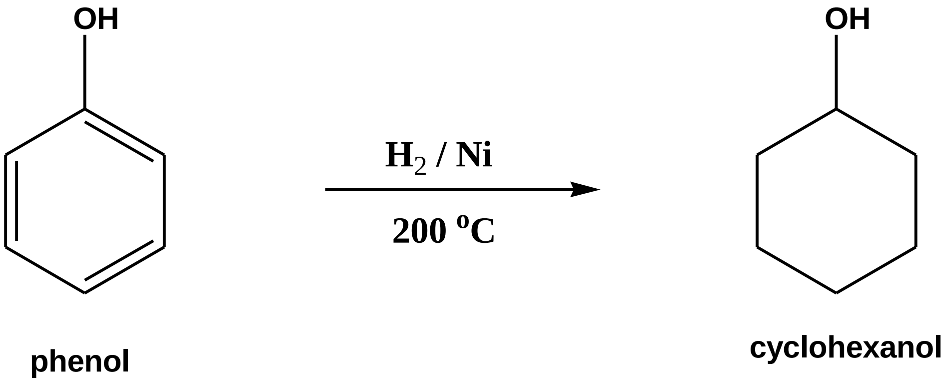
Certain halogen compounds react with magnesium which condenses internally to give cycloalkane derivatives, e. g., 6-bromo-2-hexanone reacts with **Mg** to give 1-methylcyclopentanol, which up on hydrolysis then reduction gives methylcyclopentane (Equation 6.5).



Equation 5.6

## 9. Reduction of benzene and its derivatives:

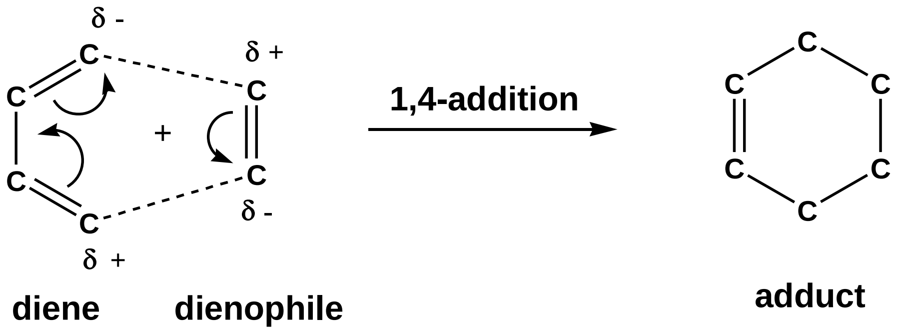
Catalytic reduction under pressure using nickel converted benzene or its derivatives into the corresponding six-membered cycloalkanes (Equation 6.6).



Equation 6.6

## 10. Diels-Alder reaction (Cyclo-addition reactions):

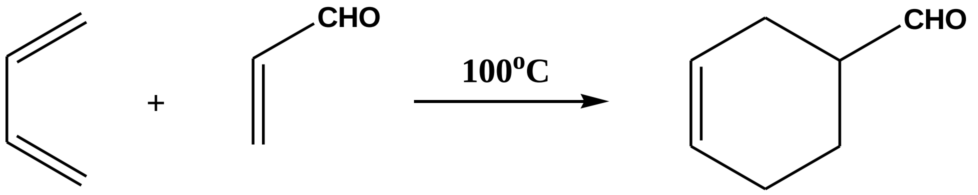
Diels-Alder reaction is an addition reaction between the diene ( a compound containing conjugated double bonds) and the dienophile (unsaturated hydrocarbon) to yield a product known as the adduct. The adduct is usually a six-membered ring, the addition taking place in the 1,4-positions. In general terms, this reaction may be written as the following (Equation 6.7).



Equation 6.7

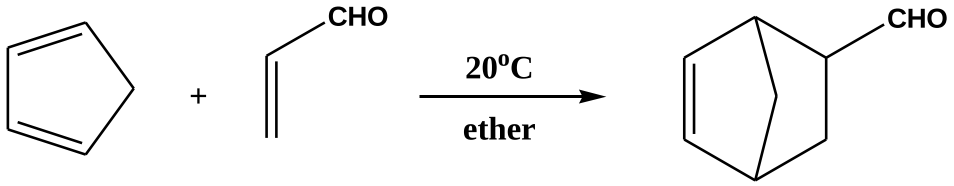
The diene may be of various types: acyclic, cyclic, semicyclic, bicyclic,

aromatic hydrocarbon with at least three linear benzene rings and certain heterocyclic compounds, also the dienophile may be: acyclic or cyclic. Some examples are in the following (Equations 6.8- 6.13).



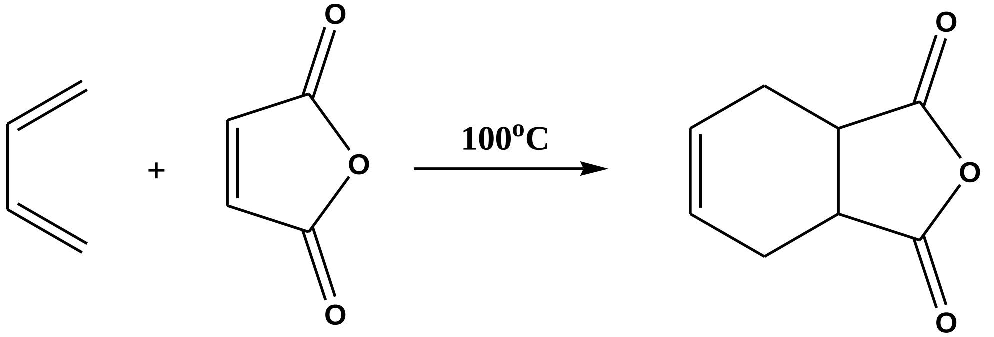
**3-cyclohexene-carbaldehyde**

**Equation 6.8**



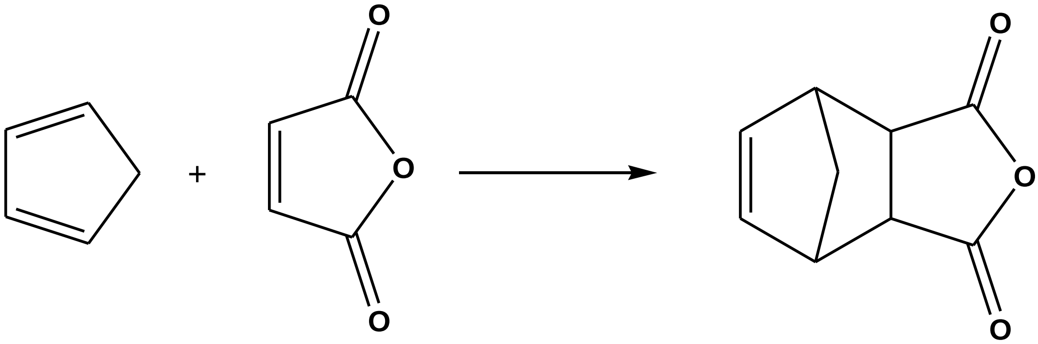
**bicyclo[2.2.1]hept-5-ene-**
**2-carbaldehyde**

**Equation 6.9**

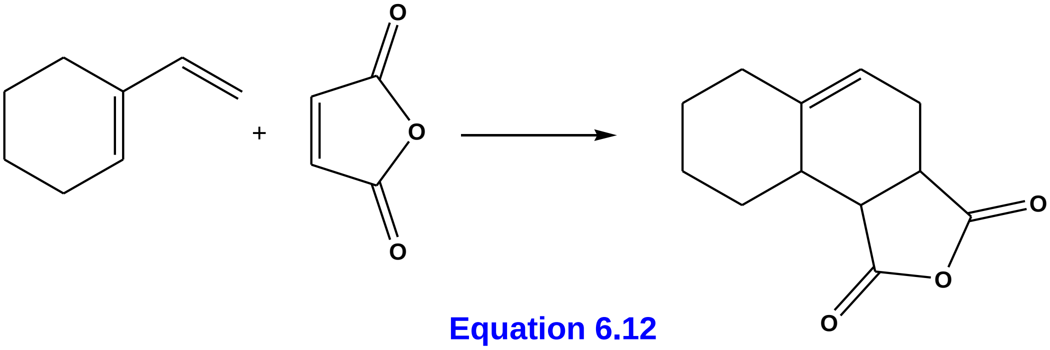


**tetrahydrophthalic anhydride**

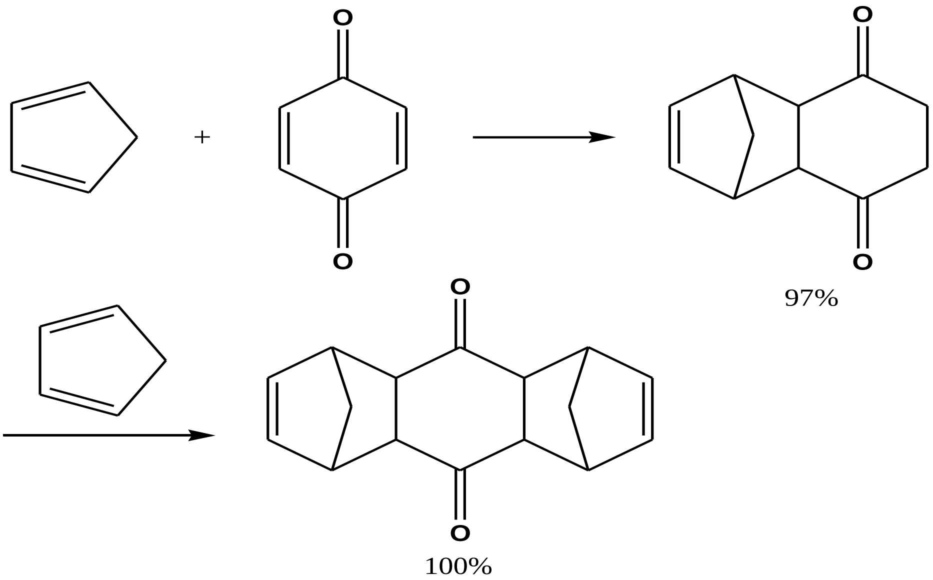
Equation 6.10



Equation 6.11



Equation 6.12



**Equation 6.13**

When the diene is cyclic, there are two *cis*-addition types, one giving the *endo*-compound and the other the *exo*-compound. The *endo*-compound is usually obtained exclusively due to the *endo*-compound is kinetically controlled, while the *exo*-compound is thermodynamically controlled. So, raising the temperature of the reaction favors the formation of the *exo*-compound (Fig. 6.14).

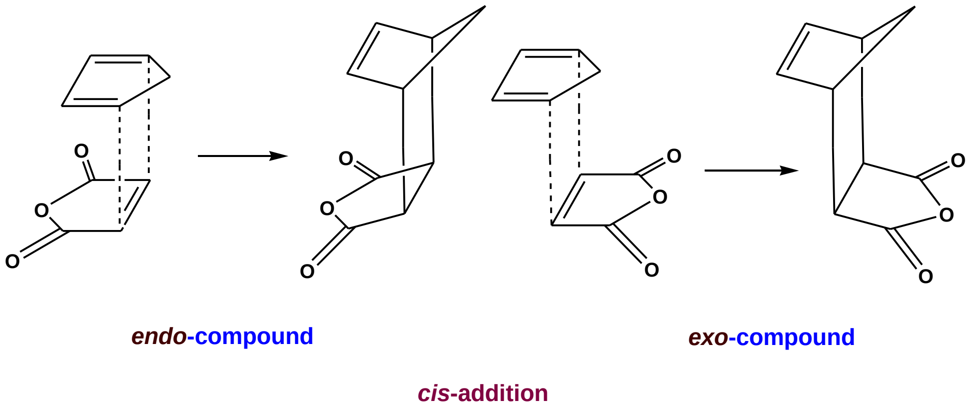


**Fig. 6.14**

# Unit 3

## Lesson 6: Cyclopropane and its derivatives

**6.1 Physical properties of cyclopropane:** b.p.= -34°C. It is used as a general anaesthetic in surgical operations. Also, cyclopropane is explusive and its explosions with oxygen are more powerful, so cyclopropane is dangerous to handle and manufacture.

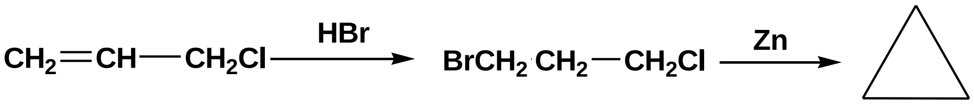
### 6.2 Chemical properties:

Several methods have been introduced to prepare cyclopropane and its derivatives as follows:

### I- Methods of preparation:

### 1. Gustavson method:

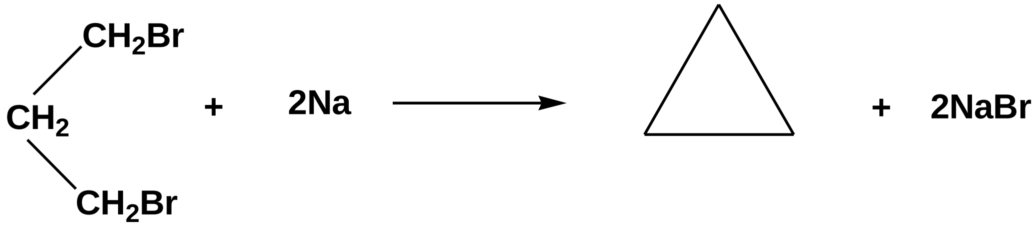
Cyclopropane is produced on an industrial scale by the action of zinc on 1,3-chlorobromo-propane, which prepared by addition of HBr to allylchloride (Equation 6.1).



Equation 6.1

### 2. Freund method:

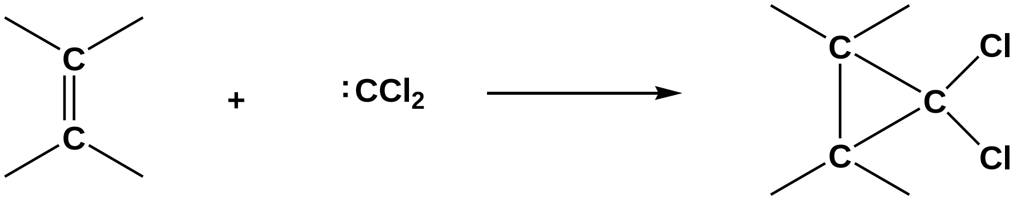
Treatment of 1,3-dibromopropane with metallic sodium gives the cyclopropane (Equation 6.2).



Equation 6.2

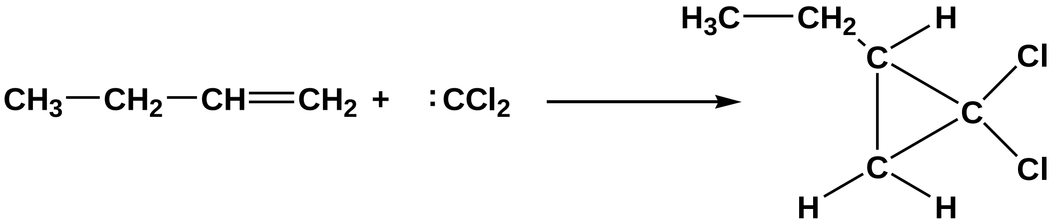
### 3. Action of carbenes on unsaturated compounds:

Addition reactions of carbenes to alkenes lead to the formation of the cyclopropanes. In general, this reaction may be written as follows (Equation 6.3).



Equation 6.3

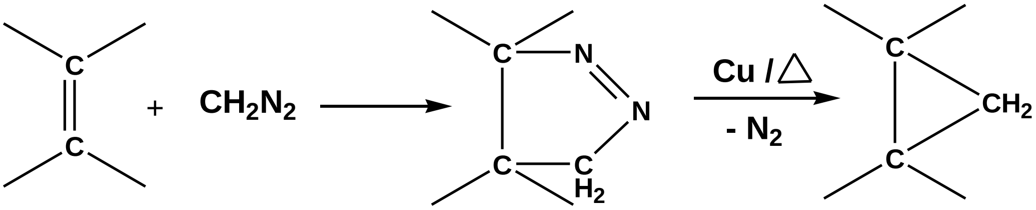
For example, (Equation 6.4).



Equation 6.4

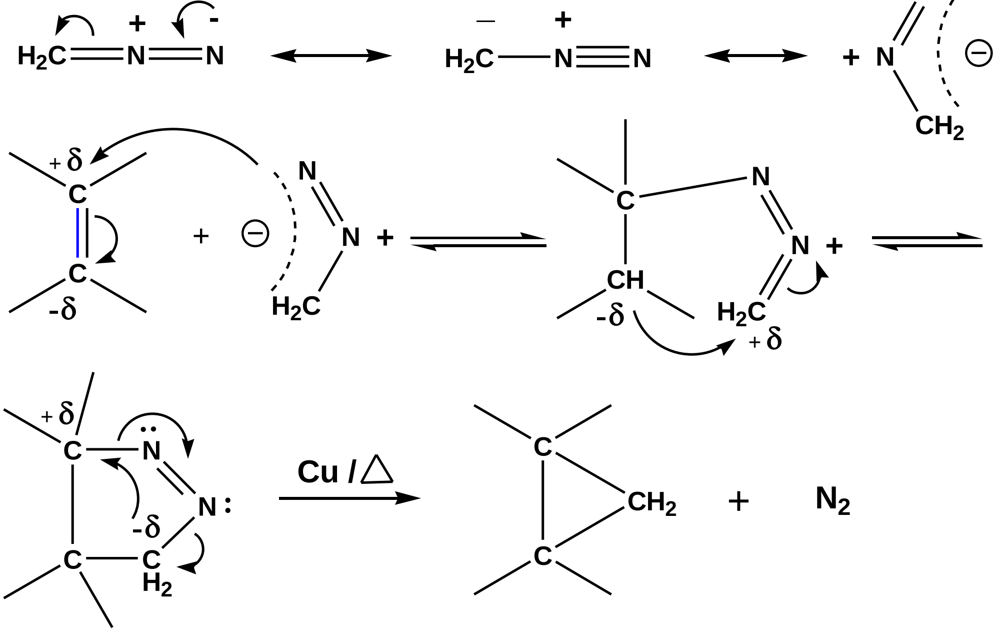
### 4. Buchner and Curtius reaction:

Addition of diazomethane to the double bonds affords the pyrazole ring, which upon heating with copper decomposed to yield the cyclopropane derivatives (Equation 6.5).



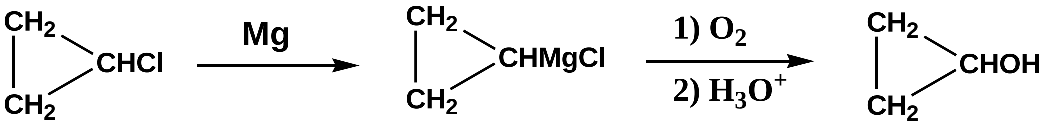
Equation 6.5

**The reaction mechanism;**



## 5. Synthesis of cyclopropanol:

Cyclopropanol has been prepared in a crude form as shown in (Equation 6.6).

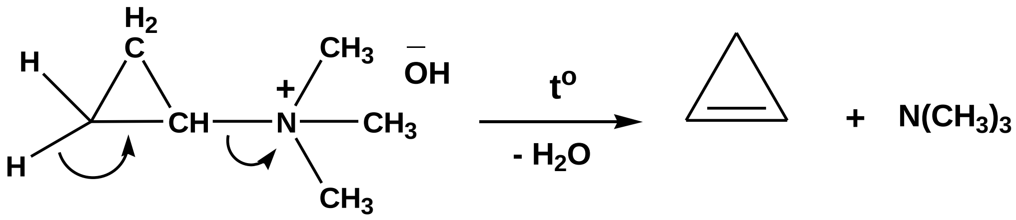


Equation 6.6

## 6. Synthesis of cyclopropenes:

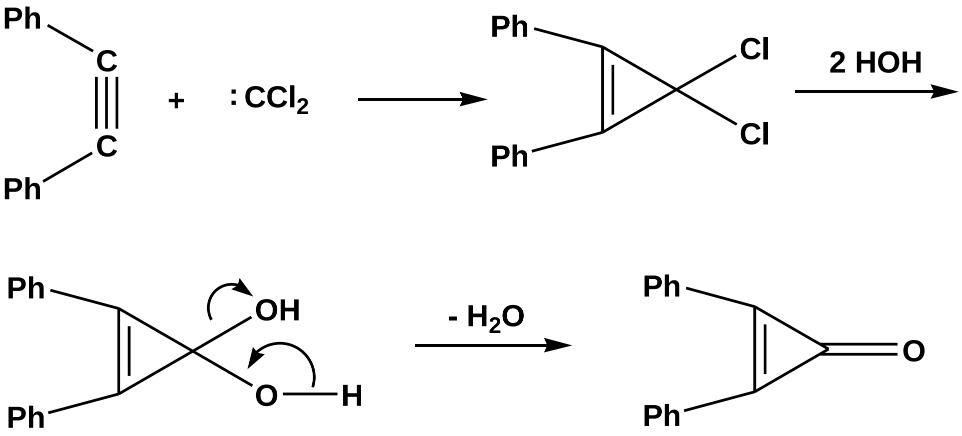
Two methods described the preparation of cyclopropene and cyclopropenenone as follows:

**i-** Decomposition of the cyclopropyltrimethylammonium hydroxide (Equation 6.7).



Equation 6.7

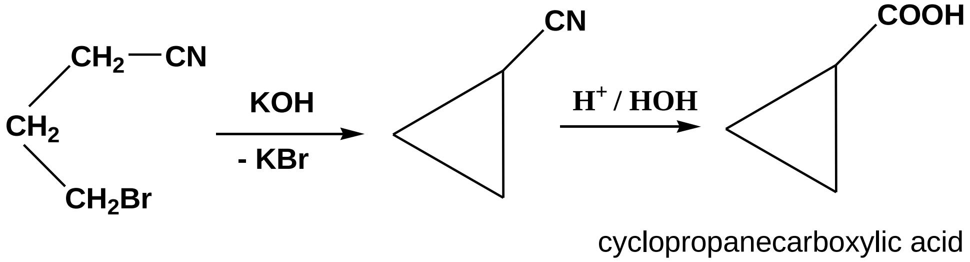
**ii-** Action of carbenes on acetylenes (Equation 6.8).



Equation 6.8

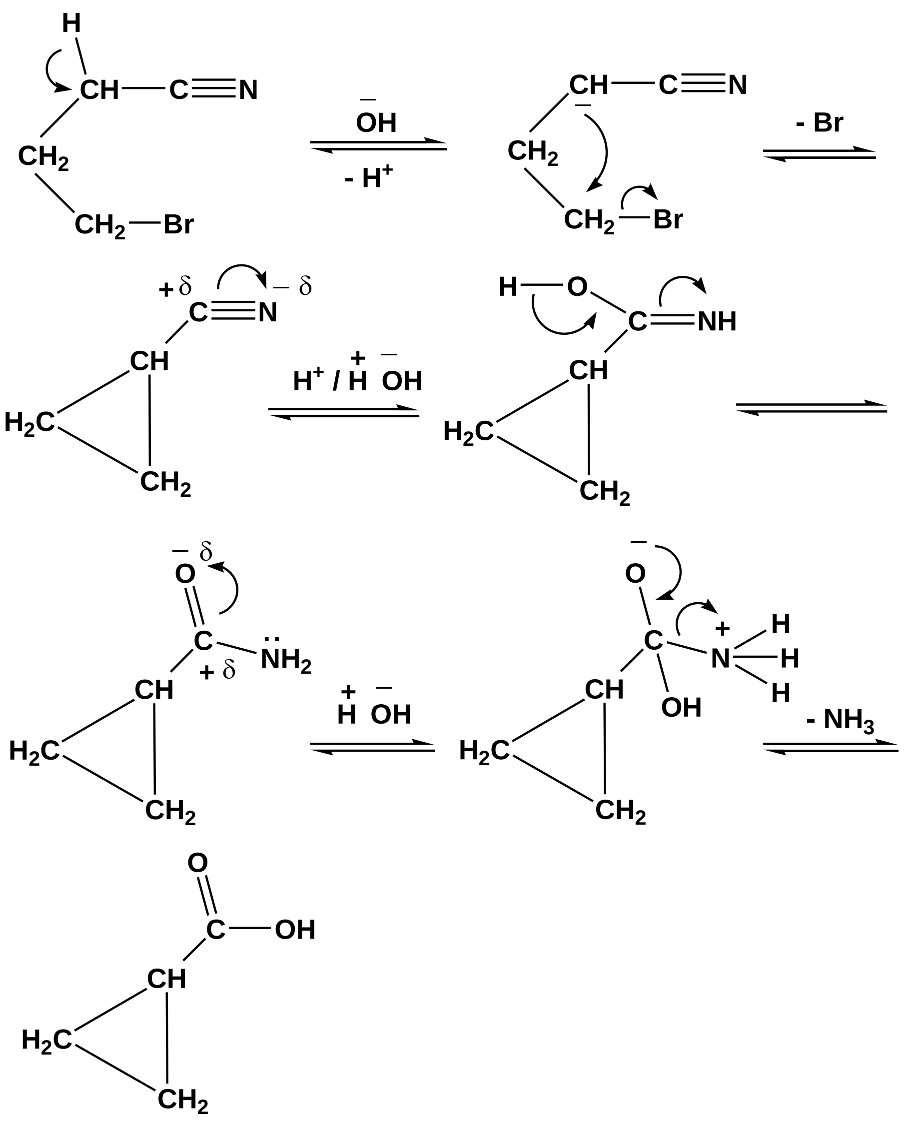
## 7. Synthesis of cyclopropanecarboxylic acid:

Cyclopropanecarboxylic acid has been prepared by the action of potassium hydroxide on 4-bromo-butyronitrile followed by hydrolysis of cyclopropanecarbonitrile (Equation 6.9).



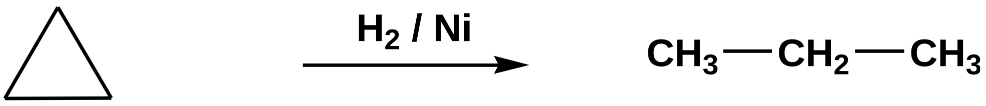
**Equation 6.9**

**Mechanism;**



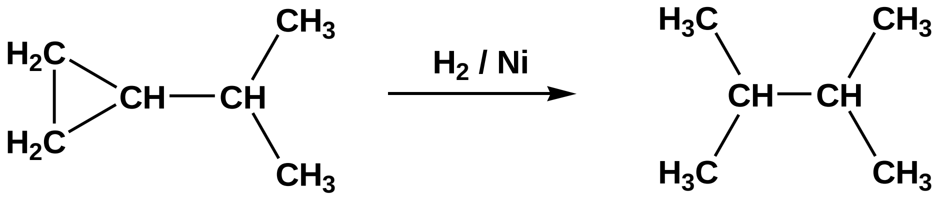
## II- Chemical reactions of cyclopropane and its derivatives:

**1. Hydrogenation:** cyclopropane turns to propane when hydrogenated over nickel (Equation 6.10).



**Equation 6.10**

Hydrogenation of isopropylcyclopropane affords 2,3-dimethylbutane (Equation 6.11).



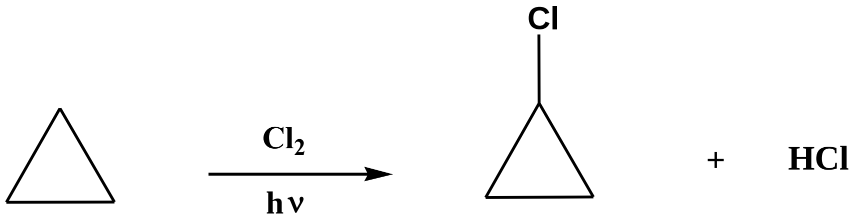
2,3-dimethyl-butane

**Equation 6.11**

**2. Halogenation:** Bromination of the cyclopropane affords 1,3-dibromocyclopropane (Equation 6.12).

**Equation 6.12**

Chlorination of cyclopropane takes place a replacement of hydrogen (Equation 6.13).

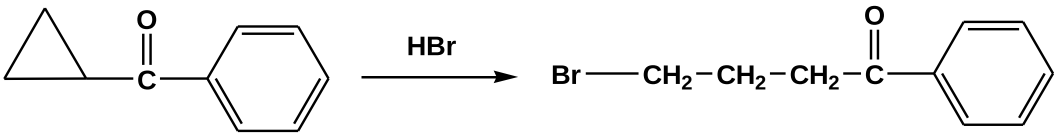


Equation 6.13

**3. Hydrohalogenation:** Hydrogen bromide reacts with cyclopropane to yield the bromopropane (Equation 6.14).

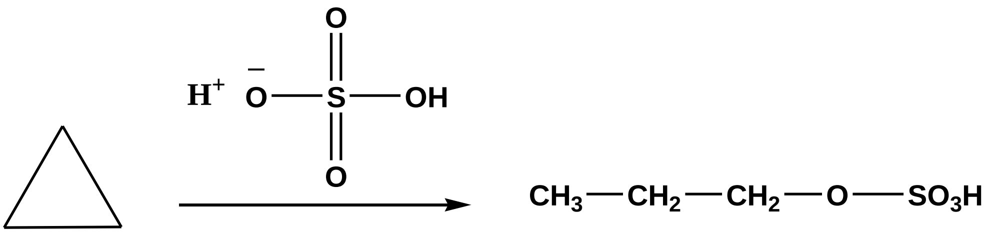
Equation 6.14

Action of hydrogen bromide to benzoylcyclopropane proceeds contrary to Markonikov's rule (Equation 6.15).



Equation 6.15

**4. Action of strong mineral acids:** Cyclopropane reacts with sulphuric acid to give sulphuric acid monopropyl ester (Equation 6.16).



Equation 6.16

# Unit 3

## Lesson 7: Cyclobutane and its derivatives

**7.1 Physical properties of cyclobutane:** $C_4H_8$, b.p.= $12.5^oC$, with a molecular mass of 56.107g/mol, is a four carbon alkane in which all the carbon atoms are arranged cyclically. Cyclobutane is a gas and commercially available as a liquefied gas.

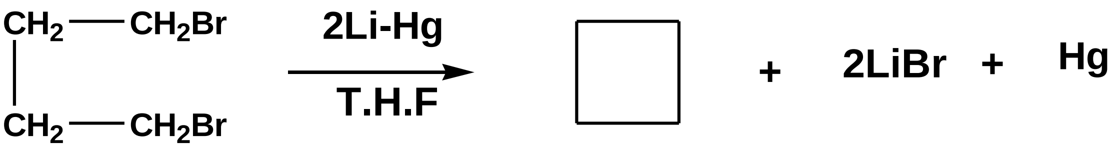
### 7.2 Chemical properties:

Several methods have been introduced to prepare cyclobutane and its derivatives as follows:

### I- Methods of preparation:

### 1. Connor and Wilson reaction (1967):

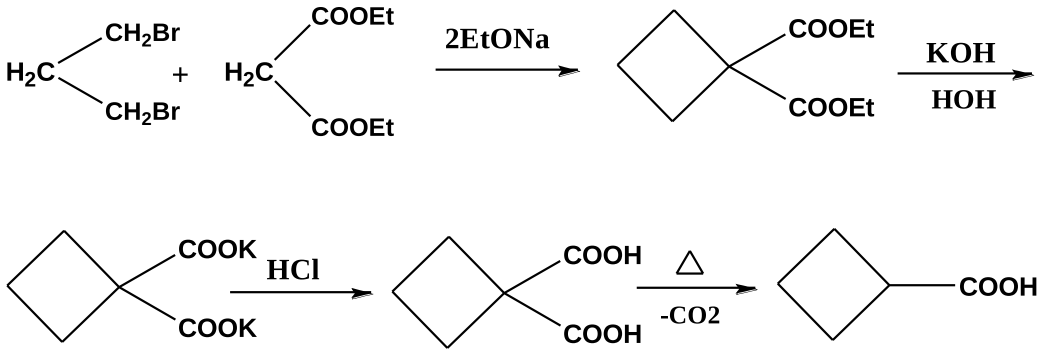
When 1,4-dibromobutane reacted with lithium amalgam in tetrahydrofuran, cyclobutane in a good yield was obtained (Equation 7.1).



Equation 7.1

### 2- Perkin's reaction:

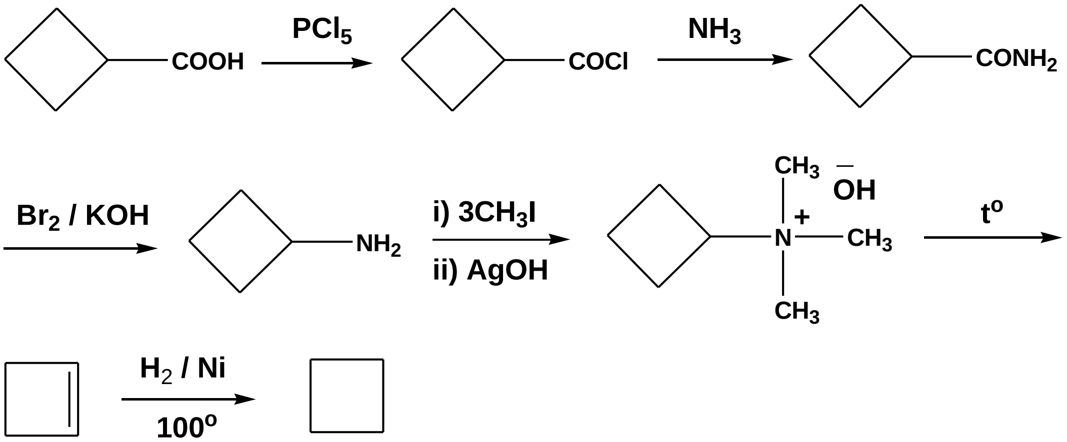
1,3-dibromobutane reacts with diethyl malonate in presence of sodium ethoxide to give cyclobutane dicarboxylic esters, which converts to cyclobutanecarboxylic acid (Equation 7.2).



Equation 7.2

## 3- From cyclobutanecarboxylic acid:

Attempts to decarboxylate of cyclobutanecarboxylic acid lead to opening of the ring, but it may be converting into cyclobutane by the following routs (Equation 7.3).



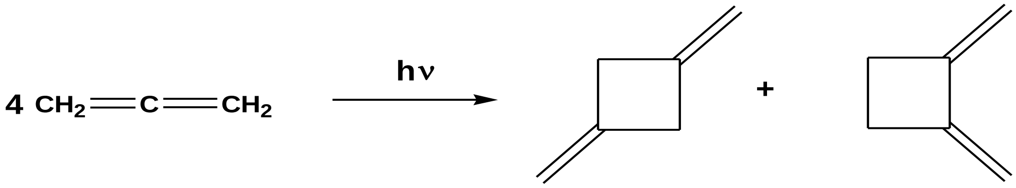
Equation 7.3

## 4- By photochemical reactions:

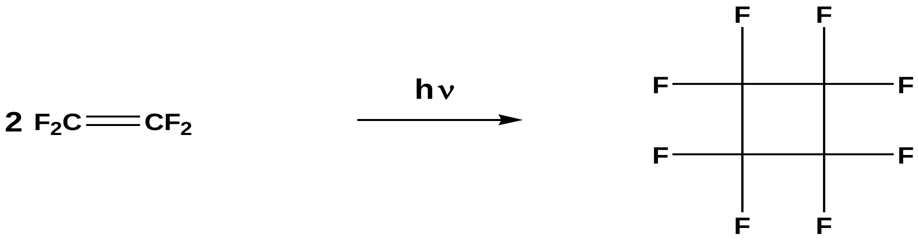
Cyclobutane or its derivatives can be prepared photochemically according to the following methods:

**a- Dimerization of allenes or perfluoro olefins:**

Photolysis of allenes or perfluoro olefins leads to formation of cyclobutane derivatives (Equations 7.4 and 7.5).

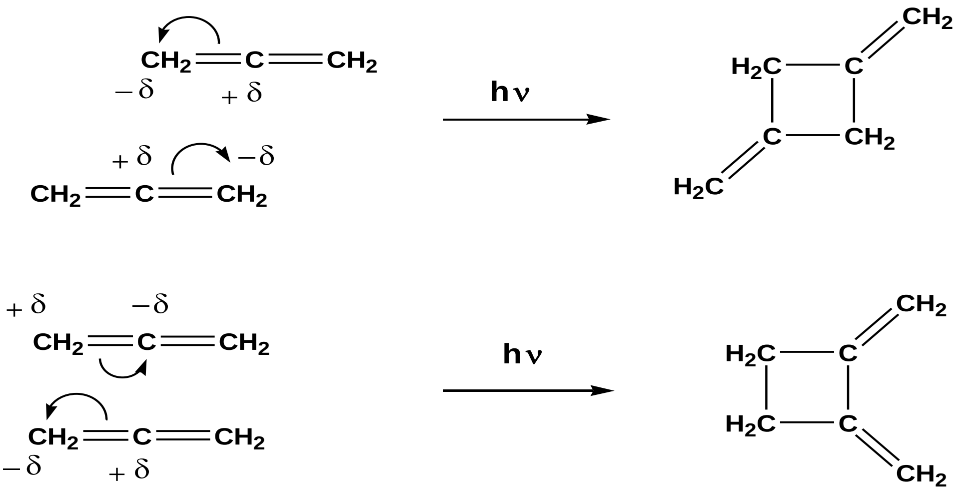


Equation 7.4



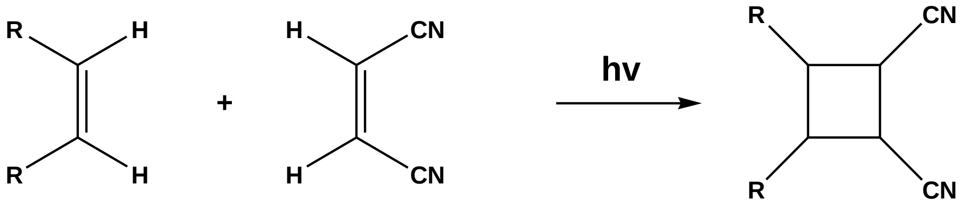
Equation 7.5

The reaction Mechanism;

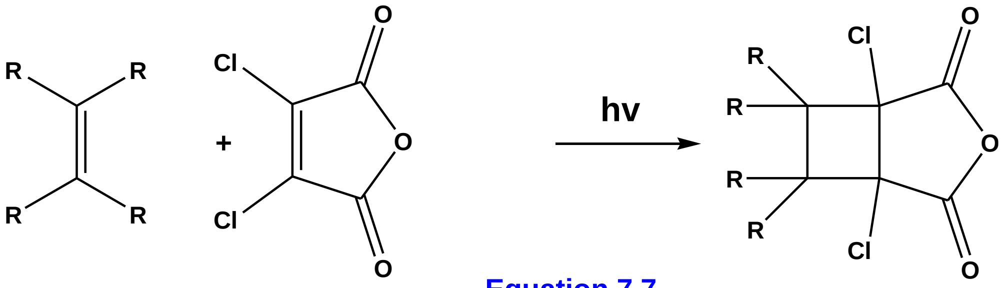


### b- Olefin- Olefin addition:

Under the action of irradiated light, olefins such as maleic anhydride and some other dienophiles are capable to adding on to olefin to form 4-membered rings (Equations 7.6 and 7.7).



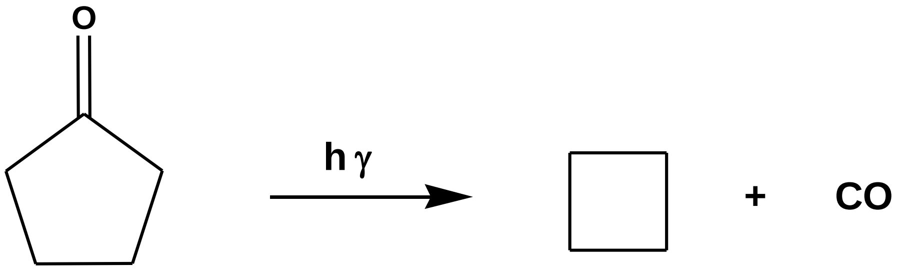
Equation 7.6



Equation 7.7

### c- Proteolysis of cyclopentanone:

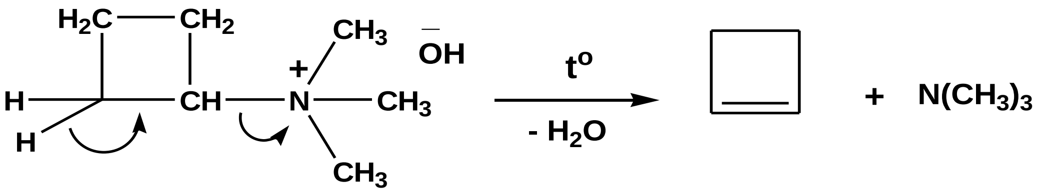
cyclobutane and carbon monoxide are the products of the proteolysis of cyclopentanone (Equation 7.8).



Equation 7.8

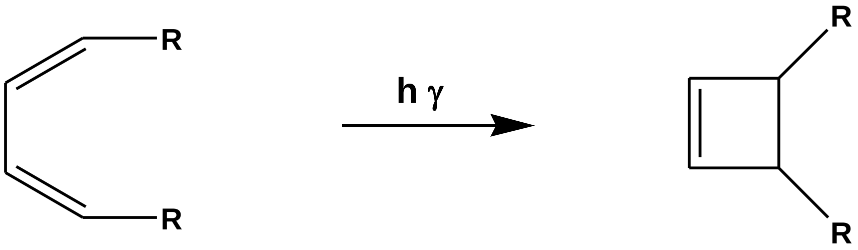
## 5- Preparation of cyclobutenes:

Decomposition of cyclobutyl trimethyl ammonium hydroxide gives the cyclobutene (Equation 7.9).



**Equation 7.9**

Irradiation of 1,3-dienes by ultraviolet rays affords cyclobutene derivatives (Equation 7.10).

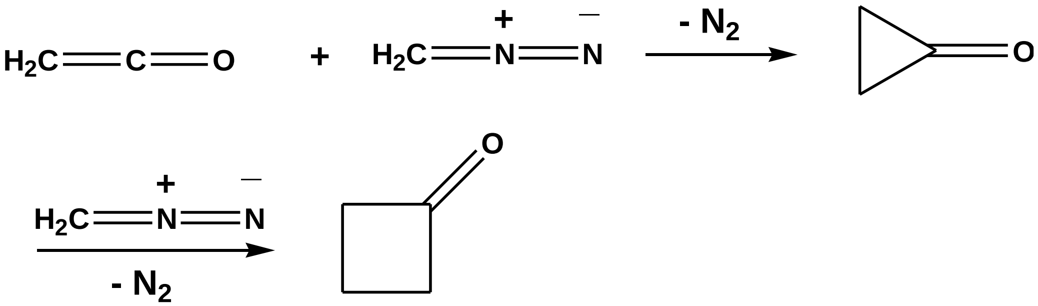


**Equation 7.10**

## 6- Carbonyl compounds of cyclobutane:

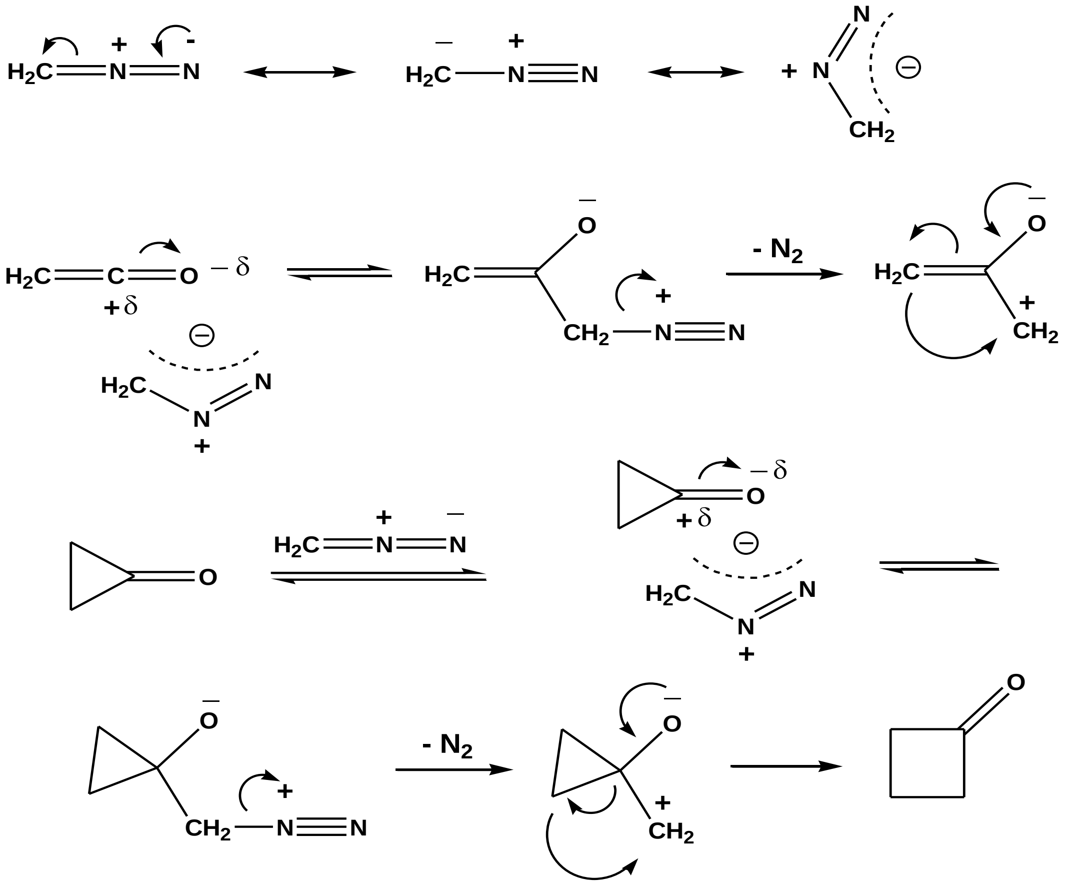
### a- Cyclobutanone:

When diazomethane reacted with ketene, cyclobutanone was obtained through the stage of formation of cyclopropanone (Equation 7.11).



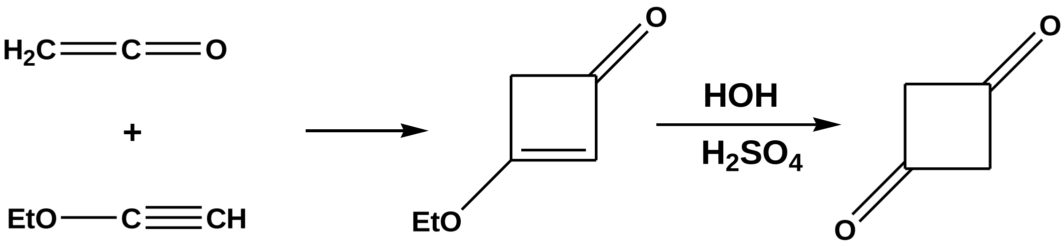
Equation 7.11

**The reaction mechanism;**



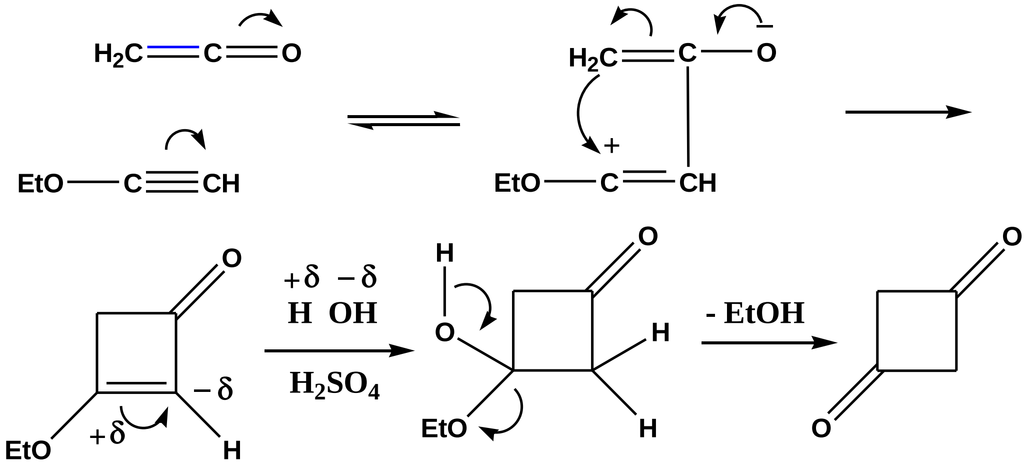
## b- Cyclobutanedione:

Cyclobutane-1,3-dione was obtained as follows (Equation 7.12).



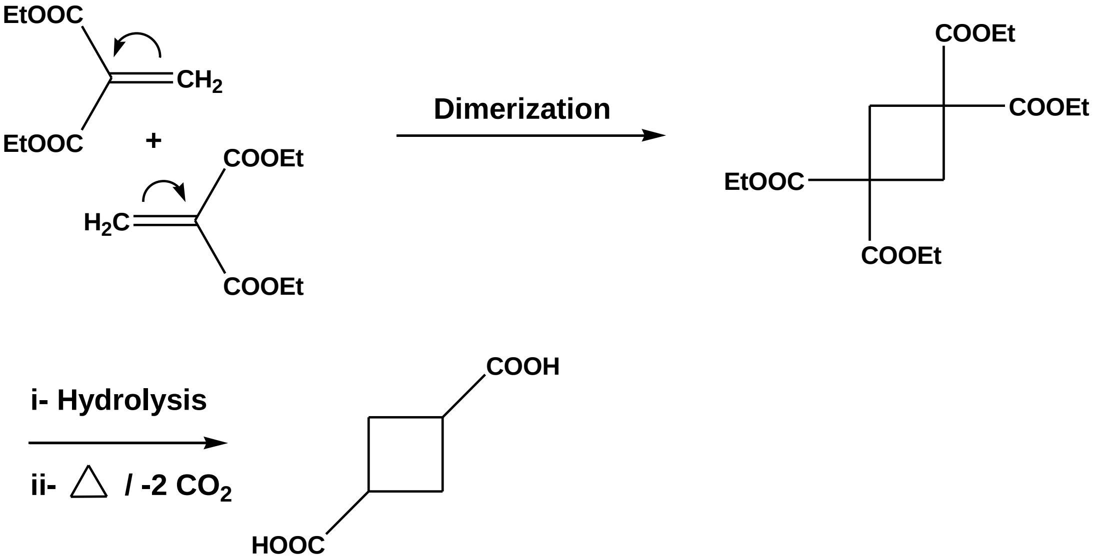
Equation 7.12

**The reaction mechanism;**



## 7- Cyclobutanecarboxylic acids:

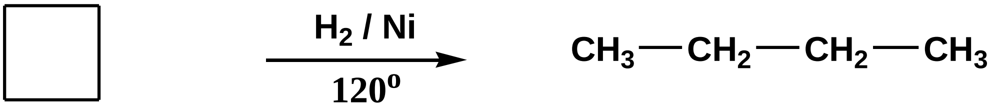
Cyclobutane-1,3-dicarboxylic acid as an example was prepared by the dimerization of 2-methylene-malonic acid diethyl ester (Equation 7.13).



Equation 7.13

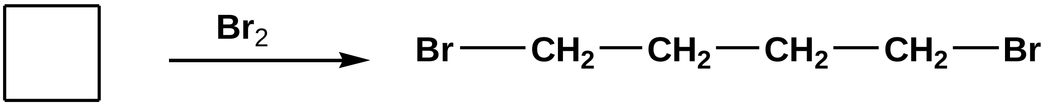
## II- Chemical reactions of cyclobutane and its derivatives:

**1- Hydrogenation:** cyclobutane converted to butane under the action of hydrogen over nickel at 120° (Equation 7.14).



Equation 7.14

**2- Halogenation:** Bromination of the cyclobutane gives 1,4-dibromobutane (Equation 7.15).

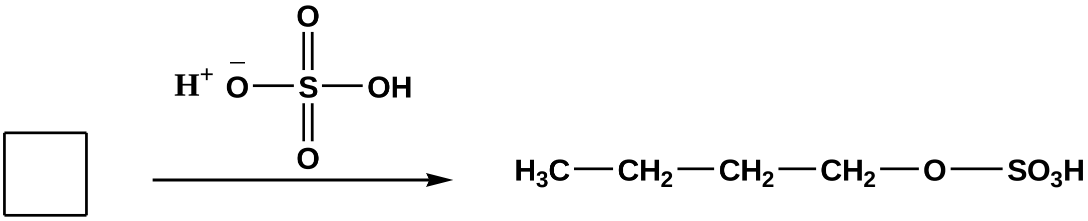


Equation 7.15

**3- Hydrohalogenation:** Cyclobutane reacts with hydrogen bromide to give the bromobutane (Equation 7.16).

Equation 7.16

5. **Action of strong mineral acids:** When sulphuric acid reacts with cyclobutane, sulphuric acid monobutyl ester was obtained (Equation 7.17).



Equation 7.17

## Unit 4

## Lesson 8: Cyclopentane and its derivatives

**8.1 Physical properties of cyclopentane:** $C_5H_{10}$, cyclopentane is a gas with bp. 49.5 $^oC$ and its molecular mass 70.1 g/mol. Petroleum contains a great variety of hydrocarbons, Markonikove and Ogloblin succeeded in isolating cyclopentane from petroleum, where the major proportion of naphthenes consists of cyclopentane and its homologues.

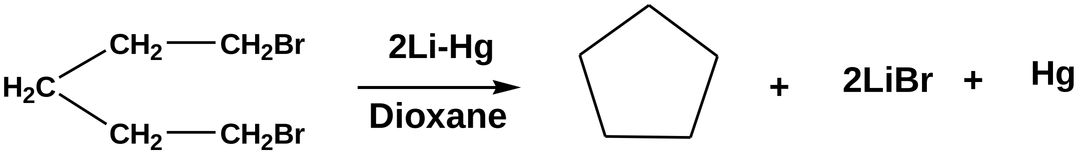
### 8.2 Chemical properties:

Several methods for the preparation of cyclopentane and its derivatives have been introduced as follows:

### I- Methods of preparation:

### 1. Connor and Wilson reaction:

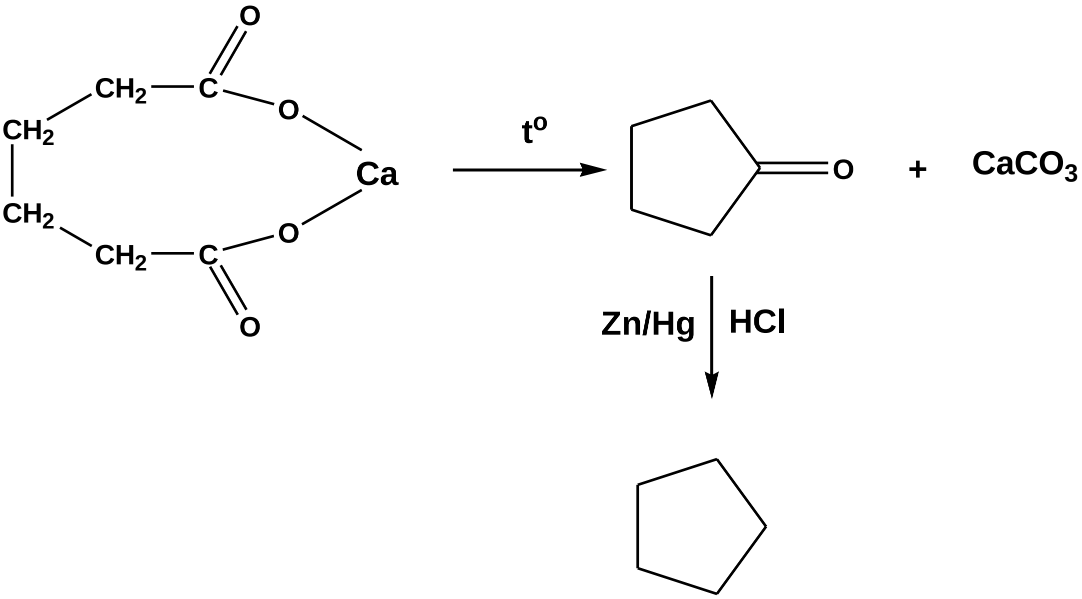
Action of lithium amalgam on a dioxane solution of 1,5-dibromopentane can give cyclopentane in 75% yield (Equation 8.1).



Equation 8.1

## 2. Pyrolysis of calcium salt of adipic acid:

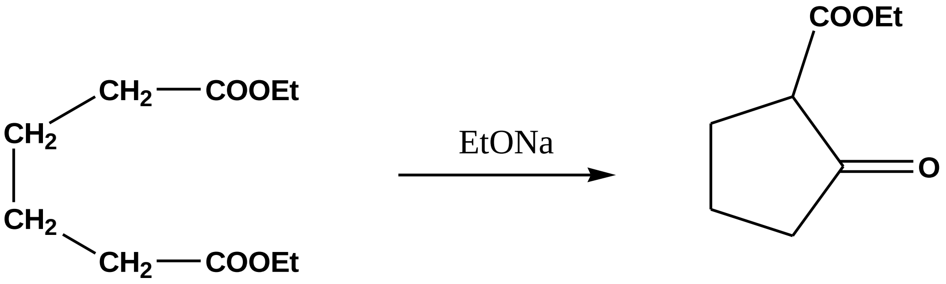
This method can be used to synthesize cyclopentanone with good yield under pyrolysis of the calcium adipate. Cyclopentanone may be converted into cyclopentane by means of the Clemmenson reduction (Equation 8.2).



Equation 8.2

## 3. Dieckmann condensation:

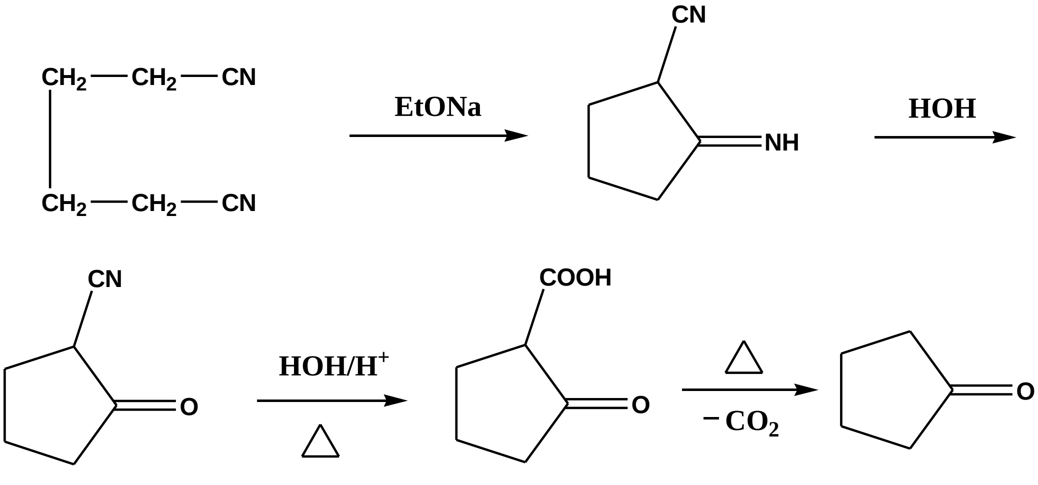
Treatment of diethyl adipate with excess of sodium ethoxide can give 2-cyclopentanonecarboxylic acid ethyl ester (Equation 8.3).



Equation 8.3

### 4. Ziegler-Thorpe reaction:

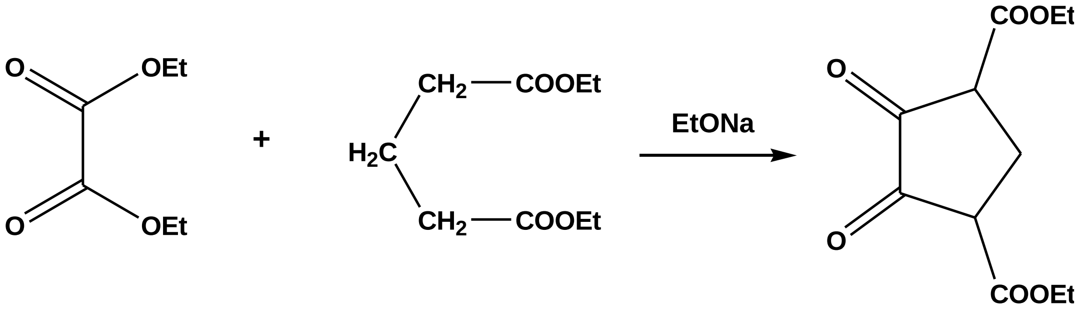
Condensation of hexanedinitrile in presence of sodium ethoxide gives 2-cyclopentanonecarbonitrile, which up-on hydrolysis affords 2-cyclopentanonecarboxylic acid. Decarboxylation of the later gives cyclopentanone (Equation 8.4).



Equation 8.4

### 5. Condensation of oxalic ester with glutatric ester:

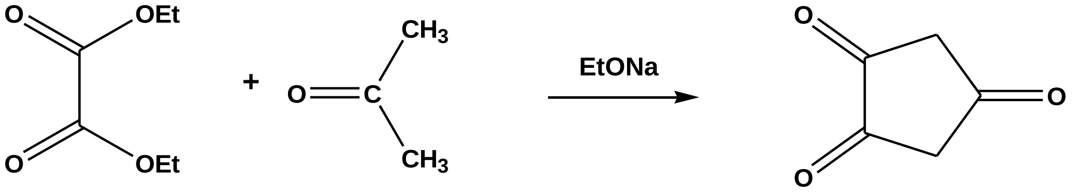
Treatment of ethyl oxalate with ethyl glutrate in presence of sodium ethoxide gives cyclopentan-4,5-dione-1,3-dicarboxylic acid diethyl ester (Equation 8.5).



Equation 8.5

### 6. Condensation of oxalic ester with acetone:

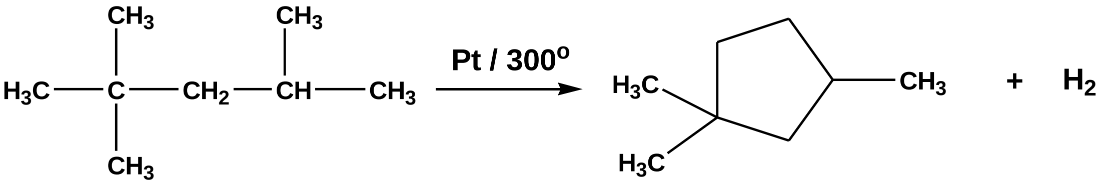
Treatment of acetone with ethyl oxalate in presence of sodium ethoxide gives cyclopentane-1,2,4-trione (Equation 8.6).



Equation 8.6

### 7. Dehydrocyclization of hydrocarbon chains:

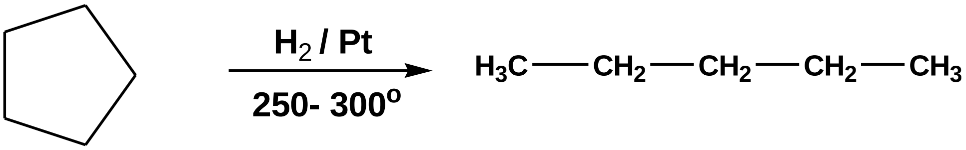
When a five carbon atoms chain contains a quaternary carbon atom is passed over a platinium catalyst at 300 $^{o}$C, cyclopentane derivative was obtained (Equation 8.7).



Equation 8.7

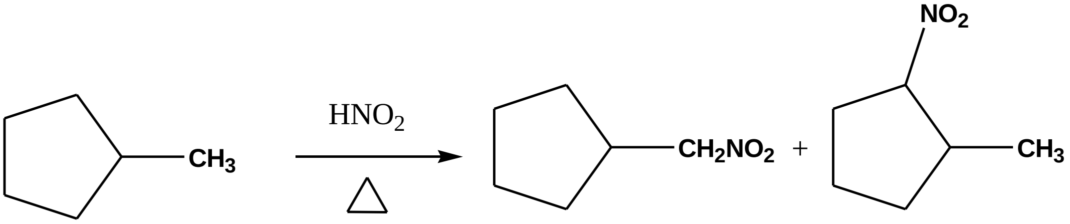
## II- Chemical reactions of cyclopentane and its derivatives:

**1. Hydrogenation:** cyclopentane undergoes hydrogenation over platinium at 250-300 °C to form pentane (Equation 8.8).



Equation 8.8

**2. Nitration:** cyclopentane and its derivatives can be nitrated, e. g., nitration of methylcyclopentane yields two products (Equation 9.9).

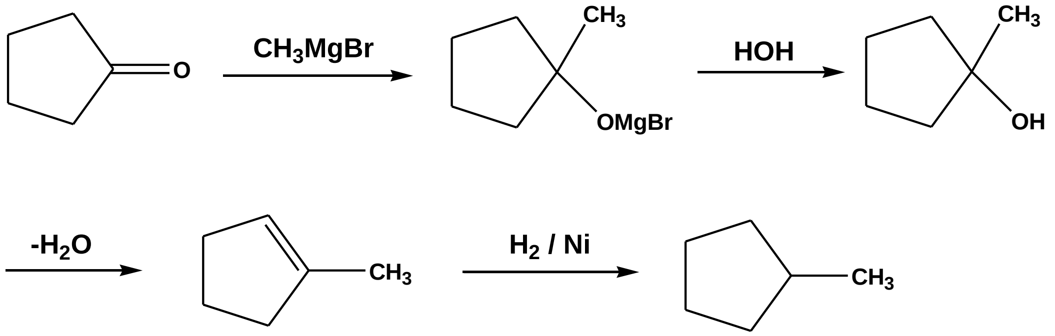


Equation 8.9

**3. Cyclopentanone:**

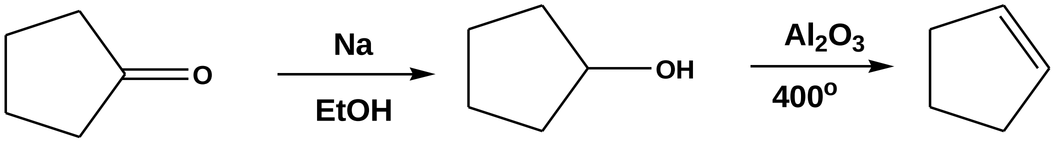
**a- Grignard reaction:** treatment of cyclopentanone with Grignard reagent ($CH_3MgBr$) followed by hydrolysis gives 1-

methyl-cyclopentanol. The later lose a molecule of water to give 1-methyl-cyclopentene, which on hydrogenation gives methylcyclopentane (Equation 8.10).



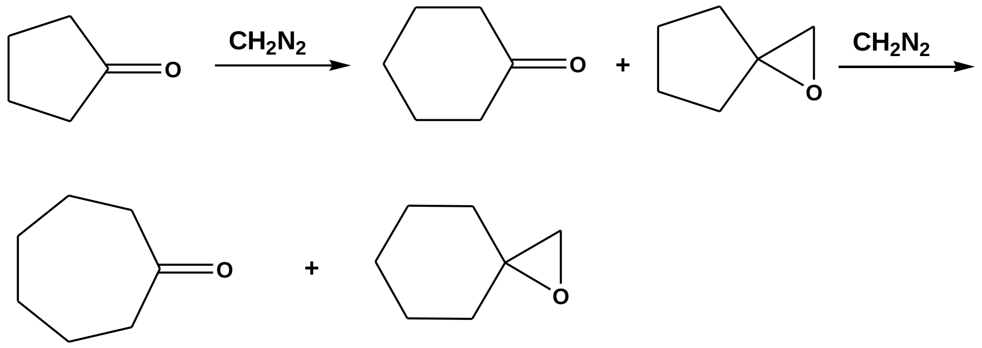
Equation 8.10

**b- Reduction of cyclopentanone:** With sodium in alcohol gives cyclopentanol, which up-on heating to 400 $^{o}$C in presence of **$Al_2O_3$** lose a molecule of water to give cyclopentene (Equation 8.11).



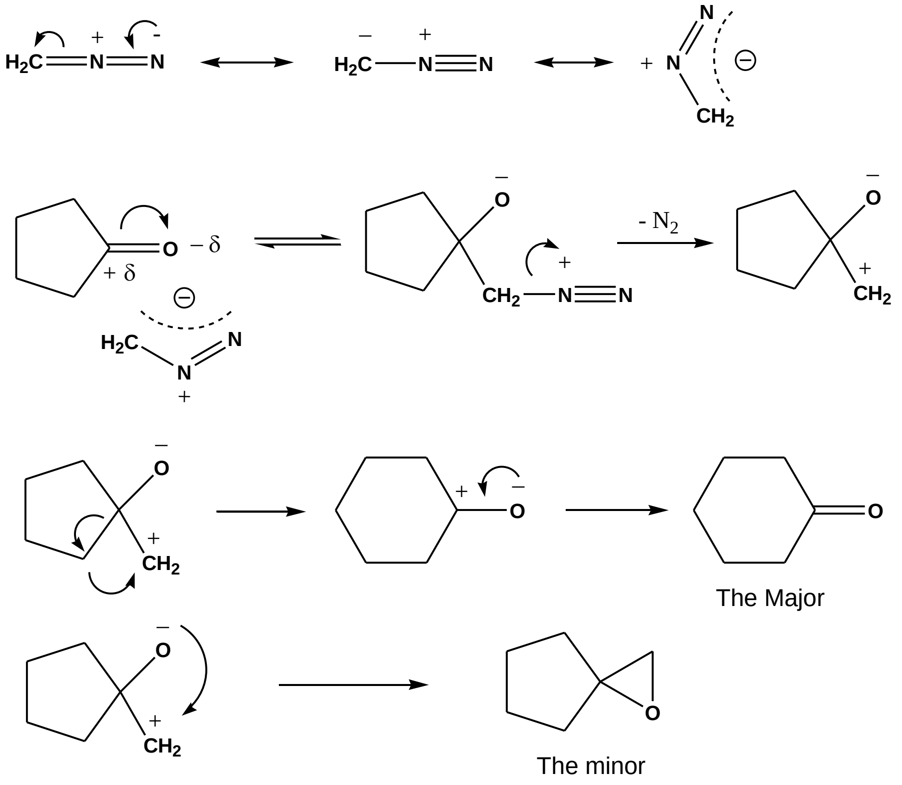
Equation 8.11

**c- Treatment of cyclopentanone with diazomethane:** undergoes ring expansion to form cyclohexanone, which reacts with diazomethane to form cycloheptanone and 1-oxa-spiro[2,5]octane (Equation 8.12).



**Equation 8.12**

**The reaction mechanism;**



## 4. Cyclopentadiene:

Cyclopentadiene is found in the crude benzene that is obtained from coal-tar.

The hydrogen atoms of methylene group are very reactive, e. g., treatment of cyclopentadiene with sodium gives sodium cyclopentadienide as shown in following figure (8.13);

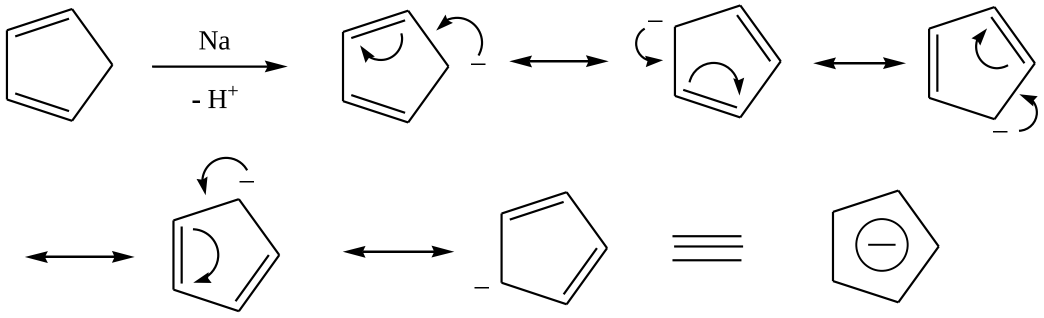
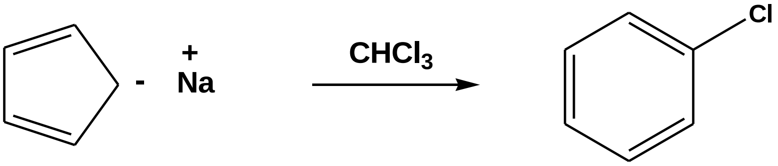


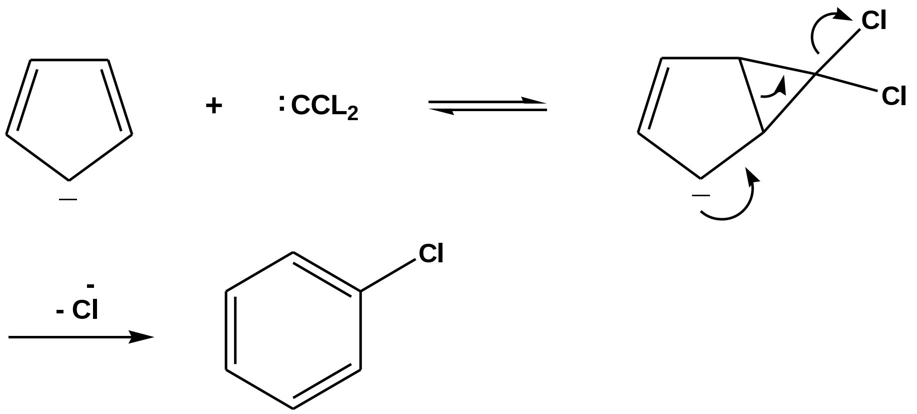
Figure 8.13

**a- Cyclopentadienyl sodium:** reacts with chloroform to give chlorobenzene (Equation 8.14).

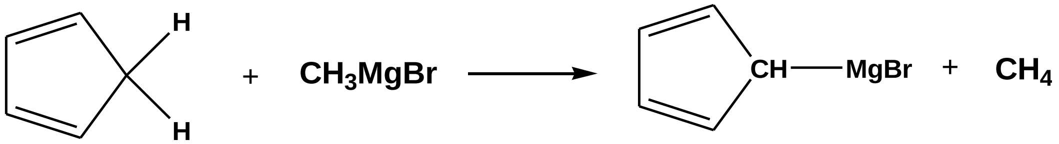


Equation 8.14

**The reaction mechanism;**

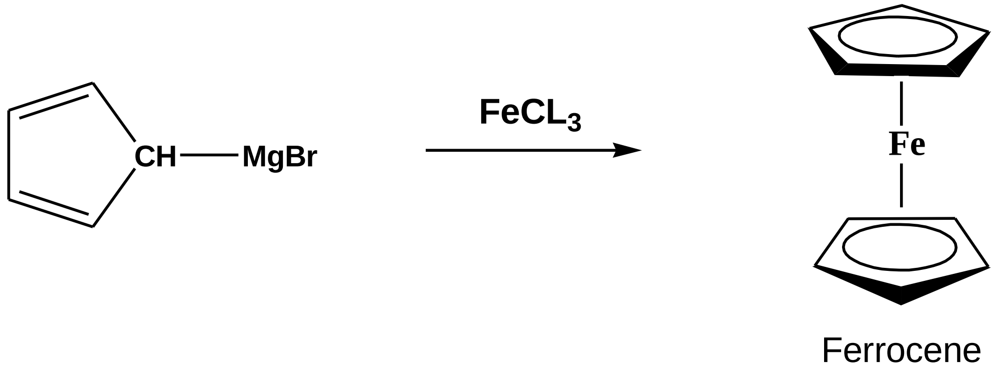


**b- Grignard reaction:** cyclopentadiene reacts with Grignard reagents to form cyclopentadienyl magnesium halide and the corresponding hydrocarbon (Equation 8.15).



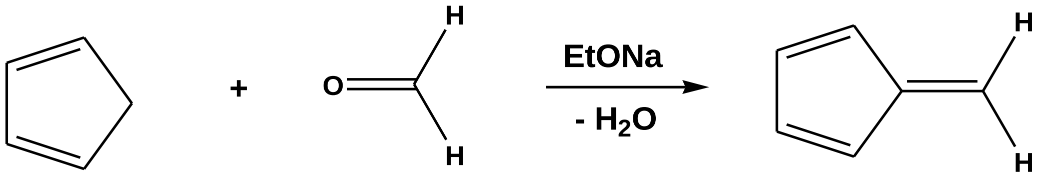
Equation 8.15

When cyclopentadienyl magnesium bromide reacts with ferric chloride, dicyclopentadienyl iron was isolated. This iron (Fe II) complex was named *ferrocene* by Woodward *et al* (Equation 8.16).



**Equation 8.16**

**c- Condensation reactions:** cyclopenta-1,3-diene condenses with aldehydes or ketones in presence of sodium ethoxide to afford *fluvenes* (Equation 8.17).



**Equation 8.17**

**d- Dimerization:** cyclopentadiene dimerizes into dicyclopentadiene, which regenerates the monomer on heating (Equation 8.18).

**Equation 8.18**

## Unit 4

## Lesson 9: Cyclohexane and its derivatives

**9.1 Physical properties of cyclohexane:** $C_6H_{12}$, cyclohexane is a colorless liquid. It is a cyclic alkane that melts at 6°C and boils at 81°C. It is insoluble in water. Cyclohexane is found naturally to some extent in petroleum and is widely used as a solvent and in making certain compounds used in the preparation of nylon.

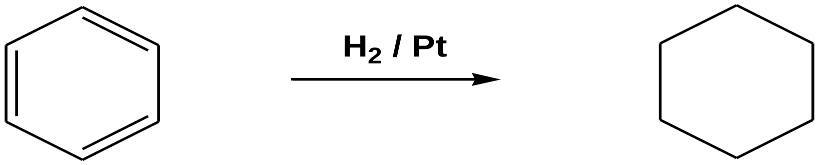
### 9.2 Chemical properties:

Many methods for the preparation of cyclohexane and its derivatives have been introduced as follows:

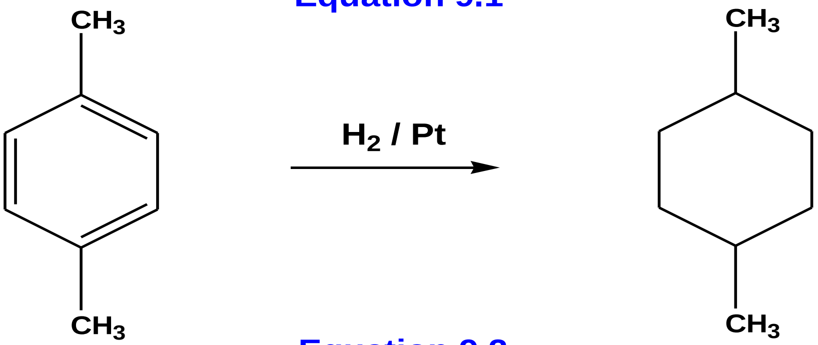
### I- Methods of preparation:

### 1. Hydrogenation of benzene and its derivatives:

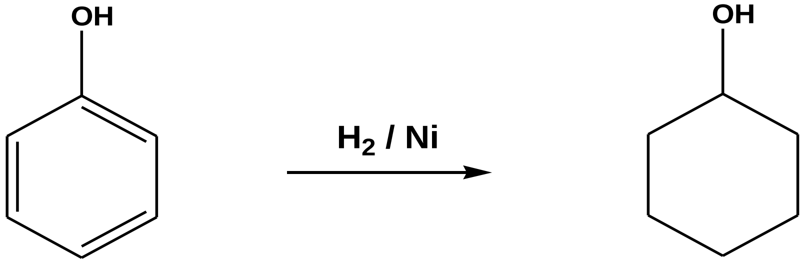
Cyclohexane is prepared commercially by catalytic hydrogenation of benzene. Certain derivatives of cyclohexane are mainly prepared by catalytic hydrogenation of certain aromatic compounds over platinum or nickel (Equations 9.1-9.4).



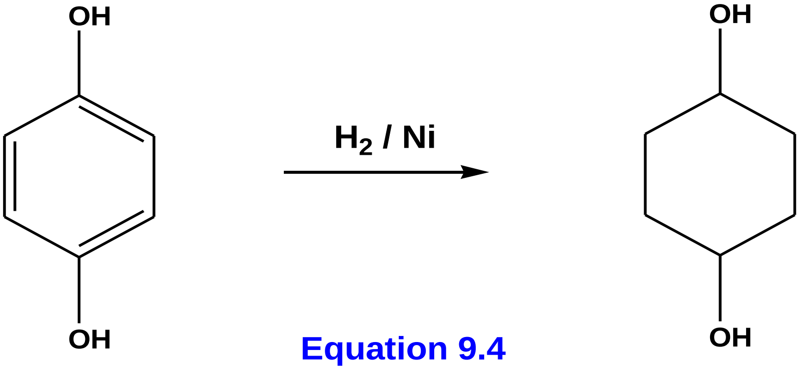
Equation 9.1



Equation 9.2



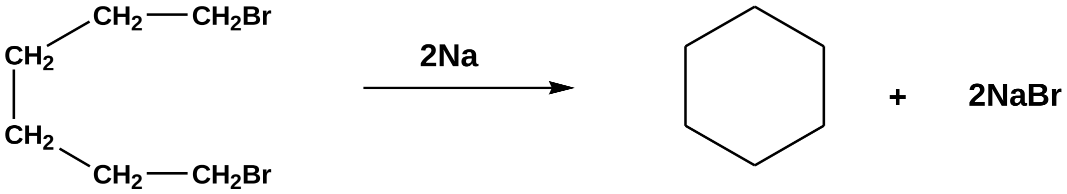
Equation 9.3



Equation 9.4

## 2- Freund reaction:

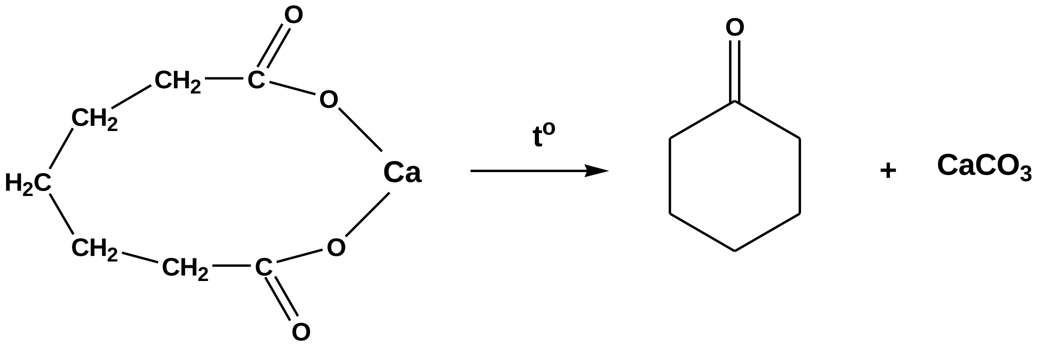
Treatment of 1,6-dibromohexane with a metal like sodium or zinc gives cyclohexane (Equation 9.5).



Equation 9.5

### 3. Pyrolysis of calcium salt of pimelic acid:

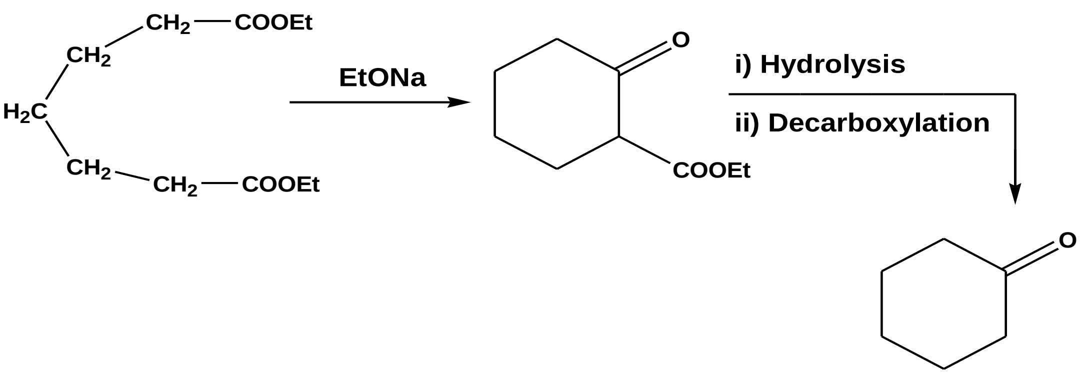
Cyclohexanone can be obtained under the pyrolysis of calcium pimelate (Equation 9.6).



Equation 9.6

### 4. Dieckmann condensation:

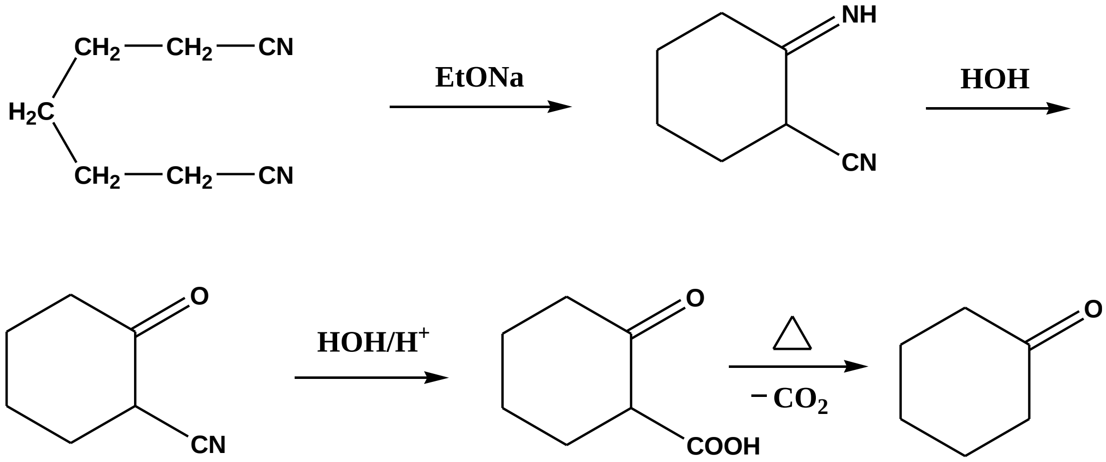
Treatment of diethyl pimelate with sodium ethoxide can give 2-cyclohexanonecarboxylic acid ethyl ester, which upon hydrolysis and decarboxylation turns to cyclohexanone (Equation 9.7).



Equation 9.7

## 5. Ziegler-Thorpe reaction:

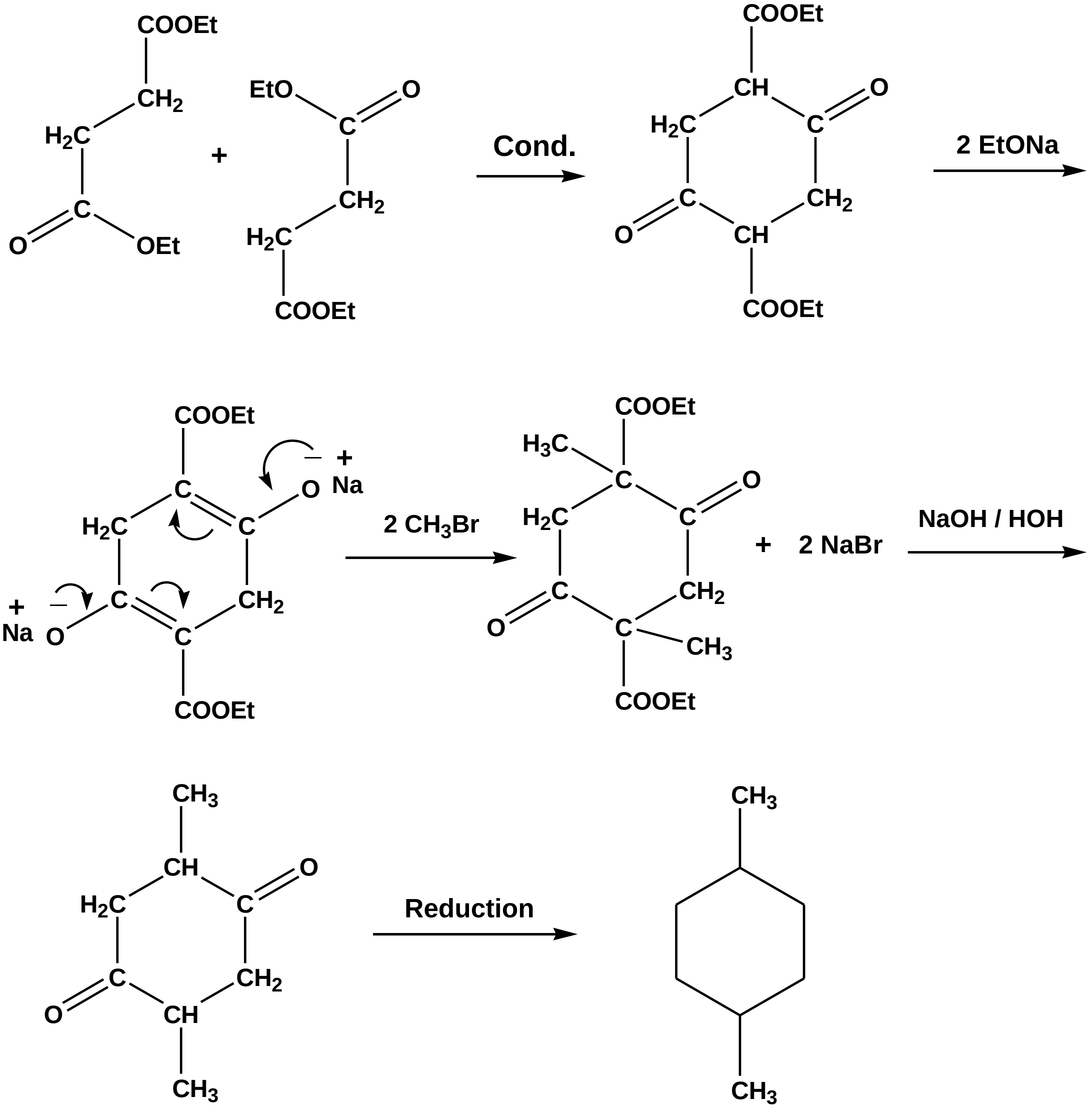
When heptanedinitrile treated with sodium ethoxide followed by hydrolysis affords 2-cyclohexanonecarbonitrile. After hydrolysis and decarboxylation of the later, cyclohexanone was obtained (Equation 9.8).



Equation 9.8

## 6. Ester condensation of succinic ester:

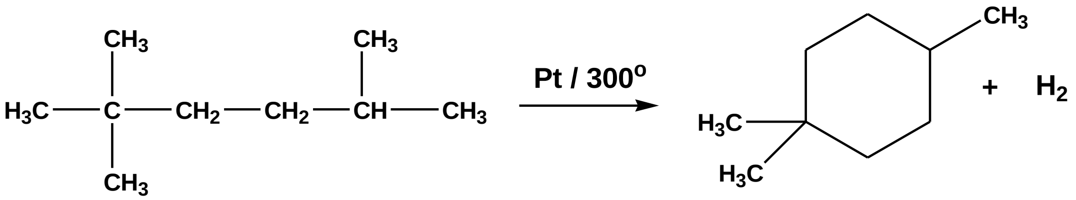
Condensation of two molecules of diethylsuccinate in presence of sodium ethoxide gives succinosuccinic ester. The sodium salt of the later was treated with alkyl halide followed by saponification and then finally Clemmenson reduction to afford 1,4-disubstituted-cyclohexane (Equation 9.9).



Equation 9.9

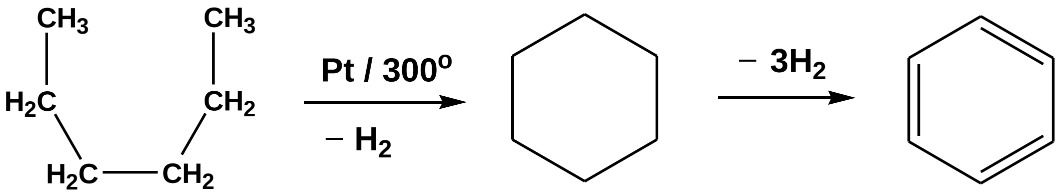
## 7. Dehydrocyclization of hydrocarbon chains:

When a six carbon atoms chain with a quaternary carbon atom is passed over a platinium catalyst at 300 °C, a six-membered ring was obtained (Equation 9.10).



**Equation 9.10**

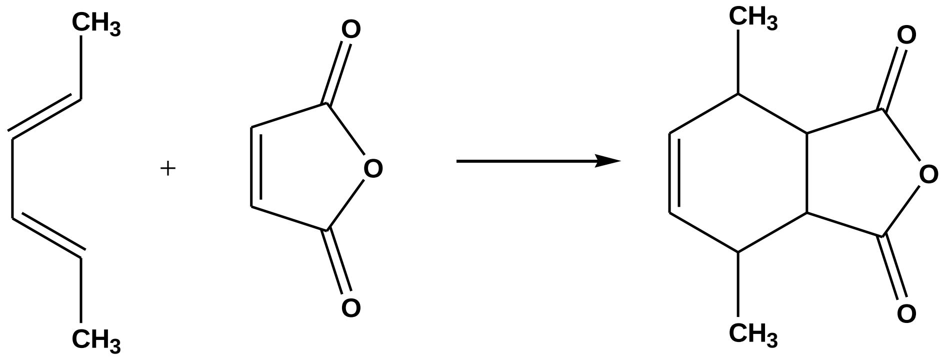
Absence of a quaternary carbon atom in the carbon chain makes the produced cyclohexane dehydrogenated to benzene (Equation 9.11).



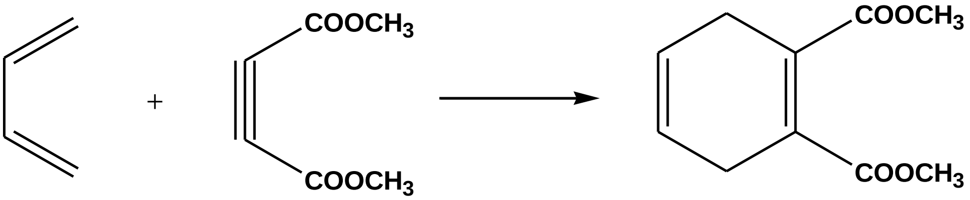
Equation 9.11

## 8. Diels-Alder reaction:

Six-membered rings with unsaturated bonds can be prepared by Diels-Alder reaction (Equations 9.12 and 9.13).



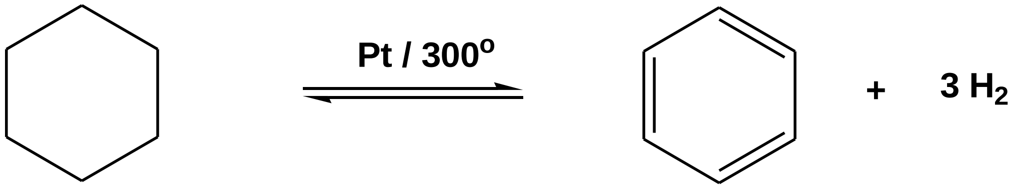
Equation 9.12



Equation 9.13

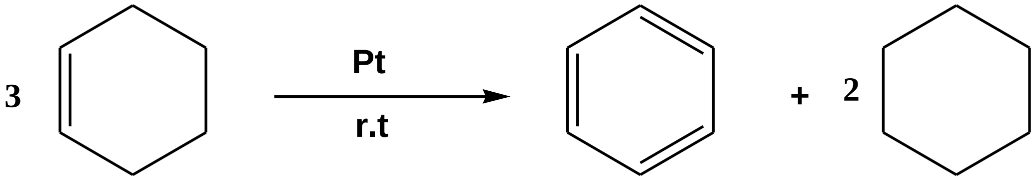
## II- Chemical reactions of cyclohexane and its derivatives:

**1. Deydrogenation reactions:** In absence of hydrogen, cyclohexane can be dehydrogenated to benzene over platinum at about 300°C (Equation 9.14).



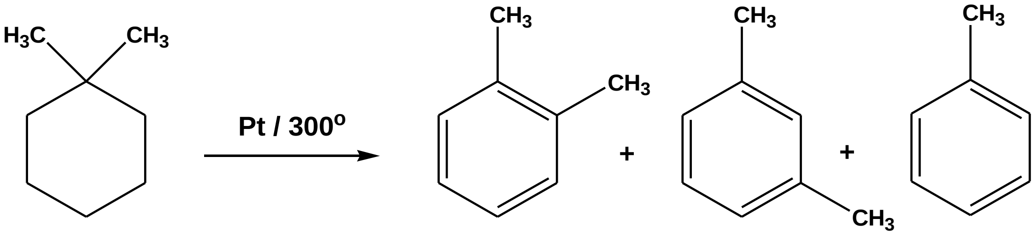
Equation 9.14

In the presence of platinum as a catalyst, cyclohexene even at room temperature disproportionate to benzene and cyclohexane as a result of an exothermic reaction (Equation 9.15).



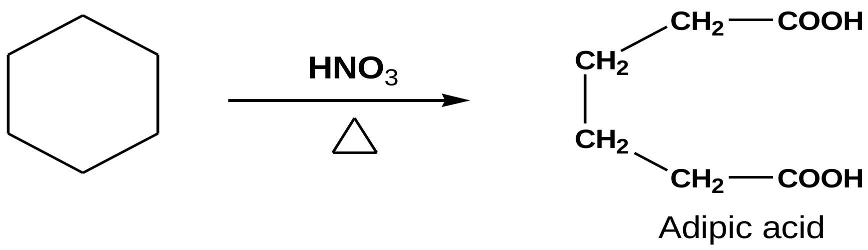
**Equation 9.15**

Dehydrogenation of 1,1-dimethylcyclohexane gives a mixture of *ortho*- and *meta*-xylenes, toluene and methane, where the dehydrogenation is accompanied by isomerization and elimination of one of the alkyl groups (Equation 9.16).



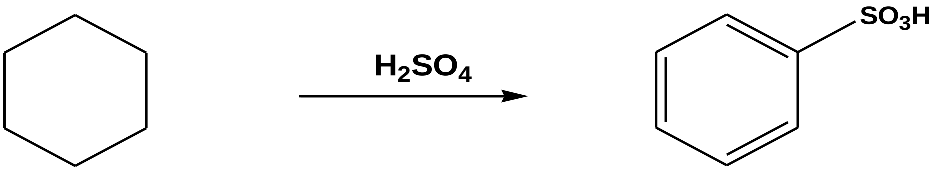
**Equation 9.16**

**2. Nitration:** in hot concentrated nitric acid, cyclohexane can be oxidized to adipic acid (Equation 9.17).



**Equation 9.17**

**3. Sulphonation:** fuming sulphuric acid converts cyclohexane into benzenesulphonic acid (Equation 9.18).

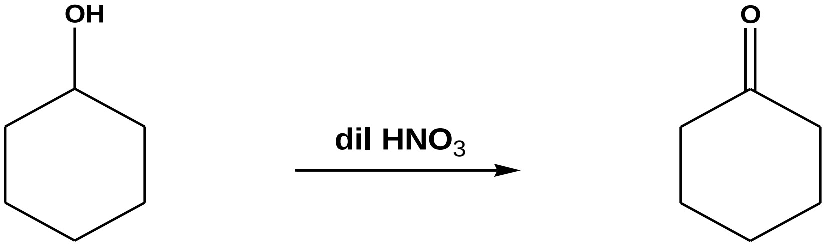


Benzenesulphonic acid

**Equation 9.18**

### 4. Cyclohexanol:

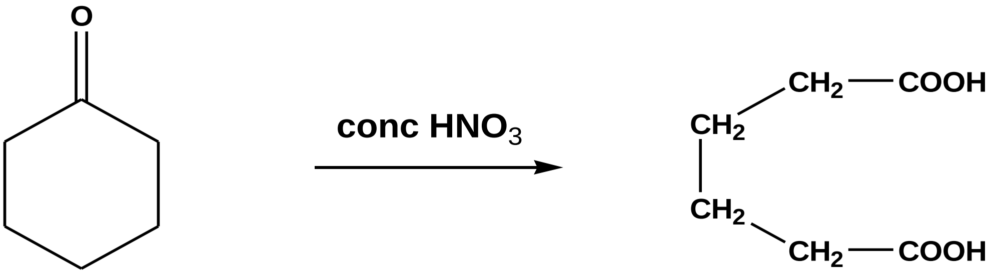
Cyclohexanol is converted by oxidation with dilute nitric acid into cyclohexanone (Equation 9.19).



**Equation 9.19**

### 5. Cyclohexanone:

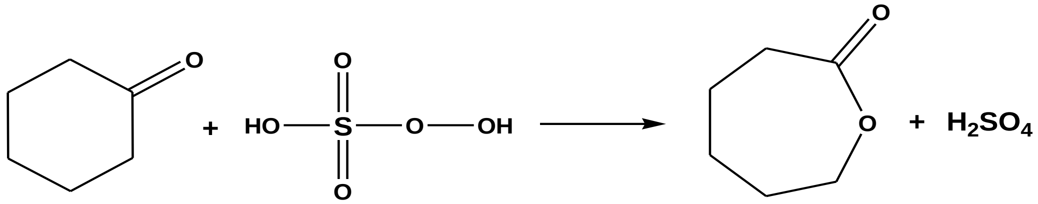
**a- Oxidation with nitric acid:** The vigorous oxidation of cyclohexanone with *conc* nitric acid produces adipic acid (Equation 9.20).



Adipic acid

**Equation 9.20**

**b- Oxidation with Caro's acid:** cyclohexanone oxidized by Caro's acid (Permonosulphuric acid) to give the caprolactone (Oxepan-2-one) (Equation 9.21).

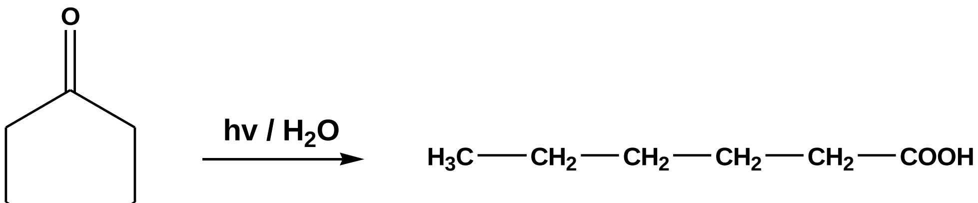


Permonosulphuric acid

Caprolactone

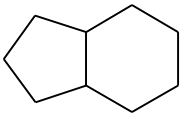
Equation 9.21

**c- The influence of light:** cyclohexanone is opened and gives caproic acid under the influence of light in presence of water (Equation 9.22).



Caproic acid

Equation 9.22



**Unit 4**

## Lesson 10: Cycloheptane and its derivatives

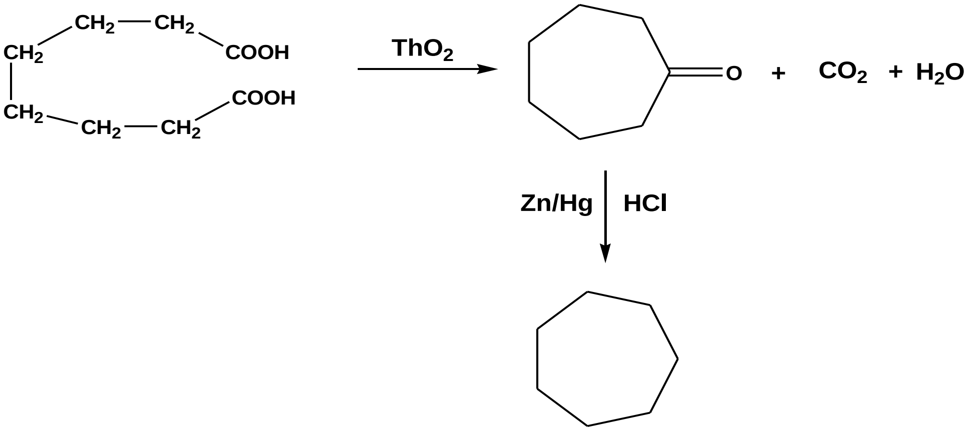
**10.1 Physical properties of cycloheptane:** $C_7H_{14}$, It is a cyclic alkane that melts at -12°C and boils at 118°C. Cycloheptane is found naturally in petroleum.

### 10.2 Chemical properties:

### I- Methods of preparation:

The following methods are suitable for preparation of cycloheptane and its derivatives as follows:

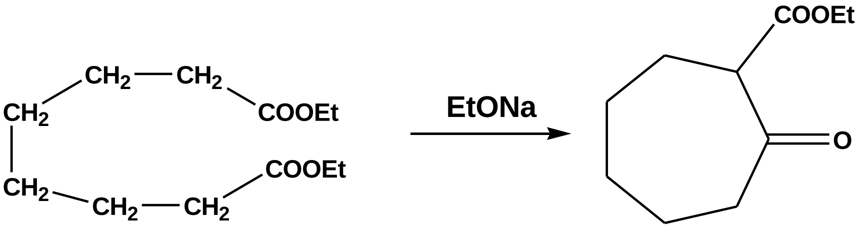
**1. Pyrolysis of dibasic acids:**
Pyrolysis of suberic acid over $\mathbf{ThO_2}$ gives cycloheptanone, which turns to cycloheptane by Clemmenson reduction (Equation 10.1).



**Equation 10.1**

## 2. Dieckmann condensation:

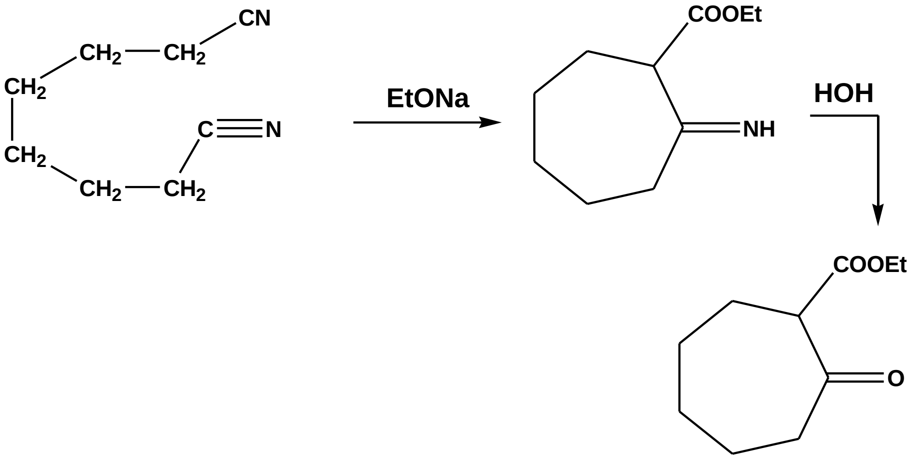
Ester condensation of octanedioic acid diethyl ester in a basic medium (sodium ethoxide) affords 2-cycloheptanonecarboxylic acid ethyl ester (Equation 10.2).



**Equation 10.2**

## 3. Thorpe reaction:

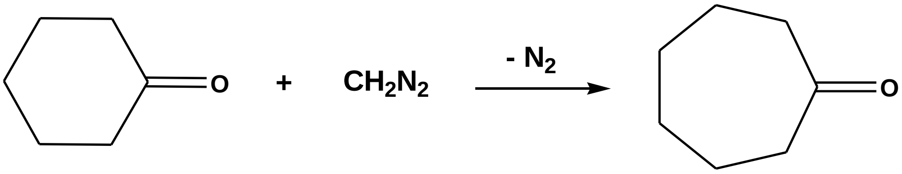
Condensation of octanedinitrile in presence of sodium ethoxide followed by hydrolysis affords 2-cycloheptanonecarbonitrile (Equation 10.3).



Equation 10.3

## 4. Action of diazomethane:

Suberone (cycloheptanone) can be prepared by the action of diazomethane on cyclohexanone in light, which an extension of six-membered ring to seven-membered one occurred (show the mechanism of this reaction in page (86)) (Equation 10.4).



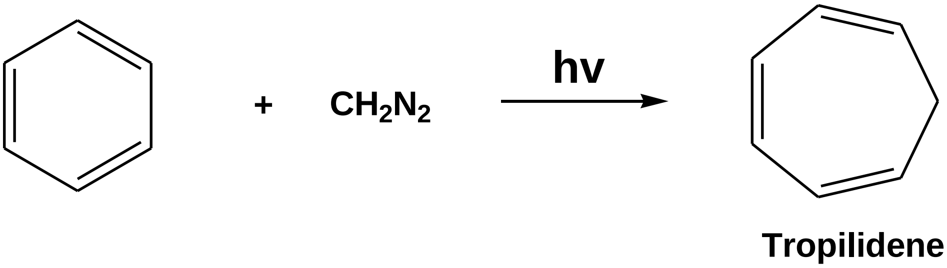
Equation 10.4

## 5. Synthesis of tropilidene:

Tropilidene (1,3,5-cycloheptatriene) may be prepared by two methods as follows:

### a- Ring expansion of benzene:

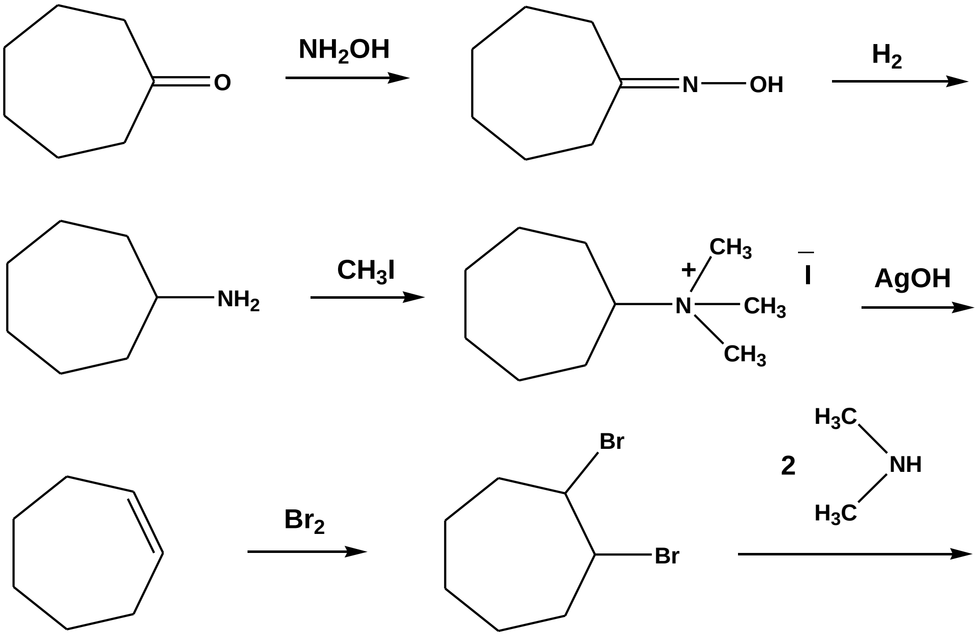
Pyrolysis of diazomethane in presence of benzene undergoes ring expansion to give the tropilidene ring (Equation 10.5).

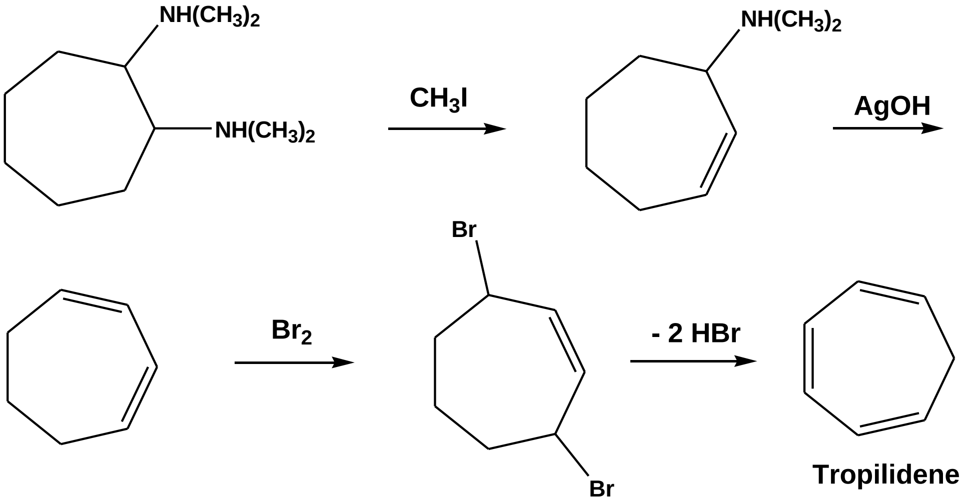


Equation 10.5

**b- From cycloheptanone:**

Willstattler used cycloheptanone as starting material to prepare tropilidene according to the following (Scheme 10.6):





Scheme 10.6

Unit 4

## Lesson 11: Alicyclic compounds with two or more Rings

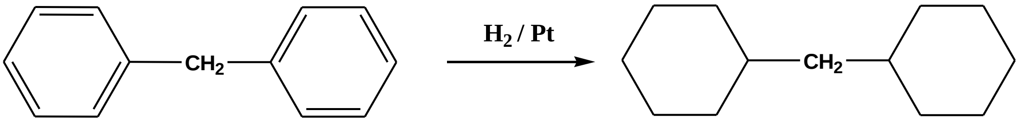
### 11.1 Bicyclic compounds with isolated rings.

- **Methods of preparation:**

The following methods are suitable for the preparation of this type of alicyclic compounds:

**1- Hydrogenation:**

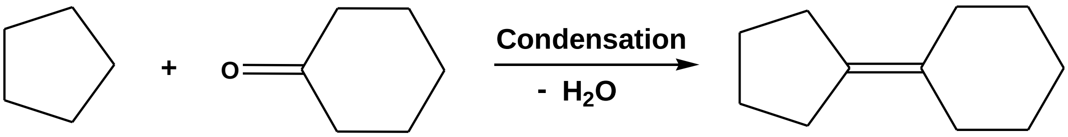
In presence of platinum as a catalyst, hydrogenation of certain aromatic compounds gave the corresponding bicyclic rings (Equation 11.1).



Equation 11.1

**2- Condensation of cyclic aldehydes or ketones:**

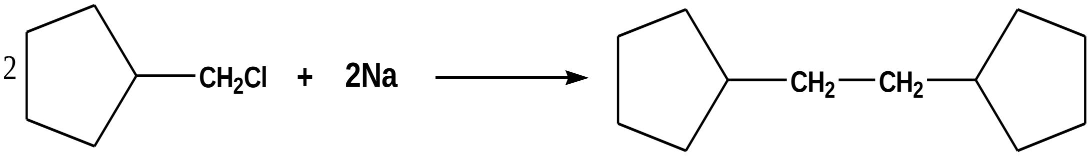
Cyclohexanone and cyclopentane may be condenses to give the cyclopentylidene-cyclohexane (Equation 11.2).



Equation 11.2

## 3- Wurtz reaction:

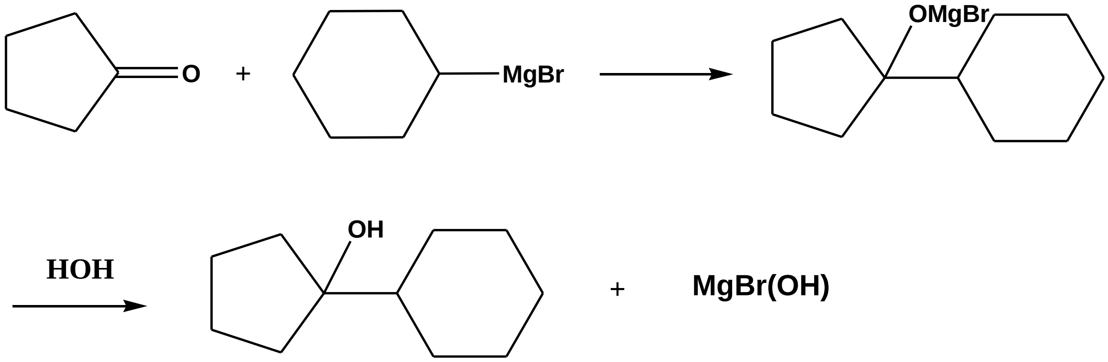
According to Wurtz reaction, the treatment of the chloromethyl-cyclopentane with sodium metal can give 1,2-dicyclopentyl-ethane (Equation 11.3).



Equation 11.3

## 4- By using organomagnesium compounds:

When cyclohexyl magnesium bromide treated with cyclopentanone, 1-cyclohexyl-cyclopentanol was obtained (Equation 11.4).

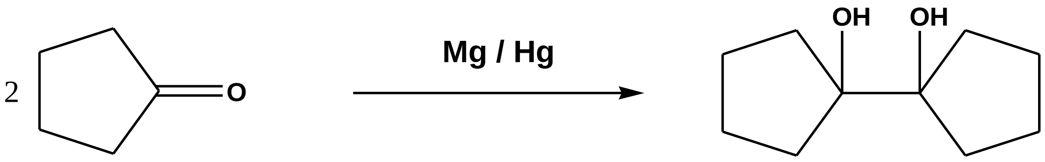


1-cyclohexyl-cyclopentanol

Equation 11.4

## 5- Reduction of cyclic ketones:

Cyclopentanone can be reduced by magnesium amalgam to give bicyclopentyl-1,1`-diol (Equation 11.5).



**bicyclopentyl-1,1'-diol**

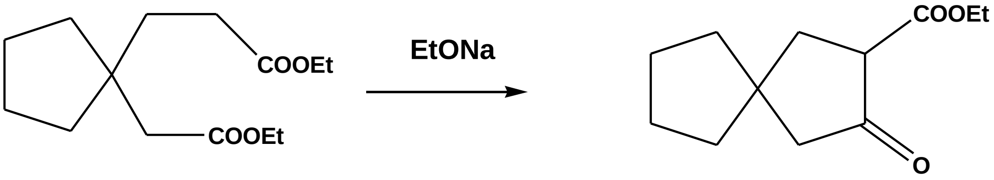
Equation 11.5

## 11.2 Spirans

Spirans are bicyclic structures in which two rings systems share one carbon atom.

Spirans can be prepared by ordinary methods of cyclization as the following examples:

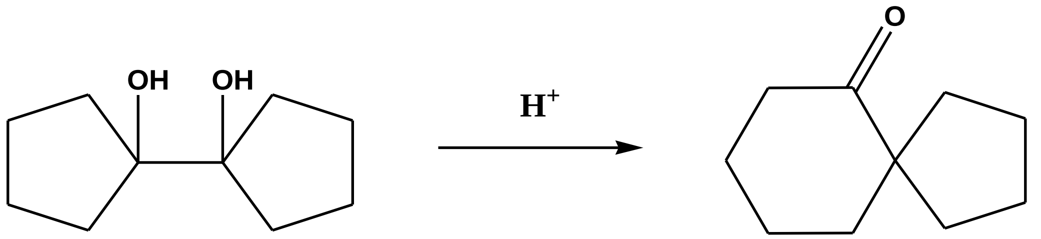
**Example 1:** (Equation 11.6).



**3-Oxo-spiro[4.4]nonane-2-carboxylic acid ethyl ester**

Equation 11.6

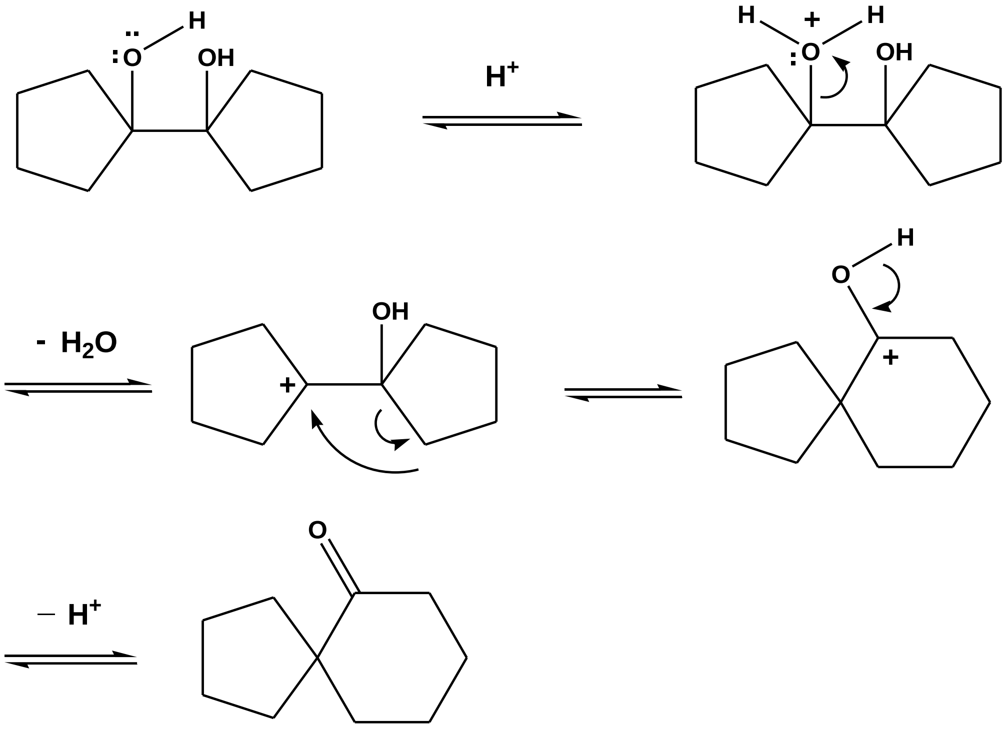
**Example 2:** Extension of the rings of certain bicyclic compounds (Equation 11.7).



**Spiro[4.5]decan-6-one**

**Equation 11.7**

**The reaction mechanism;**



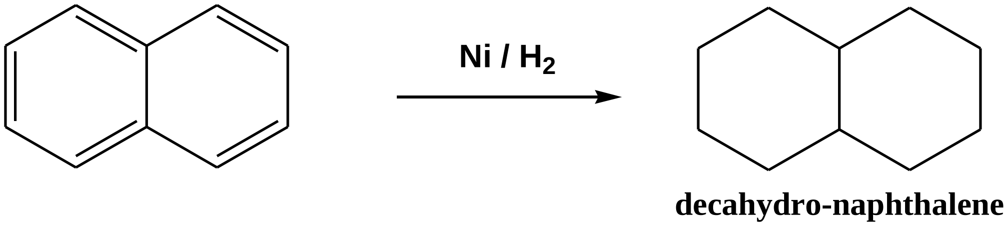
## 11.3 Alicyclic compounds with fused rings

- **Methods of synthesis:**

There are many methods used for the preparation of alicyclic fused-ring compounds as follows:

**1- Catalytic hydrogenation of condensed aromatic system:**

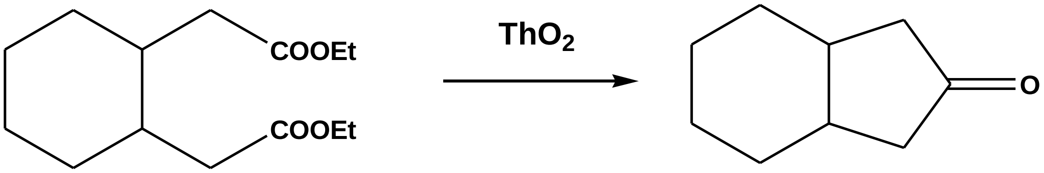
Catalytic hydrogenation of naphthalene, anthracene or phananthrene can give fused rings (Equation 11.8).



Equation 11.8

**2- Cyclization of a compound containing one ring:**

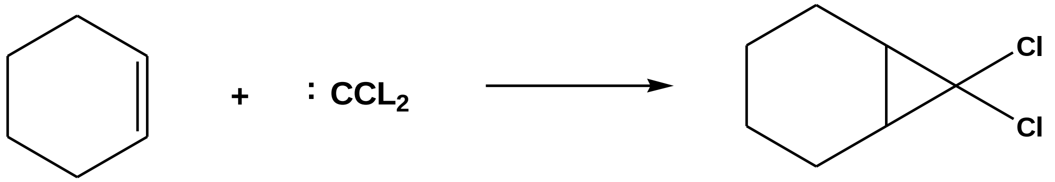
Treatment of 1,2-diethoxycarbonylmethyl-cyclohexane with thorium oxide (**$ThO_2$**) gives octahydro-inden-2-one (Equation 11.9).



Equation 11.9

**3- Addition of carbenes to unsaturated monocyclic compounds:**

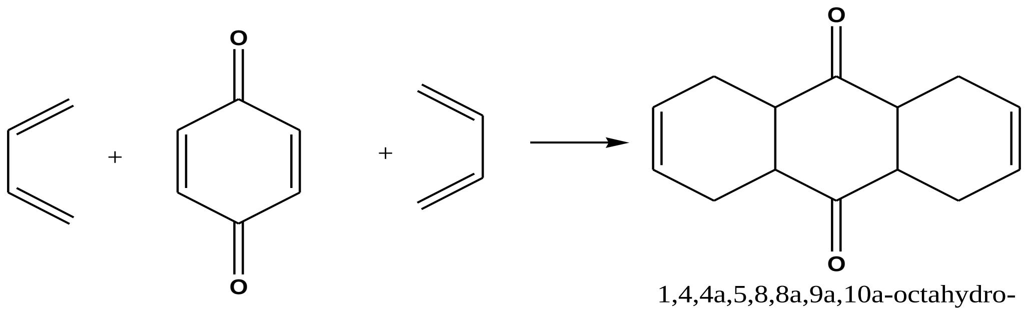
Cyclohexene reacts with carbenes to give bicyclo[4.1.0]heptane (Equation 11.10).



Equation 11.10

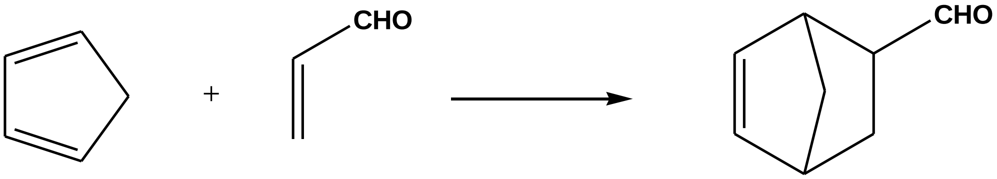
## 4- Diels-Alder reaction:

Diene reacts with dienophile to give the adduct as follows (Equations 11.11 – 11.13).



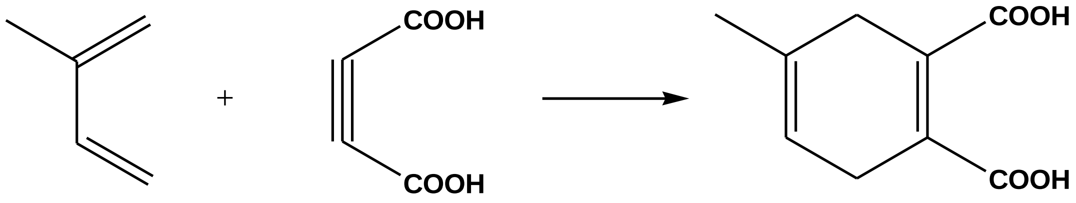
1,4,4a,5,8,8a,9a,10a-octahydro-anthraquinone

Equation 11.11



bicyclo[2.2.1]hept-5-ene-2-carbaldehyde

Equation 11.12



4-methyl-cyclohexa-1,4-diene
-1,2-dicarboxylic acid

**Equation 11.13**

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Liu, and Jie Tang *J. Am. Chem. Soc.*; 2006; 128(23) p. 7430 - 7431; doi:10.1021/ja061749y.

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**Hyperlinks**

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- http://www.chem.qmul.ac.uk/iupac/hetero/De.html
- http://people.ok.ubc.ca/wsmcneil/121/conformers.htm
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- http://www.sparknotes.com/chemistry/organic2/conformations/section1.html
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# Spectra II

# ($^1$H-NMR-Mas Spectrometry)

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كلية العلوم

قسم الكيمياء

# 2023/2022

- Faculty of Science
- Third Year
- Second Semester
- Chemistry Program

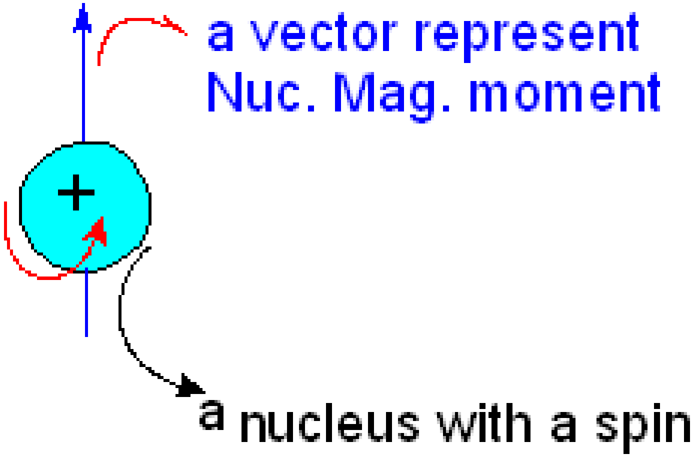
# Nuclear Magnetic Resonance (NMR) Spectroscopy

# NMR: Based on absorption of *Radio waves* of certain nuclei in strong Magnetic Field

Origin:

- Some atoms nuclei have no spin ($^{12}C$, $^{16}O$).
- Some other nuclei have spin($^{1}H$,$^{13}C$,$^{19}F$).

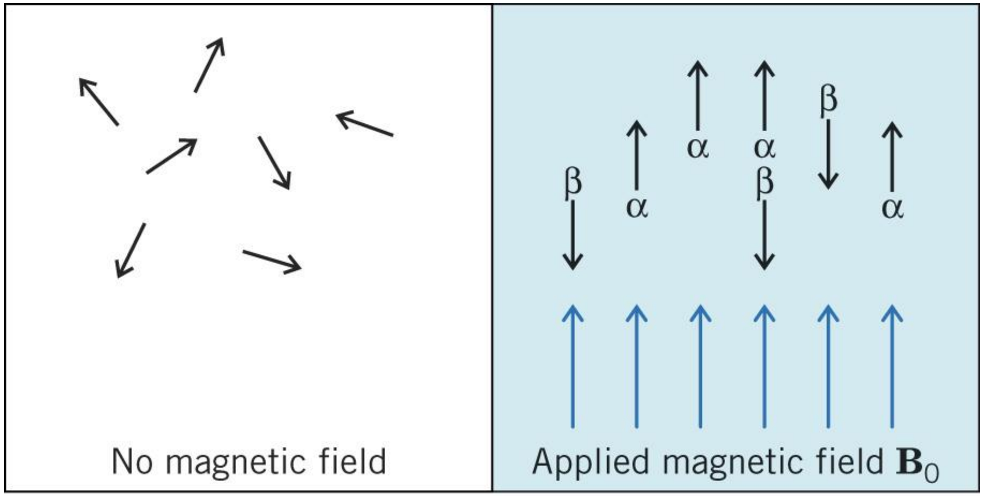
  These produce a small magnetic field = nuclear magnetic moment



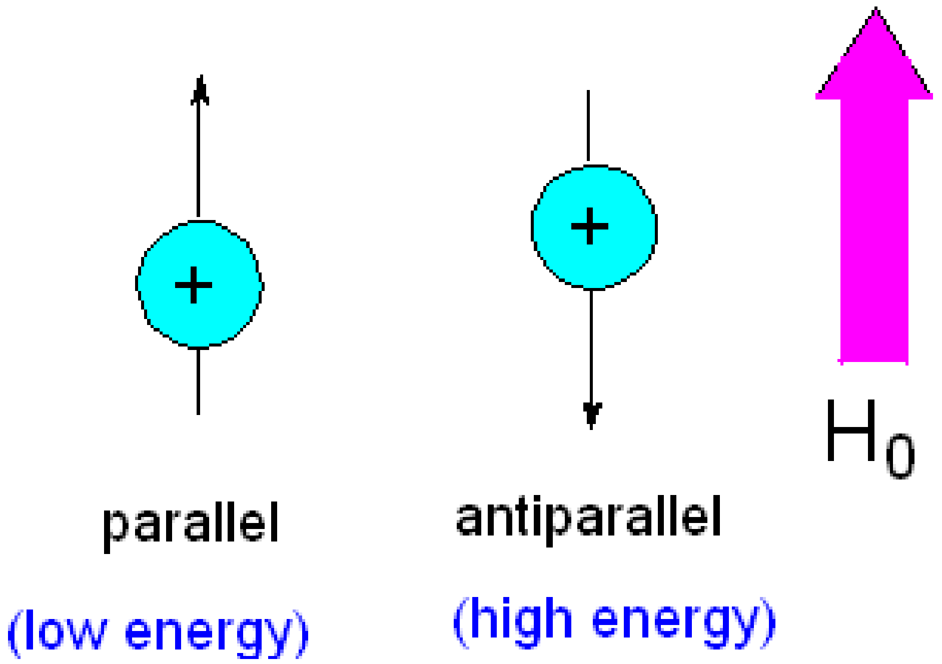
- In NMR spectroscopy an external magnetic field generated by a permanent magnet is used.
- The strength of the field is symbolized by $H_0$ (units= gauss)

# $^1$H or Proton NMR Spectra

When molecules containing hydrogen atoms are placed in an external magnetic field ; the magnetic moment of each proton nucleus aligns itself in one of two different orientations:

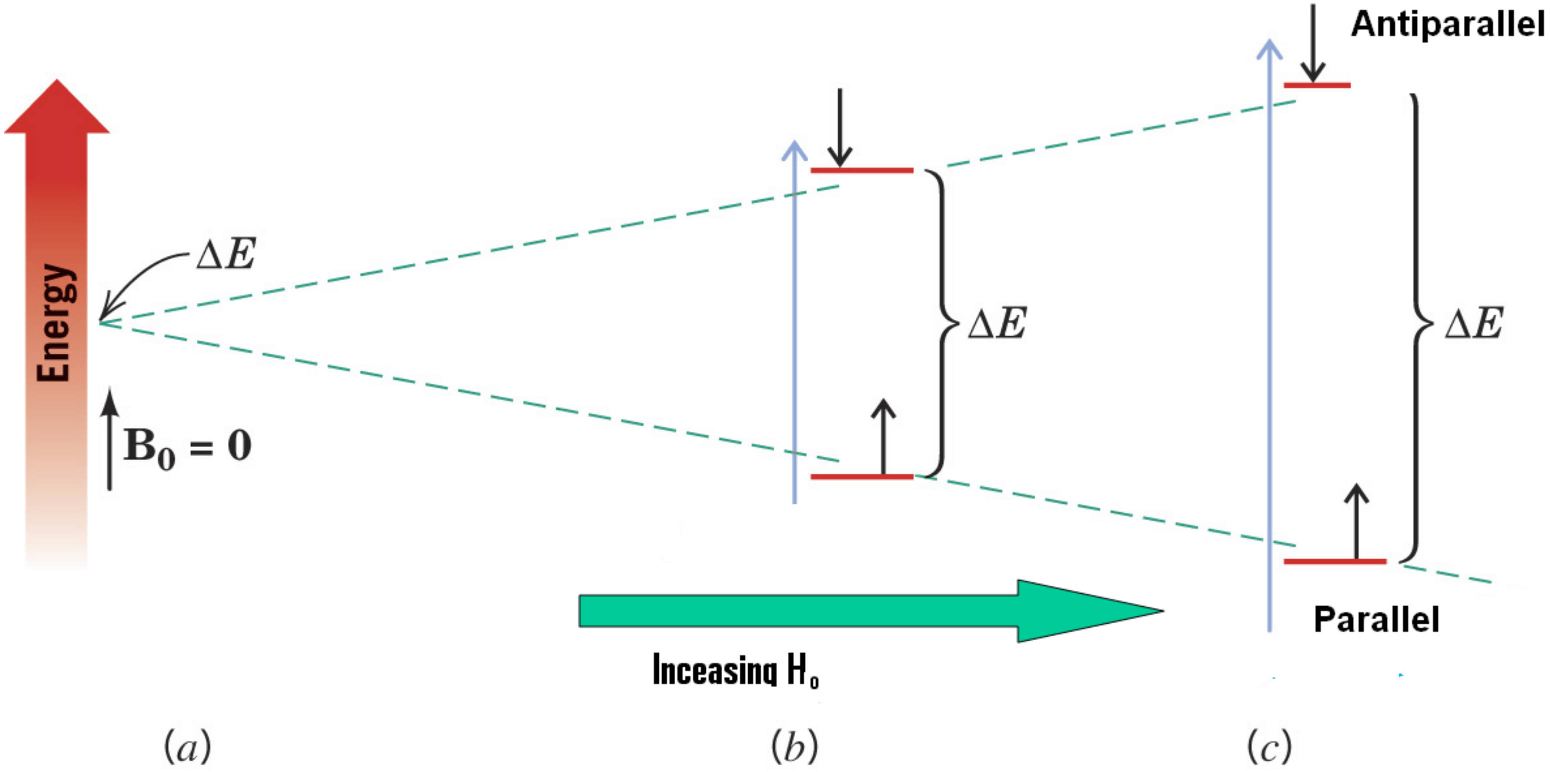


(a) (b)



- The parallel protons absorb energy (radio waves) and the magnetic moment turn around (flip) to the high energy antiparallel state (Resonance)

- The amount of energy required to flip the magnetic moment depends on the strength of the applied magnetic field $H_0$



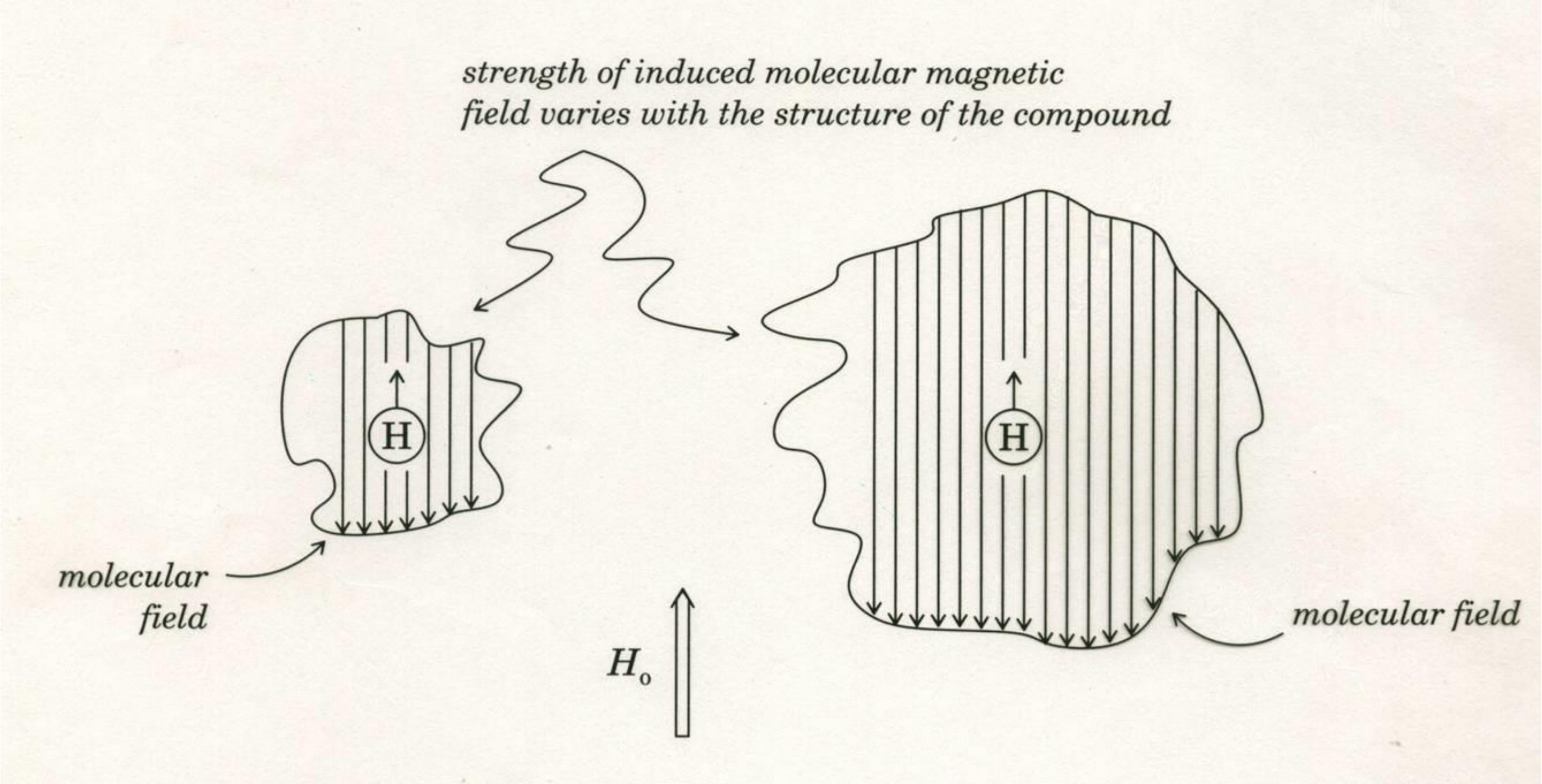
- Energy difference between parallel and antiparallel states increases with the strength of the external field $H_{0.}$

- The magnetic field observed by a proton is a combination of 2 fields

1- $H_0$ external

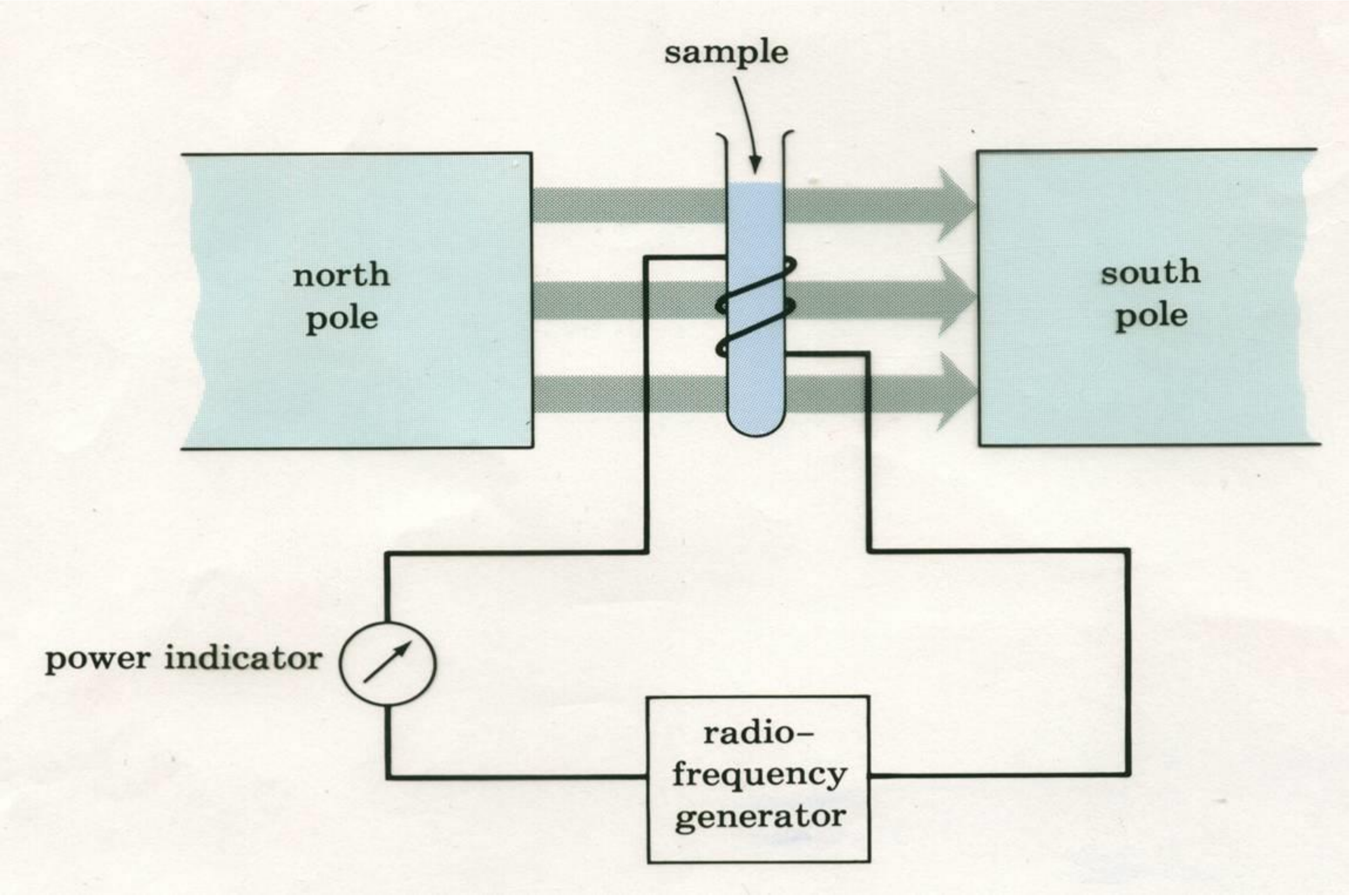
2- Induced molecular magnetic field

# Field Effects

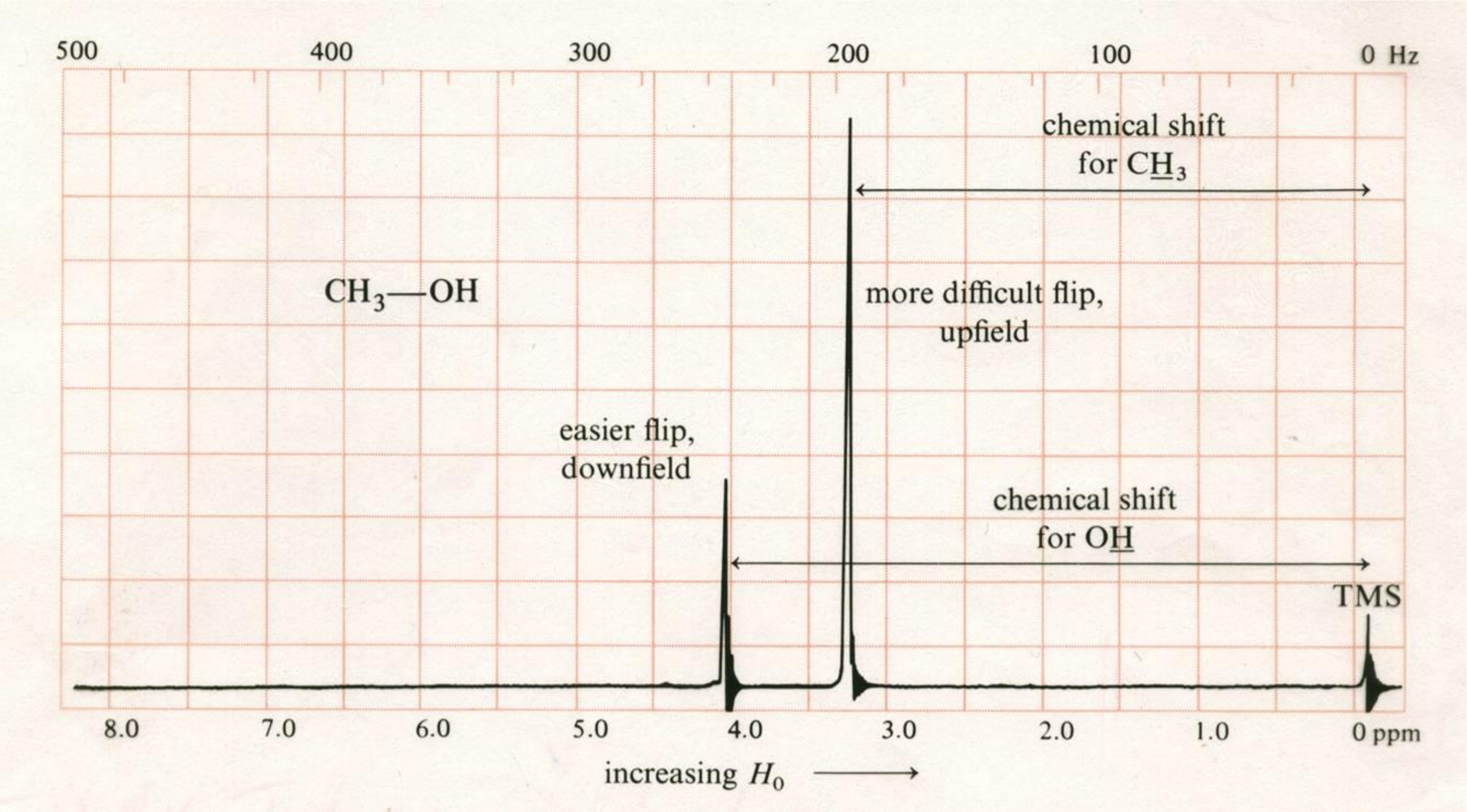


- Different protons in an organic compound are surrounded by molecular field of different strength ➔It takes stronger or weaker Ho to overcome the molecular fields
- Different protons come into resolution at different position in the spectrum.

# NMR spectrometer



# The NMR Spectrum



- The spectrum is measured on a delta (δ) scale in units of parts per million (ppm)
- Lower frequency is to the left in the spectrum; these absorptions are said to be downfield
- Higher frequency is to the right in the spectrum: these absorptions are said to be upfield
- The small signal at δ 0 corresponds to an internal standard called tetramethylsilane (TMS) used to calibrate the chemical shift scale
- The number of signals in the spectrum corresponds to the number of unique sets of protons

- Chemical shifts are measured in relation to the internal reference tetramethylsilane (TMS)
  - The protons of TMS are highly shielded because of the strong electron donating capability of silicon

- The $\delta$ scale for chemical shifts is independent of the magnetic field strength of the instrument (whereas the absolute frequency depends on field strength)

$$\delta = \frac{(\text{observed shift from TMS in hertz}) \times 10^6}{(\text{operating frequency of the instrument in hertz})}$$

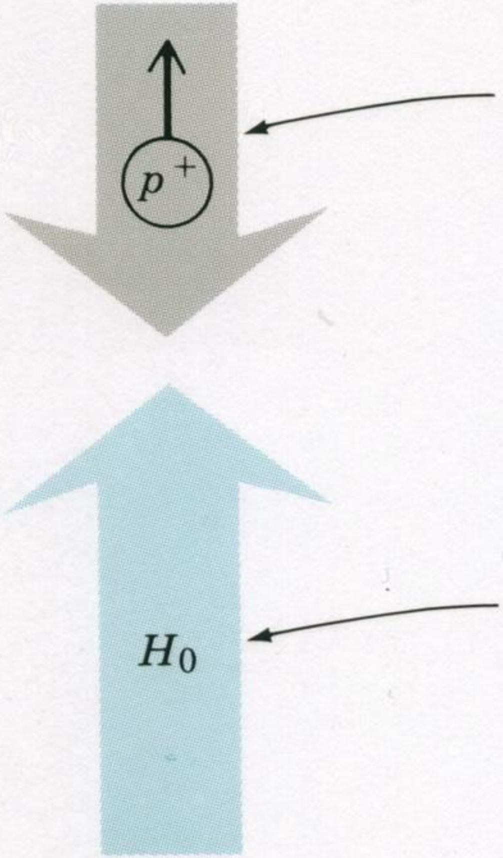
- Thus, the chemical shift in δ units for protons on benzene is the same whether a 60 MHz or 300 MHz instrument is used

$$\delta = \frac{2181\ \text{Hz} \times 10^6}{300 \times 10^6\ \text{Hz}} = 7.27$$

$$\delta = \frac{436\ \text{Hz} \times 10^6}{60 \times 10^6\ \text{Hz}} = 7.27$$

- Shielding and Deshielding of Protons
  - Protons in an external magnetic field absorb at different frequencies depending on the electron density around that proton
  - High electron density around a nucleus *shields* the nucleus from the external magnetic field
    - Shielding causes absorption of energy at higher frequencies (more energy is required for this nucleus to flip between spin states) - the signals are upfield in the NMR spectrum
  - Lower electron density around a nucleus *deshields* the nucleus from the external magnetic field
    - Deshielding causes absorption of energy at lower frequencies (less energy is required for this nucleus to flip between spin states) - the signals are downfield in the NMR spectrum

Induced molecular fields oppose $H_o$

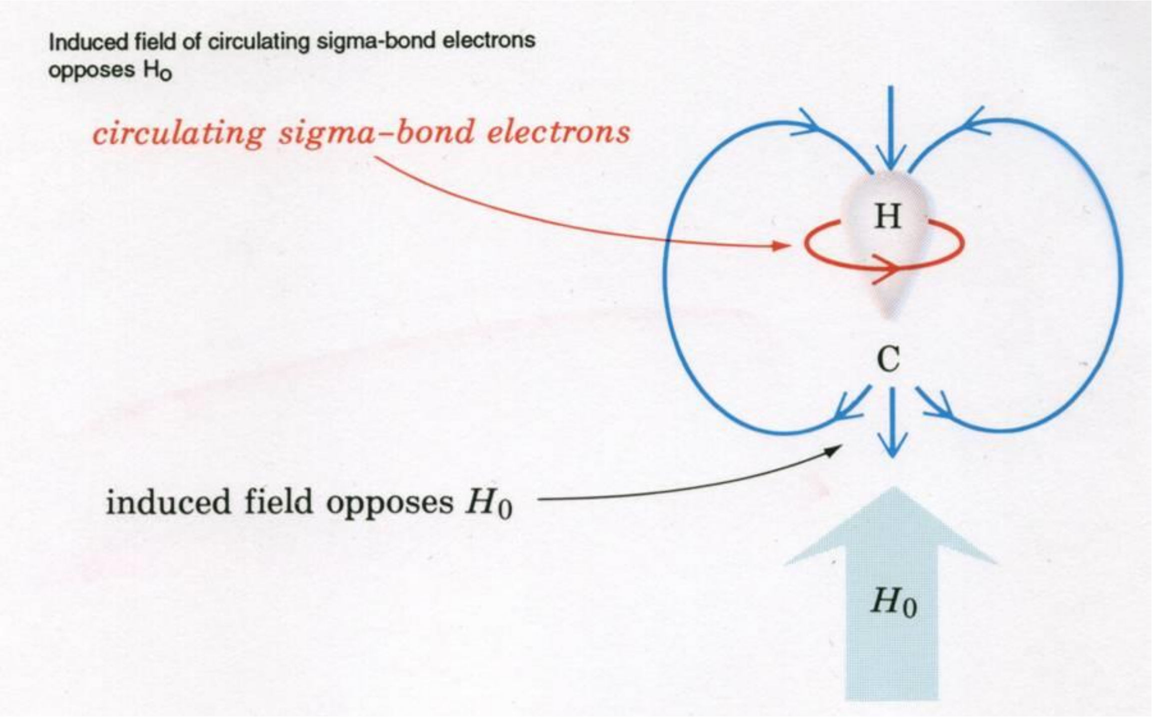


*The stronger the induced molecular field,*

*the greater must be $H_0$ to bring the proton to resonance.*

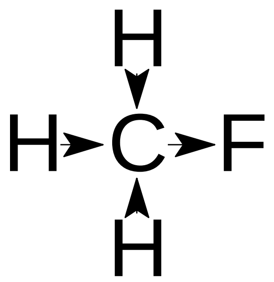
# Fields induced by sigma bonds

- The induced field from circulating sigma bond electrons opposes $H_o$ in the vicinity of proton



Induced field of circulating sigma-bond electrons opposes $H_o$

- A proton that is bonded to the same carbon as an electronegative atom is more deshielded than proton on other carbons. (Inductive Effect)



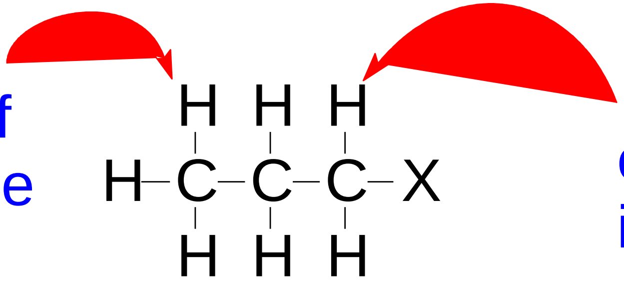
F causes a decrease in e density around each atom

| $H_3C-F$ | $H_3C-Cl$ | $H_3C-Br$ | $H_3C-I$ |
|---|---|---|---|
| δ 4.3 | δ 3.0 | δ 2.7 | δ 2.1 |

Increased shielding of H

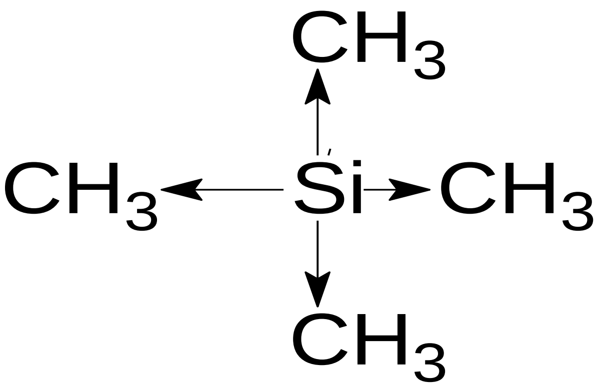
# The inductive effect

effect of X is of little importance in decreasing e density around this proton



$\mathrm{H-\underset{H}{\overset{H}{C}}-\underset{H}{\overset{H}{C}}-\underset{H}{\overset{H}{C}}-X}$

effect of X is important in decreasing e density around this proton



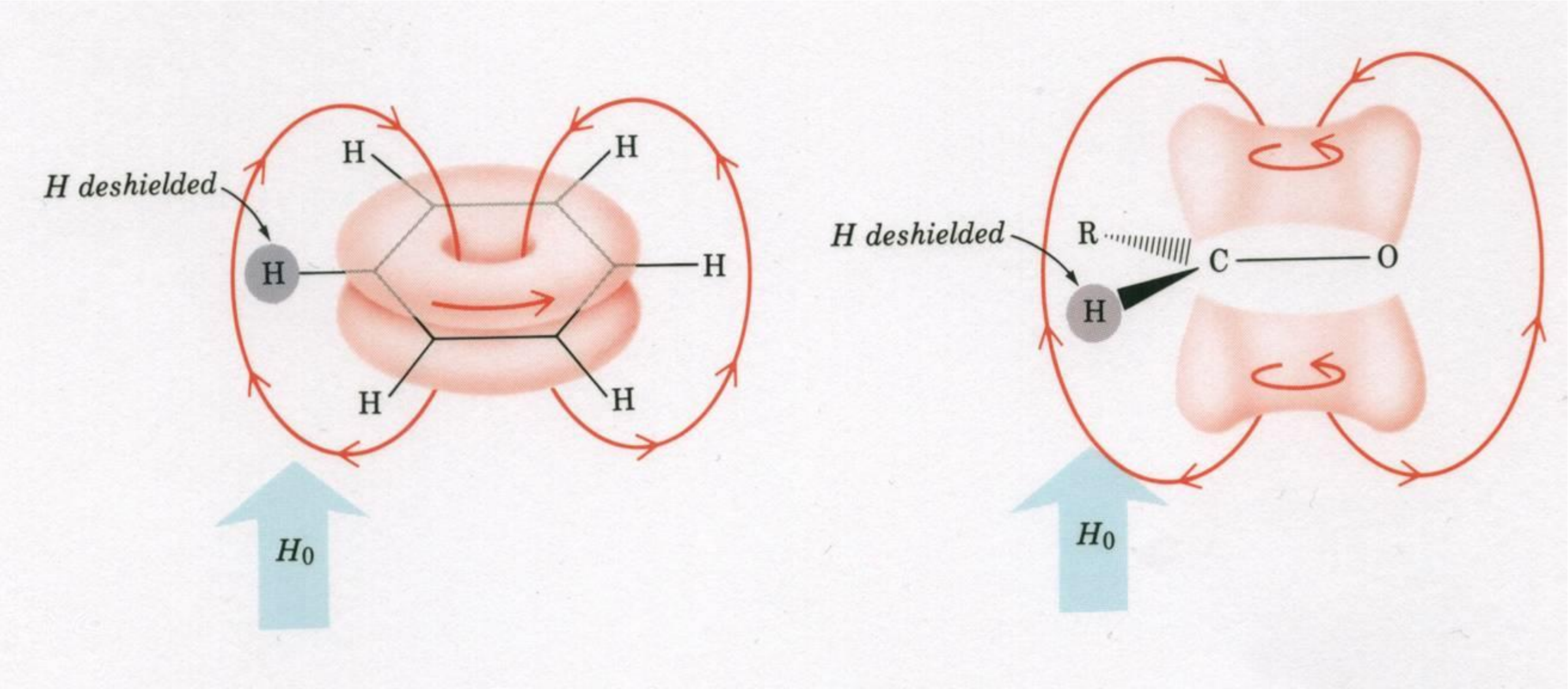
$\mathrm{CH_3 \leftarrow \underset{\downarrow\,CH_3}{\overset{CH_3\,\uparrow}{Si}} \rightarrow CH_3}$

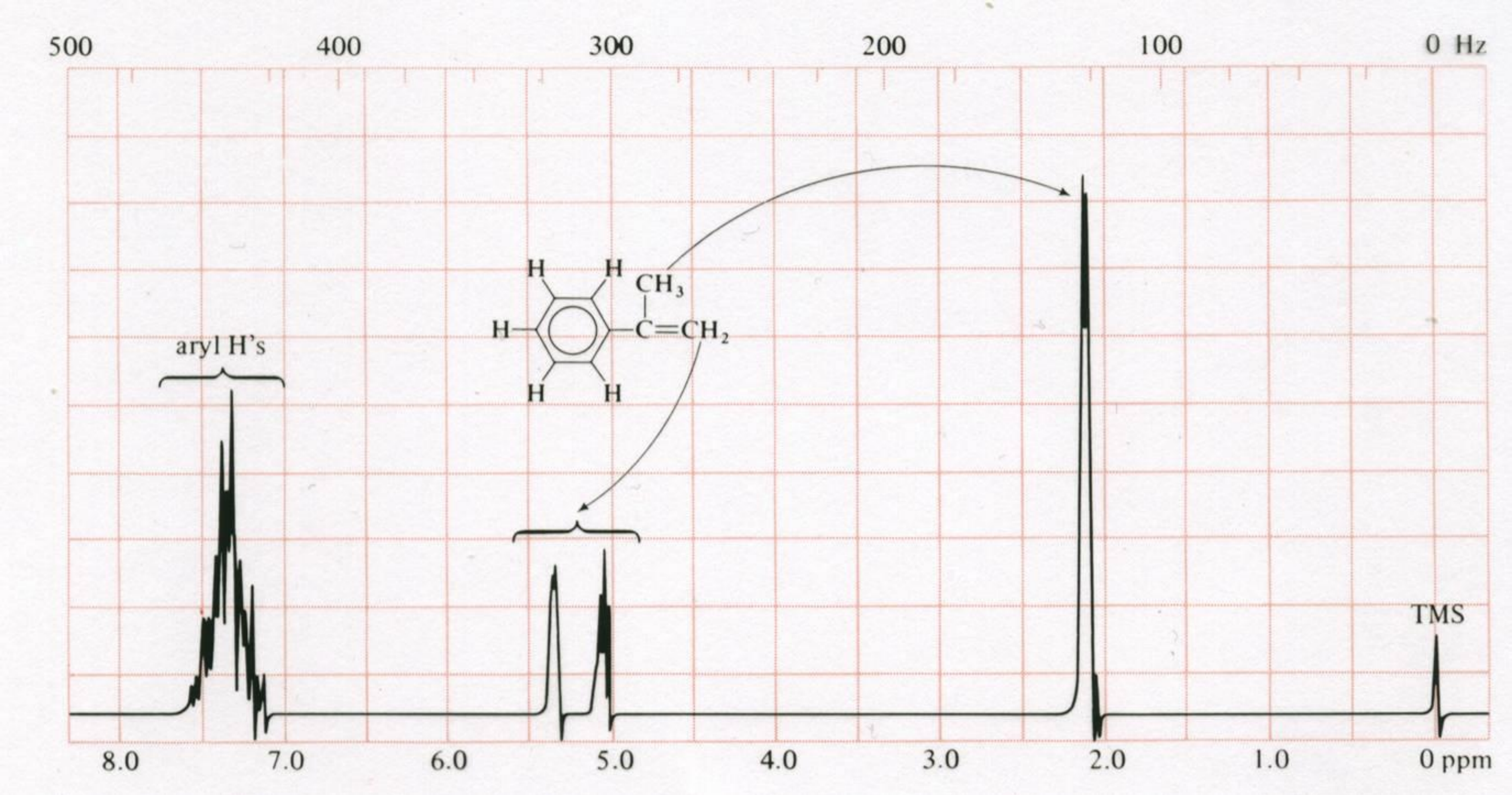
greater e density on H: highly shielded

Tetramethylsilane(TMS)

# Fields induced by pi electrons

- Circulating pi electrons in benzene and aldehydes induce a magnetic field that deshield the adjacent protons.




500
400
300
200
100
0 Hz
aryl H's
H
H
CH3
H
C=CH2
H
H
TMS
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0 ppm

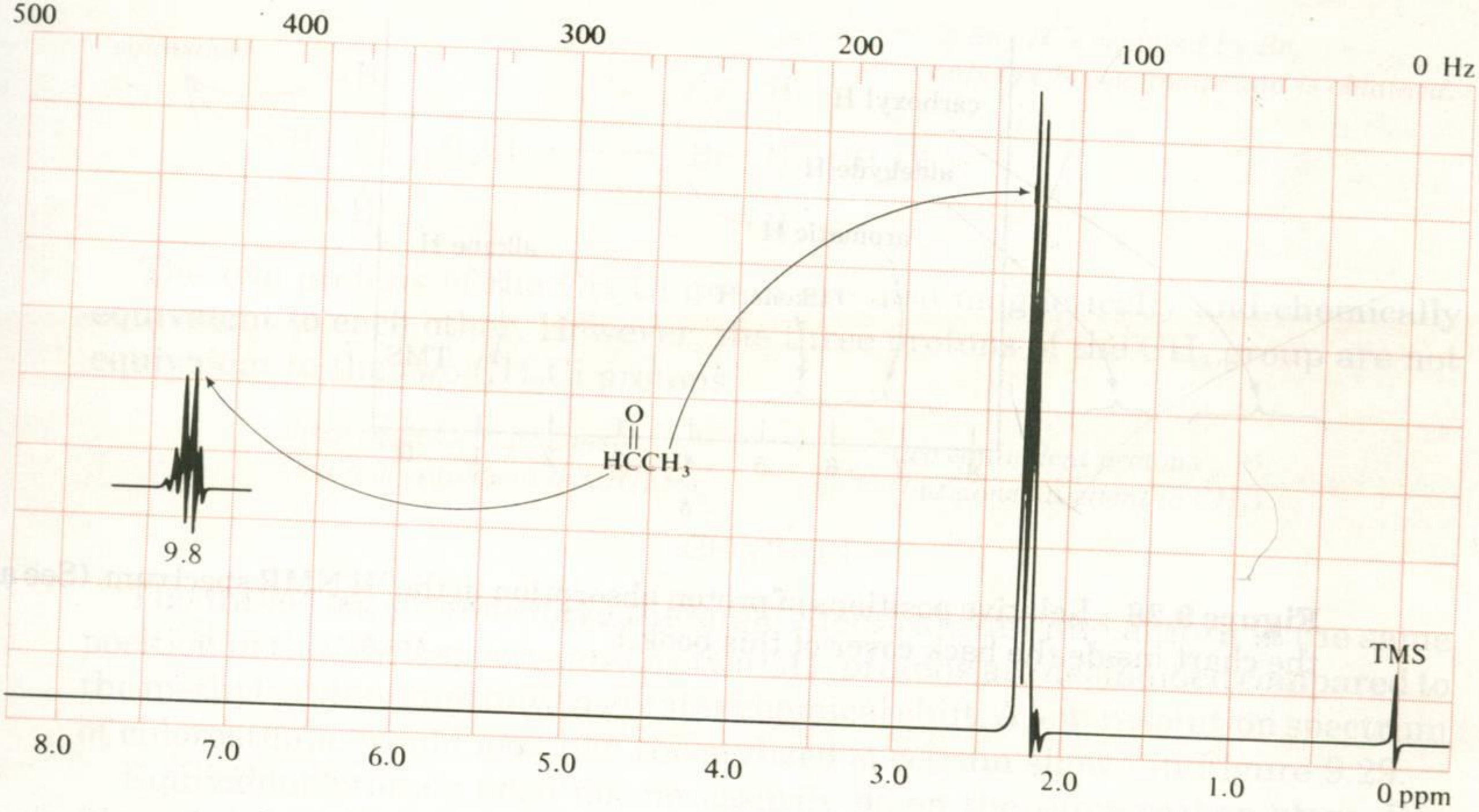
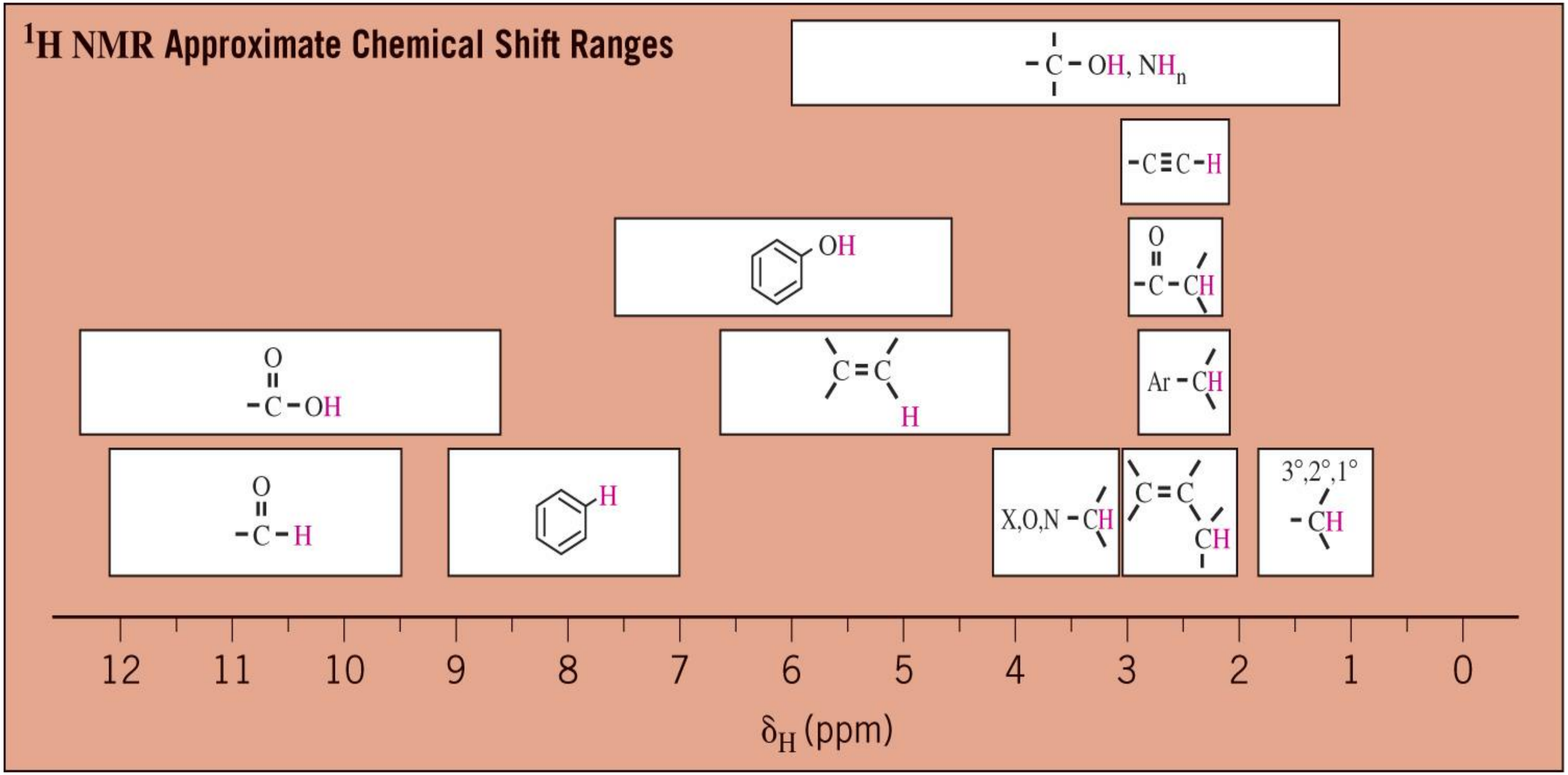
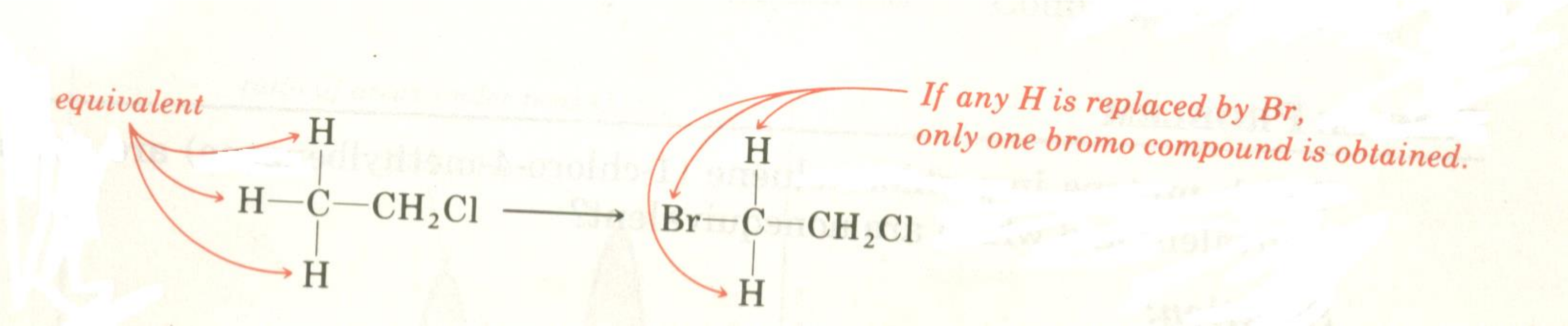


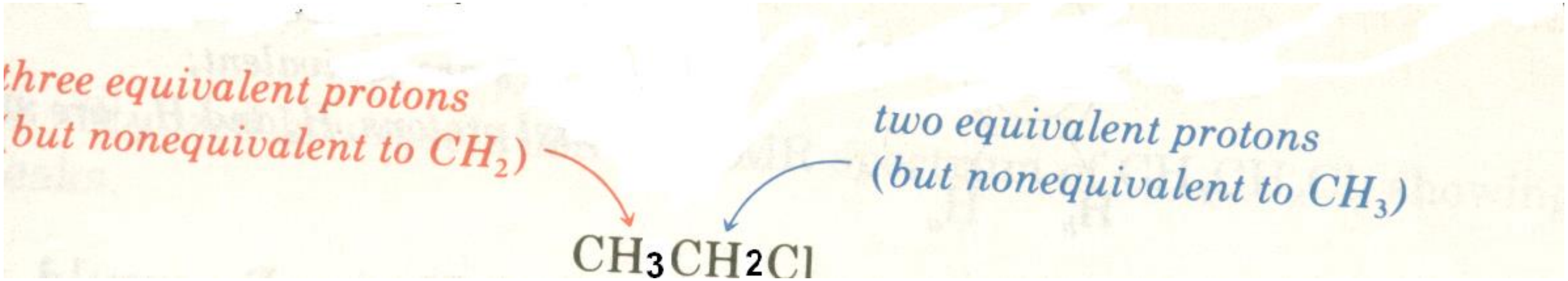
Figure 9.27 $^1$H NMR

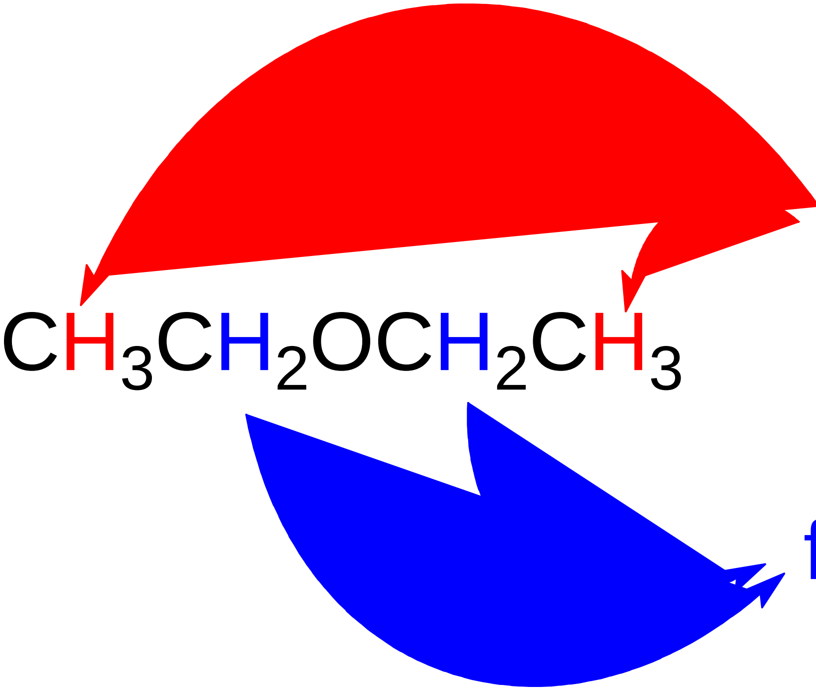
# Summary of induced field effects



# Equivalent and nonequivalent protons



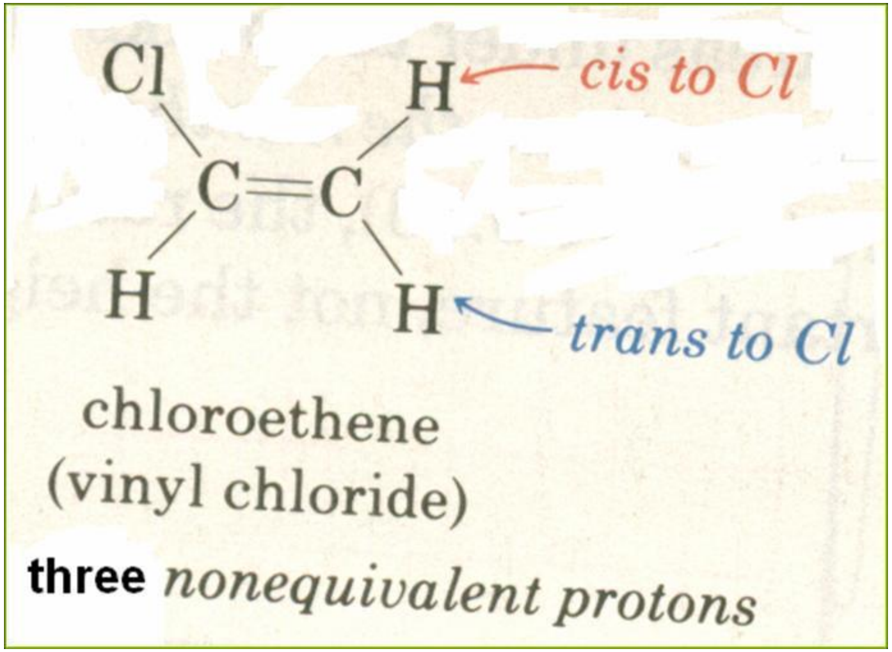




$CH_3CH_2OCH_2CH_3$

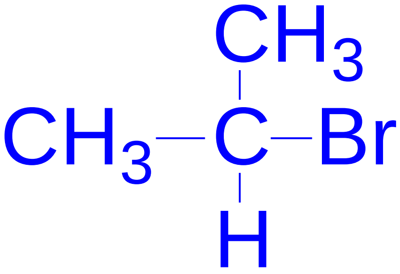
six equivalent protons

four equivalent protons



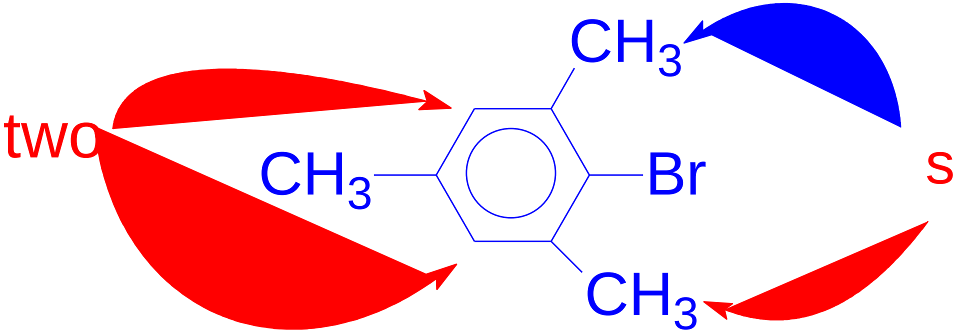
chloroethene
(vinyl chloride)

**three** *nonequivalent protons*



$CH_3-\underset{H}{\overset{CH_3}{C}}-Br$

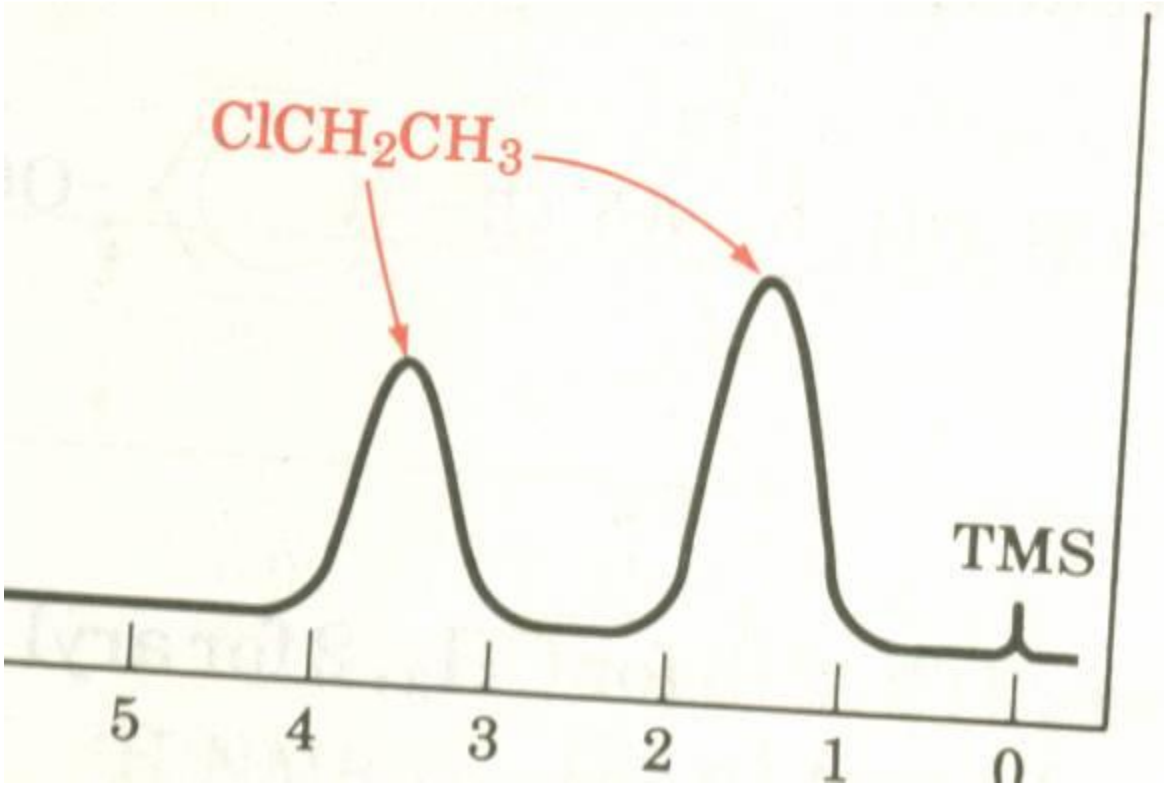
six equivalent protons



two

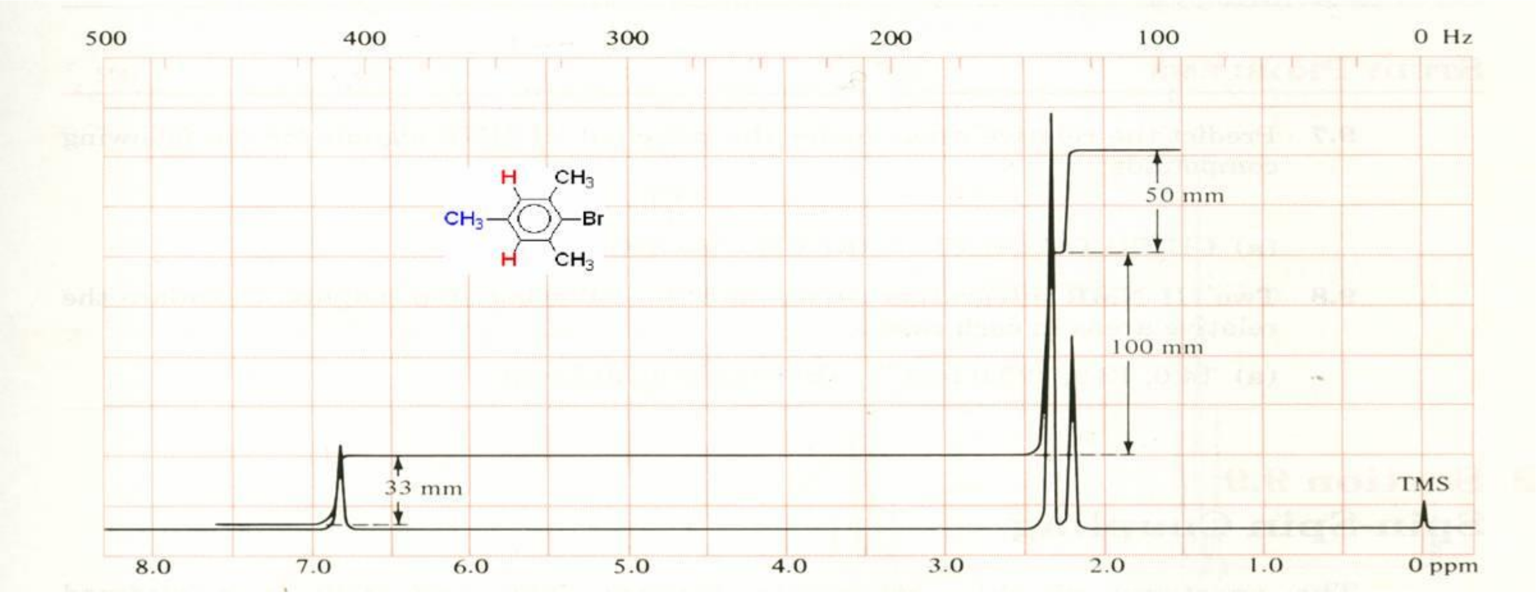
six equivalent protons

# Proton NMR spectra of $CH_3CH_2Cl$



# Integration of Peak Areas. The Integral Curve

- The area under each signal corresponds to the relative number of hydrogen atoms in each unique environment within a molecule
  - The height of each step in the integral curve is proportional to the area of the signal underneath the step



# Calculation of relative Hydrogen

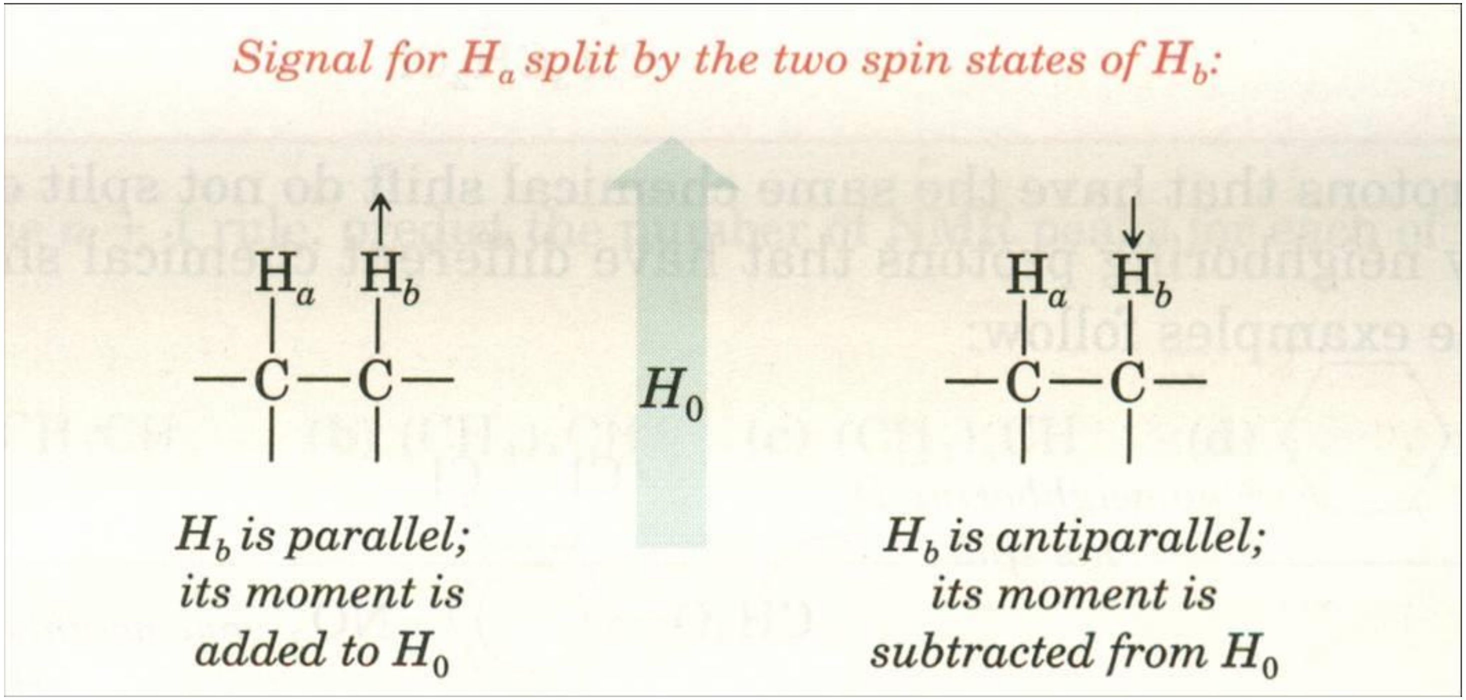
$$\frac{33\text{mm}}{33\text{mm}} : \frac{100\text{mm}}{33\text{mm}} : \frac{50\text{mm}}{33\text{mm}}$$

1 : 3 : 1.5

2 H : 6 H : 3 H

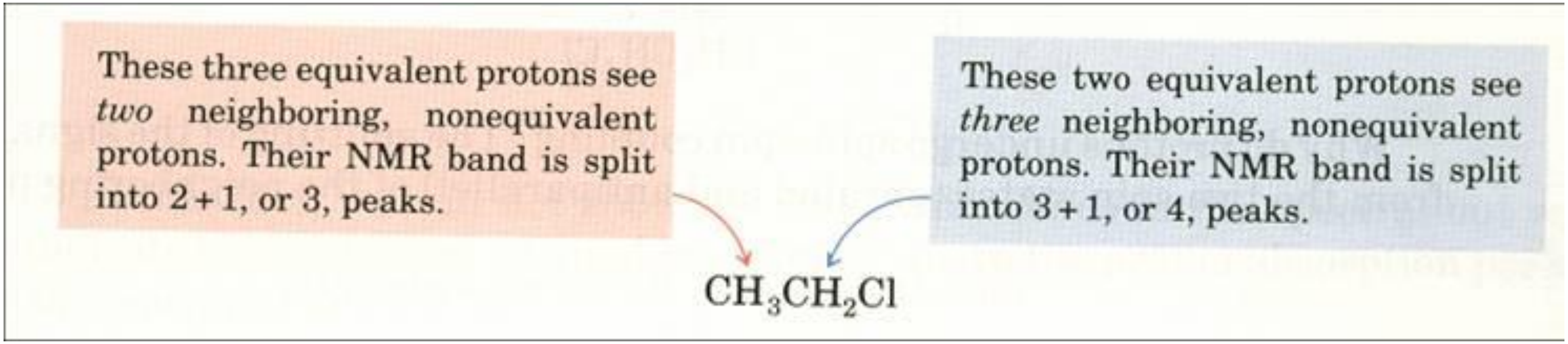
# Spin-spin coupling

- Protons that split each other signals are said to have undergone spin-spin coupling



# n+1 Rule

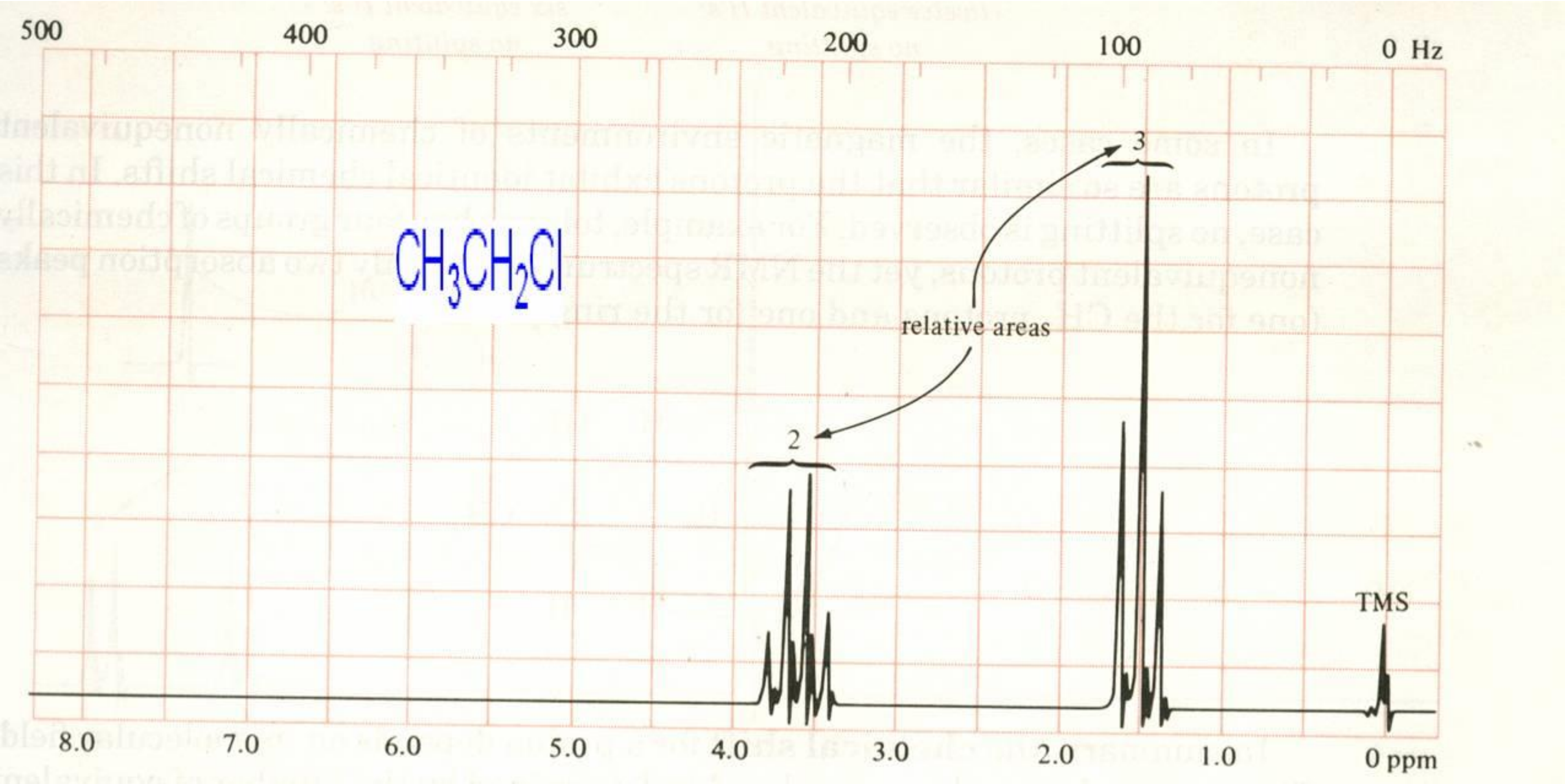
- The number of peaks of a particular proton is equal to number (n) of nonequivalent protons on the adjacent atoms + 1



These three equivalent protons see *two* neighboring, nonequivalent protons. Their NMR band is split into 2 + 1, or 3, peaks.

These two equivalent protons see *three* neighboring, nonequivalent protons. Their NMR band is split into 3 + 1, or 4, peaks.

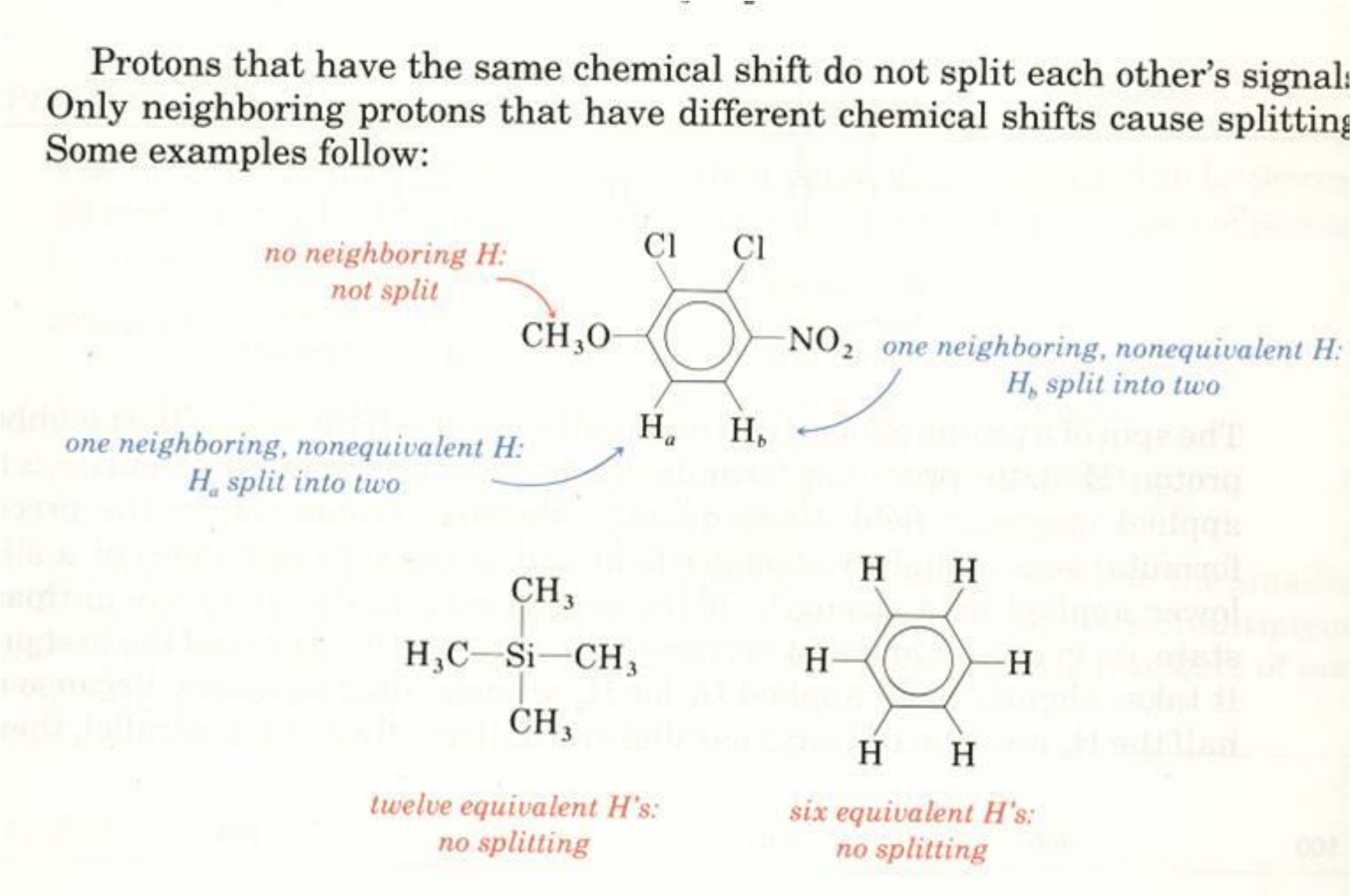
$CH_3CH_2Cl$



$CH_3CH_2Cl$

500
400
300
200
100
0 Hz
3
relative areas
2
TMS
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0 ppm

# Notice:



Protons that have the same chemical shift do not split each other's signals Only neighboring protons that have different chemical shifts cause splitting Some examples follow:

*no neighboring H: not split*

*one neighboring, nonequivalent H: $H_b$ split into two*

*one neighboring, nonequivalent H: $H_a$ split into two*

*twelve equivalent H's: no splitting*

*six equivalent H's: no splitting*

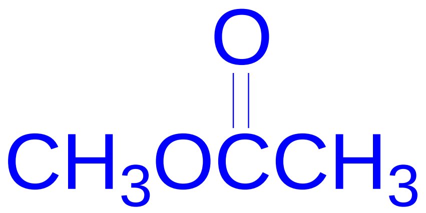
# Splitting pattern:

- The singlet

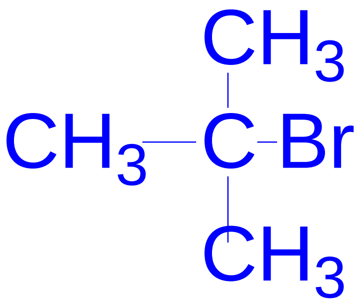
  If no neighboring nonequivalent protons present ➔ one single peak (singlet) (S).

eg.

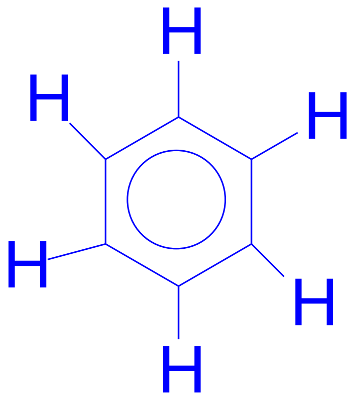
$CH_3-Cl$



$CH_3O\overset{\overset{O}{\|}}{C}CH_3$



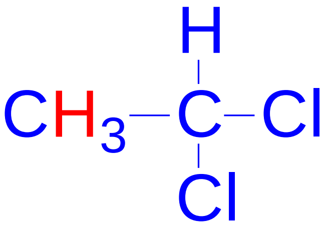
$CH_3-\underset{\underset{CH_3}{|}}{\overset{\overset{CH_3}{|}}{C}}-Br$



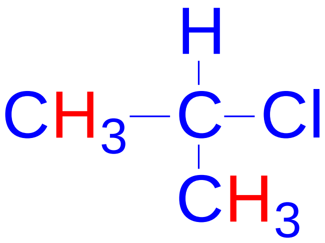
# The doublet

- If one neighboring nonequivalent proton present ➔ two peaks (doublet) (d).

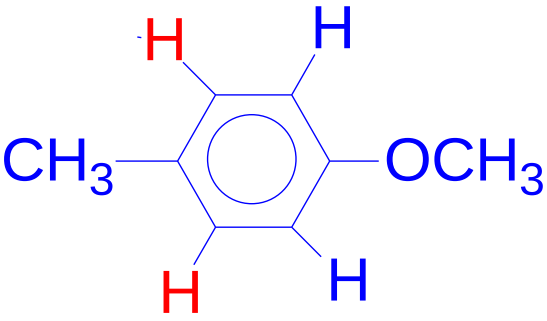
eg

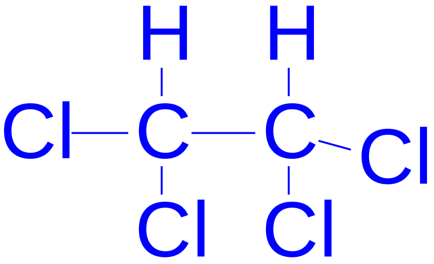


$CH_3-\overset{H}{\underset{Cl}{C}}-Cl$



$CH_3-\overset{H}{\underset{CH_3}{C}}-Cl$





$Cl-\overset{H}{\underset{Cl}{C}}-\overset{H}{\underset{Cl}{C}}-Cl$

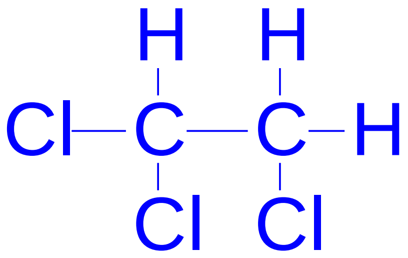
equivalent H's => S

# The triplet

- If two neighboring nonequivalent protons present ➔ three peaks (triplet) (t).

eg

$CH_3CH_2Cl$



$Cl-\overset{H}{\underset{Cl}{C}}-\overset{H}{\underset{Cl}{C}}-H$

$ClCH_2CH_2OCH_3$

# The quartet

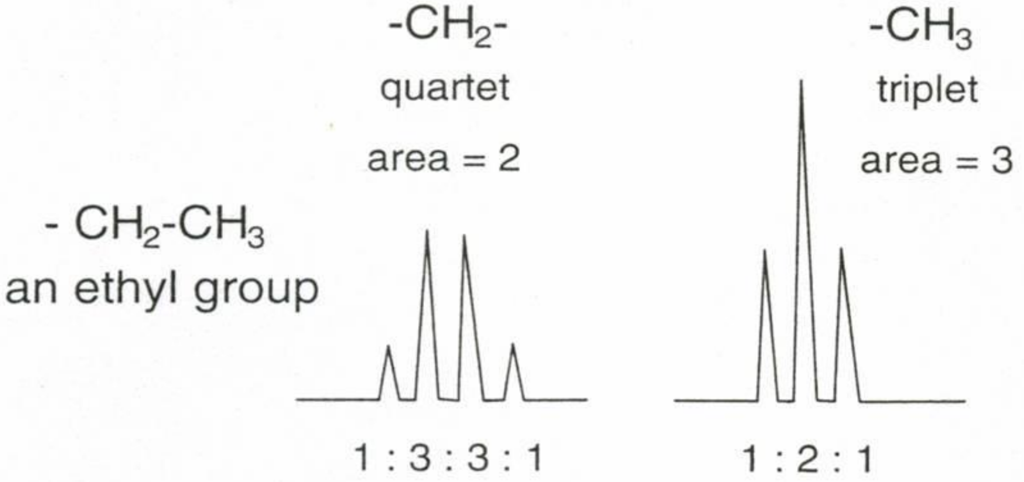
- If a proton is neighboring to $CH_3$ ➔ it will observe 3+1=4 peaks (quartet) (q)

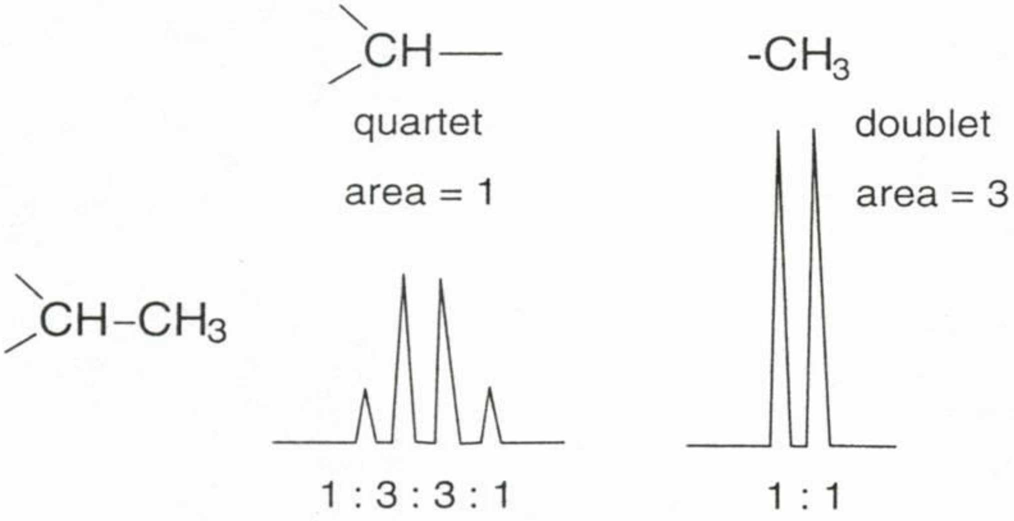
eg

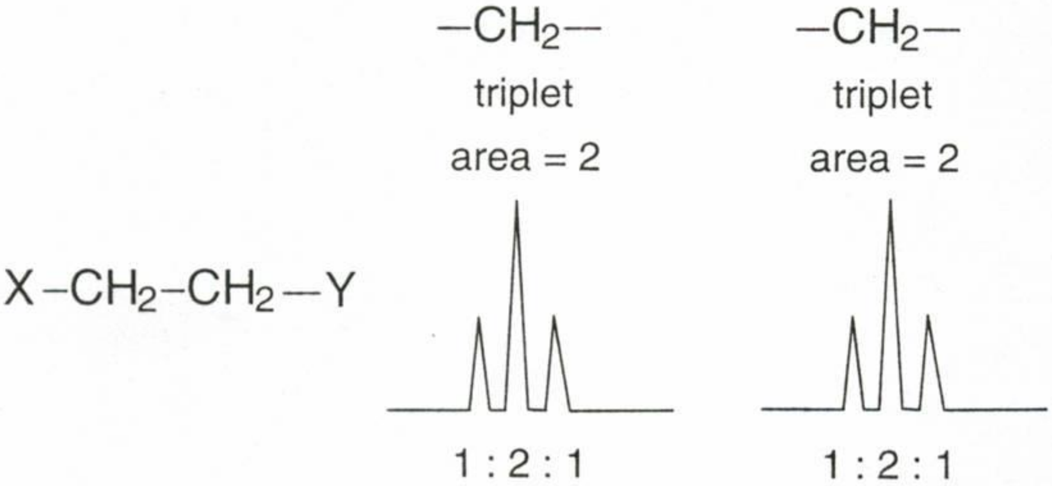
$CH_3CH_2Cl$

$CH_3CHCl_2$

$CH_3CH_2OCH_2CH_3$


$-CH_2-$
quartet
area = 2
$-CH_3$
triplet
area = 3
$-CH_2-CH_3$
an ethyl group
1 : 3 : 3 : 1
1 : 2 : 1

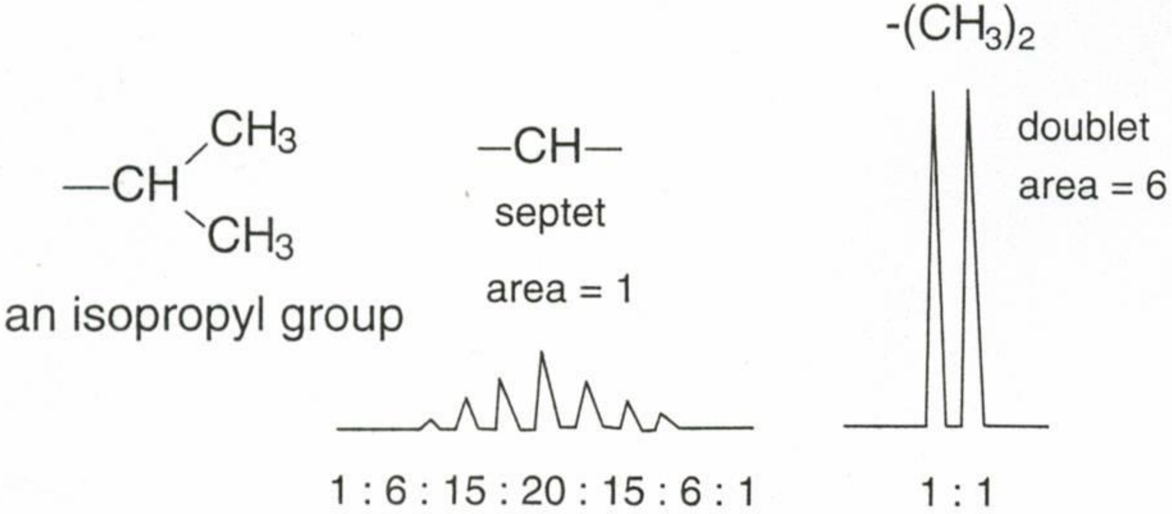

$CH-$
quartet
area = 1
$-CH_3$
doublet
area = 3
$CH-CH_3$
1 : 3 : 3 : 1
1 : 1



$X-CH_2-CH_2-Y$

$-CH_2-$ triplet area = 2 1 : 2 : 1

$-CH_2-$ triplet area = 2 1 : 2 : 1

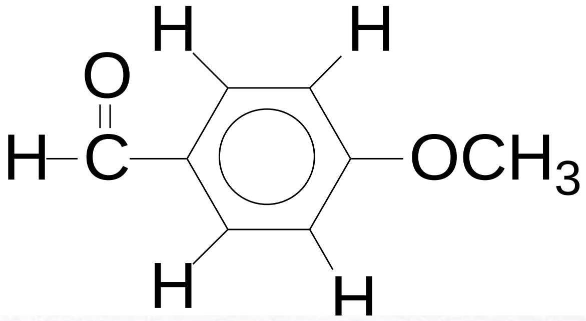


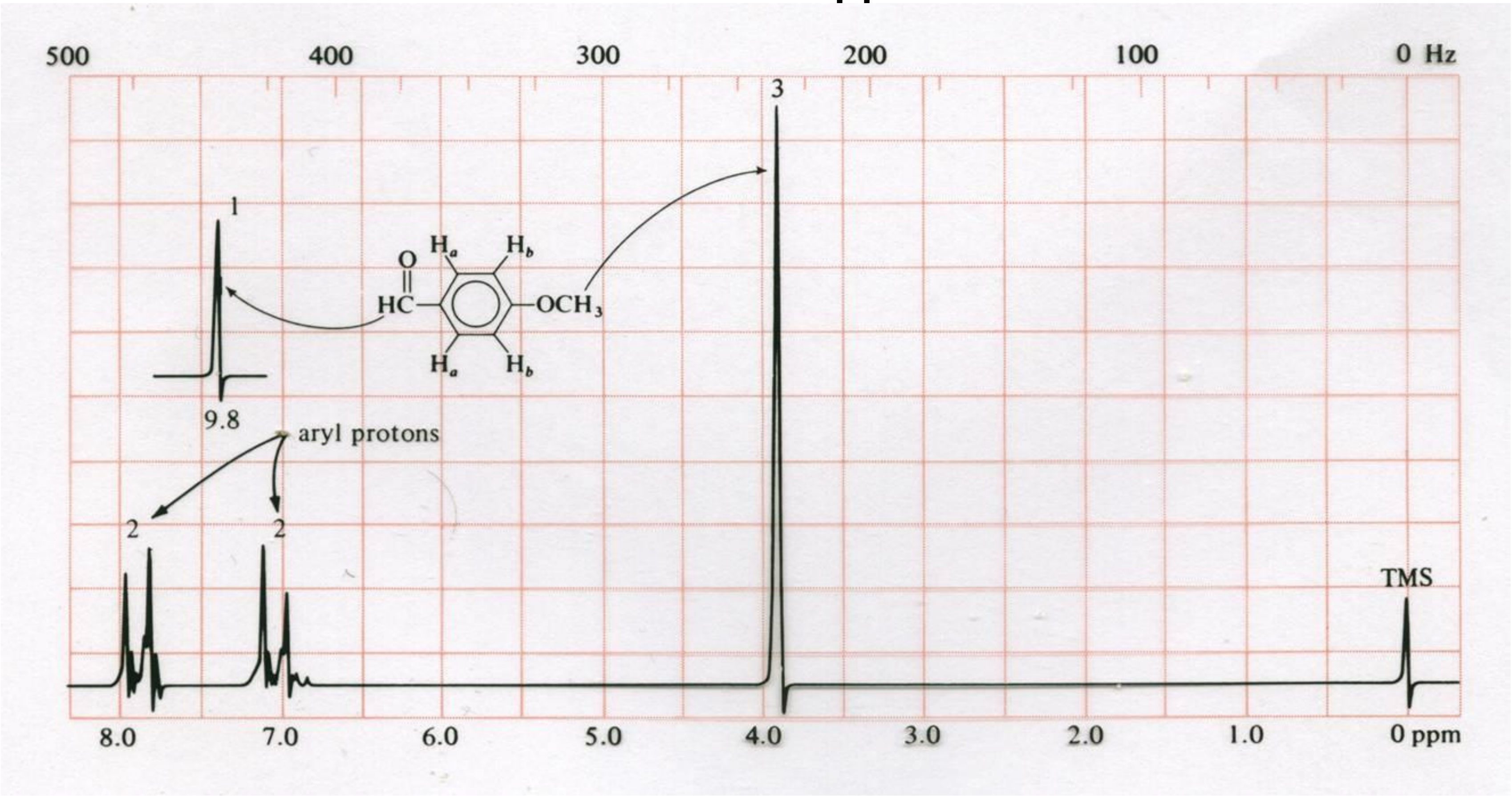
an isopropyl group

$-CH-$ septet area = 1 1 : 6 : 15 : 20 : 15 : 6 : 1

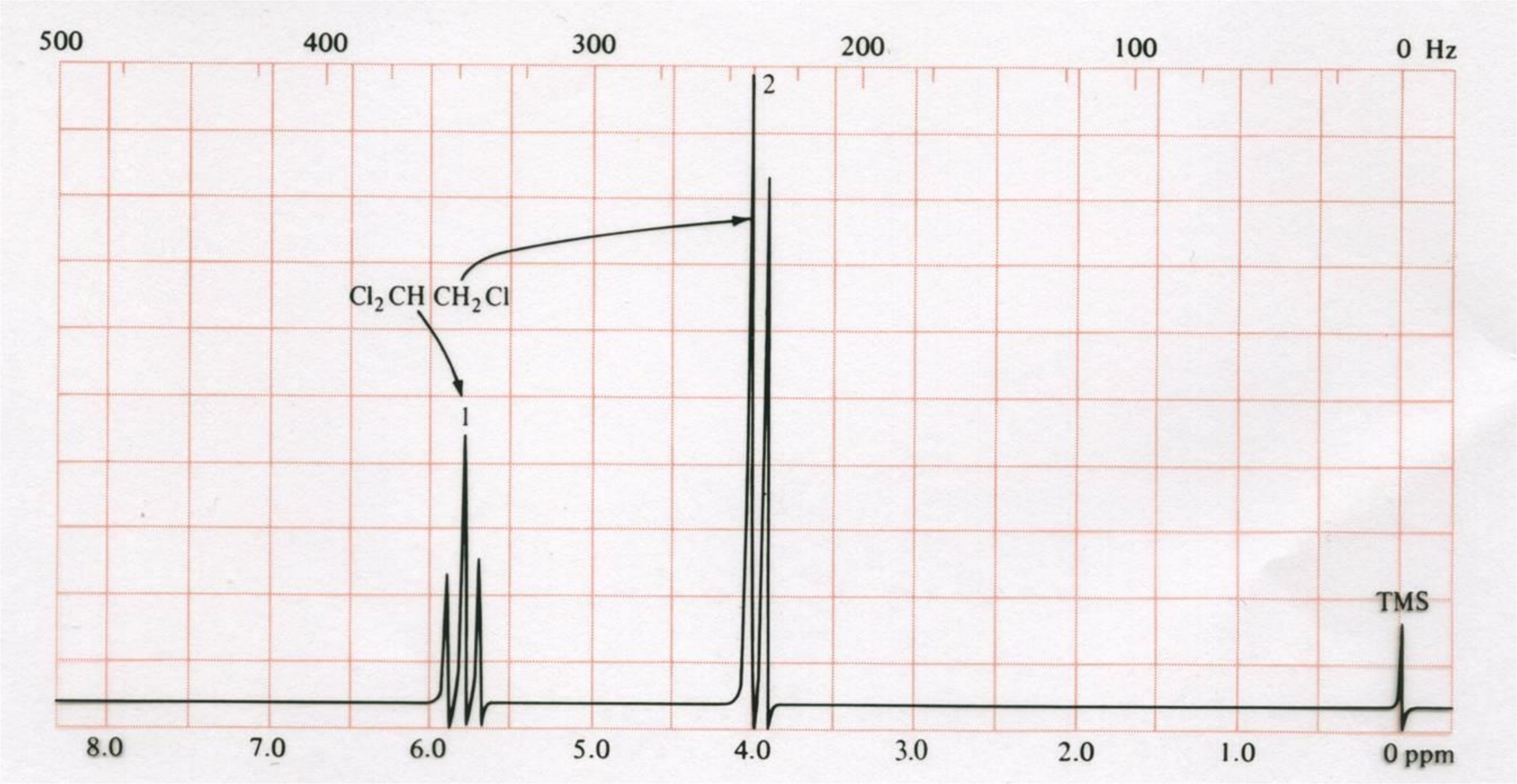
$-(CH_3)_2$ doublet area = 6 1 : 1

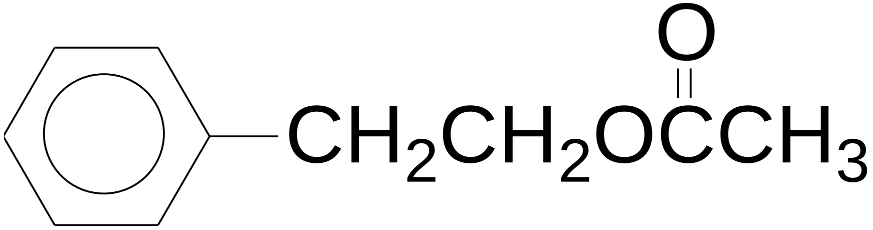
# Examples:

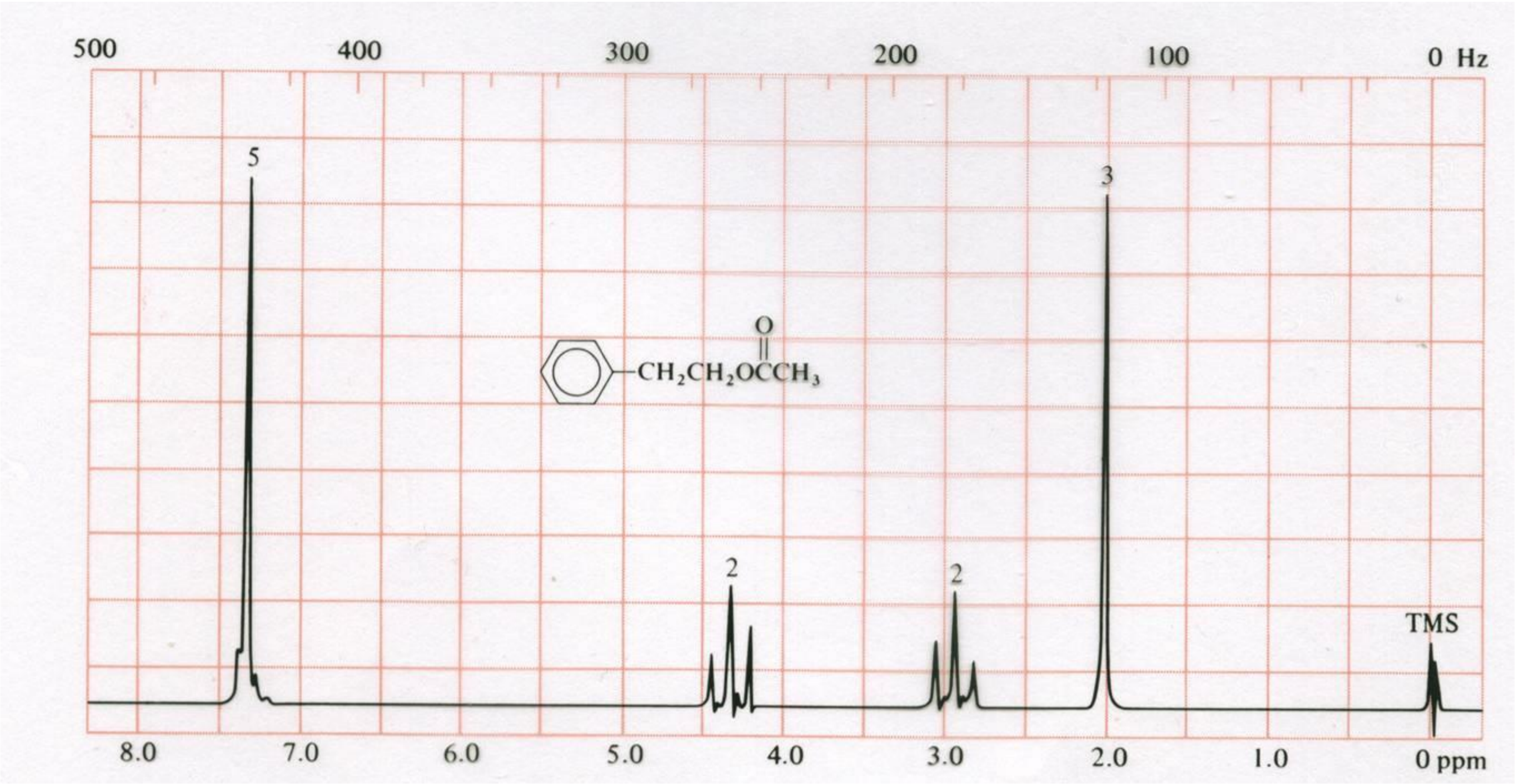

H
H
O
H–C
OCH3
H
H

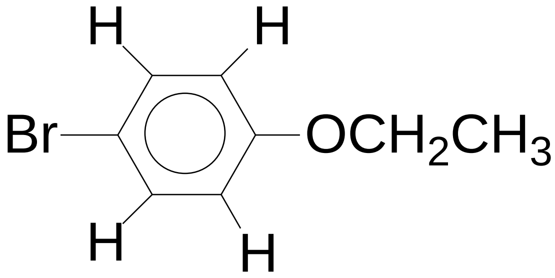

500
400
300
200
100
0 Hz
3
1
O
HC
Ha
Hb
OCH3
Ha
Hb
9.8
aryl protons
2
2
TMS
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0 ppm

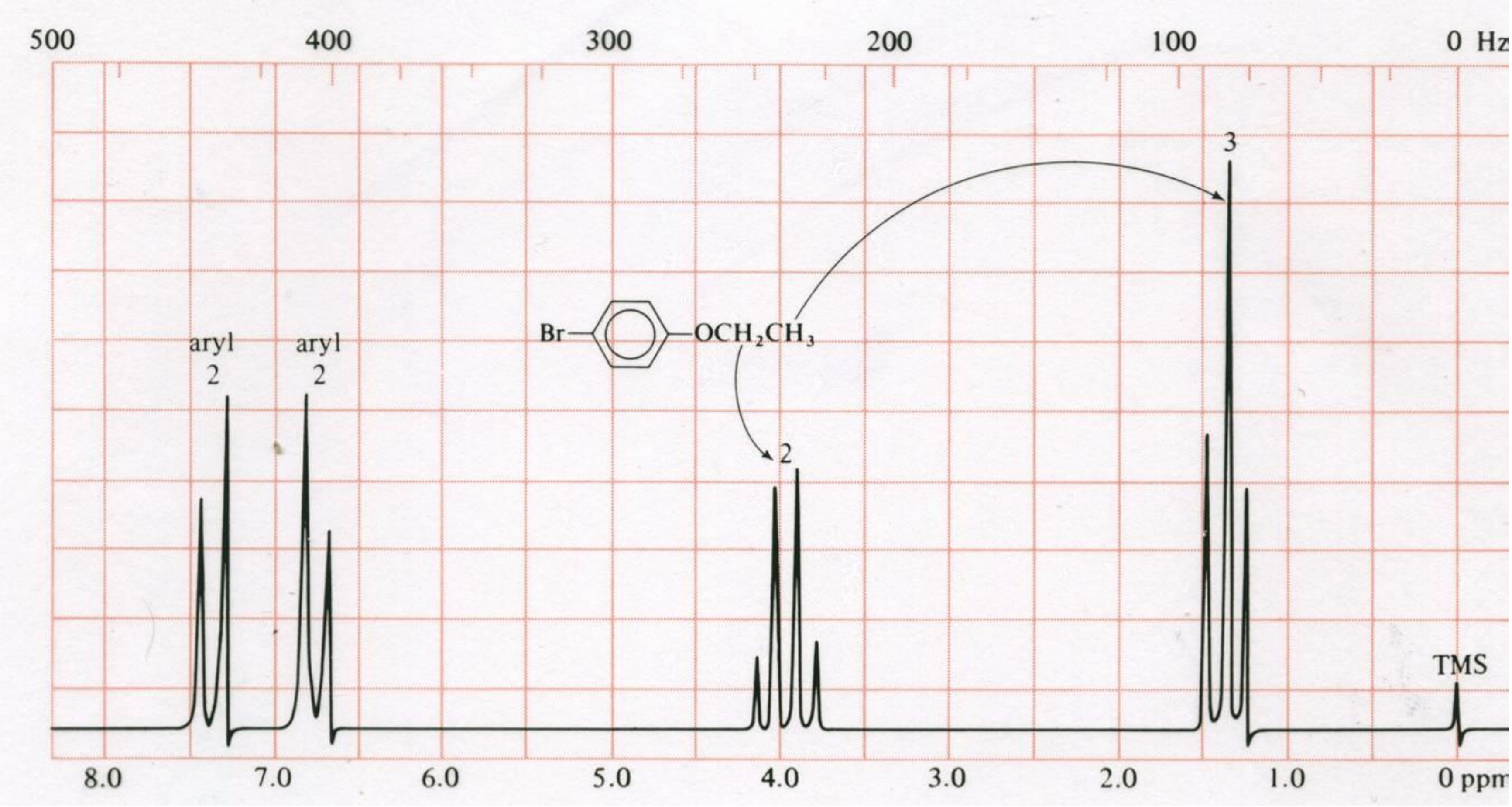
# $Cl_2CHCH_2Cl$


500
400
300
200
100
0 Hz
2
1
$Cl_2CH\ CH_2Cl$
TMS
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0 ppm

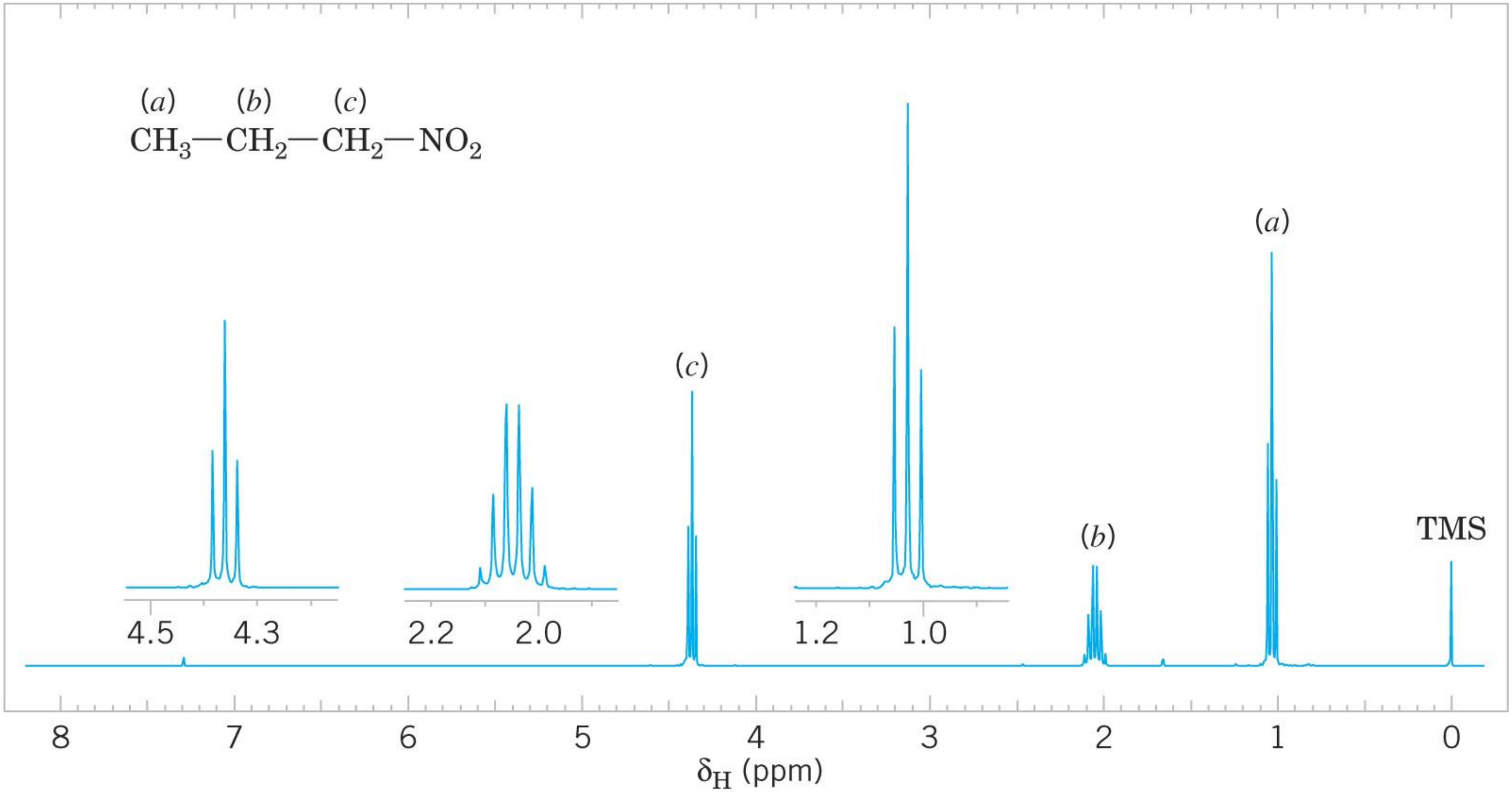



500
400
300
200
100
0 Hz
5
3
O
CH₂CH₂OCCH₃
2
2
TMS
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0 ppm

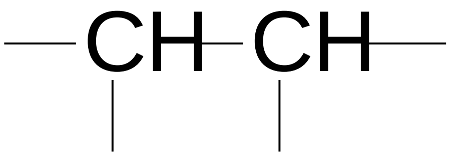

H
H
Br
OCH2CH3
H
H


500
400
300
200
100
0 Hz
aryl 2
aryl 2
Br
OCH2CH3
2
3
TMS
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0 ppm

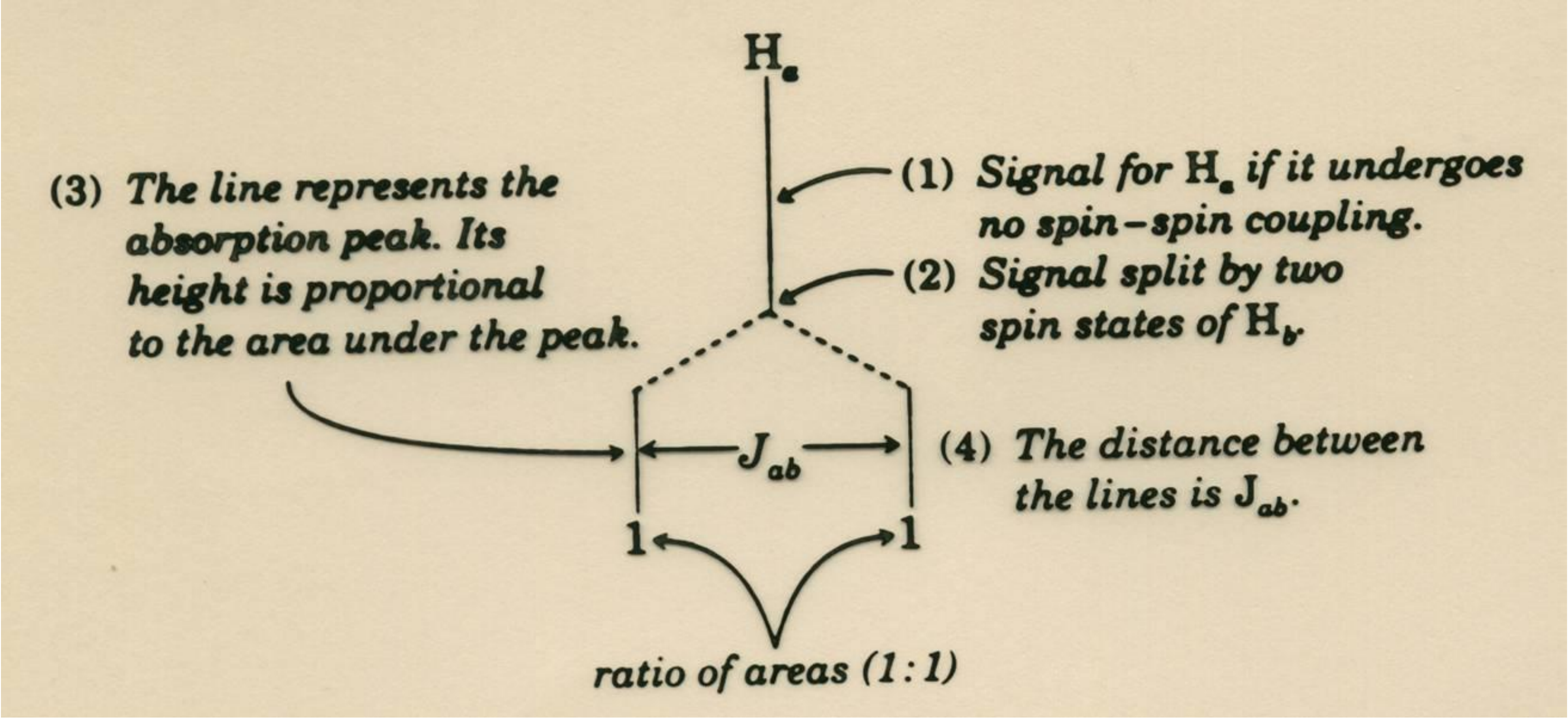
# $CH_3CH_2CH_2NO_2$



# Spin-spin splitting diagram



$-CH-CH-$



(1) *Signal for $H_a$ if it undergoes no spin–spin coupling.*

(2) *Signal split by two spin states of $H_b$.*

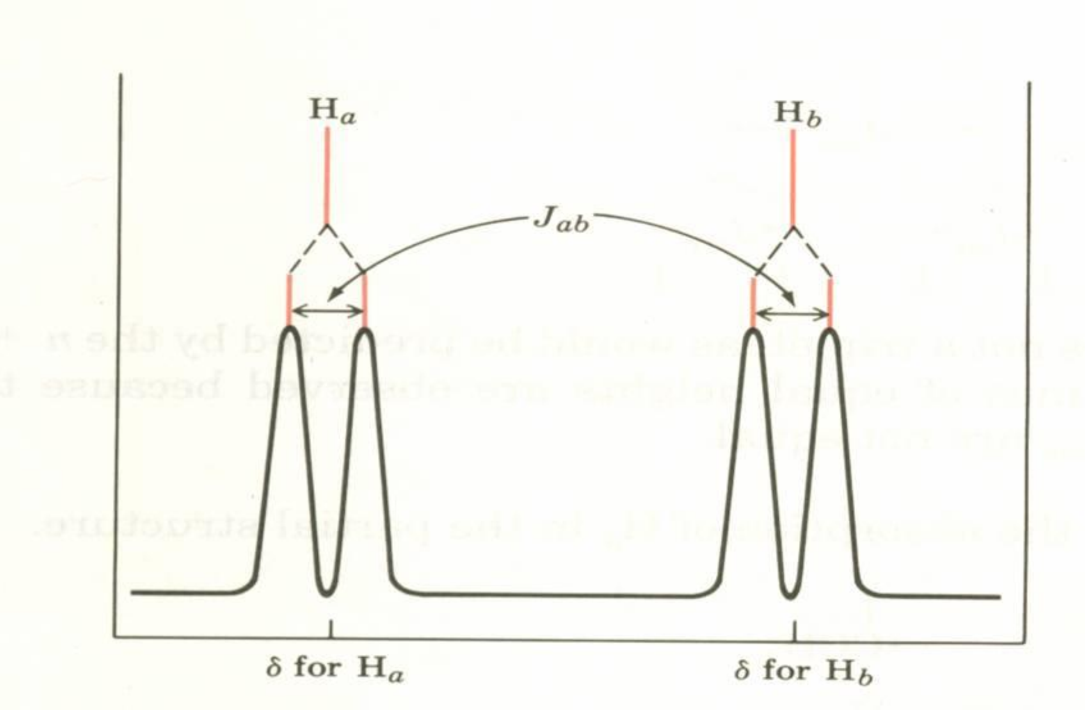
(3) *The line represents the absorption peak. Its height is proportional to the area under the peak.*

(4) *The distance between the lines is $J_{ab}$.*

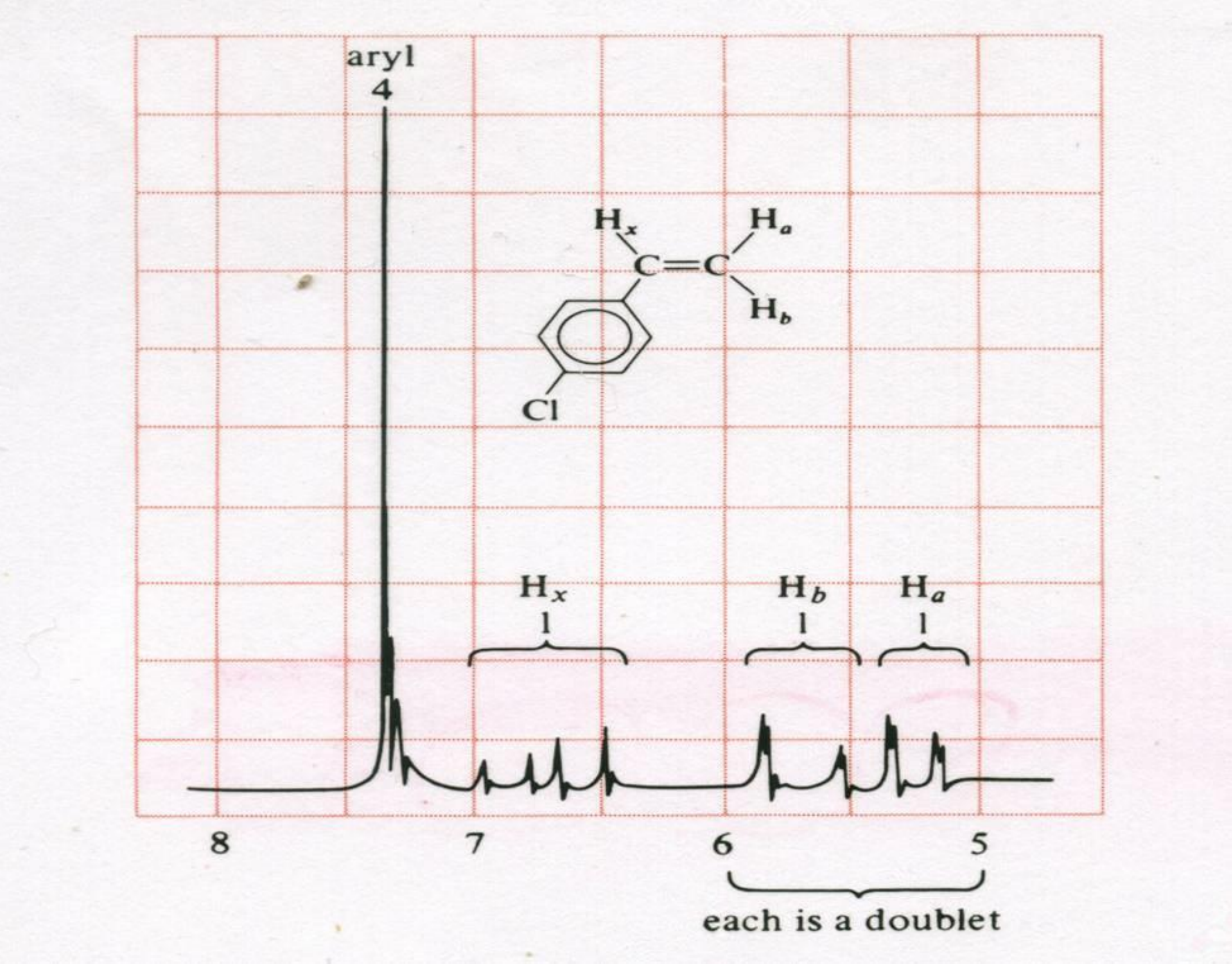
*ratio of areas (1:1)*

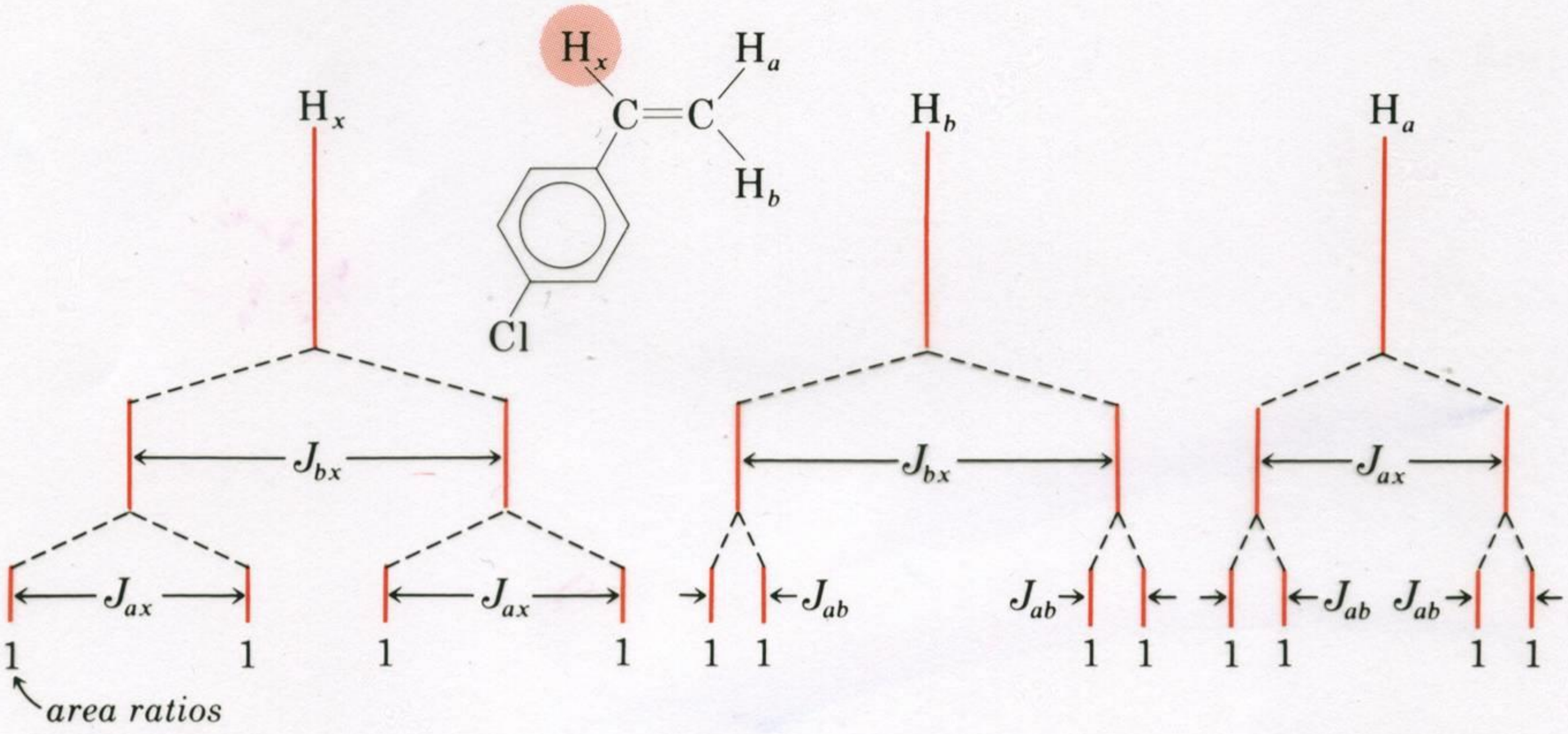
# Coupling constant

- The separation between two peaks is called the coupling constant (J)



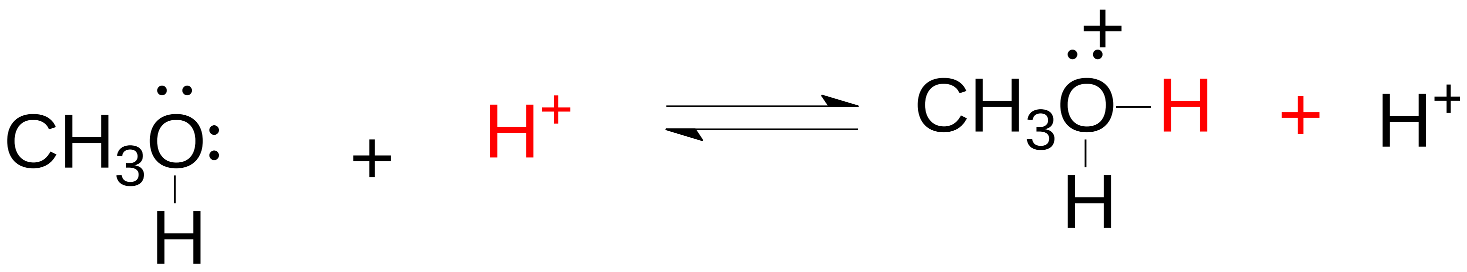
# Terminal alkene NMR





$J_{ax} = 11$ Hz, $J_{ab} = 2$ Hz, $J_{bx} = 18$ Hz

# Chemical Exchange and Hydrogen Bonding

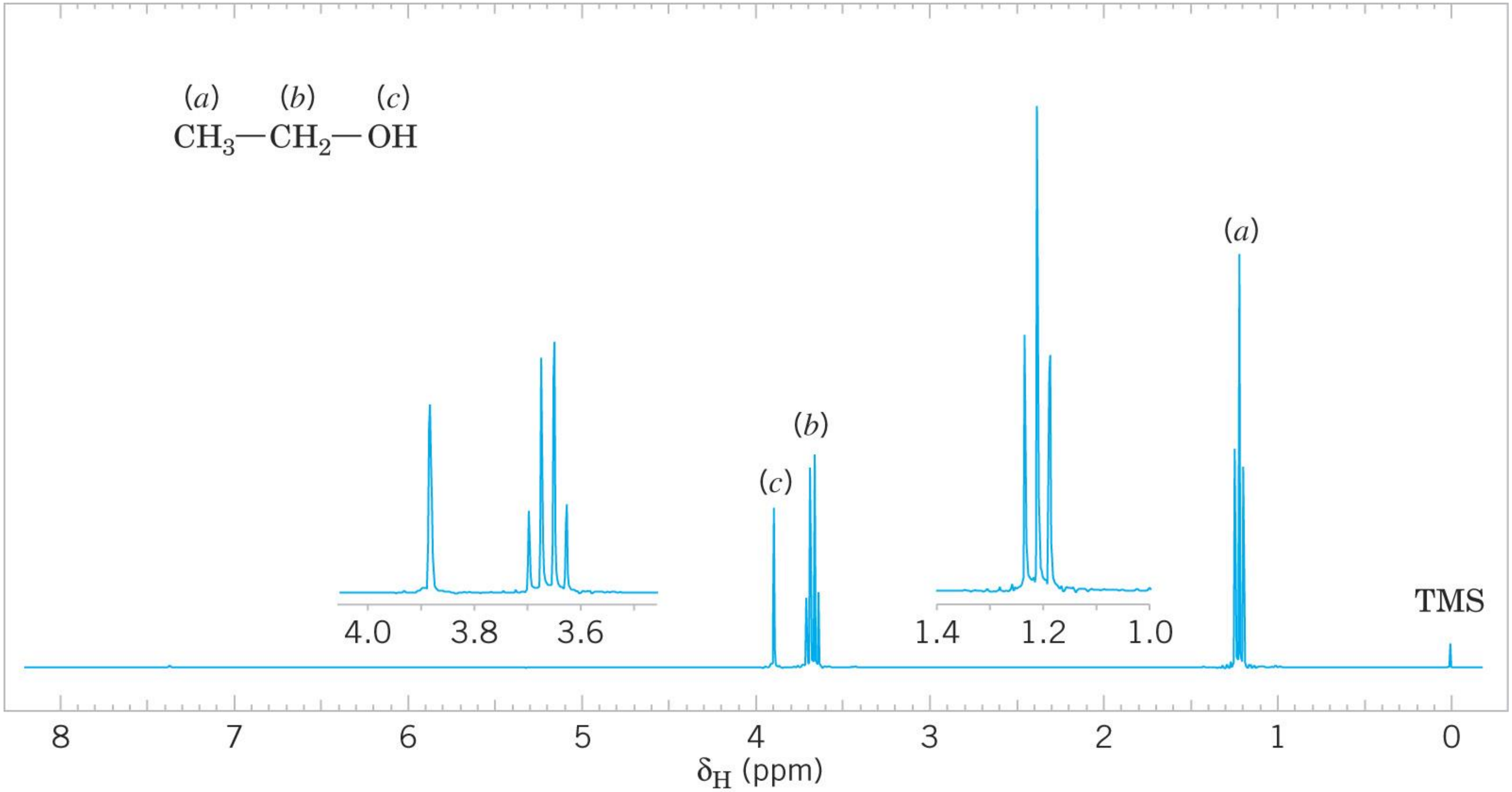


$$CH_3\underset{H}{\ddot{O}}\colon + H^+ \rightleftharpoons CH_3\underset{H}{\overset{+}{\ddot{O}}}-H + H^+$$

- Impure alcohol contains acid and base impurities which catalyze the exchange of hydroxyl protons
- This rapid exchange is so fast that coupling to the adjacent $CH_3$ is not observed
- This process is called spin decoupling

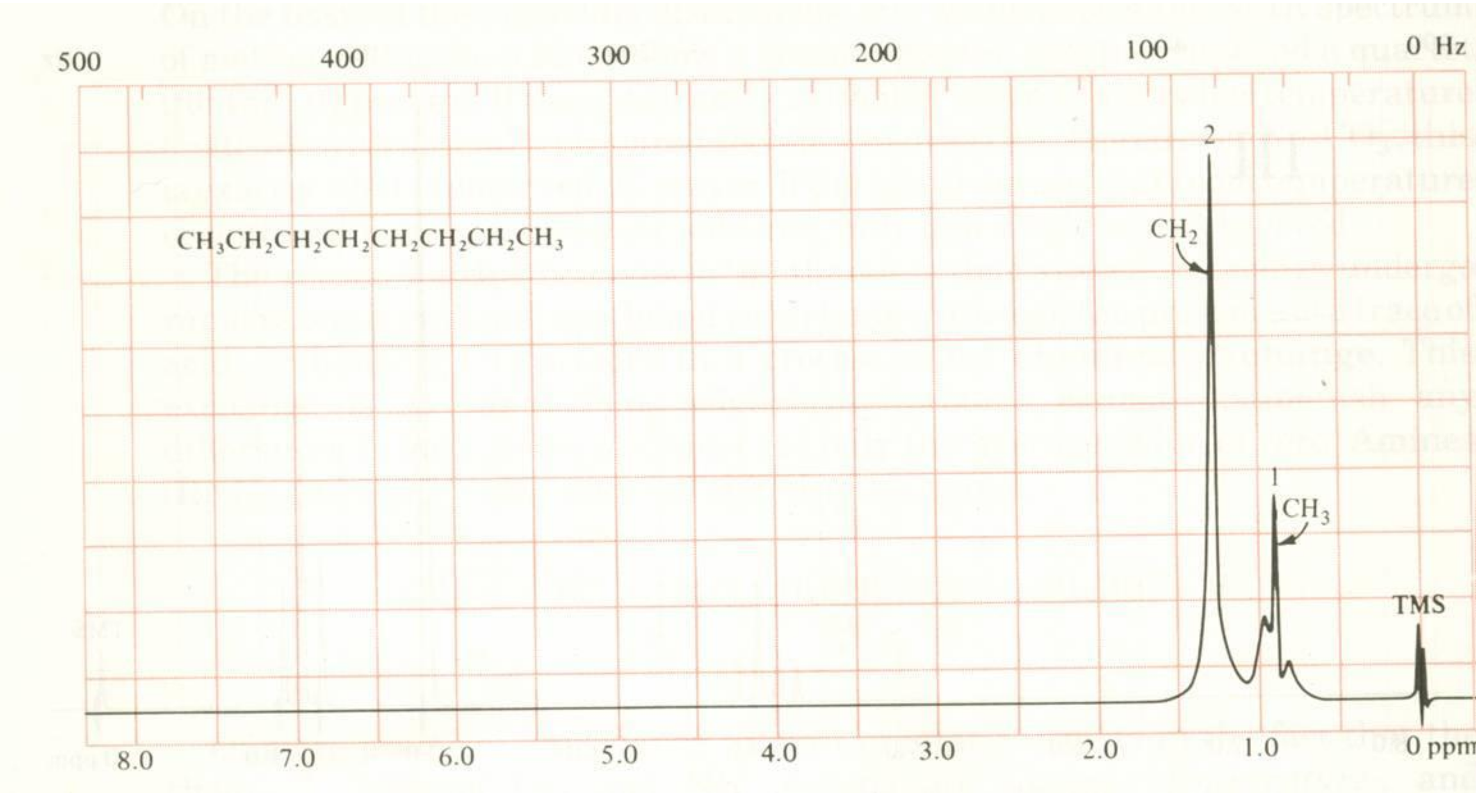
- Spin decoupling is typical in the $^1$H NMR spectra of alcohols, amines and carboxylic acids
- The proton attached to the oxygen or nitrogen normally appears as a singlet because of rapid exchange processes

# When an $^1$H NMR of regular ethanol is taken the hydroxyl proton is a singlet



# Several factors complicate analysis of NMR spectra

- Peaks may overlap ( if the chemical shift differences is very small)



- Splitting patterns in aromatic groups can be confusing.
- A monosubstituted aromatic ring can appear as an apparent singlet or a complex pattern of peaks.
- A para disubstituted aromatic ring mostly appear as two doublets (dd)

# Interpretation of proton NMR spectra

- From the molecular formula determine the number of unsaturation ( No. of rings + Double bonds)

  $C_xH_yN_zO_n$

  # of rings + db= x-1/2 y+1/2 z +1

X = # of carbon atoms

y = # of hydrogen and halogen atoms

z = # of nitrogen atoms

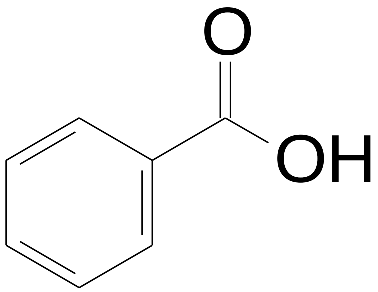
# Example:

- $C_7H_6O_2$

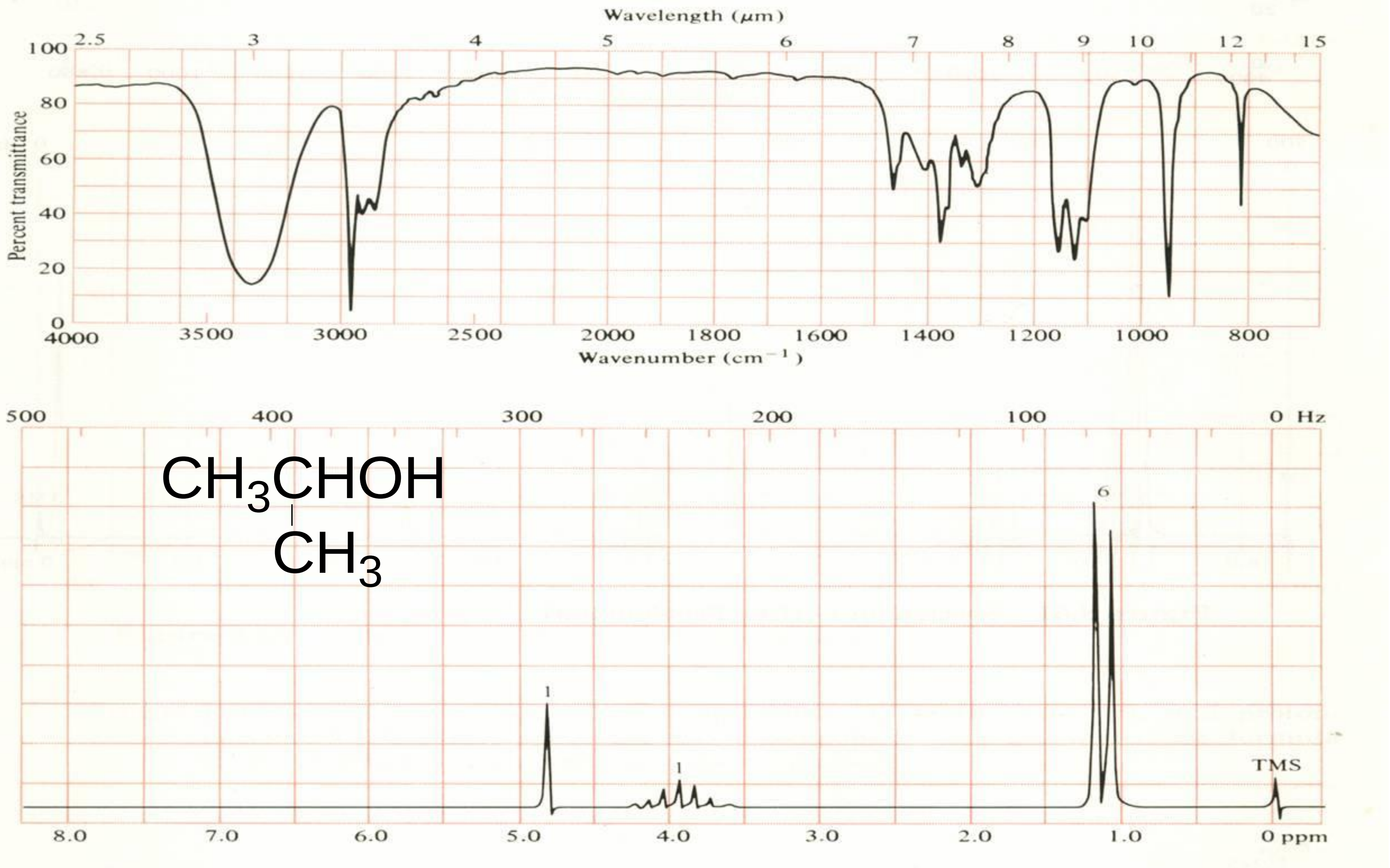
➔ #rings + db = 7- 1/2x6 + 1 = 5

➔One ring + 4 double bonds

➔ benzoic acid



# $C_3H_8O$



$$\begin{array}{l}CH_3\underset{\displaystyle |\atop \displaystyle CH_3}{C}HOH\end{array}$$

**Figure 9.50** Spectra for $C_3H_8O$, Problem 9.20.

# $C_7H_8O$

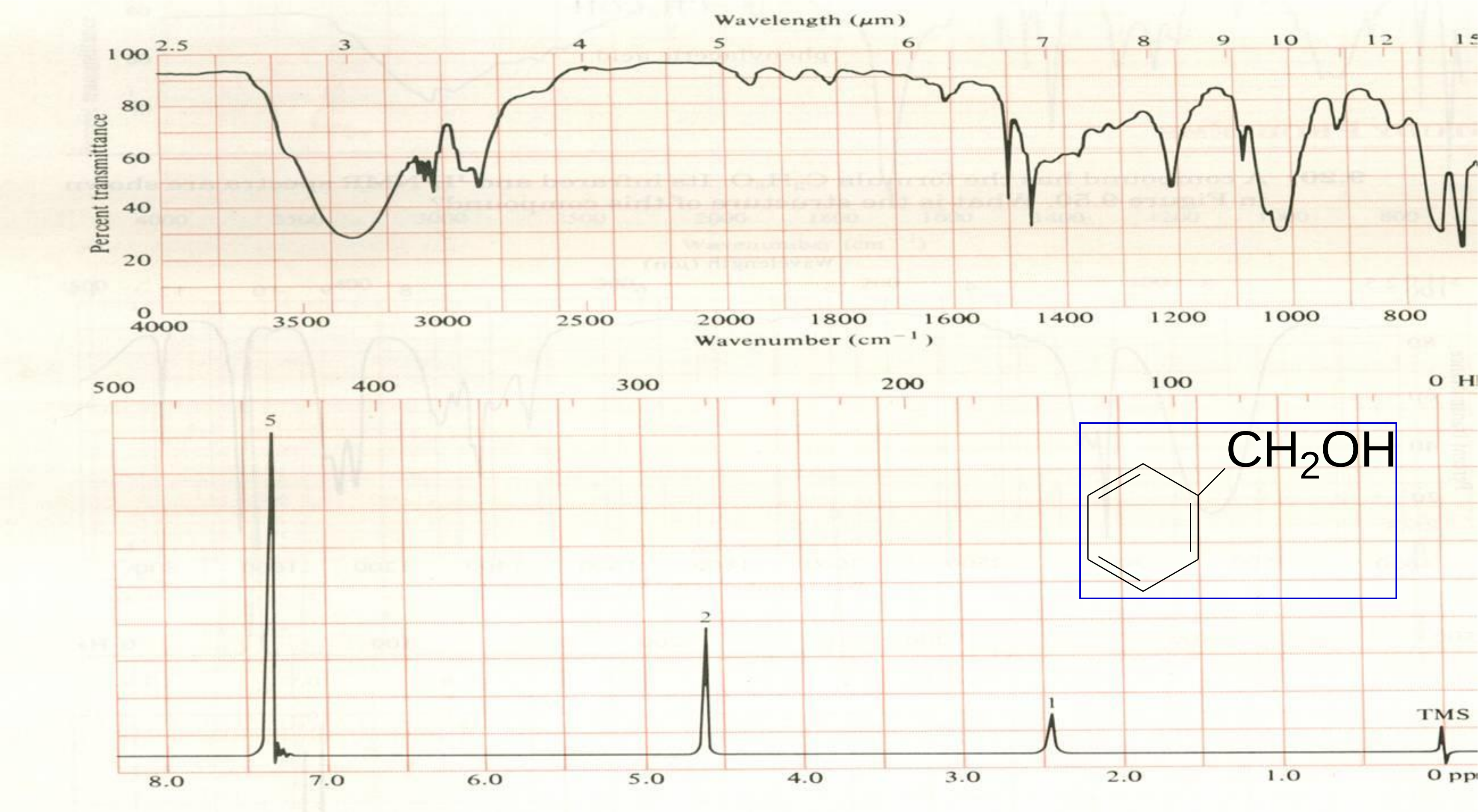
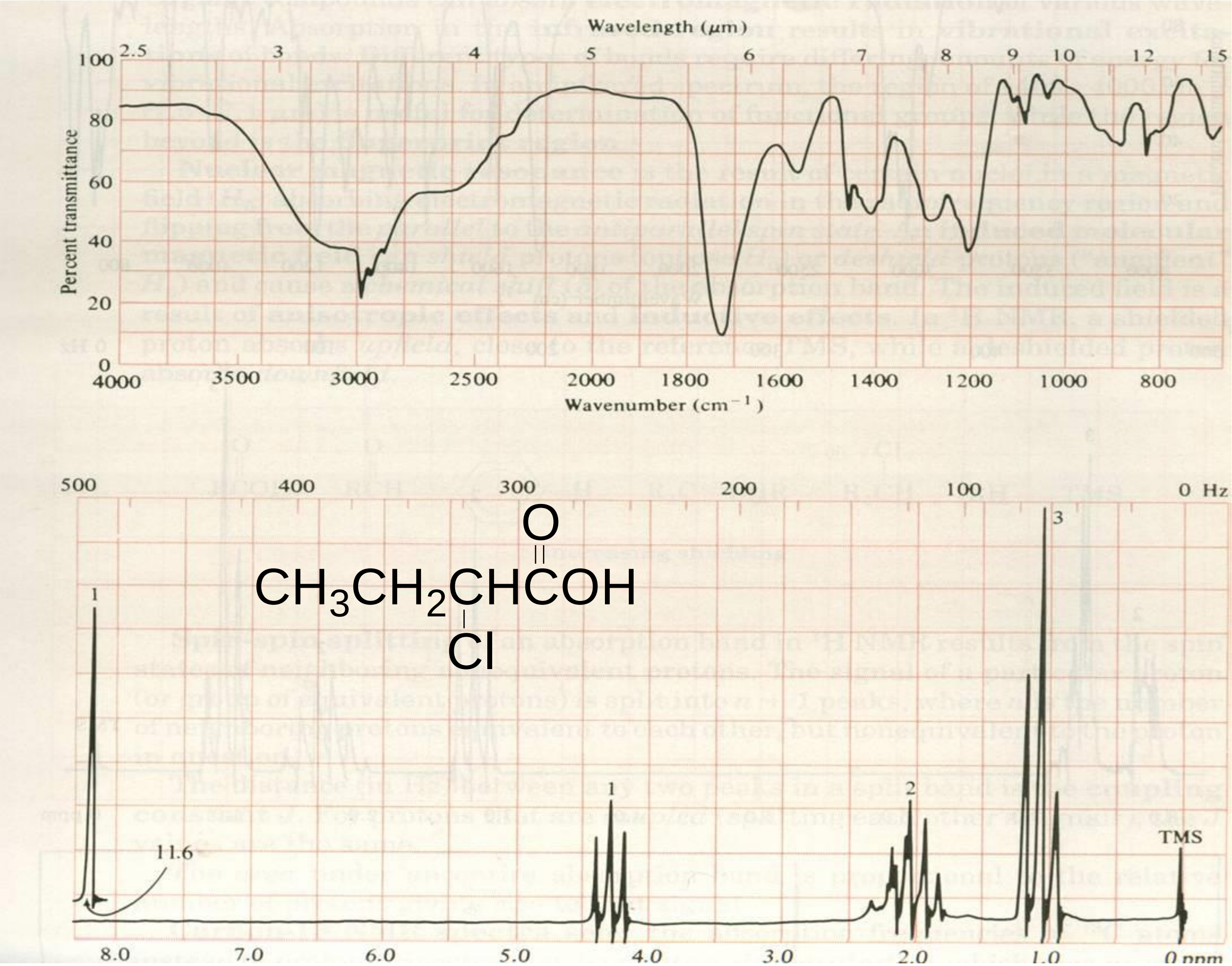


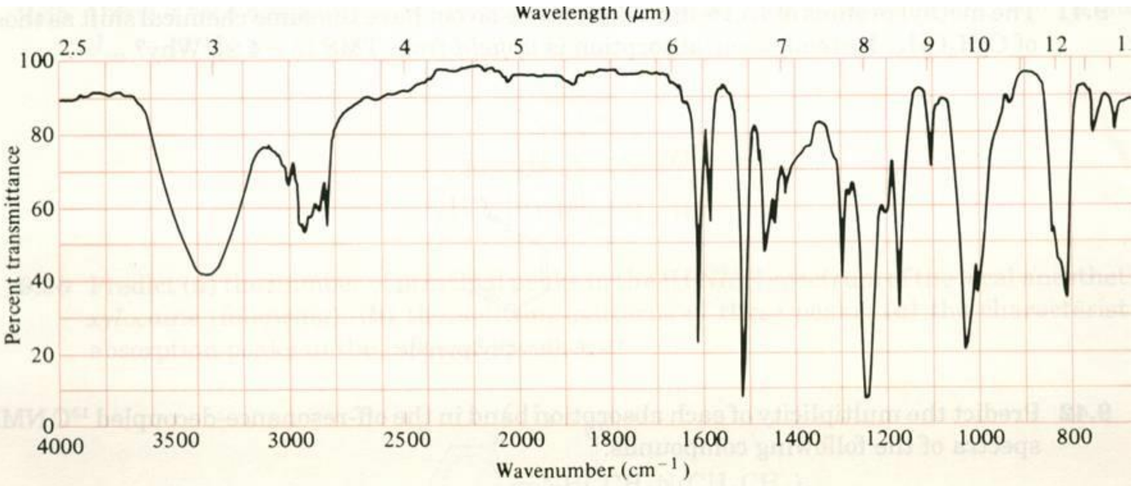
**Figure 9.51** Spectra for $C_7H_8O$, Problem 9.21.

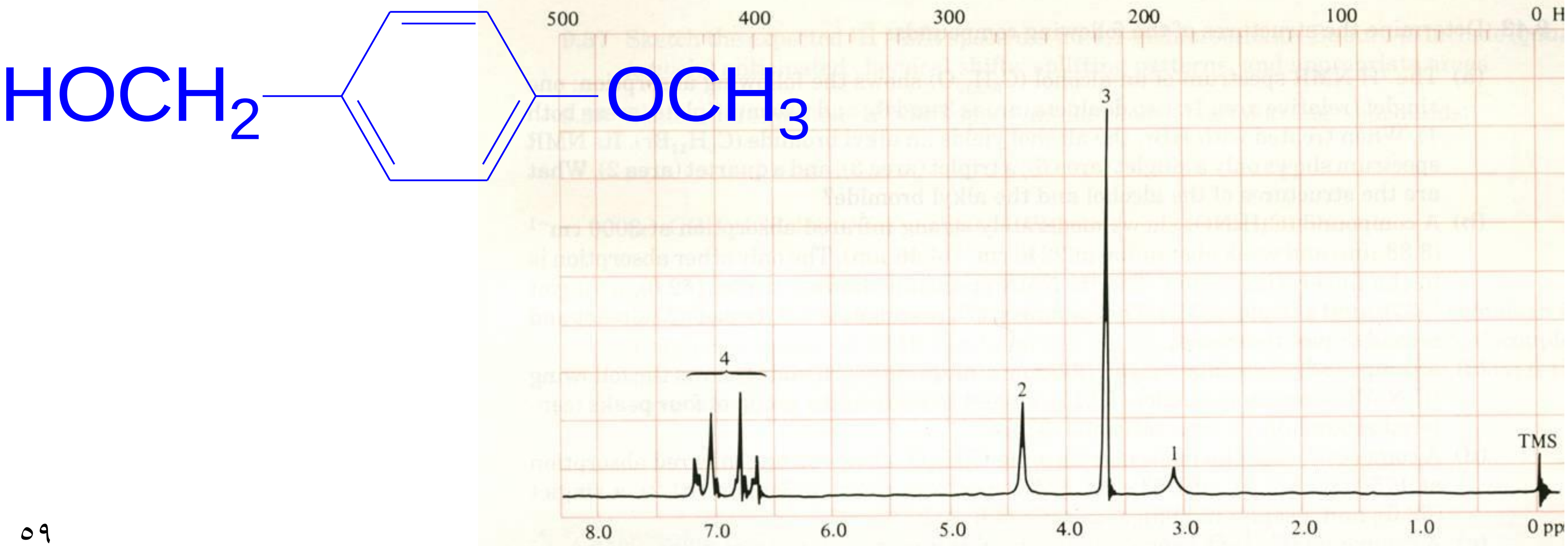
# $C_4H_7ClO_2$



$$CH_3CH_2\underset{\displaystyle Cl}{\underset{|}{C}}H\overset{\displaystyle O}{\overset{\|}{C}}OH$$

# $C_8H_{10}O_2$

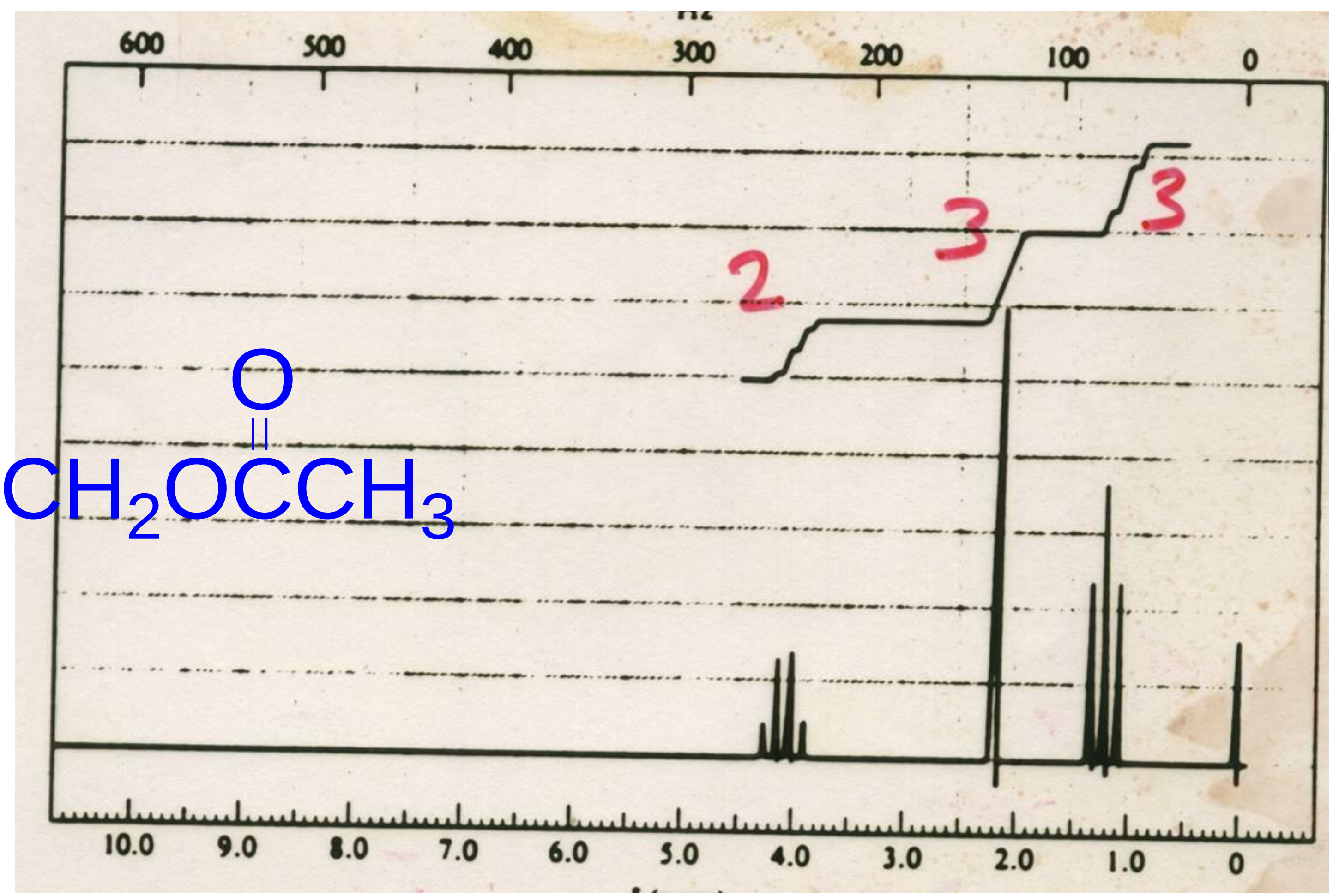

Wavelength (μm)
2.5
3
4
5
6
7
8
9
10
12
100
80
60
40
20
0
Percent transmittance
4000
3500
3000
2500
2000
1800
1600
1400
1200
1000
800
Wavenumber (cm⁻¹)


HOCH2
OCH3
500
400
300
200
100
0 H
4
2
3
1
TMS
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0 pp

# Notice: in interpreting NMR spectra

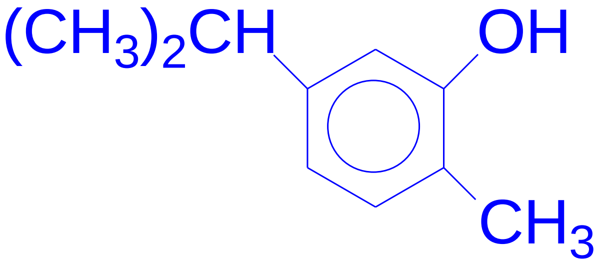
- Singlet ➔ no H on adjacent atoms
- Doublet ➔ one H on adjacent atoms.
- Triplet ➔ Two H’s on adjacent atoms.
- Quarter ➔Three H’s on adjacent atoms
- Pentet ➔ Four H’s on adjacent atoms
- Sixtet ➔ Five H’s on adjacent atoms
- Septet ➔ six H’s on adjacent atoms

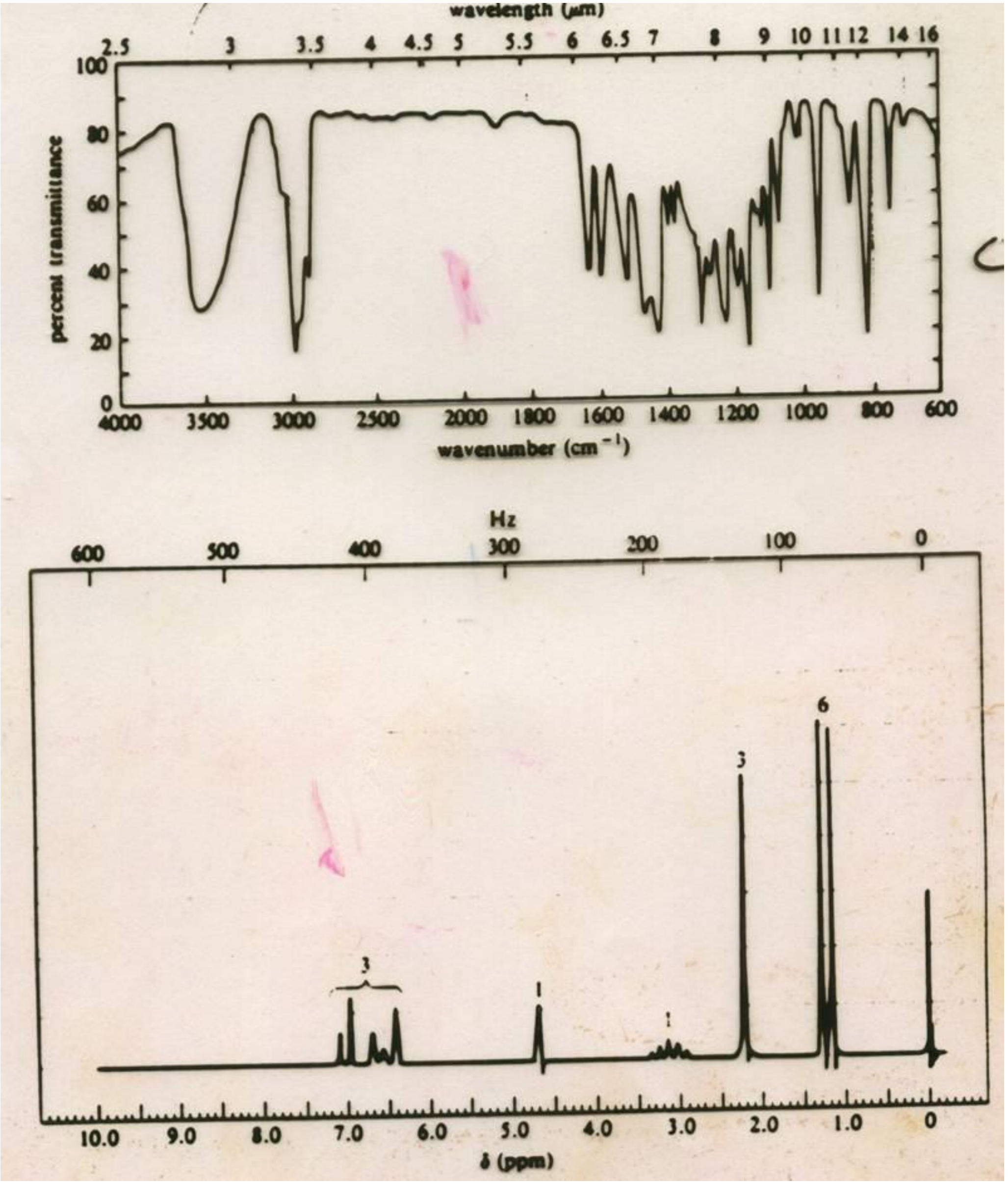
# $C_4H_8O_2$



$CH_3CH_2O\overset{O}{\overset{\|}{C}}CH_3$

# $C_{10}H_{14}O$


(CH3)2CH
OH
CH3


wavelength (μm)
2.5
3
3.5
4
4.5
5
5.5
6
6.5
7
8
9
10
11
12
14
16
percent transmittance
100
80
60
40
20
0
4000
3500
3000
2500
2000
1800
1600
1400
1200
1000
800
600
wavenumber (cm⁻¹)
Hz
600
500
400
300
200
100
0
3
1
1
3
6
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
δ (ppm)

# Carbon-13 NMR Spectroscopy

- $^{13}C$ accounts for only 1.1% of naturally occurring carbon
- $^{12}C$ has no magnetic spin and produces no NMR signal.
- C-13 NMR has $\delta$ 0 to 220 ppm ($^1$HNMR $\delta$ 0 to 12 ppm)
- No integration for C-13 spectra
- Since the $^{13}C$ isotope of carbon is present in only 1.1% natural abundance, there is only a 1 in 10,000 chance that two $^{13}C$ atoms will occur next to each other in a molecule

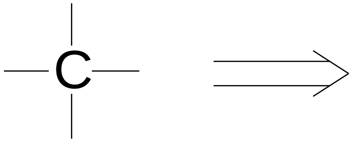
# $^{13}C$ proton decoupled spectrum

- The low probability of adjacent $^{13}C$ atoms leads to no detectable carbon-carbon splitting ➔No coupling between $^{13}C$ and C.
- One Peak for Each Unique Carbon Atom

  ( All nonequivalent carbons➔ singlets)
- # peaks ➔ # nonequivalent carbons.
- $CH_3CH_3$ ➔ one singlet
- $CH_3CH_2CH_3$ ➔ two singlets
- $CH_3CH_2CH_2CH_3$ ➔ two singlets

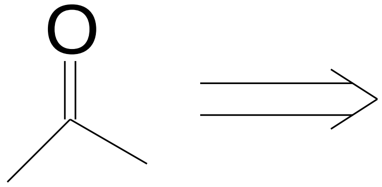
# Off-Resonance Decoupled Spectra

- Direct coupling between the carbon atom and the hydrogen on this carbon ( n+1 rule is applied)
- -$CH_3$ ➔ quartet
- -$CH_2$- ➔ triplet
- -CH- ➔ doublet



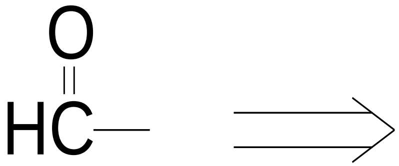
singlet

no H's



singlet

ketone



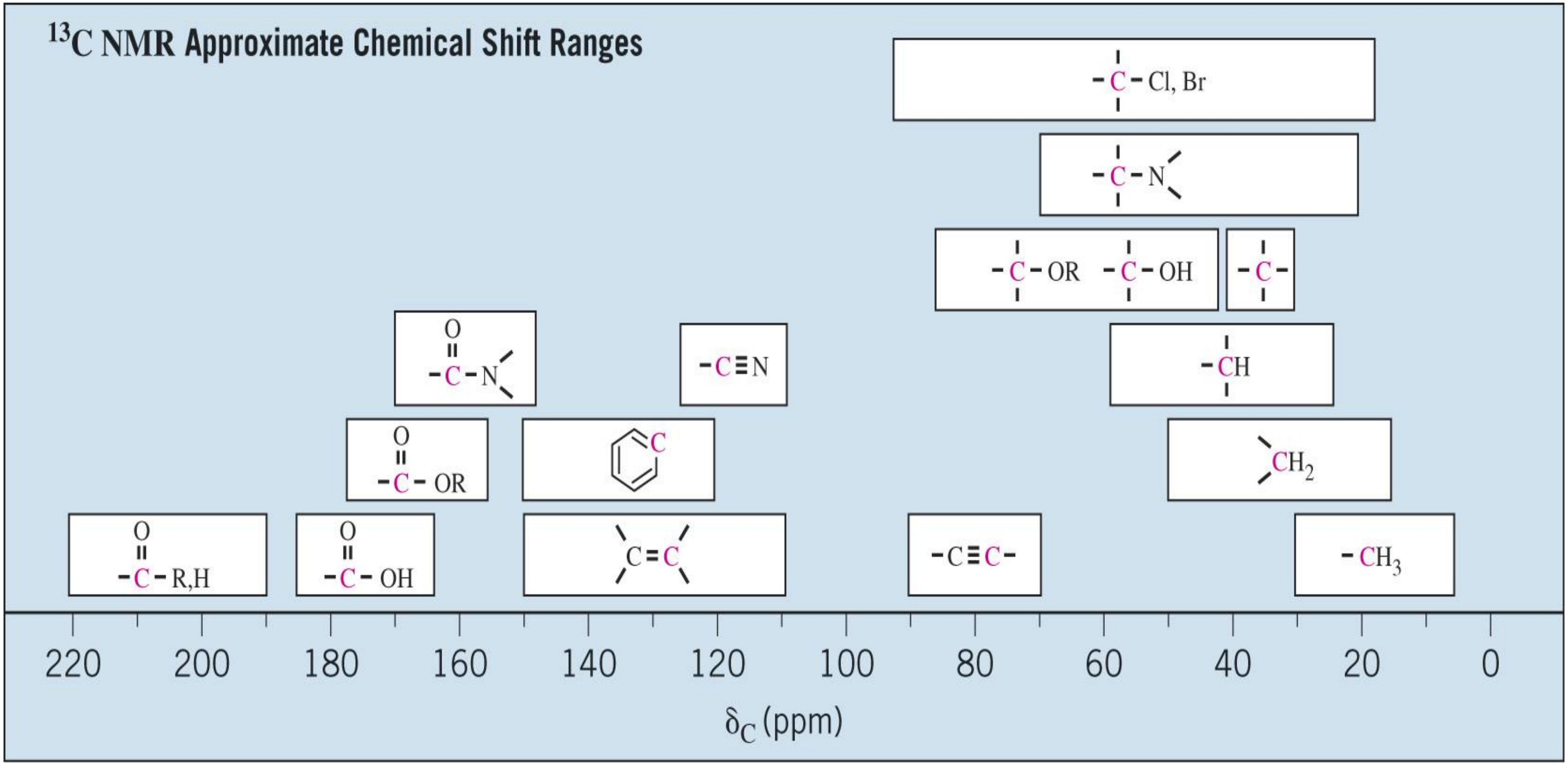
doublet

aldehyde

# $^{13}$C Chemical Shifts

- Just as in $^{1}$H NMR spectroscopy, chemical shifts in $^{13}$C NMR depend on the electron density around the carbon nucleus
  - Decreased electron density causes the signal to move downfield (*desheilding*)
  - Increased electron density causes the signal to move upfield (*sheilding*)
- Because of the wide range of chemical shifts, it is rare to have two $^{13}$C peaks coincidentally overlap
- A group of 3 peaks at $\delta$ 77 comes from the common NMR solvent deuteriochloroform and can be ignored

# $^{13}$C Chemical Shifts



# $^{13}$C Chemical shift ( simplified)

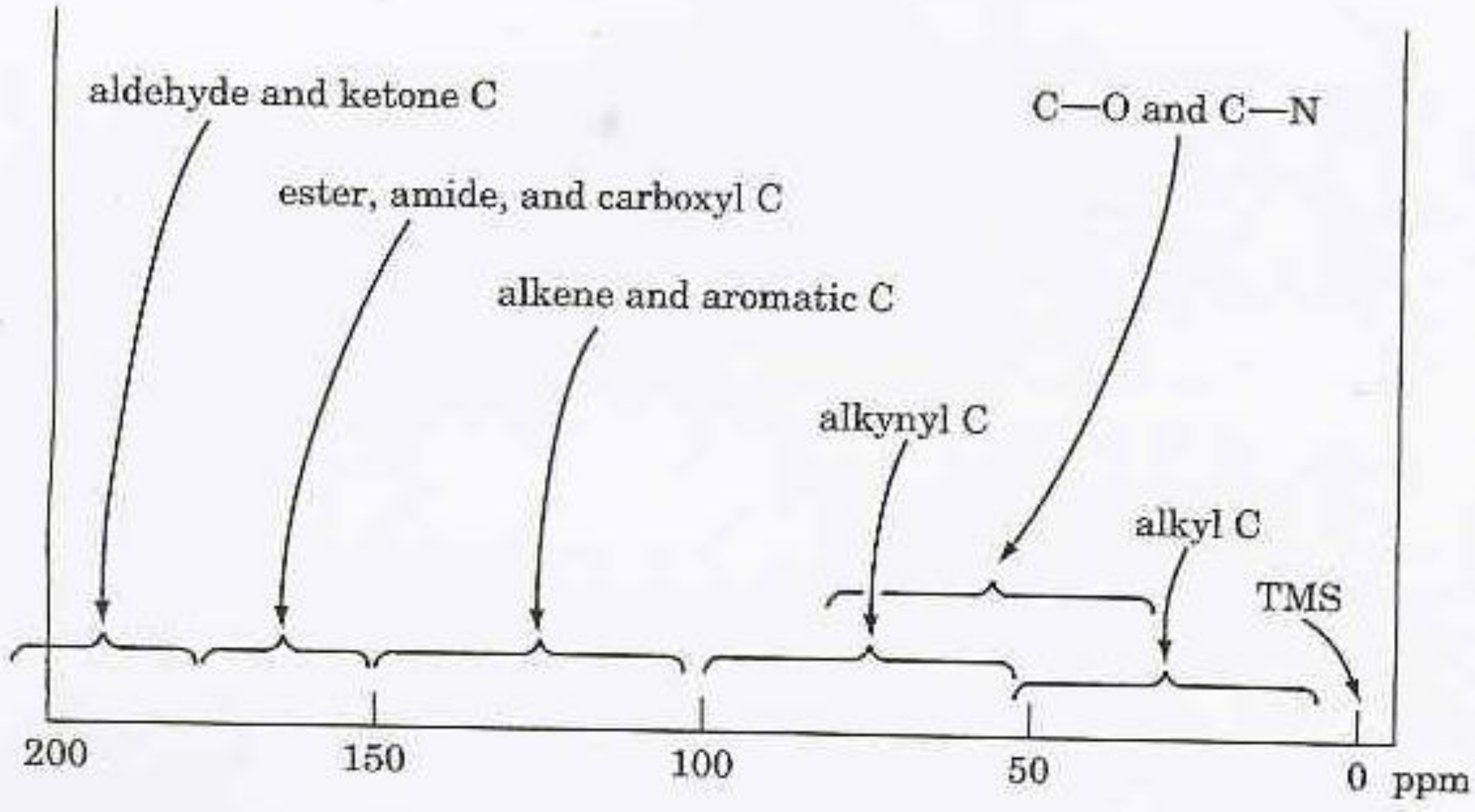


**Figure 9.46** Relative positions of $^{13}$C NMR absorption.

# Examples

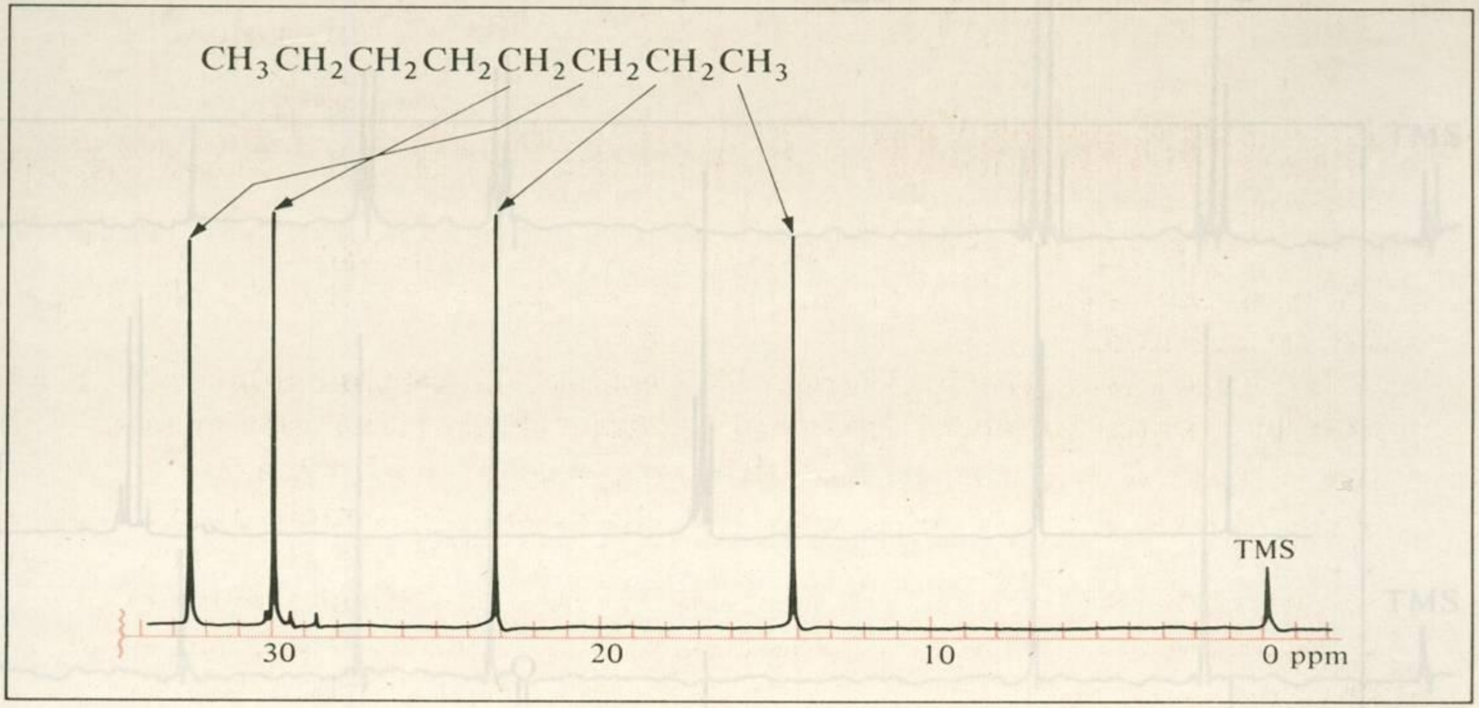
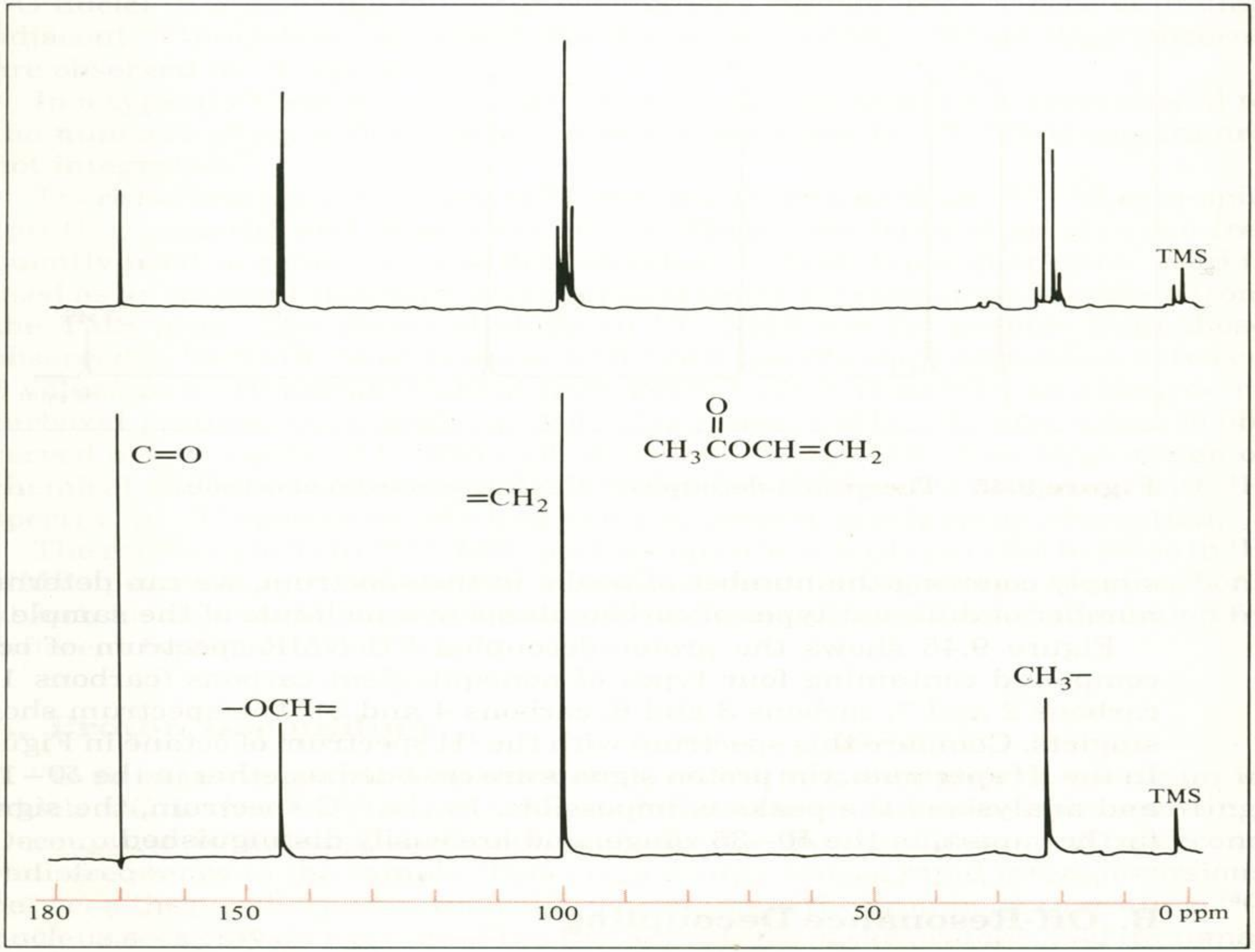
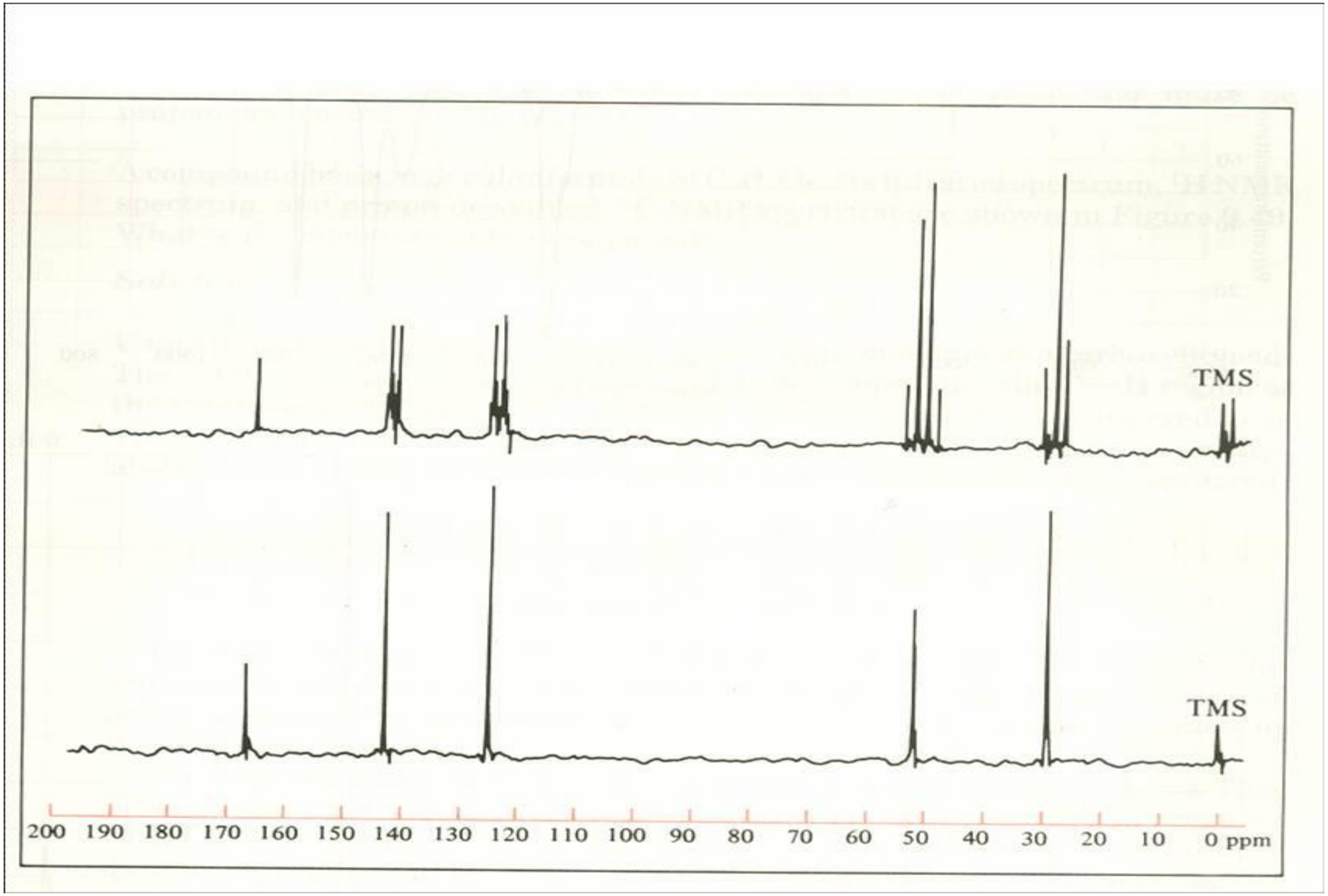


**Figure 9.45** The proton-decoupled $^{13}C$ NMR spectrum of octane.

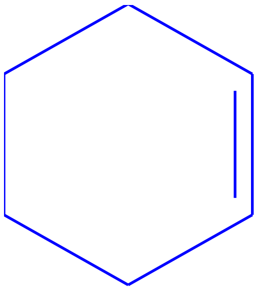

TMS
C=O
=CH$_2$
$CH_3COCH=CH_2$ (O above C)
−OCH=
CH$_3$−
TMS
180
150
100
50
0 ppm

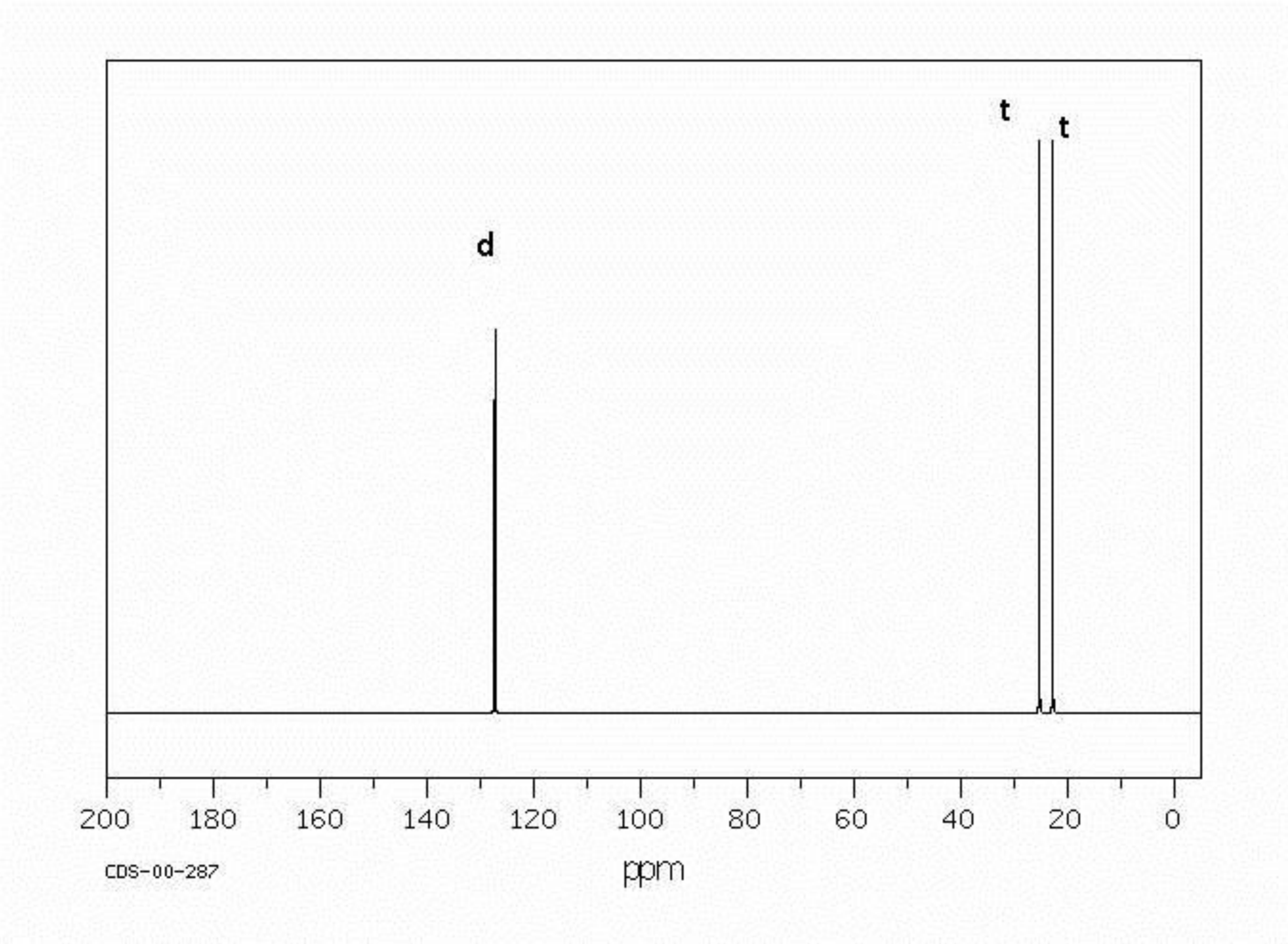
# $C_5H_7O_2Br$

$BrCH{=}CHCH_2\overset{\overset{\Large O}{\|}}{C}OCH_3$

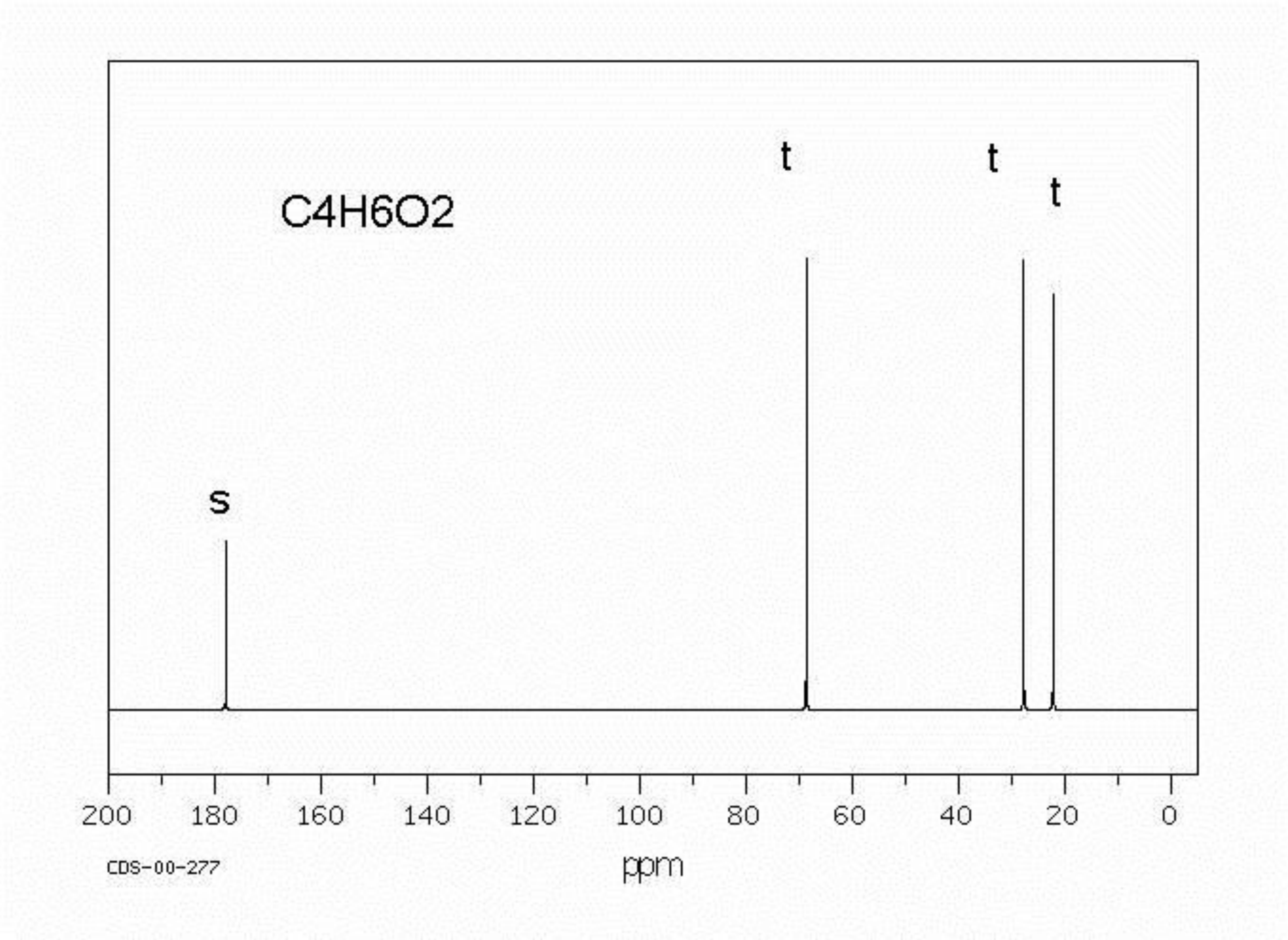


# $C_6H_{10}$





# $C_4H_6O_2$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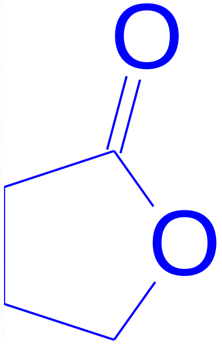
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# Lecture 1

# Mass Spectra

## Mass spectroscopy can be used can be used to:-

1) Measure relative molecular masses (molecular weights).

2) Detect the places in molecules at which it prefers to fragment.

## The principle of the mass spectroscopy:-

The function of mass spectrometer may be divided into four sections sample injection, ion generation, mass separation and ion detection.

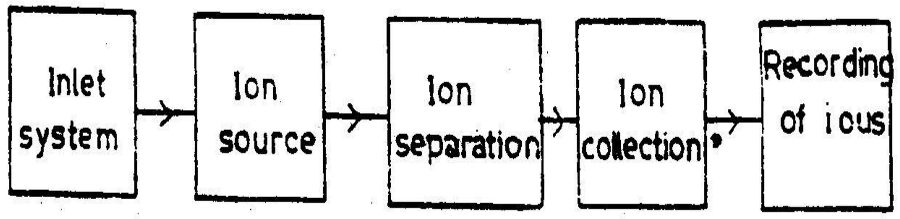


Fig. 1: Essential features of a mass spectrometer in diagrmmatic from.

## a- sample injection:-

There are two ways to inject the sample the spectrometer one is the gas inlet and the other is the direct inlet.

## gas inlet application:-

for liquid or gaseous sample, liquid can either be injected with micro syringe and it can be heated ( max. temperature during continuous service is usually 150$^{o}$c). Gaseous sample can be introduced into the reservoir though a container fitted with a break-seal, volatile substance via a gas chromatograph (GC) or liquid chromatograph (LC, HPLC).

**b- direct inlet application:-** crystalline, lacquer-like or viscous liquid samples. The sample is placed in a metal crucible, which is fixed on the tip of a heat able probe and the probe is inserted into a lock-chamber. After evacuating the chamber, the cold tip of the probe is brought into the ion source and slowly heated until the sample vaporizes.

**Ion generation:-** from one of the inlet system, a fine and constant beam of the molecules streams into the ion source where it intersect with an electron beam,

**where 60 to 100 eV can be used, although 70 eV is used for normally employed, the interaction between the electrons and the neutral molecules generates positively charged molecular ion according to:**

$$[M]\ -e^{-} \rightarrow [M]^{+\bullet} + 2e^{-}$$

**The various positive ions generated by electron impact are then accelerated through a second slit by a repelled potential applied between and (A) and (B)**

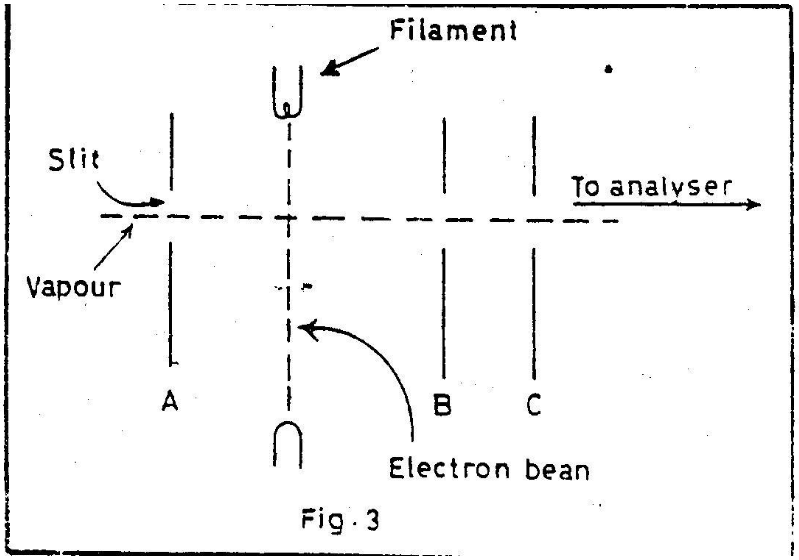


Fig · 3

**Finally, a large accelerator potential is applied between B and C, and the positive ion travel with a high velocity according to equation (1).**

**$\frac{1}{2} mv^{2} = ev$………..(1)**

**(m) is the mass of the ion, (e) the electronic charge, (v) the potential of the ion accelerating plate, and (v) the velocity of the particle.**

## Mass separation:-

**The accelerated ions then pass into the magnetic field (H) generated between the two poles of an electromagnetic in the magnetic field the ions are deflected along the circular path according to Eq. (2).**

**$r = mv/eH$ ………(2)**

**r is the radius of the path**

**From Eq. (1) and (2) we can deduce the Eq. (3)**

**$m/e = H^{2}r^{2}/2V$**

**From this we can conclude that, at given values of (H) and (V), only particles with a particular mass-to-charge will arrive at the collector slit placed along the fixed path (r) in recording mass spectra of organic compounds, most of the**

particles are singly charged, the radial paths of allowed by in the magnetic field are illustrated in Fig. (4)

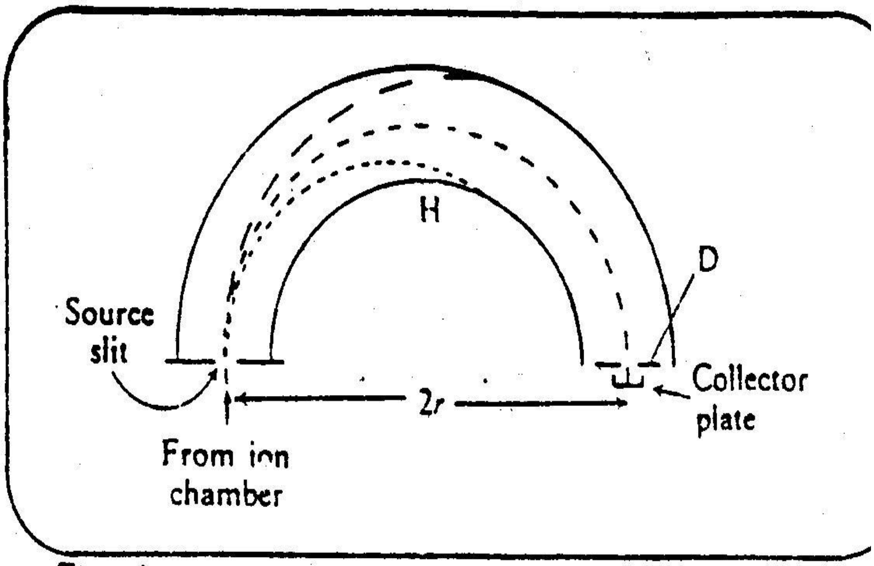


Fig.4:

# Lecture 2

## Determination of molecular formula

**The molecular weight of methyl bromide is 94.95 on chemical scale. But in mass spectra we can find the following molecular ion peaks according to isotopes occur. They called M, M+1, M+2, M+3,……..**

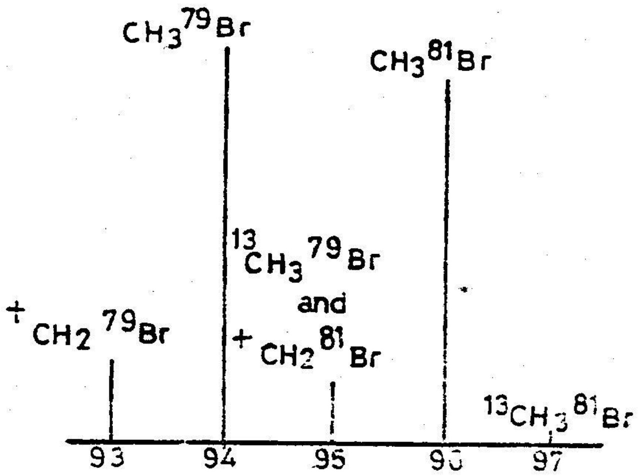
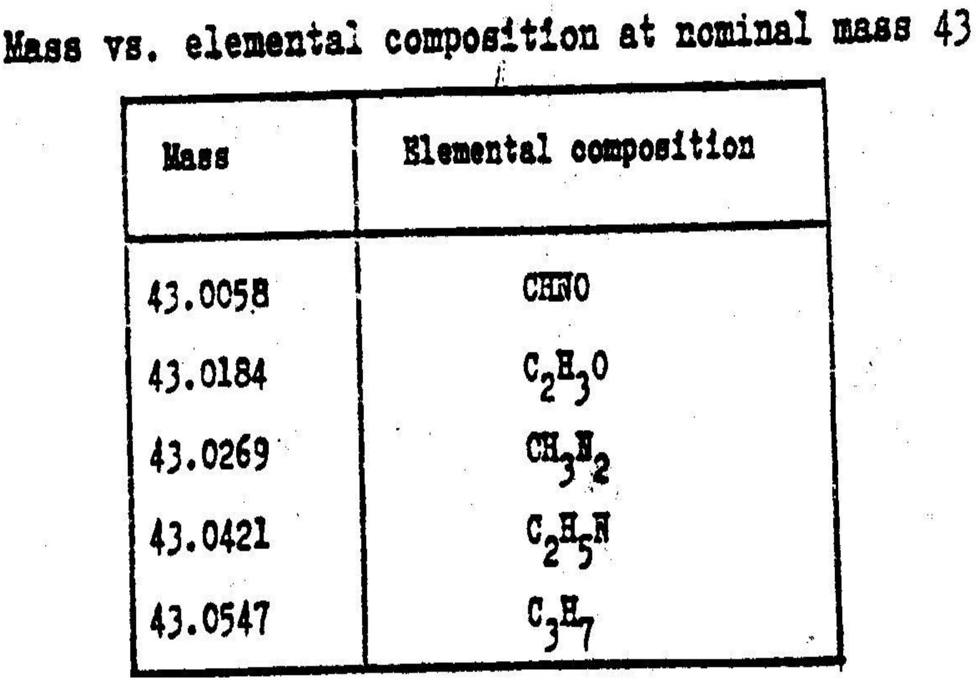


Fig. 8: Mass spectrum of methyl bromide in the region of the molecular ion.

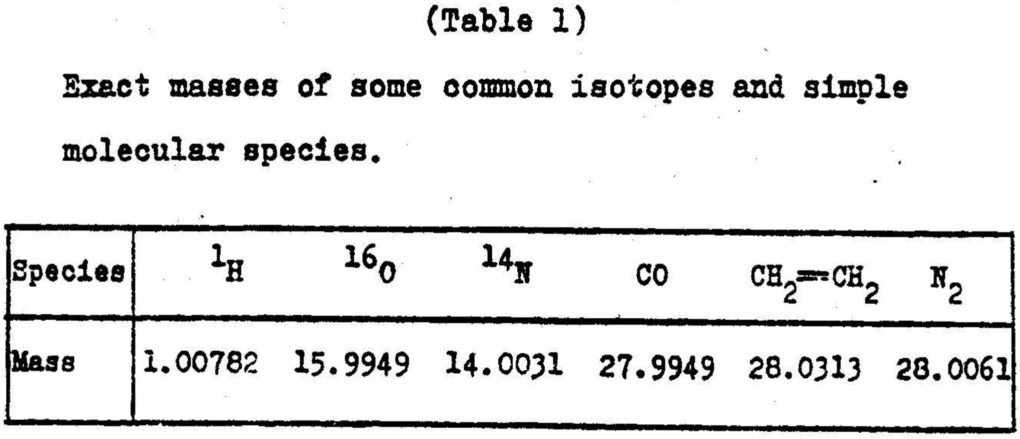
## Elemental composition at nominal mass 43



Mass vs. elemental composition at nominal mass 43

| Mass | Elemental composition |
|---|---|
| 43.0058 | $CHNO$ |
| 43.0184 | $C_2H_3O$ |
| 43.0269 | $CH_3N_2$ |
| 43.0421 | $C_2H_5N$ |
| 43.0547 | $C_3H_7$ |

## Elemental composition at nominal mass 28



(Table 1)

Exact masses of some common isotopes and simple molecular species.

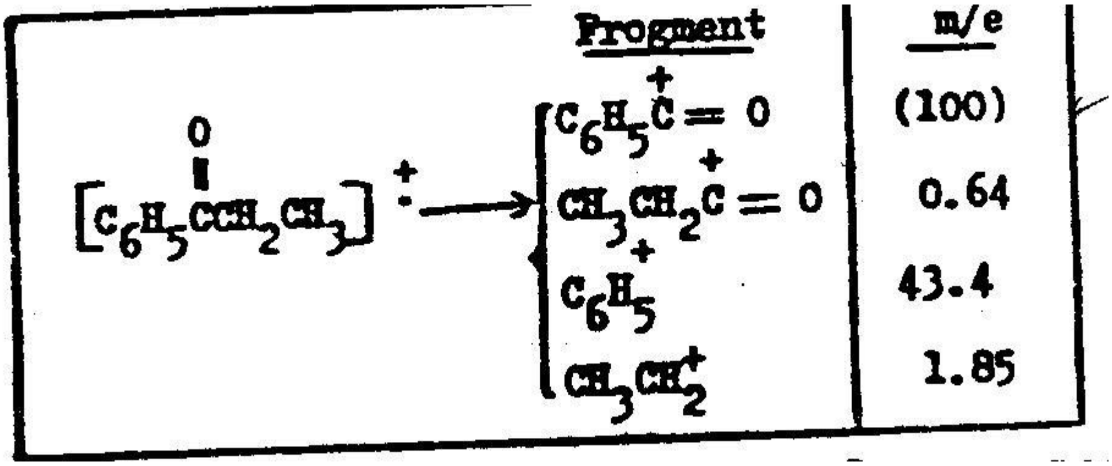
| Species | $^{1}H$ | $^{16}O$ | $^{14}N$ | $CO$ | $CH_2{=}CH_2$ | $N_2$ |
|---|---|---|---|---|---|---|
| Mass | 1.00782 | 15.9949 | 14.0031 | 27.9949 | 28.0313 | 28.0061 |

## Fragmentation

**Fragmentation are best interpreted based on the know stability of the carbonium ions and free radical.**

$$\begin{tikzcd} & A^{+} + B^{\cdot} \\ {[A\text{-}B]^{+\cdot}} \arrow[ur] \arrow[dr] & \\ & A^{\cdot} + B^{+} \end{tikzcd}$$

**In the cases where both A+ and B+ contions are of similar stability, the positive charge will reside with the highest-molecular weight cationic fragment. e.g. the following table:-**



$[C_6H_5\overset{O}{\overset{\|}{C}}CH_2CH_3]^{+\cdot} \longrightarrow$

| Progment | m/e |
|---|---|
| $C_6H_5\overset{+}{C}=O$ | (100) |
| $CH_3CH_2\overset{+}{C}=O$ | 0.64 |
| $\overset{+}{C_6H_5}$ | 43.4 |
| $CH_3CH_2^{+}$ | 1.85 |

**The C6H5O$^{+}$ ion at mass (105) in the spectrum of propiophenone can be characterized as (M-29) or the (M-C2H5) ion.**

## (i) The even-electron rule:-

**Even-electron spices will not fragment to two odd-electron species.**

$$\underset{\text{even}}{A^{+}} \not\longrightarrow \underset{\text{odd}}{\overset{+}{B}{}^{\cdot}} + \underset{\text{odd}}{C^{\cdot}}$$

**An ion will degrade to another ion and a neutral molecule.**

$$\underset{\text{even}}{A^{+}} \longrightarrow \underset{\text{even}}{B^{+}} + \underset{\text{even}}{C}$$

**Radical ion is odd-electron species so it will degrade to a radical ion and a neutral molecule.**

$$\underset{\text{odd}}{A^{+\cdot}} \longrightarrow \underset{\text{odd}}{B^{+\cdot}} + \underset{\text{even}}{C}$$

**Also radical ion also degrades to ion radical and ion.**

ion as coproduct

$$\overset{+}{A^{\cdot}} \longrightarrow \overset{+}{B^{\cdot}} + C$$

(odd) (odd)(even)

Radical ions can also degrade to a radical and an ion

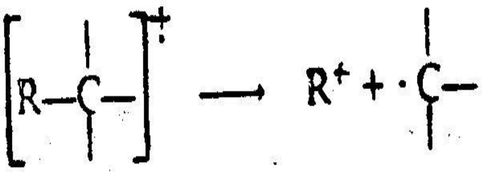
$$A^{\dot{+}} \text{ (odd)} \longrightarrow \begin{cases} B^{+} + C^{\cdot} & \text{(even) (odd)} \\ B^{\cdot} \quad C^{+} & \text{(odd) (even)} \end{cases}$$

# Lecture 3

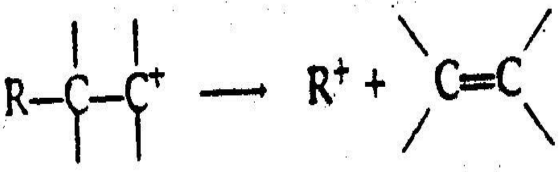
(ii) <u>Most of the important types of fragmentation</u> are summarized in general form below.

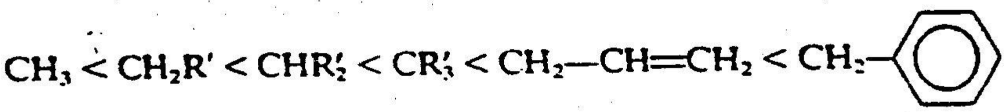
## A. Simple carbon-carbon bond cleavages

a.



b.





$$CH_3 < CH_2R' < CHR'_2 < CR'_3 < CH_2{-}CH{=}CH_2 < CH_2{-}C_6H_5$$

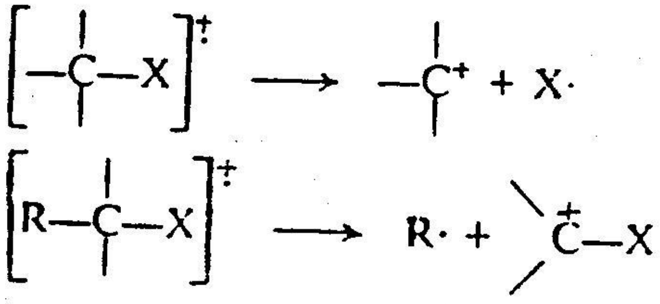
c.

$$\left[R-\overset{\overset{O}{\|}}{C}-R\right]^{\dot{+}} \longrightarrow R\cdot + R\overset{+}{C}{=}O$$

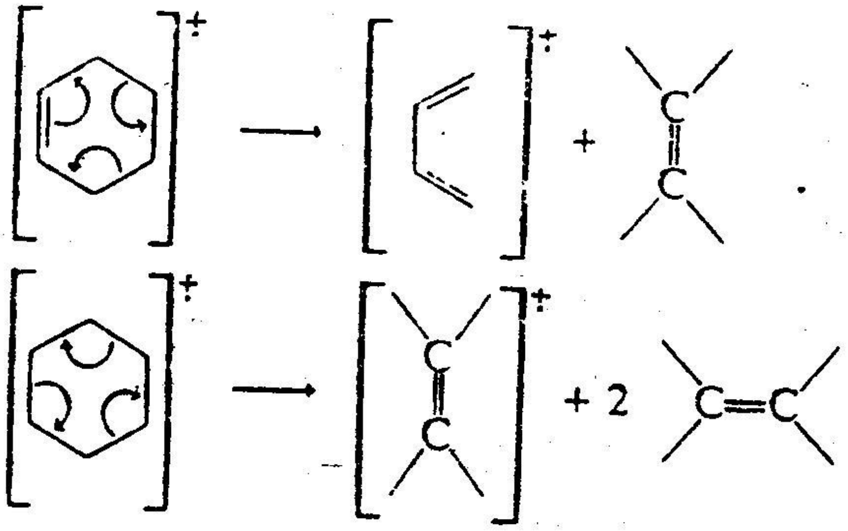
d. $R-\overset{+}{C}{=}O \longrightarrow R^{+} + C{=}O$

### B. Cleavages involving heteroatoms:

X = halogen, OR′, SR′, $NR'_2$ (R′ = H, Alkyl, Aryl)



### C. Concerted cleavages:



## (iii) Factors influencing fragmentation

### a) Functional groups:-

**Some functional groups may direct the course of fragmentation, while other functional groups may have little effect.**

### b) Thermal decomposition:-

**Thermal decomposition of some compounds may occur before ionization leading to difficulty in interpreting the mass spectra, alcohols may dehydrate before ionization, loss of water in this case leads to a peak at M-18.**

Whether the loss occurs before or after ionization, but thermal dehydration may extensive enough to eliminate entirely the appearance of a molecular ion in the spectrum.

If the thermal decomposition is suspected, the compound can be ionized in a cooled ion source, so that electron bombardment of the whole molecule takes place.

## c) Bombardment energies:-

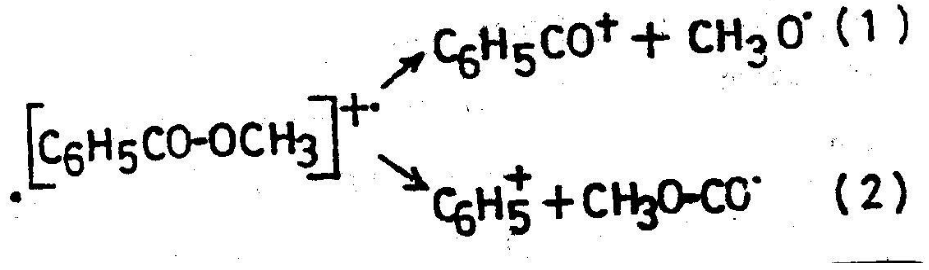
≈ 70 eV is used for ordinary spectra, molecular ions posses a maximum of ≈ 6 eV in excess of their ionization potentials, if this energy is reduced to ≈ 20 eV it will be sufficient for giving weaker spectra for the organic molecules.

## d) Relative rates of competing fragmentation routes:-

The formation of $B^+$ and $C^\cdot$ or $B^{+\cdot}$ and C from the molecular ion $A^{+\cdot}$ depends on the excitation energy possessed by $A^{+\cdot}$ and the heats of formation of all the products.

## e) Stability of fragmentation products:-

An ion fragments when it possesses an excess internal energy sufficient to exceed the activation energy for the reaction considered. (See the following figure)



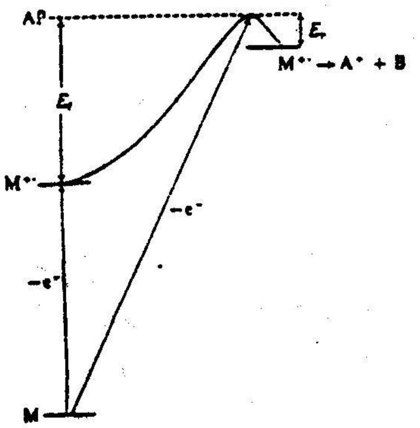


Fig. 9: Energy diagram showing the relationship between the activation energies ($E_f$, $E_r$) for the forward and backward reactions in the decomposition of the ion ($M^{+\cdot}$) to fragments ($A^{+}$, $B^{\cdot}$). The appearance potentail for the process is marked (AP).

**The activation energy for the reverse reaction ($E_r$) is very small.**

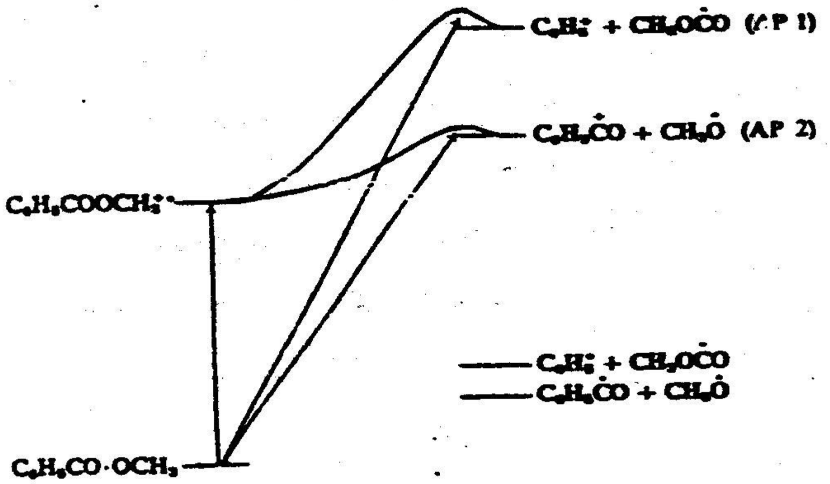


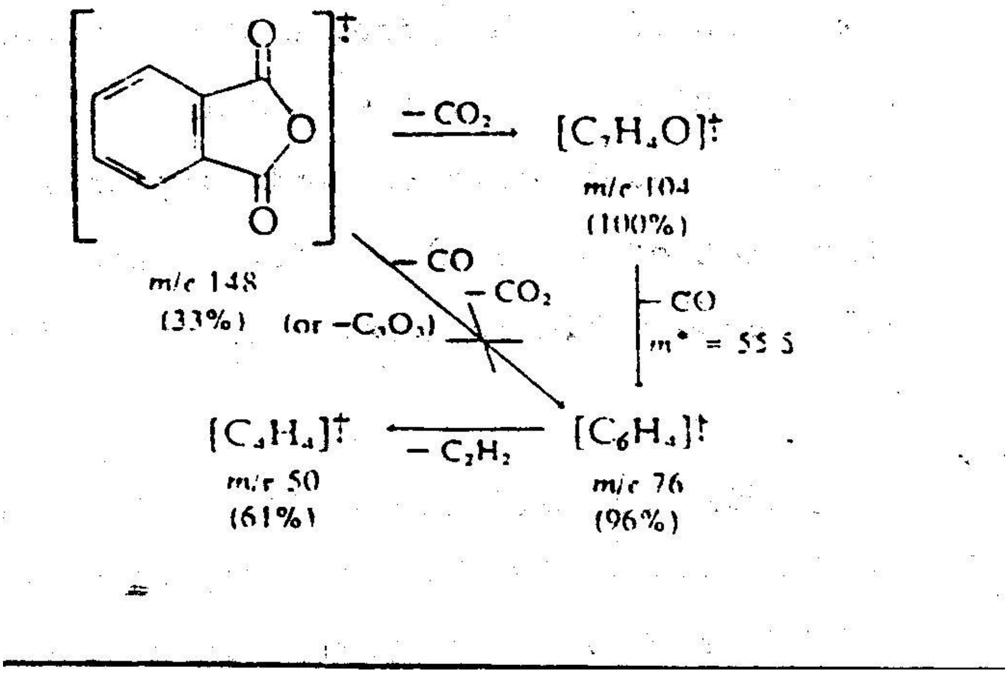
Fig-10: Energy diagram showing relation between competing fragmentation processes from one state of the molecular ion of methyl benzoate. The appearance potentials (AP1, AP 2) relate to the two reactions.

# Lecture 4

## IV- Metastable peak

**Metastable peaks are very important in the deduction of fragmentation mechanisms because they indicate that the fragment of the mass ($m_2$) is formed in a one-step process from ($m_1$) will decompose into fragments while traveling through the accelerating region of the instruments. Such ions will at first be accelerated as ($m_1$), decompose with loss of some kinetic energy to the neutral fragment, and then continue to be accelerated and deflected as ($m_2$). Which appear as abroad peak of low intensity (m*).**

$$m^* = (m_2)^2/(m_1)$$



**In the above example the metastable peak**

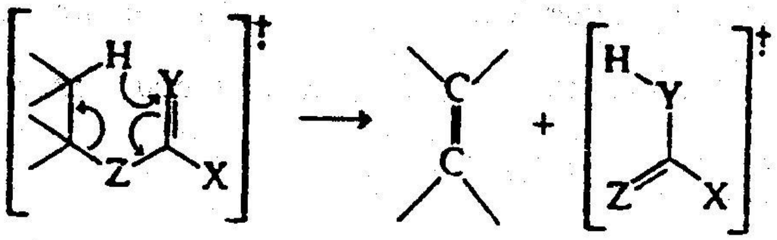
**(m*) at 55.5, this mean that the ion at m/e=76 ($m_2$) formed from the m/e 104 ($m_1$) ion and not by concerted loss of carbon monoxide and carbon dioxide from the molecular ion.**

## V-Rearrangements

**There are fragment peaks in the mass spectra which can not be interpreted by the simple methods of the normal cleavage. So there are some specific rearrangements occur to molecules as follow:-**

**<u>a- McLafferty rearrangement:-</u>**

**This type of rearrangement involves migration of hydrogen to π-electron system via a six-membered ring transition state.**

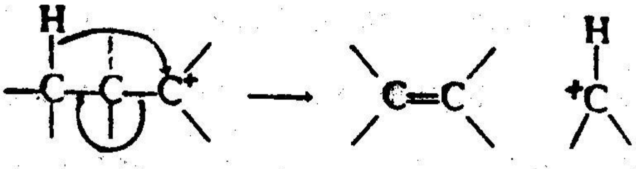


**X, Y, and Z can be O, N, C, S, and any combinations thereof.**

**<u>b- 1,3-migration in carbonium ions:-</u>**

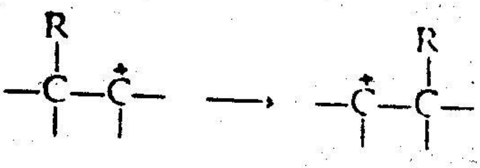
**This involves migration of hydrogen atom from C4 to C3 in the same molecule with elimination of an alkane.**

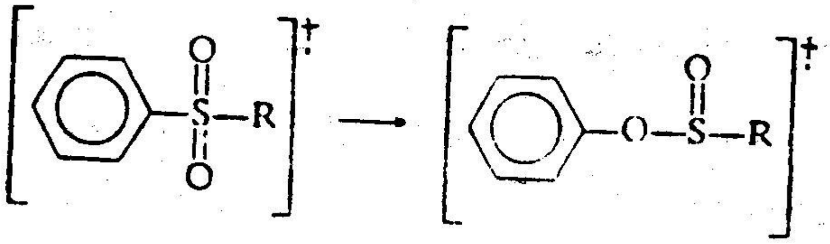
**(ii) Carbenium ions undergo 1,3 migrations with elemination of an alkene.**



**<u>c)- 1,2- shifts:-</u>**

**This type of rearrangement is to formation more stable species.**





The most famous rearrangement of this type is the formation of tropoylium ion before loss of hydrogen atom, thus tropoylium ion $C_7H_8^{+\cdot}$ has equivalent hydrogen, when it loses one hydrogen atom it converts to the most abundant ion $C_7H_7^{+}$ of mass (91) according to the following:-