Principles and Applications of NMR spectroscopy
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Module 3
Lecture No 15

We will continue now with the analysis of 1 D spectrum. So in the last class we saw that what are the different steps, which are required to be used for measuring NMR interpreting NMR spectrum. So this is what is shown here.

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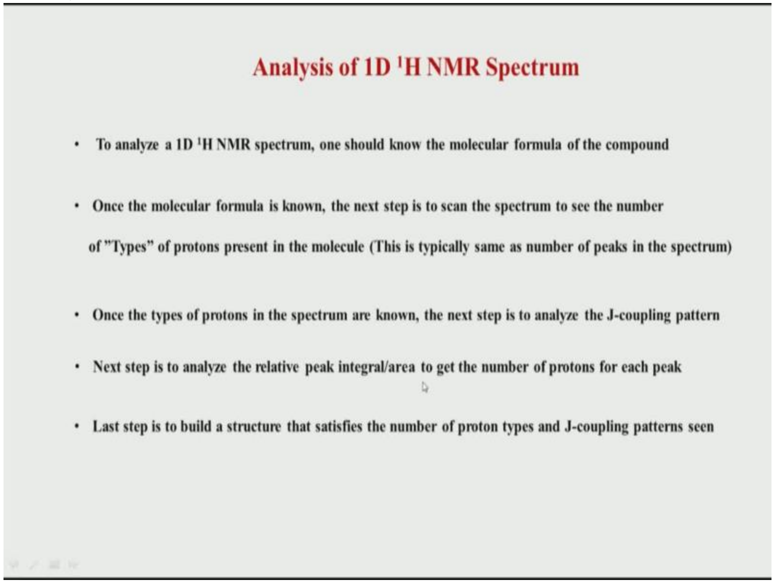

Analysis of 1D ^1H NMR Spectrum

- To analyze a 1D ^1H NMR spectrum, one should know the molecular formula of the compound
- Once the molecular formula is known, the next step is to scan the spectrum to see the number of "Types" of protons present in the molecule (This is typically same as number of peaks in the spectrum)
- Once the types of protons in the spectrum are known, the next step is to analyze the J-coupling pattern
- Next step is to analyze the relative peak integral/area to get the number of protons for each peak
- Last step is to build a structure that satisfies the number of proton types and J-coupling patterns seen

So we basically saw that we have to look at not only the, we should first of all, we should of course know the molecular formula. Then we should know the types of protons. We should know the J coupling pattern and relative intensity of peak area and when we take all of this together we can now get the total structure of the molecule based on the satisfies the number of proton types. So that means our target here is that if you know the molecular formula to know the number of hydrogens and that number of hydrogens that protons should match in the final structure which you predict from based on spectrum.

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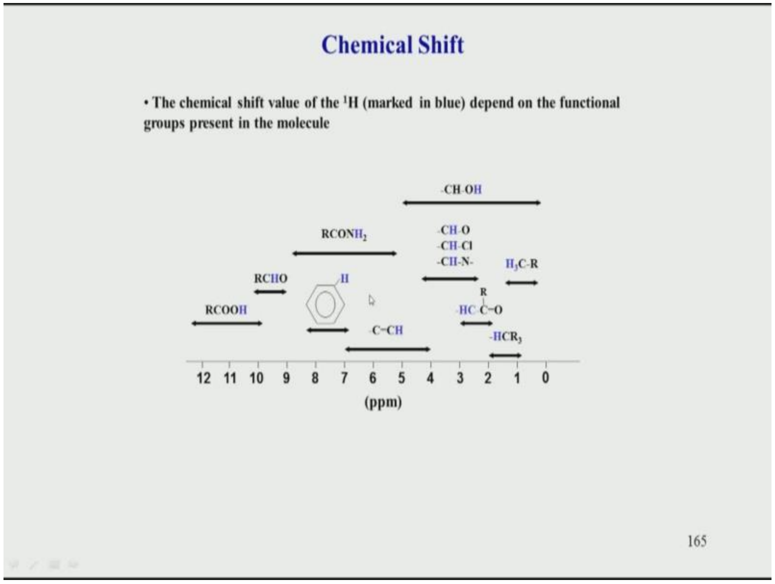

Chemical Shift

- The chemical shift value of the ^1H (marked in blue) depend on the functional groups present in the molecule

So typically it is good to have a knowledge of where the different chemical shifts come. So this is just a schematic rough diagram for a few set of function groups. So you can see here the different function groups are very characteristic ranges of chemical shifts. And they always come in that particular range. So very, very very rarely they will come out of these range. So if you know this particular range in your is mind then it is very easy looking at the peaks mole, peak of the declared molecule we can figure out what are the function groups present.

Although may be not always required this particular values to know by heart but it is good to have a some kind of picture in mind. That where the different function groups come s a o that when you analyze a data you know? You can get a fair idea of the structure. For example let us look at this one, the methyl groups, you see this is a methyl proton. Typically, the methyl protons always come between zero to two. Very unless they are of course attached to electro negative atom, which we will see.

But if they are not attach to select to negative atom they are in aliphatic part, so you see suppose this RECH 2. So the CH3CH2 this CH3 will almost always come somewhere between 0 to 2 ppm. So methyl groups are very easy to find out from NMR spectrum. Thus they are very strong peaks. They are stimulates or multiplets or they are very strong peaks. and therefore they are all they are because of these three equivalent hydrogens, the area of the peak is also very high.

It is usually the tallest peaks in the NMR spectrum is typically come from methyl groups, in a molecule. then now if you go the methyl substituted for example if these are secondary carbon are tertiary carbon then there is a slight down field shift to the proton. But even then with a tertiary or a secondary carbon group thus hydrogen atom comes somewhere between 1 to 2 ppm. Now once you start attaching electro negative groups. So for example let us say we have a ketone. If you (())(3:14) see carbonyl group and to that there is a C H and this H now gets slightly down field shifted.

So remember the word down field means toward the left, up field means toward the right. So it gets slightly down shifted and you see now it comes somewhere in this particular range between 2 to 3 ppm. So this is for typically for a ketone group and attached to this hydrogen, carbon attached to a ketone group. Now if you look at now more electro negative atoms such as oxygen, carbon halides, halogens or nitrogens you see the C H, the hydrogens they are not directly attached to oxygen but they are attached to a carbon and the carbon is attached to oxygen.

So there is a inductive effect of this oxygen on this hydrogen and that makes it go down field because of this is oxygen, chlorine and nitrogen they are more electronegative in nature. So that will cause a down field shift and this hydrogen comes somewhere between 2 to 4 ppm. So this is a typically the range observed. So what happen is, you know typically if you look at any peak as we go further we will see this kind of peaks.

Whenever there is an oxygen attached to a carbon immediately this hydrogen comes somewhere around 4 ppm. So you should that keep in mind that some peak which is coming around 4 ppm, 3.5 to 4.5 typically comes because if there is oxygen and oxygen attached to carbon and this hydrogen is attached to that particular carbon. So an hydrogen attached to a carbon which is in turn attached to oxygen typically comes somewhere around 4, 4ppm.

For example let us say, you have methyl group also attached with oxygen. Suppose this is an O like an ether an example which we will you see now in next few slide. In that situation also this methyl will not come here but it will get down field shifted and it will come somewhere here. That is because this R is now in oxygen group and that pulls electron toward itself and this hydrogens becomes deshielded. Now if you go to the double bond SP2 the ethylene, ethane group you can see their again there is a down field shift.

Remember we discussed this that the SP2 the hybridization state of the carbon is influence in factor in chemical shifts. So because of that now it is hydrogen now becomes. More down field shifted and it come somewhere between in this particular is broad range of chemical shifts. When it comes to now the amides this is very a typical in the case of many organic pharmaceutical com.s or in the case of peptides, in proteins you have amide functional groups and they always come from somewhere 5 to 9 ppm.

And this depends very much on the ph value. Similarly if you look at this here, this is an hydroxyl proton you see the range goes all the way from 0 to 5 and that is because it is very strongly dependent on the ph and the solvent. If is an hydrogen bond with the solvent it go down field shift. If not it will be up field shifted and similarly based on the ph. Similarly here CONH2 have a hydrogen bond possibility with solvent and because of that they have a wide range of chemical shifts possible.

But remember again they are typically in this range. So you will rarely see them, this particular hydrogen in amide coming somewhere here in the methyl. So that will not happen. Similarly this OH group will not show up in this side. It will be somewhere in this range. Typically, the OH groups, you will see in that particular 3 to 5 ppm.

Now coming to the aromatic. So very typical aromatic functional chemical shift range. So for any aromatic functional group it is very easy to recognize an aromatic groups based on the peaks which come here. So very rarely very rare many not function groups show peaks in this region, except the amides. But if you know there is no amide in your molecules then you can be fairly sure that the any peaks you get in this range region is coming from aromatic peaks aromatic groups.

And aromatic groups also have a very peculiar peaks splitting because they have a lot of long range coupling compared to aliphatics. So therefore the peak multiplet structure is will also looks different or little complicated compare to aliphatic. And there are also effect like strong coupling and So on. So mainly what happens typically you can do is you want to just simply identify that here is an aromatic region you just, you have to looks for peaks, in this particular range of course that given that, if you know there is no amides.

Now the aldehydes and carboxylic acid proton are very, very down field shifted and that is again very easy to find them out. and this is an again remember we saw this magnetic anisotropic concept and we saw that hydrogen comes in the deshielded region and of a in aldehyde group. And that because of that this shift very much downfield away from all the other hydrogens around 9 to 2 ppm very characteristic and carboxylic acid hydrogens again very characteristically come around 11 ppm, 10 to 12 ppm.

So this kind of a idea about different functional groups where they occurs is very useful in use just to keep in mind. We have not exhaustively look at all the possibilities. these are just simple broad ranges for majority of the function groups uh which is typically in seen in an organic com.. But for a more detailed analysis or more detailed values for each and every functional possibility you have to go you can refer to Pavia spectroscopy like Pavia.

Similarly, by Horst Friebolin and they have exhaustly, they have of tables of chemical shift for a wide range of functional and substitutions. But for our course for basic analysis interpretation we will only will looking at this set of functional group.

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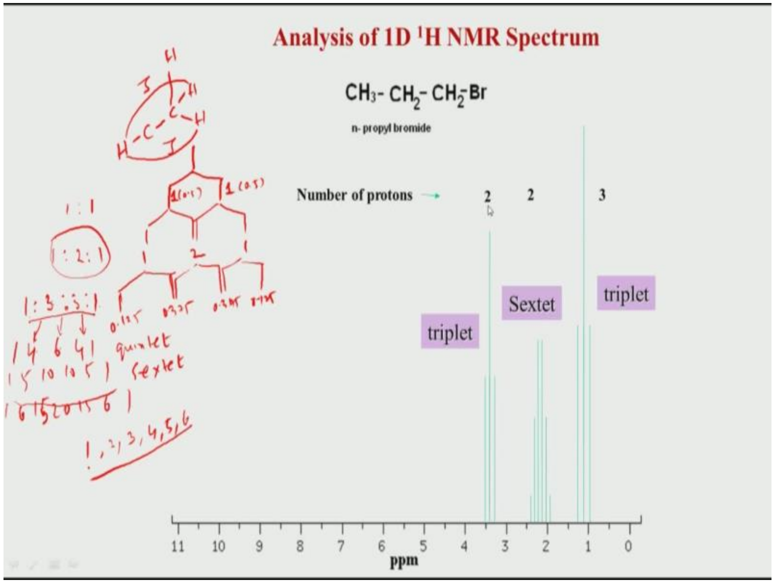

Analysis of 1D ^{1}H NMR Spectrum

$CH_3-CH_2-CH_2-Br$

n- propyl bromide

Number of protons → 2 2 3

So now let us start looking at analyzing the spectrum. So what we are going to do in todays class is only look at a few examples, examples of molecules where we gain, we know the structure. But now our thing, idea is to figure out that this structure how do we interpret the spectrum? So which hydrogens correspond to which peak and so on So forth. So the first thing as I said we should know the rough molecular formula, again remember this is a structural formula, we do not need to know this.

If I just know there are three carbons six, seven hydrogens that is enough. But that is what we will take up in the next class. But in this class we will see now that the given a structure how do we interpret the data? So this is a spectrum typically again this is schematic drawing. This is not a real experimental spectrum but close to experimental spectrum and in terms of the value and peak multiplet. But this is very good enough for us to get an understanding.

So now if you see here we are seeing remember the first step is to figure out how many types of proton are there. So that was the step number one and in step number one here, we see there are three types of proton. Because these three peaks are basically one peak, this is only J multiplet,which we look at the next step. But first this is one particular, this is one peak. This is this bunch of peaks is one peak. Because these are all coming from J multiplet.

But overall the peak is coming from one hydrogen type and similarly this is another hydrogen type. So there are three types of hydrogens in this molecule which is consistent with this molecular formula. So here you see we know that there should be three types and therefore that is what we see here. Now you can see that because of this effect shielding now what is happening is that this bromine, which is electro negative, will pull away the electron density from here.

So this hydrogen will be the most deshielded hydrogen atom and we have seen in the inductive effect concept where we saw the effects of chemical induction, inductive effect of chemical shift. So you see this will be the most deshielded. This will be the next in the line and a little bit more shielded, deshielded as compare to this and this is a least deshielded right. So because this is farthest away from bromine. So you do not expect much shielding here.

So you see now based on this idea, I can directly in fact right away say, that this particular peak which is the most deshielded should corresponds to this. This is which is intermediate should correspond to this and this is the most shielded, is corresponds to this. So in this particular example yes, it is possible to do that. But we will not take that approach. We will look at more detail, how this multiplets can be analyzed. So first thing we have seen there are three types of hydrogens.

Now the next thing we will see it, the multiplet structure. So you see what is happening here, we have a triplet, we have sextet means six peaks and we have a triplet again. So now for here, we have to keep in mind that we have to look at the Pascual's triangle. So will see that here now in the will derived the Pascal's triangle. So we saw that if you have a peak, if you have, if you have a one proton one hydrogen attached to a carbon, which is attached to two hydrogen, another hydrogen so then it will give me a doublet right.

So this is . five, that is one is to one. That is . five is to . five. I mean but the relative ratio is one is one. Now if I have another hydrogen here then each one will get further split and because the J value is same this is this J value is suppose same as this J value. Because with as they are same, you will end up with the a triplet that is one is to two is to one. That is what we saw in Pascal's triangle.

Now let us say you put one more hydrogen here. So you will end up with further splitting. So two So this will be 0 . 125,0 . 375, 0 . 375,0 . 125. So this is coming from the Pascal's traingle which we saw. So that becomes one is to three is to three is to one. That means, if I see a quartet in my molecule. This is triplet, if I see a triplet in my spectrum, where is you see in this particular case we are saying in two, two triplet here which means this particular hydrogen which I am looking at is attached to two hydrogens.

I mean coupled to two hydrogens. Therefore that particular hydrogen is getting a triplet. And if you see a quartet it means that particular hydrogens what we are seeing is coupled to three hydrogens. So therefore that hydrogens has becomes tripco quartet. Now we can continue this further. So you will see the next step, you will get as one four six four one for a quintet. And if you consider continue this Pascal's triangle further you will get 1,5,10,10,5,1. So this is six peaks this is called a sextet.

You can also get seven peaks, if you have 1, 6, 16, 20 sorry 15,15 6,1. So you see what we are you should look at this picture now, what we are trying to see here is one to one when I have, I can simply add 1 + 2 and I get 3. Similarly, this 1 + 2 I get 3. So what you do is one simple way to remember how to generate Pascal's triangle is simply write one at the both the corners and in the middle, you take one step before and add up those numbers.

So for example I will put one and one on this side take 1 + 2 which is 3, 1 + 2 which is 3. So I get one is to three is to three is to one. Now you look at this step, again I put one at the adjust then I add this two I get four, add this two I get six, I this one gives me six, this one means give me four, this one gives me four and I get one is to four is to six is to one. So in this manner, you can actually So in this manner, you can actually calculate this Pascal's triangle as long as you want.

Typically the sextets the six peaks or seven peaks this is max you will net to go. Because beyond that the number of proton goes up very high and that may not be possible in a structure. So one should basically try to remember workout what you get for a coupling to one hydrogen two hydrogen one is doublet, two is triplet, three is quartet. If it is coupled to four it is quintet. So I + N + rule up to about six proton. This is usually the maximum you will need to go about.

So let us come back to this molecule here. Now here you can say that this is a triplet. this is triplet because this is coming from ok. So before we go this, as I said the next step was to look at the integration. So from the integration it turns out that this particular peak is three peak what you are seeing here contains two hydrogens. This particular sextet contains two hydrogens.

Remember sextet does not mean six hydrogen, it means only the multiplet. But the total area under this peak is may be corresponding to two hydrogen and this turns out to be three. So when we now two is to two is to three. So one of the rule of thumb simple way is that whenever you see a three, it has to be particularly typically a methyl. Because a carbon cannot be attached to more than three hydrogens.

If it is attached to four it becomes a methane. Which is not what will see in organic com., it will typically have methyl is the maximum. So three when you see automatically it is basically a methyl group. So that is what also we expect from the structure and there is a methyl here. So now there this methyl could be this and also if you look at the chemical shift value it is coming in the range, which we saw in the last slide.

It is in the range of the zero to two. That is typically for a methyl. So you see directly we can now identify a methyl peak here in this spectrum and that methyl peak is coming corresponding to this. And it is showing a triplet and triplet is showing because this hydrogen is coupled to this two hydrogens. So if you apply the N + 1 rule this methyl is therefore is expected to be a triplet.

Now we can go to the next mole hydrogen which is two here. and that is coupled now to this side three and this side two and if you assume that these couplings are same then typically it will be the same if is a linear molecule and in the organic com.. So if you see three and two is five. So 5 + 1 the N pulse one rule says, I should expect the six peaks, that is sextet. That is what you seen here.

You see you get six peaks here. Therefore and that six peak if you look at the relative ratio, it is coming out to be in this manner. That is one this is if you consider small peak as one. This roughly five times one is to five 10,10,5,1. So one is to five to two times five one. This is what we saw here in this case. So this is what happens for a six peaks multiplet J coupling. So that is what is coming from here.

Now if you go to next CH2, which is a most down field shifted. Now that CH2 is only coupled to this hydrogen these two hydrogen. So N + 1 rule says, that for this hydrogen this two together this is equivalent. I would expect triplet and that is what you see here and the area corresponds to two protons and that is what is two, there are two hydrogens. So in this manner this correspondence we can now establish between this molecule and this specter spectrum by considering all these factors.

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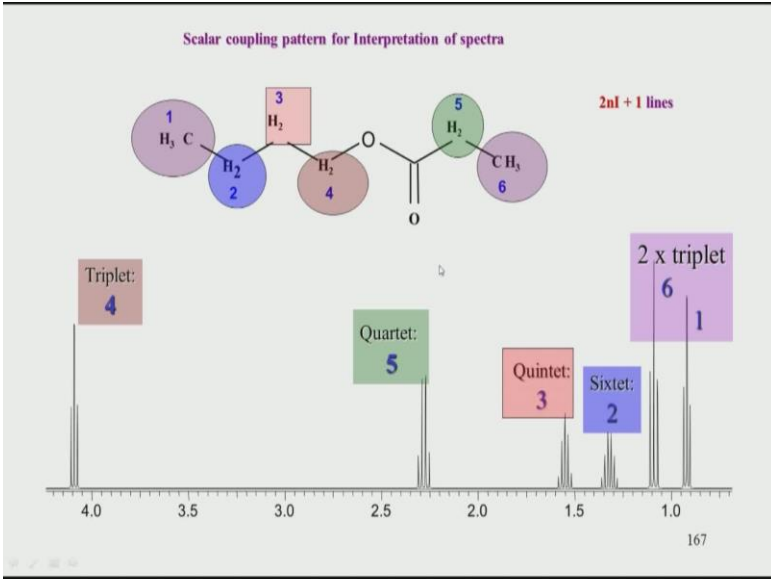

Scalar coupling pattern for Interpretation of spectra

2nI + 1 lines

Now let us look at another example, this is what is shown here. Now let us look at another example let us say we have this particular molecule. there we have a long chain but if you see here there is in center there is an ester group. Now what happens is because of this ester group this side of the hydrogens are not interacting or coupled to this side. So you can think of this ester group like a river in in a in a village, one side of the village is disconnected from the other side for the village because of the intermediate functional group.

So this is what basically is happening here. These two hydrogens will not be coupled to this side. But of course within them they are coupled to each other by J coupling. And this two are coupled by each other by J coupling. So now let us analyze the spectrum of this molecule how it looks? So this is what a spectrum shown below. Here we are showing only from 0 to 5 ppm. Because that is where all the peak are coming. So now if you look at this count the number of peaks here. Remember the first step is to see the number of proton. So you see now 1,2,3,4,5,6 and here also number are given there are six. There are six types of hydrogen and six types of peaks we are seeing here.

Six peaks we are getting here. Now we can look at the multiplet pattern. Next step the multiplet pattern is showing that there is a triplet, there two triplets here. Remember again the chemical shifts they are coming somewhere between zero to one. Therefore immediately you should consider that there are these are coming from methyl ok. But of course relative integration we are not showing here this in this particular slide.

But this triplet, remember triplet and methyl one should not confused. Triplet is something else and methyl is something else. A triplet coming because of the neighboring hydrogen and not because methyl has three hydrogen. So methyl having three hydrogen is different. That is that is reflected in the intensity of the peak. Whereas having a triplet or a quartet etcetera that depends on the neighboring hydrogen.

So in this particular two hydro this methyl group you see what happen I there is a two hydrogens here. So therefore each of this methyl this side and this methyl both of them have two hydrogens coupling I mean the methyl hydrogen is to coupled to two. So according to N + 1 rule each of this methyl shows and gives me here a triplet and both the triplet comes somewhere here. Because they are not attached any electronegative group. So therefore they come in the original 0 to 2 ppm range.

Now if you look this particular peak here sextet. Because it now having 4,2,3,5 peaks, So 5 + 1 6 rule. So this is basically a sextet. Similarly if you look at the quintet here this particular hydrogen is having basically 2 + 2 peaks here. So two hydrogens here, two hydrogen this side. So this hydrogen is coupled to four, So 4 + 1rule is a quintet. So this is what you get in this particular state ok.

Now these numbers are the integrations. So basically sorry this is not the integration. This is indicating the hydro the atom number. So this is number three here. So now if you look at this particular this hydrogen now it is coupled only the two hydrogens on this side, there is nothing on this side. So obviously therefore you will expect N + 1, 3 peaks that is what you get is three peaks here ok.

Now if you look at this value of chemical shifts. This is coming away from all the other peaks. Why? That is because of this oxygen is here. So remember the slide where we looked at the roughly the chemical shift ranges we saw that anything is attached to oxygen comes somewhere around this 3 . 5 to 4 . 5 and therefore this is a kind of outstanding peak which is standing away from others and immediately one should then conclude that this is because this hydrogen is attached to a carbon which is attached to oxygen.

So there is a slight typo here. This there is a carbon which is attached to ox hydrogen. So keep that in mind, there is carbon which is attached to hydrogen. That carbon is attached to oxygen. And therefore that is hydrogen comes way down field at around 4 ppm. Now the remaining hydrogen is this. Now this is also attached to electro negative. But this is a carbonyl, this is not directly attached this carbon here, which is not shown.

But there is carbon here and that is not attached to directly to oxygen unlike here attached to carbonyl group. And therefore this come somewhere around 2 to 2 . 5 and again this is something you can see from the slide we showed previously, the rough value is somewhere here and now this shows a quartet, quartet means it has four peaks I mean multiplet one is to three is to three is to one.

And why is that quartet coming? That is because this hydrogen knows both are equivalent and these are coupled to three hydrogens of the methyl. So according to N + 1 rule you 3 + 1, 4 peak. So you expect a four multi peak multiplet structure for this particular hydrogen. So this is how the you can see the correspondence again between a particular molecule and the peak pattern or the chemical shifts we get.

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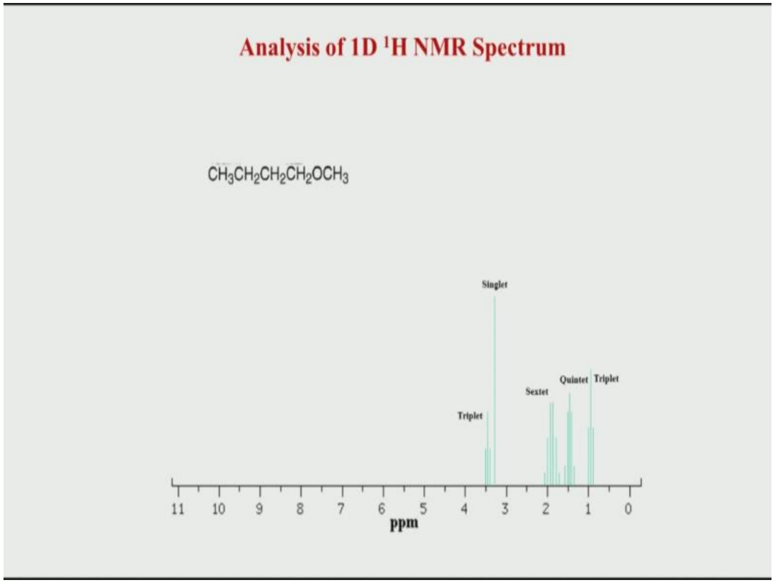

Analysis of 1D ^{1}H NMR Spectrum

$CH_3CH_2CH_2CH_2OCH_3$

We look at one more examples now, there is a last example where the this is now another long chain, long linear chain molecule. So let us again look at the same way. So you have basically that you have an NMR spectrum. So you have to count the number of protons that is number of peaks. So I get 1,2,3,4 this is all peak and the 5. So there are 5 peaks in the in the spectrum. Therefore I expect 5 different types of hydrogens and the 1,2,3,4 and 5. So you see that is figure matching with the structure, I have five hydrogen types and five peaks. Now if you analyze the multiplet structure that is a J coupling. Because sorry we are we are going to the we are not gone to the integration yet.

So if you look at the integration that part is not shown here. But what is the idea here, let us analyze the j multiplet pattern. So j multiplet pattern if you see. Let us scan from this end from the right hand toward the left, on the right you get a triplet, again remember this is coming between 0 to 2 ppm. So this most likely has to correspond to a methyl group ok this is methyl group. Now this methyl group then if it is a methyl group it is it is coupled to two hydrogens, of course value will also should match integration is three here, which is not shown.

So this three, the three protons, which show a triplet they should be attached to a CH2 and only then you can expect to get a triplet for this methyl. And that is what is shown here, So you have this this CH3 is corresponds to this peak here. Because only then it will give a triplet. Because it is attached to two protons, I mean attached in the sense coupled to two protons. So this CH3 is now this particular peak.

Now you look at this quintet, there are basically five peaks here. The five peaks basically come form where. So we have to basically look at a particular proton which is having four neighboring hydrogens, you coupled to the four neighboring hydrogens, only then you expect to get a quintet. So four hydrogen come can only be from this hydrogens. Because this is coupled to this side, with two hydrogens and this is coupled to this side with another two hydrogens.

So therefore totally it has four hydrogens coupled and So 4 + 1 gives you 5.So this particular CH2 it has to be this particular quintet. Now you come to sextet. Now sextet means six peaks and that has to now come from a hydrogen which is coupled to five protons. Only when you have five, you have 5 + 1rule, N + 1 rule, we should give you sextet. So that is this hydrogen. Because this hydrogen is now coupled to two here and three here.

So 3 + 2 is five and 5 + 1gives you six. So this particular hydrogen now is corresponding to this particular multiplet. Now look this singlet, which is at all peak and again integration would have revealed that. But integration is three and that means there is a methyl group. But why is a methyl group coming at 3 ppm? That is because this is this methyl group when it is attached to oxygen C H attached directly to the oxygen.

And because this CH3 methaoxy group is ether comes very down field shifted here relative to other methyls and is coming around 3 . 2 ppm 3 . 3. Now if you look at the last peak, which is a triplet is has to be from the remaining CH2. We already looked at all the other peaks remaining is this. You can see this CH2 is coupled to this two. And that will give you N + 1 three peaks. Remember because of this oxygen here, this hydrogen and this hydrogen are not coupled because they are far away.

So therefore this hydrogen is only coupled to this side two hydrogens N + 1 says triplet three peaks and it coming again down field shifted means it is coming below 3, 3 . 5 that is because of direct attachment to an oxygen. So therefore this is coming down field shifted. And that is where we saw that comes (())(27:59) 3 . 5 to 4 . 5, if there is direct attachment to an oxygen group ok.

So this is basically we saw now three examples in this class, how we can analyze this peak pattern, the multiplet, the integration and so on but remember you always had the molecular formula already with the structural formula and we have basically tried to do one to one mapping. We looked at the correspondence between the spectrum and the molecule but this is a fortunate case, where you already know the structure.

But many a times the problem in hand is that is we do not know the structure, we only know the formula, we know how many carbons, we know how many hydrogens, roughly we know the total composition. not the exact structure molecular formula but we know the, the composition of that and based on that our job will be to deduce the structure, molecular structure given the spectrum, given the integration, given the chemical shift values and so on.

So that is what something we will analyze in the next class. We look at few examples, where we will not have the structure in hand. We only have the, just the overall composition of the molecule, how many hydrogens carbon and then we will based on that we will go to the NMR spectrum. We will look at the multiplet structure, we will look at the integration and we will look at the chemical shift value, which is also useful a times and we will look at the number types of hydrogens and based on that we will try to deduce the structure.

And that is basically the most of the time organic chemistry requires is that given that we do not know the, what structure com. we have synthesized we want to know whether our whatever spectrum you get from a there can we deduced the structure. But some times of course to know what you are expecting to get. When we make a organic chemistry reaction we already know the end product. So therefore in that situation you already know what to expect.

So you basically try to then try to figure out, which peaks correspondence to which carbon or hydrogen. But if you extract an organic com. let us say from natural sources then we do not know anything about the structure all in have that is only the number of elemental analysis. Elemental analysis basically gives you carbon, hydrogen, oxygen and mass spectrum of course you will have with you. You may have the I R spectrum. But now for nows what will do is in the next class we only focus on hydrogen NMR spectrum and based on that we will try to deduce the structure.