



*REVIEW ARTICLE*

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**INTERPRETATION OF STRUCTURE IN ORGANIC CHEMISTRY BY  
MISCELLANEOUS TECHNIQUE**

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**Abstract:** Now a day, many molecules come in to the market. There are many methods for the synthesis of newer molecule and hence there is a chance of the impurities in the synthesis of newer molecule. So it is a challenge to the scientist to find out the impurities present in to the synthesis. For finding out the physical and chemical properties of this impurities and newer synthesized molecule, it has to find out the structure of that particular. We cannot interpret the structure with only one method; we have to use many methods like UV, IR, MASS, HPLC and NMR or any other combination of these methods like LC-NMR, MS-MS, LC-MS. Now a day, one another challenge is to find out the structure of degradants in to the formulation and it can also to find out by above methods.

**Keywords:** UV, IR, MASS, HPLC, NMR, LC-NMR, MS-MS, LC-MS.

## INTRODUCTION

### 1) HYDROGEN DEFICIENCY INDEX:

Hydrogen deficiency Index indicate the number of unsaturated bond present in to the structure and it can be calculated with the following formula

Hydrogen Deficiency Index =

$$C - \frac{H}{2} - \frac{X}{2} + \frac{N}{2} + 1$$

### 2) IR SPECTROSCOPY<sup>1-4</sup>:

IR Spectroscopy is the most important tools for the determination of the functional group. Fingerprint region is the most important for the interpretation of the functional group. Every functional group having its own characteristic IR band and hence it can be easily identified. The various functional group bands are given below.

#### ALKANES

- C-H  $sp^3$  C-H absorption always occurs at frequencies 3000 – 2840  $cm^{-1}$
- $CH_2$  Methylene groups have a characteristic bending absorption of approximately 1375  $cm^{-1}$
- $CH_3$  Methyl groups have a characteristic bending absorption of

approximately 1375  $cm^{-1}$

- $CH_2$  The bending (rocking) motion associated with four or more  $CH_2$  groups in an open chain occurs at about 720  $cm^{-1}$
- C-C Many weak peaks

#### ALKENES

- =C-H Stretch for  $sp^2$  C-H occurs at values 3095 – 3010  $cm^{-1}$
- =C-H Out-of-plane (omp) bending occurs in the range 1000-650  $cm^{-1}$
- C=C Stretch occurs at 1660 – 1600  $cm^{-1}$

#### ALKYNES

- $\equiv$ C-H Stretch for  $sp$  C-H usually occurs near 3300  $cm^{-1}$
- C $\equiv$ C Stretch occurs near 2150  $cm^{-1}$

#### AROMATIC RINGS

- =C-H Stretch for  $sp^2$  C-H occurs at values 3050 – 3010  $cm^{-1}$
- =C-H bending occurs at 900-690  $cm^{-1}$
- C=C Ring stretch absorption often occur in pairs at 1600  $cm^{-1}$  and 1475  $cm^{-1}$

#### ALCOHOLS AND PHENOLS

- O-H The free O-H stretch is a sharp peak at 3650 – 3600  $cm^{-1}$

- C-O-H Bending appears as a broad and weak peak at  $1440 - 1220 \text{ cm}^{-1}$
- C-O Stretching vibrations usually occurs in the range of  $1260 - 1000 \text{ cm}^{-1}$

### ETHERS

- C-O The most prominent band is due to C-O stretch,  $1300-1000 \text{ cm}^{-1}$

### ALDEHYDES

- R-CH=O C=O stretch appears in range  $1740-1725 \text{ cm}^{-1}$  for normal aliphatic Aldehydes
- C=C-CH=O Conjugation of C=O with C=C;  $1700-1680 \text{ cm}^{-1}$  for C=O and  $1640 \text{ cm}^{-1}$  for C=C
- Ar-CH=O Conjugation of C=O with phenyl;  $1700-1660 \text{ cm}^{-1}$  for C=O and  $1600-1450 \text{ cm}^{-1}$  for ring
- Ar-C=CH=O Longer conjugated system  $1680 \text{ cm}^{-1}$
- C-H Stretch, aldehyde hydrogen (-CHO), consists of a pair of weak bands one at  $2860 - 2800 \text{ cm}^{-1}$  and the other at  $2760-2700 \text{ cm}^{-1}$

### KETONES

- R<sup>2</sup>-C=O C=O stretch appears in range  $1720 - 1708 \text{ cm}^{-1}$  for normal aliphatic Ketones

- C=C-C Conjugation of C=O with C=C;  $1700-1675 \text{ cm}^{-1}$
- Ar-C=O-R Conjugation of C=O with phenyl;  $1700-1680 \text{ cm}^{-1}$

### CARBOXYLIC ACIDS

- O-H Stretch usually very broad, occurs at  $3400 - 2400 \text{ cm}^{-1}$
- C=O Stretch, broad, occurs at  $1730 - 1700 \text{ cm}^{-1}$
- C-O Stretch occurs in the range  $1320 - 1210 \text{ cm}^{-1}$

### ESTERS

- R-C=OOR C=O stretch appears in range  $1750-1735 \text{ cm}^{-1}$
- C=C-C=OOR  $1740 - 1715 \text{ cm}^{-1}$  for C=O and  $1640-1625 \text{ cm}^{-1}$  for C=C
- Ar-C=OOR  $1740-1715 \text{ cm}^{-1}$  for C=O and  $1600-1450 \text{ cm}^{-1}$
- R-C=OO-C=C Conjugation of single bonded oxygen atom with C=C or phenyl  $1765 - 1762 \text{ cm}^{-1}$  for C=O
- O-C=O Cyclic esters (lactones); C=O frequency increases with decreasing ring size
- C-O Stretch in two or more bands, one stronger and broader than the other, occurs in the range  $1300 - 1000 \text{ cm}^{-1}$

### AMIDES

- C=O Stretch occurs approximately 1680 – 1630  $\text{cm}^{-1}$
- N-H Stretch in primary amides ( $-\text{NH}_2$ ) gives two bands near 3350 and 3180  $\text{cm}^{-1}$ . Secondary amides have one band ( $-\text{NH}$ ) at 3300  $\text{cm}^{-1}$
- N-H Bending occurs around 1640 – 1550  $\text{cm}^{-1}$  for primary and secondary amides.

### ACID CHLORIDES

- C=O Stretch occurs in the range 1810 – 1775  $\text{cm}^{-1}$  in unconjugated chlorides. Conjugation lowers the frequency to 1780 – 1760  $\text{cm}^{-1}$
- C-Cl Stretch occurs in the range 730 – 550  $\text{cm}^{-1}$

### ANHYDRIDES

- C=O Stretch always has two bands, 1830 – 1800  $\text{cm}^{-1}$  and 1775 – 1740  $\text{cm}^{-1}$
- C-O Stretch (multiple bands) occurs in the range 1300 – 900  $\text{cm}^{-1}$

### AMINES

- N-H Stretch occurs in the range 3500 – 3000  $\text{cm}^{-1}$
- N-H Bend in primary amines results in a broad band in the range 1640-1560  $\text{cm}^{-1}$
- N-H out of plane bending absorption can sometimes be observed near 800  $\text{cm}^{-1}$

- C-N Stretch occurs in the range 1350 – 1000  $\text{cm}^{-1}$

### NITRILES

- $-\text{C}\equiv\text{N}$  Stretch is of medium intensity, sharp absorption near 2250  $\text{cm}^{-1}$

### ISOCYANATES

- $-\text{N}=\text{C}=\text{S}$  Stretch in an isocyanate gives a broad, intense absorption near 2270  $\text{cm}^{-1}$

### IMINES

- C=N Stretch in an imine, oxime, and so on gives a variable-intensity absorption in the range 1690-1640  $\text{cm}^{-1}$

### NITRO COMPOUNDS

O=N=O Aliphatic nitro compounds : asymmetric stretch (strong), 1600-1530  $\text{cm}^{-1}$ ; symmetrical stretch (medium), 1390-1300  $\text{cm}^{-1}$  Aromatic nitro compounds (conjugated): asymmetric stretch (strong) 1550 – 1490  $\text{cm}^{-1}$  ; symmetric stretch (strong), 1355 – 1315  $\text{cm}^{-1}$

### CARBOXYLATE SALTS

- O=C=O Asymmetric stretch (strong) occurs near 1600  $\text{cm}^{-1}$

Symmetrical stretch (strong) occurs near 1400  $\text{cm}^{-1}$

### AMINE SALTS

- N-H Stretch (broad) occurs at 3300-2600  $\text{cm}^{-1}$

- N-H Bend (strong) occurs at 1610 – 1500  $\text{cm}^{-1}$

### AMINO ACIDS

These compounds exist as zwitterions (internal salts) and exhibit spectra that are combinations of carboxylate and primary amine salts. Amino acids show  $\text{NH}_3^+$  stretch (very broad), N-H bend (asymmetric/symmetric), and  $\text{COO}^-$  stretch (asymmetric/symmetric)

### SULFUR COMPOUNDS

#### MERCAPTANS

S-H Stretch, one weak band, occurs near 2550  $\text{cm}^{-1}$  and virtually confirms the Presence of this group.

#### SULPHIDES

- R-S-R Little useful information is obtained from the IR

#### SULFOXIDES

- S=O Stretch, one strong band, occurs near 1050  $\text{cm}^{-1}$

#### SULFONES

- C=O Asymmetric stretch (strong) occurs at 1300  $\text{cm}^{-1}$   
Symetric stretch (strong) at 1150  $\text{cm}^{-1}$

### SULFONYL CHLORIDES

- S=O Asymmetric stretch (strong) occurs at 1375  $\text{cm}^{-1}$

Symmetric stretch (strong) at 1185  $\text{cm}^{-1}$

### SULFONATES

- S=O Asymmetric stretch (strong) occurs at 1350  $\text{cm}^{-1}$ ,

Symmetric stretch (strong) at 1175  $\text{cm}^{-1}$

- S-O Stretch, several strong bands, occurs in the range 1000 – 750  $\text{cm}^{-1}$

### SULFONAMIDES

- S=O Asymmetric stretch (strong) occurs at 1325  $\text{cm}^{-1}$

Symmetric stretch (strong) at 1140  $\text{cm}^{-1}$

- N-H Primary stretch occurs at 3350 and 3250  $\text{cm}^{-1}$ , Secondary stretch occurs at 3250  $\text{cm}^{-1}$ ; bend occurs at 1550  $\text{cm}^{-1}$

### SULFONIC ACIDS

- S=O Asymmetric stretch (strong) occurs at 1325  $\text{cm}^{-1}$

Symmetric stretch (strong) at 1140  $\text{cm}^{-1}$

### PHOSPHORUS COMPOUNDS

#### PHOSPHINES

- P-H Stretch, one strong, sharp band at 2320 – 2270  $\text{cm}^{-1}$

- $\text{PH}_2$  Bend, Medium bands, at 1090 – 1075  $\text{cm}^{-1}$  and 840 – 810  $\text{cm}^{-1}$

- P-H Bend, Medium band, at 990 – 885  $\text{cm}^{-1}$
- P-CH<sub>3</sub> Bend, medium bands, at 1450-1395  $\text{cm}^{-1}$  and 1346 – 1255  $\text{cm}^{-1}$
- P-CH<sub>2</sub> Bend, medium band, at 1440 – 1400  $\text{cm}^{-1}$

#### PHOSPHINE OXIDES

- P=O Stretch, one very strong band, at 1300 – 1240  $\text{cm}^{-1}$

#### PHOSPHATE ESTERS

- P=O Stretch, one very strong band, at 1300 – 1240  $\text{cm}^{-1}$
- R-O Stretch

#### ALKYL AND ARYL HALIDES

##### FLUORIDES

- C-F Stretch (strong) at 1400 – 1000  $\text{cm}^{-1}$   
Aryl fluorides absorb between 1250 and 1100  $\text{cm}^{-1}$

##### CHLORIDES

- C-Cl Stretch (strong) in aliphatic chlorides occurs in the range 785 -540  $\text{cm}^{-1}$   
Aryl chlorides absorb between 1100 and 1035  $\text{cm}^{-1}$
- CH<sub>2</sub> – Cl Bend (wagging) at 1300 -1230  $\text{cm}^{-1}$

##### BROMIDES

- C-Br Stretch (strong) in aliphatic bromides occurs at 650 – 510  $\text{cm}^{-1}$   
Aryl bromides absorb between 1075 and 1030  $\text{cm}^{-1}$
- CH<sub>2</sub>-Br Bend (wagging) at 1250 – 1190  $\text{cm}^{-1}$

##### IODIDES

- C-I Stretch (strong) in aliphatic iodides occurs at 600 – 485  $\text{cm}^{-1}$
- CH<sub>2</sub>-I Bend (wagging) at 1200 – 1150  $\text{cm}^{-1}$

#### 3) MASS Spectroscopy<sup>5-7</sup>

Mass spectroscopy is a powerful analytical technique for identifying the unknown compounds by determining their molecular weights, for qualitative and quantitative determination (bulk, surface and depth analysis) of trace and ultra trace levels of organic compounds and inorganic elements in different matrices and for understanding the physical and chemical properties of different molecules<sup>1</sup>.

**Common Fragment Ions and Neutral Fragments**

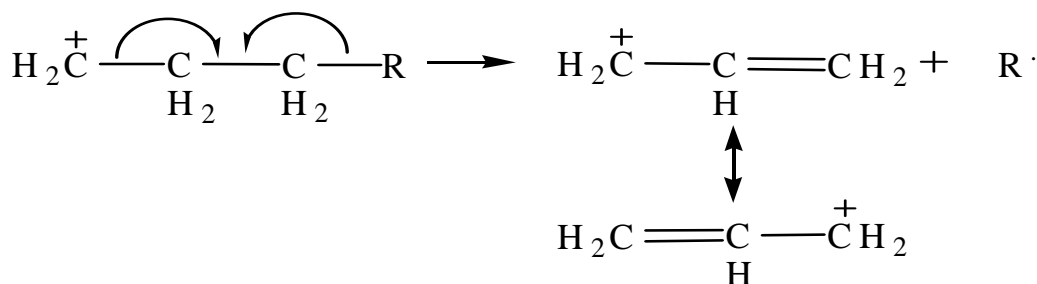
Common Small Ions		Common Neutral Fragments	
m/z	Composition	mass loss	composition
15 amu	CH <sub>3</sub>	1 amu	H
17	OH	15	CH <sub>3</sub>
18	H <sub>2</sub> O	17	OH
19	H <sub>3</sub> O, F	18	H <sub>2</sub> O
26	C <sub>2</sub> H <sub>2</sub> , CN	19	F
27	C <sub>2</sub> H <sub>3</sub>	20	HF
28	C <sub>2</sub> H <sub>4</sub> , CO, H <sub>2</sub> CN	27	C <sub>2</sub> H <sub>3</sub> , HCN
29	C <sub>2</sub> H <sub>5</sub> , CHO	28	C <sub>2</sub> H <sub>4</sub> , CO
30	CH <sub>2</sub> NH <sub>2</sub>	30	CH <sub>2</sub> O
31	CH <sub>3</sub> O	31	CH <sub>3</sub> O
33	SH, CH <sub>2</sub> F	32	CH <sub>4</sub> O, S
34	H <sub>2</sub> S	33	CH <sub>3</sub> + H <sub>2</sub> O, HS
35(37)*	Cl	33	H <sub>2</sub> S
36(38)*	HCl	35(37)*	Cl
39	C <sub>3</sub> H <sub>3</sub>	36(38)*	HCl
41	C <sub>3</sub> H <sub>5</sub> , C <sub>2</sub> H <sub>3</sub> N	42	C <sub>3</sub> H <sub>6</sub> , C <sub>2</sub> H <sub>2</sub> O, C <sub>2</sub> H <sub>4</sub> N
42	C <sub>3</sub> H <sub>6</sub> , C <sub>2</sub> H <sub>2</sub> O, C <sub>2</sub> H <sub>4</sub> N	43	C <sub>3</sub> H <sub>7</sub> , CH <sub>3</sub> CO
43	C <sub>3</sub> H <sub>7</sub> , CH <sub>3</sub> CO	44	CO <sub>2</sub> O, CONH <sub>2</sub>
44	C <sub>2</sub> H <sub>4</sub> O	45	C <sub>2</sub> H <sub>5</sub> O
46	NO <sub>2</sub>	55	C <sub>4</sub> H <sub>7</sub>
56	C <sub>4</sub> H <sub>8</sub>	57	C <sub>4</sub> H <sub>9</sub>
57	C <sub>4</sub> H <sub>9</sub>	59	C <sub>2</sub> H <sub>3</sub> O <sub>2</sub>
60	CH <sub>4</sub> CO <sub>2</sub>	60	C <sub>2</sub> H <sub>4</sub> O <sub>2</sub>
79(81)*	Br	64	SO <sub>2</sub>
80(82)*	HBr	79(81)*	Br
91	C <sub>7</sub> H <sub>7</sub>	80(82)*	HBr
127	I	127	I
128	HI	128	HI

**General rules for predicting prominent peaks in EI spectra**

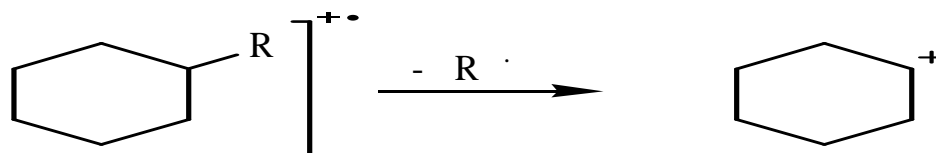
1. The relative height of the molecular ion peak is greatest for the straight chain compound and decreases as the degree of branching increases.

2. The relative height of molecular ion peak usually decreases with increasing molecular weight in a homologous series (Fatty acid esters are exception).

3. Cleavage is favored at alkyl-substituted carbon, the more substituted carbon – the more likely is the cleavage. This is because of the stability of the cation formed.



6. Saturated rings tend to lose alkyl side chains at the  $\alpha$  – bond. The positive charge tends to stay with ring.



Unsaturated rings can undergo a retro Diels – Alder reaction.

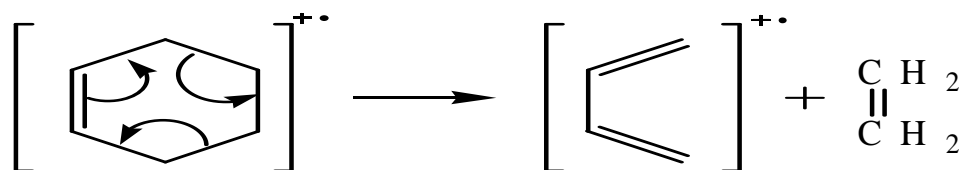
Cation stability order  $^+\text{CH}_3 < \text{R}'\text{-CH}_2^+ < \text{R}'_2\text{CH}^+ < \text{R}'_3\text{C}^+$ .

Generally a largest substituent at a branch is eliminated as radical.

4. Double bonds, cyclic structures and especially aromatic rings stabilize the molecular ion and thus increase the probability of its appearance.

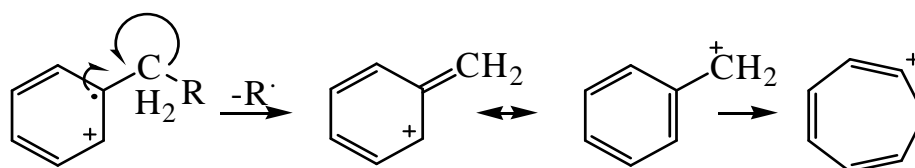
5. Double bonds favor allylic cleavage and give the resonance stabilized allylic carbocation.





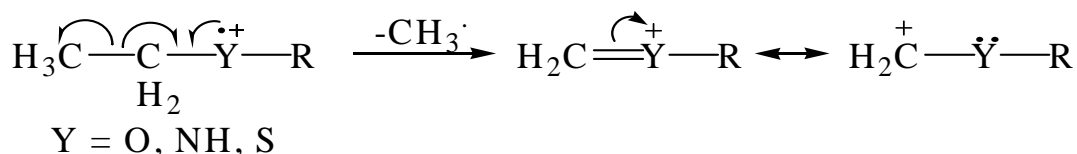
7. In alkyl substituted aromatic compounds, cleavage is very probable at the bond  $\beta$  to the ring giving rise a

resonance stabilized benzyl cation or more likely the tropylium ion.



8. The C – C bonds next to heteroatoms are frequently cleaved leaving the charge on the fragment containing the heteroatoms,

where non-bonding electrons provide resonance stabilization.



9. Cleavage is often associated with elimination of small stable natural molecules such as CO, H<sub>2</sub>O, NH<sub>3</sub>, H<sub>2</sub>,

HCN, ketene, alcohols, olefins etc. with rearrangements.

Nitrogen rule: Nitrogen atom has even aromatic weight and odd valency Other elements have both odd or even.

integral molecular weight. This is called nitrogen rule.

#### 4) NMR Spectroscopy<sup>8-11</sup>:

Due to this reason molecules containing an odd number of nitrogen atoms have odd integral molecular weight. Those with no nitrogen or even nitrogen have even

NMR spectroscopy is powerful for structure elucidation / however degradation and impurity product analysis is difficult on the micro scale.

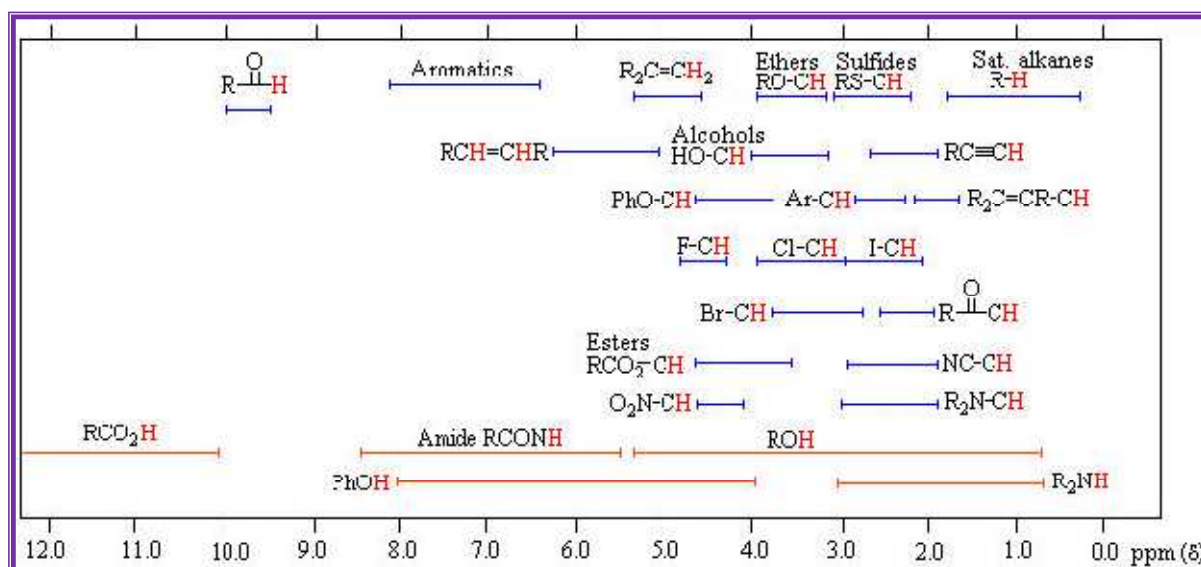
There are two types of NMR Spectroscopy:

➤  $^1\text{H}$  NMR Spectroscopy➤  $^{13}\text{C}$  NMR Spectroscopy

$^1\text{H}$  NMR Spectroscopy gives information about the hydrogen atom environment whereas  $^{13}\text{C}$  NMR Spectroscopy gives information about the carbon atom environment.

**Chemical shift** is a function of the nucleus and its environment. The difference of

absorption frequencies between protons is very small (in Hz) compared to the applied field (MHz). Therefore, chemical shifts expressed in parts per million (ppm). It is measured relative to a reference compound. For  $^1\text{H}$  NMR, the reference is usually 0 ppm for tetramethylsilane,  $\text{Si}(\text{CH}_3)_4$ .

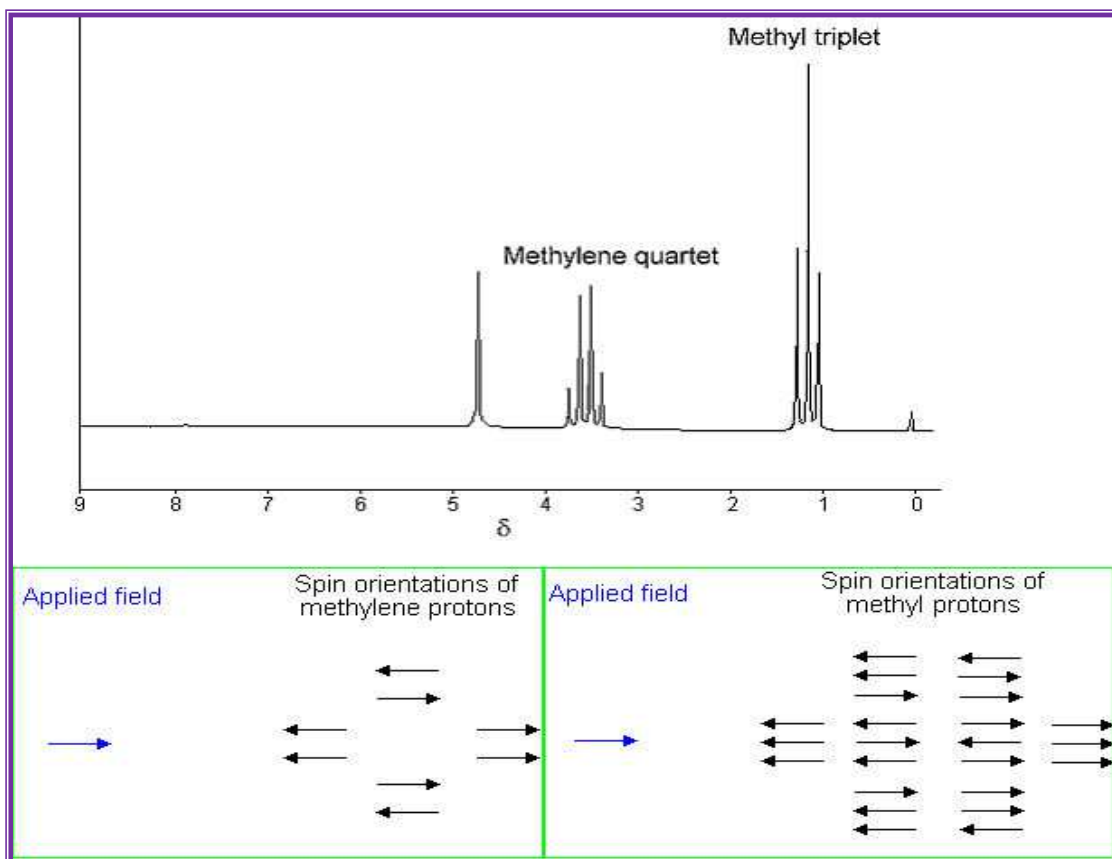


Some standard ranges of  $^1\text{H}$  NMR chemical shifts in organic compounds.

**Splitting** patterns is quite straightforward;

The multiplicity of a multiplet is given by the number of equivalent protons in neighbouring atoms plus one, i.e. the  $n + 1$  rule.

For example, in the  $^1\text{H}$  NMR spectrum of ethanol (below) the methyl peak has been split into three peaks (a triplet) and the methylene peak has been split into four peaks (a quartet) due to spin-spin coupling.



**C<sup>13</sup> NMR Spectroscopy:**

C<sup>13</sup> NMR Spectroscopy gives the information about the carbon atom environment. The basic different between the C<sup>13</sup> and H<sup>1</sup> NMR Spectroscopy is the delta value is higher than H<sup>1</sup> NMR Spectroscopy and Splitting due to the adjacent carbon atom rather than proton. The delta value for the functional group are given below

<b>R-CH<sub>3</sub></b>	<b>8 – 30</b>
<b>R<sub>2</sub>-CH<sub>2</sub></b>	15 – 55
<b>R<sub>3</sub>-CH</b>	20 – 60
<b>C-I</b>	0 – 40
<b>C-Br</b>	25 – 65
<b>C-Cl</b>	35 – 80
<b>C-N</b>	30 – 65
<b>C-O</b>	40 – 80
<b>C≡C</b>	65 – 90
<b>C=C</b>	100 – 150
<b>C≡N</b>	100 – 140
<b>Benzene</b>	110 – 175
<b>RCOOR</b>	155 – 185
<b>RCOOH</b>	155 – 185
<b>RCONH<sub>2</sub></b>	155 – 185
<b>RCHO</b>	185 - 220
<b>RCOR</b>	185 - 220

### REFERNCES

1. Sharma BK: Instrumental methods for chemical analysis, Goel publication house, Meera: 193-333.
2. Pavia and Lampman: Introduction to Spectroscopy, third edition: 13- 82.
3. Robert MS: Spectroscopic Identification of organic compounds. Seventh edition: 72 – 108.
4. Skoog: Principal of instrumental analysis, second edition: 209-254.
5. Sharma BK: Instrumental methods for chemical analysis, Goel publication house, Meera: 844- 938.
6. Pavia and Lampman: Introduction to Spectroscopy, third edition: 390-446.

7. Robert MS: Spectroscopic Identification of organic compounds. Seventh edition: 13-37.

8. Sharma BK: Instrumental methods for chemical analysis, Goel publication house, Meera: 619-736, 774-804.

9. Pavia and Lampman: Introduction to Spectroscopy, third edition: 102-153, 167-194.

10. Robert MS: Spectroscopic Identification of organic compounds. Seventh edition: 127-282.

11. Skoog: Principal of instrumental analysis, second edition: 376 - 452.