Application of Spectroscopic Methods in Molecular Structure Determination

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Lecture - 05
Nuclear Magnetic Resonance Spectroscopy
Principle and Application in Structure Elucidation

Hello, welcome to module 5 of the course on Application of Spectroscopic Techniques in Molecular Structure Determination. In this module, we see some special cases of structural elucidation. The problem-solving session is what we are going to have in this particular module. We look at those some stereo chemical aspects of compounds which can be identified by proton NMR spectroscopy.

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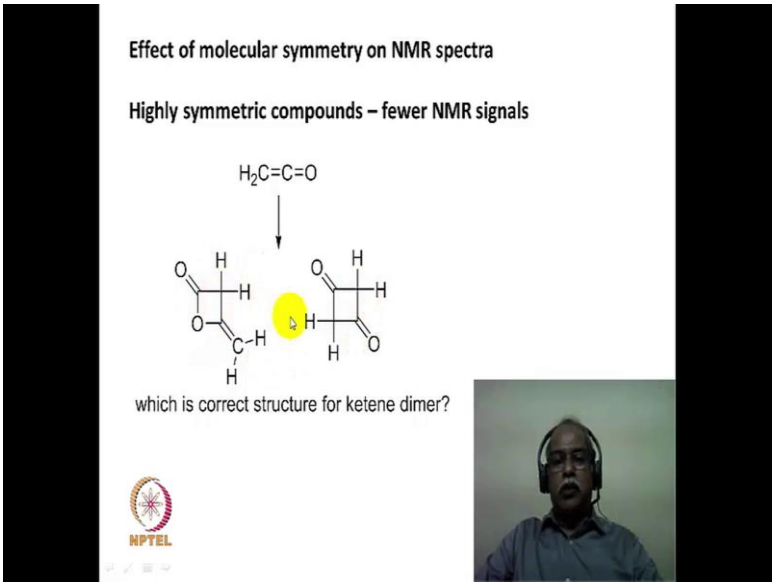

Now, let us go to the first slide. Now the question here is Effect of molecular symmetry what does it do to the NMR spectrum? We have already seen in the earlier example, if the molecule is highly symmetrical in nature then you get a fewer number of signals in the NMR.

Now, the question that is post here is, let us say it ketene is under growing dimerisation. What is the structure of the dimer, will it have a structure which is this particular structure which is lacton structure or will it have a structure which is this particular structure which is a the diketone structure? The essentially the difference between these 2 structures is that this is a highly symmetrical structure, whereas this is an unsymmetrical structure.

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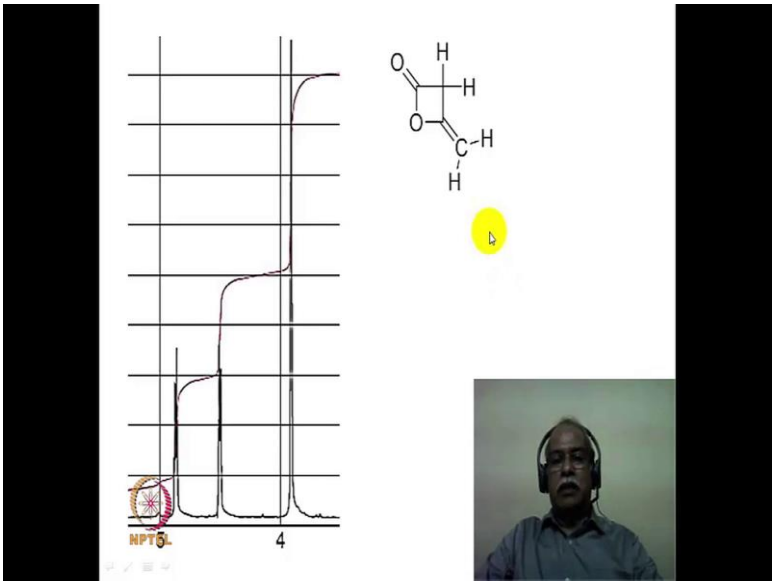

The actually spectrum of ketene seem to be showing an unsymmetrical pattern. In other words, it has 3 different chemical shift values corresponding to these 2 hydrogens, corresponding to 1 chemical shift value and this hydrogen which is trans to the oxygen here and this hydrogen which is cis to the oxygen to here comes at 2 different chemical shift value, which are shown here.

So, essentially the ketene dimer spectrum is this particular spectrum, this would match only with this particular structure, it would not match with this structure.

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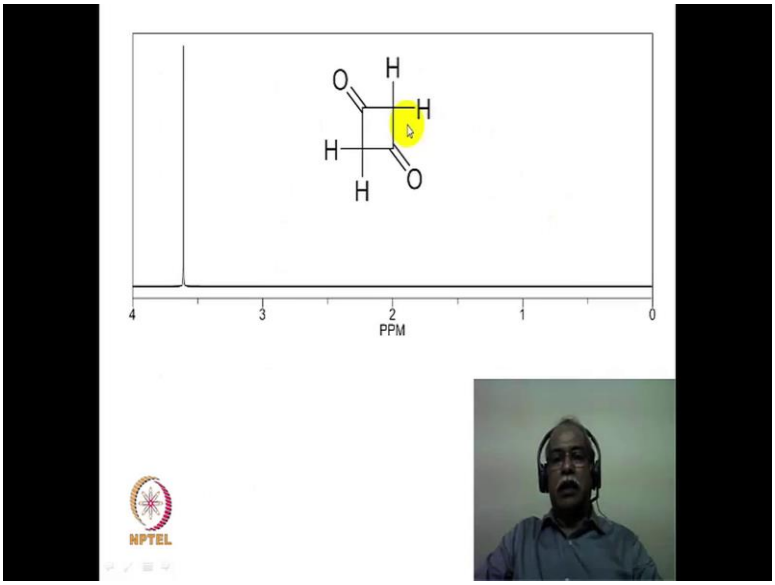

In fact, the structure of the other compound is shown here and this spectrum is also shown here. Because of the highly symmetrical nature of this molecule there is only 1 singlet that is seen for all the hydrogens around 3.55 PPM or so. So, the fact that you have 3 different chemical shift values, indicates this is the unsymmetrical structure is what is most suited for the dimer of the ketene, the structure of the ketene dimer to be this particular structure and not this particular structure here.

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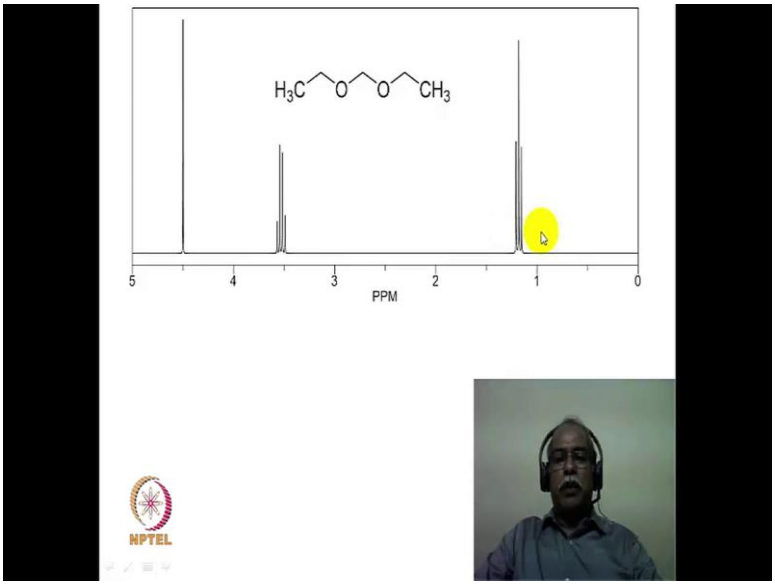

Another example we will see here; this is again a symmetrical molecule, it is a very fairly simple molecule, this CH 2 which is flanked by 2 oxygen, comes if the most deshielded region in the NMR, around 4.5 PPM it comes as a singlet because there are no coupling partners, there are only oxygen adjacent to this. Then you have an ethyl group on this side, another ethyl group on this side because of the molecular symmetry these 2 ethyl groups are identical in nature, in terms of their chemical environment. So your single set of quartet and a triplet is what you see for both the ethyl groups. So, the integration ratio would be corresponding to 2 hydrogen here, 4 hydrogen here and 6 hydrogen here in terms of the relative intensities of the ratio.

Now, let us ask ourselves this question. Suppose, I introduce a substituent here at this position in the form of a methyl group, what happens to the NMR spectrum? This simple spectrum turns into a fairly complex spectrum upon introducing a simple methyl group at this position because, now the molecule loses it is symmetry. We are now talking about this particular molecule, you can see here this spectrum is much more complicated spectrum compared to the earlier example of this particular compound spectrum, which is a simple quartet and a triplet and a singlet.

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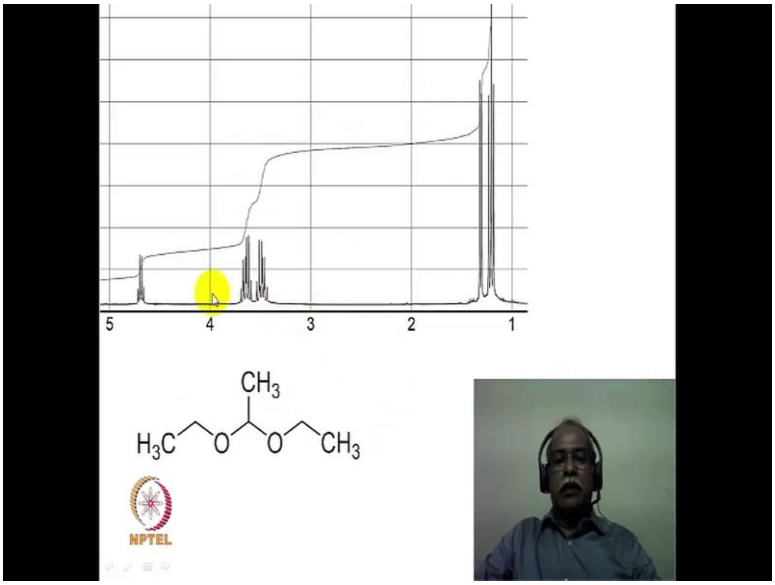

This particular introduction of a methyl group at this methylene position here has cost enormous changes in the NMR spectrum of this compound. Now, what is a reason for this? Let us analyze this, there is a quartet here and a triplet here. This quartet is essentially, 1 hydrogen intensity and this triplet here is essentially 6 hydrogen intensity. So, they are not essentially because of an ethyl group which normally we encounter in this particular case. So, the ethyl group is actually because it is connected to oxygen, this methylene should come in the region typically, in this particular region.

There is 1 hydrogen which is the methane hydrogen and that is split by the CH 3 into a quartet and that lone hydrogen alone comes in this particular region of 4.8 PPM, because that will have the highest chemical shift value because it is flanked by 2 oxygen, so the 4.8 PPM corporate corresponds to this particular hydrogen, the position that I am pointing with this cursor here. That particular position hydrogen is what is responsible for it. It is a quartet because it is split by this methyl group which is 3 adjacent hydrogen (Refer Time: 04:42) therefore, it is quartet.

Now, what happened to the methyl itself? The methyl is split in to a doublet. So, we can see a doublet here for example. And, this methyl is essentially split by this methine hydrogen into a doublet and you can see the methyl group with 3 hydrogen intensity

being a doublet in this region of about 1.3 PPM or so. Now, this methylene which should have been a quartet is not a quartet any more. It appears to be a fairly complex multiplet that, is because this is a prochiral center and that makes this 2 hydrogens pro diastereotopic in nature. In fact, the 2 hydrogens are diastereotopic in nature, so they will split each other in to a doublet of a doublet, 4 line pattern which is farther split into by the CH 3 into a quartet. So, a doublet of a doublet of a quartet is what one should see for this spectrum.

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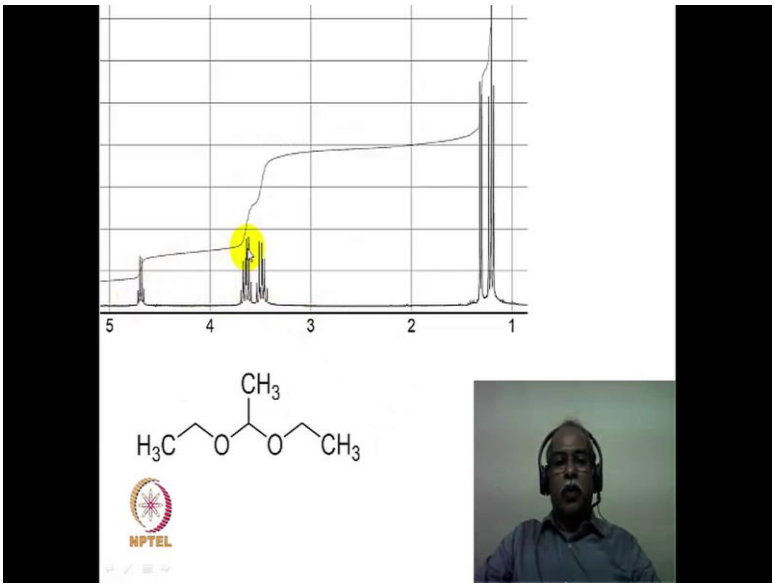

This region of quartet and this multiplet is expended and it is shown in this particular slide.

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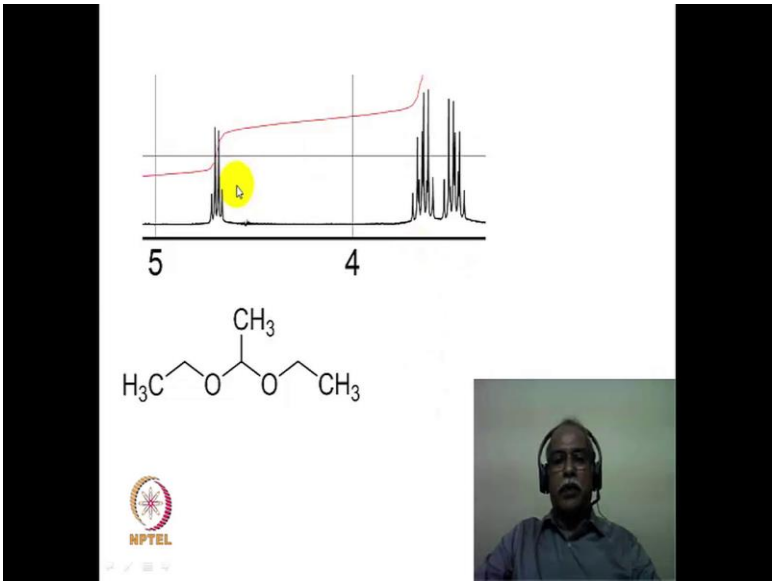

This methane hydrogen appears as a quartet and this methylene appears as a doublet of a quartet. In other words, this a overlapping quartet for 1 of the hydrogen and this is a overlapping quartet for another hydrogen. If you count carefully, you can actually see 16 line pattern in this multiplets for the corresponding to the methylene group of this. The CH 3 appears as a simple triplet which is shown here, so both the CH 3 are identical, these ether CH 3 are identical for example, and both of them appear as a single triplet of 6 hydrogen intensity for this methyl and this methyl put together. So, this example essentially illustrates that a small perturbation by introducing a methyl group causes a fairly large change in the NMR spectrum in comparison to a more symmetrical structure like this. The less symmetrical structure becomes a complex spectrum and wealth of information is obtained because of the complexity of the spectrum.

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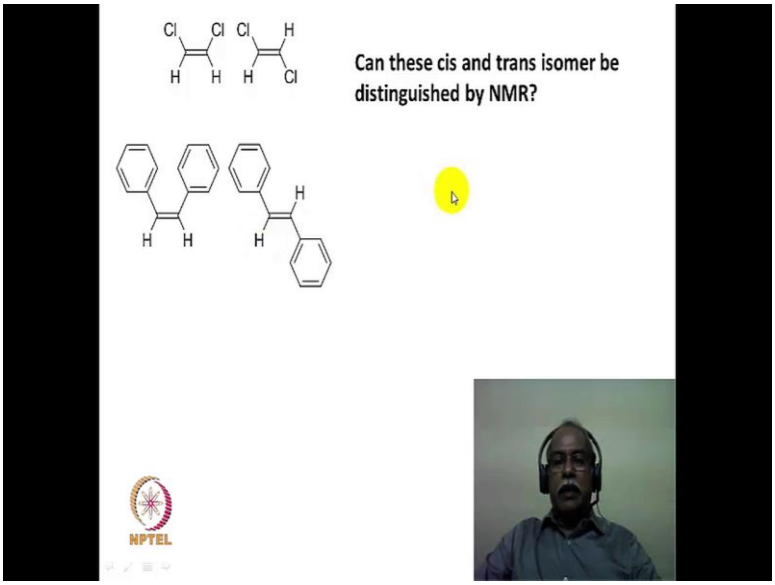

Now, quite often we asked the student, whether it is possible to distinguish this cis and trans isomers using NMR spectroscopy? The immediate conclusion or the answer the student gives is that; yes, it is possible to determine by the NMR spectroscopy by the coupling constraint between these 2 hydrogen. It is the standard answer that one gets. This is a wrong answer of course, because these 2 hydrogens in this molecule or these 2 hydrogen in the cis compound, they are chemically equivalent and they do not split each other at all. They are magnetically as well as chemically equivalent. So, what one would see in the spectrum is a singlet for these 2 hydrogen, there will not be any coupling to show whether it is cis coupling or trans coupling. Similarly, these 2 hydrogens also they are chemically and magnetically equivalent. So, there would also appear only as a singlet. We will see the spectrum in the next slide.

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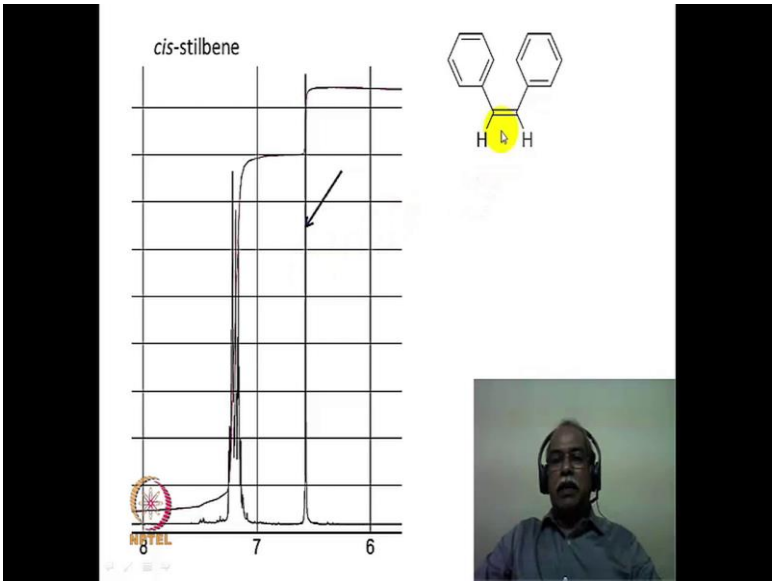

This is a spectrum of cis-stilbene. You can see here, this singlet which is shown by this arrow here correspond to these two hydrogen. The phenyl appears as a multiplet of 10 hydrogen intensity if this position here and these 2 hydrogens essentially coming as a singlet, so there is no question of J value to be distinguishing this cis isomer from the trans isomer.

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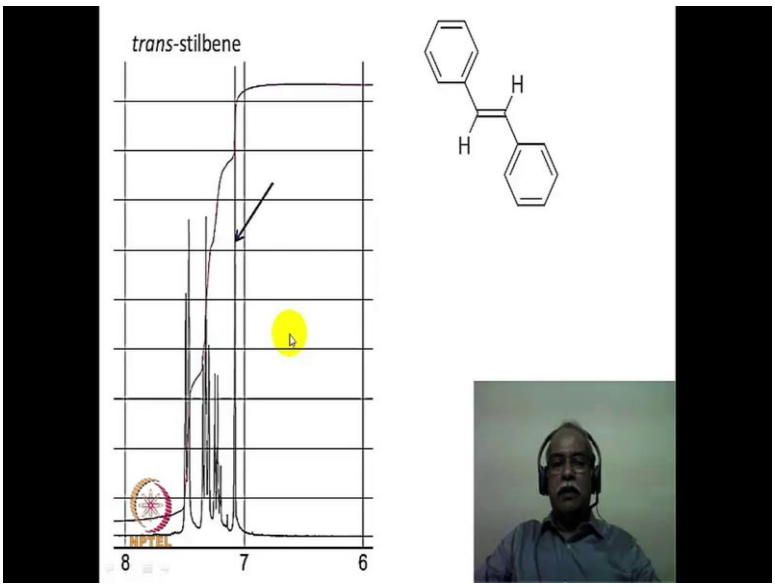

Let us see the spectrum of trans isomer. The trans isomer also is a singlet for these 2 hydrogen, olefinic hydrogen appear as a singlet of 2 hydrogen intensity and the phenyl groups appears as the multiplet, fairly complex multiplet of 10 hydrogen intensity. So, the point is that symmetrical structures do not offer you information regent coupling because of the chemical equivalence and magnetic equivalence of this type of hydrogen. So, how does one now determine which is the cis and which is trans? Now, if you have the spectrum of both the cis as well the trans isomer, it is possible to rationalize which is a cis one and which is a trans one. In the cis one the 2 hydrogens are away from the anisotropic effect of the phenyl group, so therefore, the chemical shift value of these 2 hydrogen's in comparison that trans isomer should be lower in fact, it comes around 6.5 PPM or so.

The trans isomer if you see, it is coming slightly above 7 PPM. This hydrogen is flanked by these 2 phenyl groups, so is this hydrogen by these 2 phenyl group. So, the anisotropic effect of this phenyl groups will be strongly felt by the proton, causing it to deshield itself and as a result of that compare to the cis isomer which came around 6.5 PPM, the trans isomer in fact, comes the 2 hydrogens come above 7 PPM. There by is possible to identify on the basis of chemical shift, not on the basis of coupling constant because there is no coupling constant associated in this molecule.

Now, what about this cis dichloro derivative and trans dichloro derivative? At least, in the case of phenyl derivatives we talked about anisotropic effect and incongruent effect and the deshielding effect and so on and such a facility does not exist in the case of trans dichloro derivative. Can one distinguish or can one get the J value between these 2 hydrogens which are apparently not coupled to each other?

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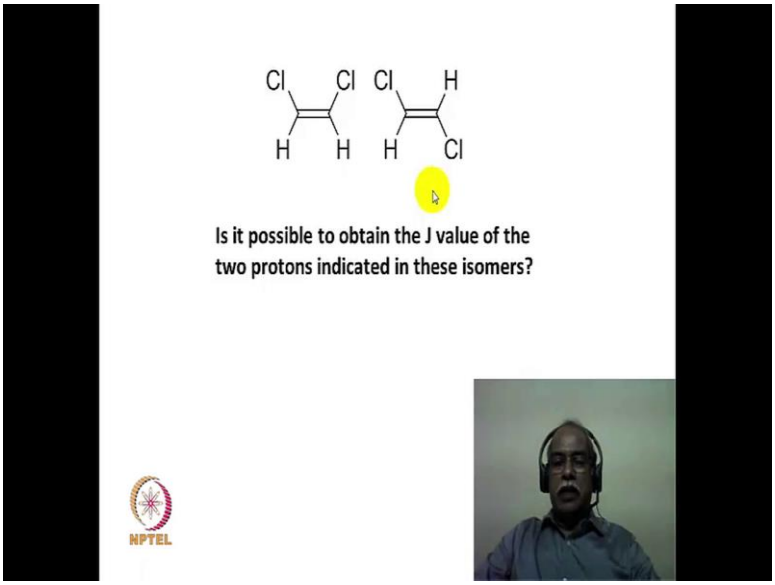

Is it possible to obtain the J value of the 2 protons indicated in these isomers? That is there is no coupling apparent coupling between these 2 hydrogen then, how does one get the J value? Is the question that we are addressing. In order to do that, we look into a phenomenon called Carbon-13 satellite peaks. We are actually referring to only a proton NMR spectrum of the compound.

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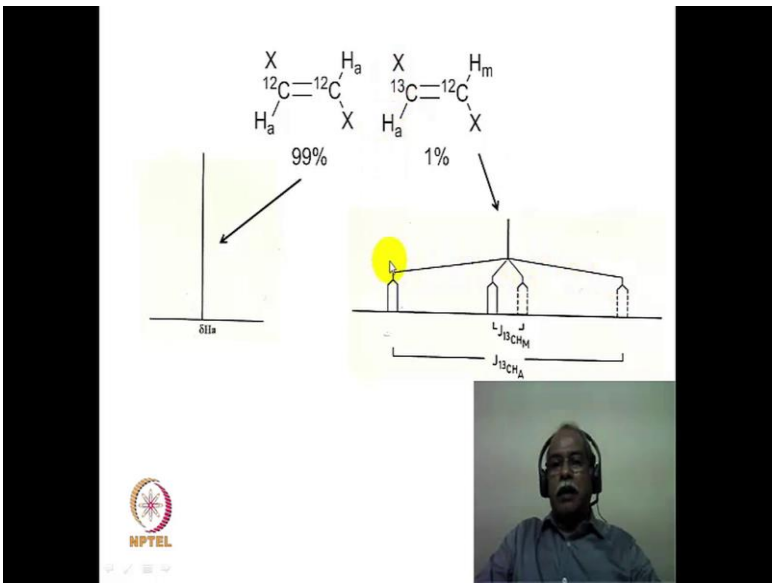

When you take this trans isomer, the trans dichloro derivative the actual sample contains mostly 99 percentage of the molecules or carbon 12 and carbon 12 molecule. And, carbon 12 of course, is magnetically inactive so, it does not matter for the NMR experiment. So, these 2 hydrogens are chemically and magnetically identical in the carbon 12 carbon 12 isotopomer of the trans dichloro derivative.

However, remember the natural abundance of carbon 13 is about 1 percent. So, the probability of having a carbon 13 labeled naturally, abundant labeled carbon 13 compound is about 1 percent. In other words, if you have 100 molecules 99 molecules would the solution would be of this type and 1 molecule will be of this type. So, it should be possible to record the spectrum of this mixture and pick out the spectrum of this particular sample. Why is it important to pick out the spectrum of this particular sample? Because, this is carbon 13, it is magnetically active and that make these 2 hydrogens non equivalent in term of the magnetic equivalence. They are chemically equivalent, but magnetically non equivalent in their nature. So, one should able to see the splitting between these 2 hydrogen's in the carbon 13 isotopomer of the trans dichloro derivative.

Now, you can ask the question how come you do not have a molecule were both carbons are carbon 13? That would be much less abundant, it will be 1 percent of the 1 percent of the molecule that you have here. In other words, 0.01 percent of the molecule would be having carbon 13 and carbon 13. So, it would not be possible to detect such an sample because of the low abundance of carbon 13 in the natural abundance.

Now, what would be the spectrum of this molecule? These 2 hydrogens are chemically and magnetically equivalent. So, it just gives only 1 line pattern. Here, these 2 hydrogens are magnetically nonequivalent, chemically also they are equivalent, chemically they are equivalent, but magnetically non-equivalent in nature so, it should actually a and a prime in terms of the label that one should give, not a and m there is a mistake here. Now, in the absence of carbon 13, only carbon 12 it would have given a singlet because of carbon 13 being present here. This particular hydrogen that is directly attached to a carbon 13 will have a large coupling of the order of 100 plus hertz or so. So, that is split into a doublet which is seen here. This will be further split into a doublet by this H, which is this particular H because this is magnetically non-equivalent in nature. So, the carbon 13

essentially splits the hydrogen in the proton NMR spectrum into a doublet and that doublet is further split into a doublet by this H m, which is this doublet that you are seeing here.

So, this large coupling is the carbon 13 hydrogen coupling, 1 bond coupling and this small coupling here that you s**ee** here is the hydrogen hydrogen coupling. That is the question we asked, can we get the coupling constraint between these 2 apparently non coupled hydrogens in a molecule like this? Yes, it is possible if you look at the carbon 13 satellite spectrum. Please remember, carbon 13 satellite spectrum is actually a proton spectrum of the carbon 13 isotopomer of the sample that you have. So, what happens to this hydrogen now, this is away from 1 carbon away from the carbon 13 so, that coupling we will be much less of the order of tens of hertz. So, that is split into a doublet here and it is further split by this hydrogen into a doublet. So, again you will see a doublet of a doublet. What you will see is a essentially a symmetrical pattern on either side with respect to the singlet which should have appeared in the system. The actually experimental spectrum is shown in next slide.

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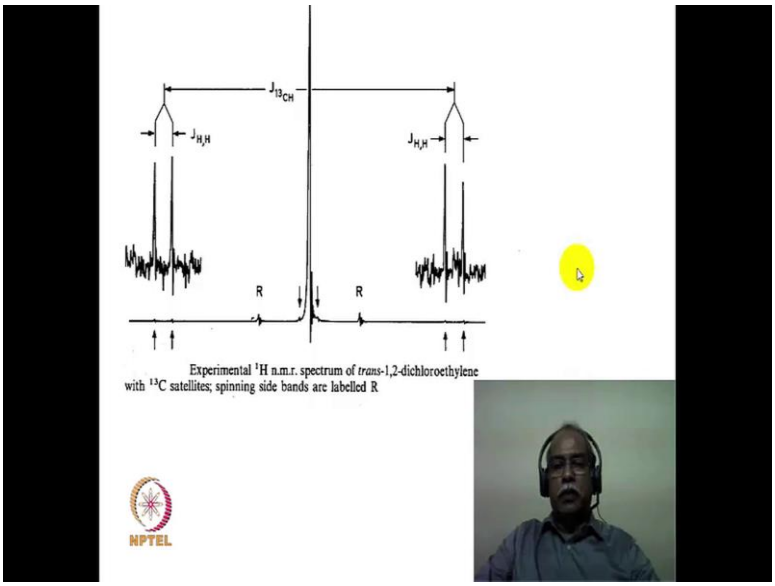

This is a spectrum of carbon 13 satellite spectrum of the 1, 2-dichloroethylene. So, this huge peak that you see in the middle is actually because of the 99 percentage of the

carbon 12 isotopomer of dichloroethylene. There is no splitting, so it just appears as a singlet. These 2 tiny lines that you see here which is expended, zoomed into the bigger picture that is seen here, indicated by the arrow there are 2 lines here and 2 lines here which are expanded and shown as an expansion here. And, this is essentially because of the carbon 13 splitting of this line into a doublet, which is further split by the hydrogen, which is these particular hydrogens are splitting each other for example. So, the J value between these 2 hydrogens are essentially gap either here or the gap between these 2 lines here. So, it is possible to get the J value of apparently non-coupled system, if you look carefully into the carbon 13 isotopomers spectrum of the corresponding molecule.

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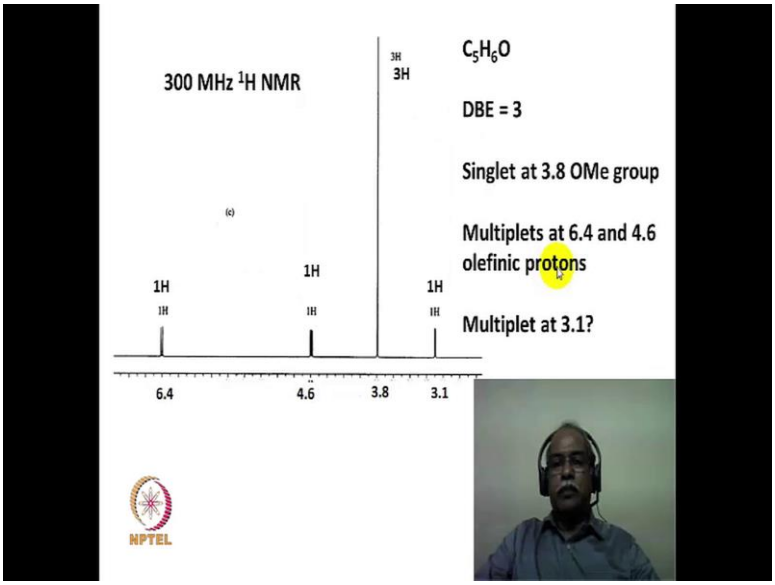

Now, let us solve a problem, a chemical structural problem here. We will try to identify the chemical shift value, J value the purpose of this exercise is essentially to familiarize with the logical way of deducing the structure of an organic compound form the molecular formula and the spectral pattern that is given here. From the molecular formula, one comes to the conclusion that double bond equivalence of this compound is about 3. Now, there is a singlet at 3.8 PPM of 3 hydrogen intensity. So, one can assume because of the presence of oxygen this to be a Methoxy functional group. Now, the multiplet at 6.4 and 4.6 we will see what kind of multipet it is next slide. For the time being assume that this is 1 multiplet and this is another multiplet, these comes in the

olefinic region. So, you have a olefinic proton, 2 olefinic protons. So, you have C 2 H 2 fragment in this particular a moitty and you have a OCH 3 fragment if this moitty. If we subtract this CH C 2 H 2 and the OCH 3 from the molecular formula, what is left with this is C 2 H. Now, you have to have double bond equivalence of 3, you have accounted for 1 olefinic bond here corresponding to a double equivalence of one. So, you have to now account for 2 more double bond equivalence. That is were this multiplet comes into picture.

What is this multiplet at 3.1? Can it be due to an acetylene because, acetylene's typically come in the region between 2 to 3. So, typically an acetylenic hydrogen can actually come in this particular region. So, if you assume this to be an acetylenic hydrogen the C 2 H fragment which is remaining after separating these 2 fragments from the molecular formula would satisfy the double bond equivalence of this particular system. So, it is possible that this molecule has a triple bonded structure. A double bonded structure connect to a methoxy functional group.

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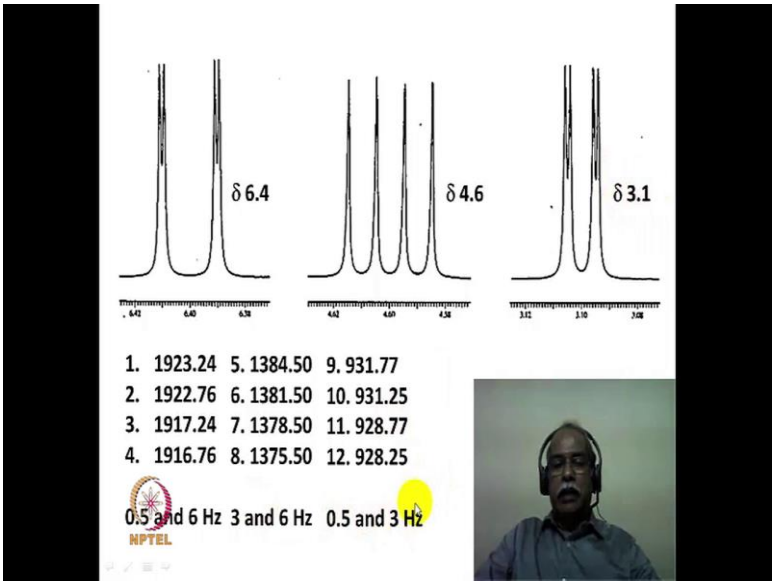

So, the multiplets that you see here or expanded and the expansion is what is shown here, there is a multiplet at 6.4 PPM, there is another multiplet at 4.6 PPM, there is another multiplet at 3.1 PPM all these 3 multiplets are essentially doublets of doublets as you can

see here. 6.4 PPM doublet of a doublet, 4.6 PPM doublet of a doublet, 3.1 PPM doublet of a doublet. In other words, these 3 hydrogens are mutually coupled to each other that is what it means. For the sake of clarity, the frequencies of these lines are also given here line 1 2 3 4 corresponds to the 4 lines of the 6.4 PPM chemical shift multiplet and lines 5 to 8 serial number corresponds to these 4 lines, lines 9 to 10 corresponds to these 4 lines or so. So, if you want to calculate the coupling constant value from this multiplets. what I have done is calculated the coupling constant value, you subtract line 2 from line 1, you get 0.5 hertz, 0.48 or something you get for the coupling constant. Similarly, you subtract 3 from 4 then also get the same value. So, one of the coupling constant is roughly 0.5 PPM or so.

Now, you take the mid portion of the between 1 and 2 you take the middle, the center point of 1 and 2 which would be something like 19, 22.5 or so, this would be 19, 16.5 or so. That is the average of 3 and 4 and a average of 1 and 2 and take the average of the average that would correspond to something like 6 hertz in this spectrum. Likewise, you can calculate the gap between these 2 lines here, that would correspond to something like 6 hertz and you can calculate the gap between these 2 lines here, that would correspond to something likes, sorry this would correspond to 3 hertz and this would correspond to something like 6 hertz or so and finally, if you calculate the mid point of this to the mid point of this that is about 6 hertz. So, you have 3 different types of coupling constant 1 set is coming from the doublet of a doublet here, as 0.5 and 6. Another set is coming from the doublet of a doublet at 4.6, coming as 3 and 6 hertz of coupling constant. The third one is coming around 3.1 delta value multiplet as coupling constant 0.5 and 3 hertz values.

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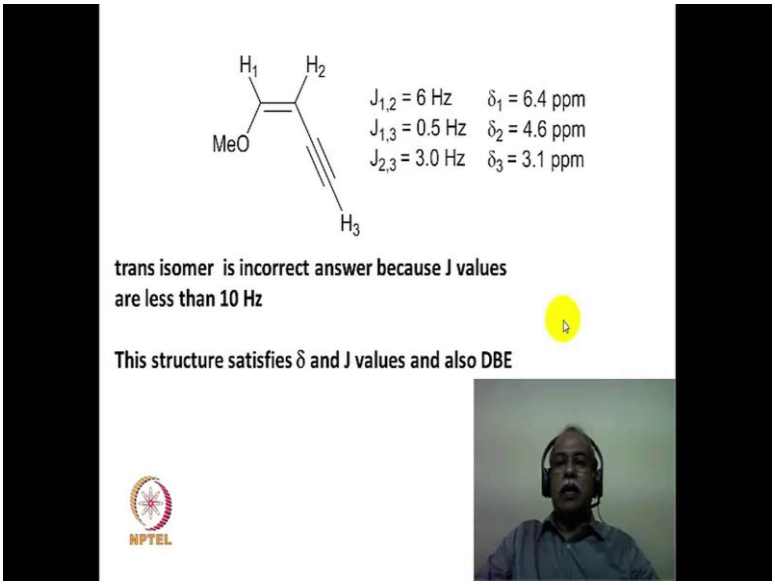

The structure of the compound is satisfied, the data is satisfied by the structure of this particular compound namely the cis isomer of the methoxy butanone. This is methoxy butanone because we have 1 methoxy peak in the NMR spectrum which corresponds to the singlet around 3.8 and then you have a olefin hydrogen. There are 2 olefin hydrogen and 1 acetylene hydrogen. If you put all this fragments together this is a kind of structure that one can come up with.

Now, what are the coupling that constants we have measured? We have put specifically the cis isomer because there are no couplings greater than 10 hertz in the coupling partners that you have here. The coupling constants are 6, 3 and 0.5 only nothing is more than 10 hertz coupling, so it cannot be the trans isomer. So, H 1 H 2 corresponds to the a vicinal coupling of about 6 hertz and H 1 H 3, which is the 1 2 3 4 5 bond coupling. So, very small coupling of a about 0.5 and 2 and 3 which is about 1 2 3 4 bond coupling is about 3 hertz or so in this particular case.

Now, the chemical shift values of this 2 olefin hydrogen's if you look at, the loan pair of electron of the methoxy and the delocalized on to this carbon. This like a enol ether, in the case of enol ether's the beta carbon is always a electron rich and as a result of that, that particular hydrogen is going to be coming at a shielded region, much lower delta

value compare to the alpha hydrogen of the enol ether. So, we put the H 1 at the highest delta value of 6.4 because it is attached directly the oxygen bearing carbon and beta position is a electron rich in nature because of the delocalization. So, that is highly shielded 4.6 PPM or so.

Finally, the acetylenic hydrogen which is the most shielded comes around 3.1. The trans isomer is incorrect answer because the J value is not, J values are less than 10 hertz. The structure satisfies in terms of delta value as well as the J value as well as the double bond equivalence of this compound. So, this give you an illustration of how to extract the information of chemical shift values and coupling constant values and logically solve the structure of this simple molecule of this kind.

Thank you, thank you very much.