Organic Structure Determination

Instrument-based methods for determination of structure of organic molecules
1) Mass Spectrometry - yields molecular weight/elements/possible molecular formulas
2) Infrared Spectroscopy - yields functional groups
3) NMR Spectroscopy - very important, yields structure

1 Mass Spectrometry
• Gives molecular weight, some elemental information, possible molecular formulas (and degrees of unsaturation)
• The sample is vaporized by heating under vacuum, then ionized by removal of an electron in an electron beam, high energy electrons impacting an organic molecule in vacuum can actually REMOVE an electron (there are other ionization techniques but this is the historically important method)
• After ionization the species is a radical AND a cation, a radical cation, that has had an electron removed, usually, from a bonding MO, which weakens the bonds and results in fragmentation of several bonds to form radicals and cations
• Usually not all of the original radical cations fragment, some remain intact, and a mixture of the radical cation and cation fragments results

For Example: Butane

\[
\text{H}_3\text{C}–\text{CH}_2–\text{CH}_2–\text{CH}_3 \xrightarrow{\text{vaporize and ionize}} \text{H}_3\text{C}–\text{CH}_2–\text{CH}_2–\text{CH}_3^+ \\
\xrightarrow{\text{fragmentation}} \begin{align*}
\text{• CH}_3 + \\
\text{H}_3\text{C}–\text{CH}_2–\text{CH}_2^+ \\
\end{align*}
\]

• The various cations are positively charged and are accelerated towards a negatively charged electrode, the electrode has a small hole in it and some ions pass through into a tube with a variable magnet
• Moving charged particles such as cations generate a magnetic field, which interacts with the field of the variable magnet to deflect the path of the cation
• Different cations have different masses and therefore different momenta, and are deflected to different extents

• Depending upon the mass (momentum) of the cation, it can be deflected exactly enough to pass through a slit at the end of the tube and be detected electronically
• Varying the external magnetic field selects cations with different masses to be detected, and so scanning the external field generates a scan over the masses of the various cations and generates a MASS SPECTRUM
An idealized mass spectrum of butane...

- mass spectrum is plot of ion current (i.e. # of ions) versus mass/charge ratio (m/z), where z is charge
- because the charge is almost always positive one (multi-charged species are rarely encountered in mass spectra), m/z is essentially the same as mass
- the largest m/z value corresponds to “molecular ion”, i.e. the unfragmented radical cation and this gives the molecular weight of the molecule being analyzed
- the molecular ion peak not necessarily the most "abundant", i.e. it is often not the "tallest" peak (called the base peak), but it has the largest m/z
- It is IMPORTANT TO REMEMBER that the sample being analyzed contains millions and millions of molecules, the peaks that are observed in the mass spectrum can NOT come from a single molecule, many of the molecules fragment in the spectrometer to generate the ion peaks with lower mass, some of them do not fragment and generate the molecular ion peak, the different fragment differently (or not at all) because they have a distribution of energies as a result of the ionization process.
- there is a lot of structural information in a mass spectrum but we will IGNORE MOST OF IT and focus only on the molecular ion peak

1.1 Important Information from Molecular Ion Peaks

A compound that contains the elements C, H and O only: The molecular ion mass is an even number
- the most abundant (largest) peak is not that of the molecular ion, it is of a fragment, the molecular ions will have the LARGEST mass, since it has not fragmented

- the M+1 peak is due to molecules that contain the isotopes D, $^{13}$C, etc., we should expect to see an M+1 peak at ca. 10% of the intensity of the molecular ion peak
- an even numbered molecular weight means that the molecule contains carbon and hydrogen, and possibly (but not necessarily) oxygen. There is no specific "signature" for oxygen in mass spectrometry.

A compound that contains the element Br: The mass spectrum has TWO molecular Ion Peaks
- the mass spectrum has TWO molecular ions, one for the molecules that contain 79Br, and one for the molecules that contain 81Br
- these two molecular ion peaks are separated by 2 mass units and have ca. 1:1 size ratio
A compound that contains the element Cl: The mass spectrum has TWO molecular ion Peaks

- the mass spectrum has TWO molecular ions, one for the molecules that contain 35Cl, and one for the molecules that contain 37Cl
- these two molecular ion peaks are separated by 2 mass units and have ca. 3:1 size ratio

A compound that contains the element N: The molecular ion mass is an ODD number for 1 or 3 N atoms

- odd molecular weight means a single nitrogen (the M.W. for 2, 4, 6 etc. nitrogens would be even)
- strictly speaking, any odd number of N atoms, but usually one in this class
1.2 Important Information From Molecular Weight

• Determine Possible Molecular Formula from Mass Spectrum

• What are POSSIBLE and also REASONABLE molecular formulae for this mass spectrum?

• Possible molecular formula will not have more than the maximum number of hydrogen atoms calculated the usual way for degrees of unsaturation

• Unreasonable molecular formulae are harder to define, they will generally have at least as many carbon atoms as hydrogen atoms and more hydrogen atoms than oxygen atoms, but there are some exceptions to these "rules"

• Divide MW by 12 to determine maximum possible number of H atoms, the remainder (R) is equal to the mass of the H atoms, the arithmetic process used to determine possible molecular formulae is…..

• replace 1 C atom by 12 H atoms, maintains the correct MW

• replace 1 C atom and 4 H atoms by 1 O atom, maintains correct MW

2 Infrared Spectroscopy

Bond Vibrations

• molecules at room temperature are very hot, they don’t SEEM to be very hot, but RELATIVE TO ABSOLUTE ZERO (where molecules have essentially no energy), molecules at room temperature have a lot of energy (they are hotter by 273 degrees C), and this energy has to "go" somewhere.

• In molecules this energy goes into kinetic energy if they are in the gas or liquid phase, but importantly also into bond VIBRATIONS

Electromagnetic Radiation (light!)

• Electromagnetic radiation consists of an oscillating orthogonal (right angles) electric and magnetic fields

• the energy in electromagnetic radiation is determined by the oscillation frequency of the electric (and magnetic) field vectors, and is given the symbol Greek n (pronounced "nu" and which looks sort of like a v)

• the energy in electromagnetic radiation is ALSO determined by the wavelength of the electric (and magnetic) field vectors, and is given the symbol Greek l (pronounced "lambda" and which looks sort of like a v)

• the wavelength and frequency of electromagnetic radiation are related via the speed of light

• we do not need to get into these equations in detail (although they are quite simple), what we need to know is that energy in electromagnetic radiation is DIRECTLY proportional to frequency, and INVERSELY proportional to wavelength, i.e, ENERGY INCREASES with INCREASING FREQUENCY
• the range of frequencies of the electromagnetic radiation in the **infrared region** matches the range of **frequencies of vibrations of bonds in molecules**
• if the frequency of the infrared radiation exactly matches that of a particular bond vibration in a molecule, then the electric field vector of the radiation can interact with the **dipole moment of the vibrating bond**, the radiation can be **absorbed by the molecule** and **used to increase the bond vibration amplitude**

- the electromagnetic frequency must **EXACTLY** match the frequency of VIBRATION of the bond (IR absorption is quantized), if the frequency is higher or lower than the bond vibration frequency it will not be absorbed
- for IR radiation to interact with a vibrating bond, the bond **MUST HAVE A DIPOLE MOMENT**
2.1 A Real Infrared Spectrum

- Infrared Vibrations are often localized on bonds or groups of atoms (the more useful vibrations are localized on specific bonds)
- Different bonds vibrate with different frequencies, this is important as this is the basis for identifying different bonds/functional groups in a spectrum, and hence in a structure
- We need to know about how many bond vibrations are possible, what their frequencies are also how STRONG or WEAK the absorptions are, i.e. how "big" they appear in actual spectra

1) How Many Bond Vibrations Are Possible in a Molecule?
- for n atoms there are MANY POSSIBLE vibrations, in fact \((3n + 6)!\)
- however, many of these are complex, i.e. are not localized on individual bonds, and occur with lower frequencies (less than 1500 cm\(^{-1}\)) in the "fingerprint region", which is the area that has signals that are specific to a particular molecule, not to a specific functional group, in this class we ignore the fingerprint region

2) What are the BOND Vibrational Frequencies?
- vibrational frequencies are determined by bond strength and atomic mass
- A bond as "spring" analogy is useful
- bonds have HIGH VIBRATION FREQUENCIES if they are STRONG, and have consist of LIGHT ATOMS
- bonds have LOW VIBRATION FREQUENCIES if they are WEAK, and have consist of HEAVY ATOMS

- a strong bond (spring) vibrates with a higher frequency
A bond (spring) with small/light atoms attached will vibrate with a higher frequency.

**Visualize the how stronger bonds and lighter atoms result in higher vibrational frequencies**

**Approximate Regions in the Infrared Spectrum**

- Bonds to the very light atom H have the highest vibrational frequencies, stronger bonds to H having the highest frequencies.
- Triple bonds to heavier atoms come next.
3) How strong are the Absorption Peaks (how big are the peaks in the spectra)?

- the electric field vector of the electromagnetic radiation interacts with dipole moment of the vibrating bond
- when the electric field (vector) of the IR electromagnetic radiation lines up with the direction of the bond dipole moment the field can "pull" the atoms apart (if the frequency is matched) and thus increase the amplitude of the vibration (the atoms separate more), in this way the IR energy is absorbed into the molecule, the energy is "used" to make the bond vibrate with a larger amplitude
- it may seem unlikely that the electric field and the bond dipole line up exactly, but in fact there are billions of molecules that are constantly tumbling in space which means that there will be plenty of bonds in the correct alignment, especially because the alignment doesn’t have to be perfect
- large (change in) dipole moment results in stronger interactions with the electric field vector, which result in absorption of a lot of IR radiation which in turn results strong IR absorptions

![Diagram](https://via.placeholder.com/150)

- to be observed in an IR spectrum a bond has to have a dipole moment
- bonds with LARGER DIPOLE moments interact more strongly with the electric field vector of the electromagnetic radiation and have STRONGER (LARGER) absorption signals in an IR spectrum

**EXAMPLES:**

![Diagram](https://via.placeholder.com/150)

2.2 Real Absorption Bands

Vibrations of C-H bonds around 3000 cm\(^{-1}\) (2700 - 3500 cm\(^{-1}\) = bonds to H atoms)

- H atoms are LIGHT, bonds to H atoms tend to be high frequency (large \(\nu\)), ca. 2700 - 3500 cm\(^{-1}\)
- stronger C-H bonds will vibrate with higher frequencies, weaker C-H bonds will vibrate with lower frequencies
- We KNOW SOMETHING about C-H bond strengths......

![Diagram](https://via.placeholder.com/150)
• We EXPECT that stronger C-H bonds will have higher frequency absorption in IR spectroscopy, and they do!

• peaks due to C-H vibrations that are found at frequencies less than 3000 cm\(^{-1}\) are due to H atoms that are attached to sp\(^3\) hybridized carbons. Bonds from hydrogen to sp\(^3\) carbons are somewhat weaker than bonds to, e.g., sp\(^2\) hybridized carbons, and thus are found at somewhat lower frequencies.

• the dipole moments for C-H bonds are very small, HOWEVER, there are usually LOTS of C-H bond vibrations, and so they "add up" so that the peaks can still be observed in the spectrum.

• peaks due to C-H vibrations that are found at frequencies just above 3000 cm\(^{-1}\) are due to H atoms that are attached to sp\(^2\) hybridized carbons. Bonds from hydrogen to sp\(^2\) carbons are somewhat stronger than bonds to sp\(^3\) hybridized carbons, and thus are found at somewhat higher frequencies.
• C-H vibrations around 3300 cm\(^{-1}\) are due to H atoms that are attached to sp hybridized carbons. These are stronger bonds with higher vibrational frequencies. They are distinguished from O-H and N-H bonds by the fact that they are not broad.

**Vibrations greater than 3000 cm\(^{-1}\) (2700 - 3500 cm\(^{-1}\) = bonds to H atoms)**
• Bonds between hydrogen and other elements are also expected to have high frequency vibrations
• AND, bonds to more electronegative elements than carbon are **stronger** and are thus expected to vibrate with **higher frequencies**
• We therefore **EXPECT** that bonds to more electronegative elements should have higher vibration frequencies because they are stronger

- N-H and O-H bonds **ALSO HAVE** larger dipole moments, their IR absorption peaks should be **STRONGER**

• The O-H bond vibration **IS** at higher frequencies than C-H bond vibrations, ca. 3300 cm\(^{-1}\), AND it is strong due to the large bond dipole moment, ONE O-H bond is equivalent to many C-H bonds in absorption strength
• The alcohol O-H stretching vibration is BROAD due to HYDROGEN-BONDING, Hydrogen-bonding "pulls" the H "away" from the O, resulting in a lower frequency vibration, a distribution in Hydrogen-bonding results in a distribution in frequencies which results in a BROAD absorption band
• The absorption is centered at ca. 3300 cm\(^{-1}\), which distinguished alcohols from carboxylic acids (see later)
The amine N-H stretching vibration is also broad due to hydrogen-bonding, but N-H hydrogen bonding is WEAKER than O-H Hydrogen bonding (nitrogen is less electronegative than oxygen), and some non-hydrogen bonded N-H vibrations can be observed as small sharp peaks on top of the broad absorption.

- The N-H bond dipole is also smaller than the O-H bond dipole (N less electronegative than O) and so N-H absorptions tend to be somewhat weaker than O-H absorptions.
- There are usually 2 small (non hydrogen-bonding) peaks for a primary amine that has two N-H bonds.
- There is usually 1 small (non hydrogen-bonding) peak for a secondary amine that has one N-H bond.
- Of course, a tertiary amine has no N-H bonds and no signals at all are observed in this region in this case.

**Vibrations of other bonds to Hydrogen around 3000 cm⁻¹ (2700 - 3500 cm⁻¹ = bonds to H region)**

- Aldehydes have 2 small peaks around 2730 and 2820 for the single C-H bond that is attached to the C=O.
- These are sometimes difficult to distinguish, and can range between ca. 2720 - 2740 and ca. 2810 - 2830, but the aldehyde also has the strong C=O stretching vibration at ca. 1700 cm⁻¹ (see further below). Observations of BOTH vibrational features helps to identify an aldehyde.
- The aldehyde C-H stretching vibration has a lower frequency than other C-H bonds due to electron withdrawal from the C-H bond by the electronegative oxygen.

- Carboxylic acids have a broad O-H peak for the same reason that alcohols do, hydrogen bonding, however, the hydrogen bonding is STRONGER in carboxylic acids, which results in a lower frequency O-H stretching vibration due to a larger "pull" on the H atom away from the oxygen.
• The stronger hydrogen bonding also results in a **very broad absorption band** broad absorption band that is distinguished from the alcohol O-H in that it is centered around 3000 cm⁻¹, basically right in top of the usual C-H region
• Carboxylic acids are also distinguished from alcohols by having the C=O stretching vibration at ca. 1700 cm⁻¹ that is very strong (see later).

**Vibrations around 2500 - 1700 cm⁻¹ (2000 - 2500 cm⁻¹ = triple bond region)**
• Bonds to atoms heavier than hydrogen vibrate with lower frequencies, the strongest of these are triple bonds
• There are only two kinds of vibrations observed in this region, the C-N triple bond of the nitrile functional group and the C=C triple bond of the alkyne functional group

\[ \text{---C≡C---H} \quad \text{---C≡N:}\]

• The C-N triple bond absorptions due to nitrile tend to be strong because the dipole moment associated with this bond is also large

• Carbon-carbon triple bond absorptions tend to be somewhat weak (the bonds have very small dipole moments) and are only usually observed for the asymmetrical terminal alkynes (alkynes in which one carbon is attached to
hydrogen, the other to an alkyl or aryl group). Internal alkynes that have alkyl groups attached to both ends of the triple bond are too symmetrical, too small dipole moments and are usually not observed
• For terminal alkynes of course, the H-C(sp) vibration is also observed at ca. 3300 cm\(^{-1}\).

**Vibrations Around 1850 – 1600 cm\(^{-1}\) (1600 - 1850 cm\(^{-1}\) = double bond region)
• This is an important region of the IR spectrum, as usual, stronger bond vibrate at higher frequencies, which means that C=O double bonds are expected higher vibrational frequencies than C=C double bonds, and they do

\[\text{C}=\text{O}\]

• C=O bonds also have larger bond dipole moments than C=C bonds, and should have stronger absorptions than C=C bonds, and they do

\[\text{C}=\text{C}\]

• Vibrations of the C=O bond in aldehydes and ketone are VERY string and occur close to 1700 cm\(^{-1}\), often ca. 1710-1715 cm\(^{-1}\).
• Aldehydes can be distinguished from ketones because they also have the 2 peaks due to C-H vibration at ca. 2730 and 2820 cm\(^{-1}\) (which means the spectrum above must be of a ketone because these peaks are absent)

\[\text{C}=\text{C}\]

• C=C double bonds tend to have small dipole moments and are usually have weak (small) absorptions, the bonds are also weaker than C=O bonds and vibrate with lower frequencies, ca. 1620 cm\(^{-1}\)
Different C=O Vibrations Around 1730 – 1680 cm\(^{-1}\) \((1600 - 1850 \text{ cm}^{-1} = \text{double bond region})\)

- Small changes in the C=O bond strength can be detected in small changes in the C=O vibration frequency
- These small changes can be quite reliable and can be used to distinguish various kinds of C=O bonds

- The electronegative oxygen that is connected to the C=O bond in the ester makes all of the bonds stronger, including the C=O bond, thus, ester C=O vibrations occur at relatively high frequencies, around 1720 - 1730 cm\(^{-1}\)
- Even though this is only slightly higher than the normal frequencies for C=O bond vibrations in aldehydes and ketones it is diagnostic enough to distinguish most esters from ketones

- "Conjugated" ketones have a C=C bond adjacent to the C=O bond, the minor resonance contributor illustrates that the C=O bond has some single bond character in these cases. The more important the minor resonance contributor, the more single bond character (the C=O is less of a pure double bond), the weaker the bond, the lower the vibrational frequency
- conjugated aldehydes and ketones have vibration frequencies around 1680 cm\(^{-1}\), the difference compared to non-conjugated aldehydes and ketones (ca. 1710 cm\(^{-1}\)) is reliable enough to distinguish these cases
• The minor resonance contributor for the amide also shows that the C=O bond has some single bond character
• In the case of an amide the minor resonance contributor is even more important than the minor contributor in the conjugated system above, because the electrons that are involved in resonance "start" as non-bonding on the nitrogen and are thus higher energy than those in the double bond above, and are thus more "available" for resonance, the minor contributor here is "less minor"
• the vibration frequency is thus further decreased to ca. 1640 cm$^{-1}$. Just like amines, the amide will have N-H vibrations (with peaks) in the 3300 cm$^{-1}$ region

**MOLECULAR vibration at 1600 cm$^{-1}$ (1600 - 1850 cm$^{-1}$ = double bond region)**
• There is one final vibration that is not of a single bond, but is associated with an entire stretching motion of a benzene ring that is useful to us

• The peak is often not very strong (because of a small dipole moment again), but is usually sharp and very close to 1600 cm$^{-1}$, and is thus often easily identified.
• If there is a benzene ring there should also be C(sp2)-H bond vibrations, and these will be observed at >3000 cm$^{-1}$
• note that you will need to be able to distinguish "real" peaks from peaks due to impurities or other artifacts
• note that a benzene ring adjacent to a C=O bond represents a common example of a the more generic conjugated C=C adjacent to C=O

Example: a hydroxy ketone

• the strong peak at 1710 cm\(^{-1}\) must be an aldehyde or a ketone, in this case it must be a ketone because the two C-H aldehyde peaks at ca. 2700 and ca. 2800 are not observed
3 NMR Spectroscopy

3.1 Basic Principles: Nuclear Spin and Radio Frequency Absorption

- All charged objects that move generate a magnetic moment, i.e. have the property of magnetism
- We can think of electrons (negative charge) and protons (positive charge) as spinning, when they spin they generate a magnetic moment; this magnetic property of these particles are described as their “spin”
- However, this is classical picture of magnetism and spin, and spin is a quantum mechanical phenomenon, the classical picture misses some maybe confusing but important details, specifically:
  1) only TWO spin states are possible for electrons and protons (the +1/2 and -1/2 quantum numbers), and.....
  2) neutrons can also have spin (even though they have no charge, this is a quantum mechanical physics thing!)
- Taking the individual spins of the protons and neutrons into account and how many there are, then the nucleus as a whole CAN have an OVERALL SPIN, depending upon whether the neutron and protons cancel or not

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- The chart below is what you are provided with on a test to help you assign peaks:

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• For NMR to work, the nucleus must have an **overall nuclear spin**, this is the case for **1H hydrogen** (the nucleus is a proton) and also the **13 isotope of carbon**, but not the most abundant **12 isotope of carbon**
• We can do NMR on nuclei of hydrogen atoms (single protons) and the nuclei of **13C** atoms (and other atomic nuclei that we do not cover in this course)
• Overall nuclear spin can also have two states, we will call these alpha and beta, and when a sample containing 1H and 13C atoms is placed in a larger (external) magnet, these two magnetic spin states align either with the field (alpha) or against the field (beta).
  • the **alpha nuclear spins are now LOWER IN ENERGY** and the **beta nuclear spins are now HIGHER IN ENERGY** in the large external magnet and its associated magnetic field

![Diagram showing energy levels in a magnet and not a magnet](image)

• **NOW THAT THEY ARE IN THE MAGNET**, there is an energy difference between the alpha and beta spins, and we can equate this energy difference to a specific frequency of electromagnetic radiation using the usual equation
• **AND**, the energy gap depends upon how large the magnetic field is, put the sample in a **LARGE MAGNETIC** (large H0) and the energy gap is **LARGE**, in a small magnetic field (small H0) the energy gap is small, in **NO magnetic field**, there is no energy difference between the alpha and beta spins
• Electromagnetic radiation energy can convert the lower energy alpha spins into higher energy beta spins

![Energy diagram showing magnetic field and resonance frequency](image)

• the frequency of the radiation required to do this conversion alpha to beta is called the **resonance frequency**, it depends upon the energy gap (Delta E), and thus the magnetic field (H0), but even in very large magnetic fields the frequency is very small, and the frequencies are much lower than IR, or even microwave, they are in the radio range of the electromagnetic spectrum
• it is a **resonance frequency** because after an alpha spin is converted to beta, the beta will eventually find a way to return to the lower energy alpha spin state, releasing the energy (as a small amount of heat), where it absorbs radiation again to form beta, then to alpha etc., the radiation induces a resonance between the alpha and beta spin states
• Scanning through all of the possible frequencies for a sample in a magnetic field reveals the resonance frequency because the sample **ABSORBS** the radiation of this frequency (ONLY), it uses the energy to induce the spin change, and so absorption versus frequency is the NMR spectrum (simple version below)

![Absorbance graph showing resonance frequency](image)
3.2 Shielding and Deshielding

• MOST IMPORTANTLY the frequency tells us the energy difference between the alpha and beta spins, \( \Delta E \)
• AND, even though all of the nuclei in a molecules are in the same external magnetic field \( (H_0) \), the LOCAL magnetic field at each individual nucleus in the molecule can be different due to electron SHIELDING
• The electrons around a nucleus generate their own field that opposes the external field, i.e. electron motion magnetically SHIELDS the nuclei

![Diagram of atomic structure showing electron shielding and induced field](image)

• NOW, it gets a little confusing, because ALL nuclei are shielding in molecules by the electrons, when the shielding is reduced, for example by reduced electron density at an atom, the nucleus is said to be DESHIELDED
• DESHIELDING can occur when there is an electronegative atom close by, the electronegative atoms effectively "pull" electron density away from proximal hydrogens
• This DECREASES the nuclear shielding, INCREASES THE DESHIELDING, which INCREASES the LOCAL magnetic field, which requires a LARGER resonance frequency to convert the nuclear alpha and beta spins

Schematic EXAMPLE:

![Diagram of chemical structures showing chemical shifts](image)

• NOT all nuclei are shielded to the same extent, this is not a problem this is the entire basis of NMR spectroscopy

3.3 Chemical Shifts

• The differences in resonance frequency are actually very small, and plotting them in an absolute scale is not as useful as plotting them on a RELATIVE SCALE, this is the CHEMICAL SHIFT scale
• Chemical shifts are resonance frequencies RELATIVE to the signal from a standard, the usual standard is tetramethylsilane (TMS)

\[
\begin{align*}
\text{Me} & \\
\text{Me-Si-Me} & \\
\text{Me} &
\end{align*}
\]

• chemical shifts are measured in the unit-less delta (it is a ratio), and range from ca. 0 - 10 ppm in proton NMR spectra and from ca. 0 - 200 ppm in 13C NMR spectra. The delta value for TMS is always zero, by definition.
3.4 Which Direction is Which in the Spectrum?

- MORE DESHIELDING means LARGER LOCAL MAGNETIC FIELD, which means LARGE RESONANCE FREQUENCY, which means LARGER DELTA means LARGER CHEMICAL SHIFT

3.5 Which Groups Deshield and by How Much?

- 2 main factors influence deshielding
  1. the inductive effect of substituents, i.e mainly electronegativity
  2. the magnetic effect of substituents, which is mainly a property of unsaturated groups.
- We are concerned with ELECTRONEGATIVITY, UNSATURATION and COMBINATIONS OF THESE TWO

**Electronegativity.** Let's look at a real spectra to illustrate...
A proximity to the electronegative oxygen results in DESHIELDING, which increases delta. 
The farther away from the oxygen, the less the electronegativity effect is, the lower the deshielding. 
Nuclei that experience the same LOCAL FIELD due to the same bonding and symmetry are MAGNETICALLY EQUIVALENT, they all contribute (add to) the same signal; in the NMR spectrum. 
NOTE the similarity between the proton and $^{13}$C spectra. $^{13}$C spectrum gives number of equivalent carbons in the molecule.

**Unsaturation** For example, the effect of proximity to pi bonds:
- Electron movement induced by the external magnetic field in the pi-orbitals that contain the polarizable electrons is responsible for generating an ADDITIONAL local magnetic field which ADDS to the external field, effectively DESHIELDING the protons and carbons that are part of pi-systems.

- deshielding by the benzene ring even larger than for alkene double bonds;
- note the characteristic frequencies of the aromatic protons, i.e. ca. 7 ppm, and 130 ppm.
- NOTE also that in the example below, all 5 protons on the benzene ring have signals that are so close together they overall (even though they are not all magnetically equivalent, this happens sometimes).
• in these spectra, the aromatic $^1$H signals overlap extensively and the magnetically inequivalent protons cannot be distinguished, although they can in the $^{13}$C spectrum

Combined Unsaturation/Electronegativity  For example, proximity to pi-bonds

• unsaturation and electronegativity combine to give largest chemical shifts
• there are ranges of chemical shifts even for similar kinds of nuclei, but the ranges are fairly well defined.
This is all slightly tricky and is worth reviewing once more……

1) Nuclear spins ALIGN in a magnetic field

\[ \text{H}_0 \uparrow \beta \alpha \beta \uparrow \alpha \downarrow \]

EXTERNAL FIELD

2) Takes ENERGY \( (E=\hbar\nu) \) to flip a spin

\[ \text{H}_0 \uparrow \beta \alpha \beta \uparrow \alpha \downarrow \]

EXTERNAL FIELD

3) The ENERGY/frequency depends upon the LOCAL MAGNETIC FIELD AT THE NUCLEUS

\[ \Delta E = \hbar \nu \]

larger local magnetic field means

4) Electrons SHIELD the nucleus from the external field, DECREASING the LOCAL FIELD

\[ \text{H}_0 \uparrow \beta \alpha \beta \uparrow \alpha \downarrow \]

EXTERNAL FIELD

5) Less Shielding/DEshielding by electropositive elements and unsaturation

\[ \beta \uparrow \Delta E = \hbar \nu \alpha \downarrow \]

6) SUMMARY....... 

\[ \beta \uparrow \Delta E = \hbar \nu \alpha \downarrow \]

Approximate chemical shift regions are shown below

\[ \text{downfield deshielded} \]

\[ \text{upfield shielded} \]

- carbonyl
- aromatic
- alkene
- halogens
- alkane

Finally, Extent of Substitution in Carbon Spectra

\( ^{13}\text{C} \) spectra are more sensitive to deshielding factors than proton spectra because there are more electrons around each C nucleus compared to H. Even the number of alkyl groups around a carbon can be determined in
carbon spectra. Even though the electronegativity difference between C and H is small, replacing H with the slightly more electronegative C results in slightly more deshielding. Specifically, going from a primary carbon to secondary to a tertiary carbon results in signals that increasingly deshielded, let's revisit a spectrum from above....

![Spectrum Image]

even though both of the circled C atoms are directly attached to oxygen, the "central" carbon of the t-butyl group, C2, is significantly more deshielded than the carbon of the methyl group C2 BECAUSE it is tertiary (has more C atoms attached to it) compared to C1, which is primary.

### 3.6 Signal Splitting: (N + 1) Rule and Coupling Constants

- **no H atoms on adjacent carbons**

![Diagram of Signal Splitting](Diagram)

- In the absence of any other hydrogen atoms, Ha (ABOVE) has a conventional resonance frequency/chemical shift that is determined by its local magnetic field as usual
- the PRESENCE OF Hb, however, alters the local magnetic field at Ha, the TWO possible spin states at Hb results in both a small INCREASE in the local field (alpha spin) and also a small DECREASE in the local field (beta spin), this results in TWO NEW resonance frequencies/chemical shifts, the peak is split into TWO, it becomes a DOUBLET

- the presence of the TWO hydrogens HB (BELOW) result in THREE local magnetic fields at proton Ha, the peak for Hα is similarly split into THREE, it appears as a triplet.

![Diagram of Signal Splitting](Diagram)

**Splitting "Rules"**
- **N+1.** The number of peaks into which a signal is split is equal to the number of non-magnetically equivalent protons with which it interacts + 1 (assumes all equal J value, which is explained below)
- in our courses, splitting only occurs with protons on ADJACENT carbon atoms, hydrogens on carbons further away usually have only7 a weak effect and can usually be ignored
- the area ratio’s of the peaks in a splitting pattern is given by Pascal's triangle
coupling constants (J) have to be identical for interacting protons (see below)

The coupling constant is the extent to which it is split, and is given the symbol J

in the example below, the 3 \( \text{H(a)} \)'s "split" the two \( \text{H(b)} \)'s (and vica versa).

The splitting of both signals are identical because they are "coupled"

J is usually ca. 7 Hz for protons on alkyl chains with free rotation

Here is the carbon nmr spectrum of the same molecule as in the proton spectrum above

**IMPORTANT POINTS**

1) All of the \( ^{13} \text{C} \) spectra in OUR organic chemistry courses are "PROTON DECOUPLED", i.e. no splitting is observed in our carbon spectra

2) The same factors that determine chemical shift in the proton spectrum determine chemical shifts in the carbon spectrum

3) There are more peaks in the carbon spectrum compared to the proton spectrum, which means that one of the carbon atoms does not have any hydrogens attached (the \( \text{C}=\text{O} \) carbon in this case)

**Example Problem:** Assign the protons to the peaks in the provided spectra
• how are the benzene protons C and D distinguished in these spectra?

• minor resonance contributors tell us about minor changes in electron distribution in the benzene ring
• a partial negative charge means increased electron density, more shielding, LESS DEshielding, smaller chemical shift, these are the protons indicated a D in the structures above

• a partial positive charge means decreased electron density, less shielding, MORE DEshielding, larger chemical shift, these are the protons indicated a C in the structures above
### 3.7 Signal Sizes: Integration

- In $^1$H spectra, the signal size relates to the number of contributing protons.

* NMR spectrometers provide **relative signal sizes**, historically as an integration trace.
* It is the INTEGRATED AREAS under the peaks that determine signal "size", not peak height.
* Signal size is related to the # of equivalent H's in proton spectra.
* In most of the spectra you will see, however, the ABSOLUTE number of hydrogens that contribute to a signal are given (which is a lot easier).
* **Signal size is NOT related to # of equivalent C's in $^{13}$C spectra due to spin relaxation effects.**

### 3.8 Complex Splitting

- Breakdown of the (N + 1) rule occurs when protons are split with different coupling constants (J).
- Splitting by different protons with different J values results in complex splitting patterns, usually best understood with the aid of a "splitting tree" (note the "order" of the splitting does not matter).

* The protons Ha and Hc are also doublets-of-doublets, although one of the splittings is so small that they look like simple doublets at the resolution of this spectrum.

### 3.9 Exchangeable Hydrogens

- Under usual conditions, N-H and O-H protons exchange on the NMR timescale due to hydrogen bonding with each other and with small amounts of water and particularly acid or base impurities (it is quite difficult to completely dry most organic solvents).
in many of the nmr spectra the timescale of the hydrogen atom exchange is faster than the timescale of the nmr experiment, and "blurred" or averaged signals for O-H protons are observed

the chemical shifts of O-H (and N-H) protons are thus very condition dependent (e.g. they vary with concentration, see below), AND, it is not really possible to use our usual understanding of deshielding to predict their chemical shifts

Because of this "blurring" or averaging of exchanging protons, splitting is not observed (they are SINGLETS), they are not split and they do not split

because they are exchangeable, O-H (and N-H) signals ALSO usually disappear upon shaking with D₂O because the H is exchanged for D, and D is not visible in a proton nmr spectrum

signals may or may NOT be indicated as exchangeable on a nmr spectrum, but if they are then this is very useful diagnostically, it shows that the protons are bonded or oxygen (or nitrogen)

3.10 Real Spectra

real spectra are often not as simple as those provided in this lecture course!
you are usually given the absolute number of hydrogens for each peak in ¹H NMR, however, real integrations give only relative numbers of hydrogens, peak ratios have to be converted into absolute hydrogen atom count

spectra are run in solvents in which the H's have been exchanged for D's, however, exchange is never complete and peaks due to solvent are often observed
real spectra often contain peaks from impurities and other contaminants
small peaks, e.g. on tertiary carbons, may get "lost" in the noise in ¹³C NMR spectra

Example:
4 Solving Spectral Problems: A Suggested Procedure

• For most of the spectrum problems you will be asked to solve in this class you will be provided with the molecular formula: here is the suggested procedure for these problems

1. Get degrees of unsaturation from the molecular formula
2. Get functional group information from the IR
3. Get the number of chemically inequivalent carbons, and confirm functionalities from $^{13}\text{C}$ NMR
4. Compare # of signals in proton and $^{13}\text{C}$ NMR's to determine whether there are carbons without hydrogens
5. Build molecular fragments and put them together to make tentative structures
6. See if the structures fit the proton NMR. Important! Try to get as much information from the other spectra before going to the proton NMR

Example Problem 1: Determine the structure and assign the peaks in the proton NMR spectrum

Molecular formula = C$_6$H$_{12}$O$_2$

• this implies 1 double bond OR 1 ring but not both

• The IR spectrum clearly shows no C=C unsaturation (no C-H stretch above 3000 cm$^{-1}$), and clearly shows a carbonyl group. This is around 1740 cm$^{-1}$, and so must be an ester, which means that we have "found" the one degree of unsaturation

• the $^{13}\text{C}$ NMR confirms the carbonyl carbon with high chemical shift
• the spectrum has only 4 additional peaks, which means that there must be 2 magnetically equivalent carbon atoms, this is commonly an isopropyl group
• look for the methyl groups in the proton NMR, they come in integral multiples of 3, they tend to be less deshielded because they have to be at the end of a chain, and from their splitting patterns you can figure out what they are connected to

**Important!** After you have your structure, **predict** a proton spectrum and see if it matches the provided spectrum. You should not be in any doubt as to whether you have the correct structure

**Example Problem 2**
Molecular formula = C₁₈H₁₀O₄
• therefore we immediately think about there probably being a benzene ring (which has 4 degrees of unsaturation on its own)

* The IR spectrum clearly shows an –OH group, and C=C unsaturation (C-H stretching vibrations above 3000 cm⁻¹), and evidence for a benzene ring stretch at ca. 1600 cm⁻¹
• the 13C nmr spectrum confirms the benzene ring, and there are TWO other peaks in "aliphatic" region that can not be magnetically equivalent
• there are 4 signals in the aromatic region, thus the substitution pattern on the benzene ring must be either a monosubstituted ring, or a 1,4 substituted ring

• 5 protons in the aromatic region conform that the benzene must be monosubstituted
• NOTE: in this case the aromatic region have a 5 H peak that is split, this doesn't mean that the 5 H atoms on the benzene are magnetically equivalent but that the chemical shift differences are small and that the signals OVERLAP, this is often observed when a benzene ring has a simple alkyl substituent
• the two 2H doublets tell us that there are no methyl groups (which would have a 3H signal) and that the structure has to be as shown, the more desigield 2H signal must be the one attached to the electronegative oxygen
• REMEMBER: H atoms connected to O (or N) are exchangeable and are never split and do not split and have chemical shifts that are very variable and difficult to predict

Example Problem 3: Determine the structure and assign the peaks in the proton NMR spectrum
Molecular formula = C\textsubscript{10}H\textsubscript{12}O
• therefore we immediately think about there probably being a benzene ring
• the IR spectrum confirms the presence of a benzene ring and also suggests a conjugated C=O

• the 13C NMR confirms the benzene ring (signals in the aromatic region) and the presence of a C=O (the highly deshielded signal) and 3 other carbons, none of which are magnetically equivalent
• the four signals in the aromatic region suggest either a mono- or a 1,4-disubstituted benzene

• 5 hydrogens are observed in the aromatic region, which means that the benzene must be mono-substituted
• the alkyl chain structure is obtained from analysis of the splitting patterns
• the aromatic signals are assigned on the basis of their integrations, splitting, and shielding

Important! After you have your structure, predict a proton spectrum and see if it matches the provided spectrum. You should not be in any doubt as to whether you have the correct structure.