Heterocyclic Chemistry
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Lecture - 5
Overview of Structure Determination in Heterocyclic Chemistry

Good morning, so today's topic is the first topic of course, as usual and all of us know that, structure determination is often taught in one semester, sometimes two semester, sometimes for few years, such a vast subject all of us know. But, you studied in the B.Sc, M.Sc and then again we are going through it, but this is a kind of a special topic, subject is special heterocyclic chemistry. Similarly, the structure determination in heterocyclic chemistry also is tough, why tough, I will give you some of the examples basically today. And also we will stress upon the use of carbon NMR and nitrogen NMR, these are the more more useful techniques in heterocyclic chemistry, why difficult, etcetera, all these things actually just basically will give you some ideas.

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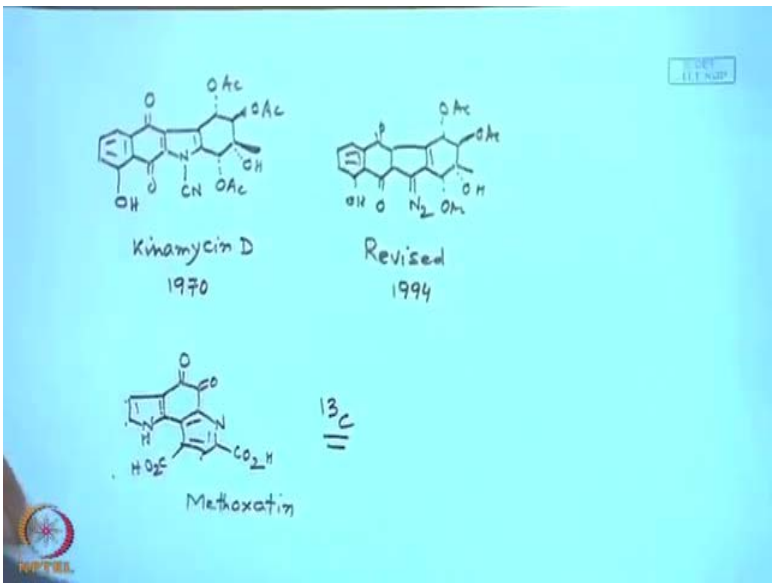

For example, a topic which could be from my research area and this is a molecule, which was you see here, I am just drawing the structure, it is a little big structure zone. It is a big structure, we say a big structure here and then you have this coulomb motive and a double bonds then you have O A C and here also one O A C. So, likewise methyl group, it is a beta methyl group then prehydroxy then a O A C group. So, you see then what

then the nitrogen is substituted by cyano group, which is called cyanamide and the name of this molecule is a kinamycin D and which was isolated in 1970.

And then structure was established on the basis of NMR, IR, etcetera all this thing including X ray. Then in 1994, somebody like Steven gold from Oregon state where I worked, he found that structure is wrong. What could be wrong, actually she mind it, this was established by an X ray examinations, X ray crystallography. But, eventually in 1994, here is the OH group of here, he could show that, the real compound, what could be the real compound?

Student: ((Refer Time: 03:32))

C N should be N C acetonide, basically because this mass is incompatible with this structure, all of the functional groups in agreement. So then what is the problem that means, this particular compound defied the crystallographic determination, structure determination. And eventually, it was found to be a molecule of this kind, is a bench in the known kind of a molecule. So, everything remain as it is O A C and O A C here then methyl group then alpha hydroxyl, alpha O A C and what.

And you say, nitrogen compound which is quite unusual, all of us know di isomethane is pretty unstable, diphenyl di isomethane unstable, but this is sufficiently stable to survive in naturals products by microorganism and it could be isolated, it could be chromatographed, it could do all kinds of things. So, what it means that, this is just an example, where the structure determination in heterocyclic chemistry could be too complicated, where you had all kinds of hydrogens and acetyl acetone, nothing was changed.

But, when it comes to the heterocyclic part, this is the molecular change that means, X rays was unable to map the M C N and C C N, C N N unit. Likewise, let us look at one more molecule, here you have a pyrrole moiety then ortho quinone kind of moiety they are and then you have a pyridine and nucleus and then carboxylic acid, this molecule is a known as a methoxatin. So, if you look at, how many hydrogens are there all together, there are only five hydrogens and there is no aliphatic hydrogen, 1 2 3 4 5 6 hydrogen, 6 hydrogen.

But, out of which many of you know that, in NMR under normal routine experiments, we do not detect the carboxylic hydrogen, unless we stop the exchange flow process then what else then you have all this aromatic hydrogen, etcetera. While from the chemical, you can make out somewhat as you will see, you can make quickly, I will give you some examples, how to distinguish pyrrole and pyridine by just by proton NMR, you can do it very quickly.

That means, from there you can make out that, there is a pyrrole unit, there is a pyridine unit, but how to ascertain the position of the nitrogen is tough. So, there are OH, classically people should do by degradation means, bigger molecular into smaller pieces. Then you write down the structures, determination structure, then of course, then do the little back calculation to find out the structures. For the such molecules, one thing which could be important is this carbon 13 NMR.

What is the use of carbon 13 NMR, first of all it is a high resolution NMR, it works for a wide range, all of us know. In addition, it is particularly useful for the carbonyl compounds, that you have to remember. And carbonyl compounds are nicely distinguish, let us say you have an ester, you have an amide, you can quickly distinguish them. Especially, if you have a carbonyl group, ketone carbonyl or aldehyde carbonyl, they can be distinguish very easily from this other carbonyl groups. So, often we will say that means, in other words, for molecule which are proton poor, proton poor means that very few protons then structure determination is very tough.

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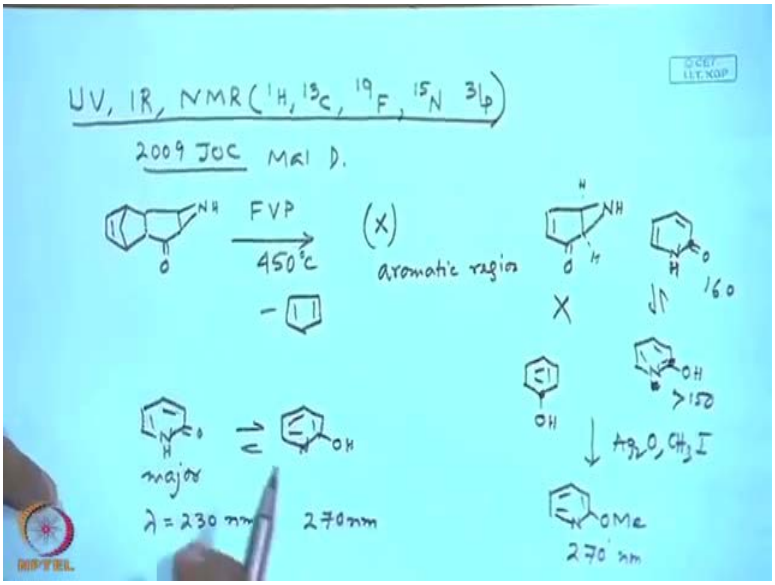

But yet, but what are these typical methods, I think often you will see here in books, in books you will have UV, as usual IR then NMR. Then within NMR, what are the nuclei of toulene, there are plenty now, about 40 different nuclei are regularly investigated to find out this structure, 40 more, many more means, including silicon, iron, cobalt all this, tin, aluminum, boron, all this. So, but commonly in heterocyclic chemistry, will be dealing with proton carbon and...

Student: Fluorine

Fluorine, I will take fluorine, fluorine also important nucleus, phosphorus, I will put that in the back side, first 13 1 phosphorous and I will have to put something more here, which is 15 nitrogen, this is very important one. Because, most commonly we encounter nitrogen, so these are the nuclei in heterocyclic chemistry are very useful. There is a group of compounds, phosphorus compounds so but if you go to the Silver Styne's books, what will find, there is no chapter on UV.

Let in be, then what useful, but I give you only two examples today, which are of recent examples, which are recent times. And even today, let UV can be useful in heterocyclic chemistry, in normal carbon cyclic chemistry, etcetera, UV may not be useful, but in heterocyclic chemistry, it is still very useful. I just give you two example, one is from my paper and all form other paper and then one paper published in last 2010 that, how could UV was used.

For example, we did a chemical reaction and the molecule looks like this, ((Refer Time: 10:38)) have a cyclic arylidene, so arylidene is a cyclic by tricyclic or into pentacyclic or whatever you say, this was the molecule. Then we did a reaction for fan vacuum pyrolysis at high temperature, which is at 450 degree centigrade. I do not know whether you know or not, the technique called fan vacuum pyrolysis, what is it. So, you say normally it is high temperature reaction beyond 300 degree centigrade and vapor phase reaction.

That means, you vaporized the solid and then allow to pass through the preheated oven under vacuum. That means, when you allow it to pass fully preheated oven and the contact time with the heat is less, this is just for a few second maybe. So that means, the if it is unstable, after formation, immediately drawn to the cold trap. So, I mean, if we have a ((Refer Time: 11:53)) in our lab, how many apparatus you can do this. And then we got a compound here and as usual, when we took the NMR, NMR was too complicated.

But, one thing which was clear that, it was not in aliphatic compound, all the peaks were present in the aromatic region. So, in NMR aromatic region was identified, so what is the product, this is the kind of first report is new way of making an heterocyclic compound. One thing I can tell you that, flash vacuum pyrolysis exclude cyclopentadiene that means, say reverse electro ((Refer Time: 13:00)) reactions. So, one would expect that is so the product should have been this one, cyclopentadiene arylidene, but unfortunately the product was not this one, because it is a aliphatic, you have aliphatic hydrogen, all these things.

Now, alicyclic hydrogen I should say, but those were not present, so what do you expect then I will give you the structure state without spending much time, the structure is, what is 2 pyridone, it is a special kind of a pericyclic reaction, pi to a, pi to a, pi to s. So, what can all do that, now this compound also could be, they also could be 2 heterodoxy pyridone. So, this was the problem actually, so how to establish that?

Student: ((Refer Time: 14:16))

So, how to establish this that means, it is the problem of a tautomeric mixture of compounds, how to establish which are tautomers are present in the molecule. Let us say, if you are handling with beta cadastros, ethyl actoacetate, you can quickly see it by

proton NMR. Because, in all form hydrogen is there, that comes hydrogen bonded, because the hydrogen bonding, it appears at a point beyond 10 or 12. So, you have nice hydrogen bonded proton can be visible in proton NMR, that is the ((Refer Time: 15:05)) tautomerism in as shown in simple cases could be easily established.

But, in these case, how do to it, if you look at the NMR and if you see the NMR, you can actually propose both these structures, because this part is same, double lead, double lead, double lead, all this, etcetera. And this N H I had basically, we have to distinguish between N H hydrogen and OH hydrogen, how to do it. If you do normally, for if is the ((Refer Time: 15:37)) hydrogen, all of us know, we do D 2 exchange, this will walk actually both the structures.

So then what is the other proposition, if you let us say, few minutes ago I said that, carbon NMR is a very important one, that is what I thought in fact, but it did not work. For your information, this is what paper published in 2009 and JOC and I do not have page number, but if you just go through this certain, go to our name, this will find this. So, but you have to also keep it in mind, if you have an oxygen attached carbon, that also has very high chemical shift value. For example, a chemical shift value of this carbonyl of the pyridone should be around any guess?

Student: 200, 210

210, no you have to little careful, it is amide, ester is around 170, amide means the first two digit is 1 6 and the third digit could be 9 or 1 or even less, so it is less than 170 for sure. And for example, if you take phenol, these are the thing you have to be little for example, if you take phenol here, what is the delta value of the carbon having the hydro oxyl, any idea. If you are practicing the organic chemistry, especially research scholars, you have to keep in mind I mean, not exactly, roughly. For example, a benzene what is the base value of the benzene carbon NMR?

Student: ((Refer Time: 17:35))

carbon, no carbon roughly you have to remember, 128, so add another 30 how much?

Student: 158.

So, 158 so that means, if you put an oxygen then big increment of this, that is the very unique property of carbon 13 NMR. So, this is very that means, if you want to identify oxygen continuum aromatics, it is easier rather to conclude with carbon 13 NMR. So, in case of pyridone, let us say 2 hydroxyl pyridine, what has to be estimated with the carbon 13 NMR, having this carbon chemical shift of this carbon having this OH group. So, it was benzene 120, another is 150 then you have a nitrogen, electron with the nitrogen.

So, it definitely could be greater than 150 that for sure, this is around 160, so it is very difficult to distinguish, I do not like exactly remember what are the value, but it is complex. So, eventually, but people will suggested that, if the molecule this kind exist in a literature, there will be ratio of 9 is to 1. That means, 9 is to the ketone form and 1 is the quinole form, but how to establish. The way it was established is like this, this is standard protocol available in the literature and this was the major form.

And UV in this case was useful and the UV was 230 nanometer and the lambda max for the other compound, this one and this was 270 nanometer. And so but we have not established the structure of the product of the reaction, because it a mixture then after you have both, 230 and 270, so you have to had a pure compound. So, what we did, we reacted this mixture with silver oxide and methyl halide and eventually, we locked this and this experiment, obviously this locking is this one and it...

Now, you see this one is very close to the quinole form and this particular compound given NMR of this UV of 270, exactly 270. So that means, because a substitution of hydrogen by methyl group would not have any UV difference. So, both the compound; that means, locked enol form was checked and it nicely match. And so at least we could assume that, the compound was the in this form, but we cannot say, which one is more, which one is less.

At least, the conclusion was that, this reaction gives a pyridone, but from this experiments, we could make out only that a pyridone form, but still we could not establish, whether it was a... Then you go back to the UV, etcetera, all this thing again to establish or the NMR rather to find out. So, once you know that, pyridone is formed then you can go through the NMR again and there are many other techniques called solvochromatic studies from, there you can find out the ratio of the different all forms.

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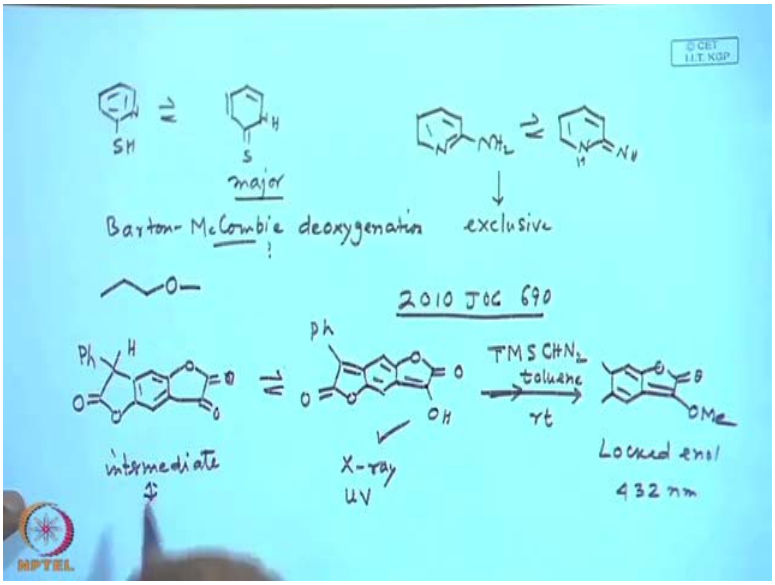

And for heterocyclic chemistry, this prototropic, tautomerism is very important, let it me give you one more example. Let us say, if you have napthelene sulpha substituted pyridine let us say. So, again all of us can guess, the equilibrium would be this thio equilibrium on this kind. That means, pyridine to mark kept in even equilibrium, but which one is more, which one is less. In case of oxygen, it was pyridone was the major, 9 is to 1.

But, in this case, what should be the, again it is a guess, again this ion is the, this one is the major one, but this is in equilibrium. Most of the reactions were the react to mark kept up pyridine reacts, they undergo reactions through sulfur and why do use to mark upto pyridine.

Student: ((Refer Time: 23:05))

To mark upto pyridine...

Student: ((Refer Time: 23:07))

Louder...

Student: ((Refer Time: 23:09))

No, LPG, there is some other compound, that is benzphyl sulphide, but it has to be volatile though, but at two mark, it is not volatile. But, it is used as a reagent in a very important reaction called bottom...

Student: ((Refer Time: 23:32))

Louder...

Student: ((Refer Time: 23:34))

Bottom...

Student: ((Refer Time: 23:37))

No, bottom is famous of many things, nitrosomonas reaction, all this thing, but Barton McCombie deoxygenation. I may note exactly spelt this McCombie something like this, this spelling could be little wrong and it is called deoxygenation. What is it, it is nothing but we have to also know this things, this is very important reaction, you just go through ((Refer Time: 24:16)) and this is there, which is a Mccombie reaction. And if you have this oxygen up here and then you have to some derivatisation you have to do with this to mark up to pyridine something, I have forget little at this moment.

So, something then you have to do radical reaction, I think it is a kind of radical reaction, at this moment I have forgotten, may be you have to see, any case. So, if you have sulfur and oxygen, the major tautomerism the ketone form and go to next one and the other possible structure, let us say if you have 2 amino pyridine. In most cases, this is there and there are other possibility then the other possibility is corresponding amine form.

I mean, it is very difficult to distinguish them, but again from the UV study, you can make out that, this is purely aromatic and this is not purely aromatic one and for nitrogen, it is the exclusive form that is, the amino form is the exclusive form. Let us take one more example, this is a nucleus, I will be talking about benzene then furon on structures with two compound then other side we have again a furon, but looks like a lepton and hydrogen and this is phenyl.

Now, but normally, whatever we know of, from there we cannot really write an equilibrium, we do not write in equilibrium, because ketone tautomerism requires say,

ketone and alpha hydrogen, that is there here. So, one can assume that, there is a tautomerism towards this direction, but it has been eventually established again through UV study. Let this the initialization, the initialization actually breaks the aromaticity, and the compound that is found in all that is found is this ones.

And so this is actually, the equilibrium lies here and this particular compound in all form has been crystallized and examine by X ray and the structure is proven now. Structure is proven of course, it requires all kinds of study NMR, IR, UV, everything, everything was studied, but this was the special feature. I mean, what is the driving force that we have to see and that means, this is a published work again and this was published into 2010 JOC page number 690.

So, X ray, what is this all form and then you have to support the X ray also, because very first example I said, X ray is not the final answer, X ray could be wrong, especially when you have ((Refer Time: 27:55)) and other things. And it was also supported by UV and this UV in this case, so obviously, we have to first know, what is UV and we do that, what they did reaction here, room temperatures reactions. I will write this, TMS CH N 2 and toluene is the solvent, the temperature is room temperature, so what do we guess?

Student: ((Refer Time: 28:38))

Dimethyl ether O CH TMS, yes that is what I guess, but eventually actually, the reaction that take place, I will just write only part structure here, this would be ethyl ((Refer Time: 29:11)) goes out under the reaction conditions. Because, it is slightly acidic hydrogen, so acetic hydrogen it comes out, so it is just like basically high boiling substitute of dimethyl ether. And so what is it, it is again a locked enol or in all ether and if you look at the UV of the starting one and this one, this has an UV 432 nanometer, so it is I mean, similar kinds of compounds of this in all forms they had been.

But, what is the diverging force here, that is what we have to find out, what is the driving force to break the aromaticity of the starting compound, this is actually intermediate for a commercial dye and I could not get the literature, because it is a patented, but it was very useful and commercial available dye, but I cannot tell you the purpose, for which they are meant or they are commercialized and what. So, when you guess, why the in all form should be more stable are more predominant and then this aromaticity.

Normally, aromaticity is the driving force for most of the reactions, D aromatisation is not, but in this case, something different.

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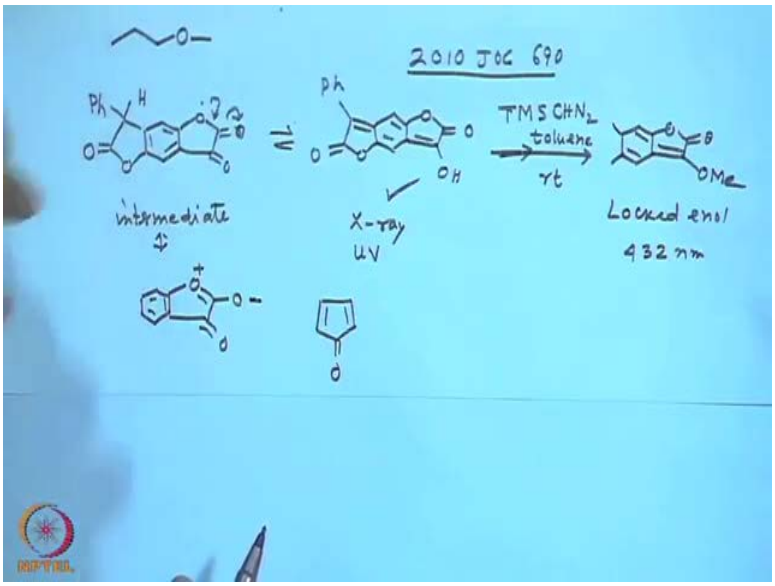

And it is if you draw the residing structures of these molecule, what you will find, it could be... If you draw the resulting structure here, so you have a five membering and oxygen and this is nitrogen. So, once again this is a kind of the sydnone structure, polarized one this when discharge resides also at the skeleton. So, this is sydnone kind of a structure, so can you make out and that means, it is in a regional field such a structure. And this structure is not stable one within the, just like if you recall, I think all of this recent seminars, I raise this point then this molecule cyclopentanone is a unstable molecule today, even today it is not isolable.

Student: ((Refer Time: 32:02))

So, this anti iodicity is actually it has this molecule for the ionizations, but this example is to tell you that, the UV is still required in certain cases, some especially keto enol tautomerism and this case like this enol ketone forms. And so let us look at, maybe one more important area that is, a UV we talk about.

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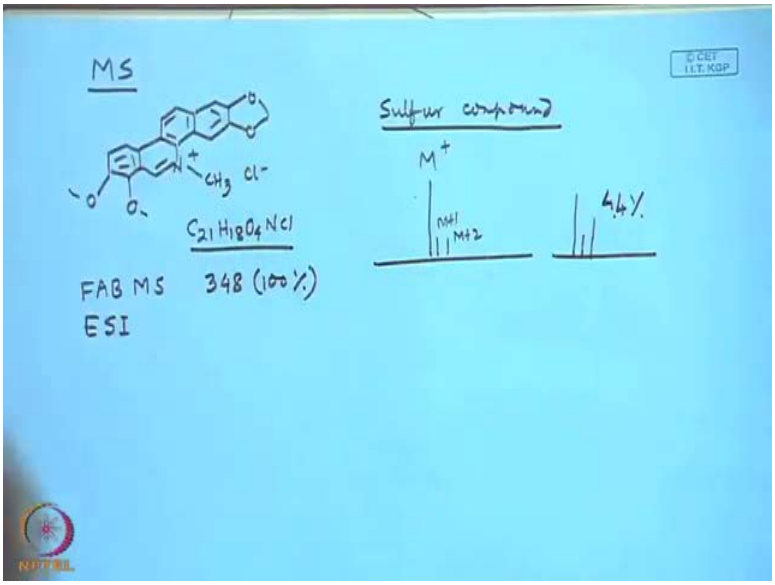


And then all of us know this mass spec, mass spec is very useful then we will go to NMR. In NMR, we have all kinds of experiments, in mass spec how to use mass spec in heterocyclic chemistry. All of us know, nitrogen odd rule, what it tell, this nitrogen rules in mass spec, it be molecular ion peak, if the molecular ion peak is odd then the compound must have odd number of nitrogens. But, that is not always true though I mean, first of all it is not true, because of what, because of the presence of even number of nitrogen, that is a one thing.

Secondly, you have to note that, molecular ion peak may not be visible, that is the important thing, it is not visible, it could be misleading. And thirdly, we could be this even odd number of nitrogen compound may be accompanied by halides. I have an example here, this was published in 1995, I said in alkaloid what we will see, if you do this chemical analysis etcetera, will get the molecular formula, etcetera.

See, it is heterocyclic molecule and you have clusters here then this methoxy and methoxy all these, I said basic state and molecular formula is found out to be from analysis, which follow mass spec is found out to be C 21 O 4 nitrogen and C. So, what you see here, just you have a single nitrogen, but if you recall the FAB mass, this is no longer used, FAB mass is not very popular after the invent of ESA mass. You have to know this terminology.

Student: ((Refer Time: 35:02))

FAB is first atom must to take, this not popular, now it has lost it is popularity, now the most common one is what we have now ESA Electron Spray Analyzation. So, this mass actually, mass spectral data value 348 has the highest peak and this was 100 percent. So obviously, one would jump to the conclusion that, this peak is due to the molecular ion peak and this even number. So that means, it must have even number of nitrogen, but what you see here, eventual conclusion that, the compound is not.

And that means, you have to little quasi, this is just an example, I have many more minimum rather I pointed the information here , but I do not want to give you those information. But, this is just an example that allow molecule has odd number of nitrogen...

Student: ((Refer Time: 36:16))

Which one?

Student: ((Refer Time: 36:20))

No, this is methyl group, this one...

Student: ((Refer Time: 36:26))

Yes, it is actually that, this is a natural product, so natural products and it has a hydrochoride salt, what else. The other I mean, mass spec of coppers, it gives you the exact pressurized molecular formula, so if you have a hydrogenesis mass and the quickest, if you do not have a hydrogenesis mass, you can also make it easy of it, especially for the detection of the sulfur compounds. How to detect sulfur compounds, to say you are given a molecule and you have to find out, whether the molecule content is sulfur, how do you do, it could be aromatic, it could be non aromatic, it does not matter, how do you do.

So, sodium fusion test no, we do that, yes many times it is very useful, but most often probably from all now years, nobody will do that those sort of test. I mean, theorically, one can do it by ESCA, electrons calling microscopy for chemical analysis, electron microscopy for chemical analysis ESCA. Then XPS a proton electrons scope, so all kinds of spectroscopy are there, which will basically find out the ionising potential or binding energy for injection of the electrons.

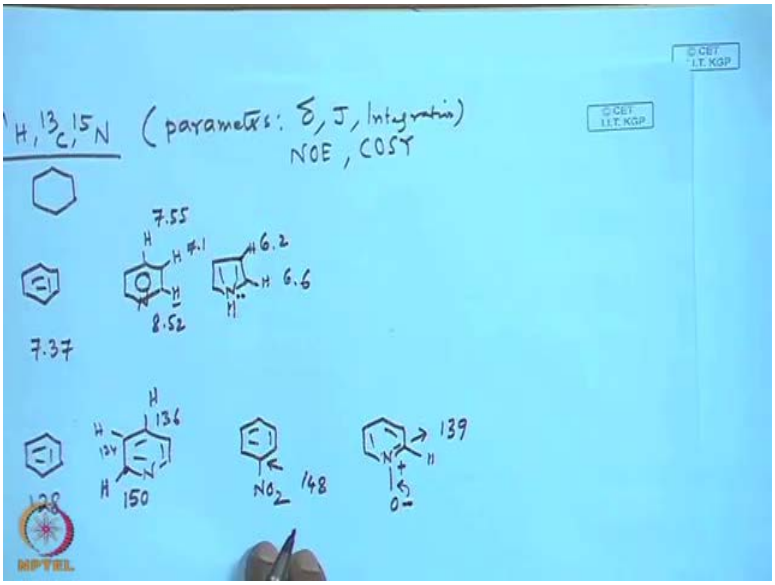
But, other than that, ask for the chemist, actually base useful is the, I mean if you like to know that mass, mass is very important. If you have a record, you must here, let us say this is M, this peak is called as a M plus ((Refer Time: 38:27)) then immediately after, what you see here, M plus 1 of course, then next what you see M plus 2. But, in case of sulfur, if you are just careful, in sulfur what will you find, M then M plus 1 and then M plus 2 is little longer, that just basically they all are minute thing, but this give you nice indication, why?

Student: ((Refer Time: 38:59))

34 no, but this natural abundant in case of nitrogen, nitrogen let us say 14 15, what is abundant of nitrogen 15, how much, this is also very important in NMR spectroscopy. What is the natural abundant of nitrogen 15, something like 0.4 percent that means, 99.6 percent is basically nitrogen 14 or 0.4 percent of this one. And then in case of sulfur, that 34 sulfur is 4.4 percent, so it is significantly high, so from there, you can actually make out, whether the sulfur is present or not.

And we has to do small calculation, from there also you could make I mean, there is a old version of ((Refer Time: 40:01)) would give you small calculation to find out that, how many carbons are there, how many hydrogen are there, how many nitrogen are there. But, these are, if we have hydrogenous mass, straight away you get the molecular formula done, so there is not a problem at all. But, so that means, from there also you can make out, but unless if you do not have then of course, you have to go to something else. And rest is basically, next thing will be proton NMR, how do we distinguish, let us say I will give you, basically I will give you the problem.

(Refer Slide Time: 40:40)



That means, in NMR, so you have proton and then 15 NMR and of course, the carbon NMR, with this the H, C, N seems like this. There we have plenty of experiments and then you have to also read the parameters, what are the parameters we deal with, chemical shift what else, coupling constants, integration that is all. And anything else, yes other experiment would require NOE...

Student: ((Refer Time: 41:26))

COSY, that means correlation spectroscopy, these are this and correlation spectroscopy could be of many kinds. And so if you that means, just NMR is too complex, actually again for NMR, there may be 50 different experiments are there, may be more not less and all kinds of NMR programs are there to evaluate coupling constant, to evaluate chemicals shifts, all these things. But, some of them are reliable, some of them are not, but we had again trying to calculate chemical shift by using standard technique called DFT, what is DFT?

Student: ((Refer Time: 42:09))

So, you all of us know, so and how do we quickly, basically you have to do little quick test here in case of the aromatic chemistry. Suppose, you are expecting a compound could be a pyridine or it could be derivative of plus pyrrole, how do I do, how do I evaluate without going to the chemical and other things mentally. In NMR, reference

compound is a very important, just you know just one or two values for reference compound then you can extrapolate the chemical shift.

For example, all of us know, for benzene what is the chemical shift value then what should be the chemical shift value of pyridine. You have three different kinds of the protons, grossly if you do not remember any value, let us say you are handling the pyridine, you have taken the NMR, how do you quickly come to the conclusion that, that is the NMR of the pyridine?

Student: ((Refer Time: 43:23)

No, which one you look for basically, let us say I am expecting or suspecting this molecule as a pyridine. Now, we check the NMR, now we have to conclude that, this is a pyridine or not pyridine, how do I know. Now, in case of let us say in case of...

Student: ((Refer Time: 43:51))

Chemical shift should be higher, because in whole system you have benzene, now carbon has been substituted by more electronegativity atom. So, overall somewhere at some point, one of the hydrogen should be down field shifted, that is all. So in fact, in this least case, you can see this one is 7.55 and this one is pretty close to benzene, it is 7.1. But, this one, the one that is alpha to nitrogen, it is 8.52. So that means, you do not have to remember the values, you just look for a signal, which will appearing at an higher delta value.

Similarly, if you are suspecting let us say pyrrole, so for the pyrrole what should be the value, just guess, again you put the electro negative atom. So, I mean, you can always expect a little high delta value, because you have, but at the same time, you are now a heterocyclic chemist. We know that, the lone pair of electron is delocalized and it is shared by all the carbon atoms and that means, at least two electron divided by five atoms, two by fifth electro densities are around.

So that means, electro density has increased, so the chemical shift up field that is all, that means, what is the reference point, benzene. So, it should be on the right hand side of benzene and in this case, what will find again, this is 6.2 this hydrogen and this hydrogen is 6.6. So, basically just your reference point, either benzene or chloroform, if you see

something on the right hand side, lightly to be this as usual compound, five member heterocyclic compound.

And there are plenty of books I mean, there are very few books, so which will give me, but initially we have purchased one book called hand book of hetero cyclic chemistry, there you will get all these details data, but roughly you have to have this idea. And let us say, now if you let us say, we go for carbon, this is for the proton, similarly you go for the carbon here. What is base value for the benzene...

Student: ((Refer Time: 46:25))

120 few minutes ago I said, now let us say if you are suspecting the pyridine derivative what you expect, pyridine divert at down field. Let us see, how much is it, let us the remotes test one, in the remote test, carbon from hydrogen, this is 136 and this one is 124. This meta one, you see here meta one is little, that gives you polarized structure, because of that, it is less and then as you can see here, the one that is address to nitrogen...

Student: ((Refer Time: 47:08))

150 remember few minutes ago I said, the oxygen is plus 30, so roughly that means,. So, this is pretty diagnostic that, this carbon have chemical sheet line. So, I mean, you can just draw the resembles from your compound of this kind for example, what should be the chemical shift value of this carbon, you know now, the base value 128. So, you have a nitrogen now attached to it and the electron will then go. So, again 150, well in this case it is close 148.

So now, heterocyclic chemistry again, so let us take another molecule, I think all of us know this molecule, what is it called?

Student: Pyridine

It is pyridine enough site, you take pyridine, just hydrogen peroxide, acetic acid, acetic acid it will state away give this compound, ((Refer Time: 48:17)) crystalline compound and it is reactivity is different. You all know the resonance, because of this resonance of this oxygen electron pair and what you will find this pyridine thing is now a electron reach compare to the ((Refer Time: 48:40)) pyridine. That means, if the electron density

increases around the ring, obvious conclusion would be that, the electron density would be increased means, chemical shift decreased.

And that is what, you will see for this carbon here now, so it is 139, so you can just extrapolate all this thing, we have the much problem. And so let me think basically trained in electro density or this chemical shift is important here then there are examples also we will give you, where you can go for the coupling constant.

Student: ((Refer Time: 49:21))

Just draw this structure eventually basically I mean, it is very difficult at the moment say, you have to just draw this and see, which one has higher weightage and which one has not weightage. You say polarized one, not like benzene it is like homogenously delocalized, in case of heterocyclic chemistry it is not rightly I mean, all the carbon will have same electron density, because of the polarized structures.

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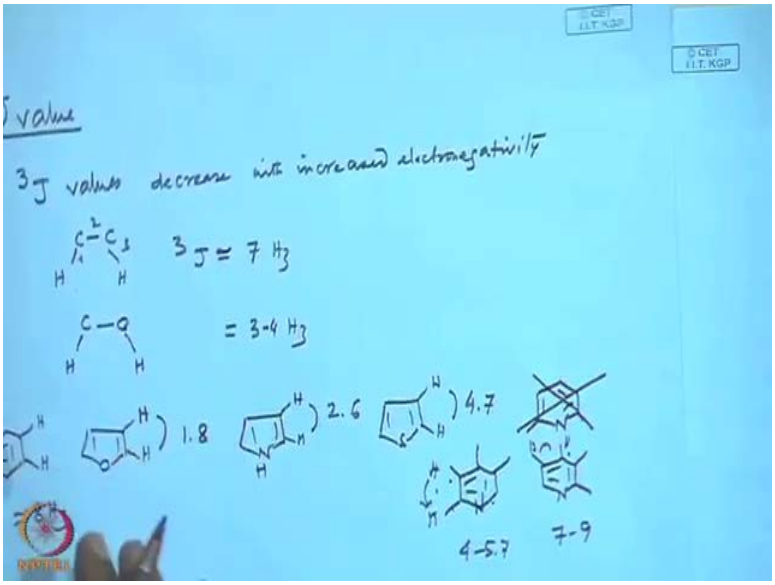

Let me give you, this is very important one J value, J value is very important again in heterocyclic to distinguish the heterocyclic nucleus from non hetero cyclic nuclei. How do I know, there is a guide line, J value I think this is standard formula, J value decreased with I think with increased electro negativity. When I say J value that means 3 J, 3 J value is decreased with increased electron density. What is it mean, it is mean that, if you

have a coupling, let us say this is all of us know, these two hydrogen 1 2 3, so the coupling between this is known as 3 J.

What is the standard value for aliphatic compound, you have to remember, coupling constant 7 Hertz. Let us say, ethyl ester, methyl ester, ethyl ester means you had a quadrate and electric plate. For the coupling constant, if it was a aliphatic one, it was to be around 7. Now, just what you do, just change this carbon into an hetero atom and put hydrogen. So, what is the coupling constant, now the coupling constant should be between 3 to 4 Hertz, that is what I mean to say.

That if you incorporate an electronegative atom into this skeleton of a 3 J coupling then the coupling constant decreases. This is the very diagnostic, because many of you know that, we often deal with furon compounds. In our lab, when I do the furon compounds, so our reference again let us say, this hydrogen and this hydrogen and our reference is here 3 J in benzene. What is the coupling constant, for benzene ortho hydrogen...

Student: 7 to 8

7 to 8, standard value is I think is 8, so now you see, what should be coupling constant between these two hydrogen in furon. Yes, even electro negative atom by the way and this is of course, the angle, etcetera also have changed, but this value is, I will give you this value is 1.8, very small. So that means, you are having in aromatic protons and then you see coupling constant, very small coupling constant, almost always likely to be heterocyclic compounds.

For example, let us take a another example like pyrrole, in this case of pyrrole, this hydrogenous would couple to each other with a constant 2.6. In case of pyrofil, you can see electron negativity decreases in this order furon, pyrrole and pyrofil. Now, so what do you expect, it should be little more and in this case, it is ((Refer Time: 54:02)) I mean, to give you one more example probably, this is quite interesting. Suppose, you are expecting a dye substituted pyridine let us say, I just mono substituted pyridine for example.

So, there are two possible structure, let us say this is a possible structure and then another structure could be this structures. How do you distinguish, it is very difficult, but let me give you one most structure, I think without that, I think this is better option, this one let

us say. Let us say, forget about this one, let us say between these two, this dimethyl pyridine, these dimethyl pyridine, how do you distinguish them?

Student: ((Refer Time: 55:07))

Yes, ((Refer Time: 55:11)) of course, that is the number 1, number 2, chemical shift also useful, you have two down fill protons here, in this case one. Thirdly, you can just use the coupling constant values, this coupling constant this one, these two hydrogen indicated hydrogen could be more than these two coupling constant. That means, this is what, 2 3 hydrogen and 3 4 hydrogen, 2 3 hydrogen has a coupling constant, this has a coupling constant 4 to 5.7.

And if you go to the 3 4, the coupling constant goes to 7 to 9, what does it means, because this hydrogen are closer to the nitrogen, that is all. If the hydrogen are projected electronegative atoms, the coupling constant likely to be less, so this is very important diagnostic. And so I think a let me just quickly go to one more example then in tomorrow we will talk about this nitrogen 15.

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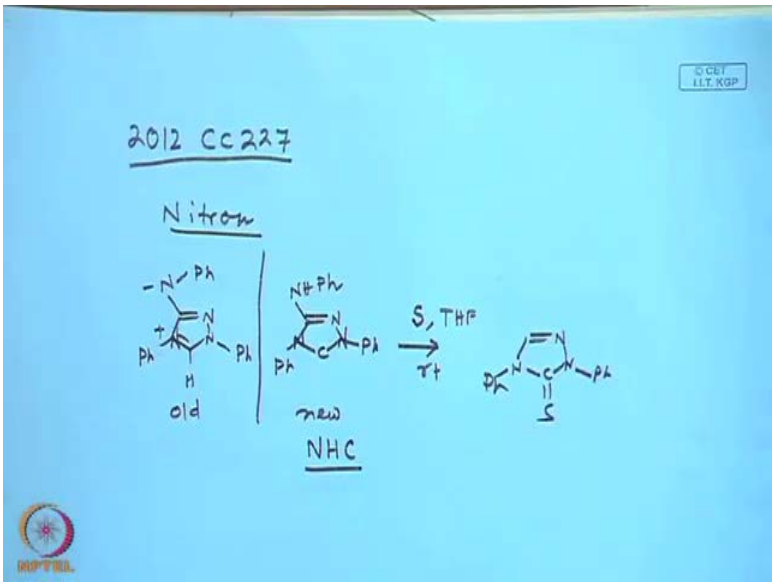

This is paper from 2010, this is fresh paper actually and this is a CC means, chemical communication and page number 277, this is very interesting compound. Only just in last month, they are found different structure for example, there is a structure, the name of the compound is the I forgot, I guess nitron something like that, from nitron not n i

nitron. And the structure was originally proposed to be triazole, this is nitrogen and nitrogen here, hydrogen and this mind it and this was the structure and proposed and people believe that, this is the structure.

But, only recently, a group of scientist has proposed that, this structure is wrong, this structure is this, there is a nitrogen up here, triazole, so nitrogen should be also here and also here. So that means, only on left what you see, this was the old structure, old one and this is new one, difference the old one is proposed to be a signone structures or mesoionic compound, charge lying outside this, there is no proper regarding structure. And in this case also, the right hand side also this new one, this is not a really structure and what is it, by now all of us know, who will take up this topic for research scholars, anybody is it interested.

If you know NAC, anybody interested in review NAC, because all research scholars have to write a ((Refer Time: 58:48)) paper, write it on paper and so pick up this topic NAC in heterocyclic carbene, nitrogen heterocyclic carbene. What do you see, the carbene is a stable now, this molecule is commercialized, but this is stable. And who is the discoverer of our stable carbene, do you remember...

Student: ((Refer Time: 59:17))

Good, which year?

Student: 1991

1991 and this is another carbene, 2010 you see in stable carbene, you can brought it, you can sell it, this is a nice one. But, how to establish this structure I mean, what did they do, basically they did a reaction with sulfur, just sulfur THF at room temperature. What is the expected product, expected product is nitrogen, carbon and nitrogen and this molecule here is this.

So, what do you see, carbon and again in example of carbon NMR, this carbon appear at 229. So, that means, carbon NMR is again useful for the heterocyclic compounds and so next time, we will have little more on these nitrogen heterocyclic and nitrogen NMR rather.