Heterocyclic Chemistry
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Lecture - 6
15 N NMR in Heterocyclic Chemistry

Last time basically we talked about the initial things about the structure determinations, we already said that heterocyclic requires special kind of attentions with regard to the structure determinations. Simply because they are plot on poor and in heterocyclic chemistry, carbon 13 is also a very useful tool, in addition nitrogen 15, these are the NMR tools. But before we talked about NMR, we also briefly talked about the mass utility x-ray.

X-ray is the ultimate answer but certain cases, we have cautioned you that it could be also misleading like the example of kinamycin, if you recall. And then the ketoconazole drug and that is best studied by UV, of course it has to be supported by other things, other means NMR and other things. And then when you came to the one dimensional NMR actually, when you come to one dimensional NMR, we normally deal with three different parameters.

What are the three parameters? This chemical shifts and then size and the shape, that is also true for all I mean, all kinds of the nuclei including I mean, whatever the 40 to 50 different nuclei, NMR active nuclei. For all these nuclei, actually all the three parameters are equally important, fine. We gave you examples, when I say I mean chemical shift means, it is basically delta parameter, and what is a size means integration, and shape means multiplicity. Then so we have seen that, that in case of benzene, whatever the chemicals shift is ((Refer Time: 02:11)) just basically electronics is one of the important guidance.

In case of pyrrole also with reference to benzene, this pyrrole is considered to be pi excessive heterocycle, this is a term called pi excessive heterocycles ((Refer Time: 02:26). Because, a pair of electron is shared by 5 atoms, so that is why, it is pi excessive electron is increase, so chemical shift decreases, that is the typical. So that means, from there you can make out, whether you are dealing with a 5 member or 6 member, which are more commonly encountered in this chemistry.

And then also, we left looked at the coupling constant, we give you a very important guideline, what was the guideline, that with increased electron negativity, the coupling constant decreases. It is a very important guidelines, you can quickly distinguish, whether you are dealing with a 5 member or 6 member or with hetero atomic compounds or not. Now, there are many other factors, which influence the coupling constants then we also give you some of the examples of this NHC carbene.

So, NHC carbene, that we have even a small molecule which was thought to be sydnone or mesoionic compound, only in 2012, it has found to be a stable carbene that is called nitron. And today, what we do, today we will have again little bit of the chemical shifts, little bit of the coupling constant, we will ignore. But, we will exclusively talk about nitrogen 15 NMR and also, we will talk about 2 D NMR. 2 D means, application of 2 D in 2 D NMR application so all of us know the 2 D NMR. So, what is 2 D NMR, how does it differ from 1 D NMR, what is the speciality, Abhishek, what is the speciality of 2 D NMR?

Student: 2 D NMR describes interaction between the special, for each NMR interaction between two different protons, which is not expected by normal observation or something like that.

No so basically yes, what you said is correct but to be more precise, it only deals with coupling, how is that, only deals with coupling. So that means, from the 2 D NMR you get coupling information so just to very briefly introduce so that means, what we do, normally in NMR, what we do delta.

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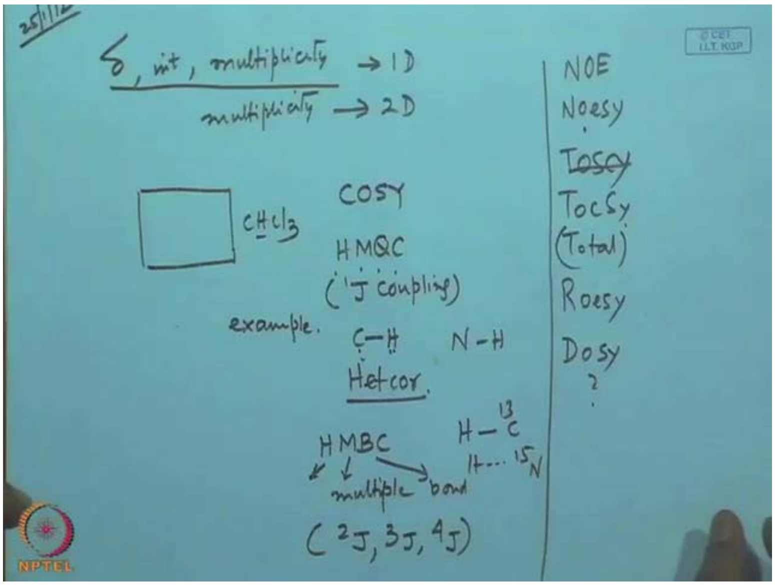

Then, integration means, how many protons, etcetera and then multiplicity, these are the three things often, this is in 1 D NMR. In 2 D NMR, it is basically we deal with multiplicity. Multiplicity this is basically, refer to this coupling that is all, the coupling information is embedded in 2 D NMR. Now, let us look at 2 D NMR half for example, chloroform for example, chloroform so what is the expected 2 D NMR of chloroform, how many contour will be finding here.

Let us say, when I say chloroform means proton NMR, in proton NMR in case of 1 D NMR, you get a single that is all. In the 2 D NMR, what you get nothing, again a single contour that means, you do not get any additional information, that is important. That means, where there is no coupling, 2 D is useless as simple as that. So, in heterocyclic compounds, as you know, most often protons are less so obviously, couplings are less. But then there are other things also so in 2 D NMR then what are the other items often we deal with.

So, all kinds of spectroscopy in 2 D and ((Refer Time: 06:40)) COSY, COSY NMR correlative spectroscopy basically, correlates the couplings, the nuclei which are coupled to each other. And then under this COSY, this is called homo COSY means that implies so hetero COSY means, hetero atoms and then other that hetero that means, sometime called homo COSY spectra and hetero COSY spectra. Then what else you have, the other categories are HMQC, HMQC stand, H stands for Hetero nuclei Multiple Quantum Coherence.

So, it is basically 1 J coupling how is that, 1 J coupling means for example, let us say you have a coupling between this carbon and hydrogen, and number of intervening bond between them is 1 so this is called 1 J. Coupling, if these sort of couplings are shown in a spectrum that is, in a 2 D NMR, that is called HMQC sometimes, we call hetcor means, hetero atom Correlations spectroscopy. When I say, hetero atom, hetcor so what it means, actually there are plenty of other names, hetcor means it is basically, 1 J coupling.

Then, one more important kind of spectroscopy or 2 D technique is, this is one of the very useful one, HMBC. HMBC, I do not have to write, this is again a hetero nuclei and M stands for Multiple and B stands for Bond and correlations. Normally, this refers to 2 J means, 1 J is skipped that is important, direct coupling is avoided then 3 J and very rarely, 4 J atleast, I just once, I came across this 4 J. These are the techniques, now then you have all kinds of sub techniques, sub techniques means, like in this case, when I say hetcor means carbon hydrogen, it could be nitrogen hydrogen, it could be any other hydrogen.

Similarly, HMBC talking about when I say, HMBC talking about, this is essentially is an hetcor so hetero nuclei implies hetero atom. Now, it could be 2 J, 3 J, the all are in the same spectra by the way, they are not separate spectra, all the same spectra. And then you have to build little cautious about this 4 J, it could be seen, it may not be seen but quite often 2 J and 3 J are seen. Not only that, the nuclei could also be differing means, let us say, like in this case, hydrogen can undergo coupling with this 13 C and hydrogen can undergo coupling with 15 N, all kinds of things.

So that means, it could be of different kinds but most commonly, that hydrogen is one of the commonest nuclear because it is populous, it is population is very high. So, these are the techniques normally we deal with but basic idea is chemical shift, size and the coupling, nothing else so throughout. Then other special techniques all of us know, NOE, Nuclear Overhauser Effect, Overhauser is name of a scientist then now, people say, NOESY.

In two dimensional, equivalent of this one, this basically gives you again a coupling but direct coupling, not the indirect coupling. There are two terminology, often used direct and indirect, direct means true space, there is no I mean, perpendicular distance and indirect means true bonds, that often we deal with. So, that gives you the direct coupling and then there are many other techniques actually, we do not often use, that is a called TOSCY I think, TOSCY something like that, TOCSY, Total Correlation Spectroscopy.

So, actually it contains all the couplings, all the direct couplings, all the indirect couplings but this spectrum becomes, all of you can understand, becomes too complex to understand. So, we have other things that is called ROESY Remote Correlation Spectroscopy, I never come across that but people use it. Then some people use DOSY, DOSY is Diffusion Correlation Spectroscopy, something like that. So, I think this is used by mostly the physical chemists, physical chemist they use solution structure, solution dynamics all these things are like ((Refer Time: 11:57)) uses DOSY spectrum.

Suppose, you have an amine bond to a solid surfaces and freely floating in the solution, how do you differentiate them. Both of them would look like in the NMR but if we by using DOSY, you can differentiate them. So, we have but for us, for practical purpose, what are the things, will be 1 D ((Refer Time: 12:20)), which could be with respect to hydrogen carbon and HMBC and HSQC, that is all. So now, with this little background, we will look at maybe some of the examples only, in certain cases will identify the chemical shifts, certain cases the correlations, certain cases the trends. In between, we also talk about the exclusively actually nitrogen NMR, may be we will begin with nitrogen first, rather would be nicer. Let us say, nitrogen NMR what should you know, active nuclei by now, all of us know and so active nuclei most often used.

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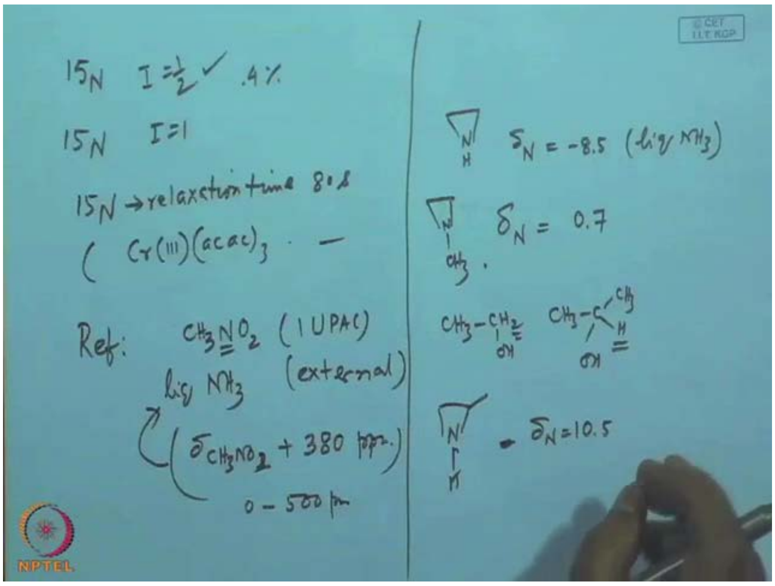

^{15}N $I = \frac{1}{2}$ ✓ .4%

^{15}N $I = 1$

^{15}N → relaxation time 80 s

(Cr(III)(acac)$_3$. —

Ref: CH_3NO_2 (IUPAC)

liq NH_3 (external)

($\delta_{CH_3NO_2}$ + 380 ppm.)

0 – 500 pm

$\delta_N = -8.5$ (liq NH_3)

$\delta_N = 0.7$

CH_3-CH_2-OH $CH_3-CH(CH_3)-OH$

$\delta_N = 10.5$

In NMR heterocyclic chemistry is nitrogen 15, what is the I value, nitrogen 15 I value is half and what is the frequency, that also you have to know roughly. Let us say, if hydrogen has frequency 100 megahertz then what should be the frequency of carbon, 285, all of you know, one fourth. Similarly, with reference to hydrogen, what is the nitrogen frequency, nitrogen frequency it is much less, I think around roughly, I can just guess, it is less than 25 that is for sure.

The frequency in that region, why we need to know all these things simply, because when you adjust the machine, you have to see, where to fit it. I mean of course, every channels are already fixed, nitrogen channel, hydrogen channel, carbon channel, they are fixed. But, you have to know, at least which side you have to look for number 1, number 2 that, sometimes dual probe, multiple probe you have to handle, all these things if you go up, any cases.

So, this is important and then all of us know now I think, what I said the natural abundance is 0.4 percent, this is very less compared to the, most populated one is hydrogen all of us know, followed by I mean fluorine, fluorine frequency is close to hydrogen then comes phosphorous, phosphorous I think then phosphorus also 100 percent then the carbon most often used is carbon 1.1 percent. So, even this nitrogen 15 is less than that that means, less sensitive.

So, you have two more scans but that is not all, if the frequency is not adjusted, it can overlap with nitrogen 14 frequency, nitrogen 14 also very close to these nitrogen 15 frequency. So, you have to little cautious about that and then nitrogen 14 has a quadrapole movement so that means, I equal to 1. So, what it does, it actually induces faster relaxation, induces faster relaxation means this I mean, if you just apply the uncertainty principle, the signal will just merge with the baseline so that means, we may not see it.

So that means, that is the reason, why it is not followed but as it has some advantages also, if you have a hydrogen attached with nitrogen, you can almost always see some sort of broadening. Let us say, you are expecting an OH and then NH in the same region, how to distinguish them. If you try to do the extends experiment, it can be applied to the both, that will not distinguish NH and OH. Then how do we do, after exchanging will see the broadening is retained with the case of nitrogen, not with the OH group.

So, that inherent broadening also there, that is in the helpful sometime any case but there is another disadvantage actually, the disadvantage with nitrogen 15 NMR, that nitrogen 15 relaxation time is pretty high. What is relaxation time of hydrogen let us say, these are the things you have, these all the common vocabulary taken from NMR course, what is relaxation time, rough idea. Relaxation time of hydrogen, relaxation time of carbon, roughly at least it can be 5 minutes also, 5 hours also. So, and for hydrogen, microseconds till the minus 6 seconds, maybe I mean, less than 1 second for sure.

That means, that tells you how much relaxation delay you will be giving in the machine, for nitrogen 15, it is about 80 second actually, 80 second. So, occasionally what you do, now here, you come with this inorganic people, inorganic people would come they will put a chromium complex with acetyl acetonitrile complex of the chromium 3, what is it, it is a paramedic substance. If you have right paramedic substance is optimally induces the relaxation that means, relaxation time decreases.

If you have paramedic substance, relaxation is faster, signal is broadened, in this case what you do, yes maybe signal is being broadened but at the same time, you are compromising with the relaxation time so that means, occasionally depending on the situation, etcetera. And next most important thing in nitrogen NMR is reference, it is a critical reference, actually this morning also I got confused, in one node I had something like minus 8.5, in the other node I got some 300, 400 for the same compound, I really got confused.

Then, I had a visitor also, I asked him, he is from Oxford and today's seminar speaker, I asked him how you are used NMR nitrogen 15, he said no but he could not say which one is the reference. So, the recommended reference is nitromethane, nitromethane nitrogen, this is internal reference, this is recommended by IUPAC. But, unfortunately people do not follow, people follow external reference, this is a liquid ammonia so this is actually reference.

So, whenever you look at it nitrogen NMR, you have to be little careful about it, what is the reference. To give you a hint, if your let us say dealing with nitromethane so whatever the chemicals shift you get that is, if you want to convert these into liquid ammonia. So, what you do, you just add take this nitro nitromethane chemical shift and plus 380 PPM. So, if you follow that, that goes to the reference of liquid ammonia and normally, the range is from 0 to 500 PPM.

Student: ((Refer Time: 20:10))

It depends on, why?

Student: ((Refer Time: 20:14))

That is upto the convenience, actually it is upto the convenience maybe because you see external means once you standardise then you can routinely do it one after another, you do not have to add nitromethane, that is all. But, some people have used liquid ammonia, nitromethane also, I have references and for example, Silverstein reported again with liquid ammonia and but I contacted a review vertical, that also is the liquid ammonia so all this thing mostly but there are examples where…

So, that is important and this chemical shift is very important in this case, chemical shift ranges high but quite unpredictable. So, whenever you are required, just go consult a book and see the trend for example, I will begin with the smallest heterocycle acridine and in this case, this delta nitrogen here is minus 8.5, when I say. So, basically it is refer to liquid ammonia so that is the oldest reference so that is followed.

Now begin with, now just put one more methyl so I mean, anybody can predict anything actually, I mean with my understanding, I would predict higher chemical shift value and it has been true in this. And the explanation, many of you know, it is not…

Student: ((Refer Time: 22:12))

Electronegativity…

Student: ((Refer Time: 22:16))

Not really, if the electric density is increases chemical shift decreases but in this case, chemical shift increases.

Student: ((Refer Time: 22:23))

Carbon is, no… I will take you back to the, I do not know whether I taught you my NMR in your class, no this is very important. For example, just quickly then go through let us say, we are talking about the ethanol, let us say these two examples. So, this is a hydrogen oxygen and this is CH 2 ethanol and isopropanol, underline hydrogen, which one will have higher chemical shift value, ethanol or isopropanol. Isopropanol should have a higher chemical shift value why, of…

Student: ((Refer Time: 23:23))

That is it, it is not the inductive effect, often we get confused with inductive effect, it is the carbon carbon sigma bond that gives you this. So, this is the reason why, in this case of acridine you can say so and then but these are all there are plenty examples. For example, if you just take an example of let us say acridine, the substitution elsewhere and two position then the delta nitrogen would be coming to again delta nitrogen is 10.5. So, delta is increasing, delta is increased again so I mean, these are all the standard value of the let us say for example, in case of just typical value here.

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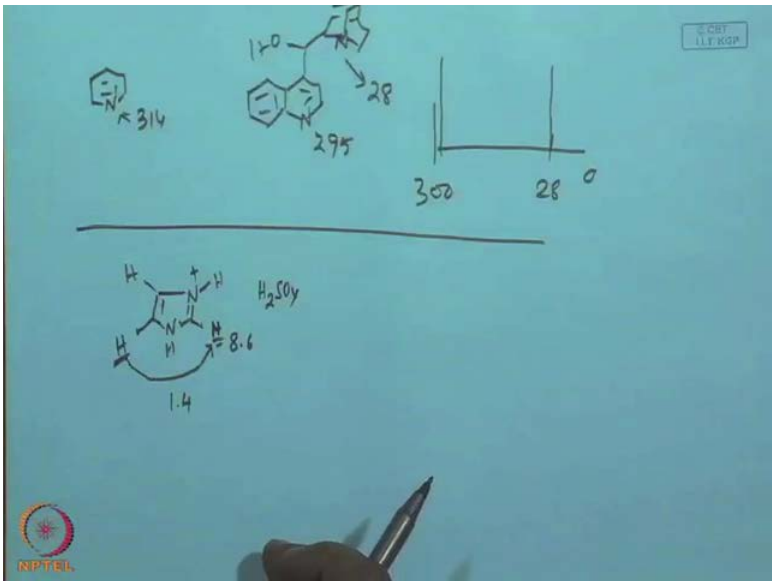

Typical value of pyridine, it is 314 so you can just make out from these things here and that means, you can quickly distinguish aromatic and aliphatic. For example, this is a known compound quinine, quinine is a known compound all of us can quickly write this structure quinine. How do we write this, 314 quinine will have OH of here and then you have a hexabicyclic system I mean, I am just giving you a rough idea, do not worry about this thing here, there is nitrogen oxygen.

So, there is a two different nitrogen, in this case it is this aromatic nitrogen is 295 and aliphatic nitrogen is 28. So, it is clear that means this spectrum, how this spectrum look like. Just basically, if you let us say begin with 0 here, 28 here let us say, you make it 300 so that means, that solve that means, it have only two lines, so simple very simple. That means, if you have access to nitrogen NMR, you can quickly look at this two steps without any problem and…

Student: ((Refer Time: 25:55))

Not mighty, it is the nucleus nitrogen.

Student: ((Refer Time: 26:03))

Ring is a…

Student: ((Refer Time: 26:10))

But, those guys said, he said hexabicyclo 2 2 2 2 octane how is that so that means, we have given enough background. Now, let us have examples only, the techniques and the enough that means, aromatic nitrogen will have higher chemical shift, aliphatic that is quite obvious. So, but whenever you are dealing with a right problem, you have to just go through the literature and find out, what are the state of the ((Refer Time: 26:44)), do not try to remember all these values.

But, you have to know how to use the techniques, how do you use the technique means, you have to know what to know about the techniques and what to know about the structures, etcetera all this things. Just we will have, from now onwards we will have only a few examples for example, I have a problem here, imidazolyl problem let us say, imidazolyl problem. I think by now, all of us know imidazolyl means, it is a five numbered ring with 2 nitrogen, that you have to remember because it is a biomolecules so you have to remember like this.

Now, this is an example because this is a commonly encountered…

Student: ((Refer Time: 27:30))

Actually, the imidazolyl itself is not really soluble in organic solvents so what you do actually, you put a little bit of sulphuric acid, occasionally what you do, try for acetic acid, many attempts you have done it, many insoluble compounds there are insoluble. So, you just add, you are expecting in a basic nitrogen put sulphuric acetic acid so then it gives you this salt here. So, what is the difference do you expect so obviously, the chemical shift should be increased because you have added a proton, positive charge and that is what you see, this is 8.6.

So, like these all these, I will not give you the value here but what is important in this case is that, I will like your attention to be drawn to the fact that, very interestingly let us say, this hydrogen and this hydrogen that means, is coupled in the NMR. That means, number of intervening bond between this indicate the hydrogen, this one and this one, 1 2 3 4 normally, 4 bond couplings are very little. In this case, it is significant and the value is here 1.4 occasionally, it can go upto 2, 3.

So, what is the reason, reason is all the carbon switch are is s p 2 carbon atoms, if the things are the system you have plenty of s p 2 carbon atoms then you can go upto 9 J.

That means, number of intervening bond could be after a maximum 9, I have seen upto 11 so provided those are all align system. So, this is just an example that means, where you can find out the coupling can be existing if you have a hydrogen and then there are other things. This is a case, I think we will ignore that, I will come back maybe sometimes later let us say, we will have an example of HMBC.

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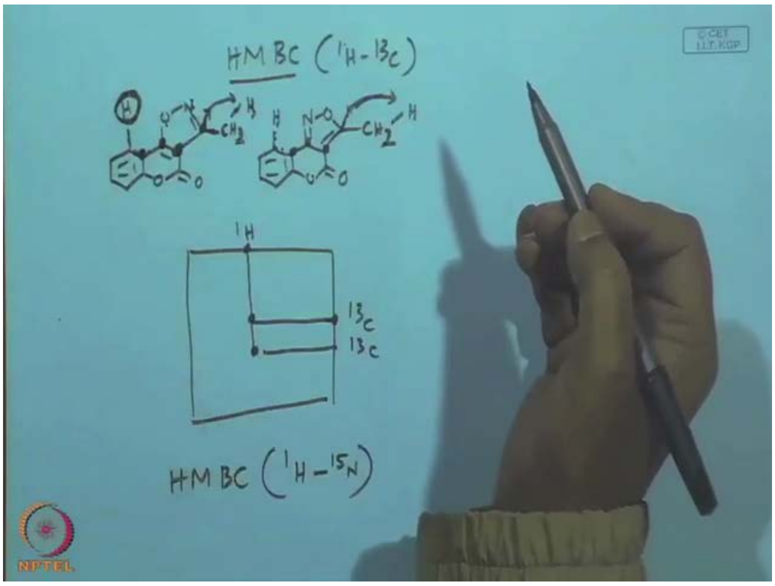

HMBC may be taken from, it is a case of let us say, if you have a structure of this kind, it is isomeric and nitrogen and this structure also it is isomeric. This structure what I am writing on your right or rather on my right it is something like this, exchange the nitrogen and oxygen up here, just interchange the position of nitrogen and oxygen. So, how do you differentiate them, isomeric so mass spectrum will give the same mass, molecular formulae same exactly, is very difficult.

But, seems to be know now that, HMBC experiment so one can quickly decide, let us see so what is the starting point of HMBC, starting point of HMBC, what could be the starting point, where you start from. In any NMR analysis, you have to have a nice reference for example, Sam yesterday made an acetate so whether the NMR is correct or incorrect, how do I know. We start from acetate because we know acetate comes almost arise at 2.0 something so if that is there, the compound has to be there, with reference to that we just explained.

So similarly, here also, you have to find a proton or something, which is for sure existence and giving a signal. In this case which one, methyl, methyl is nice singlet, nice singlet you can just see but it does not undergo any coupling, you have a CH 3 here. HMBC means, let us say for now, we talk about carbon 13 for example, what you see, I will make it 2 here, I will make it 2 here and hydrogen. HMBC takes care of 2 J, 3 J most commonly so that means, this hydrogen would undergo coupling with 1 2, with this carbon, with this one, this carbon so that means, this would undergo coupling.

So, similarly this carbon would undergo coupling with this so in both the compounds, you have that coupling so you cannot really make out. So, what do you see actually, how does the spectrum look like, spectrum look like let us say, if this is a proton scale, this is a carbon scale, if you have a spot like this that means, just basically vertical line and a horizontal line. Tthat means, this hydrogen is coupled to this hydrogen that is all, unlike in 2 D COSY NMR, you look for cross fix so just basically a sort of linear connectivity kind of things.

So that means, if this is the hydrogen up here, this carbon is let us say is this, just supposing so that means, in both the cases, you will have a very similar chemical shifts, similar coupling so you cannot distinguish them. So, what else you do, go to the 3 J, 3 J means 1 2 3 that means, this one would be coupled with this original hydrogen, this one would be coupled original hydrogen, you can see the environment, they are very much alike. So, it is very difficult to distinguish that means, there would be a spot corresponding to that one.

That means, this hydrogen let us say would also have a spot here and this one is the second carbon, that is the second carbon so that means, this hydrogen would also coupled to another carbon but it does not differentiate them. So, what we do, let us take another reference, what is the reference, here is a hydrogen, here is a hydrogen, this hydrogen is distinctly difference from all other hydrogen reason being, close to second aromatic, this one is in aromatic 1.

So, influence of aromatic one would make this one decelerate, just like naphthalene perihydrogen, naphthalene perihydrogen more decelerate than the other pheripherial hydrogen so that means, it will be most downfield at hydrogen in aromatic region. So, let us look at the HMBC of that one so HMBC means, this is our reference 1 and 2 bond that means, these should be coupled this one, this one would be coupled. So, in this case also, you have a coupled hydrogen then 3, 1 2 3 this one is coupled, in this case 1 2 3 this one also would be coupled.

Mind it, you have here oxygen, you have nitrogen, it is very difficult to distinguish, the chemical shift twice, both are electron negative, both are aromatic systems so it is kind of a difficult. So, you have to have something, which would be unambiguous so what should I do, what should we do, let us let us see, we will do again HMBC but in this case, we will do HMBC with nitrogen 15, how is that. Nitrogen 15 means, what you see let us say again in this case, on the left most hydrogen is this one and the bond is 1 2 that means, it can coupled this hydrogen, in this case also this.

And then 1 2 3, it can coupled with these, in this case also 1 2 3 so it does not make any difference but if you come with the other reference hydrogen, methyl hydrogen, 1 2 3 that means, hydrogen couples with nitrogen, in this case hydrogen coupled with nothing, oxygen does not couple, that is what. So, quickly that means, these are the things we have just look for, we never did any nitrogen HMBC but in this particular example, nitrogen HMBC is perfectly all right and this is very useful especially, in case of nucleus at chemistry.

Let me see, if I have an example, example maybe let us say, nitrogen HMBC, I do not have any example of nitrogen HMBC. All I have is carbon HMBC, let us try with one carbon HMBC and see, whether you can distinguish two isomeric compounds, which are heterocyclic.

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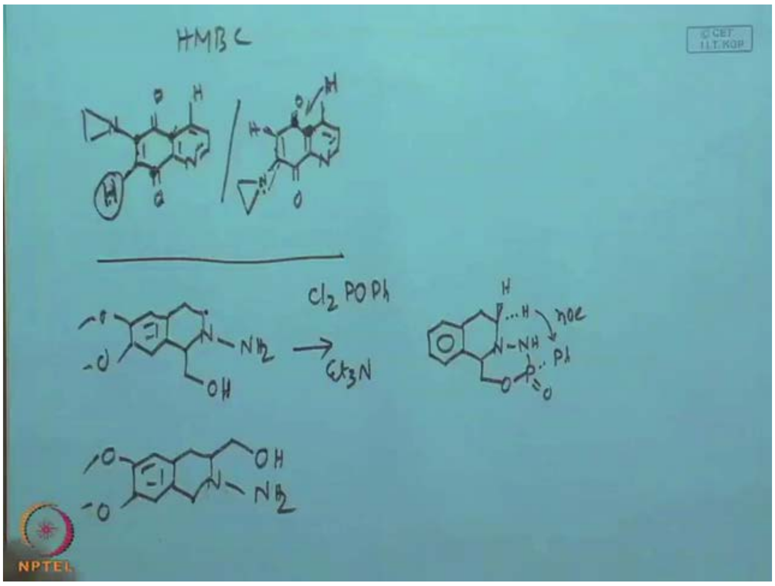

Again it is a quinine kind of heterocyclic quinone and I have this thing then you have a hydrogen up here and it is an uridine kind of structure. Similarly, one can guess, this versus you have again a quinine, it is pyridine nucleus, just interchange the position of and acetylene and the hydrogen. So now, the problem is to, what technique could be used to differentiate them, what technique would be use. How do I know, what technique where to start with let us say, just give your answer first, how to start with.

Student: ((Refer Time: 39:19))

Structure is given now, just tell me, just where to start from, a reference point, what is the reference hydrogen, this hydrogen because para 2 hydrogen all of us know because of the resonance effect, this hydrogen is most decelerate number 1 and then you have carbonell anisotrophic effect, this oxygen is facing the hydrogen. So, you have a strong effect on hydrogen so this hydrogen would be most decelerate.

So that means, you start from that means, very quickly actually, a spectrum where you look at actually left to right or most populated or a less populated area, less populated area that is right, either your extreme right or left are less populated area. So, exactly you do the same thing, this is important this starting is very important, starting and your confidence in assigning the reference, that is important. Once you have a right confident reference then rest of the problem should be easier so that way so you have these two then.

And then let us see I mean, whether you apply homo COSY, hetero COSY, all these things so you know all the meaning. But, since I have already told you that, we will be dealing with this HMBC, let us see what happens I mean, if you just deal with this one this one, 1 2 that means, the carbon here, second carbon then 1 2 3 carbonyl carbon so angular carbon and carbonyl carbon with this. So similarly, here also, you see angular carbon and carbonyl carbon let us say, then what else, this is most up field hydrogen, this is not in aromatic hydrogen so it should be most up field hydrogen.

So, what do you see here, this one again, one carbonyl carbon and what else 1 2 I mean, you can nitrogen carbon, 1 and 2 nitrogen and 1 2 nitrogen. So, you cannot really differentiate so what to do.

Student: ((Refer Time: 42:05))

Normally, these days people do not use, when we did Ph.d we did that because coupling constant is so high I mean, whole spectrum becomes too complex, either you have any idea about the coupling constant direct, the coupling constant of carbon and hydrogen would be 120, 200, 300, 400, 500 so you can have such falls in the spectrum. So, the quickest I mean, although there are ways to solve this problem, if you have this, basically these comes from confident level.

For example, all of us know the chemistry part, chemistry part means, if you look at this nitrogen here, there is some conjugation. Although it is not a fully conjugated to these carbonyl go, this carbonyl that means, some conjugation is there, the chemical shift would be increased decreased in this case. So, I mean, that way you can find out which one is better conjugated, nitrogen in this case the one, here it is got a conjugated so that way one can determine.

I think the one I have here has no definite answer but they did this experiment so best thing probably would be which one, nitrogen, no, nitrogen also would not do anything because the hydrogen here 1 2 3, in this case 1 2 3. So, nitrogen also would not help so only thing the way we work and do that is this, the distinguishing these two carbonyl first. Once you distinguish these two carbonyl first then we can go for the analysis so essence is I mean, what is the essence, the things are not that easy.

In certain cases quite easy, depending on the situation, whether we switched to carbon, we switch to nitrogen but you have to have all this thing in mind. And let us assume, by now many of you know for example, in this case, there is an experiment also, all of you know this NOE experiment. NOE experiments, what does it demand, it demands that the two nuclei should be close enough, when I say close enough means, this is the absurd answer you have to have a…

Student: ((Refer Time: 44:43))

How much?

Student: ((Refer Time: 44:45))

No, much more it is close to 5 Angstrom.

Student: ((Refer Time: 44:51))

No, close to 5 Angstrom, twice the hydrogen bond, what is the standard hydrogen bond distance 2.45 or something like that so roughly that so below 5. I said it is just a random guess but point something is not for sure, maybe I am wrong, if I am wrong, no it is possible but any case that is what, you have to… Whenever you just try to do NOE, you have to make sure that these things and I think if you know NOE then I will give you a advanced problem actually.

Let us say, how to distinguish, this is again an experiment to distinguish isomeric compound and in this case, this structure again bicyclic structure, nitrogen CH 2 is NH 2 OH and this is OME. And the other compound that will I look at would be again a isocoolant derivatives, this is OH and NH 2 and OME and OME. So, how do you distinguish, tetrahydra isocoolant. So, how do you do that means, this portion is common so only thing that, once CH 2 group is just exchanged, this whole CH 2 group has been placed here so rest of the things are all right how do you do.

Student: ((Refer Time: 47:31))

Number of benzene product here 2, here also 2, here also on this side.

Student: ((Refer Time: 47:44))

Benzene is multiplied by 2, will have little difference yes, integration will…

Student: ((Refer Time: 47:53))

Chemical shift, this is difficult if you let us say, if you often we deal with tetralene kind of compound, which is difficult to deal with. How is that, I will accept your answer but you have to support by another complimentary technique, it is a suggested complimentary technique. Let us I mean or I can straightaway ask to this question, just do a kind of derivatives so that, your NOE study would be better of means, would be more suitable.

That means, one of the requirement of what I said, the nuclear should be in close proximity that is one of the requirements. The other possible requirement that means, to make this or to bring the nuclei in close proximity, what you do, you have to cyclize. So that means, if you have some kind of derivative you have to do, it is just basically your derivatized, so that these hydrogens and other things or something comes close to proximity.

In this case actually, what is done, I will just give the answer, this answer is here you say first was oxygen chloride, di ethyl amine, I will just give you only one example, top one. And this example would be so I will just quickly write and oxygen just to one can quickly also write this structure, this first product CH and NaOH, it is a cyclic structure that is all, what else, what you see. So, what you will find, if you just think of this structure in three dimensional, this is let us say pointing towards down and you have a hydrogen up here and you have this alpha hydrogen.

You can visualize that, this hydrogen will have a NOE effect but if you write the corresponding structure here then the alpha hydrogen of this CH 2 on the other case, in this case that is, this one is far away from, that is all. So that means, by cyclizing the compound, you have brought one of the groups to a neighbouring hydrogen that is all. So, you can do this that means, this is the shift trick. So, many times if you have let us say, you are suspecting let us say, diol compound, many of the often we will make diol.

What you do, find out the steady chemistry of the diol is a tough because they can move, they can rotate all kinds of possibilities. So, you just convert into corresponding acetonitrile and acetonitrile, that is one of the other trick is corresponding sulphate I guess, sulphide or sulphate something like that so it should be sulphide so convert it into sulphide and you get to the corresponding things. And so I think we have many more examples at this, last example this is a nothing to do with the 2 D NMR, it is an example of the multi nuclear NMR let us say.

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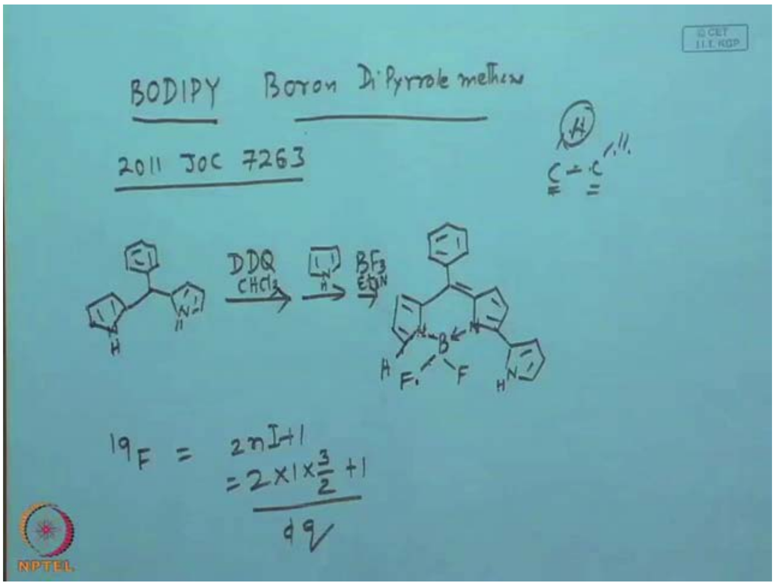

Let us say, we will take up this, Sushmit this is your homework, write it on paper on BODIPY di, bodipy BO stands for Boron, Di stands for Di and this is pyrole. Pyrole methane, a group of dye, it is a fluorescent dye, very important fluorescent dye. Someone very recently in 2011 JOC, Ii will give you the basic reference so that, you do not have to spend much time this is the reference. What they did, they took a compound di pyrole methane compound and so this is di pyrole methane compound and they have done a series of reactions, you workout mechanism by yourself or you can look at the literature.

DDQ or first node DDQ Dichloride Dichloro quinone is oxidising agent then you put extra pyrole. Eventually, what you got, you got a compound very similar to this 5 membered again on this site so and then he got also an additional 5 membered pyrole. And so something then this then in between actually, what we did, we did BF 3 and triethylamine so it is a 3 step reaction. So, what is the suggested product, suggested product is I say, boron and this is coordinated and this is this that means, now it is BF 2.

So, BF 2 has been incorporated, 1 fluoride is expelled now, how do you confirm it, we are now we do not go to wet lab and do there, we all go to the spectroscopy lab only.

How do you know there is a BF 2, how do we know, spectroscopically, NMR through which NMR.

Student: ((Refer Time: 54:33))

Fluorine so 19 fluorine so what should be nature of the pick so you will get a singlet now, what is the multiplicity. See mind it, how to evaluate coupling, when I say coupling would take this, which side of coupling will use the for example, as quickly I will give you the let us say, you have something like this, what you see about this. You will see the doublet, because of the hydrogen, we always just jumped to 1 2 3 but you are ignoring the fact that, this carbon is also have a nucleus called 13 C, that can also coupling that can also coupling.

So, you have to take care of the abundance, abundance also you have to keep this in mind, so whenever you study the nuclei, you have to have the frequency known, you have to be stream quantum number known, you have to abundance known. And then whether it will appear or non appear or whether you will see or not see that, all depends on your spectrum. Many times recall satellite spectrum, satellite pics, satellite pics are nothing but those small couplings, invisible couplings any case.

So, in this case what you will see, that boron so that means, boron would split this fluorine, what is the splitting pattern should be, formula is 2 n I plus i. In this case, n is 1, boron 11 is 3 by 2 and quadrate so it should be quadrate, find what else nitrogen population is very low but this hydrogen. So, 1 2 3 4, 1 2 3 4 so 4 bond coupling is possible and because you have an s p 2 atom here, boron is electron deficient so you have s p 2 clouding.

So, it should be that means, this is the fluorine would appear as a doublet of a quadrate so likewise what should be these splitting pattern of the boron then. Boron, you have to think about this, fluorine is population is very high so that is why, you could see the hydrogen coupling also, But, in case of boron, the population is not that high but boron should be split by only fluorine. So, what should be the multiplicity so like this actually, you can just quickly establish that, boron is there, fluorine is there without much problem, it has been a regular practice now.

Routinely, heterocyclic chemistry do all these experiments so I think we have talked about most of the important things I think I guess then it is a matter of practice and use. I think, we will take care of… so next time next class, we will be talking about actually the reactivity, what does nitrogen do, list let us say, question I will give you the question. Let us say, you have a carbon cycle, you put a nitrogen, what sort of reactivity difference do you like to see, which will arise out of nitrogen, cyclo action as a cyclo-action for example.