Course on Stereochemistry
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Mod08 Lecture 40
Revisiting the Contents Covered

Okay welcome back to this the course, in the last session or in the last session and whatever we planned to cover has been covered over this the lectures that were being that were delivered which were brocken down into modules. So basically 39 lectures of mostly half an hour. Now let us first have a glimpse of what has been covered in this entire syllabus and then we plan to again revisit some of these issues, the some of these concepts workout some problems and then workout some problems and that will be, that will clear if any dought remains, okay.

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Stereogenicity & chirotopicity
Stereochemistry; Stereoisomerism, chirality, symmetry properties, optical activity,
enantiomerism & diastereomerism
dextro & Levo,
specific rotation
optical purity
enantiomeric excess
2D projection formula
Fischer, Newman, Sawhorse,
Absolute & Relative Configuration
D, L, R/S, E/Z Threo/Erythro/ like/unlike, Syn/anti
Pref/Parf
Pro stereogenic centre: proR/proS
faces: Enantio & diastereotopic re/Si
Chirality due N, P
Conformational Analysis
Acyclic, Cyclic compds (n=6)
detailed analysis of cyclohexane
decalin (cis & trans): Energy diff. optical activity

So we actually covered, the first day we introduced the subject of stereochemistry then under it, stereoisomerism, then chirality, then symmetry properties, under stereoisomerism we have divided into we have shown what are these enantio enantiomerism and diastereomerism, okay. So that was the initial few days symmetry properties then we went to optical activity dextro and levo rotatory specific rotation, optical purity, enantiomeric excess. So these are the concepts that were cleared and then how to calculate the optical rotation, all these things (())) (3:01).

After that we went for this 2D projection formula and here, we have covered Fischer, Numan and Saw Horse, okay. Then we went for the absolute and relative configuration. Here, we have done for absolute dL then R/S and E/Z for relative we have done threo-erythro then like/unlike and we have done also syn/anti. There are some other methods like (())(4:34) which I decided not to cover, but if you are interested you can check that pref and (())(4:43) okay. So I put a star mark, those who want to know this, you can go through the books and then see what are these. Then also we have done the pro-chirality at a here chirality and at that time we introduced stereogenicity and chirotopicity that means local chirality, okay.

We have seen carbons which are stereogenic, but not chirotopic which are syn carbon, which are non-stereogenic, but chirotopic solve source combinations are there then we went for pro-stereogenic center and then we have assigned an faces. So here we have done proR/proS and here we have done enantio topic and diastereotopic faces and then accordingly we have using domains ray/psi, okay. So then we have we went for conformation conformational analysis and that is a huge topic the conformational analysis we first covered the acyclic compounds then the cyclic compounds up to n equal to 6 that means cyclohexane then we have specifically done the detail analysis of cyclohexane, so in between, I think what we have done? We have also pro-stereogenic center before conformational analysis we had the chiral compounds chirality due to nitrogen and phosphorus. So that was done chirality due to nitrogen and phosphorus.

So acyclic cyclic compounds and detail analysis of detail analysis of cyclohexane and then we went for we went for the decalin also, Cis and the Trans decalin Cis and Trans. What we have checked? We have checked the energy differences and we have check the optical activity whether they are optically active or not, okay. So after the conformational analysis with respect to energy then we went for we have seen also of different types of boat systems unusual systems where the unexpected result happen compounds with axial groups compounds which exist in boat conformation that were covered.

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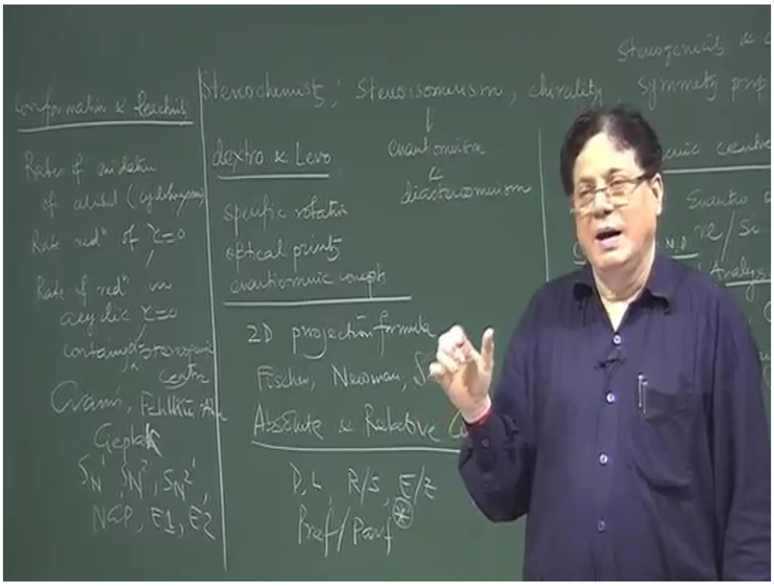

Then we went for conformation and reactivity**.** So we went for rates of oxidation we have given some example rate of oxidation of alcohols of in a cyclohexane system and we have done reduction rate of reduction of carbonyl but when we did the rate of reduction of carbonyl, before that we have done the rate of reduction the reduction rate of reduction. In acyclic carbonyls containing alpha stereogenic center, okay.

Then we did all this crams rule, then felkin and then Ceplak, sorry k Ceplak all this models were discussed, okay and then we have SN1, SN2 reactions, SN2-prime then NGp then 1 and 2 even we did not discuss much, but because stereochemistry is involved any two, so we went for E2 and did worked out what is the situation in case of cyclohexane, okay and after going through all these, then and these are all with respect to inversion of configuration or retention of configuration that means the stereochemistry of these reactions were discussed, in detail and then we have finally we came to what are called asymmetric synthesis, stereo specific synthesis.

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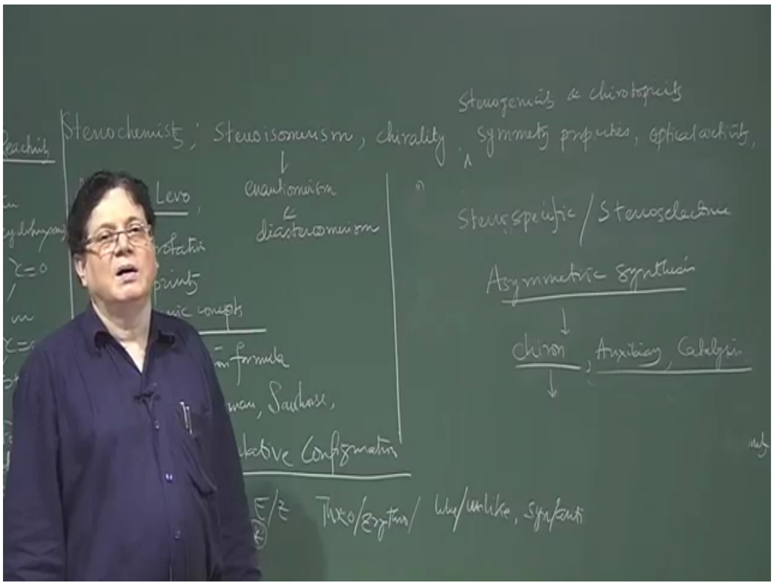

So first we did stereo specific synthesis stereo specific, stereo selective and finally, asymmetric synthesis there is not much difference, I told you between the stereo selective and asymmetric synthesis. A stereo selective synthesis giving chiral compounds, becomes giving one of the chiral compounds out of the chiral compounds out of may be becomes an asymmetric synthesis, okay. Specific is little bit different specific is the if A gives B A gives C and D gives D gives another compound, A gives C and B gives D and C and D are stereo isomers then it is stereo specific that means the product depends on the configuration of a starting material and I gave you a classic example of what is called cyclohexene, which cannot exist in the trans form.

So nobody can prove what is the state of bromine addition. So addition of bromine in cyclohexene cannot be called a stereo specific reaction; however it is a stereo selective reaction, okay. So asymmetric synthesis and finally we did some asymmetric synthesis we said that there are many approaches one is chiron approach, that means you have a chirality to start with, you have auxiliary based approach auxiliary based and you have catalysis based approach okay.

We have given some examples chiron is that the same thing as crams rule, these are predicted, we have one more crams rule and then we have done the prelogs rule also here Prelog prelogs rule okay and then the chiron approach that is actually basically when you have chirality already built in. So those are like Prelog where you apply the crams rule, Prelogs rule, felkins model then auxiliary, we have done the Evens auxiliary chemistry of alkylation and finally, catalysis we have given just one modern example of Barry Sharpless.

So who discovered this asymmetric epoxidation, okay and we ended off with a mnemonic device and I said that it is good to end up with sharpless epoxidation, because he is the Nobel (())(13:49) prize win and not in 2002, I think last time I told you 2002, it is in 2001when he shear the Nobel prize with noyori who discovered asymmetric hydrogenation that when the hydrogen comes and saturated double bond, you can get chirality at that point also and there are very important components like L dopa, which has been which is synthesized by Noyories method and then there was the third phelop (())(14:19) whose name was nolls (())(14:21) and (he was) he started this asymmetric hydrogenation. So these three sheared the Nobel Prize okay.

So you see, this stereochemistry subject is so important, ultimately all this concepts are very applicable in biology and in medicine. Biology any biological world is chiral. So any system you deal with in biology is a chiral system, DNA is chiral, RNA is chiral, proteins are chiral, carbohydrates are chiral. So whatever molecules we take it chiral. So whenever there is an interaction in the (())(15:02). So it is the stereochemistry that matters most.

So these concepts that what you will be having after at ending this course will be extremely helpful. For medicine also you know that medicines as I said, I gave you one story real life story of thalidomide tragedy. What happens to the babies born from mother who are taking the thalidomide in the plus minus form in the racemic form and ultimately the babies are borned with deformity that was called the teratogenic effect. Then people realized that drug should be given only in one chiral form. So that is the entire syllabus that we have covered, we promise to covered this part that was in the in their in the in the course outline and we have done this over this 39 lectures.

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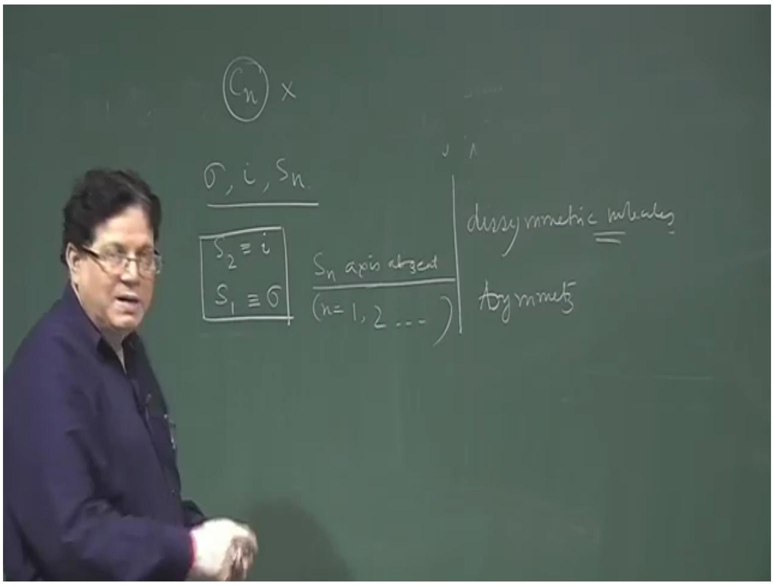

Now this 40th lecture what I plan to do is to just to revisit, whatever concepts we have covered and then work out some problems and see just to clear out some droughts if you have, okay. So first question is that you know what is a which property of a molecule makes the molecule chiral, again going back to the very basics. Chiral molecules are those which have got non-superimposable mirror images, okay and to have non-superimposable mirror images; it has to lack certain elements of symmetry, which are called improper elements of symmetry. So each should lack, it should lack sigma, it should lack i and it should lack Sn later on I said that Sn is equivalent to S2 is equivalent to i and S1 is equivalent to sigma. So that you also you know that.

So it is sufficient to say that Sn axis absent is the minimum condition for chirality, okay. When these are at, but here you better write, because see in we have to be careful the careful in the sense that just go and write only that Sn axis is absent, because there may be problem, some people may not like it. So you start with this that it should not have sigma, i and Sn, but then since S2 is equivalent to i and S1 is equivalent to sigma. So it is sufficient to say that Sn axis absence is the minimum criteria for optical activity, okay.

Now an n equals to 1, 2 and then dot dot dot. The molecules which lack this elements of symmetry are called dissymmetric molecules, okay, because they could not, so you can again another if you are saying it in a line, you can say dissymmetry is the is the minimum criteria for us for optical activity, because dissymmetry means of absence of this. So that is another way to say these things, but you cannot say asymmetry is the minimum criteria, because asymmetry contains another element of symmetry that is i, okay asymmetry means divide of all kinds of symmetry, but that you do not want in a chiral molecule. Chirality demands only the absence of sigma, i and Sn. So the Ci, Cn axis that has nothing to do in the chirality. So that was very clear on the very first day or the second day.

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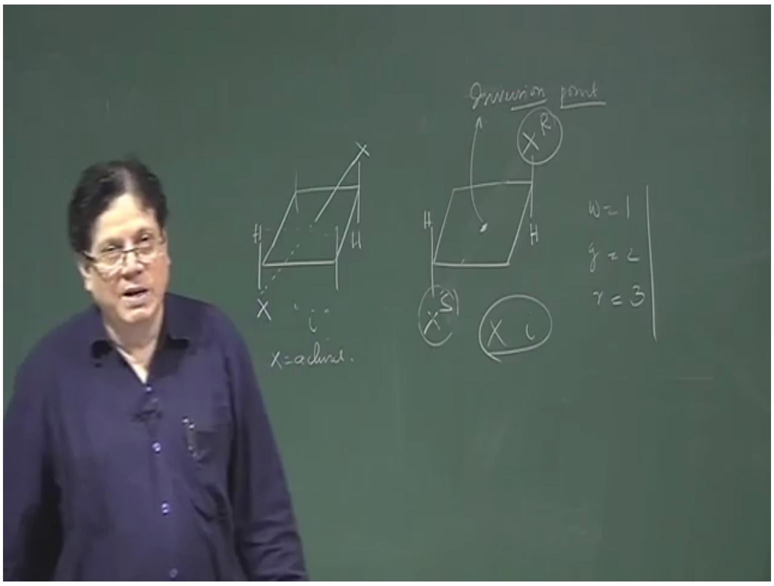

Now let us do some problems. Now we define i, remember what is i is the inversion point, earlier called center of symmetry. Now this center of symmetry, the definition was that if you join one group, one substituent in a molecule to the point to that central point and then extend it backwards you will find, a same group at equal distance and this is applicable to all the groups present in the molecule okay.

Now the question is why it is called an inversion point, because I do not see the word inversion coming in while defining the center of symmetry. Now you will see that the definition has some problem. When I say that it hits (())(19:44) an identical group at identical distance in the opposite direction. There is one condition, which it should also satisfy and that is when these groups have chirality. So what we have earlier said is X and X. so we did not bother whether X is chiral or not. So if that is a case X is achiral then there is no problem that this matches with this at equal distance and this hydrogen also matches with this at equal distance and these hydrogens will of course, because you have to check all sides okay. So it has got a i, but why it is call inversion point, suppose the X has got a stereogenic center, okay. So if it has got stereogenic center, so that can exist in R or S form.

Suppose I write that I have a molecule both are R form, okay. Now I ask you that whether it has got a center of symmetry or not, okay. We start a problem from the very basics. We try to move forward and see to clear your droughts. So we will extend this class a little bit. So if this is a seen arrow, now I ask whether this has got a plane of symmetry or not. Now according to the definition that I have gave you to start with. Initially, I did not introduce this concept. Now I am introducing that if you add this and extend it backwards you get the same groups, yes both are same groups, both are X and R , but actually what happens you will never get the this XR is not the same as this XR, because I can show you in a model that , see this is suppose XR and this is XR and suppose it is in the R configuration, R configuration means suppose this is the group of least priority, this carbon and these are white is one red is 2 and green is 3.

So suppose white is one, then green is 2 and red is3. If this is the situation and the carbon is the 4th priority. So this what is the configuration of this white, green and red, so that is I see it clockwise, I see it opposite from this 4th group. This I assumed that this is the 4th group. So this becomes a clockwise direction. So that becomes R, so my lower thing is R. Now what about if I make another R here, so I have to make white then green then red, but it is in the opposite configuration, you see it is in the it is in the anti-clockwise direction. So you have to change it, any interchange will go to the other that is the rule if you do any one interchange then the molecule changes, okay for 1 asymmetric carbon atom center like this, it goes to the other enantiomer okay and other enantiomer for diastereomers, it goes to the diastereomers okay, but R becomes S, S becomes R if we interchange the groups, I hope this is clear.

If we have only one asymmetric carbon center, if we interchange any groups, you get the enantiomer. If there is another chiral center present in the molecule then interchange of groups will give it to diastereomers okay. So now let see, whether we are following these R again, this is white, this is green, this two were red. So again it is clockwise. So these two are same configuration.

Now let see when now you have to be careful, because there are 3 substituents for achiral compounds we did not bother what are the substituents, but for chirality, because these are different. Now you have to match the red also with the red one, means when you add this when you draw this line. So this is the line center and then you draw it on these sides. So the red is not at least it is not placed on these sides. So red if I place it on this side as see that yes, red is no not that one sorry, red should be here. So if red should be here.

Now you see I and red place red in such a fashion that it meets red in the opposite direction. What about the green? The green is here, okay red is matching with the red and the green is matching with the green and the white is matching with the white. Let see, so this is green this is 1, 2, 3. So that is a clockwise direction. So that is R. this is white green red. This is anti-clockwise. So there is a change in configuration here, so again I will just repeat it, I have to make the configuration same both RR and I assume that white is one, green is two and red is three. So that was not the case actually, sorry. So now you change it, again just double check white, green and red is clockwise keeping this as the 4th group and here white, green and red again clockwise. So they have the same configuration.

Now come to the point, so this red is matching as you add as you draw this point join the red to this point and extend it backwards you get red, no problem, but what happen to the green? If you add the green to this point and then extend it backwards you find white. Now you can say that I will put the green there. The moment you put the green there, the red is disturbed; the red has gone from here to there, so red will not match now. The moment you try to match white from here to there, the other two will not match, okay you see the point, so that means when these groups are in the same configuration, it does not have any center of symmetry. Now we have to revise the definition little bit, center of symmetry for achiral is that a substituent join to the group extend it backwards and you get the same substituent and that is true for all the substituents present in the system. This is for this is for molecules without any without any chiral center.

Now if you have a chiral center like this on two sides then what happens? If you have chiral center some 2 sides and you have then what happens, because there is possibility of RR or RS combination or SS combination and interestingly when there RR, I just showed you that it does not have i, i is absent, so which form has i**.** So for achiral molecules now you see, if I change it, so this was the earlier, this was clockwise blue this white, green, red is in a clockwise direction, but you cannot if you change one make from the clock to the anti-clock then see the interesting point.

So this goes to here that goes to there and now you see, you will have an have a center of symmetry, if you have to you just push it in the actual way. So red matches with red, white will go to this direction, just see white through go to that direction white is on this side, green was earlier on that side. So when you join this line extend it backwards, it will come to this side green is on this side, red is going down, here red is going up. So when you join the up one it will go down and the red is in the down. So what is happening now?

So if this is R and this is S then you have a center of symmetry, so because R going to S is kind of an inversion of configuration. So this is called an inversion point. So you have to define in two ways for systems which are which are not having any stereogenic center, earlier definition stands for systems where there are asymmetric centers then inversion center is there when the groups opposite to in positions opposite to each other have different configuration. So RS has the center of symmetry and that is why these there is a change of configuration. So it is called an inversion point okay, so that is an interesting, very interesting situation okay, I can tell other important problems that also to you will have to encounter and that is regarding plane of symmetry. This is regarding center of symmetry.

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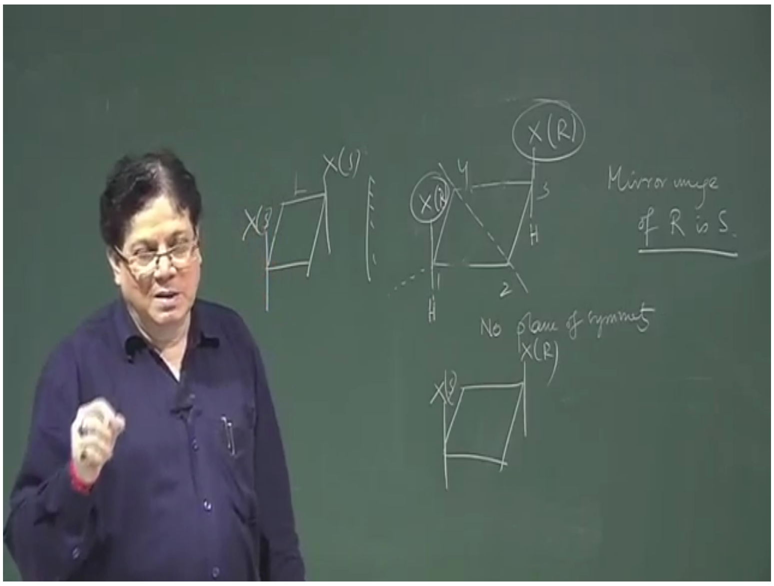

Now all these problems come when there is a group which is **s** chiral. Now suppose, if I say whether this compound is having a plane of symmetry or not. The apparently, if these XX are not chiral definitely it has got a plane of symmetry through this and also it has got a plane of symmetry going through this one and suppose this is 1, 2,3 and 4 that C1 and C3 and containing this X and I H bonds. So you cut it and you see this is the mirror image of this part when you cut this, so it as if this is the mirror image of this part, but that is something wrong, if I say this is the mirror image of this part that is wrong, because mirror image of R is S. So this cannot be the mirror image of this, okay. So this is not a plane of symmetry, so no plane of symmetry, okay and so which one has plane of symmetry, you can easily make out that the one which has got plane of symmetry is this one XX and XR, okay.

Now there are many ways to do these problems, I can give you this is one way that you actually see the molecule and then divide it and see whether it is one half is the mirror image of the half, some people who are clever, they can immediately tell that this cannot be this cannot have a plane of symmetry, because if it has a plane of symmetry, it becomes achiral, it is not chiral. So they will immediately take a mirror image and in the mirror image what happens, R becomes S, S becomes R. So this will become XS and this will also become XS. Now S cannot superimpose on R, so this is the mirror image of this non-superimposable. So it cannot have any type of symmetry. It does not have i, it does not have sigma, it does not have S also, oaky that is another way to do the problem okay.

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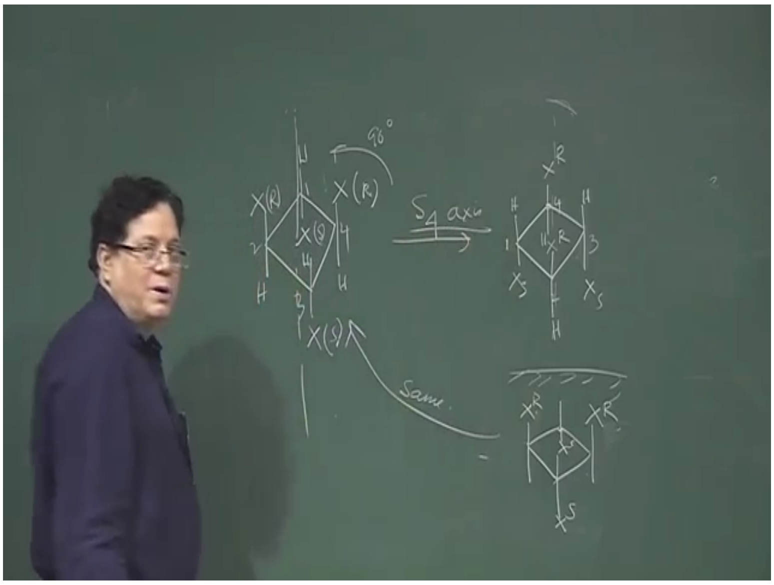

Now I can go on and continue various types of problems, I think which will be given when you take the course and that yes, we will definitely do that, I will give you one more example that this is a compound containing 4 XX. These are all hydrogens hydrogens hydrogens. This is in R configuration, this is S configuration. This is in R configuration and this is in S configuration okay. So now the question is which type of symmetry element it has or is it chiral or not. If it is chiral then it does not have any symmetry element, okay I am talking about improper symmetry element, because it has got a C2 symmetry, but C2 does not count for the chirality of the molecule.

Now to do this what you need to do to arrive at a decision, so what you need to do, see the problem is if you draw a mirror image you are still not you will not be in a comfortable position, because there are two R and 2 S and in the mirror image there will be 2 SS and 2R, okay. So you have to again think over it whether it is a matching on this or not. The other way is that if you are that is why is the stereochemistry, I said the visualization is so important, I see an exchange of this X up down and also at the same time the configuration changes. So what I do? I give it a, so as if every 90 degree there is a change happening.

So keeping that fact what I do, I may be just I draw it in a different way keeping that fact, I suppose this is one, this is two, this is three and this is four. So I again rotate it say anti-clockwise by 90 degree and if I do that. So this is your 4 position and this is your 1 position, this is 2 and this is 3. Where are the groups now? So XR will be here, XS will be here; because that was attached to one then your two XR will be here and this is your 3 carbon **3** XS is here, put the hydrogens okay put the hydrogens. Now I have rotated the axis was what the axis was like this. So it is a vertical axis, I have rotate it by 90 degree and then if I take a mirror image along this axis. So I take a mirror image. The molecule structural image the cyclo-butane remains the same looks like the same.

Now we have to put the groups in the top of the XS just look at the XS. So this is the 3 carbon, X is down, now in the mirror image X is up that is no 1 and no 2 is S becomes R. So this will be R. Now at the 4 carbon this carbon is now this 4 or is carbon is now this carbon okay. So that carbon what happens. It was X X was R and the top, now X will be S are the bottom okay, both changes are happening up becomes bottom, bottom becomes up and R becomes S and S becomes R. So this is S then this is XR and finally you have this carbon and here X is S.

So now you see the similarity between these two. So X say they are same now so they are same. So that tells you that it has got a S4 axis okay. So this is quite tricky you know, these type of problems obviously you have practice and practice and you can generate your own problems not cyclo-butane take cyclohexene, cyclopenten and put the groups specially with the chiral groups the system becomes very interesting okay. So that has got this S4 axis.

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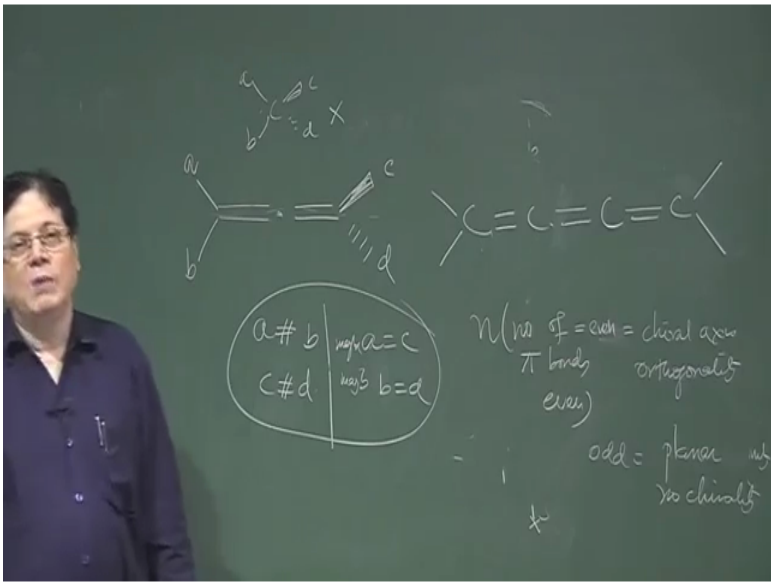

Now there are there are several problems, I could have gone into but the time is short. So I will not go to many, one compound I gave it to you and that was the allene system. In the allene (())(36:50) system what we have said that these two groups occupy a plane which is orthogonal to the plane occupied by this and if AB and CD if A is not equal to B and C is not equal to D, it does not matter A is not equal to B, A may be equal to C may be A equal to C may be D equal to B equal to D, but this becomes if it this contains it maintains. The major condition is that A not equal to B, C not equals to D, it does not matter whether A equals to C or B equals to D. So there it becomes chiral okay, because of the this can be consider that if you push this carbon and try to bring it here and then they meet each other compressing this pi bonds, so you get a tetra hydral. So this is, but in a tetrahedral you know that what happens?

In a tetrahedral if A becomes B that means if the two substituents becomes same that is not chiral, but as you break tis carbon as if you are breaking it and then and then extend it, then that sort of plane of symmetry, which was present here is gone. So allene becomes chiral. Allene can be regarded as an extended tetrahedron, but while doing that you see that your condition becomes more friendly that means you do not have to have all 4 groups different. Here only the two groups at the end have to be different in a allene (())(38:38).

Now if you increase the carbon chain more what happens? So if you have a (())(38:46) then what happens okay? (())(38:51) again the thing is that these groups are again back to in the same plane again back in the same plane. So basically it all depends on the number of pi bond, which will take care of this that whether the groups at the two ends will be orthogonal or they are in the same plane. So if n equals to even if the number of pi bonds n number of pi bonds even then what happens? The molecule is has a chiral axis then the possibility of chiral axis, because this has then this is a chiral then orthogonality is there orthogonality. If **if** n is the number of pi bonds is even, sorry is even then that happens okay. If it is odd then it is planar, so no chirality, because the plane of the system becomes the plane of symmetry, any planar system the plane itself is a plane of symmetry for the molecule.

So if you look at this see this is a molecule, which was got which is now, 3 pi bonds here and if you take this 3 pi bonds that means n equals to 3 you see. Now the 2 ends have become planar the planes are coplanar with each other. So this is the blue and the green and this is the white and you can take any other whatever you take it does not make, it chiral, because it is a planar molecule. The plane itself I repeat the plane itself is the plane of symmetry, okay. So that will continue to do.

If you put another one then it becomes orthogonal. If you put another one, it becomes planar okay. So just to end I again show the allene molecule. Allene molecule will have only one double bond, not this one allene molecule will have I just rough, it is a rough showing. So allene molecule will be something like this. This is what is the status of the allene molecule. The pi bonds are mutually ortho, see these are PX this is the sp carbon sp hybridized then it has got py and pz. So if it supplies the py then the other one supplies the pz. So the two p orbitals that the pi bonds are basically orthogonal to each other and that makes the two hands orthogonal to each other. So this is allene, because n equal 2 then n equal to 4 another allene chiral axis will come, n equal to 6 another chiral axis to come and we have seen how to give the nomenclature system of the allene okay. These are all covered okay.

So I think now when the courses start who will put all the questions, all the assignments so that things will be clear to you as we go along with the course okay. So I wish you very wish you a very that you have a very interesting journey ahead and you will ultimately can have very good concept about this topic of stereochemistry, okay. Thank you.