# Principles and Applications of NMR spectroscopy

**Professor Hanudatta S. Atreya**
**NMR Research Centre**
**Indian Institute of Science Bangalore**
**Module 4**
**Lecture No 20**

In the last class, we saw how the carbon chemical shifts in one dimensional carbon NMR can be calculated predicted based on the structures. We looked at a few examples, given some rules, these are all empirical rules and how we calculate. Similarly we had seen this also for protons few classes ago.

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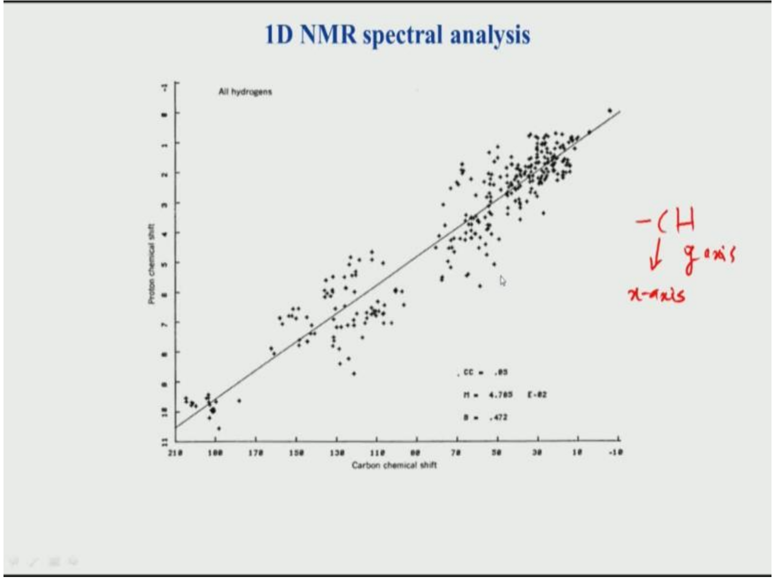

1D NMR spectral analysis

So if you now look at this slide what this slide is depicting is a very interesting thing and the thing is in chemical shifts if you see on the x-axis is carbon chemical shifts and on the y-axis is hydrogen Proton chemical shifts. So for a given CH carbon hydrogen pair is plotted here. So for example if a Proton has a chemical shift close to 0 this carbon is around - 10. Similarly if some particular this is again from a large number of molecules large number of CH chemical shifts this has been taken. This is a plot again from one of the research articles.

What it says is that that whenever you have a carbon proton pair. So we are basically looking at this kind of a system, so we are looking at a CH pair. So this is a H is on the x-axis y-axis what is plotted and for the same hydrogen carbon this is plotted on the x-axis. Ok? So this is for a particular pair. So we take a large number of such pairs from large number of molecules and is plotted shown plot is shown here. What it says is that if the for a given CH moity like this if the hydrogen chemical shift goes upfield, upfield means towards upward side, the carbon chemical shift is also upfield towards the 0 side.

Similar if carbon chemical shift goes down which happens typically in the case of aromatics you see aromatic comes downfield, down means downfield shifted. The hydrogen for the aromatics is also we know comes around 7 to 8. So that is also downfield shifted. So that means carbon and hydrogen chemical shifts in CH moity are correlated. They have a positive correlation. So this is interesting thing which was discovered sometime long time back.

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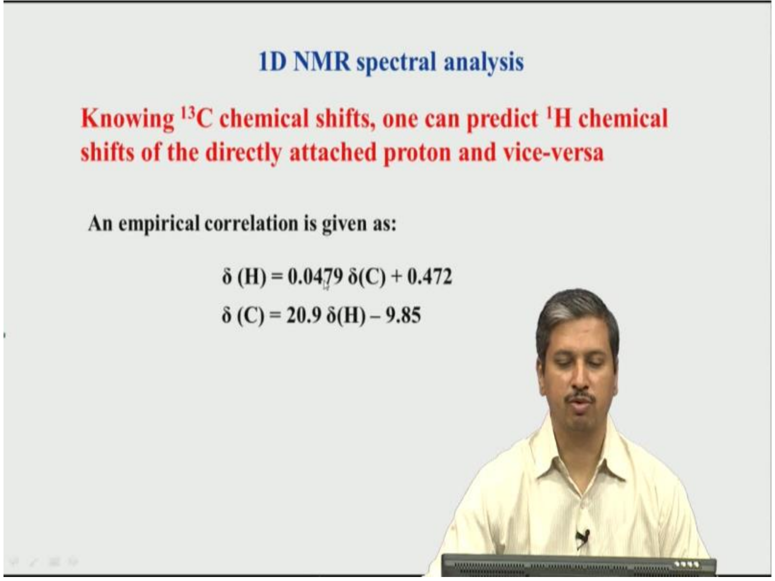

1D NMR spectral analysis

Knowing $^{13}$C chemical shifts, one can predict $^{1}$H chemical shifts of the directly attached proton and vice-versa

An empirical correlation is given as:

$$\delta(H) = 0.0479\,\delta(C) + 0.472$$

$$\delta(C) = 20.9\,\delta(H) - 9.85$$

And in fact there is a formula which we will show in the next slide which says that if you know the hydrogen chemical shift from 1D NMR you can approximately calculate the carbon chemical shifts of the CH system by using this formula. So you just have to take that, sorry, if you know the carbon chemical shifts, you multiply the carbon chemical shift with this and then you get the Hydrogen chemical shift of a given CH pair. Similarly if you know the proton chemical shifts, you can multiply the proton chemical shifts into this value and subtract 9.85, you get the carbon.

For example let us take methyl system, in a methyl, let us say you have a chemical shift which is around 1 ppm, so remember chemical shifts of methyl, hydrogens they come somewhere between 0 to 2 ppm. So let us say we have a system where we get 1 ppm as a chemical shift of a methyl proton, I multiply 1 into 20.9 - 9.85, will give me roughly 10 that means this carbon, of that methyl carbon will be 10 ppm, roughly. Similarly for hydrogen, let us say we take aromatic system, so aromatic we know comes typically somewhere around 140 ppm, if you multiply this 140 with this and actually you do the math, it will come somewhere around 7 ppm.

So you see that hydrogen for aromatics we know, comes somewhere around 7 ppm and this is what is basically coming out of this, that was between 7 to 8, let us say 7.5 ppm. So the carbon will be around 140 ppm. So this a very interesting correlation, an empirical correlation which was discovered that whenever a proton-chemical shift increases, the carbon chemical shift also increases and this will be of some relevance when we come to 2D NMR, especially when we look at the hetero-nuclear NMR spectroscopy.

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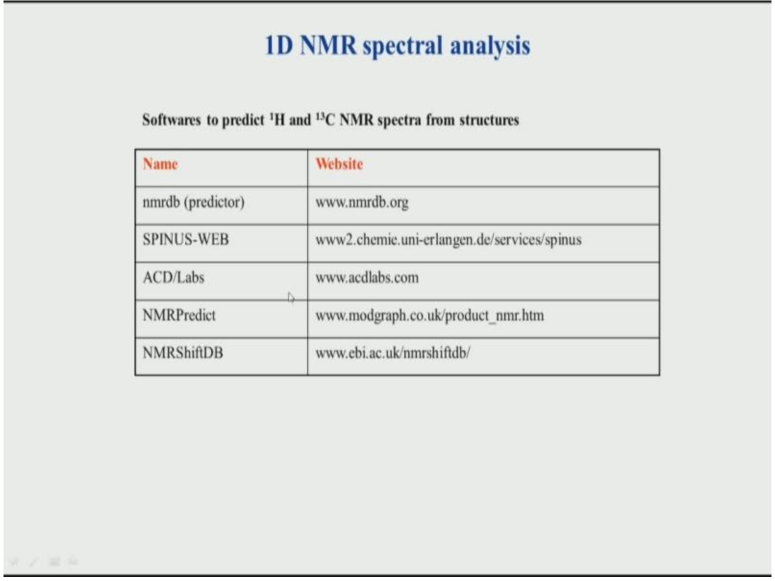

1D NMR spectral analysis

Softwares to predict $^1H$ and $^{13}C$ NMR spectra from structures

| Name | Website |
|---|---|
| nmrdb (predictor) | www.nmrdb.org |
| SPINUS-WEB | www2.chemie.uni-erlangen.de/services/spinus |
| ACD/Labs | www.acdlabs.com |
| NMRPredict | www.modgraph.co.uk/product_nmr.htm |
| NMRShiftDB | www.ebi.ac.uk/nmrshiftdb/ |

Now this slide here, we are listing some of the websites where you can actually visit, hence it will be a very good exercise for you if you can go to this website. Some of them in fact have online where you can try out that you give a structure of the molecule and it will predict the chemical shifts. So these are basically softwares to predict proton and carbon NMR chemical shifts. When we say spectrum basically it means we are trying to get the chemical shift values given the structural information.

So if you know the structure of the molecule, you feed the structure and to one of the softwares and the software will then give you the chemical shift values, what you expect and then that if you compare with your spectrum, you can now do what is called assignment. Means given a chemical shift value, a peak in a spectrum you want to find out to which carbon or proton it belongs to in the molecule. So if you know the structure, you predict the chemical shifts of hydrogen and carbon and you match it with the chemical shifts you get from the NMR spectrum.

So that is called assignment and many of this help you to do that. Some of them are free freely available, some of them are paid but overall you get a good idea from. So all these things which we worked out, in the previous slides was, basically are all implemented in these softwares.

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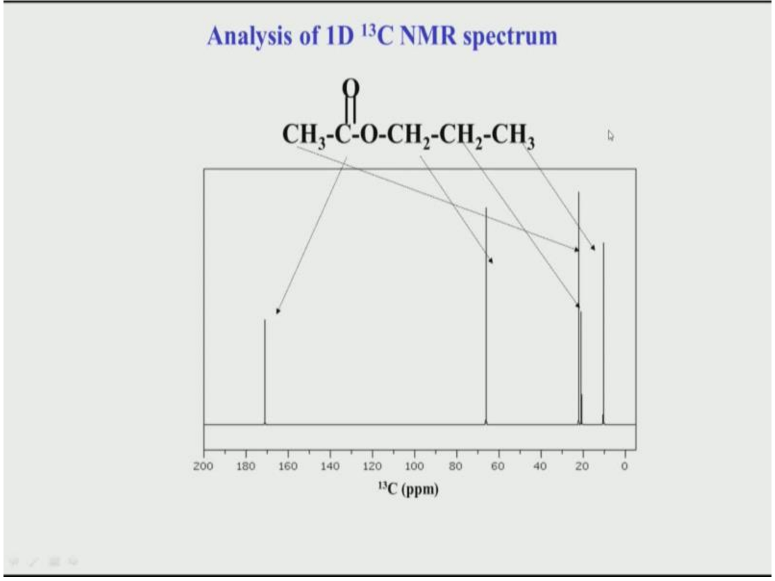

Analysis of 1D $^{13}C$ NMR spectrum

$CH_3-\overset{O}{\overset{\|}{C}}-O-CH_2-CH_2-CH_3$

So now let us continue with how we analyse the chemical shifts of carbon spectrum 1D NMR. So what we are going to do is the first approach, that given a structure can I find can I try to assign the peaks which I get in the 1D spectrum? So remember what we did last time was that given a structure, we tried to predict using some rules. But now we are not going to predict the chemical shift values, rather what we will do is, we will see the spectrum and try to figure out which peak in the spectrum corresponds to which carbon atom in this molecule.

So similar to what we did in hydrogen, that given a structure and the spectrum, we want to now assign the particular carbon to a proton. So again some recapitulating, we are basically doing three things in this proton and carbon NMR. First thing we are doing is that we are trying to predict the chemical shifts of proton or carbon using some rules which we saw, that is one thing. Second thing what we did was given a spectrum and the structure again, we want to try to figure out that based on the J-coupling, based on the chemical shift value roughly, what is the which peak will correspond to which proton or carbon.

So same thing we are going to do here and the third thing which we did, which we will do here as well, is that we looked at given only the molecular formula, we do not know the structure and we are given the molecular formula and a spectrum, we have to now find the structure. Ok? So right now what we will do is, given a spectrum, find the assignment. So this is the spectrum shown here for this particular molecule so now our now our objective is that to figure out which proton which carbon corresponds to which carbon here. So first thing if you notice in this molecule, look let us try to look at the functional group.

So here we have an ester functional group so remember for ester, if you remember the chart or if you can go back to the chart, you will see that the ester carbonyls comes somewhere between 160 to 175 and that is what we are seeing, we are seeing a peak around 170 ppm which definitely has to now correspond to this carbonyl carbon. So this carbon is coming from here. Then let us start from this corner, so this is, you see this CH 3 which is away from all the functional groups. I mean all the electronegative functional groups. So that means this will have the most a field shifted carbon because the inductive effect is the lowest. So therefore you would expect that this carbon would now correspond to a most field shifted carbon peak which is here.

So that is basically the carbonyl assignment which we just discussed and this is the CH 3 which is this peak. Now come to this CH 2, now this CH 2 is closer coming to here but this CH 3 is also coming close to this. So that means there are two peaks which are very close to each other and that means one of them is corresponds to this CH 2 this carbon and another C another peak corresponds to this carbon. Why we are saying this because the idea is that you go away from functional group, I mean the electronegative groups, your deshielding effect reduces.

So that means this is more shielded with respect to this but it is less shielded with respect to this, it is somewhere in between, in middle. Similarly this is also close to this. So therefore, this and this will come very close to each other and that is what is this happening here. So the smaller peak corresponds to this of course their chemical shift difference is very small. So obviously it is not straightforward to find out whether this tall peak is corresponding to this carbon or this tall peak corresponds to this carbon.

For that we will have to go to 2D NMR, which we will see, that is where the 2D NMR helps us but right now we will only look at 1D. So now based on these, we can say that one of them is this carbon and the other one is this carbon. So we will now tentatively or we will assign that these two are coming from those two carbons. Typically what happens is, methyls are very strong peaks in NMR. In proton also, we get the very strong peak. Similarly in carbon also we get very strong peaks.

So therefore we use typically the tall peaks are usually associated with CH 3. Now coming to the remaining peak, has to correspond to then this CH. Now why is this coming so much at 60 to 70 ppm, that is again remember this is directly attached to Oxygen. So because of the electronegative effect, the shielding it is directly influenced by this one bond, carbon-oxygen bond and therefore this CH 2 comes very much downfield shifted and it comes at 65 to 70. This is also something which we saw in the proton in the in the beginning that CO group comes somewhere between 60 to 70.

Now if you record a proton spectrum which is not shown here, we are not going to look at the hydrogen-proton spectrum right now, but that proton also remember, was coming around 4 to 5 ppm because of this oxygen electronegative. So this is how we can assign for this particular example.

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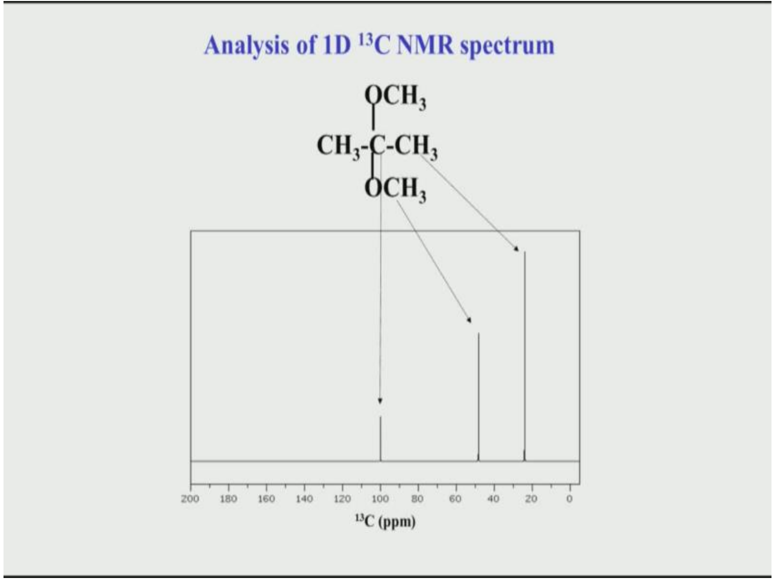

Analysis of 1D $^{13}$C NMR spectrum

Let us look at another example. This is also, remember all these molecules, we have been looking at from the proton angle. So we saw the proton spectrum earlier a few classes ago and there also we saw the same molecules. So therefore we are going to look at the same molecules again but now we are analysing the carbon spectrum rather than the proton spectrum. So let us look at the spectrum of this molecule. So what do you see?

Now let us look at how many types of carbon are there. If you see there are only two types carbons or three types rather. This is a quaternary carbon, so this is one carbon. Second is these two are symmetrical, so they will be equivalent, so they are having the same chemical shift. So this is another carbon, second type. And the third type of carbon is this, because both of them again are equally asymmetrical and they are chemically equivalent.

So there are three types of carbon, so we expect three types of peak, three peaks. Similar to what we saw in the proton, counting the number of peaks, a group of peaks in proton, a bunch. So let us say, we would call the multiplet structure as one bunch called looking at the one bunches of peaks, we saw that we can find out the number of types of hydrogens, protons.

Similarly here, by counting the number of peaks, we can find out how many types of carbon are there but we will see this rule does not always hold true because sometimes some peaks are missing, sometimes the OH peaks are broad. Similarly in carbon, we will look at aromatic cases.

There also it is sometimes not easy to count the number of peaks but roughly you can actually estimate the number carbons simply based on looking at the number of peaks.

So if I go back to the previous problems, there we had one, two, three, four, five types of carbons and here also we have one, two, three, four, and fifth, five carbons. So five carbons we got peaks, five types of carbons and five peaks. Similarly here, we have three types of carbon, we expect three peaks. So let us begin the assignment, how do we assign which peak is which carbon again we can use simple logic that whenever you have an oxygen attached to a carbon it comes somewhere around fifty, sixty ppm but remember this us OCH 3.

So therefore, the CH 3 also comes somewhere between 0 to 20 but 0 to 20 is now will not hold if there is an oxygen attached. So again if you look at that chart which was we have seen earlier it was **some** somewhere between 50 to 100 ppm is given for the OCH 2 or CH 3 and this is basically coming from there and this lone carbon is attached to 2 oxygens. So if you see this quaternary carbon is attached to 2 oxygens and therefore you expect double inductive effect and therefore it will be much more downfield shifted this carbon compared to this carbon because this is attached to only one oxygen.

So by that logic, this will become the quaternary, quaternary means C carbon and this will be the OCH 3 and then what remains that is of free shifted that is a pure methyl that is at coming at this standard value somewhere between 0 to 25 ppm and this is what is shown. So this is the exact assignment which we just discussed, One thing we can keep in mind from a practical point of view is whenever you have a quaternary carbon, a lone carbon, it is always a little lower in intensity compared to other; and why is this so?

The reason for that is, that whenever you do not have any hydrogens attached to a carbon it has a very long T1 relaxation. So whenever you have something which has a long T1 relaxation, it is not completely recovered to its original magnetisation when we apply 1D pulse. So this is something we saw earlier that you need three to five times relaxation time T1 for the relaxation delay value. So you have a long relaxation time, you need correspondingly longer relaxation delay but we do not practically is possible to do that because this may run into several tens of seconds.

So you cannot afford to wait for five times 10 seconds which is about a minute whereas this carbons may have a short relaxation time, they may have only a few seconds. So idea is to quickly capture the chemical shifts without waiting too long, but if you do not wait sufficiently long, the intensity is reduced because of the incomplete relaxation, T1 relaxation and that is why the peak intensity of this quaternary carbons usually are very weak. We will see also this in case of aromatic systems, aromatic quaternary carbons.

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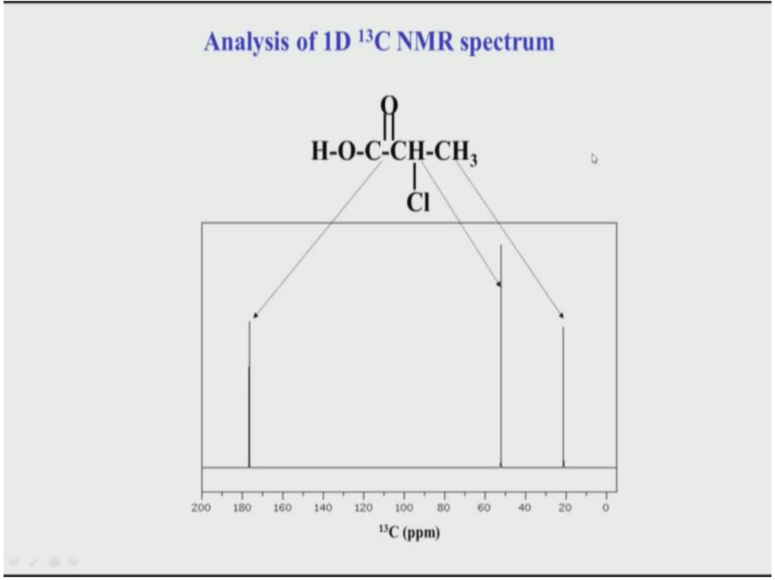

Analysis of 1D $^{13}$C NMR spectrum

So let us move on to the next example here. So this is a CHCO which is attached to this. This is an acid, carboxylic acid group and this is a secondary halogen. So secondary carbon which is having a halide substitution. So this is the molecule also we looked at when we analysed the 1D proton Spectrum. So same molecule has been taken up here. So if you now like I see the spectrum of this molecule, here you can see now. Again there are three types of carbon, this is this methyl carbon one, this is CHCl, carbon one C and this oxygen is attached carbonyl carboxylate group at this C and therefore it is coming at this position.

Now again, if you look at the chart of carbon expected peaks of the values, we saw that carboxylate comes somewhere around 180 ppm and that is what is shown here, that there is a peak at 180 ppm and that is little bit downfield compared to the ester group. So if you recollect there is a slight distinction between ester and acid. In case of ester it comes somewhere around

160 to 170 whereas in the carboxylate acid and carboxylate group, the carbonyl, this carbon is comes around somewhere in between 170 80 to 190.

So this is the peak which corresponds to this carbon, and this side, this is a methyl group and because this carbon is attached to electronegative carbonyl halogen, so you expect this carbon to be deshielded and that is what is coming, it is coming quite deshielded at around 50 ppm whereas this CH 3 which is a regular methyl group is away from this and that will be therefore less deshielded when it comes at its regular position. So again, look see if you look at the intensities of these peaks, keep in mind the intensities of these peaks are no longer proportional to the number of carbons.

For example, if I expect they are proportional, then I would have expected all of them equal in intensity. Why? Because they are seven carbons. So this represents one carbon, this represents another carbon, this represents third carbon. So there is one is to one is to one so you expect one intensity but equal intensities for all the three but that is not the case in carbon and because again the reasons were given as T1 relaxation, long T1 relaxation and second is the NOE effect because we decouple.

So look at these lines, they are sharp single peaks, why? Because they are decoupled. The protons have been, I mean the J-coupling has been removed from protons by decoupling and that also affects their intensities.

So the intensity is no longer directly reflecting the number of carbons unlike in the proton. In the proton case, this is not the situation, they are very quantitative. So looking at now the assignments, this is what we discussed. The three carbons are very easy to assign and basically we are using logical arguments here. The logical arguments, electronegative effect, the carbonyl where you expect them, where you expect the methyl and so on. If you want to do get an exact match, you have to look at, you can calculate based on the rules we saw and from there also you can see which is matching.

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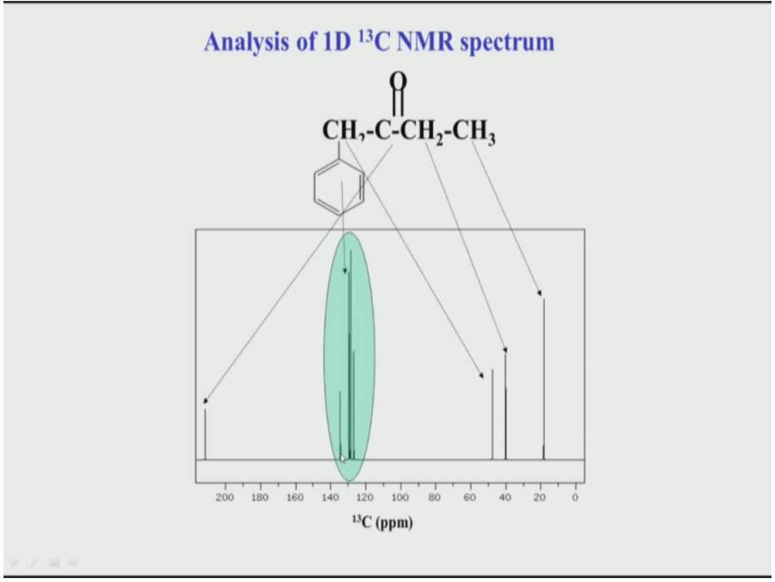

Analysis of 1D $^{13}C$ NMR spectrum

So we will look at an aromatic spin system aromatic case where aromatic is system is shown here and there is this carbonyl attached to this. So this is a ketone. So now we are looking at a ketone function group. we have seen carboxylic acid, we have seen ester, now let us see how what happens in case of a ketone. So Ketone, the spectrum of this molecule is given here. So let us try to assign means match which carbon could be which. Again, by logically you can say that this carbon which is away from all these groups could be the most off field shifted because and that comes it is a regular methyl, so this is something what you can directly say this coming from here.

Similarly this ketone group, again if you look at the chart, we saw in the in that the chart of chemical shifts there you will see, the ketone is the most downfield shifted carbon. It comes close to 220 ppm. So that is what you see here, there is a very downfield shifted peak, coming around 220 ppm and that therefore has to come from this ketone C carbonyl group of the ketone. Now if you look at this region, somewhere between 120 to 140, that is where your aromatic spin systems comes.

So typically, what happens is when you are trying to simply assign, this molecule to this spectrum, we do not look at the details of this peaks here, in the aromatic region because again like we saw in proton, you have a complication here called strong coupling and so on, and it may happen that there is lot of overlap and there is more of signal intensity loss etcetera. So what typically is done is by just qualitatively, qualitatively you just look at the region and if you see peaks in this region, you can very well be assured that there is a aromatic spin system.

So this is how qualitatively you assign. Also if you look at this peak which is a little isolated from this bunch and it is lower in density, that could be therefore that could be coming from the quaternary carbon, this carbon here which is not attached to any proton, like we saw in the previous case. So therefore, this type of a signature, this type of a profile and this type of a spectrum is typically then assumed that there is an aromatic group here and we do not go into detail analysis of each and every peak.

But this is we can say, there is an aromatic moiety in our molecule and that is basically this moiety. Now the remaining aliphatic, we can assign base on the isolated peaks. So with this CH 3 we already saw, is could be this and this CH 2 now, is close to this. Similarly this is close to this, both are equally from this but if you see this CH 2 is little bit downfield shifted more would be because it is attached to an aromatic group which is an electron withdrawing group. So that will also withdraw the electron density from this carbon and similarly this carbon will also will have so it has a double inductive effect.

So you can expect that this carbon will be slightly more downfield shifted compared to this carbon and that is what you can see here. So we will see the assignment, let us see the assignments, so this carbonyl is this peak which we already saw, this methyl is this and you can see here that because of the double electron withdrawing groups present on this carbon, it is little bit downfield shifted more compared to this carbon which is only attached to one CO which is electron withdrawing whereas this carbon has two electron withdrawing groups close to each other, directly bonded, therefore you expect downfield shift.

So you see by this kind of a logic, typically you can assign the carbon chemical shifts and we rarely record the coupling, coupled spectrum usually it always decoupled spectrum and therefore it is just based on the qualitative aspects. Of course if you have the multiplicity idea and so on, remember we saw that that we do not get multiplicity from 1D carbon for that you have to do a special experiment separately to get that information and that experiment if you have, if you do, then you will again further see whether it is a methyl carbon or a methylene carbon or a methine carbon for example in aromatics, they are all CH.

So that kind of information comes from a separate experiment, not from this 1D, and that is also usually done. So we will take that up later when we actually go for a full structure determination example in the later classes. So let us now look at continue with this. So this is aromatic group, this is what I was saying that if you have bunch of peaks at this region 125 to 135 or 120 to 140 we can very confidently be sure that there is an aromatic group present in the molecule.

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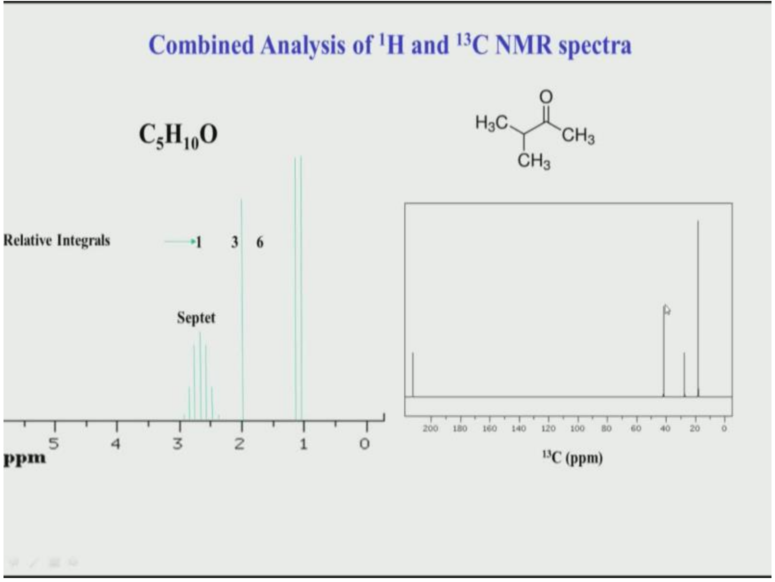

Combined Analysis of $^1H$ and $^{13}C$ NMR spectra

$C_5H_{10}O$

So now let us look at the, the last aspect where we look at given molecular formula again this is an example, which we have already seen in hydrogen proton spectrum analysis and now we are going to add a information on top of that. So we already had the proton spectrum and based on that we have analysed. Now what I am going to do is only add one more spectrum to this example and see whether our structure what we got, is it confirming the, confirmed based on the carbon spectrum.

So if you it look at this case, immediately so this from here this is a structure, this is a molecule. So if I had only the proton spectrum with me, I would have not been sure whether they what kind of CO moiety is here, it could be an alcohol. If there is an Alcohol, it is OH, ok? But if there is a carbonyl, it is CO. So that information is not coming from here.

Of course it can come from IR spectrum, but suppose I do not have an IR spectrum, I have only NMR, by looking at the spectrum immediately I can see here that there is a peak at 1 220 ppm and that 220 ppm is very strongly for coming going to come from ketone group according to that chart which we saw. So therefore, immediately I can conclude that there is a ketone functional group in this molecule that means there is a C double bond O.

Now I have remaining four carbons to look at and the remaining ten hydrogens, so there could be now the aliphatic system. So again remember, this is repeat of what we saw that if you have a septek means seven peaks most likely it is an isopropyl group, CH 3 CH CH 3. So that could be the CH 3 CH CH 3 attached to a carbonyl group and there could be isolated methyl because there is no J-coupling. So that means there are three types of protons and three types of carbon in the aliphatic.

Of course this is the fourth type of carbon but that is ketone. So this is basically fairly straightforward, we already analysed from the proton side and carbon is only helping us to confirm. So this is the structure of the molecule which we saw earlier and this is explaining the carbon spectrum because the carbonyl is a ketone which comes very downfield shifted and because of this these CH 3s are isolated will be coming from here and the one which is attached to CO this CH is slightly downfield shifted which will come from here, but again which carbon is which carbon not we are not sure from here that that connection between this proton spectrum in which carbon that is the part of the 2D experiment, we will do that later.

So right now we are looking at isolation, means I am looking at this spectrum in isolation with this spectrum separately. But a combination of these two would also give me the information as to which carbon, which peak here matches with which carbon proton here. Ok? So that information is not in this because we are looking at separate 1D.

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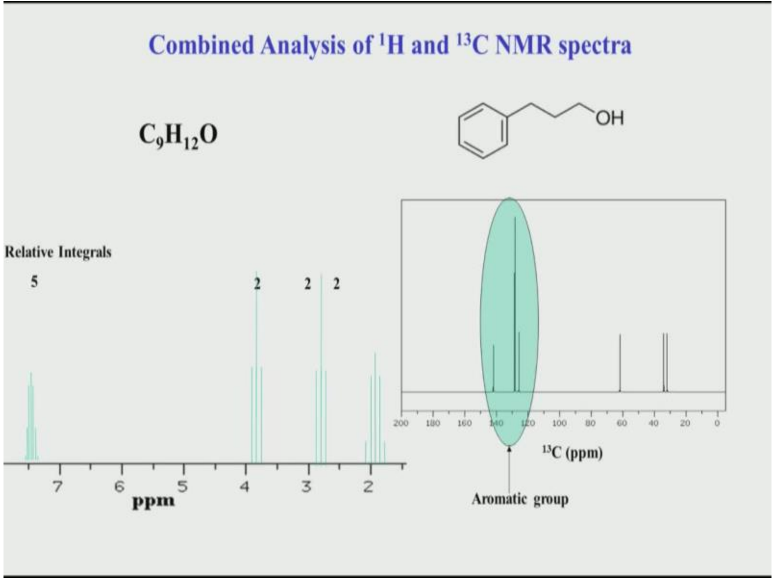

Combined Analysis of $^1H$ and $^{13}C$ NMR spectra

$C_9H_{12}O$

So let us come back to this particular case. If you see here, again there is a single oxygen but again I do not know whether it is a ketone functional group or there is a alcohol OH and so on. So how do I find that out? Again if you look at the carbon spectrum, you see there is no peak here in carbonyl region. So that means there is no carbonyl group here. There is no ester, Ester of course; there is no two oxygens so only one oxygen so there is no carbonyl peak in this region.

So it has to be a alcohol, OH. Now if you look at the bunch of peaks here between 7 to 8. Similarly a bunch of peaks here, remember this all corresponds to aromatic groups. So therefore there is an aromatic moiety in this molecule. There is an aromatic moiety, there is an OH group. Now if there is an OH group, you expect a downfield shift for the hydrogen which is near to the OH that is CHOH. Similarly here also the this peak which is between sixty to seventy is again CHO kind of a molecule moiety in the molecule.

And this quartet and triplet could be ethyl group, CH 3 CH 2. CH 3 will get CH 2 will be quartet and CH 3 will be the triplet. So let us see this molecule, this is what is shown here. This aromatic system and this is this particular molecule. So you can see that there is an OH group, so this CH 2 corresponds to this is a triplet and this CH 2 which is in the middle is actually a quintet, so this is not a methyl, this is a CH 2 which is a quintet; and why is it a quintet, because there are two hydrogens this side, two hydrogens this side so 2 + 2, 4 + 1 makes it 5. So this is in the middle.

Now if you look at this peak here, this carbon and hydrogen, this is attached to an electron withdrawing group, the benzene aromatic ring therefore they are expected to be downfield shifted. So out of these two peaks here, the methylene, one of them is this carbon, other is this, but what about the protons? The protons, this one, which is here will be more downfield shifted relative to this because of the electron withdrawing group of this. Ok?

And that is this peak here because it is coming in at three ppm, it is downfield shifted and there are triplet here because this two is coupled to two protons here. So according to the N + 1 rule, these two protons will be equivalent and they will have triplet, multiplet from J-coupling and this hydrogen and this proton is downfield shifted because of the OH that is coming from here. And now coming to carbon side, this 60 ppm which is downfield shifted is this carbon and between the two carbons, the upfield shifted will be this one because it is less shielded, it is away from the deshielding effects. It is in the middle, whereas this is close to this group so therefore this carbon here could be this carbon.

So this is how we assign the carbon spectrum. So we have looked at some of the examples how we can assign carbon spectrum based either on the structure directly or in combination with protons spectrum or we can actually predict the carbon chemical shifts directly based on the rules which we have seen some of the rules. So we will now complete this part of the course here that is looking we have looked 1D NMR of proton and carbon and their interpretation in different ways. how what factors affect the chemical shifts? How to analyse 1D NMR? and so on.

So this completes the second part of the course. Next part of the course now we will be begin with 2D NMR where we will now look at 2D NMR correlation between proton and proton, and proton and carbon and we will see how they are recorded, what are the practical aspects and how do we actually analyse them.