Spectroscopic Techniques for Pharmaceutical and Biopharmaceutical Industries
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Lecture 32
Structure of Information from NMR

Hello students, welcome to lecture 32 of this course. In the last lecture I discussed about principles of NMR. I started with the 1D NMR and I introduced how to represent signal and what are the factors on which signal depends. In this lecture I will discuss how to get a structure information from NMR.

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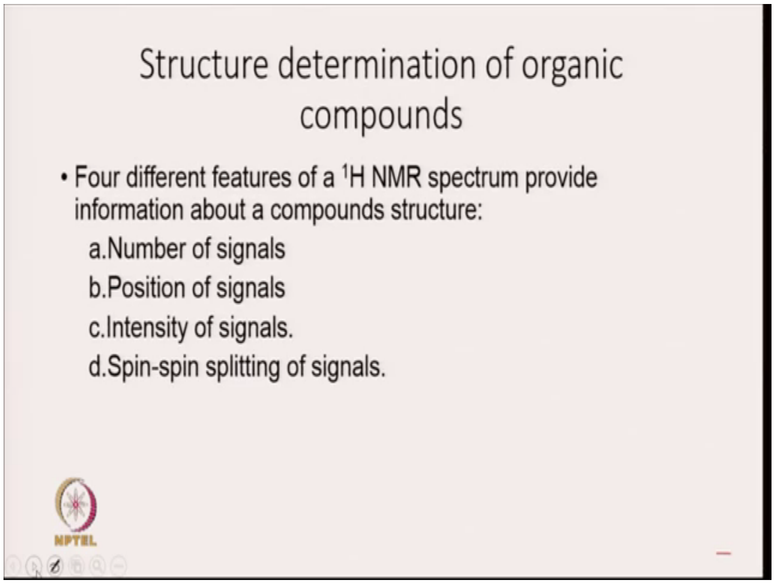

Structure determination of organic compounds

- Four different features of a ^1H NMR spectrum provide information about a compounds structure:
  - a.Number of signals
  - b.Position of signals
  - c.Intensity of signals.
  - d.Spin-spin splitting of signals.

So, we will start with a structure determination of organic compounds, 4 different features of proton NMR spectrum provide information about a compound structure and 4 different features are number of signals, position of signals, intensity of signals and the splitting of signal. These 4 features gives important information through which we can derive the structure of organic compounds. I will go one by one to each of the features and discuss the importance of those 4 features.

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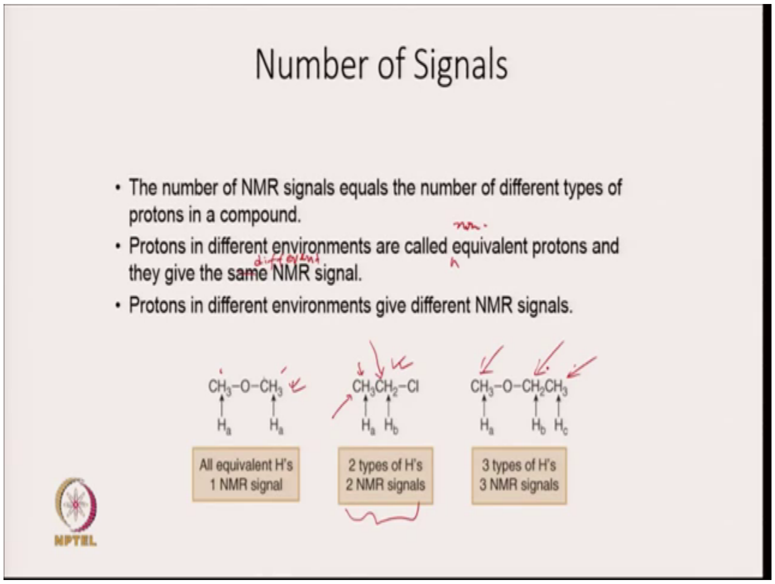

Number of Signals

- The number of NMR signals equals the number of different types of protons in a compound.
- Protons in different environments are called non-equivalent protons and they give the ~~same~~ different NMR signal.
- Protons in different environments give different NMR signals.

All equivalent H's
1 NMR signal

2 types of H's
2 NMR signals

3 types of H's
3 NMR signals

First feature is number of signals. So, the number of NMR signals equals the number of different types of proton in a compound. So, if there are 4 different kinds of protons in a compound you should expect 4 different signals. Protons in different environments are called non-equivalent protons and they give different NMR signal whereas the protons in same environment are called equivalent protons and they will give same NMR signal.

So, proton in same environment gives same signal whereas proton in different environment gives different NMR signal. For example, if you take this case this is your Dimethyl ether all 6 protons 3 protons attached to this carbon, 3 protons attached to this carbon has same environment, same environment. So, any 1 of the proton is attached with 1 carbon and that carbon is attached to 1 oxygen and again that oxygen is attached to 1 carbon. So, environment of any of the proton which you take in dimethyl ether is same what does that mean is that proton has only 1 kind of environment and so you will get one NMR signal.

Now, take this case 1 Chloroethane or Ethyl Chloride these 3 proton has same environment whereas these 2 proton has same environment but different then these 3 proton, these 3 protons. So, 1 Chloroethane has 2 different kind of protons and so you will get 2 NMR signals, you will get 2 NMR signals. If we take methyl ethyl ether there are 3 different kind of proton. For example, if you see this 3 protons are in same environment whereas these 2 protons are in different environment then these 3 protons whereas these 3 protons again is in different environment then these 2 and so you have a 3 different kind of protons and so you expect 3 NMR signals, 3 NMR signals.

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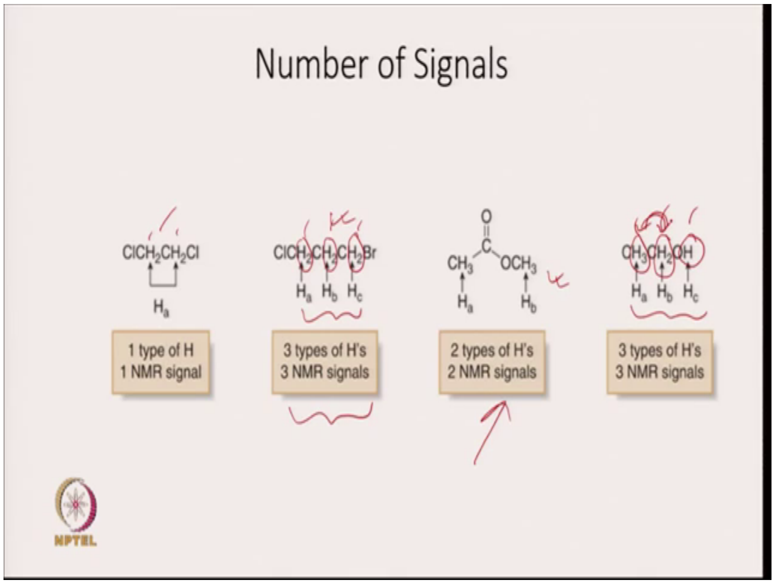

Number of Signals

$ClCH_2CH_2Cl$

$ClCH_2CH_2CH_2Br$

CH_3COOCH_3

CH_3CH_2OH

1 type of H
1 NMR signal

3 types of H's
3 NMR signals

2 types of H's
2 NMR signals

3 types of H's
3 NMR signals

So, number of signals will gives you an idea about how many different kinds of protons are present in a molecule. Now, take this case 1 Chloro, 2 Chloroethane in that case all protons have similar environment and so they will give 1 NMR signal. In this compound, whereas this is 1 Chloro and 3 Bromo, 1 Chloro and 3 Bromo Propane there are 3 different kind of protons 3 different kind of protons and so there will be 3 NMR signal. So, you see this carbon these protons these 2 protons the they are attached to the carbon which is attached to a Cl group and a C group whereas these 2 protons is attached to carbon which is attached to 2 different carbons whereas these 2 protons are attached to a carbon which is attached to a Bromo group and 1 carbon group. So, all so these 2 protons these 2 protons and these 2 protons are in different environment and so you should expect 3 NMR signals.

In this compound, we have 2 different kind of protons and so there will be 2 NMR signal whereas in this compound there are 3 different kind of protons, these 3 Hydrogens has different environment in comparison to these 2 Hydrogens and this Hydrogen. All 3 types of protons have different environment but these 3 protons they have similar environment, they have same environment. So, these 3 protons do not differ in their environment and so they are known as 1 kind of protons. Whereas these 2 protons also have same environment and so they are called of same type of the same type but in between these 2 groups their environment are different and that is why they are assigned 2 different groups.

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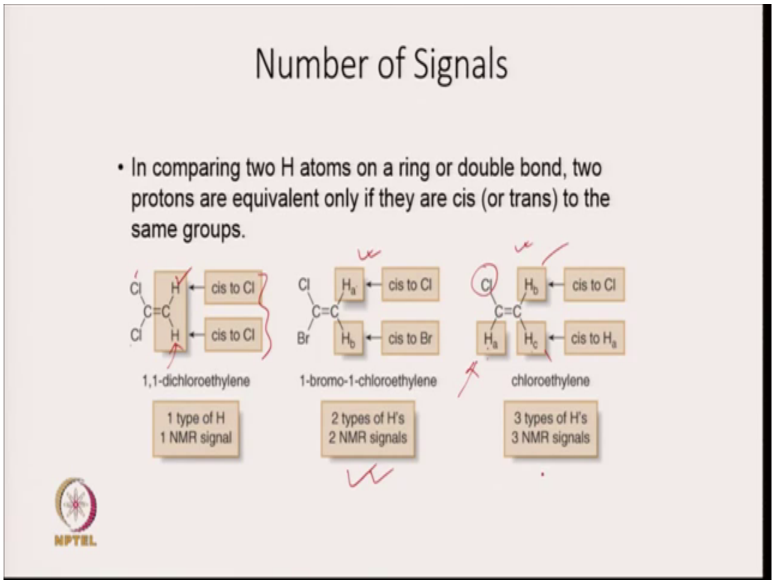

Number of Signals

- In comparing two H atoms on a ring or double bond, two protons are equivalent only if they are cis (or trans) to the same groups.

1,1-dichloroethylene

1 type of H
1 NMR signal

1-bromo-1-chloroethylene

2 types of H's
2 NMR signals

chloroethylene

3 types of H's
3 NMR signals

In comparing 2 Hydrogen atoms on a ring or a double bond 2 protons are equivalent only if they are cis or trans to the same group, cis or trans to the same group. For example, if I take this proton this is cis to this Chloro group whereas this proton is also cis to Chloro group and hence these 2 protons are same and so we expect only 1 signal but if you take in this compound this proton is cis to Chloro group whereas this proton is cis to Bromo group and hence these 2 proton do not have same environment and so we get 2 NMR signals.

In this compound, you see this H b basically is our cis to this Chloro group whereas H c is cis to Ha group so these 2 protons are different, these 2 protons are different and this is different since this H is attached to carbon which is attached to this Chloro group. Whereas these 2 are these 2 protons are attached to Carbon which is not attached to Chloro group. So, all 3 protons are in different environment and so we should expect 3 NMR signals and that is what we get.

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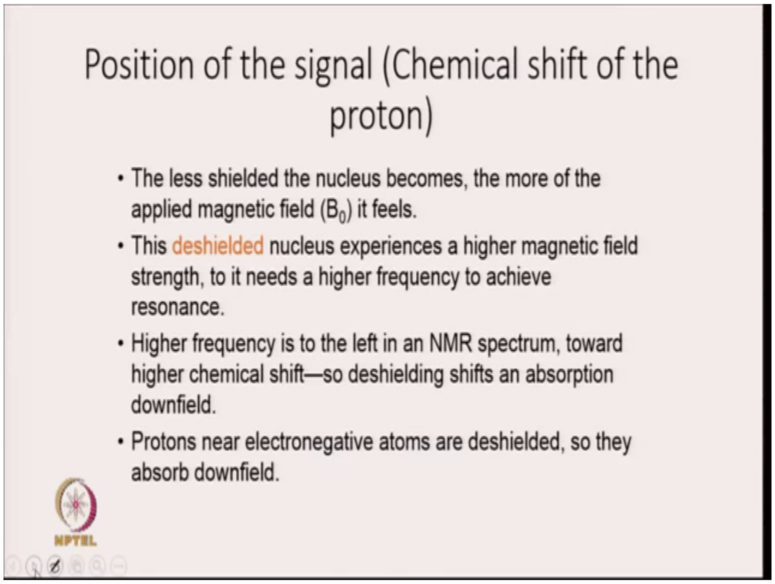

Position of the signal (Chemical shift of the proton)

- The less shielded the nucleus becomes, the more of the applied magnetic field (B_0) it feels.
- This deshielded nucleus experiences a higher magnetic field strength, to it needs a higher frequency to achieve resonance.
- Higher frequency is to the left in an NMR spectrum, toward higher chemical shift—so deshielding shifts an absorption downfield.
- Protons near electronegative atoms are deshielded, so they absorb downfield.

Now, the second feature of the NMR spectrum is position of the signal which is basically chemical shift of the product. So, chemical shift of proton also gives an idea about the idea about the functional group, the idea about the functional group. The most important part about a chemical shift is that the less shielded the nucleus becomes the more of the applied magnetic field it fills and this I have already discussed about the chemical shift in the last lecture. Why in certain case chemical shift is high? Why in the certain cases chemical shift is a small Delta value, the main factor is shielding of nucleus.

The deshielded nucleus experiences a higher magnetic field strength and it needs a higher frequency to achieve resonance. Higher frequency is to the left in the NMR spectrum and towards higher chemical shift so deshielding shift and absorption downfield, downfield. Protons near electronegative atoms are deshielded, so they absorb downfield and again absorbed downfield means higher chemical shift, higher chemical shift. So, these are the things which I have already discussed in last class so please look at the, you know content of the last class.

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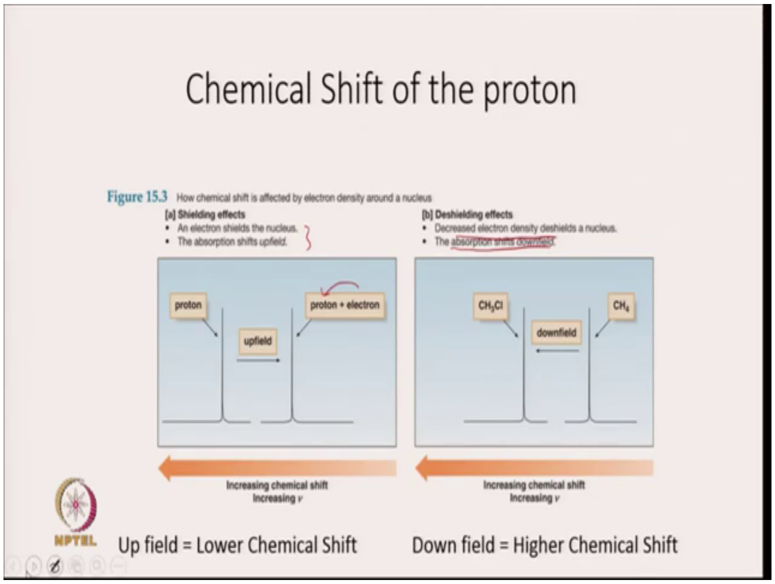

Chemical Shift of the proton

Figure 15.3 How chemical shift is affected by electron density around a nucleus

[a] Shielding effects
- An electron shields the nucleus.
- The absorption shifts upfield.

[b] Deshielding effects
- Decreased electron density deshields a nucleus.
- The absorption shifts downfield.

Up field = Lower Chemical Shift

Down field = Higher Chemical Shift

So, if you take a proton and if an electron shields this proton then your pick shifts up field that is what it is written that electron shields the nucleus and proton in presence of electron around the nucleus basically shift the absorption up field. If somehow we decrease the electron density electron density near any nucleus we are basically deshielding it, we are basically deshielding it, we are basically deshielding it and in that case absorption shifts downfield and again downfield means higher chemical shift there is up field means lower chemical shift.

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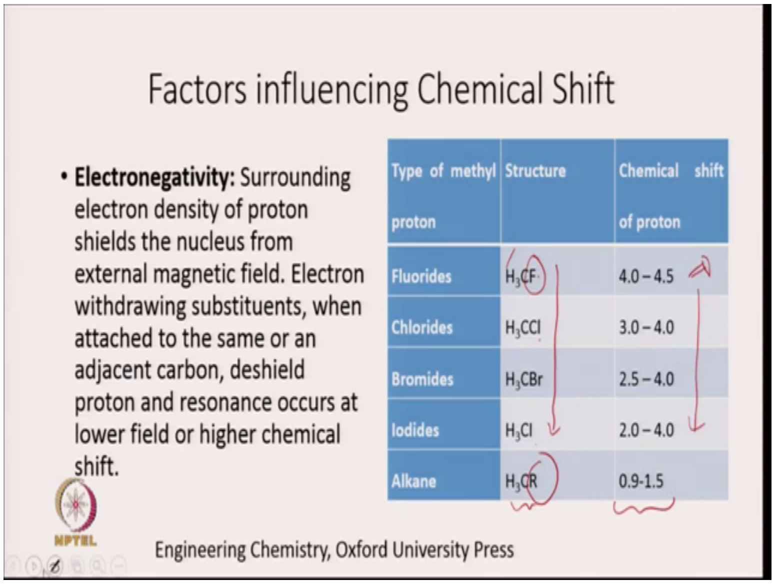

Factors influencing Chemical Shift

- **Electronegativity:** Surrounding electron density of proton shields the nucleus from external magnetic field. Electron withdrawing substituents, when attached to the same or an adjacent carbon, deshield proton and resonance occurs at lower field or higher chemical shift.

Type of methyl proton	Structure	Chemical shift of proton
Fluorides	H_3CF	4.0 – 4.5
Chlorides	H_3CCl	3.0 – 4.0
Bromides	H_3CBr	2.5 – 4.0
Iodides	H_3CI	2.0 – 4.0
Alkane	H_3CR	0.9-1.5

Engineering Chemistry, Oxford University Press

In last class I started discussing about factors influencing chemical shift again I will start with the electronegativity. The surrounding electron density of proton shields the nucleus from external magnetic field. So, if I have electron withdrawing substituent attached to a nucleus they can be attached to the same or adjacent nucleus. It basically deshield proton and resonance occurs at lower filed or higher chemical shift, higher chemical shift. So, if electronegative atom is attached to the carbon to which these 3 protons are attached they will take away electrons from the carbon and proton and that is how they deshield this proton.

And resonance of the these protons happens at lower field and that means they have higher chemical shift it means they have higher chemical shift. As you go down electronegativity decreases when you go down from Fluorine to Chlorine to Bromine to Iodine and so less electron will be shifted from the proton and so deshielding will be small and hence resonance will occur at higher field or lower chemical shift. And so you can see that as you go down that chemical shift value decreases. In alkane the carbon is attached to R group which is electron donating group and that is why we expect a small chemical shift.

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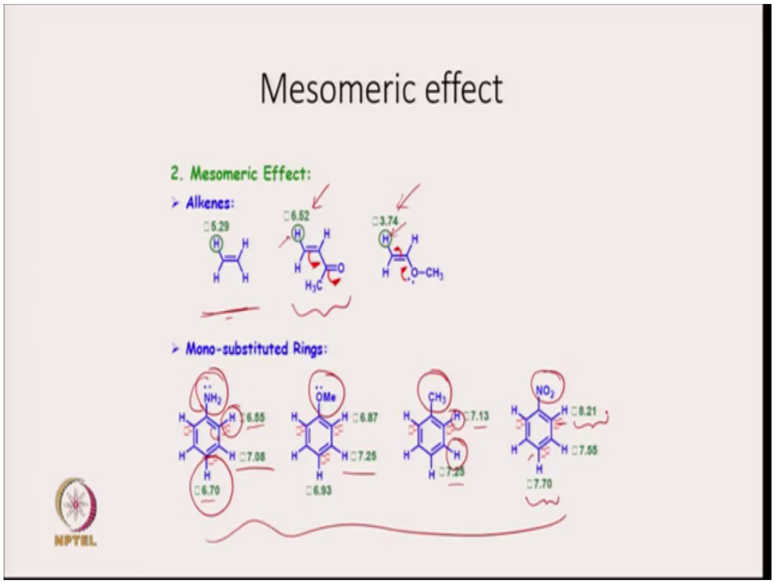
Mesomeric effect

2. Mesomeric Effect:

- Alkenes:

- Mono-substituted Rings:

The second effect which we have started discussing in the last lecture which effect chemical shift is Mesomeric effect. Again Mesomeric effect can withdraw electron from the proton or it can enhance the electron, electron surroundings of a proton. If it remove the electron then we expect chemical shift to be higher if it donates electron then we expect chemical shift to be smaller and that is what we see here.

If we go from simple Alkene to an Alkene substituted with CO CH3 group the CO group is in conjugation with this double bond and so there will be Mesomeric shift and shift will be in this direction and so what you are doing is you are removing electron from this proton and so this proton will be in resonance at higher chemical shift. In this case, when double bond is attached to a lone pair plus M effect will operate and proton is going to have more electron, this proton is going to have more electron and so this proton will resonate at frequency which is lower so chemical shift will be lower 3.74.

And similarly we can discuss about Mono-substituted rings. Here, if the ring has NH2 group its lone pair is in conjugation with the double bond and the lone pair is will be if you take this lone pair here and this will go at this position and this will go to this position and so you can see that this is going to be of higher chemical shift and these 2 are going to be of lower chemical shift since here electron is reaching. Electron this proton is more electron rich, this proton is more electron rich so NH2 has plus M effect and so the protons at ortho and para position are going to be more rich in electron and hence they will have lower chemical shift. Again OMe has plus M effect and so proton at ortho and para position are going to be are going to have lower chemical shift comparison to a proton at meta position.

CH3 is electron donating group and this has plus I effect and so this proton will be more electron rich compared to a proton at your meta position and hence this will have lower chemical shift in comparison to a proton at para position. NO2 is electron withdrawing group so it has minus M effect and so proton will be less rich at ortho and para position and so they are going to be, they are going to have higher chemical shift. So, the electron around a nucleus will affect electron around a nucleus will affect this chemical shift value if there is more electron near a proton then it is going to have smaller chemical shift.

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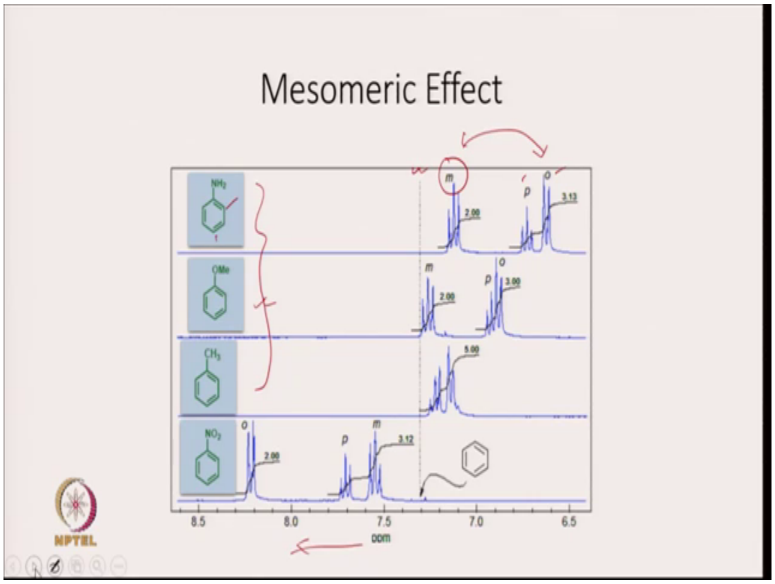

Mesomeric Effect

Now, here you see the effect of Mesomeric effect and at this position comes the Benzene ring. If I put NH2 then it will go to lower chemical shift, I put OMe it will go to lower chemical shift whereas if I put NO2 on the benzene ring it will go to higher chemical shift. So, this is lined for benzene ring, NO2 is withdrawing electron away, withdrawing electron away from the ring. So, all proton either in ortho position, para position or meta position is going to be electron deficient in comparison to benzene ring, electron deficient in comparison to benzene ring and so your chemical shift will be high.

Whereas these 3 groups NH2, OCH3 and CH3 group they are donating electron and so they are going to be at higher chemical shift than benzene. The electron donating plus M effect will be, will be more predominant in ortho and para position and so ortho followed by para position is going to be of a smaller chemical shift, meta position will be, meta will be of highest chemical shift, proton at meta position is going to be of highest chemical shift among all these 3 protons. Same with the case with OCH3 group and you can see ortho, para and then meta. So, this is the effect of the substituent on a benzene ring.

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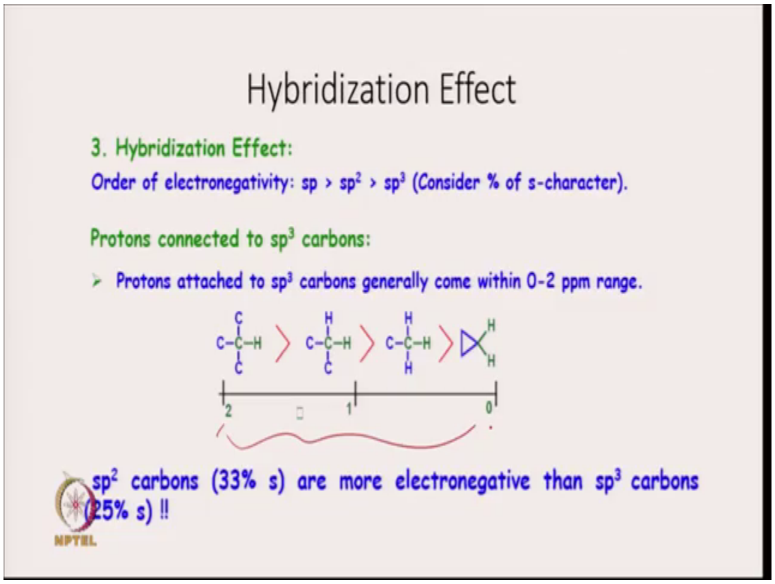

Hybridization Effect

3. Hybridization Effect:

Order of electronegativity: sp > sp^2 > sp^3 (Consider % of s-character).

Protons connected to sp^3 carbons:

- Protons attached to sp^3 carbons generally come within 0-2 ppm range.

sp^2 carbons (33% s) are more electronegative than sp^3 carbons (25% s) !!

Now, third effect which I am going to discuss is Hybridization effect. Hybridization of carbon will also affect the chemical shift value. Order of electronegativity as we know that a nucleus with hybridization sp is going to be more electronegative than a nucleus which is sp2 hybridized and similarly a nucleus which is sp2 hybridized is more electronegative than a nucleus which is sp3 hybridized and that is because of because of s-character so if s-character increases electronegativity is more.

So, if protons attached is with sp3 carbon then the proton chemical shift is going to be in 0 to 2 ppm range and some value is given here, this is for proton attached to tertiary carbon and since so proton attached to tertiary carbon here proton is attached to secondary carbon and among these 3 you just apply the concept of electronegativity and you will understand why this one has higher chemical shift and this one has lower chemical shift.

sp2 carbon, if we compare between sp2 carbon and sp3 carbon we know that sp2 carbon is more electronegative than sp3 carbon and hence if proton is attached to a sp2 carbon then electron is withdrawn from that proton more strongly in comparison to a proton attached to sp3 carbon. So, we discussed about the substitution effect on proton chemical shift of benzene ring but the very high chemical shift value cannot be explained just only based on electronegativity.

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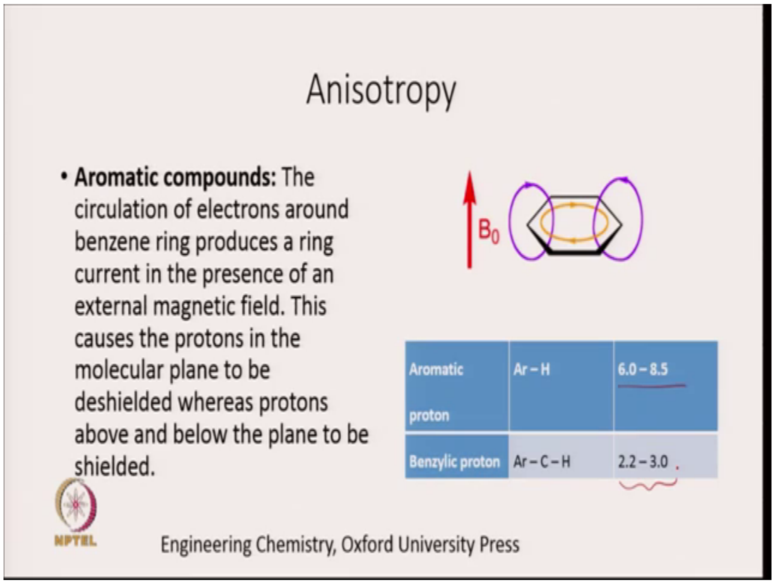

Anisotropy

- **Aromatic compounds:** The circulation of electrons around benzene ring produces a ring current in the presence of an external magnetic field. This causes the protons in the molecular plane to be deshielded whereas protons above and below the plane to be shielded.

Aromatic proton	Ar – H	6.0 – 8.5
Benzylic proton	Ar – C – H	2.2 – 3.0

Engineering Chemistry, Oxford University Press

Value of chemical shift can only be explained on the basis of Anisotropy. The circulation of electrons around benzene ring produces a ring current in the presence of an external magnetic field. So, there is a circulation of electron in the plane of benzene ring and that produces a ring current in the presence of external magnetic field and this causes the protons in molecular plane to be deshielded and protons above or below the plane to be shielded and so Benzylic protons, Aromatic protons has very high chemical shift it is 6 to 8.5 because they are deshielded. Whereas protons in above, protons above or below the planes are shielded and that is why they are low chemical shift value.

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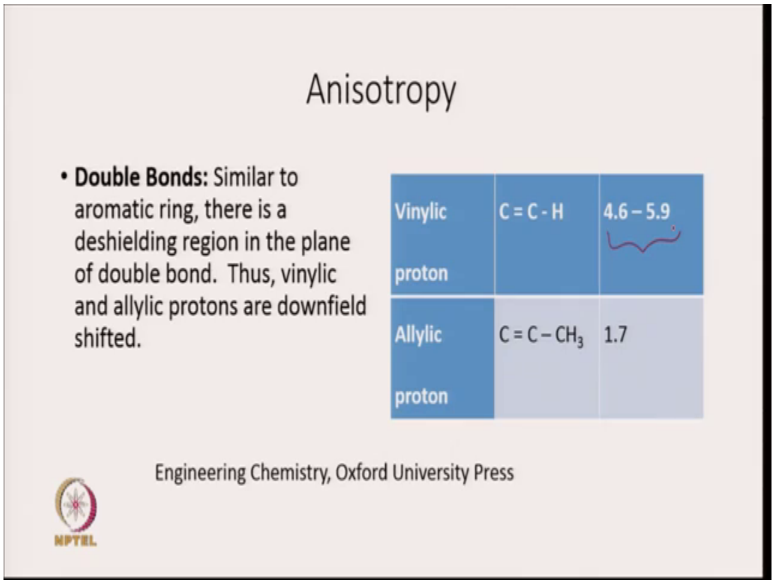

Anisotropy

- **Double Bonds:** Similar to aromatic ring, there is a deshielding region in the plane of double bond. Thus, vinylic and allylic protons are downfield shifted.

Vinylic proton	C = C - H	4.6 – 5.9
Allylic proton	C = C – CH_3	1.7

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Similar to aromatic ring, anisotropy also plays a role in double bond. So, similar to aromatic ring there is a deshielding region in the plane of the double bond and thus, Vinylic and Allylic protons are downfield shifted and this is the value of Vinylic proton.

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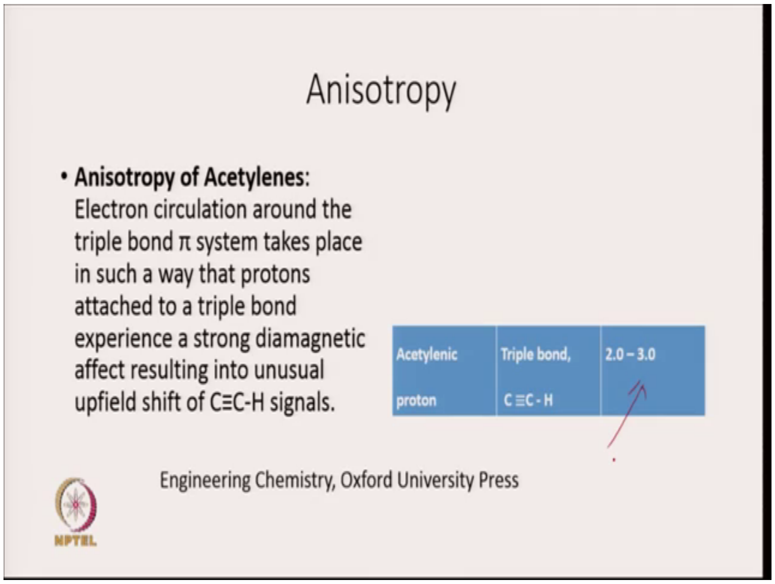

Anisotropy

- **Anisotropy of Acetylenes:** Electron circulation around the triple bond π system takes place in such a way that protons attached to a triple bond experience a strong diamagnetic affect resulting into unusual upfield shift of C≡C-H signals.

Acetylenic proton	Triple bond, C≡C - H	2.0 – 3.0

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Anisotropy also effects Acetylene protons. The electron circulation around the triple bond pi system takes place in such a way that protons attached to a triple bond experience a strong diamagnetic field resulting in unusual up field shift of C triple bond C H signal, C triple bond C H signal. So, this is unusual up field shift.

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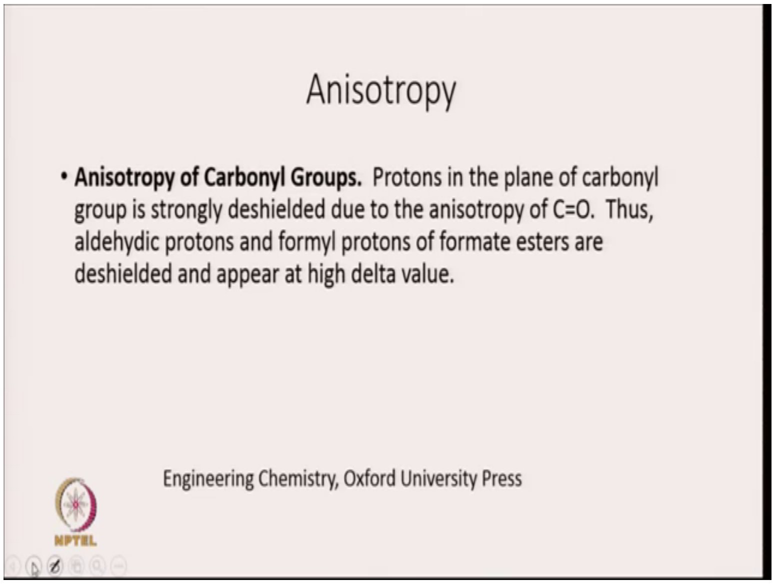

Anisotropy

- **Anisotropy of Carbonyl Groups.** Protons in the plane of carbonyl group is strongly deshielded due to the anisotropy of C=O. Thus, aldehydic protons and formyl protons of formate esters are deshielded and appear at high delta value.

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Anisotropy of the carbonyl group again protons in the plane of carbonyl group is the strongly deshielded due to anisotropy of C double bond O and thus aldehydic protons and formyl protons of formate esters are deshielded and appear at higher delta value. So, it is deshielded then higher delta value if it is shielded then it then it is going to have lower delta value, so please keep that thing in mind.

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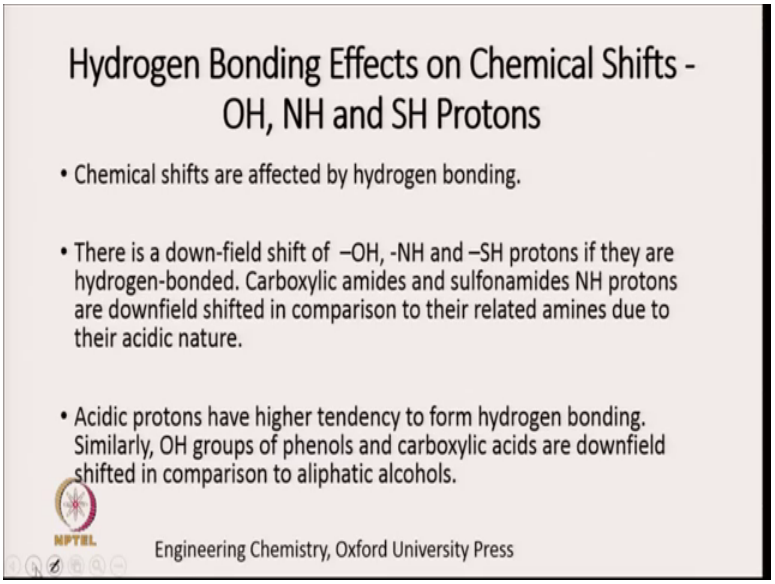

Hydrogen Bonding Effects on Chemical Shifts - OH, NH and SH Protons

- Chemical shifts are affected by hydrogen bonding.
- There is a down-field shift of –OH, -NH and –SH protons if they are hydrogen-bonded. Carboxylic amides and sulfonamides NH protons are downfield shifted in comparison to their related amines due to their acidic nature.
- Acidic protons have higher tendency to form hydrogen bonding. Similarly, OH groups of phenols and carboxylic acids are downfield shifted in comparison to aliphatic alcohols.

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Chemical shifts are also affected by hydrogen bonding. So, there is a downfield shift of OH, NH and SH proton if they are hydrogen bonded. So, they will come at high chemical shift value.

Carboxylic amide and Sulfonamide NH protons are downfield shifted in comparison to their related amines due to their acidic nature and that is why these NH protons will come at higher chemical shift value. Acidic protons have higher tendency to form hydrogen bonding. Similarly OH group of phenol and carboxylic acids are downfield shifted in comparison to aliphatic alcohols.

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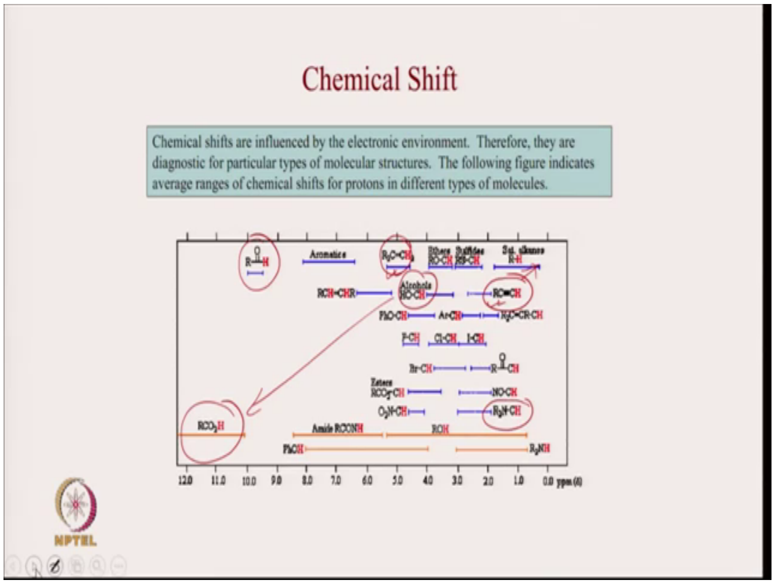

Chemical Shift

Chemical shifts are influenced by the electronic environment. Therefore, they are diagnostic for particular types of molecular structures. The following figure indicates average ranges of chemical shifts for protons in different types of molecules.

And this is your a typical chemical shift value of some of the groups. So, RCO2H has highest chemical shift whereas you can see that these values, these amine values CHRNR2 these are going to have lowest chemical shift value, saturated alkenes has lowest chemical shift value. If you look at R2C double bond CH2 it is having higher chemical shift value comparison to, in comparison to your, this triple bond RC triple bond CH and this is because of anisotropy.

And then you can see here that alcohol and compared between this alcohol and RCO2H group so these acidic protons, acidic protons is more downfield shifted or higher chemical shift compared to an alcohol proton it is because of they are very acidic they are very acidic. So, this proton of your aldehyde is going to have higher chemical shift value because of anisotropy. So, these are the some of the values of chemical shift and depending on the value of chemical shift also you can guess a depending on chemical shift of the proton which you obtained through NMR, through NMR you can tell that which kind of functional group may be present in that compound.

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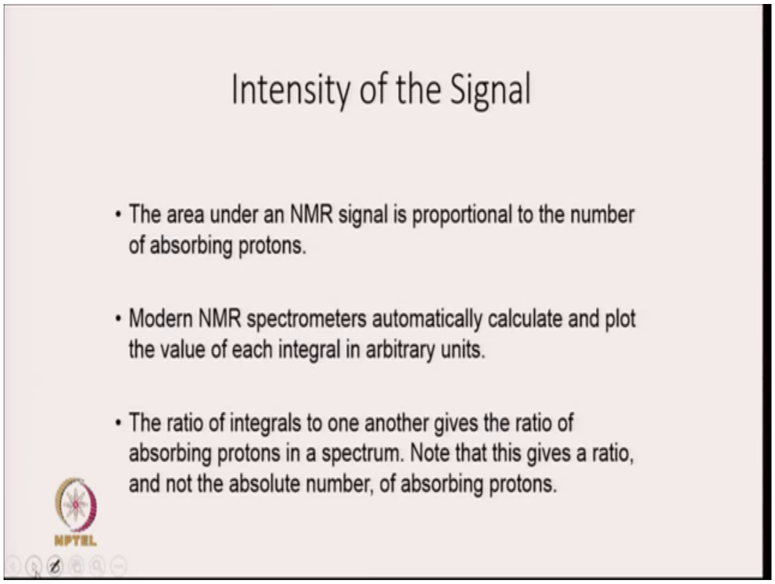

Intensity of the Signal

- The area under an NMR signal is proportional to the number of absorbing protons.
- Modern NMR spectrometers automatically calculate and plot the value of each integral in arbitrary units.
- The ratio of integrals to one another gives the ratio of absorbing protons in a spectrum. Note that this gives a ratio, and not the absolute number, of absorbing protons.

The third important factor is intensity of the signal and the area under an NMR signal is proportional to the number of absorbing protons and this can also be used to obtain a structural features from a NMR spectrum. Modern NMR spectrometer automatically calculates and plot the value of each integral in arbitrary unit. The ratio of integral to one another gives the ratio of absorbing protons in a spectrum and that is very important. Note that, this gives a ratio and not the absolute number of the absorbing protons so please keep this thing in mind but it is important that if I get the ratio of integral I know what will be the ratio of absorbing protons in that spectrum.

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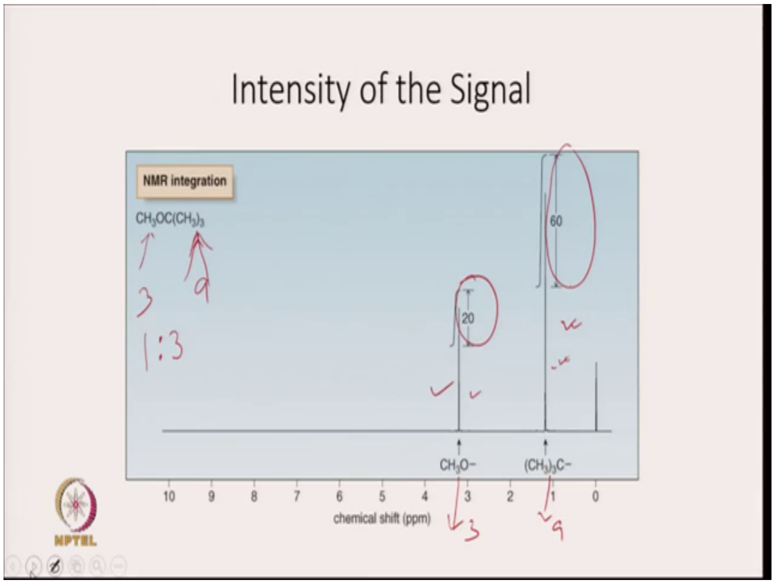

Intensity of the Signal

NMR integration

$CH_3OC(CH_3)_3$

So, now see in this case this is your CH3OCCH3 thrice, CH3 thrice. Now, if you notice they have 2 different kind of protons so you get 2 signals and now just based on their intensity you can tell that which proton gives which signal. So, now here you see this is there are only 3 protons and there is 9 protons here and so what you expect that one if this is if intensity if we normalize intensity this should be in the ratio 1 is to 3. And now you see this is the this if you look at the intensity this is 20 unit, if this is 20 unit this is your 60 unit this is your intensity of the signal and so now you know that ratio of protons having this signal is one third of protons having this signal. So, it is quite easy to assign this is CH3 thrice C and this will be CH3O, this has 3 protons, this has 9 protons. So, it is quite obvious that the signal of this peak will be thrice that of signal of this peak. So, just based on intensity we are able to assign the spectrum in this case.

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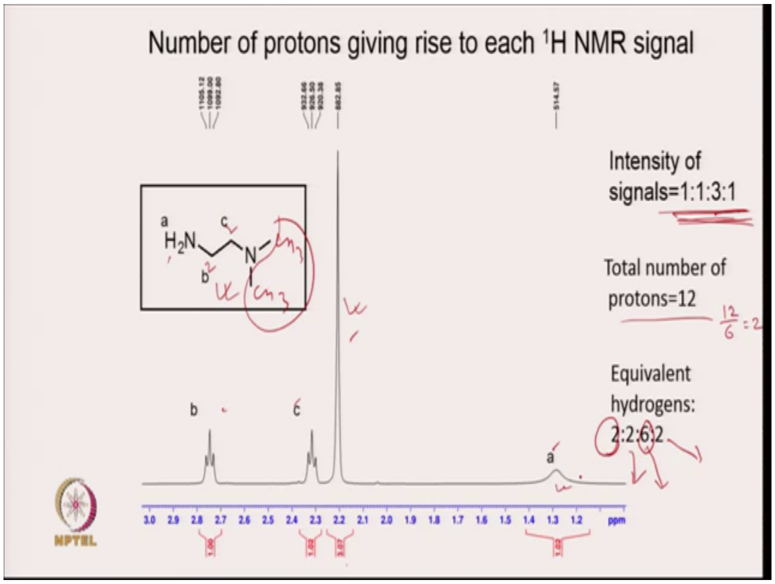

Number of protons giving rise to each ^{1}H NMR signal

Intensity of signals=1:1:3:1

Total number of protons=12

Equivalent hydrogens: 2:2:6:2

Now, let us think about this molecule. So, this is NH2 CH2 CH2 and CH3 twice so this is CH3 and this is CH3. So, 3, 3, 6 and there is 2 proton attached to this carbon 2 proton attached to this carbon and 2 proton attached to this nitrogen. So, you have a 4 different kind of protons so you expect 4 different signal and these 4 signals are here and if you look at this intensity ratio here is the ratio given and this is 1 is to 1 is to 3 is to 1. So, this is the ratio which you obtained from the spectrum NMR a spectrum which you obtain through the NMR experiment and the intensity what you got is in the ratio of 1 is to 1 is to 3 is to 1.

Now, look at the total number of protons here 2, 2 4, 2 6, and 6, 12 so total number of proton is 12 and the sum of this is 2 plus 3 plus 1 so 5 plus 1 6 and if I divide 12 divided by 6 this will give you 2 and so just you multiply this number by 2 so equivalent hydrogens will be your 2 so 1 equivalent hydrogen group will have 2 protons. The second group will have 2 protons and third group is going to have 6 protons and fourth group is going to have 2 electrons. So, there are 6 plus 6 12 protons 2 plus 2 plus 6 plus 2 is 12 protons and if you see the third one it has a 6 proton so certainly you will be able to assign this peak to these 6 protons because this is almost thrice of other peaks and the others can be assigned based on the chemical shift.

This b is going to be most upfilled since this proton is attached to an electronegative atom n, electronegative atom N, so b will be this, c will be this one and since this the proton attached to this carbon and carbon is attached to NCH3 twice group which is less electronegative than NH2 group because this N is attached to electron donating group and so the NCH3 twice in less electronegative than NH2 and hence the second will come at this position, third we have already assigned and forth since this is attached to and so it is attached to N group directly and so it will come at this position. So, just based on what we expect of chemical shift value we can assign your this spectrum there are another characteristic which is the splitting of signal I just I will discuss that also that basically ensures that the spectrum is correctly assigned.

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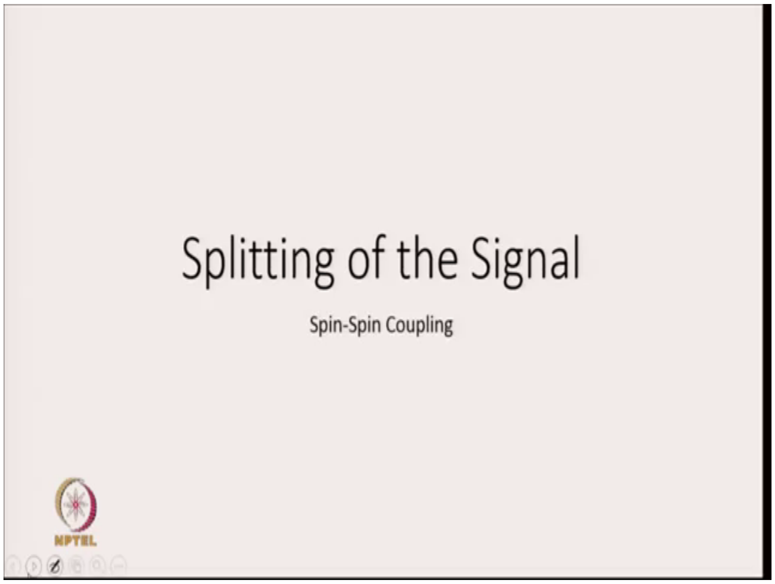

Splitting of the Signal

Spin-Spin Coupling

So, the fourth feature another important feature of the NMR signal is they split in presence of each other protons.

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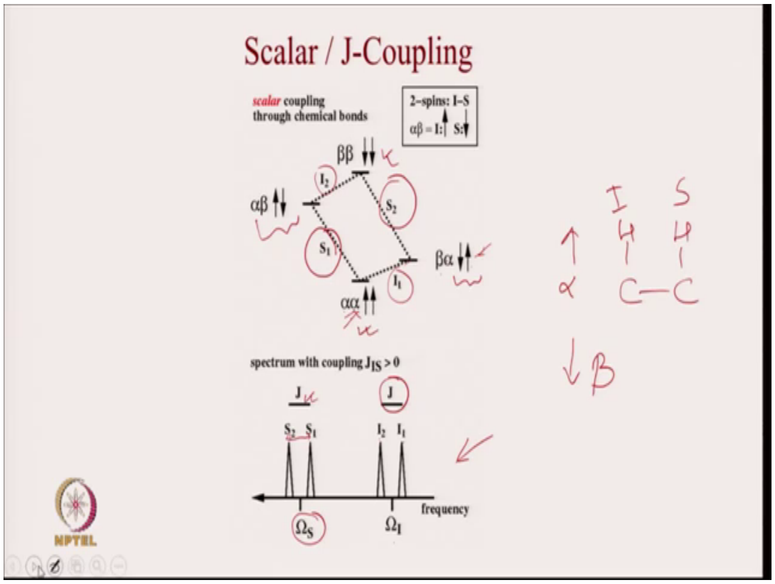

Scalar / J-Coupling

scalar coupling
through chemical bonds

2-spins: I-S
αβ = I:↑ S:↓

spectrum with coupling $J_{IS} > 0$

And that I will that is explained by a scalar J coupling or J coupling. So, if there are 2 spin so if there are 2 spin adjacent to each other they will split, they will a split the signal. To explain this let us assume that this spin is given by I and this spin is given by S and if spin is in this direction then I give this alpha sign if the spin is in this direction and I give it beta sign. So, the 2 spins can arrange in 4 different ways. First when both are up, in the second one, one is up another is down, the third one, one is up another is down and fourth one both are down. So, in this the spin of both I and S is up and this spin of I is up, the spin of S is down and so spin of I is given by alpha, spin of S is given by beta, in this spin of I is down and a spin of S is up and so beta alpha.

These are the 4 different states and if the transition happens from (alpha to) alpha alpha to alpha beta it means the S is changing sign. So, S is going from alpha to beta whereas for I sign is same alpha alpha and that is why this is called S1 transition and similarly if you look at this beta alpha to beta beta, the change in sign is happening for the spin S and that is why this is known as S2 transition. Whereas if you see this transition alpha alpha to beta alpha the spin of I is changing direction which is going from alpha to beta. Whereas in this also the spin of I is changing direction and that is why these are known as I1 and I2 transitions.

So, now you can see that we have 2 S transition and 2 I transition and that is what we say that in presence of S, the (I the transition) the I transition is split into 2 part whereas in presence of I, S transition splits into 2 and that is what is shown here and this is for I so this is your chemical shift of I suppose and then in the presence of your S it is splits into 2, one is I1, I2 and the splitting between these 2 signals is known as J, J value I scalar coupling. Here you see the S also splits into 2 because of presence of I and this is your chemical shift of S and split is in the other 2 direction and the your this gap between these two value is known as J it is known J value or is a coupling constant value. So, the presence of nearby proton split the signal or protons.

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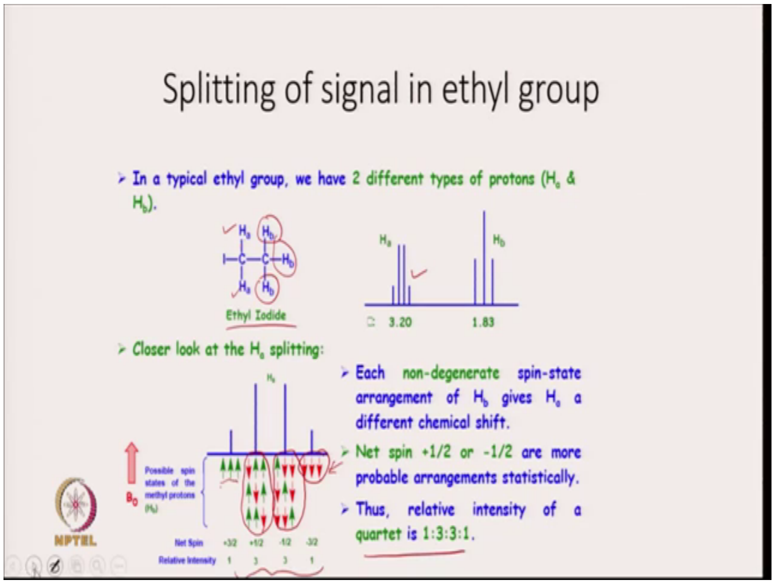

Splitting of signal in ethyl group

- In a typical ethyl group, we have 2 different types of protons (H_a & H_b).

- Closer look at the H_a splitting:

- Each non-degenerate spin-state arrangement of H_b gives H_a a different chemical shift.
- Net spin +1/2 or -1/2 are more probable arrangements statistically.
- Thus, relative intensity of a quartet is 1:3:3:1.

So, let us talk about some molecule and see how many splitting is possible so. Take, the case of ethyl iodide and this carbon has 2 proton, this carbon has 3 proton, this carbon has 3 proton and if I look at the splitting of this Ha due to this Hb. Now, think of how many levels it will split? The so this is for Ha and now you see all Hb can be up direction, 1 is down 2 is up and there are 3 different possibilities possible for 1 down 2 up, for 1 up and 2 down these 3 are possible and for 3 down this 1 combination is possible.

So, splitting will happen the signal of Ha will is split into 4 with this intensity ratio 1 is to 3 is to 3 is to 1 this ratio because there is only 1 combination for all 3 spin up. This there are 3 different combination for 2 up 1 down 3 different combination for 1 up 2 down and 1 combination for all 3 down and so the relative intensity of quartet will be 1 is to 3 is to 3 is to 1. So, the signal of Ha splits into 4 because your presence of 3 Hb protons and that can be converted into rule that if there is a N protons nearby then there will be the splitting will a splitting of nearby proton will be

N, N plus 1 peaks. So, 3 protons are present so signal of H a will split into 4 and since 2 protons are present near to these Hb protons so the signal of Hb will split into 3, 2 plus 1 3.

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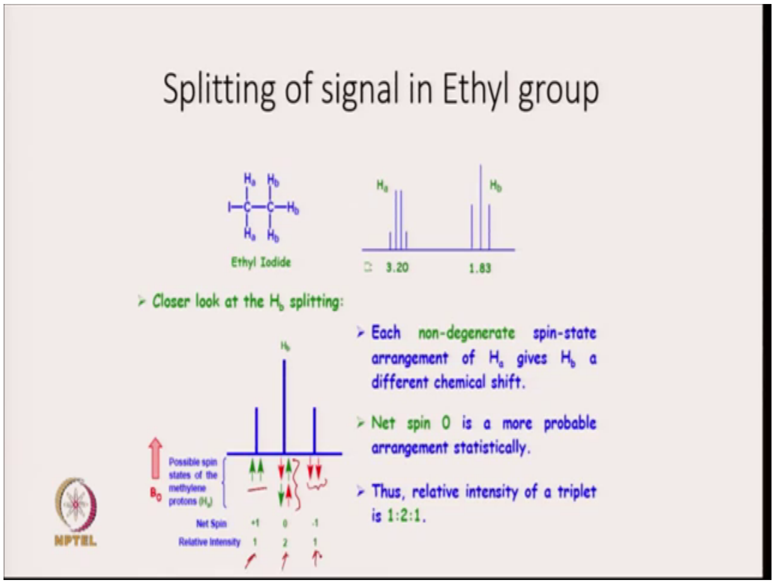

Splitting of signal in Ethyl group

- Closer look at the H_b splitting:
- Each non-degenerate spin-state arrangement of H_a gives H_b a different chemical shift.
- Net spin 0 is a more probable arrangement statistically.
- Thus, relative intensity of a triplet is 1:2:1.

And that you can see here that if we go for Hb then what happens that possible spins are combination of both up is 1, the combination of your 1 up and 1 down is 2 and combination of both down is 1 and so a split will be in the 3 peaks in ratio 1 is to 2 is to 1.

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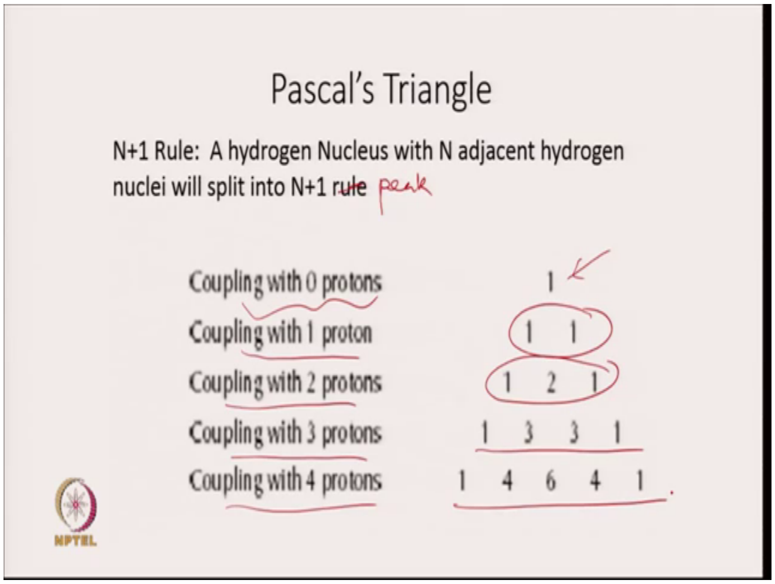

Pascal's Triangle

N+1 Rule: A hydrogen Nucleus with N adjacent hydrogen nuclei will split into N+1 ~~rule~~ peak

Coupling with 0 protons	1
Coupling with 1 proton	1 1
Coupling with 2 protons	1 2 1
Coupling with 3 protons	1 3 3 1
Coupling with 4 protons	1 4 6 4 1

So, from this example comes what is known as N plus 1 rule. A hydrogen nucleus with N adjacent hydrogen nuclei will split into N plus 1 peaks. Nuclei I will split into N plus 1 peak and what does that mean is coupling is with 0 protons there is no nearby protons then you will get only 1 peak so 0 plus 1 1 peak. If coupling is with 1 proton you will get 2 peak 1 plus 1 2 peak,. in the ratio 1 is to 1. If the coupling will be with the 2 protons the peak will split into the proton peak will be split into 3 different peaks with the ratio 1 is to 2 is to 1 and coupling is with 3 protons 4 peak will result with the intensity 1 is to 3 is to 3 is to 1. Coupling with 4 protons will result into your 5 different peak with the intensity 1 is to 4 is to 6 is to 4 is to 1.

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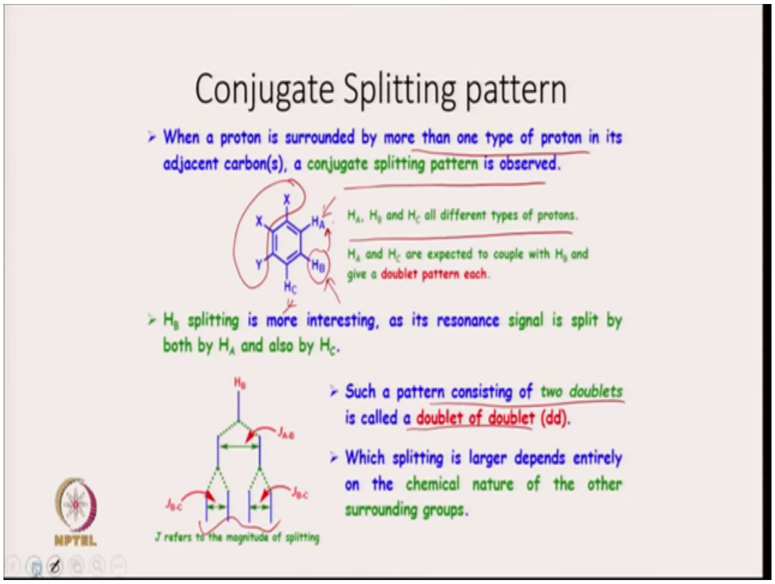

Conjugate Splitting pattern

- When a proton is surrounded by more than one type of proton in its adjacent carbon(s), a conjugate splitting pattern is observed.

H_A, H_B and H_C all different types of protons.

H_A and H_C are expected to couple with H_B and give a doublet pattern each.

- H_B splitting is more interesting, as its resonance signal is split by both by H_A and also by H_C.

J refers to the magnitude of splitting

- Such a pattern consisting of two doublets is called a doublet of doublet (dd).
- Which splitting is larger depends entirely on the chemical nature of the other surrounding groups.

When a proton is surrounded by more than 1 type of protons in it is adjacent carbon then a conjugate splitting pattern will be observed. For example, here if you HA, HB, HC they are all different types of protons if the substitutions are X X and Y at this position HA and HC are expected to couple with HB only and so since there is coupling of HA with HB and so this will split into 2 peaks, HC will also be split into 2 peaks but interesting is your splitting of HB since it will be split both by HA and HC and the splitting will like be this.

So, HB this is splitting because of it is coupling with A and this is the splitting and now since B is also coupled with C and so this 2 peak again will split and this is your coupling constant between A and B and this will be the coupling constant between B and C. So, there will be 4 peakse. 4 peaks, 4 peaks and what this is called 2 doublets or doublet of doublet dd, doublet of doublet. Which splitting will larger depends entirely on the chemical nature of other surrounding group. So, J AB is higher or J BC is higher it will depend on chemical nature of other surrounding group.

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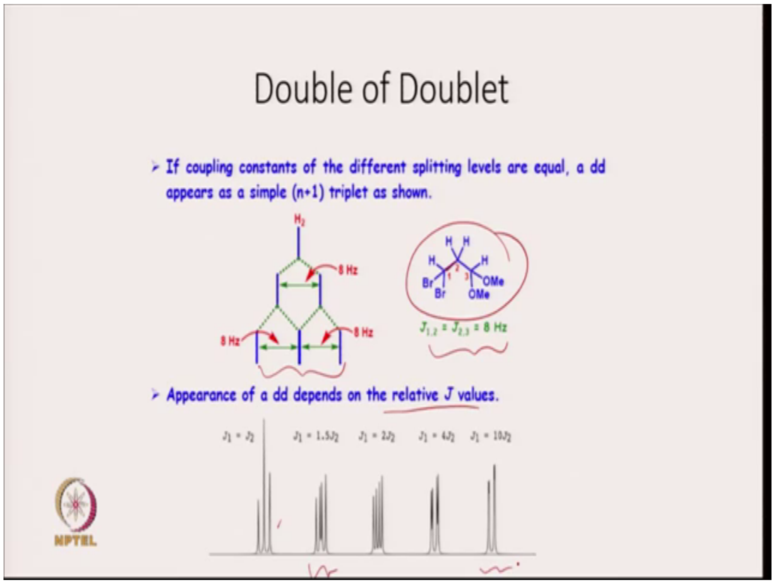

Double of Doublet

- If coupling constants of the different splitting levels are equal, a dd appears as a simple (n+1) triplet as shown.
- Appearance of a dd depends on the relative *J* values.

If the coupling constant of the different splitting levels are equal our dd will appear as a simple n plus 1 triplet. So, look at here this the second one the J 12 is equal to J 23 if you take this molecule, this proton is being split by this proton and this proton but the coupling constant is, coupling constant between 1 and 2 and 2 and 3 is equal, a coupling constants between these 2 and these 2 are equal and that are equal to 8 hertz in that case we will get a triplet. So, appearance of dd depends of on the relative J value and if J 1 is equal to J 2 we looked at this triplet we will get if J 1 is equal to 1.5 J 2 then you will get like this. Then depending on the different values you will get different kind of dd, dd signal.

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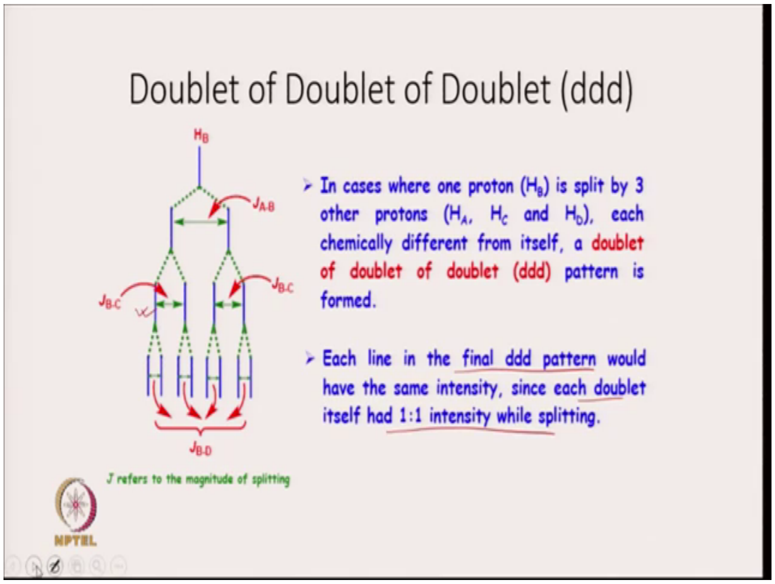

Doublet of Doublet of Doublet (ddd)

J refers to the magnitude of splitting

- In cases where one proton (H_B) is split by 3 other protons (H_A, H_C and H_D), each chemically different from itself, a doublet of doublet of doublet (ddd) pattern is formed.
- Each line in the final ddd pattern would have the same intensity, since each doublet itself had 1:1 intensity while splitting.

Now, there is doublet of doublet of doublet ddd signal also present in cases where this happens when 1 proton HB is split by 3 other protons HA, HC and HD each chemically different from itself a doublet of doublet of doublet pattern is form. Each line in final ddd pattern would have same intensity since each doublet itself has 1 is to 1 intensity while is splitting. So, let us look here this is the first splitting and then this gets split, this is the second splitting and this is your third splitting. So, this is because of coupling between A and B, this is because of coupling between B and C and this is because of coupling between B and D and so doublet of doublet of doublet signal will be seen.

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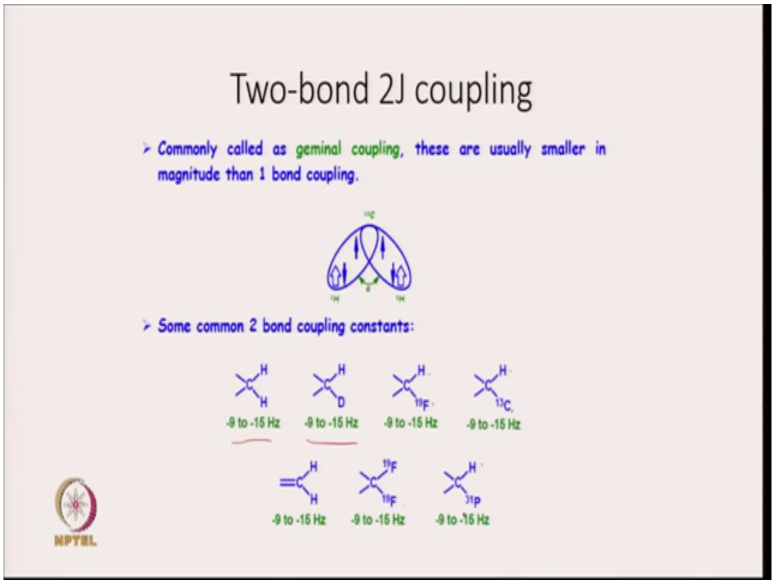

Two-bond 2J coupling

- Commonly called as geminal coupling, these are usually smaller in magnitude than 1 bond coupling.
- Some common 2 bond coupling constants:

Then there is a two bond 2J coupling commonly known as geminal coupling, they are usually a smaller in magnitude than 1 bond coupling. So, this is your geminal coupling and you can see that C is attached to this H and this H and this is known as 2 bond 2J coupling and some 2 bond coupling constant are given here. So, between proton and proton you will get this 9 to 15 Hertz and these are between proton and D, this is between proton and fluorine, this is between proton and carbon, this between proton and proton attached to sp2 carbon, this is between 19 F and 19 F and this is between proton and 31 phosphorus.

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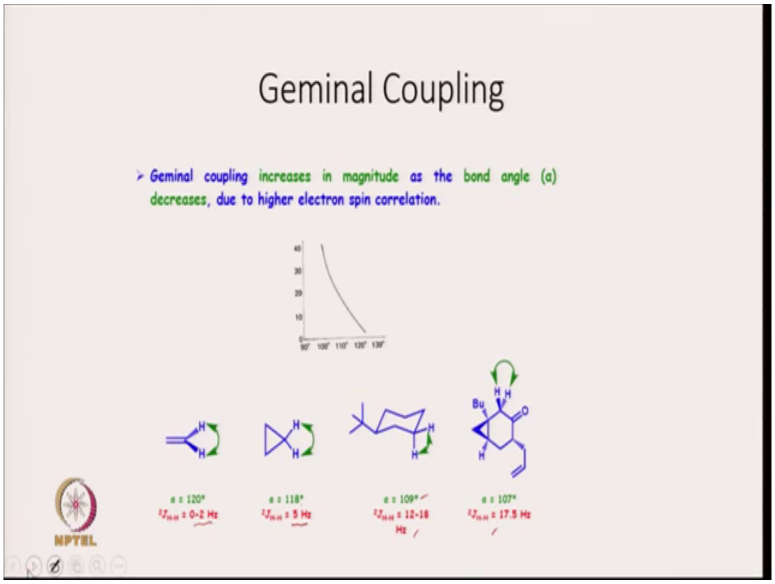
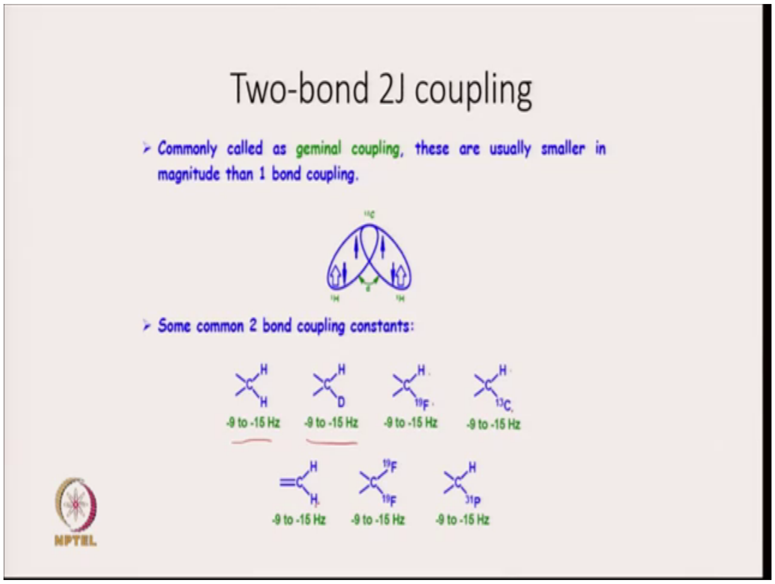


Geminal Coupling

- Geminal coupling increases in magnitude as the bond angle (α) decreases, due to higher electron spin correlation.



Two-bond 2J coupling

- Commonly called as geminal coupling, these are usually smaller in magnitude than 1 bond coupling.
- Some common 2 bond coupling constants:

Geminal coupling increases in magnitude as the bond angle alpha decreases. So, this alpha value affects the coupling constant value. Geminal coupling increases in magnitude as the bond angle alpha decreases and due to high electron spin correlation. So, if this is 120 degree alpha is 120 degree then it is 0 to 2 Hertz, if it is 118 degree then coupling increases to 5 hertz, if it is 109 degree then coupling 12 to 18 hertz, I angle is 107 degree the coupling is 17.5 hertz.

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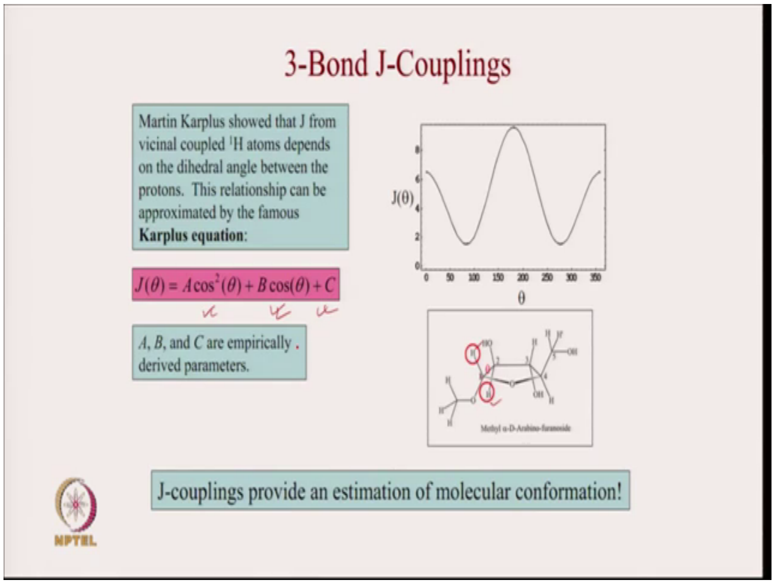

3-Bond J-Couplings

Martin Karplus showed that J from vicinal coupled ^{1}H atoms depends on the dihedral angle between the protons. This relationship can be approximated by the famous **Karplus equation**:

$$J(\theta) = A\cos^2(\theta) + B\cos(\theta) + C$$

A, *B*, and *C* are empirically derived parameters.

J-couplings provide an estimation of molecular conformation!

Similarly, there is also coupling between 3 bond and that is very important if you want to get dihedral angle. So, there is a relation between coupling which is for 3 bond H coupling. For example, this proton the 1 bond 2 bond and 3 bond this proton and this proton if we can get coupling constant, they can give you the dihedral angle between these 2 proton. So, Martin Karplus showed that J from vicinal coupled proton atoms depends on dihedral angle between the protons and this relationship can be approximated by the famous Karplus equation

And J value is given by A cos square theta plus B cos theta plus C where A, B, C are empirically derived parameters and this is very important if you want to estimate the molecular conformation. Today, I will stop here because time is over and in the next lecture I will discuss about how to get the Structural Information using 3 different kind of information, (4) basically 4 different kind of information I have only discussed I believe 3 or I have discussed also I have discussed 3, 4th is still I am discussing. In the next lecture, I will discuss about the COSY and other 2D experiment which are generally done to get a structure of complex molecules, thank you very much, bye.