Circular Dichroism and Mossbauer Spectroscopy for Chemists

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Lecture – 13
Chirality and Biology – III

So, coming back to the original question uh posed by Soman. Is that why we talk about two different sigma? So, actually when we talk about that I am taking a mirrored image and looking into that particular reflection that we got and try to rotate it so that to see that whether it is super imposable or not? Over there when you are taking the mirrored image the mirrored plane is actually outside of the molecule. Okay

I did not put that mirror plane inside the molecule. So that is why it does not really matter where I am putting the mirror plane outside the molecule. Because over here, my goal is not to find whether the molecule itself it is reflecting because when you talk about a reflection plane, the reflection plane generally stays inside a molecule and that is not the case over here. Over here, what we are doing we are trying to get the mirror image as simple as that.

So, it does not really matter where I am putting the mirror plane so, anywhere you are trying to take the mirror image that will be the same. However when you are talking about the original improper axis of rotation S_n, over there what we say that we have to have a C_n axis of rotation that means there would be an axis of rotation which belongs in the belongs to the molecule and there will be a σ_h plane that has to be inside the molecule.

I cannot put that sigma plane outside the molecule because the symmetry element has to belong inside the molecule so that is the big difference we are talking about. So, during the time when I am trying to find out whether, I am having a media image which is super impossible or not. I am taking the mirror image outside. So that means that is actually going to have a sigma plane and now that mirrored image will obviously going to match the same result.

If I take a sigma plane in any of the possible plane present inside the molecule it has to be. So that is why now the change I can make it where I am putting the C_n axis, I have to put it just perpendicular to the sigma plane and only then I can say I have a perfectly ordered S_n axis. So, the big difference again when I am talking about a sigma plane, σ_h, σ_v, σ_d with respect to symmetry elements that has to be present inside the molecule that has to go through the molecule.

Whenever, I am talking about a mirror image of a molecule I am taking the mirror plane outside the molecule that is the big difference. Does it answer your question Soman? Yes Sir. Sir are you writing something? No, I am not. Okay So, any more question? Sir I have a question? Sir I have a question, yes yes go. Sir, actually the molecule molecules is of D_3 point group I know that but, I feel that the molecule means the four uh oxygen atom is there that containing a plane.

If we take that is a molecular plane and then I think that σ_h is present mean, I feel that it uh It is sigma, it is the σ_h or not.

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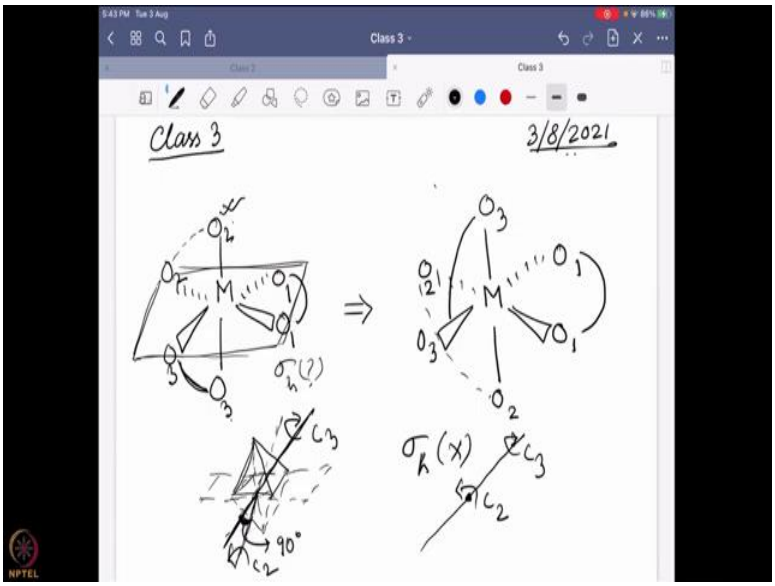

Sir, you get my question? Yeah, I think you are talking about this metal bound with 3 bidented ligand, you were talking about? Yes Sir. Sir, It is you have shown in that like that that one oxygen is uh upward to the plane and one is below to the plane but generally when we are talking about when we put in a means when we try to draw the molecule in a plane, we just saw that that four oxygen atom that is in the in a simple plane means it is a in it is a plane only.

So, in that way if we found that that could be the σ_h because C_3 is perpendicular and it will reflect the upper oxygen to the lower oxygen. um So, is it possible that that plane is the σ_h? So, if I understood your question you want to say like this particular four oxygen containing plane is it a σ_h or not? That is your question? Yeah, I feel that that is the molecular plane and σ_h also because that is the perpendicular to the C_3 axis also. Okay

So, let us take a route on that and let us discuss this molecule. So, now first of all first find it out whether it is a sigma plane or not? So, let us do a sigma orientation over there. So, first all the oxygen as it is we will draw first.

So, these two oxygen say I am putting O_1, O_1, O_2, O_2, O_3, O_3 for my understanding. So, O_1, O_1 will remain in the same plane, fine then this O_2 will remain in the same, this O_3 is remaining the same plane.

What happens to this O_2, if I am doing a sigma orientation or sigma operation through this plane? This O_2 will go down. okay This O_3 will go up. So, now you can see O_2, O_2 and O_3, O_3 have to connect, the oxygens are remaining but the connectivity is different. Yes Sir and that is why there is no sigma plane. Okay Okay Sir, thank you. Ok. Any more questions? Okay So, you might guys, you guys might have a lot of questions regarding the quiz do not worry about that we will have that at the end of the class.

And this is a little bit different quiz than probably you have faced so far. It is not going to be checking your, I would say like how much you actually, probably studied too much about this particular course? Or how much you studied the last two classes? Not much on that to be honest and it is obviously, not going to depend on how much you can remember? So, there will be a few questions where it will ask you a question a little bit philosophical in nature.

And that will require whatever we have gone through that class, on that particular portion how much we can use that particular knowledge, to probe those answers. So, do not worry about that too much. It is more of for my understanding like, if you guys are following the points I want to deliver or not and it has a minimal effect on your grades. Because I generally, over there will be grading with respect to like whether you are following the correct thought process or not and not really on that what is your actual answer. Okay

So, it is not a binary kind of mathematical question that if you have that answer you get full marks. If you do not have the answer you will get zero. Nothing like that so, the questions will be a little bit as I said philosophical in nature. So, you will put through your answers and then you will go through that but anyways, we will come into that little bit later. So, we will proceed forward and before that over there I want to write no σ_h plane present over there.

And the other thing over here is that this plane over here what you have drawn and actually it is better to see if you actually draw the octahedral side probably better. So, this is I am actually trying to draw the octahedral field. How it looks like so, it is called octahedral because there are 8 hedral or faces. So, C_3 actually passes through here Okay and your σ_h plane that you are trying to tell or go that is over here.

So, they are not really perpendicular to each other okay and then that what Soman was asking, what happens to the C_2? Now C_2 is over here it may look like it is actually not in the perpendicular plane that is because it is a line not a plane. So, now if I look into this particular angle this angle is actually 90 degree. okay Because it is actually a line like this and on the top of that I am putting my C_2 over here, if I look through this C_2 over here.

So, now you can see the C_2 is sitting perpendicular to that right because there are two lines. Because I am looking in such a way, it may looks like it is not. But if you look through the C_2 you can find the C_3 is lying like this so, this is the C_2, this is the C_2. So, they are actually perpendicular. okay So, Soman give it another try do not always try to look into a molecule, try to visualize in your head that is the best way you can see it. So, generally if you try to find out whether they are perpendicular or not.

The best way to do that is put your visionary angle or visionary direction through one of the axis or through one of the plane that is the best way to find out whether they are perpendicular or not. Okay So, give it a try later and if you still have issues please let me know okay So, okay Sir. Okay thank you. So, we will go to the next portion.

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So, so far what we have done in this particular class that we have gone through the molecular interaction, uh sorry molecular recognition that we, have find out that that is actually has a big role to play and we, have discussed that molecular recognition system has a big role to play with the chirality and that is why we are actually interested in chirality and then we figure it out biology is actually a system which actually has a lot of chiral centres. Okay

And those chiral centres are coming from the proteins. Coming from the carbohydrates and even from of the nucleic acids RNA's and DNA's all those things and again this chiral centre does not always mean it has to it have to have only a chirality present instead of the molecular ah level. That means that molecule with a carbon with four different groups not always.

It can have a secondary structure made out of like a polymer of a even a achiral molecule. But the secondary structure is such oriented that this molecule can be a chiral in nature. Okay We will come into that little later like alpha helical, beta sheet all these structures of the protein and how they are choral? Even though the original molecules which are actually making it may not be chiral.

For example glycine, glycine is not a chiral molecule right we, actually have gone through the structures and if you make it a polyglycine and this polyglycine can make a alpha helical structure and this alpha helical structure can be chiral whereas, this glycine itself is chiral. So, do not always look into what is the ah I would say that the backbone or even say like the primary units that is actually forming the polymers or the polymeric or the overall structure of a system, instead in in the terms of protein, carbohydrate or nucleic acids.

It is not always to be the the forming units has to be chiral the overall unit can be chiral. For an example nucleic acids, the nucleic acids the simple system the nucleotides they are not chiral. But when they make the RNA and DNA form the helical structure they become chiral. Okay So that we have learned and then the other thing we learned we learned what is an L amino acid? And we now learn how to draw a L amino acid and we actually learned, all the 20 naturally occurring amino acids and how they are actually drawn?

What is their one letter and three letter code and how they are actually defined over here? So, that we have learned. Now, the question comes in this particular fashion over here, Is that does this L amino acid and D amino acid really actually matters? And, what is the effect of the presence of L amino acid and D amino acid mixture in the system so that we will discuss in details today. So, the first question is if I look into biology.

In biology you will find L amino acids at the predominant ones so, if you find any amino acid in biology or it is coming from a biological origin. You will find it is L in nature and the L terms defined that it is actually having a particular special orientation of the groups of the carboxylic acid group of the R group of the NH_2 group. And they form in such a way that my amino acid structure.

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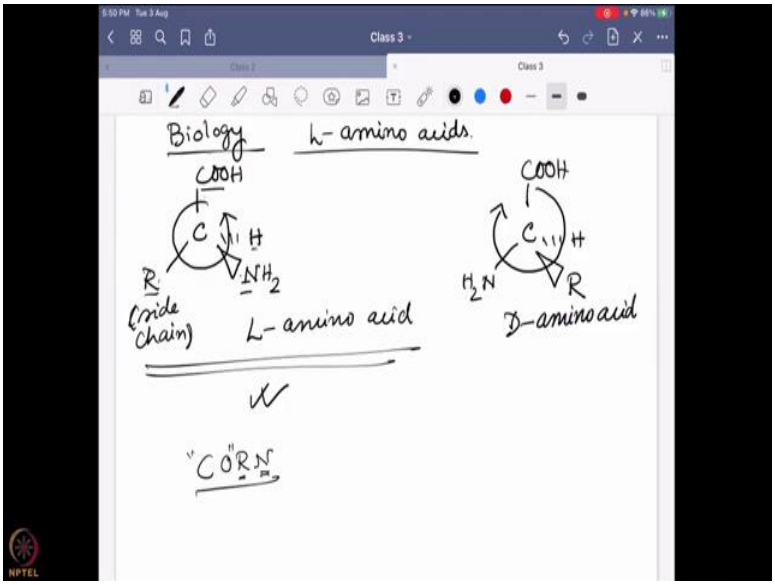

So, when you draw this amino acids in such a way the hydrogen goes at the back, carboxylic acid the R group which is also known as the side chain of an amino acid and that is the most important part because the rest of them are actually very similar for all the amino acids and they are actually makes generally the backbone of the system forming amide bonds. So, this is form in such a way that the if you connect the carboxylic acid group R group and NH_2 group they form a left-hand rotation or anti-clockwise rotation.

So, this is known as the L amino acid. Whereas if you take the opposite one, it puts the hydrogen over there now you put R group over here in NH_2 group over here. Now you can see CO, R, N goes to this side and this is known as the D amino acids. So, if you look into biology, most of them falls in this part. So, their special orientation is in such a way that the carboxylic acid group R group and NH_2 is to group form this left hand orientation which we already discussed as the CORN rule.

CO stands for the carboxylic acid, R is the side chain, N defines the amide groups. Now, the question is why it is important? So, for that I will give you some examples and from those examples we try to understand, how important the presence of the D amino acid or the L amino acid are for the functions of the biological entities.

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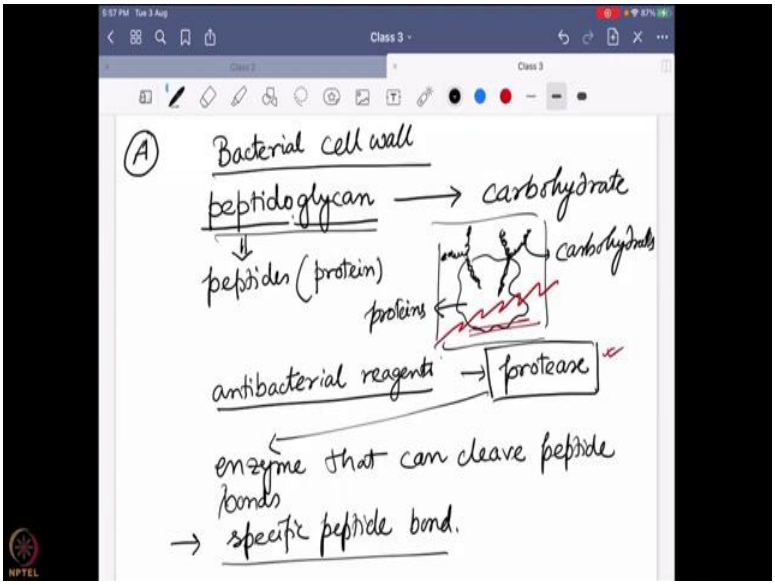

So, the first example, I will be giving is the following we will talk about the bacterial cell wall. So, whatever the biology we all studied from our school we know there are important feature in the bacteria which is known as the cell wall. Which stays on the outermost part of the bacteria and it actually helps it to survive all the uh toxic behaviour any other things coming towards this way and helps us to survive.

So, cell wall is actually the very important protective layer for the bacterial. Now, we learn it all together all these things in schools but now as we are chemist and most of our in the PhD., on the masters level or higher standard of the bachelor's level. Now we have a better idea like what this particular cell walls are made of? So, if we look into carefully we found the cell walls are made out of this very important factor called peptidoglycan.

So, if we divide it up one side is peptide, one side is glycan. So, peptide is nothing but peptides that means protein. It is again forming between amide bonds or peptide bonds between different amino acids so that is why it is name and the glycan defines carbohydrate molecule. We have discussed that a little bit earlier that what we have we actually have a protein entity a protein structure and on the top of that we actually have a carbohydrate motive, something like that.

So, these are the carbohydrates and these are the proteins and this full section will be called the peptidoglycan and these are actually the building blocks of the bacterial cell wall. Now the bacterias can have different effects on human life, some of them are good which are actually living in harmony with us and some of them are bad which actually try to get our metabolic systems, out of our way and use them for their own purpose.

So, those are actually not bad and for that what we use? If I want to kill a bacteria we use in common term antibacterial reagents and how this antibacterial reagents in typically it works. Antibacterial reagents are nothing but chemicals because now as we are in a chemistry class we try to look everything under the scanner of chemistry. So, when you say a bacterial reagent if you add the bacteria dies that is what life science or biology says.

And as a chemist we try to understand wait a minute, It dies it is fine but how it is actually working? What is the reaction is happening? So, what we found this anterior antibacterial reagents are nothing but something called protease or some chemicals that actually activate protease. What is protease? Protease is nothing but an enzyme that can cleave peptide bonds and why it is critical?

Because once you start cleaving the peptide bonds you are going to create some fusions inside the wall. So, you are going to breach the wall around the bacteria and once you are starting breaching the wall the protective layer around the bacteria will be gone and once this protective layer is gone now it is vulnerable. Now it is going to get attacked by all the different conditions for an example in our gastric juice, it is a very strong acidic region is present over there which goes to even $_{P}$H 2 to 3.

If you put any protein over there that is going to be just stewed up. However, the bacterial even survive over there how? Because this peptidoglycans are actually putting a protective layer and fighting with it and make it survive. But the proteins present inside the bacteria they might be or even the nucleic acids present in the bacteria they are vulnerable to this strong acidic condition but the bacterial cell wall is actually protecting.

But once this protease come into the picture and start cleaving that proteins present in the cell wall that is going to put a fissure and through that the acid or the protons can get into the system and kill the bacterial proteins that are important for their metabolism or the nucleic acid they are important for their survival. So that is how a protease work and that is how the antibacterial reagent generally works.

Now, it is the survival of the fleetest. So, generally this protease when they are working they actually work in such a way that they generally clip a particular specific peptide point and depending on which particular peptide bond they like they actually have different names. So, I am not going into the details of that so, this protease for example one kind of

protease is such that it likes if there is an arginine, I will detect it.

How they will detect it? If you remember the arginine has a huge side chain which contains a guanidine group. So, they probably detect the guanidine ion and sits over there and then whatever the peptide bond present just next to it, it just cleaves it. So that is how the protease actually detects the side chain what is the functionality and cleave one of the peptide parts and that is how the protease work.

Now, as we are just saying the bacteria are not going to leave this wall as it is they are saying okay you have protease. I cannot defend myself very well against it because that is very strong reagent and a very strong actually said acid base reagent which actually can cleave my amide bond, amide bond cleavage is nothing but an acid-base reaction. So, how I can survive it? That is the thought process of the bacterial.

So, bacteria says like okay let us see how the protease is actually detecting the peptide bond.

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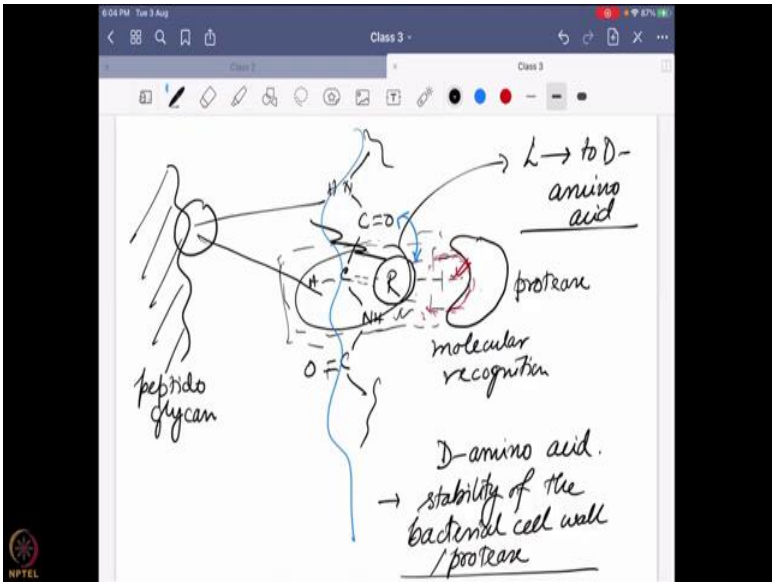

And as I just said the protease so, for an example this is my side chain of this peptidoglycan. So, there is a huge peptidoglycan and I draw it such a way but in reality if I look closely but we will find that is nothing but amide bonds next to each other. right C-H and there is this R group and then there is this NH Group there is this carboxylic acid group and so on and so forth. And say this R group is very critical for understanding or recognizing this protease when it is coming through say this is the protease it is coming through.

So, it is understanding this particular R group detect in it again molecular recognition and then it cleaves this

particular peptide point and that is how this protease works. So, the bacteria thought like okay I cannot stop it because I have to make my bacterial wall in such a way that it has to have protein, I cannot get it without protein. But how can I change it without a huge amount of uh different things in inclusion of different things?

So, for example you can totally change your the sequence of the peptides that is possible. But for that just imagine, how much change you have to do into your gene? You have to totally put a totally new genetic material. You will end up putting up a new species. Yeah That is a possibility that you evolved to new species to survive. But that kind of evolution does not happen at a day.

It requires millions years of evolution to reach there. So, how the evolution start? Evolution typically starts with one point mutation. So, it just change one amino acid at a time or something like that. So, biology can try that but the issue is that when they are trying it the problem is that they change one amino acid but the protease can still work and bind a different portion of this system and cleave it?.

So, what they want leave everything as it is so that the protease still try to find this particular R group. But I want to change such subtle change that even in the presence of this R group the protease will not be able to detect it. so, how it actually done? So, what the bacterial does? Keep the R group same? Keep it an arginine group. But instead of L arginine they change the whole system L to D amino acids.

So, now when you change the system to L to D amino acid, now you know enantiomers their actual properties are not that different and over here you can argue that different chiral centres are also present. So, they are basically diastereomers not the enantiomers but for the sake of our discussion making it simple. We said if I change from one L to D amino acid the overall property overall structure is not going to change a huge amount.

But the subtle change the orientation of the R group will be subtly different and such a small difference play a huge role because this protease when it comes and try to detect it, it try to bind it, it has a particular binding pocket. The binding pocket already have a particular orientation present over there that can envelop that R group. However, as I go from L to D amino acid, it changes subtle way it moves in so much little way.

But it totally breaks down the interaction between the protease binding site and this R group when it is near to this

peptide backbone. Because you have to stay near to the peptide backbone so that it can act. It is not only binding to that R group but also, staying close to this amide bonds because that you have to break. Now, when I change this argument from L to D the inter the inter inter nuclear distance between the R and carbonyl group changes and that actually shifts the whole scenario.

Now, the protease cannot bind the R and cleave the carbonyl group the amide bond together because that is not the binding pocket of the proteins. So that is why you can still go under the radar without activating the protease and that is what some of the bacteria actually does. They actually very smartly change only a few of the points L to D amino acid and they understand which of the amino acids are close to my binding pocket of my proteins and only those amino acids they actually change and once they change it what happens?

They actually can goes around the system without getting detected by the protease because protease has to first detect it through molecular recognition and only then can bind and cleave it and the bacterial are smart enough to change from L to D. Without changing the overall structure a lot and get undetected and that is how it actually works. And what it is found that it is reality that some of the D amino acid inclusion actually increases.

What is called the virulence? Or I would generally particularly say the stability of the cell wall bacterial cell wall even in the presence of the protease. So, that is how a D amino acid, L amino acid mixture is actually very important and it is find out that when the bacteria are trying to do that. They generally try to put only those amino acids which are generally a part of this molecular recognition program.

So, it can disrupt the molecular recognition pattern and get undetected. okay So, at the end of the day, I will share you some reading materials that you can read more in details and try to get some more ideas more information about this system. So, over here I am giving you the overview how it actually works now there are multiple examples of it. I am not going to go through each and every example but I am just going to give you how it is actually work over there? So that is one of the system, how it actually works.