Organic Structure Determination Analytical Chemistry

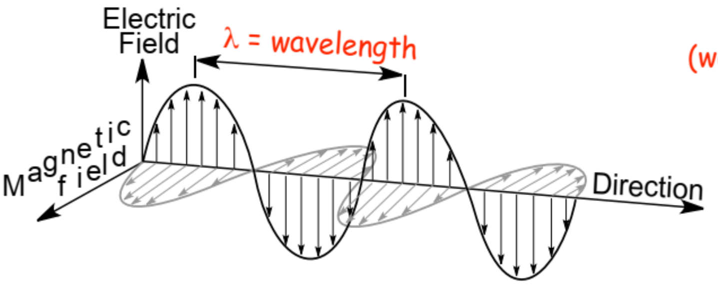
Instrument-based methods for determination of structure of organic molecules
1) Infrared Spectroscopy - yields functional groups
2) NMR Spectroscopy - very important, yields structure - described in the next section of the notes

1 Infrared Spectroscopy

- 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.**



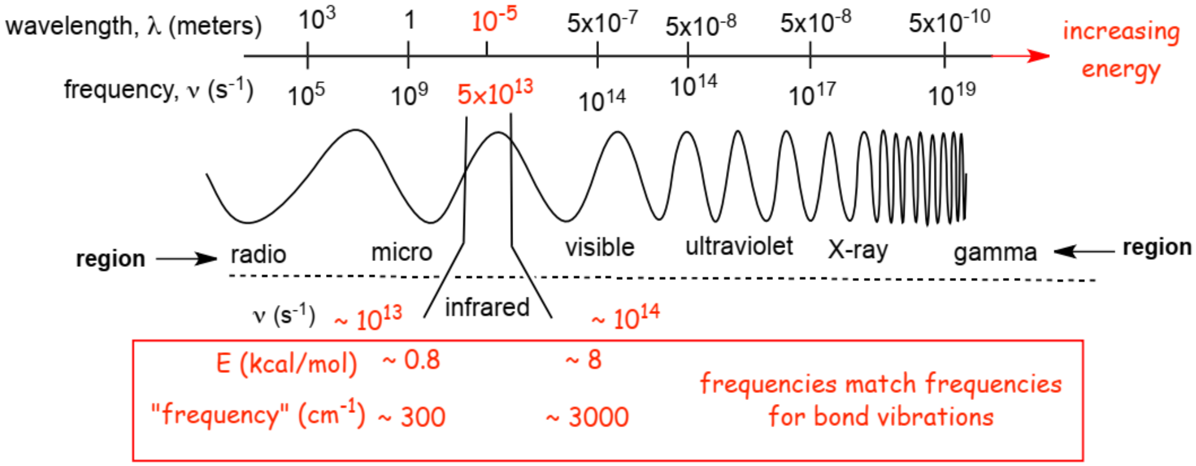
$$\underset{\text{(wavelength)}}{\lambda} = \frac{\text{c (speed of light)}}{\nu \text{ (frequency)}}$$

c = speed of light
h = Plank constant

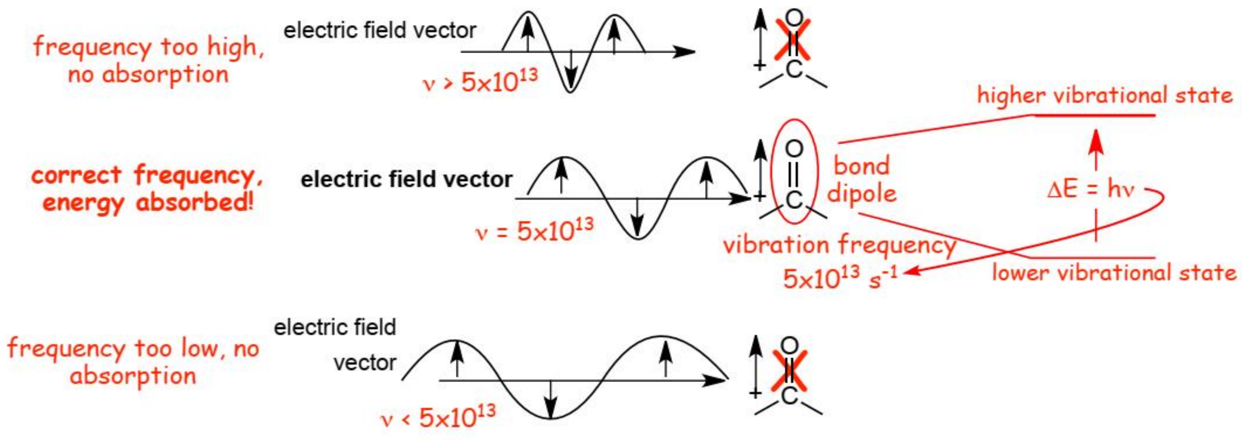
$$\text{Energy (E)} = \frac{h\,c}{\lambda}$$

$$\text{Energy (E)} = h\nu$$

The Electromagnetic Spectrum

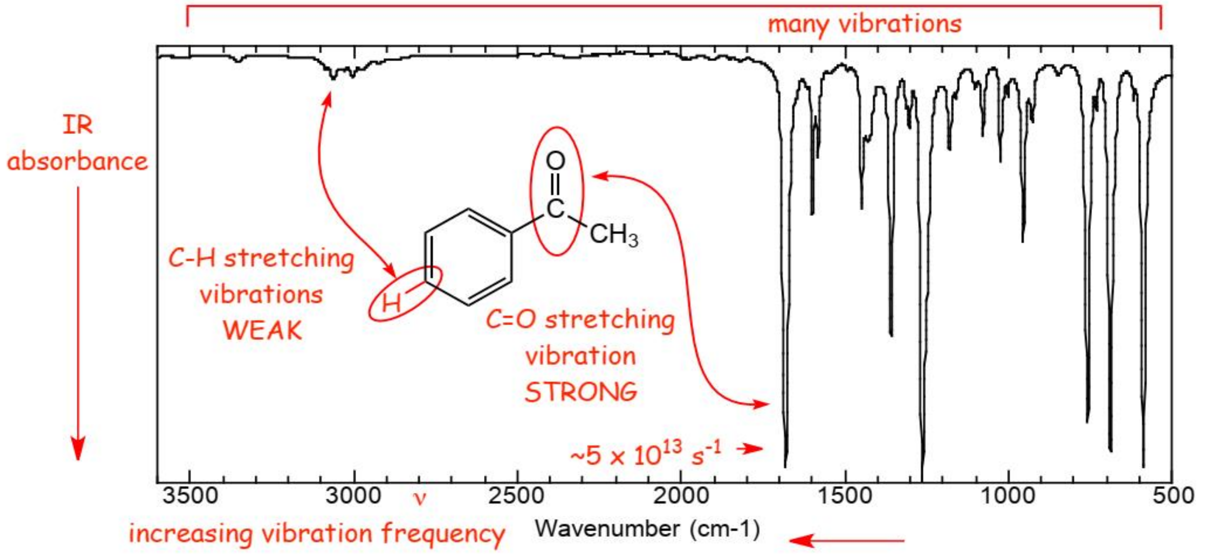


- The range of frequencies of the electromagnetic radiation in the **infrared region** matches the range of **frequencies of vibrations of bonds in molecules.**
- If the frequency of the infrared radiation exactly matches that of a particular bond vibration in a molecule, then the electric field vector 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**

1.1 A Real Infrared Spectrum



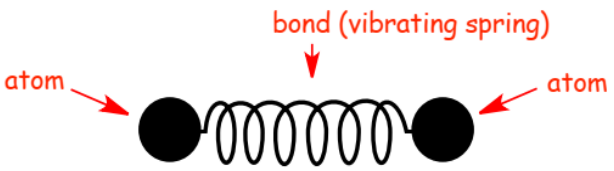
- Infrared Vibrations are often localized on bonds or groups of atoms (the more useful vibrations are localized on specific bonds)
- Different bonds vibrate with different frequencies, this is important as this is the basis for identifying different bonds/functional groups in a spectrum, and hence in 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?

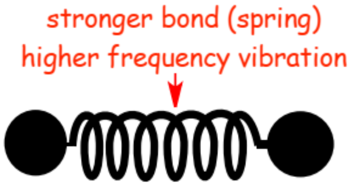
- For n atoms, there are MANY POSSIBLE vibrations, in fact (3n + 6)!
- However, many of these are complex, i.e. are not localized on individual bonds, and occur with lower frequencies (less than 1500 cm-1) in the "fingerprint region", which is the area that has signals that are specific to a particular 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**

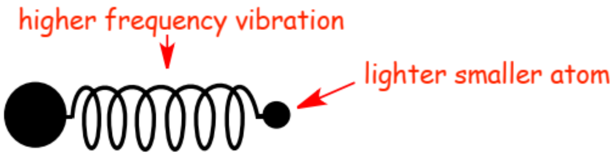


INCREASING bond strength

INCREASING frequency

bond	BDE (kcal/mol)	ν (s^{-1})	E (cm^{-1})
C—C	~85	3×10^{13}	1200
C=C	~145	5×10^{13}	1600
C≡C	~200	6×10^{13}	2100

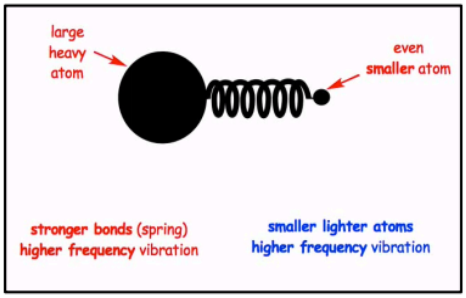
- A bond (spring) with small/light atoms attached will vibrate with a higher frequency



DECREASING mass

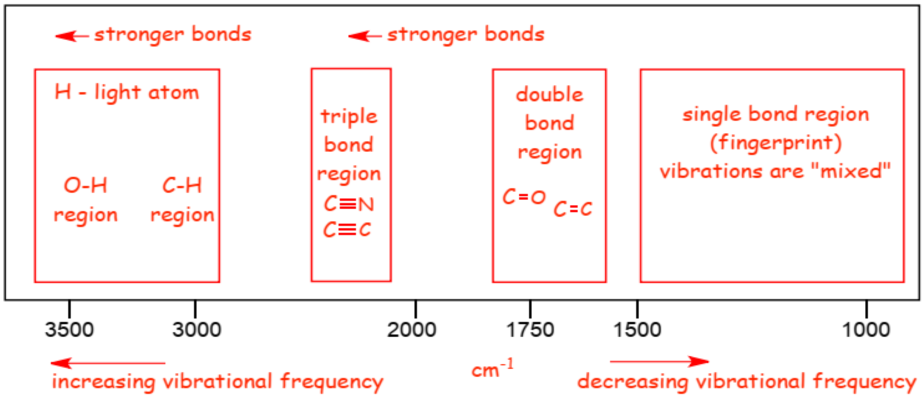
INCREASING frequency

bond	BDE (kcal/mol)	ν (s^{-1})	E (cm^{-1})
C—C	~85	3×10^{13}	1200
C—D	~100	6×10^{13}	2100
C—H	~100	10^{14}	3000



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

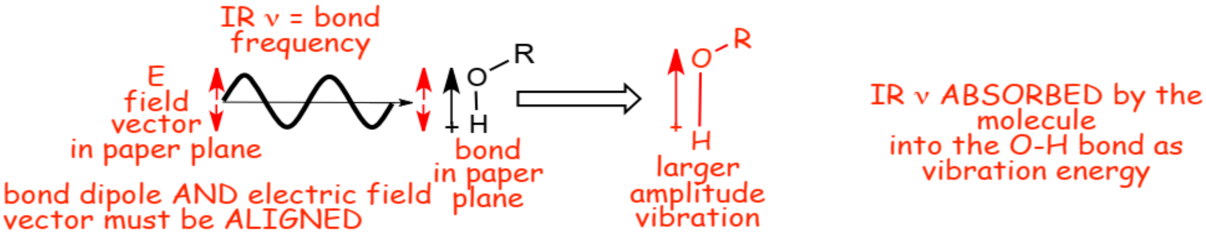
Approximate Regions in the Infrared Spectrum



- 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.
- Double bonds to heavier elements come next, with higher frequencies for stronger bonds.
- Single bonds to heavier elements have the lowest frequencies, usually in the fingerprint region where identifying functional groups is difficult, and is not included in this course.

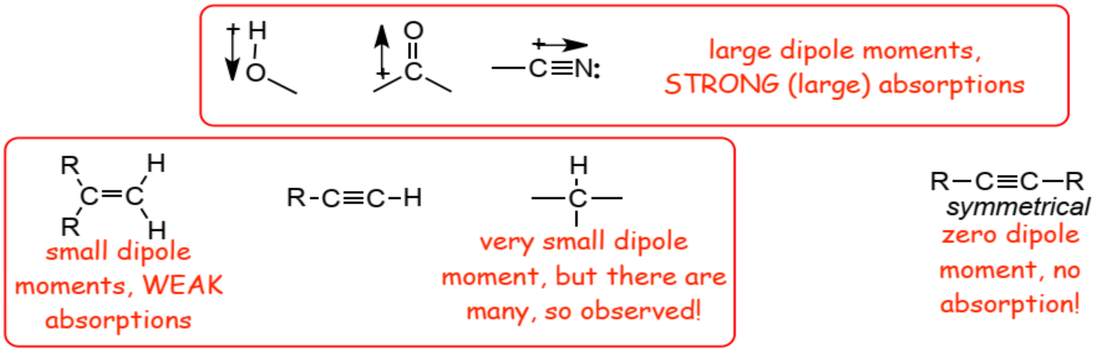
3) How strong are the Absorption Peaks (how big are the peaks in the spectra)?

- The **electric field vector** of the electromagnetic radiation interacts with **dipole moment** of the vibrating bond
- When the **DIRECTION OF THE electric field (vector)** of the IR electromagnetic radiation is **ALIGNED 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 bind 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 results in absorption of a lot of IR radiation which in turn results strong IR absorptions



- 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.

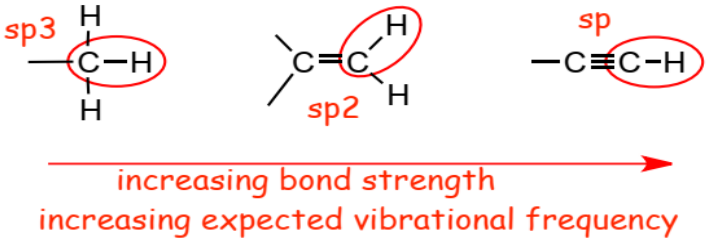
Examples:



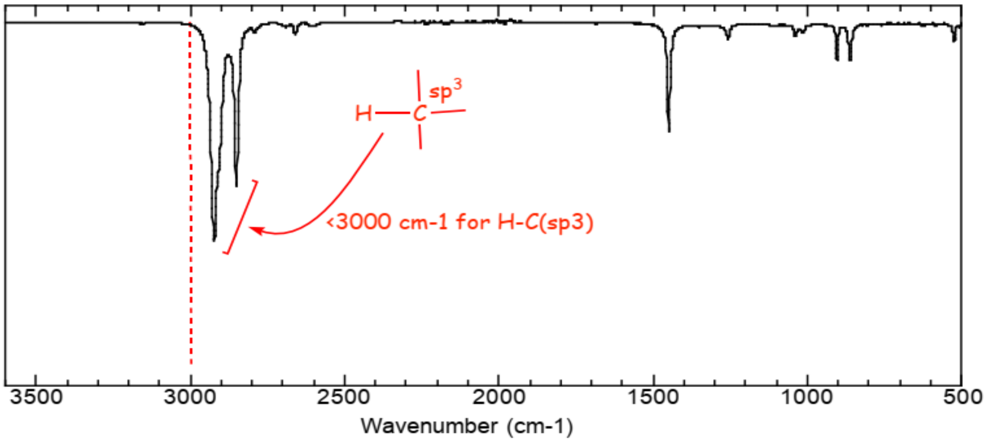
1.2 Real Absorption Bands

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

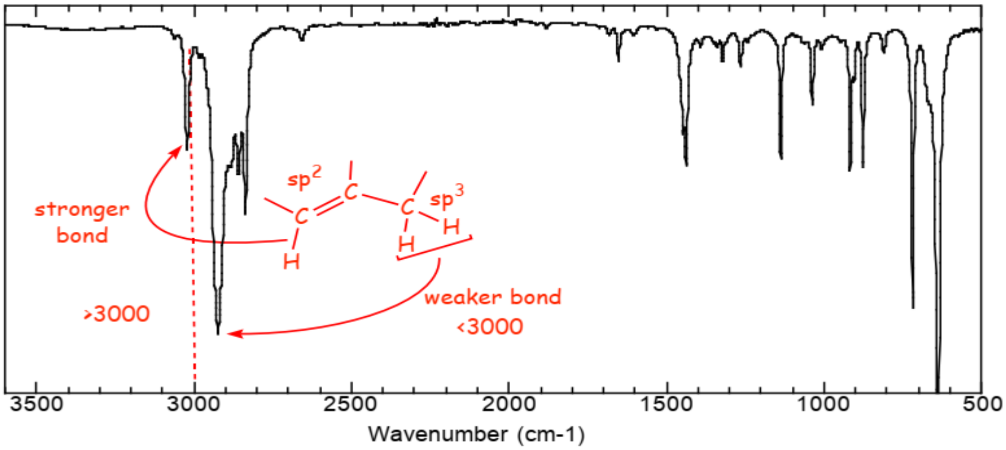
- H atoms are LIGHT, bonds to H atoms tend to be high frequency (large nu), ca. 2700 - 3500 cm-1
- stronger C-H bonds will vibrate with higher frequencies, weaker C-H bonds will vibrate with lower frequencies
- We KNOW SOMETHING about C-H bond strengths……



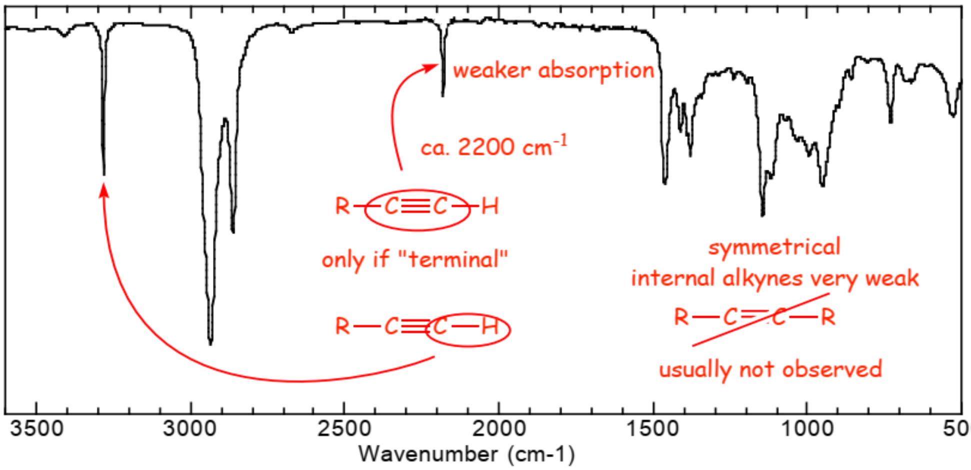
- We EXPECT that stronger C-H bonds will have higher frequency absorption in IR spectroscopy, and they do!



- 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 sp3 hybridized carbons. Bonds from hydrogen to sp3 carbons are somewhat weaker than bonds to, e.g. sp2 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



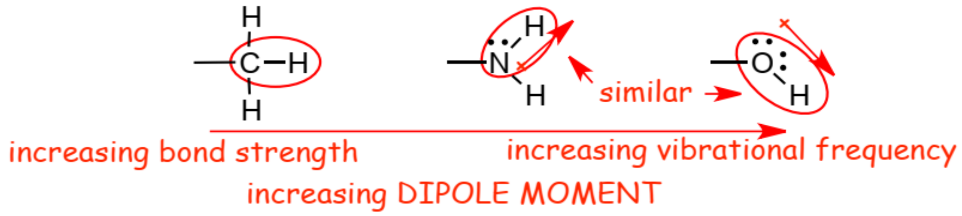
- peaks due to C-H vibrations that are found at frequencies just above 3000 cm-1 are due to H atoms that are attached to sp2 hybridized carbons. Bonds from hydrogen to sp2 carbons are somewhat stronger than bonds to sp3 hybridized carbons, and thus are found at somewhat higher frequencies



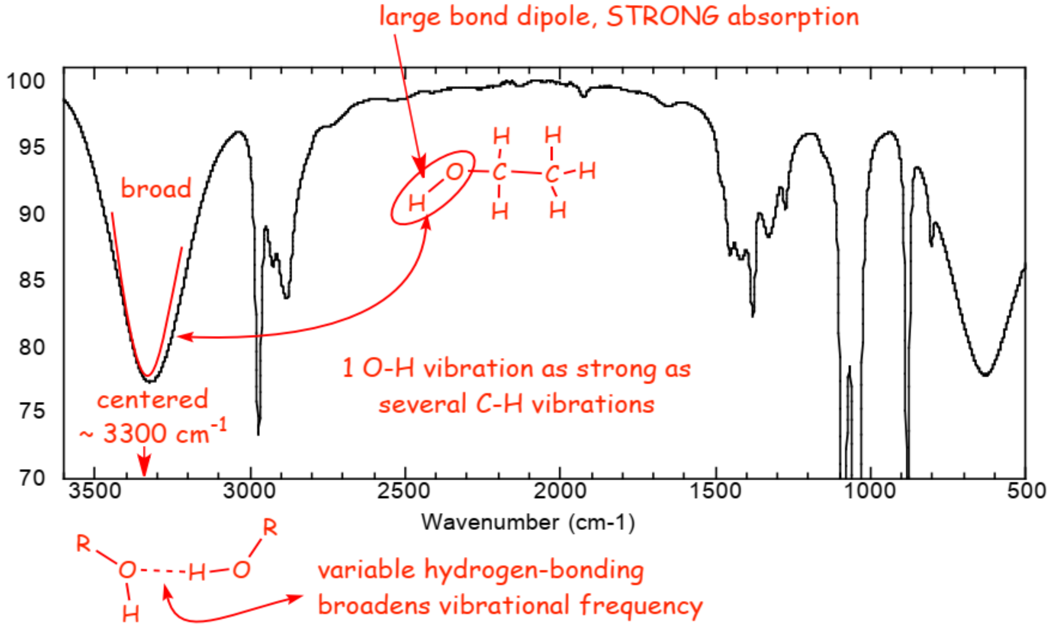
- C-H vibrations around 3300 cm-1 are due to H atoms that are attached to sp hybridized carbons. These are stronger bonds with higher vibrational frequencies. They are distinguished from O-H and N-H bonds by the fact that they are not broad

Vibrations greater than 3000 cm^{-1}: (2700 - 3500 cm^{-1} = bonds to H atoms)

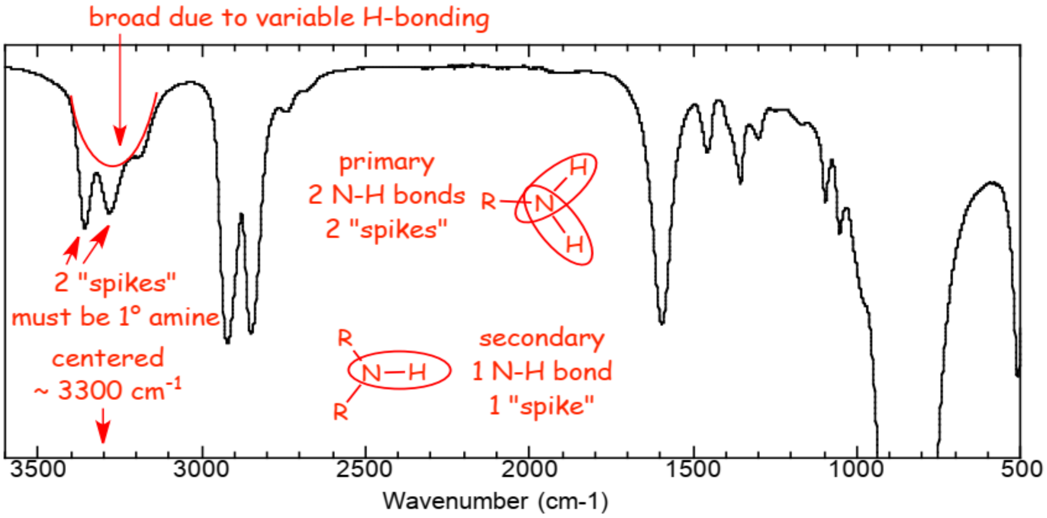
- Bonds between hydrogen and other elements are also expected to have high frequency vibrations
- AND, bonds to more electronegative elements than carbon are **stronger** and are thus expected to vibrate with **higher frequencies**
- We therefore EXPECT that bonds to more electronegative elements should have higher vibration frequencies because they are stronger

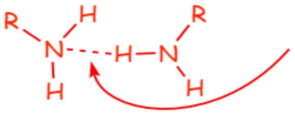


- N-H and O-H bonds ALSO HAVE larger dipole moments; their IR absorption peaks should be **stronger**



- 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)

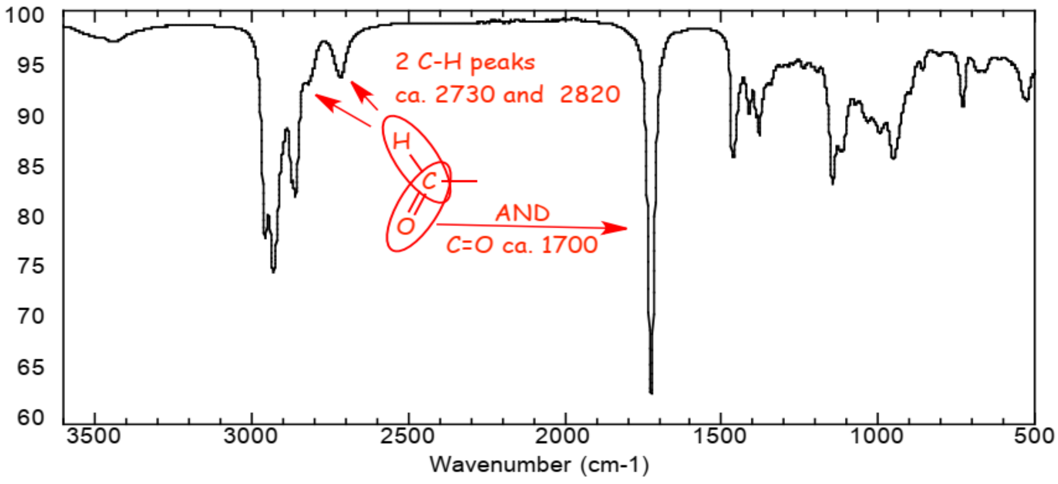




WEAKER Hydrogen-bonding
therefore sharp N-H vibration peaks CAN be observed

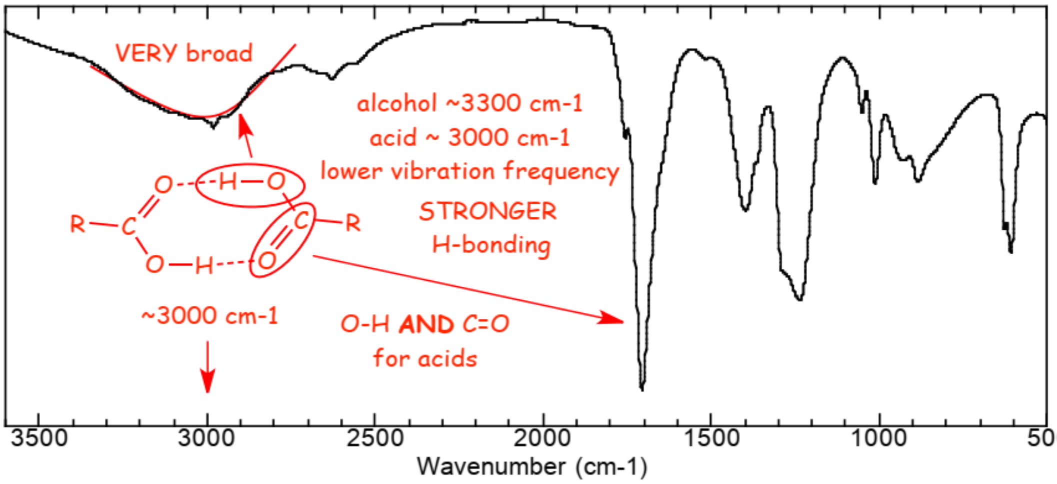
- The amine N-H stretching vibration is also broad due to hydrogen-bonding, but N-H hydrogen bonding is WEAKER than O-H Hydrogen bonding (nitrogen is less electronegative than oxygen), and some **non-hydrogen bonded N-H vibrations** can be observed as small sharp peaks on top of the broad absorption
- 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

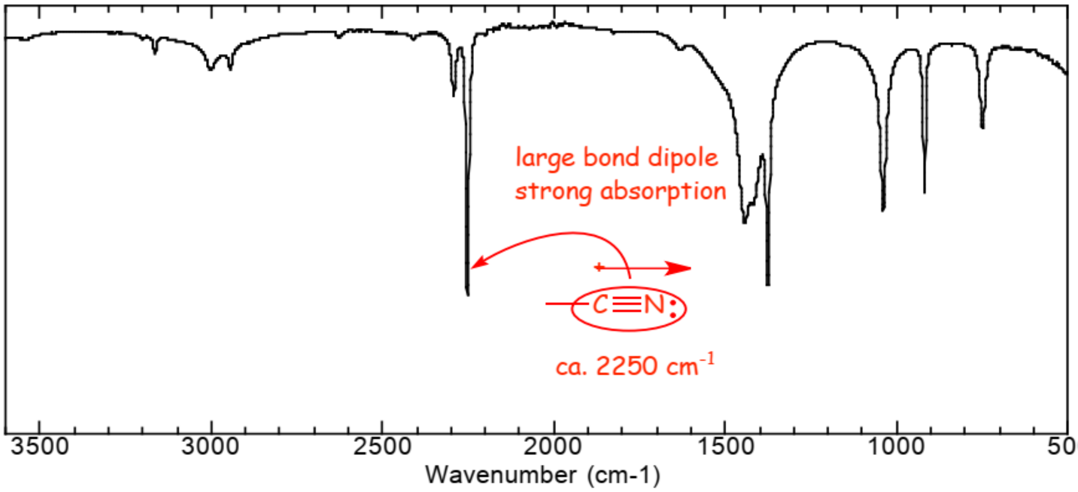
- These are sometimes difficult to distinguish, and can range between ca. 2720 - 2740 and ca. 2810 - 2830, but the aldehyde also has the strong C=O stretching vibration at ca. 1700 cm-1 (see further below). Observation of BOTH vibrational features helps to identify an aldehyde
- The aldehyde C-H stretching vibration has a lower frequency than other C-H bonds due to electron withdrawal from the C-H bond by the electronegative oxygen



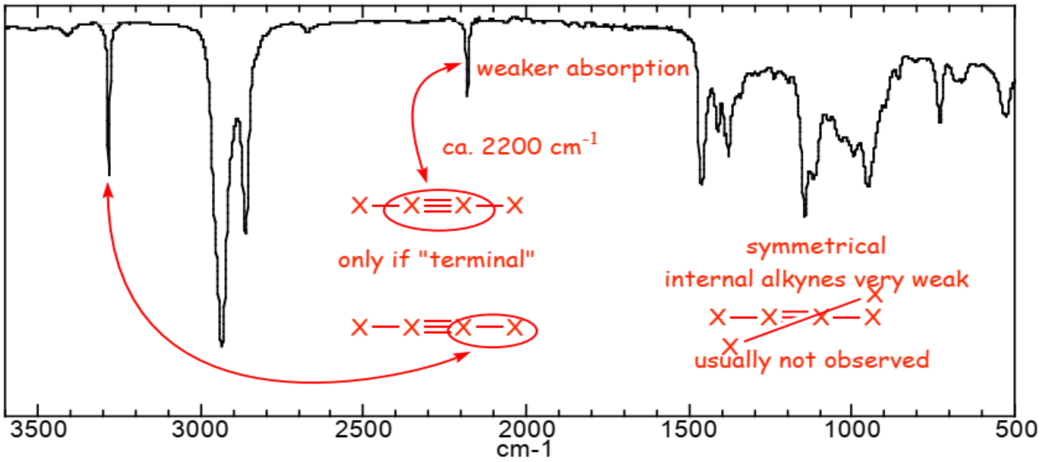
- **Note: Two absorption peaks are observed for carboxylic acids corresponding to O-H and C=O vibration**
- Carboxylic acids have a broad O-H peak for the same reason that alcohols do, hydrogen bonding, however, the **hydrogen bonding is stronger in carboxylic acids**, which results in a lower frequency O-H stretching vibration compared to an alcohol 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



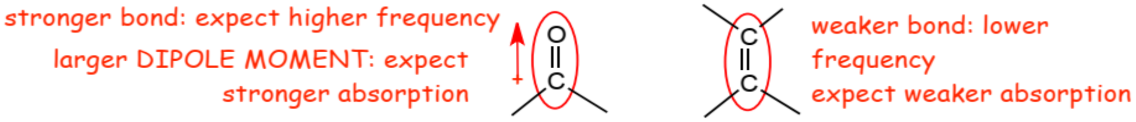
- The C-N triple bond absorptions due to nitrile tend to be strong because the dipole moment associated with this bond is VERY large!



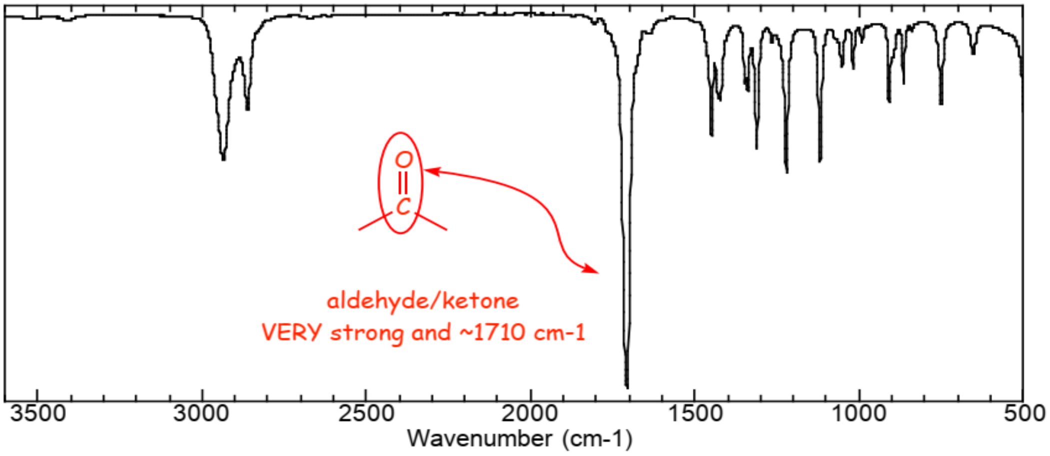
- Carbon-carbon triple bond absorptions tend to be somewhat weak (the bonds have very small dipole moments) and are only usually observed for the asymmetrical terminal alkynes (alkynes in which one carbon is attached to hydrogen, the other to an alkyl or aryl group). Internal alkynes that have alkyl 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)

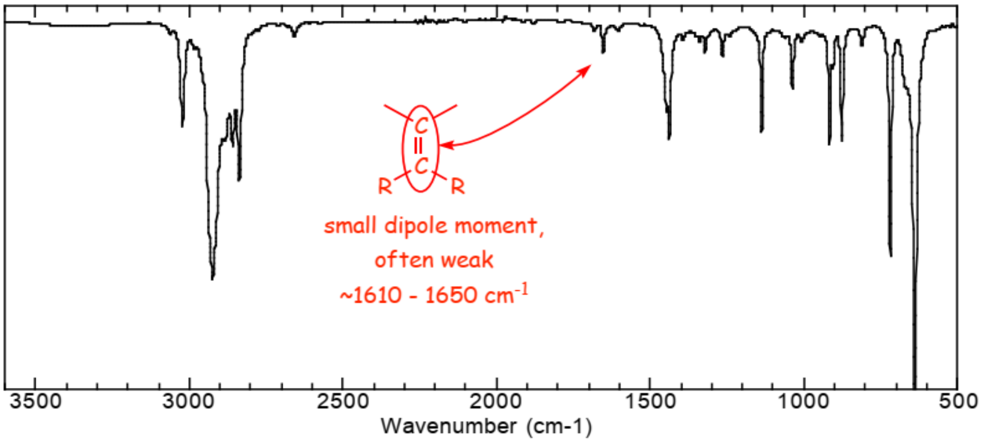
- This is an important region of the IR spectrum, as usual, stronger bonds vibrate at higher frequencies, which means that C=O double bonds are expected higher vibrational frequencies than C=C double bonds, and they do



- 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



- Vibrations of the C=O bond in aldehydes and ketone are VERY strong 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)

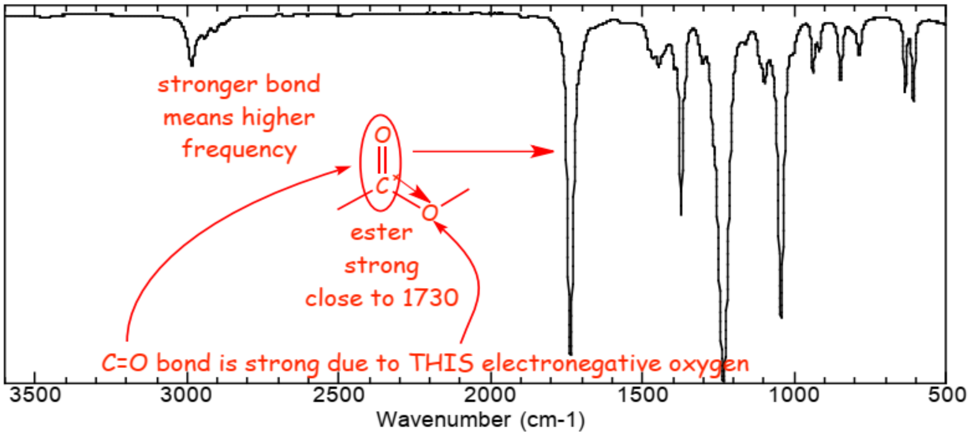


small dipole moment,
often weak
~1610 - 1650 cm^{-1}

- 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 cm^{-1} = 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

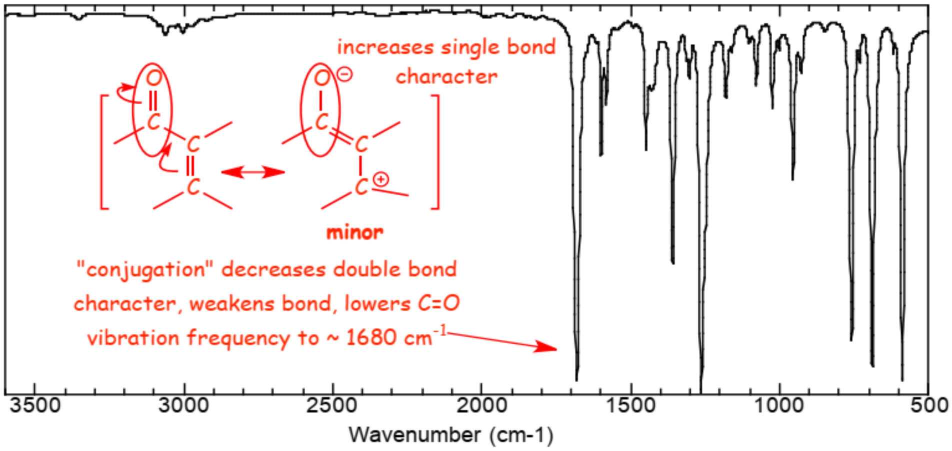


stronger bond
means higher
frequency

ester
strong
close to 1730

C=O bond is strong due to THIS electronegative oxygen

- 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

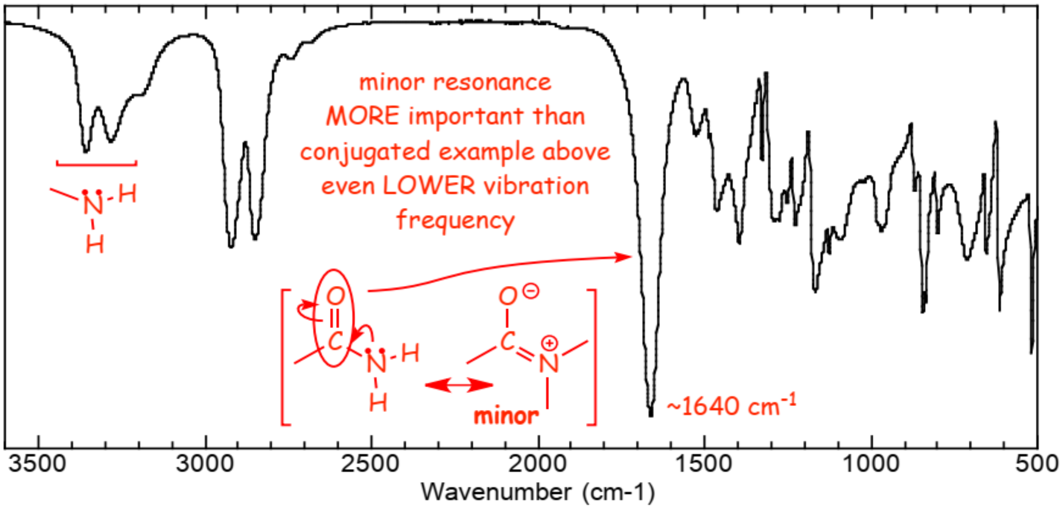


increases single bond
character

minor

"conjugation" decreases double bond
character, weakens bond, lowers C=O
vibration frequency to ~ 1680 cm^{-1}

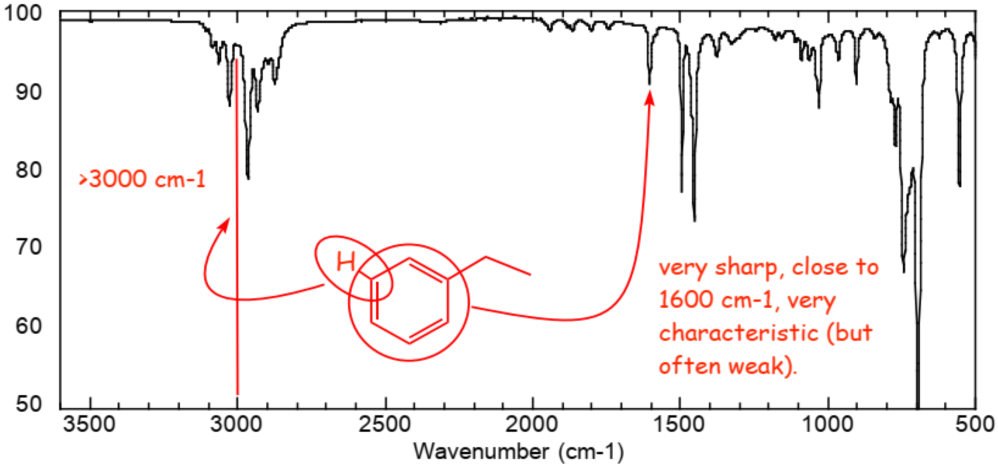
- "Conjugated" ketones have a C=C bond adjacent to the C=O bond, the minor resonance contributor illustrates that the C=O bond has some single bond character in these cases. The more important the minor resonance contributor, the more single bond character (the C=O is less of a pure double bond), the 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.

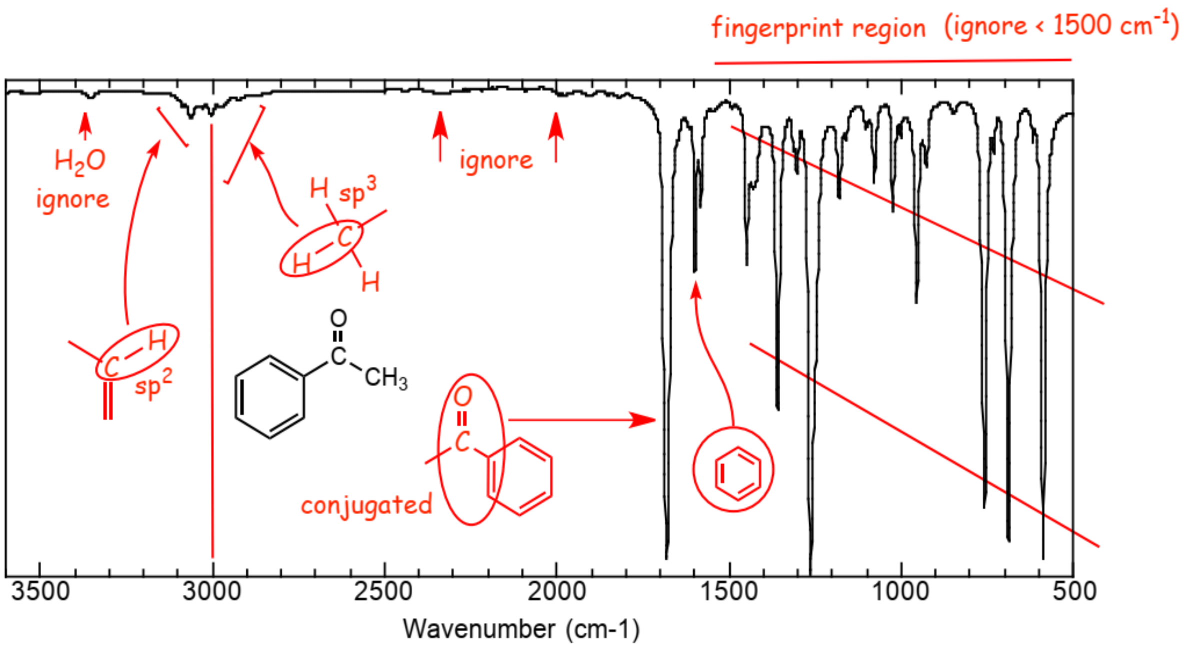
MOLECULAR vibration at 1600 cm^{-1}: (1600 - 1850 cm^{-1} = double bond region)

- There is one final vibration that **is unusual in that it is not of a single bond**, but is associated with **a stretching motion of an entire benzene ring** that is useful to us.



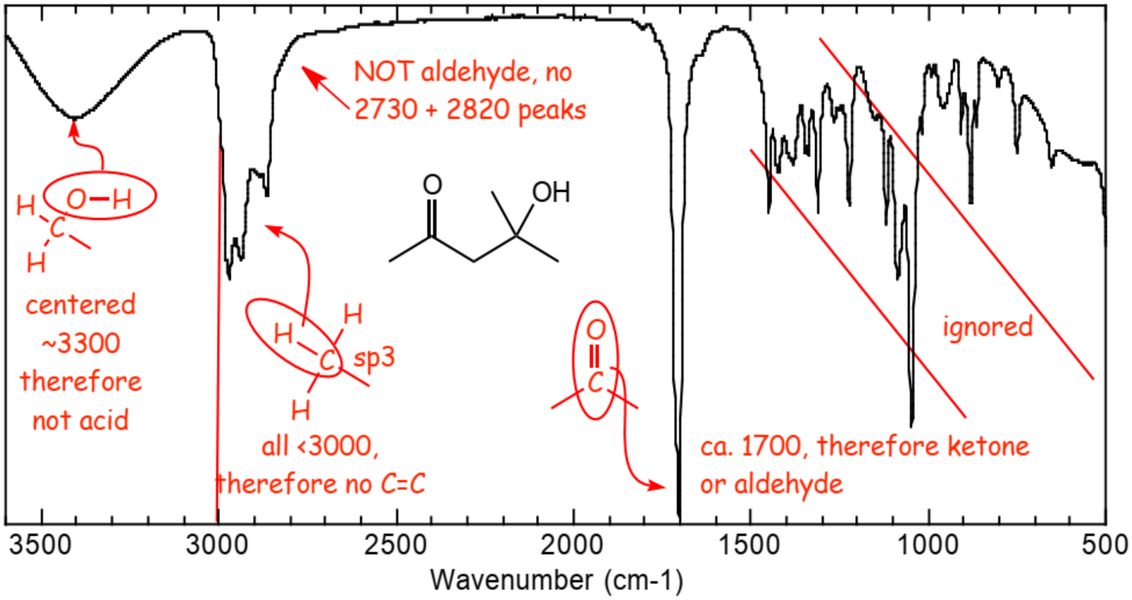
- The peak is often not very strong (because of a small dipole moment again), but is usually sharp and very close to 1600 cm^{-1}, and is thus often easily identified.
- If there is a benzene ring there should almost always also be C(sp2)-H bond vibrations, and these will be observed at >3000 cm^{-1}.

Return to Real Spectra: Example: Acetophenone



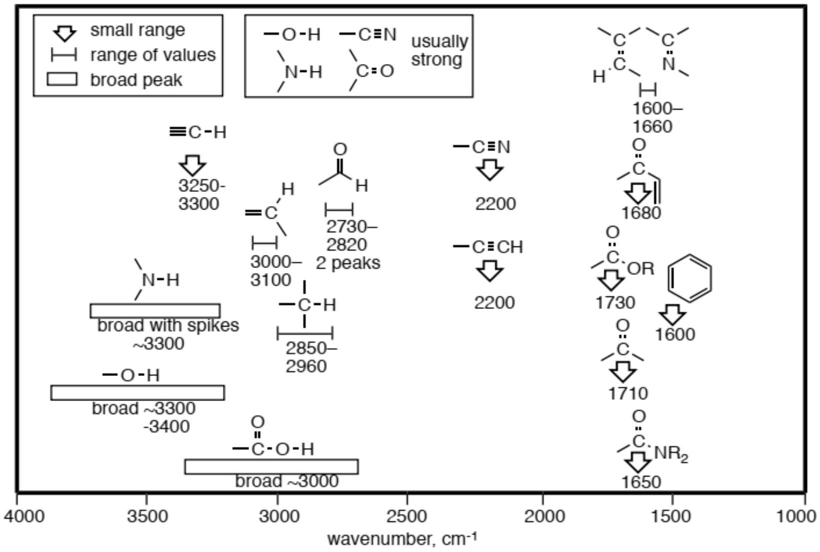
- Note that you will need to be able to distinguish "real" peaks from peaks due to impurities or other artifacts, such as water as a contaminant, which is often seen as a **weak** peak around 3300 cm^{-1} (any “real” peaks in this region would be **strong**).
- Note that a benzene ring adjacent to a 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.

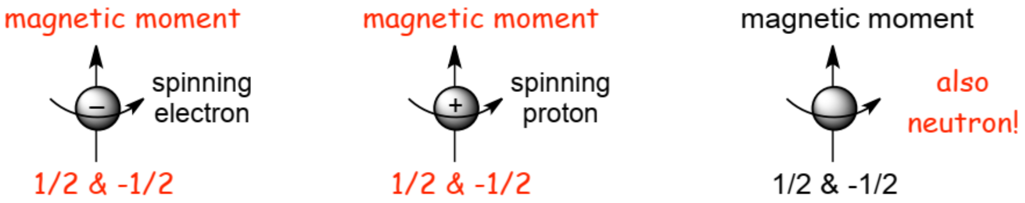
The chart below is what you are provided with on a test to help you assign peaks



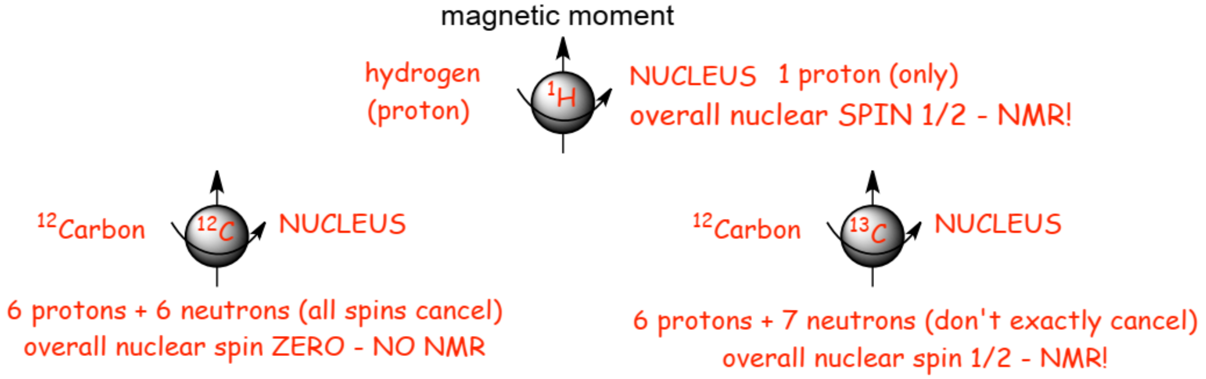
2 NMR Spectroscopy - Structure Determination

2.1 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".
- This spin is the information that is contained in the spin quantum number for electrons (+1/2 and -1/2).

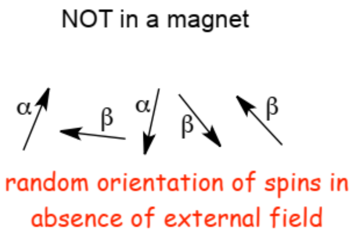


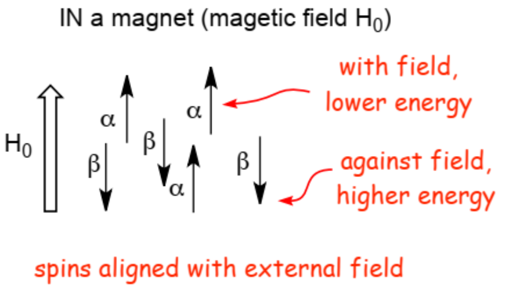
- HOWEVER, this is classical picture of magnetism and spin, and spin is a quantum mechanical phenomenon, the classical picture misses some maybe confusing but important details, specifically:
  1) only TWO spin states are possible for electrons and protons (the +1/2 and -1/2 quantum numbers), and…..
  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.



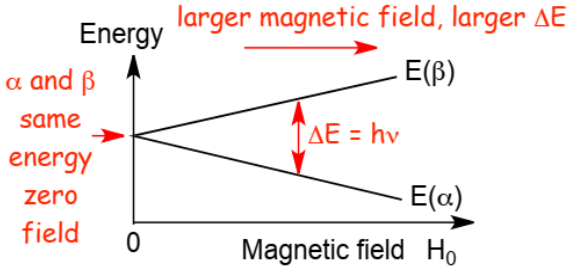
- For NMR to work, the nucleus must have an **overall nuclear spin**, this is the case for **1H hydrogen** (the nucleus is a proton) and also the **13 isotope of carbon**, but not the most abundant 12 isotope of carbon

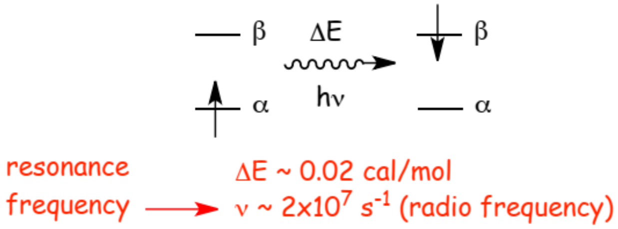
- We can do NMR on nuclei of hydrogen atoms (single protons) and the nuclei of 13C atoms (and other atomic nuclei that we do not cover in this course).
- Overall nuclear spin can also have two states, we will call these alpha and beta, and when a sample containing 1H and 13C atoms is placed in a larger (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.



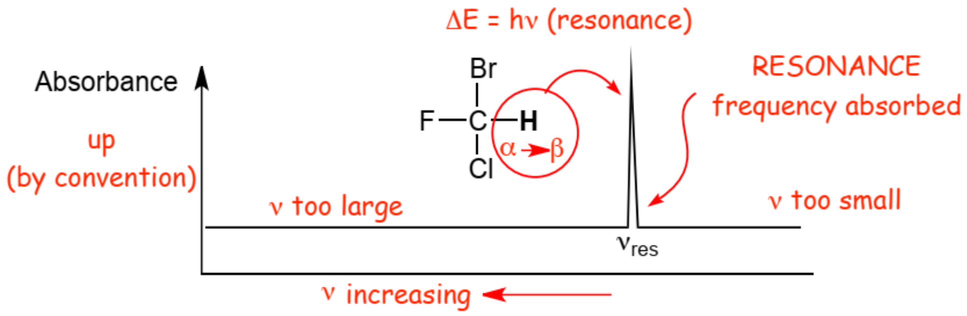


- **Now that they are in a magnet**, there is an energy difference between the alpha and beta spins, and we can equate this energy difference to a specific frequency of electromagnetic radiation using the usual equation
- AND, the energy gap depends upon how large the magnetic field is, put the sample in a LARGE MAGNETIC (large H0) and the energy gap is LARGE, in a small magnetic field (small H_0) 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.



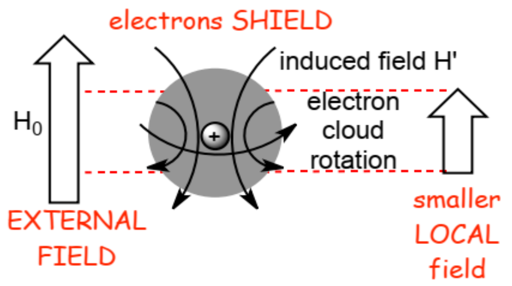


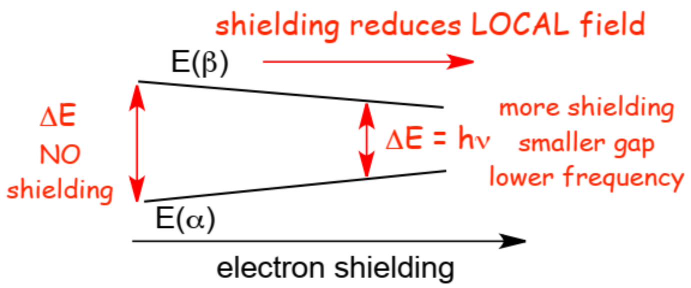
- The frequency of the radiation required to do this conversion alpha to beta is called the **resonance frequency**, it depends upon the energy gap (ΔE), and thus the magnetic field (H_0), but even in very large magnetic fields the frequency is very small, and the frequencies are much lower than IR, 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).



2.2 Shielding and Deshielding

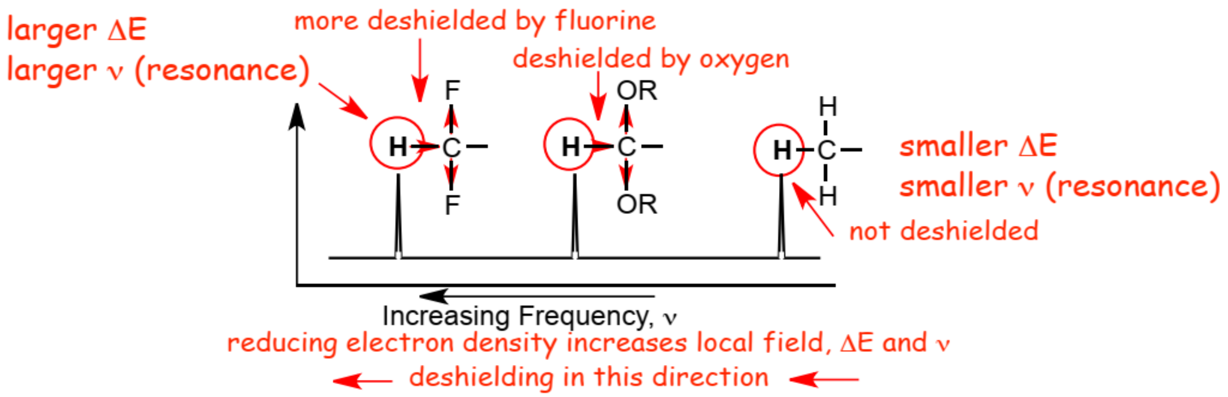
- MOST IMPORTANTLY the frequency tells us the energy difference between the alpha and beta spins, Delta E
- AND, even though all of the nuclei in a molecule are in the same external magnetic field (H_0), the **local magnetic field at each individual nucleus in the molecule can be different due to electron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





- **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

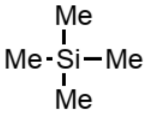
Schematic EXAMPLE:



- **Not** all nuclei are shielded to the same extent, this is not a problem this is the entire basis of NMR spectroscopy

2.3 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).

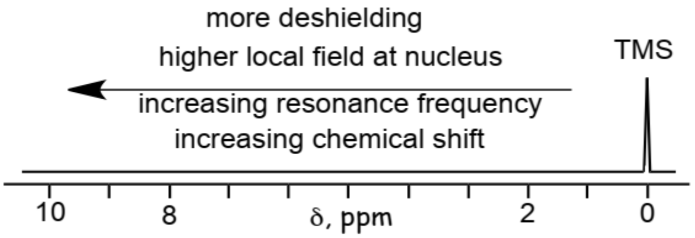


$$\mathrm{Me{-}\overset{Me}{\underset{Me}{Si}}{-}Me}$$

TMS

- 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.

2.4 Which Direction is Which in the Spectrum?



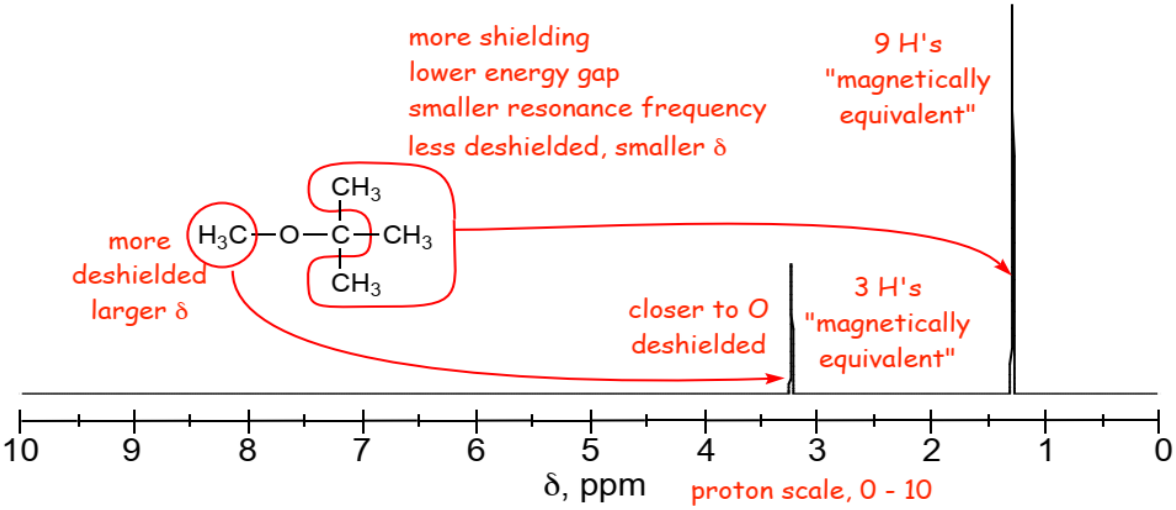
chemical shifts measured relative to TMS (δ scale), TMS is very "shielding"

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

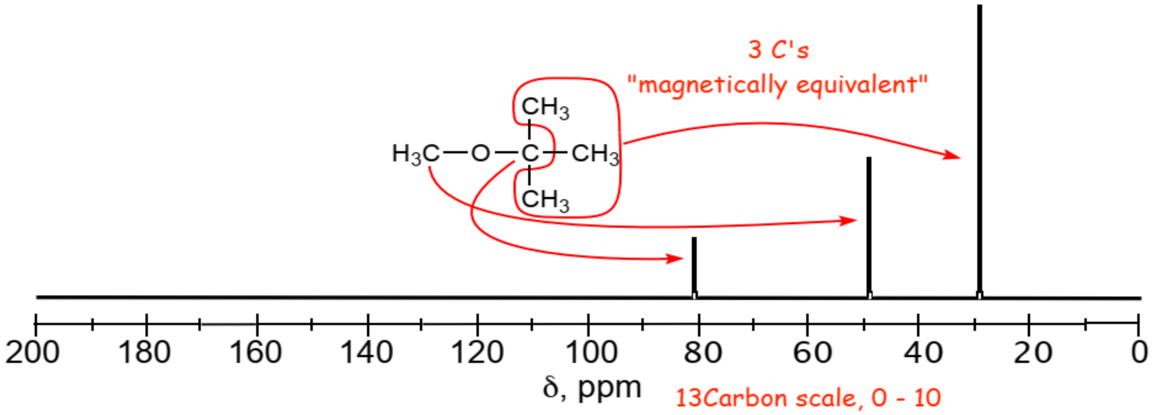
2.5 Which Groups Deshield and by How Much?

Two 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 spectrum to illustrate.
Electronegative elements "pull" electron density from atoms via the **inductive effect**



(the nmr spectra given here were not run on an nmr spectrometer, instead they are simulated using a computer program obtained from: https://www.nmrdb.org/. This has the advantage that the spectra are very clean and easy for students to read, but the miss some realistic features such as noise, contributions from impurities, etc.)

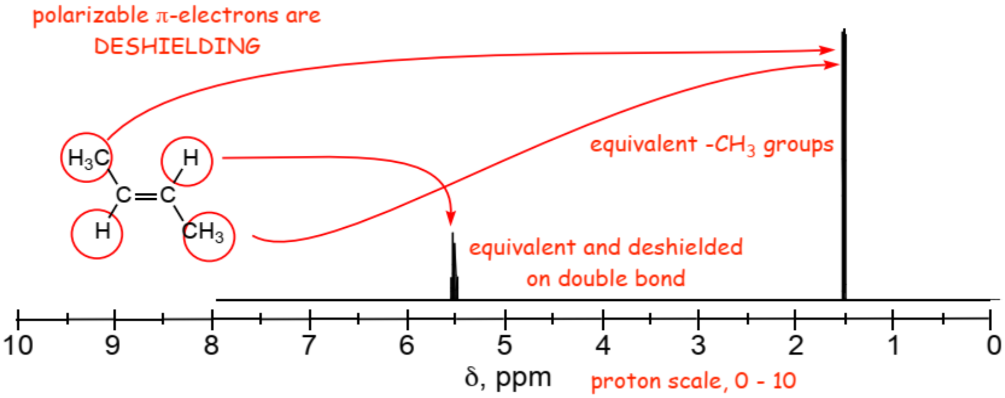


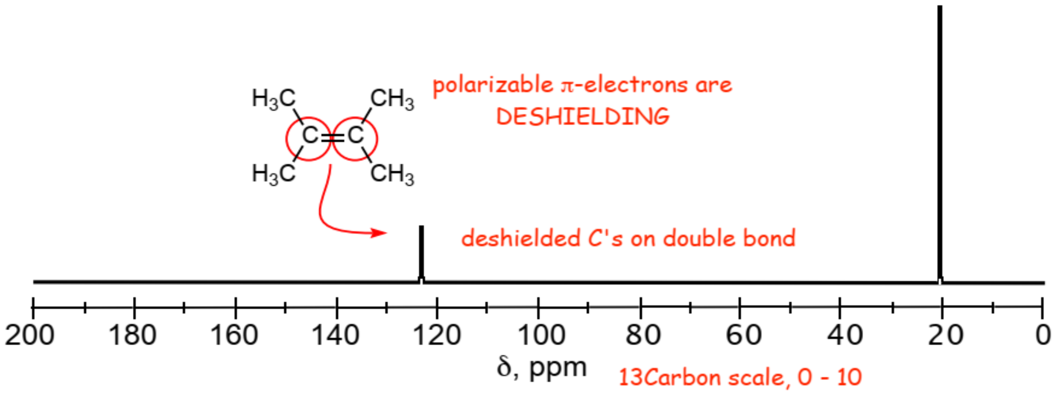
- Proximity to the electronegative oxygen results in reduced electron density due to the **inductive effect**, resulting in **deshielding**, which increases the chemical shift, delta.

- The farther away from the oxygen, the **smaller the inductive effect,** 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. The ^{13}C spectrum gives number of equivalent carbons.

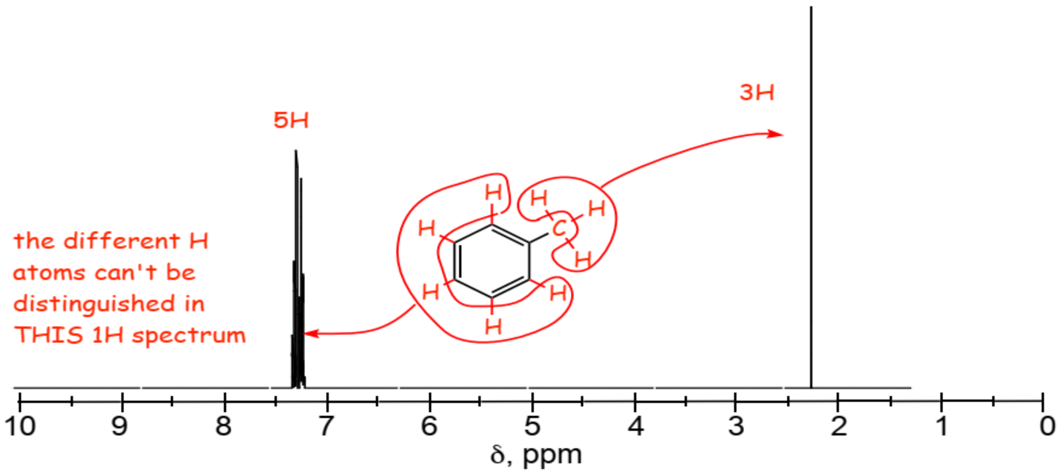
Unsaturation: For example, the effect of proximity to pi bonds

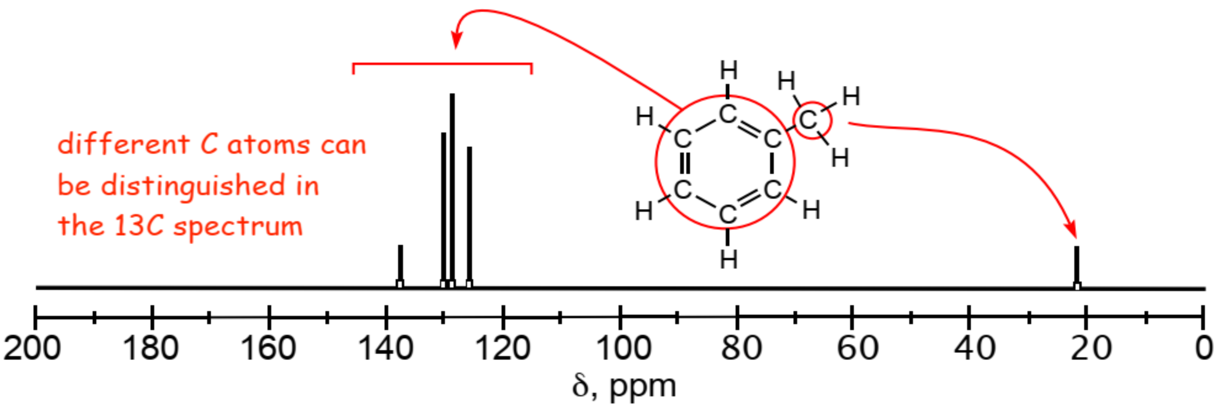
- Electron movement induced by the external magnetic field in the pi-orbitals that contain the polarizable electrons is responsible for generating an **additional** local magnetic field which **adds** to the external field, effectively **deshielding** the protons and carbons that are part of π-systems.





- 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).

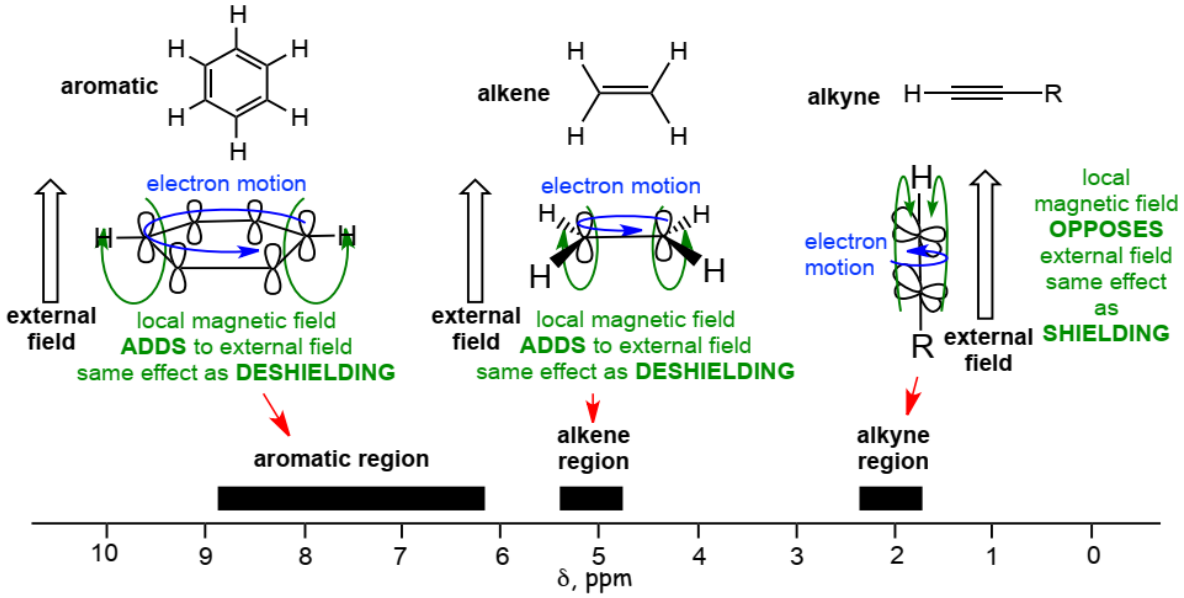




- In these spectra, the aromatic ^{1}H signals overlap extensively and the magnetically inequivalent protons cannot be distinguished, although they can in the ^{13}C spectrum.

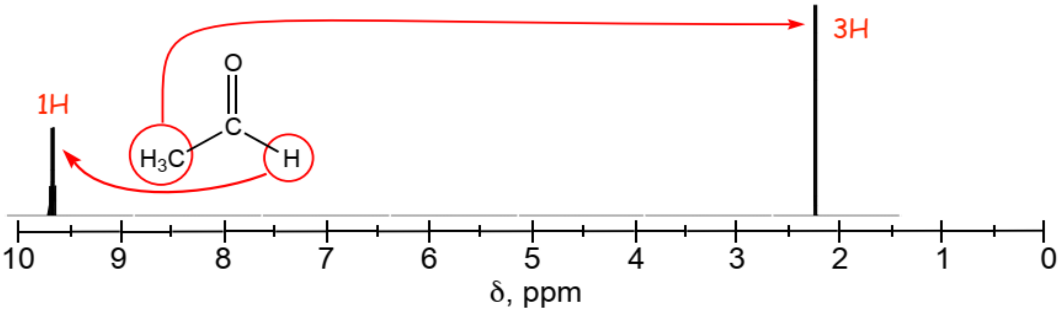
Origin of the Deshielding (and Shielding) Effect of Unsaturation

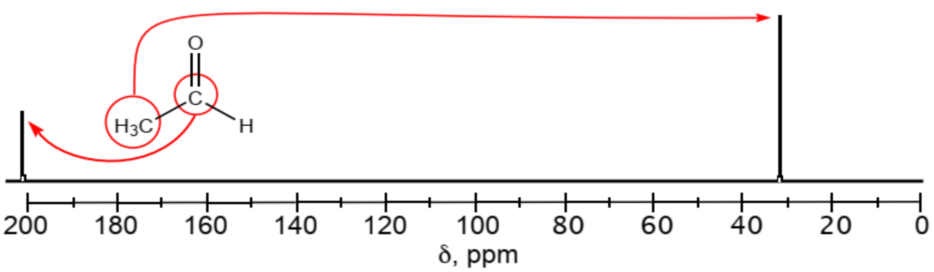
- Deshielding by electronegative elements via the INDUCTIVE EFFECT is easy to understand, it is the electrons that do the shielding and so reducing electron density due to the inductive effect results on DESHIELDING
- Deshielding by unsaturation is different, in this case the movement of π-electrons in π-molecular orbitals generates local magnetic fields that result in decreased (or sometimes increased) overall magnetic fields at nuclei



- The **different shapes** and **orientations** of the π-Molecular Orbitals result in **different** extents of **deshielding** and in the case of alkynes, **shielding.**

Combined Unsaturation/Electronegativity: For example, proximity to π-bonds AND electronegative oxygen

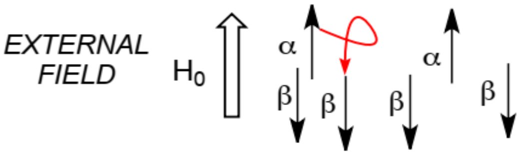




- Unsaturation and electronegativity combine to give largest chemical shifts
- There are ranges of chemical shifts even for similar kinds of nuclei, but the ranges are fairly well defined.

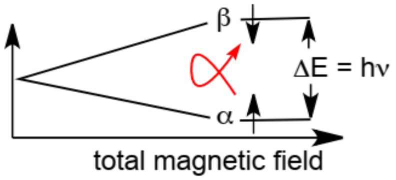
This is all slightly tricky and is worth reviewing once more……

- **It Takes ENERGY (E=hν) to flip a nuclear spin in the magnetic field of an NMR spectrometer...**



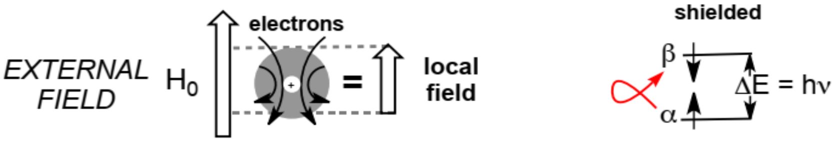
E = hν
ν = resonance frequency

- **The ENERGY/frequency depends upon the LOCAL MAGNETIC FIELD AT THE NUCLEUS...**



LARGER local field means larger ΔE means larger hν

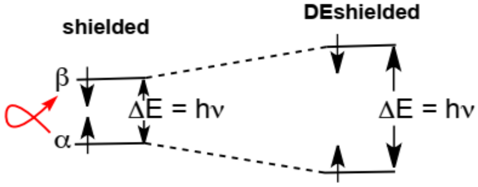
- **Electrons SHIELD the nucleus from the external field, DECREASING the LOCAL FIELD**



more shielding means smaller ΔE means smaller hν

- **Less Shielding/DEshielding by electronegative elements and unsaturation**

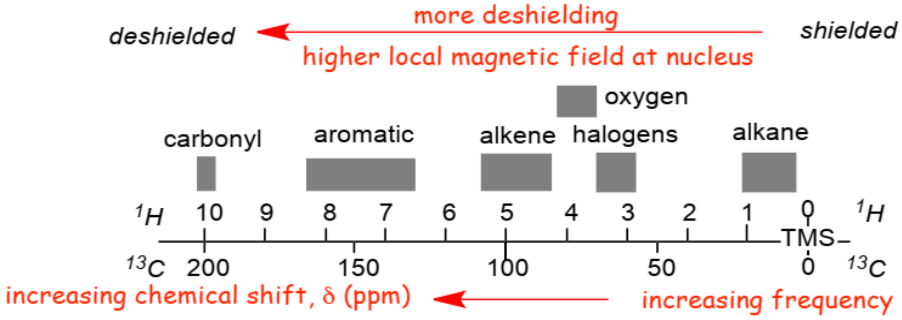
more shielding means smaller ΔE means smaller hν



more DESHIELDING means larger ΔE means larger hν

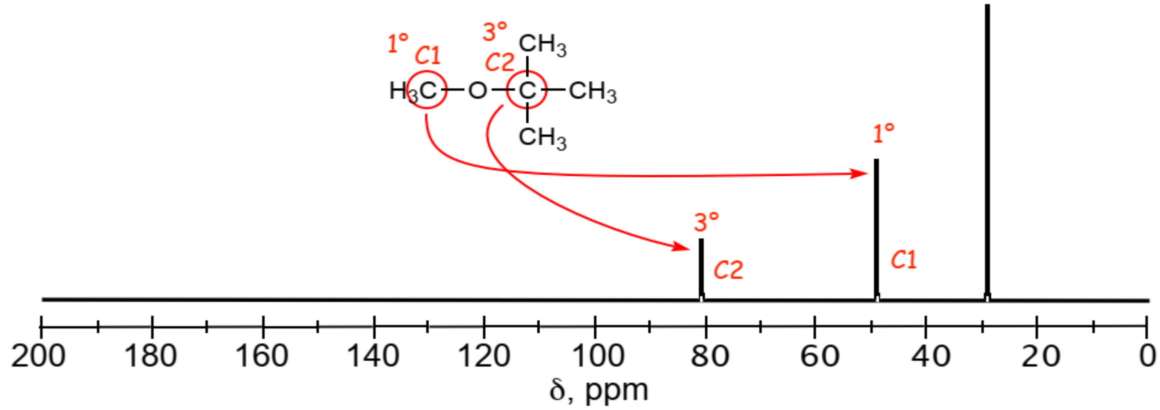
- **SUMMARY...** MORE deshielding = Larger local magnetic field = Larger ΔE

  Larger ΔE = Larger resonance frequency = Larger chemical shift, δ



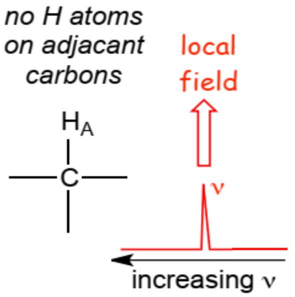
Finally, Extent of Substitution in Carbon Spectra

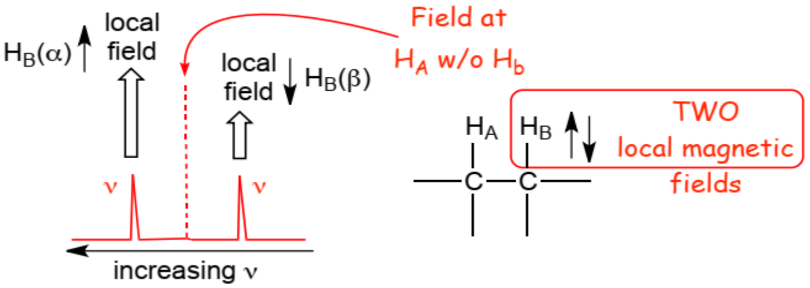
^{13}C spectra are **more sensitive to deshielding factors** than proton spectra because there are more electrons around each C nucleus compared to H. Even the number of alkyl groups around a carbon can be determined in carbon spectra. Even though the electronegativity difference between C and H is small, 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....



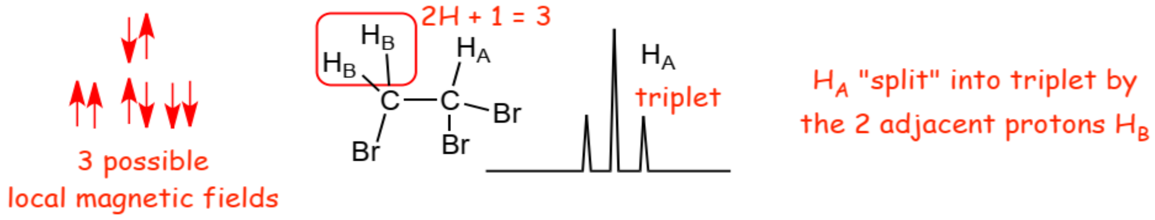
- Even though both of the circled C atoms are directly attached to oxygen, the "central" carbon of the t-butyl group, C2, is significantly more deshielded than the carbon of the methyl group C2 **because** it is tertiary (has more C atoms attached to it) compared to C1, which is primary.

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





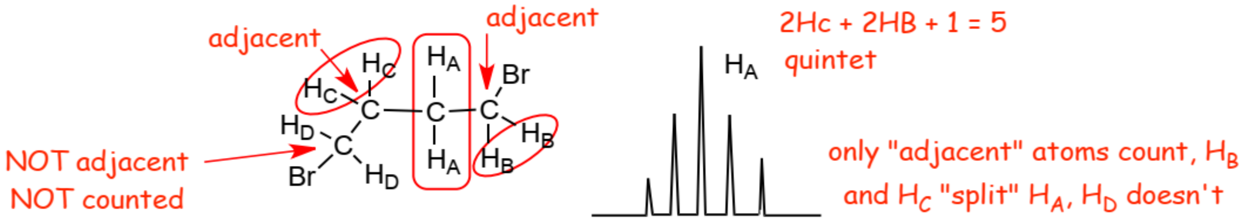
- In the absence of any other hydrogen atoms, Ha (**above**) has a conventional resonance frequency/chemical shift that is determined by its local magnetic field as usual.
- The **presence of Hb**, however, alters the local magnetic field at Ha, the **two** possible spin states at Hb results in both 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 H_A is similarly split into **three**, it appears as a triplet.



Splitting N+1 "Rule":

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)

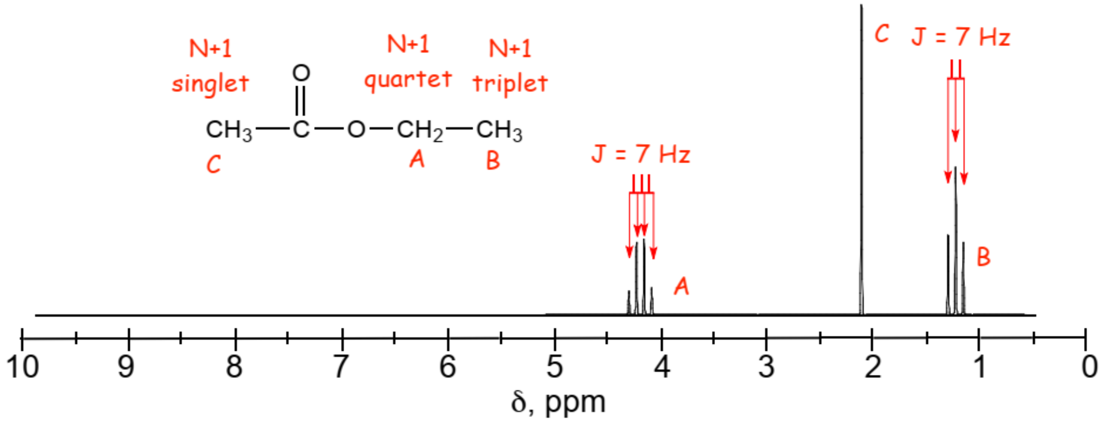
- in our courses, splitting only occurs with protons on **adjacent** carbon atoms, hydrogens on carbons further away usually have only7 a weak effect and can usually be ignored.
- The area ratios of the peaks in a splitting pattern is given by Pascal's triangle.



- coupling constants (J) have to be identical for interacting protons (see below)

The Coupling Constant: Measures the frequency difference between the peak positions in a spilt peak, and is given the symbol **J**, which has units of frequency, usually Hertz, which is reciprocal seconds

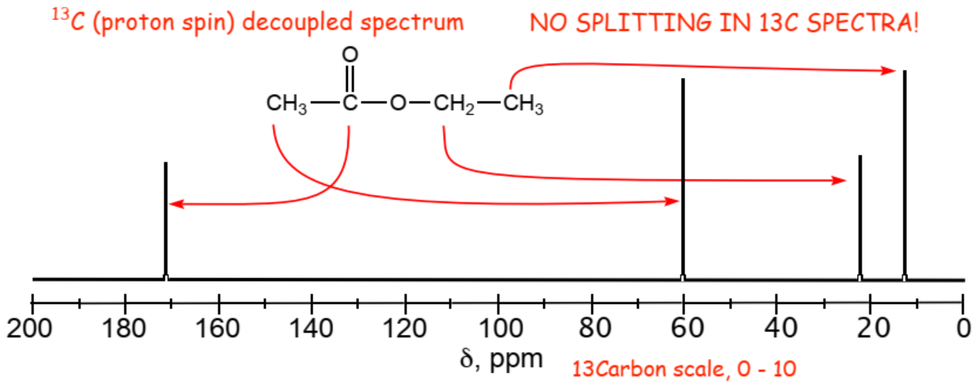
- In the example below, the three H(a)'s "split" the two H(b)'s (and vice versa).



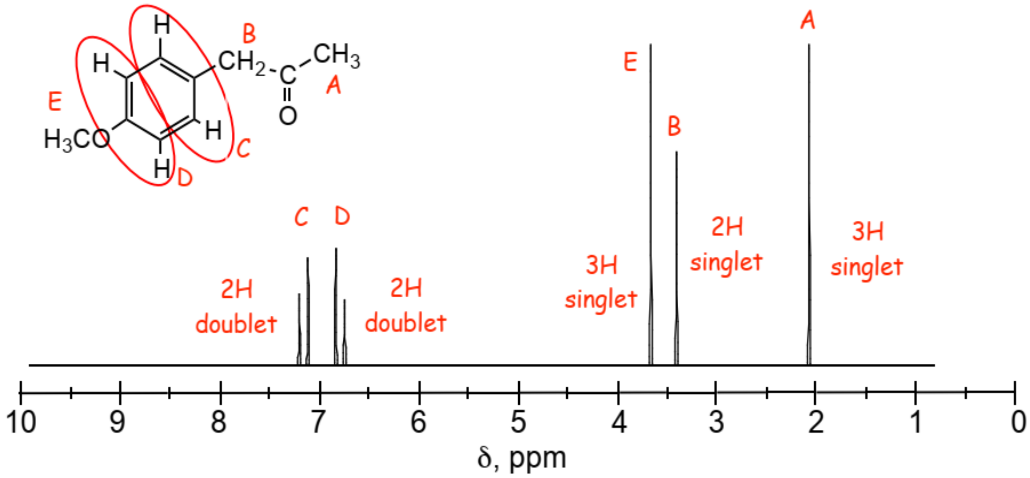
- The J coupling constants, the splitting, for both signals are identical because they are "coupled".
- J is usually ca. 7 Hz for protons on alkyl chains with free rotation.
- The carbon nmr spectrum of the same molecule as in the proton spectrum above shows **no splitting.**

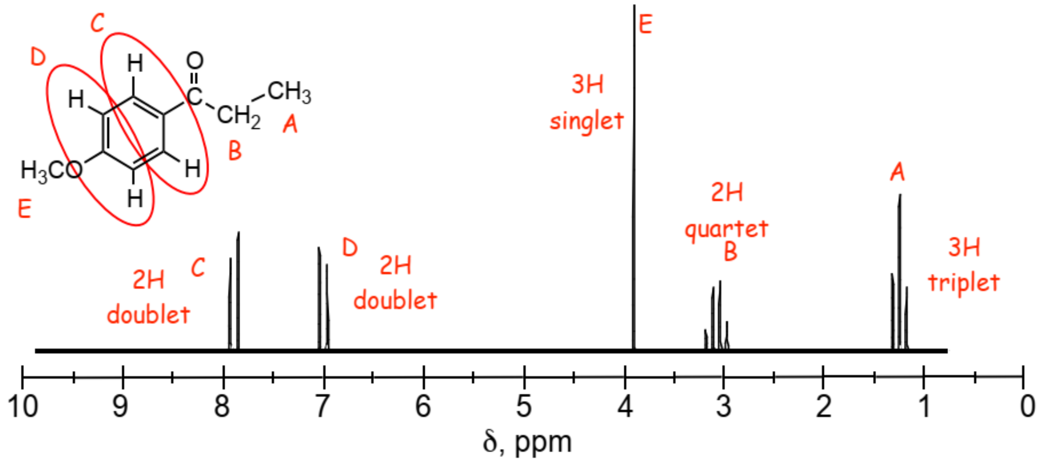
Important

1) All of the ^{13}C spectra in OUR organic chemistry courses are "**proton decoupled**", i.e. **no splitting is observed in our carbon spectra peaks, only singlets** are observed.
2) The same factors determine chemical shift in both the proton and carbon spectra.
3) There are often 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 C=O carbon in this case)



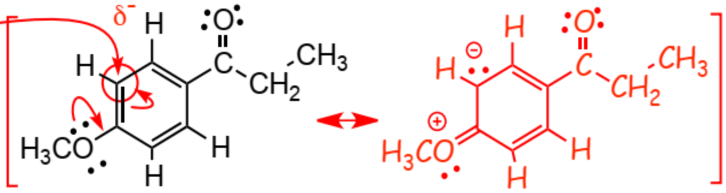
Example Problem: Assign the protons to the peaks in the provided spectra





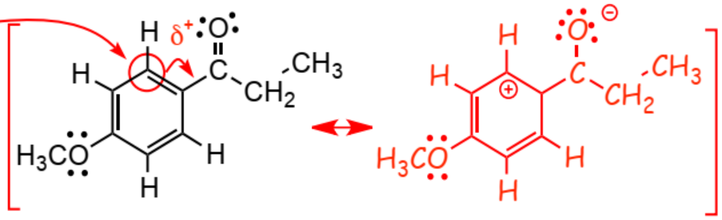
- How are the benzene protons C and D distinguished in these spectra?

partial negative charge
more shielding
LESS deshielding
SMALLER local magnetic field
SMALLER resonance frequency
SMALLER chemical shift



- 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.

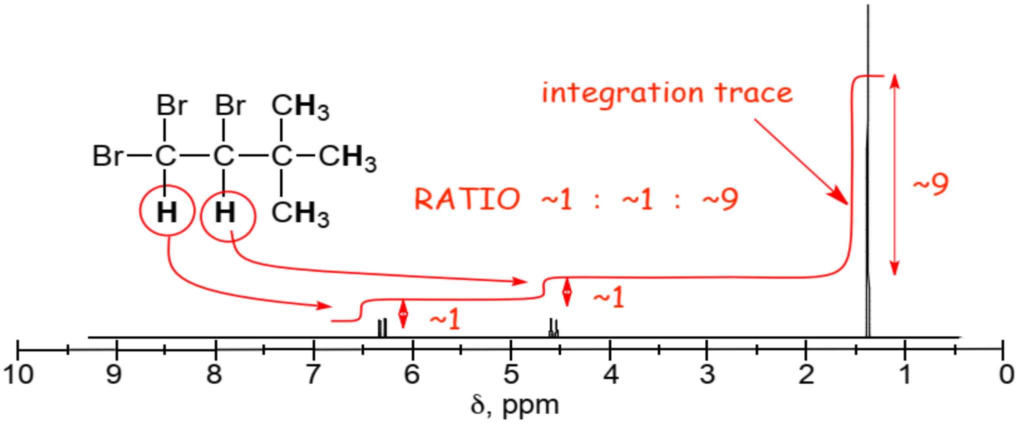
partial positive charge
less shielding
MORE DEshielding
LARGER local magnetic field
LARGER resonance frequency
LARGER chemical shift



- 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.

2.7 Signal Sizes: Integration

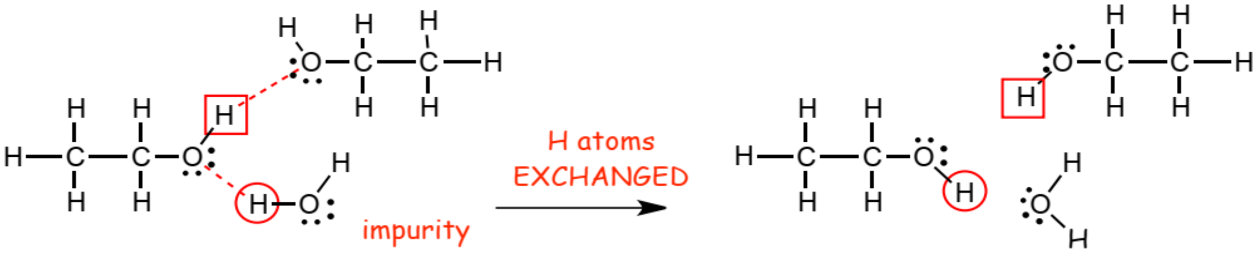
- In ^1H spectra, the signal size relates to the number of contributing protons.



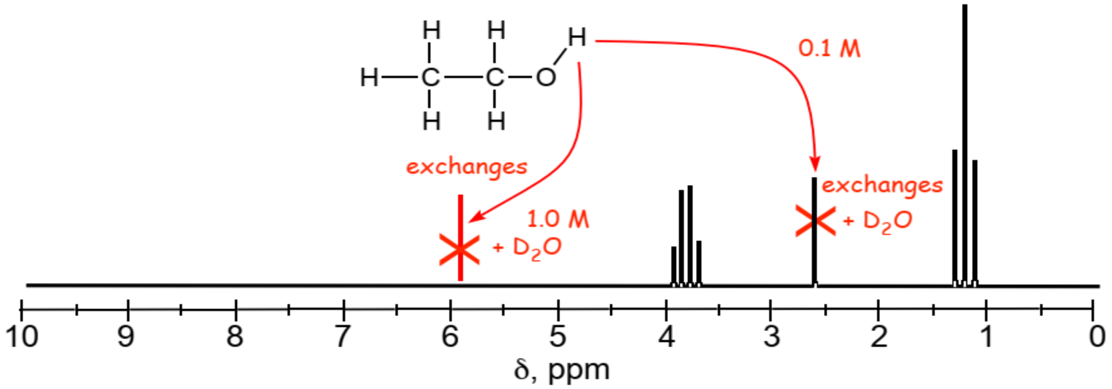
- NMR spectrometers provide **relative signal sizes ONLY**, historically as an integration trace, such as that shown superimposed on the spectrum above.
- It is the **integrated areas** under the peaks that determine signal "size", not peak height.
- signal size is related to # of equivalent H's in proton 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 13C spectra due to spin relaxation effects.**

2.8 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 the chemical shifts of O-H and N-H signals!**



- 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 D_2O 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).

2.9 Real Spectra

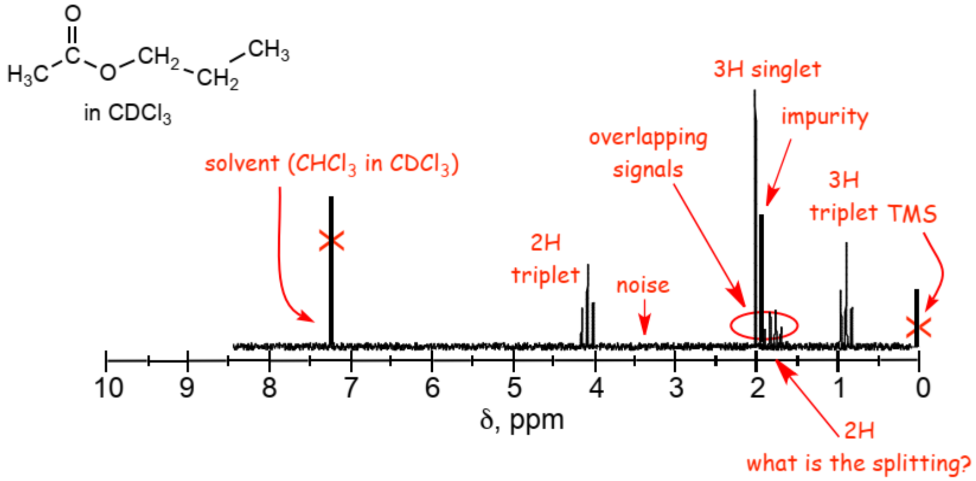
- Real spectra are often **not as simple as those provided in this lecture course!**
- You are usually given the absolute number of hydrogens for each peak in ^1H NMR, however, real integrations give only relative numbers of hydrogens, peak ratios have to be converted into absolute hydrogen atom count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

$CHCl_3$
chloroform
CAN'T use solvents with H atoms for NMR!

$CDCl_3$
(always has some $CHCl_3$ as an impurity)
deuteriated chloroform as an NMR solvent

- In addition to peaks from the solvent, real spectra often contain peaks from impurities and other contaminants
- Small peaks, e.g. on tertiary carbons, may get "lost" in the noise in ^{13}C NMR spectra.
- The peak from the TMS is, of course, not part of the spectrum of the compound being studied, it is present in order to calibrate the chemical shift scale (TMS is often not observed in modern spectra).

Example:



- Determining the exact splitting is difficult for peaks that are highly spilt, for example, what is the splitting pattern for the 2H signal in the spectrum above?
- In some cases, it is only possible to say that a signal is split, without actually saying exactly how many peaks it is split into, such a peak is described as a **multiplet.**
- Finally, there are often cases where different signals overlap, again, as shown above.

3 Solving Spectral Problems; A Suggested Procedure

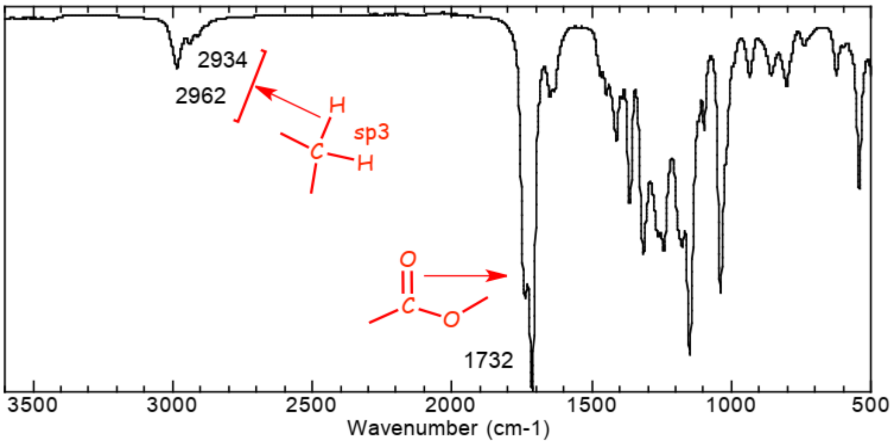
Here is the suggested procedure for these problems

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}C NMR
4. Compare # of signals in proton and ^{13}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

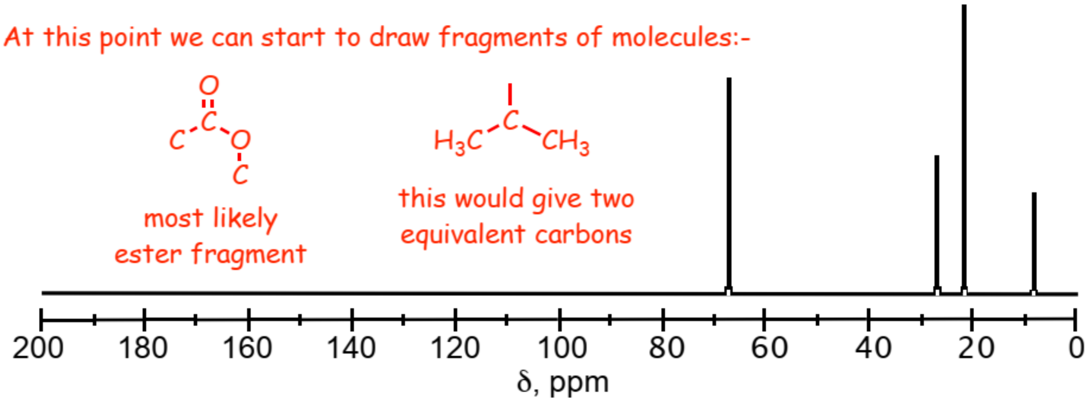
Example Problem 1: Determine the structure and assign the peaks in the proton NMR spectrum.

Molecular formula = $C_6H_{12}O_2$ 1 degree of unsaturation

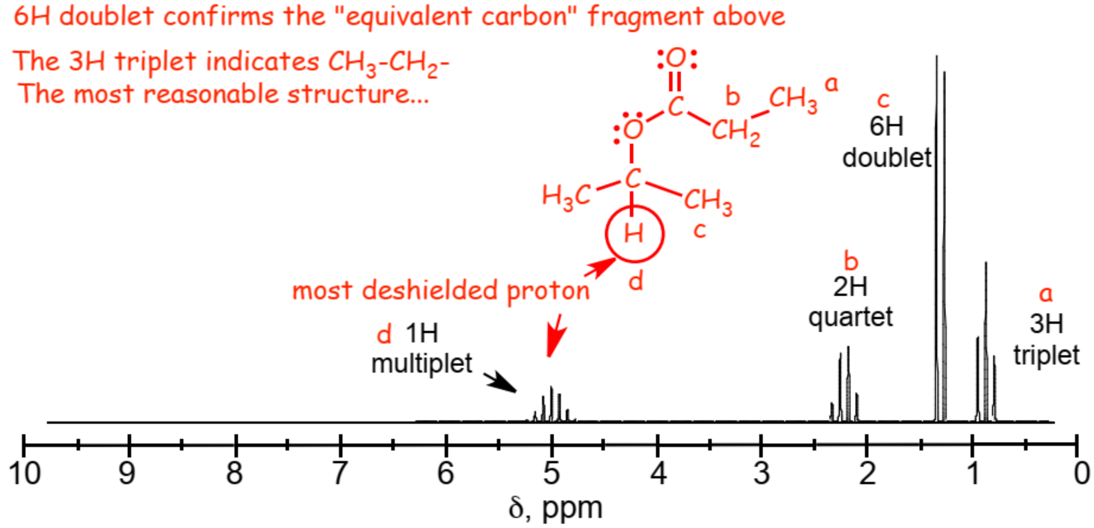
- This implies 1 double bond OR 1 ring but not both.



- 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 13C 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.



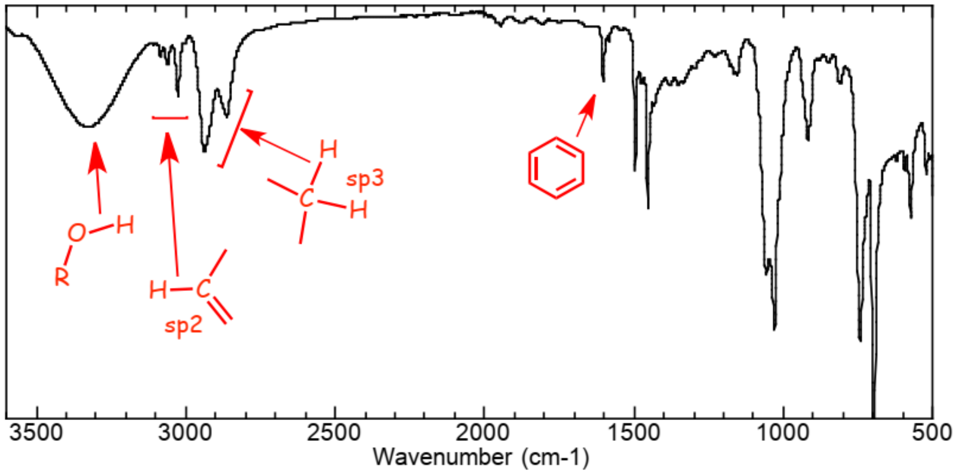
- Look for the methyl groups in the proton NMR, they come in integral multiples of 3, they tend to be less deshielded because they are at the ends of chains, and from their splitting patterns you can figure out what they are connected to.

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.

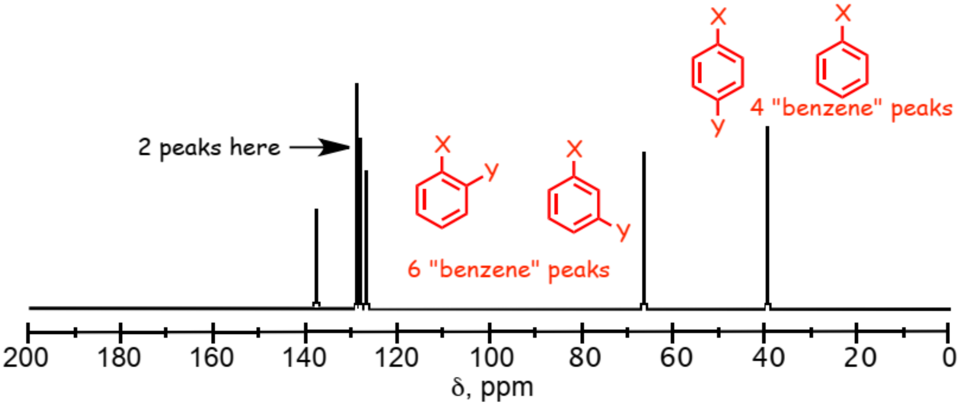
Example Problem 2

Molecular formula = $C_8H_{10}O$ 4 degrees of unsaturation

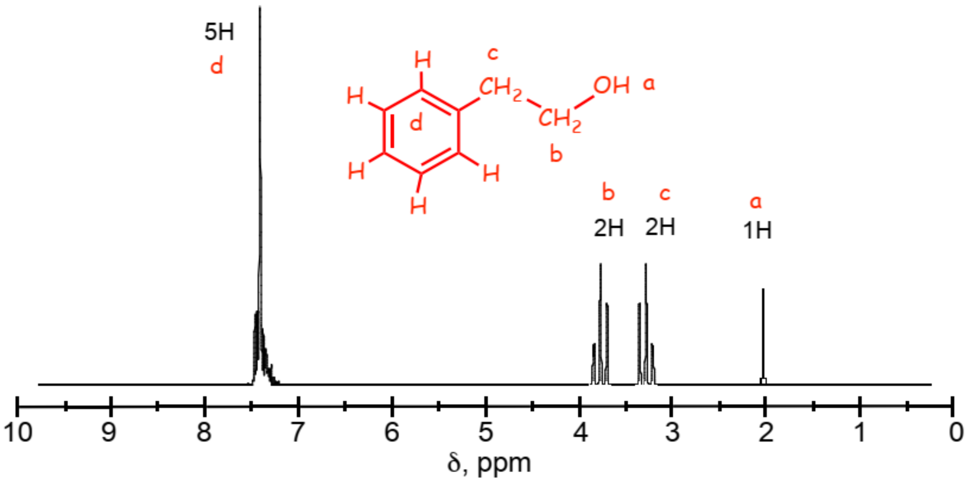
- We immediately think about a possible benzene ring (which has 4 degrees of unsaturation on its own)



- The IR spectrum clearly shows an –OH group, and C=C unsaturation (C-H 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 cannot 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.

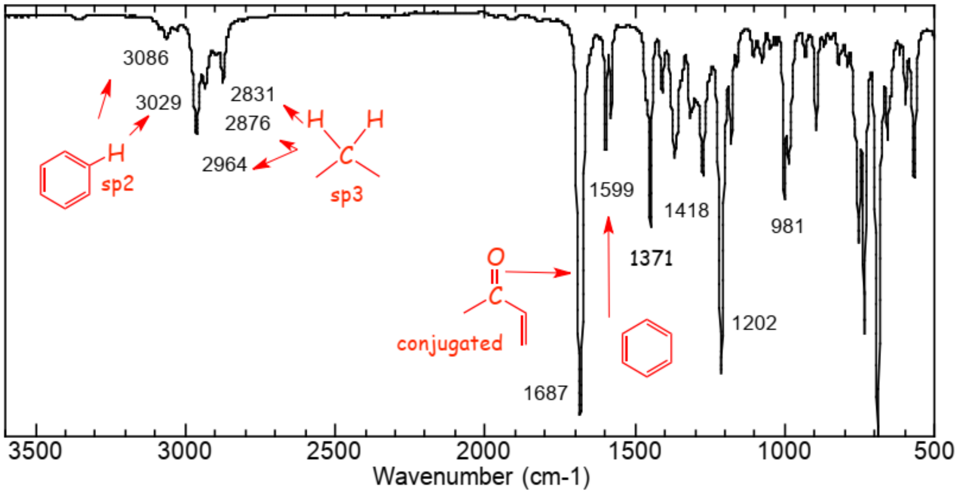


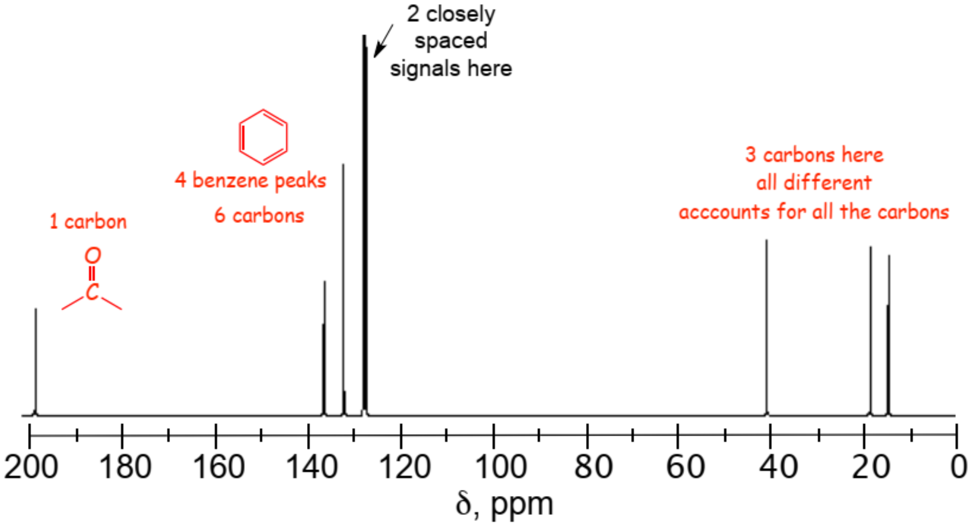
- 5 protons in the aromatic region conform that the benzene must be monosubstituted.
- **Note**: **in this case, the aromatic region has a 5H peak that is split**, this doesn't mean that the 5 H atoms on the benzene are magnetically equivalent **but that the chemical shift differences are small and that 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 deshielded 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**

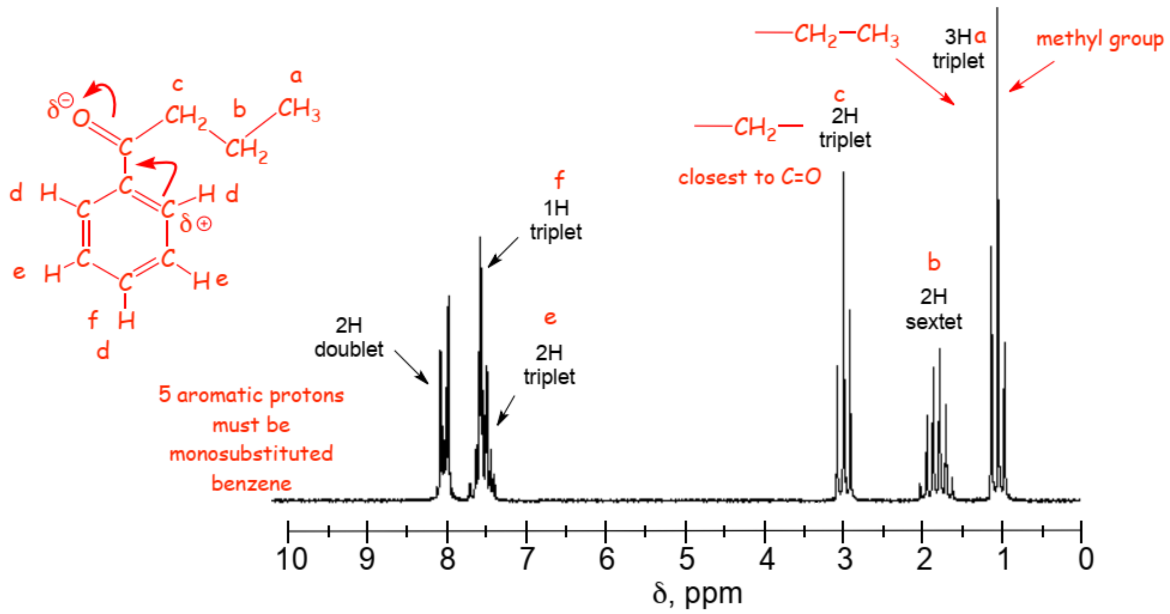
Example Problem 3:

Molecular formula = $C_{10}H_{12}O$ 5 degrees of unsaturation

- 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