

3B Analysis:

What is Nuclear Magnetic Resonance - NMR

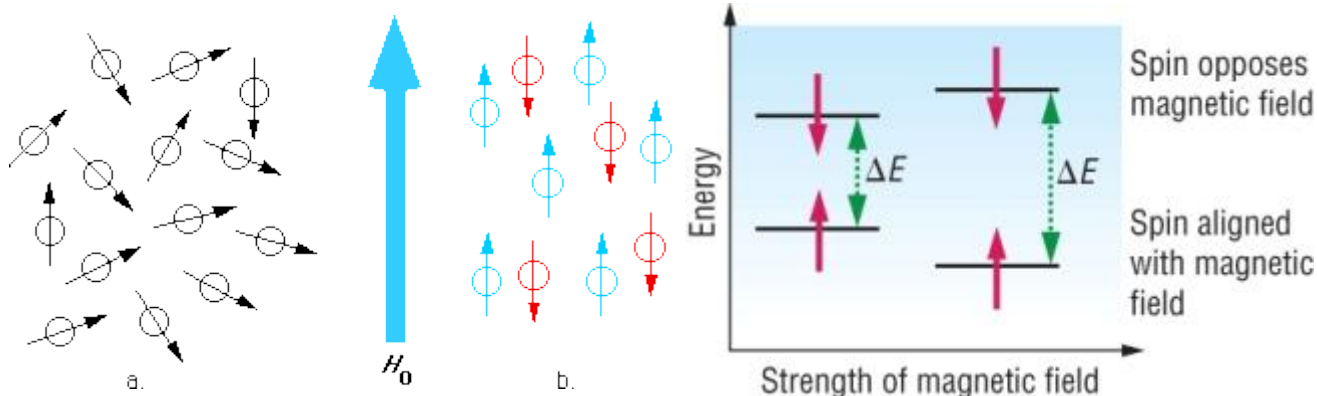
- A very powerful analytical technique allowing chemists to identify even the most complex of structures.
- Developed by chemists and physicists together it works by the interaction of magnetic properties of certain nuclei and their chemical environment.
- This technique only works with atoms with an odd number of nucleons (protons and neutrons).
- At A2 this will be applied to ^1_1H and $^{13}_6\text{C}$ NMR.

Nuclear spin

- All nucleons spin, and pair up just as electrons do.
- Those with an odd number of nucleons will have a nucleon that has not been able to pair up.
- A spinning nucleus such as hydrogen behaves as a spinning charge and generates a magnetic field.
- For example - ^1_1H and $^{13}_6\text{C}$ possess spin whereas $^{12}_6\text{C}$ does not.
- It can be likened to a bar magnet:

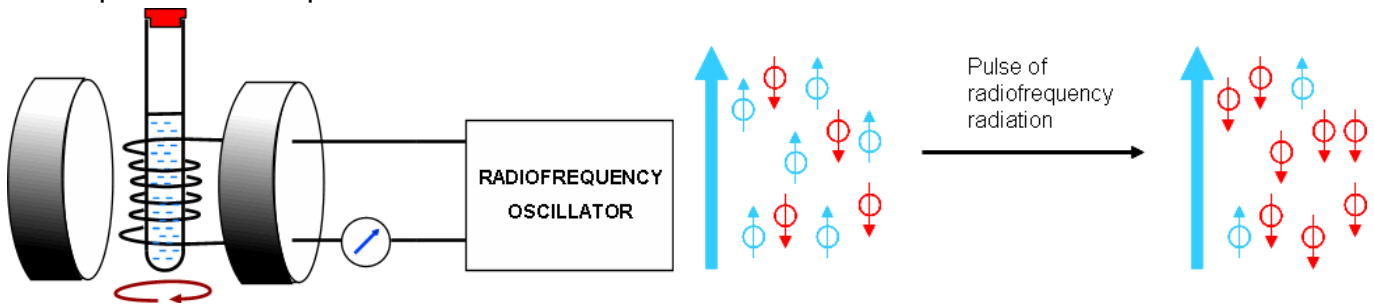


- When this is placed in an external magnetic field it will align with or against the field.
- The nuclei which align parallel are at a lower energy than those aligned anti parallel:



Resonance:

- When they are subjected to a pulse of radiofrequency radiation, some nuclei flip from parallel to anti parallel:



- This promotes the nuclei from low energy spin (parallel) to high energy spin (antiparallel) thus absorbing energy - **excitation**.
- The frequency required to make this happen is specific to the difference in energy between the 'parallel' and 'antiparallel'
- The excited nuclei will at some point drop back to its low energy state (parallel) **emitting the same amount of energy** (that is specific for those nuclei)
- As electrons surround the nuclei, the energy needed to flip the nuclei depend on the **environment** they find themselves.
- This pulse oscillates so the nuclei continually flip or resonate back and forth, **absorbing and emitting energy**.
- The resonance is recorded as a trace.
- By looking at the field strength at which the nuclei absorb energy while resonating, we can work out the structure of a molecule

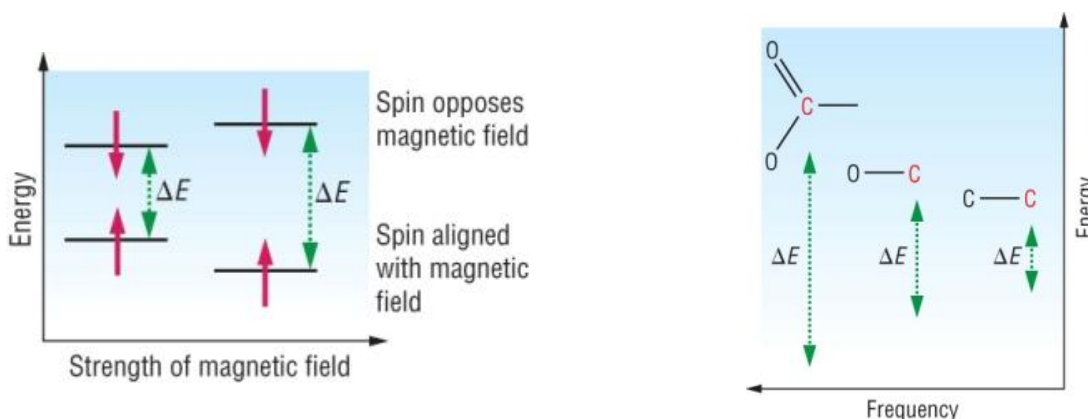
Nuclear shielding and chemical shift:

- The magnetic field felt by a nucleus depends on:

1) Applied magnetic field

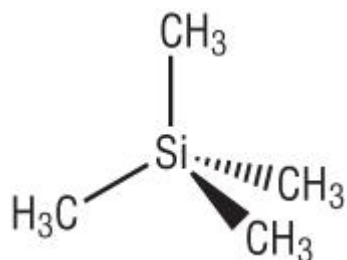
2) The weak magnetic fields generated from electrons surrounding the nuclei and nearby atoms (the environment)

- The electrons in an atom also produce tiny magnetic fields which '**shield**' the nucleus from the applied magnetic field.
- This is called **nuclear shielding** and the extent depends upon nearby atoms or groups of atoms.
- It alters the **environment** of a nucleus changing the energy gap.
- Nuclei in different environments will have **different chemical resonance frequencies**:



Chemical shift, δ :

- This is a place in the NMR spectrum where a nuclei **absorbs and emits energy - resonates**
- The scale is in ppm or δ scale.
- The scale is measured against a reference signal, **TMS = 0** chemical shift is measured from this.
- **TMS** is **T**etramethyl**S**ilane:



- This molecule has 12 equivalent protons giving rise to a single peak.
- This peak is assigned the value = 0
- All peaks of a sample under study are related to it and reported in parts per million.

Solvents for NMR spectroscopy:



¹H nucleus



Deuterium nucleus, ²H

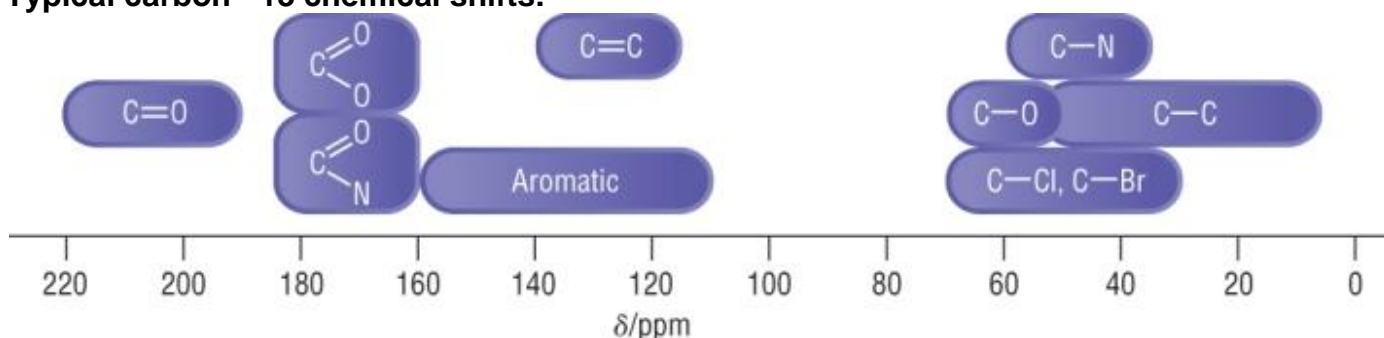
- NMR is carried out in solution.
- The best solvents are usually hydrocarbons which will also produce a signal.
- Deuterated solvents are used as these have an even number of nucleons. These do not give a signal.
- CDCl₃ is usually used.
- This is volatile so can be recovered by evaporation.

Qu 1 - 2 P85

Carbon - 13 NMR spectroscopy

- **99%** of any sample of carbon - ¹²C
- **1%** of any sample of carbon - ¹³C
- This 1% has an uneven number of nucleons, this means it will have a magnetic spin and be detected using NMR

Typical carbon - 13 chemical shifts:



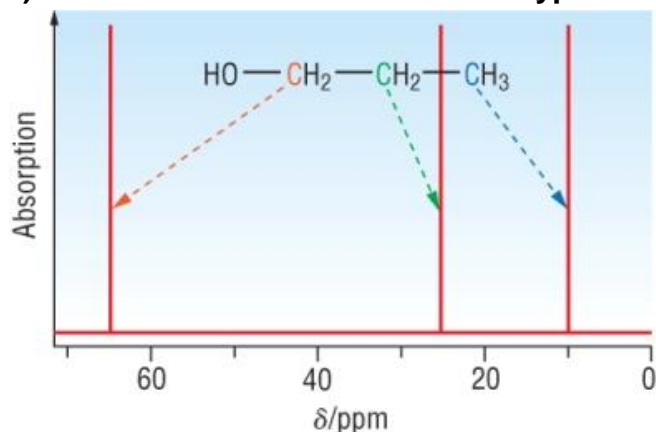
- The chemical shift indicates the environments the 'carbons' are in.
- An electronegative element causes a significant shift as carbon - 13 is sensitive to nuclear shielding.

- The scale ranges 0 - 230, this means that each carbon is likely to have its own separate signal.
- Values will vary with different solvents.

Interpreting carbon - 13 NMR spectra

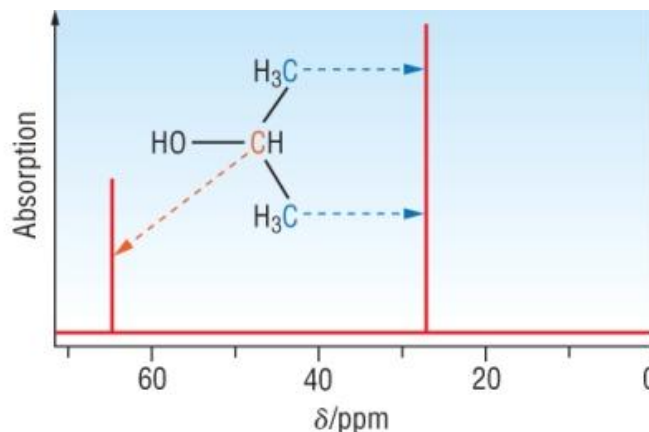
- 3 things obtained from a carbon - 13 NMR is:

- 1) The number of different carbons
- 2) The carbon environment
- 3) The relative ratio of each of the types of carbons



Propan - 1 - ol:

- 3 equally peaks indicating 3 different carbon environments
- A peak at ~ 64ppm: C - O
- A peak at ~ 27ppm: C - C (nearest the electronegative element O)
- A peak at ~ 10ppm: C - C (furthest from the electronegative O)



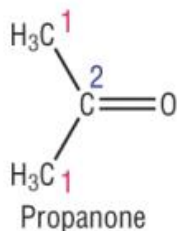
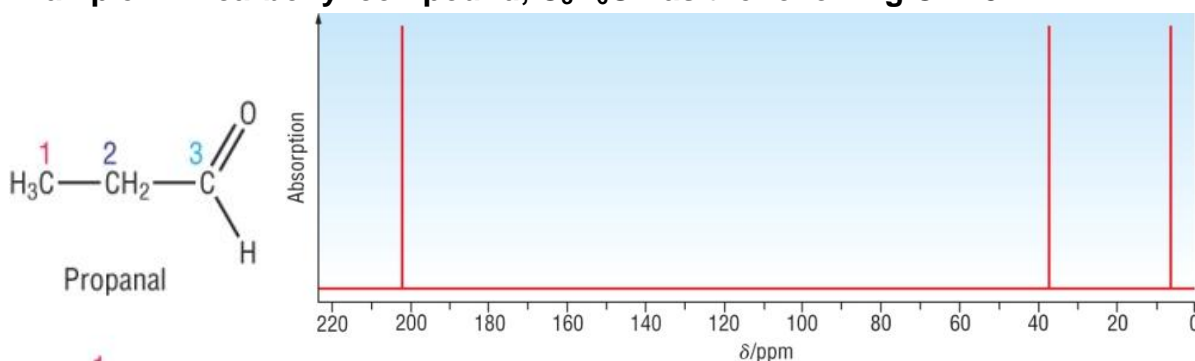
Propan - 2 - ol:

- 2 different sized peaks indicating 2 different carbon environments with different amounts of carbons
- A peak at ~ 64ppm: C - O
- A peak at ~ 27ppm: C - C
- The peak at ~ 27ppm is 2x the size of the peak of the one at ~64ppm as there are 2 equivalent carbons responsible for this peak

Analysis of carbon - 13 NMR spectra

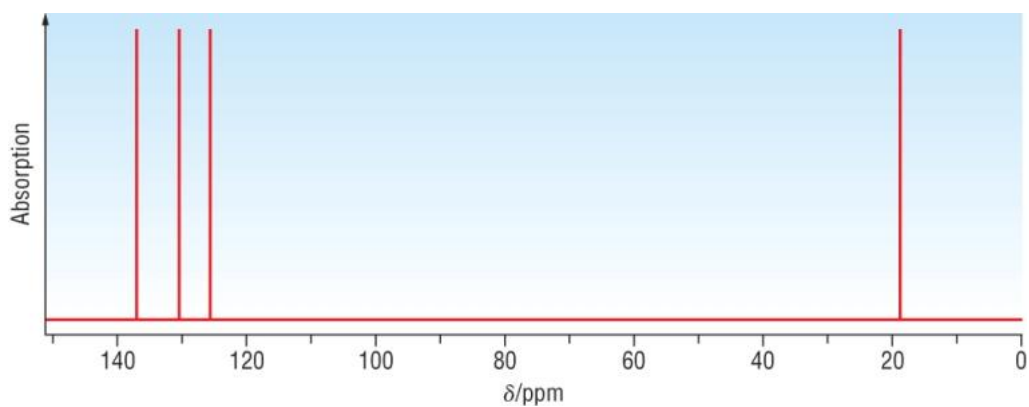
Making predictions:

Example 1: A carbonyl compound, C_3H_6O has the following C - 13 NMR:

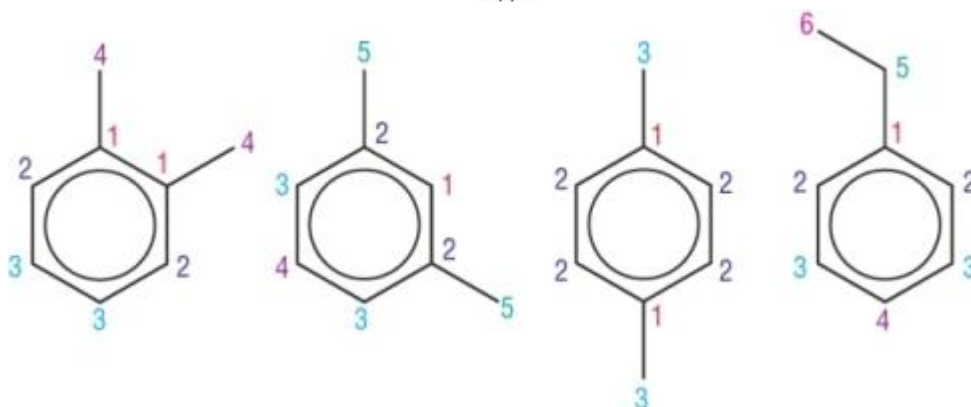


- 3 peaks indicating 3 different carbon environments
- A peak at ~ 205ppm: C = O
- A peak at ~ 37ppm: C - C (nearest the electronegative element O)
- A peak at ~ 6ppm: C - C (furthest from the electronegative O)
- Must be Propanal

Example 2: An aromatic compound, C_8H_8O has the following C - 13 NMR:



Possible structures:



Carbon environments

4

5

3

6

Aromatic environments

3

4

2

4

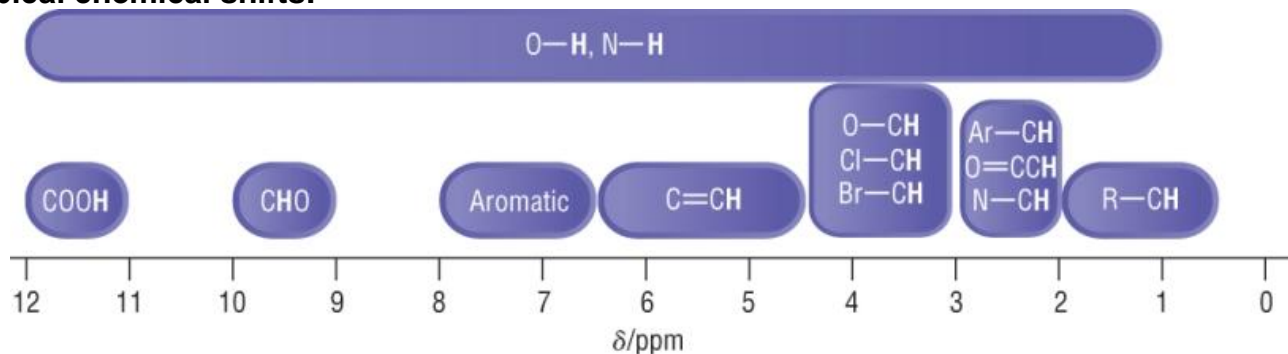
Qu 1 - [2](#) P87 / Qu 1 P89

Proton NMR spectroscopy

Proton NMR:

- Is based around the ^1H which is a single proton.
- ^1H is much more abundant than ^{13}C . **99.9% ^1H to 1.1% ^{13}C .**
- This means less needs to be used.
- Proton NMR is done in the same way as ^{13}C NMR and gives all the same information as ^{13}C NMR but for protons.
- In addition - it gives you information about adjacent protons (later)

Typical chemical shifts:

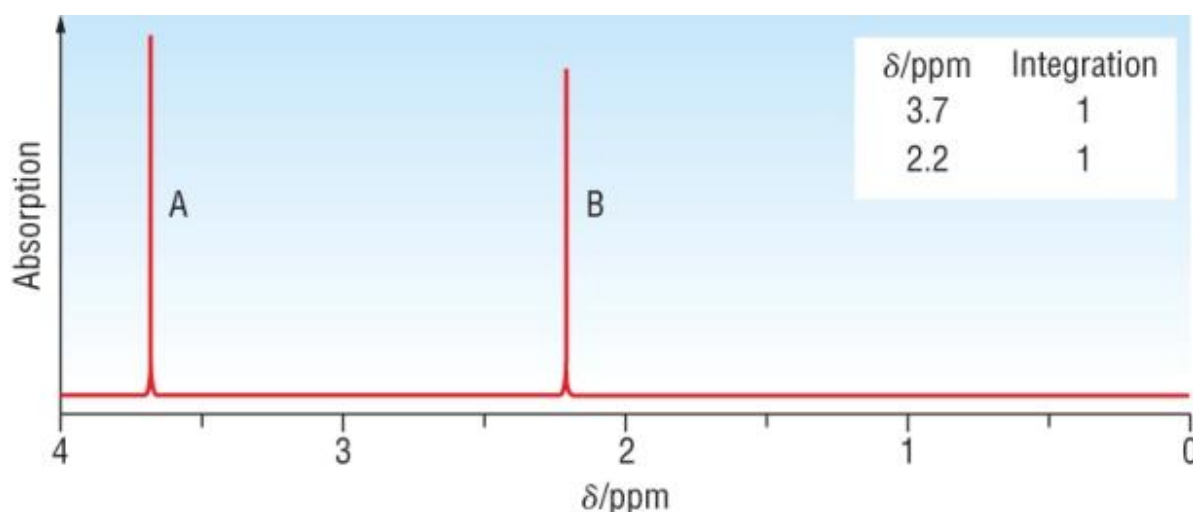


- The scale is narrower which means some signals will overlap.
- Actual chemical shifts can vary depending on environments.
- The scale should be used as a rule of thumb.

Integration traces:

- The area under the peak is proportional to the number of protons.
- On the NMR spectrum, the spectrometer measures this and is recorded as an **integration trace**.
- This is usually an integration line above the peak and can be measured for relative abundances.

Example: This is the proton NMR for $\text{C}_3\text{H}_6\text{O}_2$



- 2 equally sized peaks indicating 2 different proton environments
- This means that there are 2 areas of 3 protons
- A) peak at $\sim 3.7\text{ppm}$: O - CH_3 (nearest the electronegative element O)
- B) peak at $\sim 2.2\text{ppm}$: OC - CH_3 (furthest from the electronegative O)
- Must be methyl propanoate - $\text{CH}_3\text{COOCH}_3$

Spin - spin coupling in proton NMR spectra

Spin - Spin coupling:

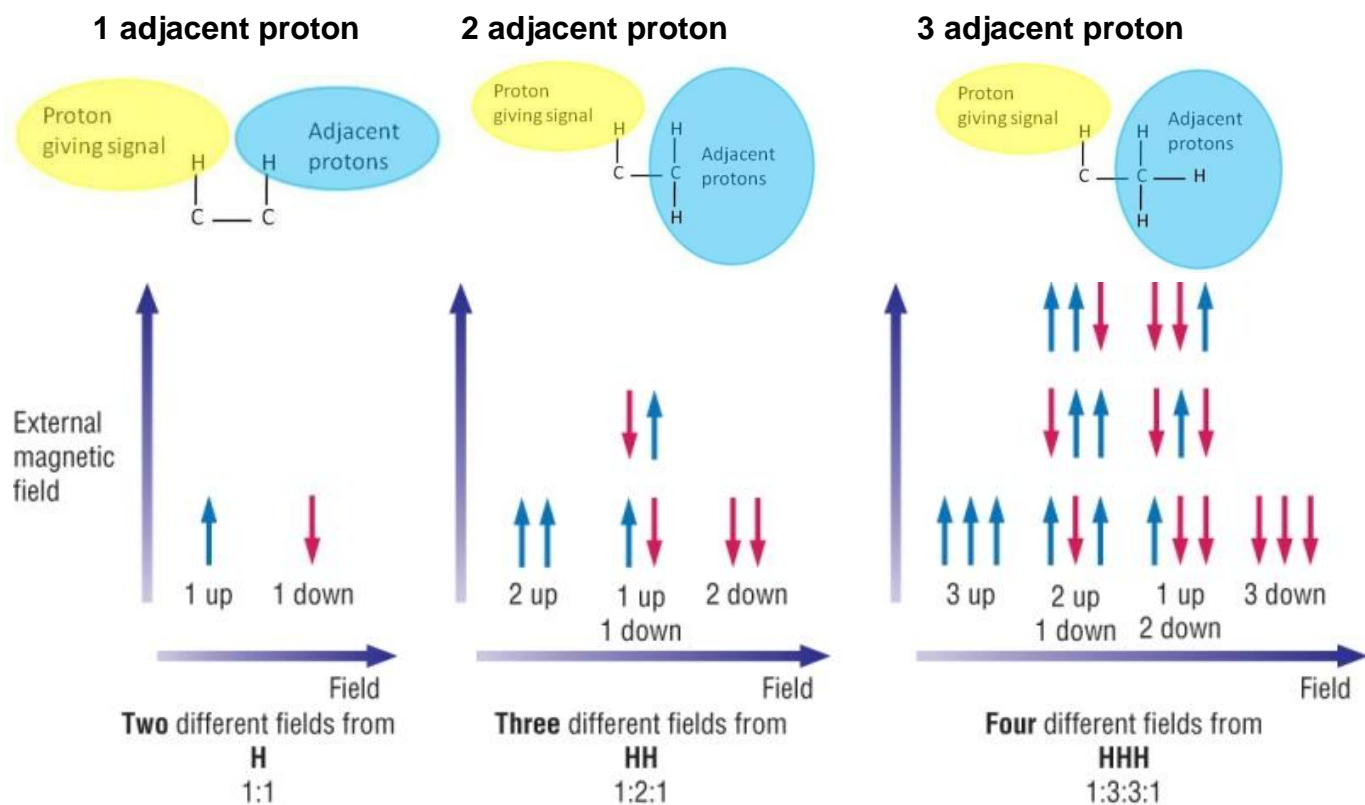
- Splitting patterns are worked out by considering the effect that adjacent, chemically different hydrogen's have on another signal in a given environment.
- The spin of the proton producing the signal is affected by each of the two forms of the adjacent hydrogen's (parallel and anti parallel).
- One orientation enhances its field and the other reduces it.
- We can work this out by calculating the various possible combinations of alignment of adjacent protons.

Theory:

- The proton gives a signal by its magnetic field from its spin.
- Its signal is influenced by adjacent protons (on neighbouring carbons).
- Each proton will either spin in the same direction or the opposing direction.
- This means that each adjacent proton either enhances the magnetic field or diminishes it.
- There are 2 possibilities of equal chance per adjacent proton - enhancing or diminishing the magnetic field.
- This **splits** the signal given by the proton

Analogy:

- Imagine you had an opinion on something. If nobody influenced you, your opinion would be the same.
- If another person had a view on the topic, they would either agree or disagree with you.
- Their ideas would either enhance what you thought or diminish it.
- There would be 2 possibilities of equal chance per person agreeing or disagreeing with you:



- The adjacent proton spins in the same or opposing direction.

- **Agree**
- **Disagree**

- Each of the 2 adjacent protons spins in the same or opposing direction.

- **Agree - Agree**
- **Agree - Disagree / Disagree - Agree**
- **Disagree - Disagree**

- Each of the 2 adjacent protons spins in the same or opposing direction.
- **Agree - Agree - Agree**
- **Agree - Agree - Disagree / Disagree - Agree - Agree / Agree - Disagree - Disagree - Agree**
- **Disagree - Disagree - Agree / Disagree - Agree - Disagree / Agree - Disagree - Disagree**
- **Disagree - Disagree - Disagree**

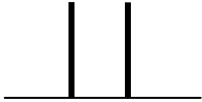
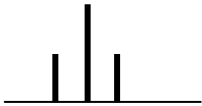
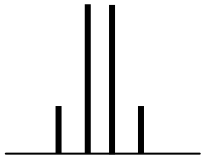
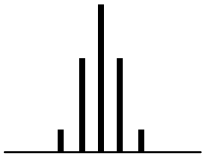
2 fields of equal intensity

3 fields with an intensity of 1:2:1

4 fields with an intensity of 1:3:3:1

- There is always an extra field than the number of adjacent protons - known as the n+1 rule:

n+1 rule:

n + 1 rule: Number of peaks = Number of different H's on adjacent atoms + 1				
1 Neighbouring H	2 Peaks	DOUBLET	1:1	
2 Neighbouring H	3 Peaks	TRIPLET	1:2:1	
3 Neighbouring H	4 Peaks	QUARTET	1:3:3:1	
4 Neighbouring H	5 Peaks	QUINTET	1:4:6:4:1	

Signals for H in an O - H bond are unaffected by hydrogen's on adjacent atoms = singlet only

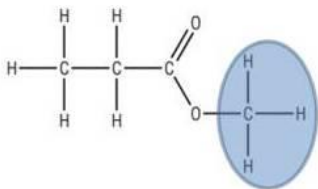
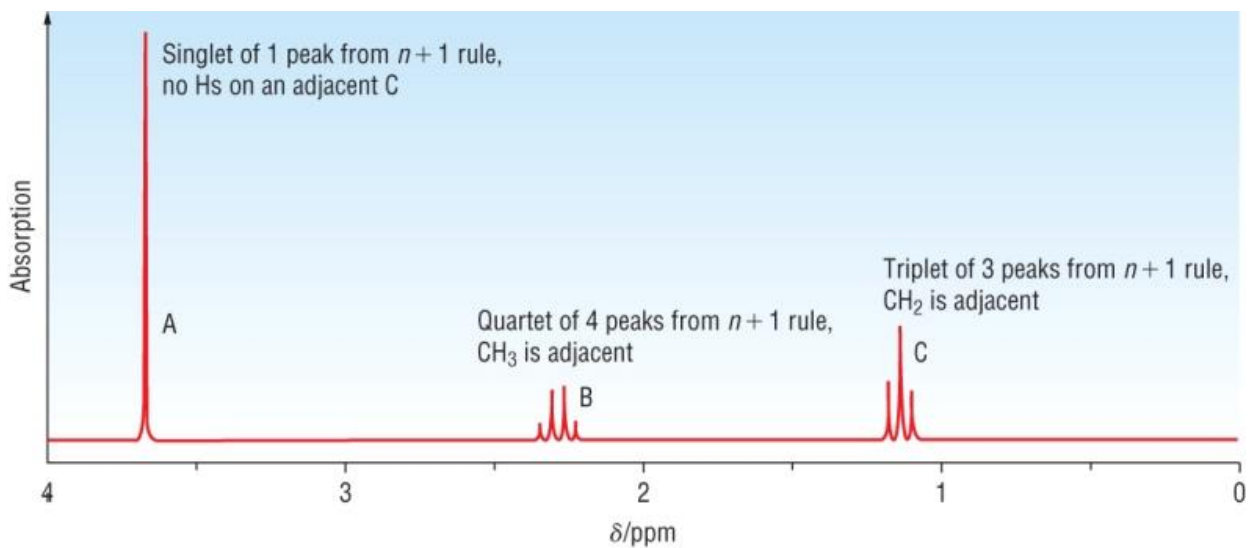
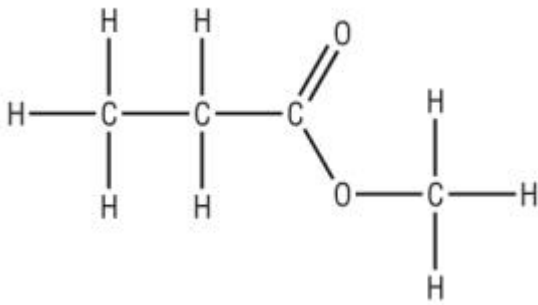
NOTE: Pascal's triangles

- Just a note of interest. The signal peaks show the patterns described by Pascal's triangles:

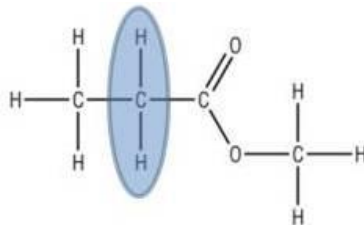
1
1 1
1 2 1
1 3 3 1
1 4 6 4 1

The proton NMR spectrum of methyl propanoate:

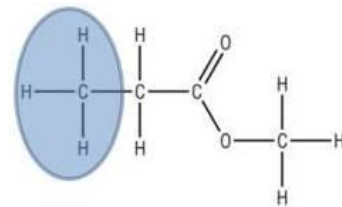
- There are 3 areas of protons - this will give 3 areas of signal:



- These protons are adjacent to = 0 protons
- $n+1 = 1$ field
- Singlet



- These protons are adjacent to = 3 protons
- $n+1 = 4$ field
- Quartet



- These protons are adjacent to = 2 protons
- $n+1 = 3$ field
- Triplet

NMR spectra of OH and NH protons

- These are not only difficult to identify but can also confuse the rest of the spectra.
- The reason for this is:

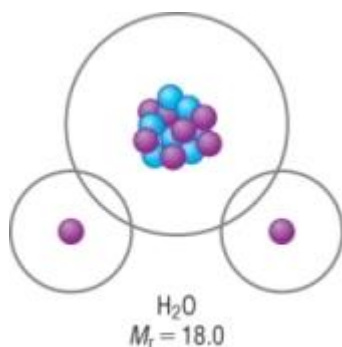
1) Peaks can appear over a wide range of chemical shifts

2) Signals are often broad

3) There is no splitting pattern (due to ease of proton exchange in OH / NH - not needed)

- These signals can be removed by using **heavy water**, deuterium oxide, **D₂O**
- It is the same as water but the hydrogen's are replaced with deuterium.
- **Deuterium does not give a signal in NMR**

Use of D₂O



How D₂O is used:

1) An NMR is run as normal

2) A small amount of D₂O is added to the mixture, shaken and a second NMR is run

The OH or NH signal disappears

How it works:

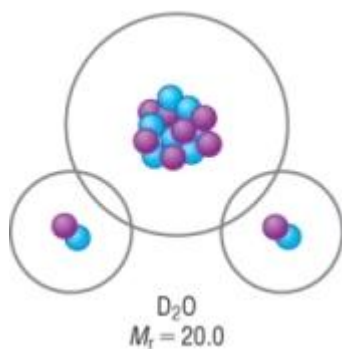
The Deuterium atoms in heavy water can replace the protons on OH or NH:



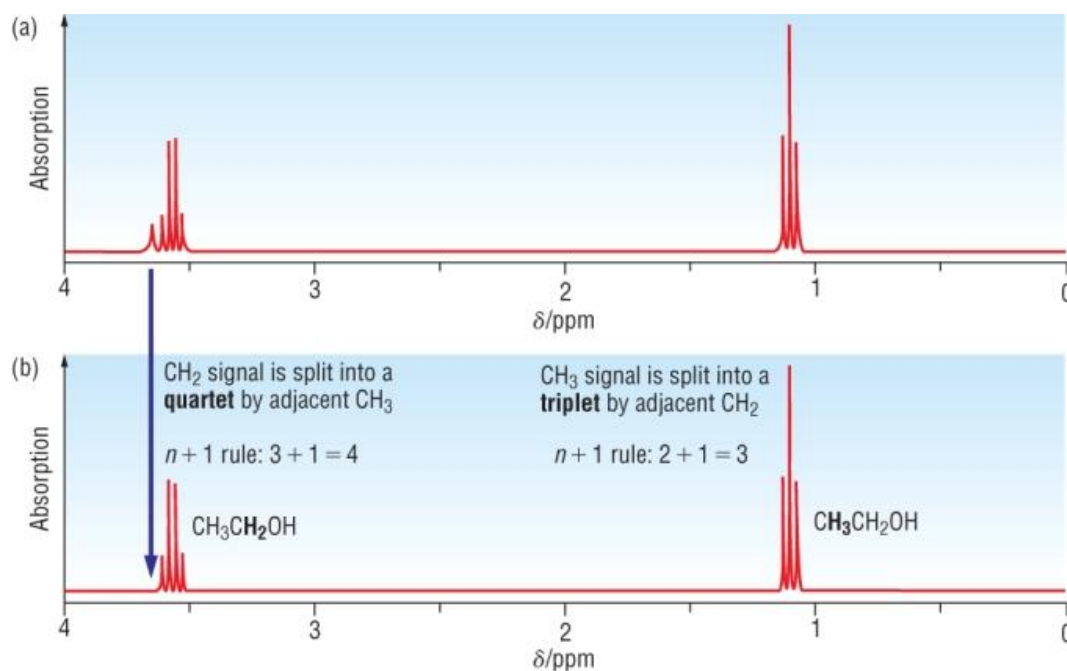
Remember only atoms with an odd number of nucleons gives an NMR peak.

This means that the -OH → -OD and -NH → -ND

Deuterium has an even number of nucleons which means the -OD and -ND will no longer give a signal.



Example: NMR spectra of ethanol, (a) CH₃CH₂OH in water and (b) in D₂O, CH₃CH₂OD



THE OH SIGNAL HAS DISAPPEARED

Splitting from -OH and -NH protons:

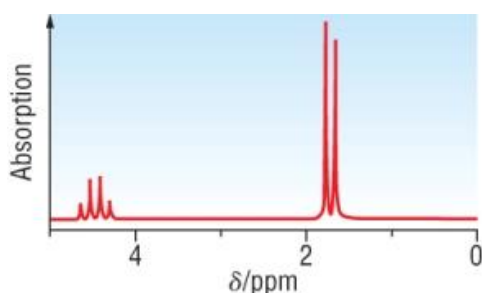
- -OH and -NH peaks **DO NOT** split and **DO NOT** contribute to splitting
- Hydrogen bonding between water (solvent) and -OH / -NH protons broaden the peak

Qu 1-2 P95

Spin - spin coupling examples

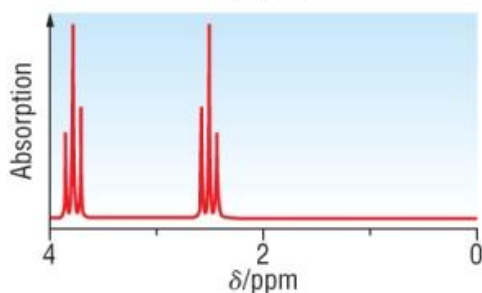
1) Using splitting patterns:

H - NMR of 2 isomers of C₃H₅ClO₂: 1) CH₃CHClCOOH and 2) ClCH₂CH₂COOH both run in D₂O



As it is run in D₂O, we do not need to worry about the COOH signal.

- **Quartet**: is made from **proton(s) adjacent to 3H (CH-CH₃)**
- **Doublet**: is made from **proton(s) adjacent to 1H (CH₃-CH)**
- This leads to isomer 1) CH₃CHClCOOH
- **Triplet**: is made from **proton(s) adjacent to 2H (CH₂-CH₂)**
- As there is 2 of them, there must be 2 lots of CH₂'s next to each other
- This leads to isomer 2) ClCH₂CH₂COOH

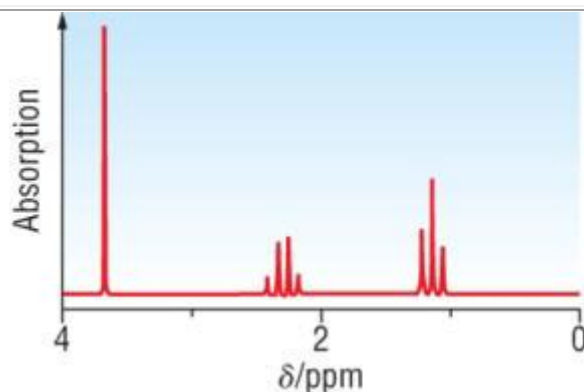


2) Using splitting, integration and chemical shift:

H - NMR of 4 isomers of the ester, C₄H₈O₂:

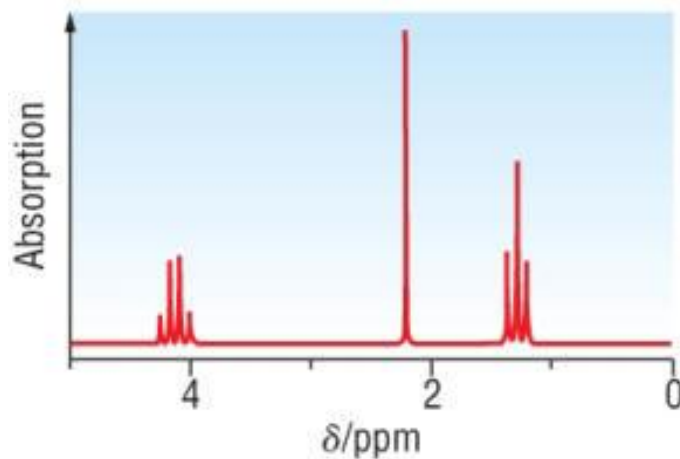
A) CH₃CH₂COOCH₃ B) CH₃COOCH₂CH₃ C) HCOOCH₂CH₂CH₃ D) HCOOCH(CH₃)₂

2 of these esters are shown below, match the ester to the spectra:



Chemical shift:	1.1	2.1	3.6
Integration	3	2	3
Splitting pattern	Triplet - signal adjacent to 2H's	Quartet - signal adjacent to 3H's	Singlet - signal adjacent to 0H's
Interpretation	3H's adjacent to 2H's	2H's adjacent to 3H's	3H's adjacent to 0H's
Assignment	CH ₃ CH ₂	O=CCH ₂ CH ₃	O-CH ₃

Put the assignments together: CH₃CH₂COOCH₃

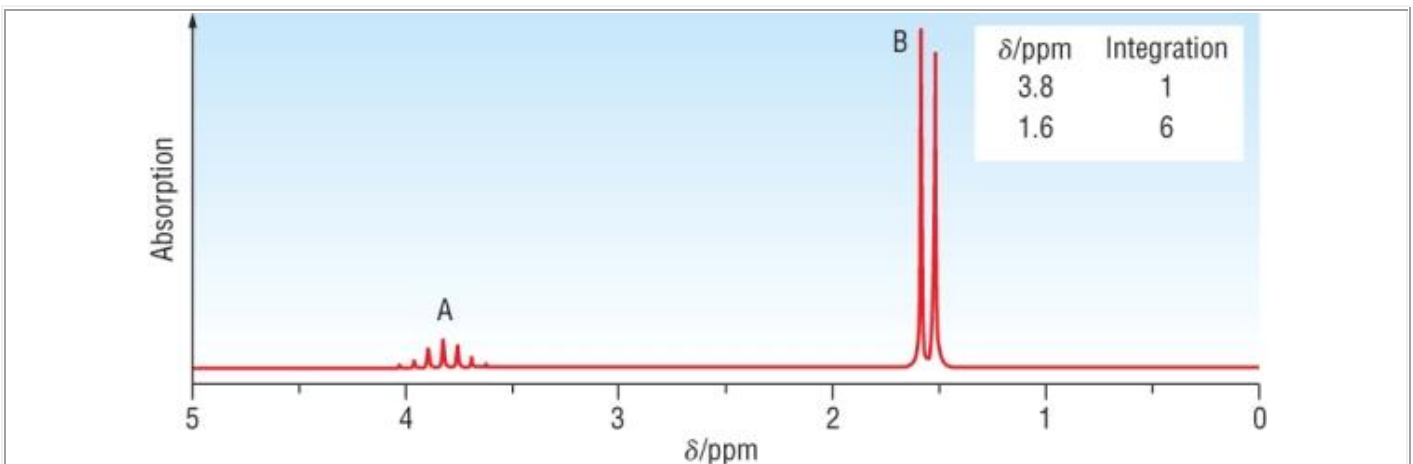


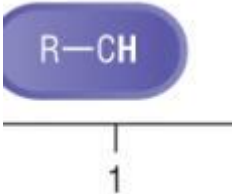
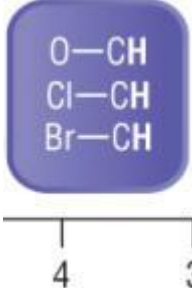
Chemical shift:	1.1	2.1	4.1
Integration	3	3	2
Splitting pattern	Triplet - signal adjacent to 2H's	Singlet - signal adjacent to 0H's	Quartet - signal adjacent to 3H's
Interpretation	3H's adjacent to 2H's	3H's adjacent to 0H's	2H's adjacent to 3H's
Assignment	CH₃CH₂	O=CCH₃	O-CH₂CH₃

Put the assignments together: CH₃COOCH₂CH₃

3) Protons adjacent on both sides:

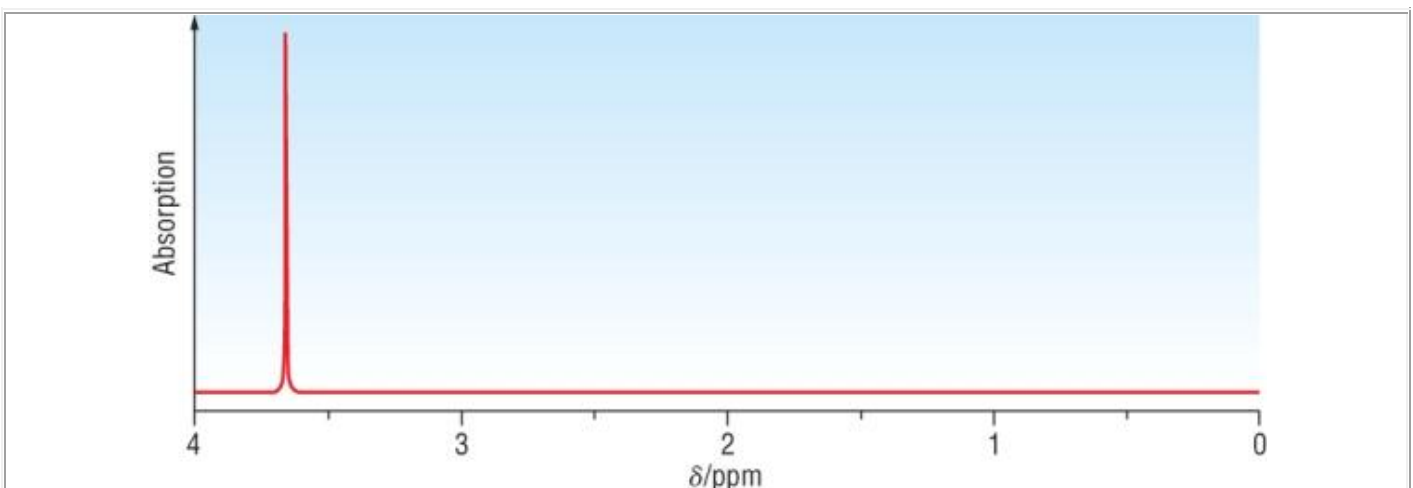
The spectra below is for $\text{CH}_3\text{CHClCH}_3$

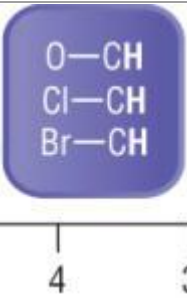


Chemical shift:	1.6	3.8
		
Integration	6	1
Splitting pattern	Doublet - signal adjacent to 1H's	Heptet - signal adjacent to 6 equivalent H's
Interpretation	6 equivalent H's adjacent to 1H's	1H's adjacent to 6 equivalent H's
Assignment	$\text{CH}_3\text{CHClCH}_3$	$\text{CH}_3\text{CHClCH}_3$
Put the assignments together: $\text{CH}_3\text{CHClCH}_3$		

4) Equivalent protons not split:

The spectra below is for $\text{ClCH}_2\text{CH}_2\text{Cl}$



Chemical shift:	3.8
	
Integration	4
Splitting pattern	Singlet - signal adjacent to 2H's
Interpretation	2H's adjacent to 6H's
Assignment	$\text{ClCH}_2\text{CH}_2\text{Cl} \times 2$
Put the assignments together: $\text{ClCH}_2\text{CH}_2\text{Cl}$	

Qu 1 P97

NMR in medicine

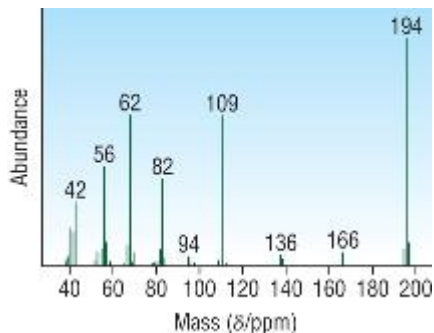
- It is used to determine the structure of synthetic drugs.
- It is used in **MRI** scans - **M**agnetic **R**esonance **I**maging.
- The word Nuclear was dropped as it was thought people would associate it with radiation.
- The patient is the sample and although their protons are resonating, it is painless and harmless.
- Only patients with **ferromagnetic metal implants (Fe, Co, Ni)** should not use **MRI** such as pacemakers.
- **MRI** takes a **3D** image of the water in tissue as slices which a computer then puts together.
- Diseases affect the water in tissues and this can be identified - cancers / spinal injuries
- Used in sporting injuries to identify tendon / muscle / ligament tears as dense materials such as bones appear darker due to less protons.

Qu 1 - 4 P 99

Combined techniques:

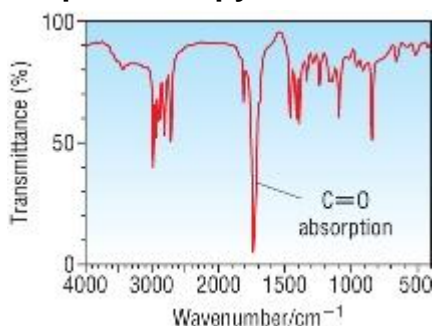
- A single spectroscopic technique tells you 'bits' of information on the structure of a molecule or compound.
- Combining the techniques give you lots of 'bits' of information that can be used to determine the actual structure of the molecule or compound:

Mass Spectroscopy:



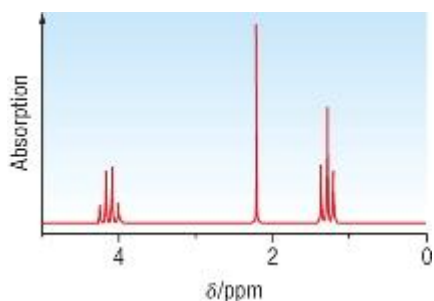
- Chemical analysis provides the empirical formula of the compound.
- Mass spectroscopy gives the Mr and hence the molecular formula.
- Fragmentation patterns give clues about the carbon skeleton.

IR spectroscopy:



- IR spectroscopy gives information about functional groups present in the molecule:
- O - H
- C = O
- C - O
- However many functional groups can have these bonds present

NMR spectroscopy:



Carbon - 13 NMR:

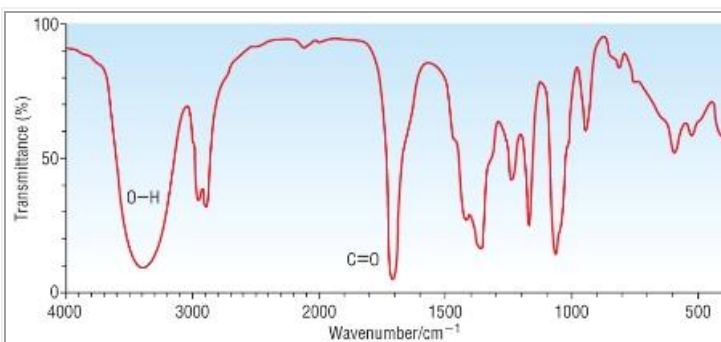
- Gives information about the numbers and types of carbon environments.

Proton NMR:

- Gives information about the numbers and types of protons.
- It also tells you the environments the protons are in.

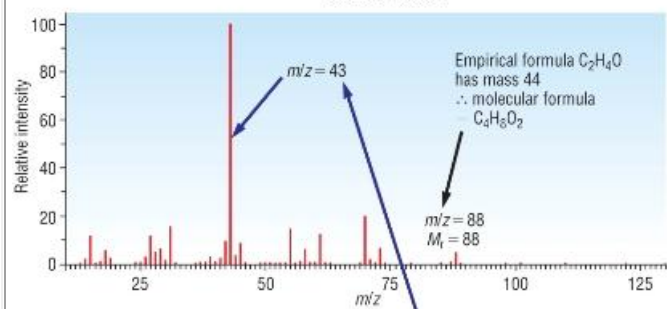
Worked example:

Chemical analysis has identified the empirical formula as C_2H_4O ($M_r = 44$)



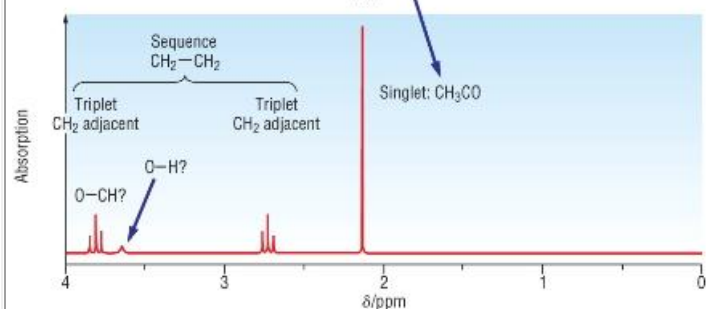
IR spectra:

- O - H present
- C = O present



Mass Spectra:

- Molecule has a mass, $M_r = 88$
- Molecular formula = $C_4H_8O_2$



NMR:

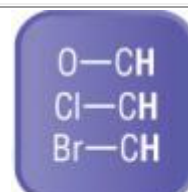
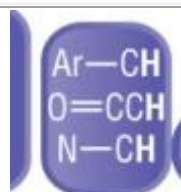
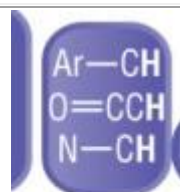
Chemical shift:

2.1

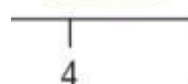
2.7

3.8

3.6



O-H can be in any region between 1.0 - 5.5



Integration

3

2

2

1

Splitting pattern

Singlet - signal adjacent to OH's

Triplet - signal adjacent to 2H's

Triplet - signal adjacent to 2H's

Singlet

Interpretation

3H's adjacent to OH's

2H's adjacent to 2H's

2H's adjacent to 2H's

O-H?

Assignment

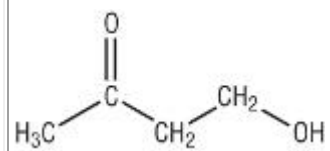
$O=CCH_3$

$O=CCH_2CH_2-$

$O-CH_2CH_2$

-O-H

Put the assignments together:



Qu 1-2 P103 Qu 3-8 P105 Qu 2 - 8 P108/109