Structure, Stereochemistry and Reactivity of Organic Compounds and Intermediates: A Problem-Solving Approach

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Lecture - 08

Concept of Pseudoasymmetry; Reflection Variance/Invariance Problem; Methods of Nomenclature System

Hello. Welcome back to this course on Structure, Stereochemistry and Reactivity of Organic Molecules and Intermediates: A Problem Solving Approach. Today we will be discussing an important concept of stereochemistry which is called Pseudo Asymmetry.

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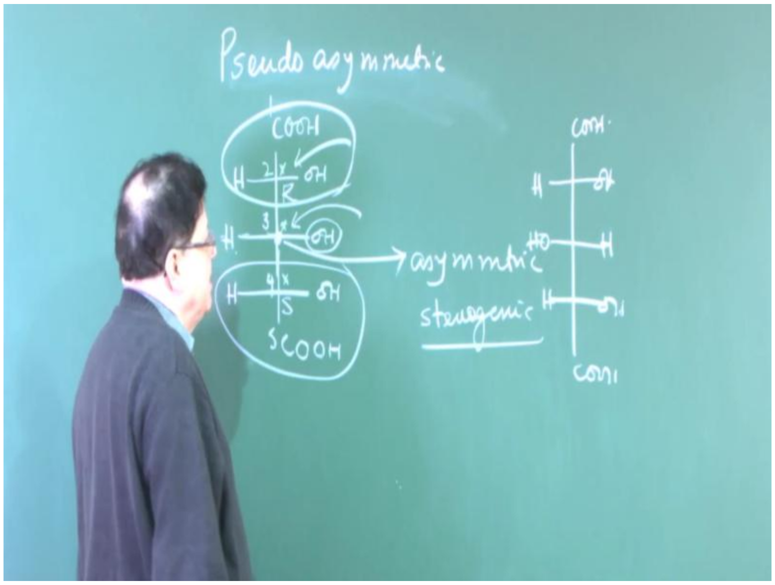

Pseudo asymmetry as the name suggests Pseudo means not real, so it is little bit different from a proper asymmetric system or a carbon. We will go through that what is a pseudoasymmetric carbon and what is a pseudoasymmetric system we will discuss that.

But anyway let us start from the very basic principle that what pseudo means not real. Not real means so sometimes it shows the typical behavior of the asymmetric carbon which is now known as stereogenic carbon and sometimes it is not depending on the environment that is present or depending upon the groups that is attached to it .

The whole thing started with trihydroxy glutaric acid . You know trihydroxy glutaric acid this is the structure of trihydroxy glutaric acid. Here there are 3 centers where 4 different groups are attached 3 carbon centers where 4 different groups are attached . Now this molecule what has been represented here is not chiral because it has got a plane of symmetry in the conformation that is drawn here .

Now, suppose this is your number 1 carbon 2, 3, 4 and 5. Now C2 carbon has if I want to assign the absolute configuration of the C2 carbon then you will see what will happen that this is 1, that is 2 and that is 3 so that becomes R that becomes R .

Hydrogen is on the horizontal side and if you do this 1, 2 and 3 so now it becomes S . So what is the status of the C3 carbon now? C3 carbon is now attached to 4 different groups because these 2 groups are differing in their configuration.

So, when I say different groups attached to a stereogenic center that includes groups which have got same constitution but may have different absolute configuration and by that notion they can be different . So this is now in this case this is R, this is S. So this carbon that middle carbon the C3 carbon is now asymmetric by the older term or you can now say that it is now become a stereogenic.

If it has become stereogenic that means if you change the position of the OH and the H you will get another stereoisomer which is obviously true in this case that if you change this position of the OH and H you get another stereoisomer . So this is now basically a stereogenic center and stereogenic center because these 2 have different configuration . Now if you now change the structure a little, now if I change the configuration of C2 by putting the OH on the left and the hydrogen on the right. That means I interchange the position of the two.

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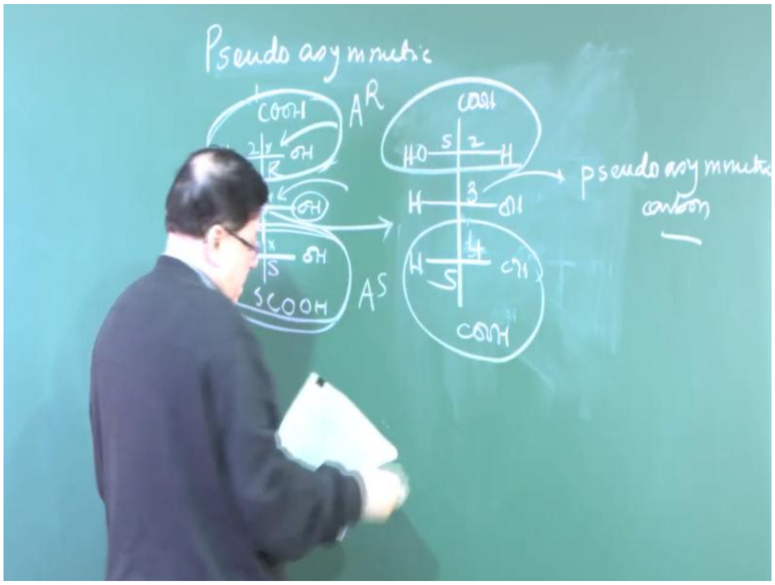

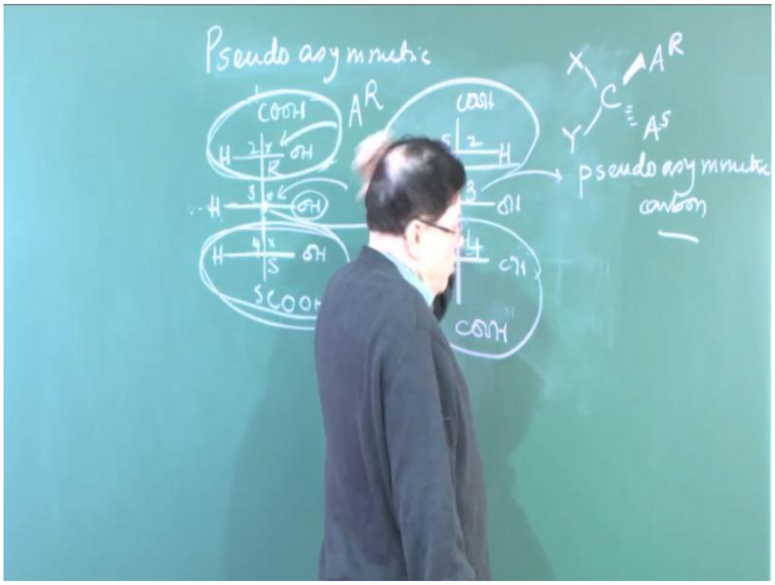

So, I get another diastereomer but by doing that I have changed the configuration of C2, C3 remaining the same, sorry C3 not C4 remaining the same. C4 I do not change. Earlier this molecule was not chiral because there is a plane of symmetry passing through this C3. And so C3 is actually an achirotopic point but it is stereogenic.

In this case this is chiral so that means every point in this molecule is chirotopic. The question is what about C3? Is it having 4 different groups? That means groups which are having different configuration or not or is it a symmetric carbon. Now if you do the RS nomenclature this will be obviously S and that was we have already done that was S. So that means now you have same groups on both sides.

So if same groups are present so that actually destroys the stereogenicity of this C3 . Now earlier this carbon stereogenicity term came much later. So it was all known as asymmetric carbon 4 different groups. So in this case what we are seeing that if the molecule exist in this structure, this C3 carbon is asymmetric.

On the other hand if it exists in this structure the C3 carbon is symmetric, it loses its asymmetry. So this is the carbon which is called a pseudoasymmetric carbon . Now according to iupac nomenclature, iupac definition of a pseudoasymmetric carbon is that it is a carbon attached to, attached to a pair of enantiomorphic ligands.

Enantiomorphic ligand means this one, this and this, these two are attached to C3 but these two groups are basically they are called ligands and they are enantiomorphic because their absolute configuration is different .

So, the iupac definition says that pseudoasymmetric carbon is a carbon which is attached to a pair of enantiomorphic ligands and along with two other groups and none of which are same as the enantiomorphic pair. I can repeat whatever the iupac has said. The iupac defines pseudoasymmetric center as a tetravalent carbons attached to a pair of enantiomorphic ligands like AR and AS.

So, if I call this as AR and this I can call AS what are enantiomorphic ligands? They are constitutionally same but having different configurations I have repeated that. With the other two ligands suppose x and y constitutionally different from A and are mutually non enantiomorphic . So that was the iupac definition.

So, basically what it says according to iupac a pseudoasymmetric carbon is this AR AS and x and y. AR and AS are enantiomorphic the pair of enantiomorphic ligands and x and y are constitutionally different from A and also they are not and they are mutually non enantiomorphic that was the that was the definition of they are mutually non enantiomorphic that was the definition iupac has given .

Now, let us try to see that the asymmetric the pseudoasymmetric carbon basically has a carbon when it is asymmetric like in this molecule. So it has got a configuration, a absolute configuration that you can assign at C3 and let us do that and let us observe a very interesting phenomena which is usually overlooked by us.

Remember when we introduce stereochemistry and absolute configuration we always say that the mirror image of an S molecule or an S center is R center . However, the mirror image of a double one which is in the suppose e geometry or suppose in the trans geometry it remains trans in the mirror image that means there are 2 aspects that was very clear from the very beginning or told very emphatically.

One is that mirror image of S is R or vice versa on the other hand that means that is the what is called reflection variant that means if you take reflection then it changes R becomes S, S becomes R. On the other hand mirror image of E remains E. Mirror image of Z remains Z .

So, that is, that means double bond geometry is reflection invariant . So these are the two things which are basically embedded in our mind from the very beginning. However, today we will see that there are some, there are some issues or this type of pseudo asymmetry breaks down those type of notions.

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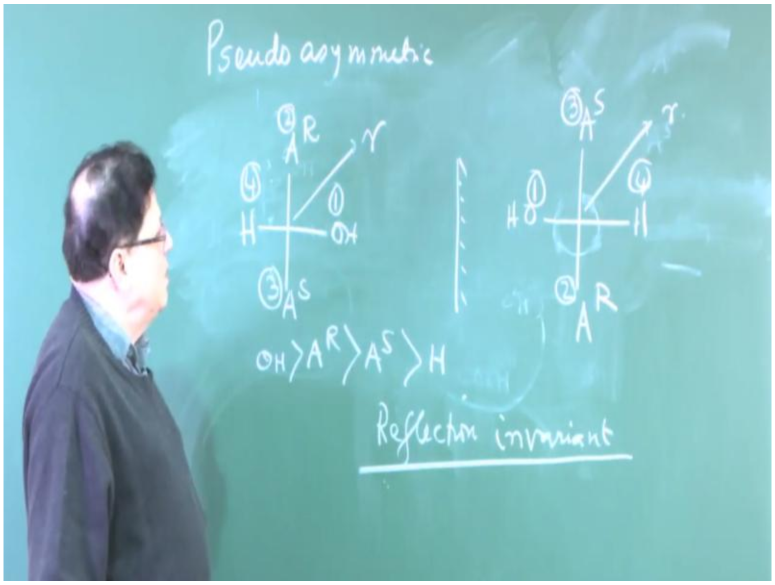

Like if I take this molecule suppose I draw a Fischer projection of this molecule this is AR AS and suppose this is OH and this is H. Now let us see let us assume that OH has a higher priority than AR than AS you know that R precedes S and then hydrogen. So that is the, that is your sequence, preference of sequences.

So, now that will be your 1, that will be your 2, that will be your 3 and this will be your 4. So if you do that your absolute configuration will come out to be 1, 2, 3. So looks like anticlockwise hydrogen is in the horizontal side so that will be having R configuration.

Now, in order to differentiate between an a pure asymmetric carbon and a pseudoasymmetric carbon what has been decided that we should mention this as small r, small r, small s is reserved for pseudoasymmetric carbon, absolute configuration of pseudoasymmetric carbon.

Now, if you take the mirror image of this if you take the mirror image of this, so that will be OH on the left H and then this will be AS because mirror image of AR is AS and that will become AR. So that is the situation now of the mirror image. Now what we expect that the configuration of this carbon should change in the mirror image. So if it is r, small r it should be small s in that case.

But if you do the sequencing if you do the absolute configuration determination this is 1, that is your 2 and this is your 3, that is 4 and you see this is again going in the anticlockwise but hydrogen is in the horizontal side. So this is still become R. So that is I think quite interesting. R remains R for a pseudoasymmetric carbon that means I said pseudoasymmetric carbon is absolute configuration is reflection invariant.

So, that is quite interesting. Now in this molecule what you can say, what you can argue that this carbon is an achirotopic, is achirotopic. So possibly it will not matter if R remains R or S remains S although that is kind of strange.

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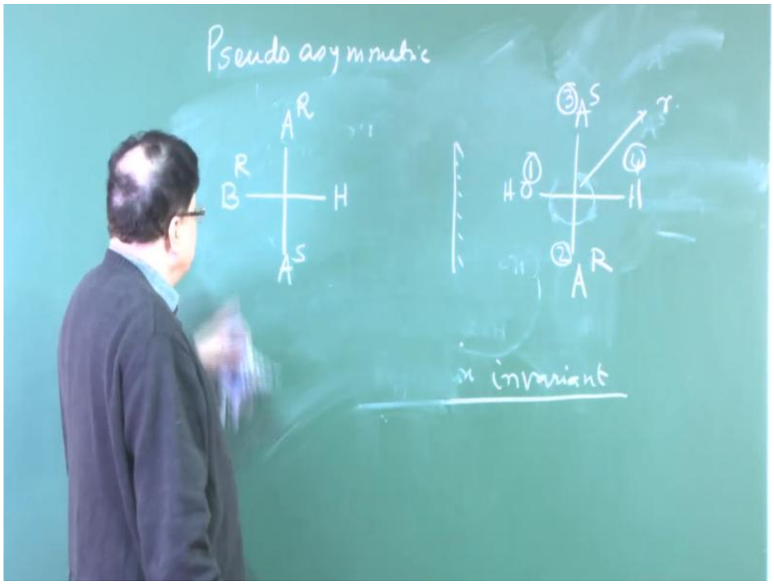

However, for molecules where you have the pair of enantiomorphic ligands remember iupac definition says that pseudoasymmetric carbon there should be a pair of enantiomorphic ligands and then other 2 ligands which are different from the pair of enantiomorphic ligands and they are mutually non-enantiomorphic .

So, you can now but it does not say whether you put a, whether your 3rd ligand or the 4th ligand they also had a asymmetric center or not. Now if you put another group suppose B here and suppose a hydrogen. So now B could be in the B has an asymmetric center so B can be B can have R configuration or S configuration. So this is basically now the molecule becomes chiral. If you look at the system the molecule is now a chiral system because that plane of symmetry is gone now.

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Now, let us see what happens if you take the mirror image and try to do the configuration the absolute configuration at the center. Remember this carbon still remains pseudoasymmetric because the asymmetry is lost the moment this AR and AS has the same configuration, AS has the same configuration.

So, either AR or AR so there is no asymmetry at that center at that point. So that is destroyed so it is a pseudoasymmetric center. Now if you try to do the RS configuration, suppose this is just suppose that A is having a higher priority than B and B having higher priority obviously than hydrogen so then this will be your 1, that will be your 2, this will be your 3 and that will be your 4. So what is the configuration now?

The configuration is 1, 2, 3 so it is now S. We write it again I say that we write it in small s and if we do the mirror image so hydrogen is here this is B. Now this will be S and this will be AS, this will be AR. And now you do the, do your preference order so that will be your 1, this will be your 2, this will be your 3 and that will be your 4.

So, that will become so that will still become S, looks like clockwise but actually anticlockwise. So again you see that even for chiral pseudoasymmetric systems where the pseudoasymmetric carbon is stereogenic as well as chirotopic then also you do not see the reflection variance that is usually expected for an asymmetric carbon.

So, again this is reflection invariant. So S remains S. So one important conclusion from this is that there are cases if you apply the rules of iupac system whatever the rules of the that CIP systems it tells that for pseudoasymmetric carbon your, the absolute configuration is of the pseudoasymmetric carbon remains reflection invariant. So R remains R, S remains S. So that is a significant departure or a major departure from our concept of an asymmetric carbon.

Now, people have tried to solve this issue because whatever the configuration comes out by putting the CIP system but in fact that when you take the mirror image it is always true that this H and B has interchanged their places, their positions in the mirror image. There is no denying of that fact that there is an interchange of groups that has taken place.

And if that is the case interchange of groups that has taken place but that is not leading to difference in configuration, absolute configuration simply because of our the whatever CIP rules that we have that R precedes S. R precedes S so what happened here why the configuration remain same because this AR which was earlier having the number 1 priority because of the change of configuration in the mirror image so that became 2.

And whatever was earlier 2 that became 1 in the mirror image. So that is the reason that in spite of change of the, interchange of position of 2 groups your configuration still does not change because there is a change in the preference order because of this RS inversion in the mirror image. Now there are, there is a, there it could be ways to solve this.

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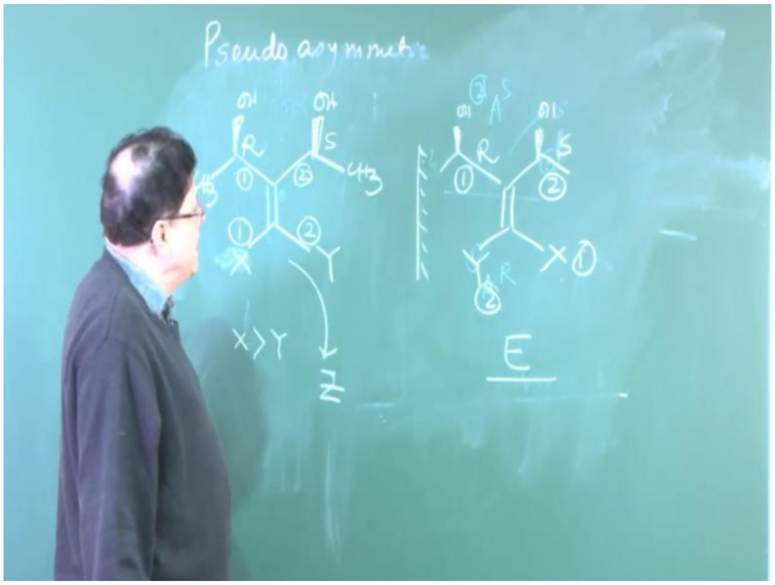

One of the way, I, before I go into that this Pseudoasymmetry can be extended into double bond also alkene. Here also you will see the same type of fallacy, same type of fallacy means the double bond geometry should be reflection invariant but I will show you that double bond geometry becomes reflection variant in case of pseudoasymmetric system.

What happens? Suppose I have a compound which is, suppose this is x and this is y and now in the mirror image you have double bond. There is basically no change here the, it looks like the same but here there will be x and that will be y. Now suppose if you want to do the configuration here so this is 1, that is 2, that is 3 so that means this is your R configuration and this will be 1, 2, 3 that will be S configuration.

And if x has higher priority than y then what will happen this will be your 1, that will be your 2, this will be your 1, that will be your 2. So that means this becomes a geometry z geometry that means because of the higher priority groups on the same side, similar priority groups of the same side .

If you do the same thing here now this is the mirror image so this is still becoming R remain R, this is S and now this is 1 and that is 2 and this is 1 and that is 2. So what happens here now? Now you are getting an E isomer. So the, what happens in the mirror image that means you are changing the double bond geometry which is unusual because double bond geometry should not change upon reflection.

But here that is happening and that is happening again there must be some limitations somewhere that we could not discriminate between these two forms we are changing the this scenario, the changing the normal notion of reflection in variance in a double bond system.

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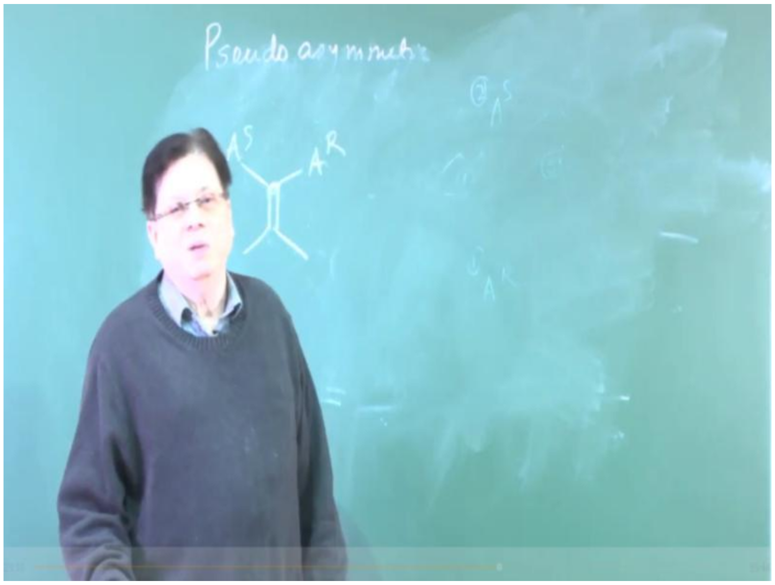

You can also try to do, the another question the question that can come, Sir, whether, why you are considering it as a pseudoasymmetric system because the double bond geometry this EZ geometry nomenclature system or isomerism will be lost if, you if the configuration of these two groups remains same, becomes same.

That is why you can include this because if you expand that concept of pseudoasymmetry it should be that the, that whatever asymmetry actually asymmetric term should not be is not very proper because we know that that has been replaced by stereogenicity. So the stereogenicity is lost when these 2 groups become or have same morphology that means same absolute configuration.

Then you lose the EZ isomerism and there is a proposal that instead of calling it pseudoasymmetric carbon, one should generalize and call this type of carbon where the, where there are two pair a pair of enantiomorphic groups then the stereogenicity is lost when they become the same when they have the same absolute configuration. The same thing also happens in allene system, the same thing also happens in planar chirality.

You can have various types of this pseudo stereogenicity present in different molecules and if you try to assign absolute configuration you will land into always that that paradigm that reflection invariance in RS system and reflection variance in EZ system which is entirely different from the normal asymmetric center.

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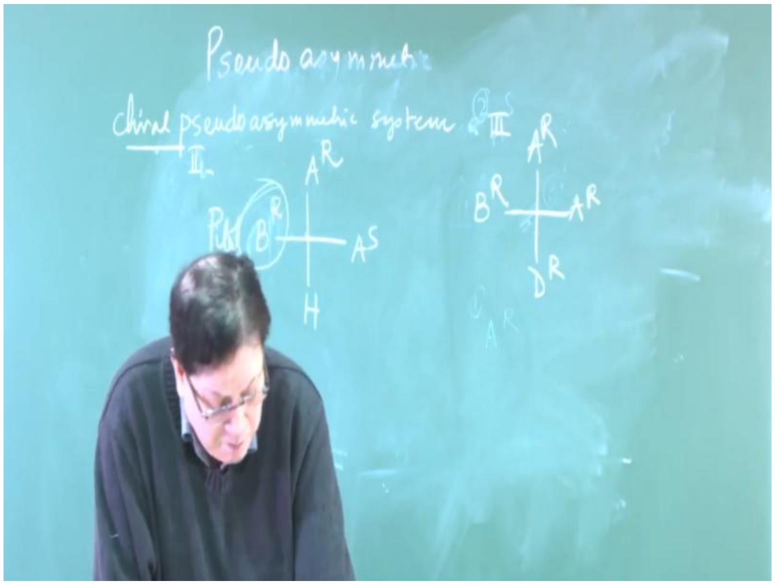

Now, there is a proposal to solve this type of reflection invariance in a pseudoasymmetric center containing an SP3 chirality, SP3 system. Because now we have different types of pseudoasymmetric system, one is containing double bond that EZ and another is containing the tetrahedral carbon.

So, let us talk about the tetrahedral carbon which is pseudoasymmetric. So AR AS and then you have just 1 pair. So we are talking about chiral pseudoasymmetric system. We are not talking about the system which is also called class 1 systems that is like glutaric acid trihydroxy where the molecule itself is achirotopic.

So, here we are talking about pseudoasymmetric system with chirality or chiral pseudoasymmetric systems. That is a better way. So that means you have another asymmetric center present in a different group and suppose this is hydrogen. Suppose this is hydrogen does not have any configuration. Now the rules the new set of rules says that what you do basically that you select out of the 2 non-enantiomorphic ligands.

This is the pair of enantiomorphic ligands out of the 2 non-enantiomorphic ligands the 1 the 1 this is remember this is a chiral pseudoasymmetric center . So it has got, in this system it has got one system B which has got a chirality. So you take this as a pilot atom and then based on the configuration of the pilot atom you assign the number 1, 2, 3 to the other ligands.

So, I can still clarify that, that in case of like systems like this what you do that if you have just 1 second you have to take a pilot atom. The question is what is the pilot atom? The pilot atom cannot be selected from the pair of enantiomorphic ligands that is number 1. For molecules belonging to class 2, class 2 means this is where there is which has chiral pseudoasymmetric system containing 1 extra asymmetric ligand.

And there is a another class where both are, the other 2 ligands are also having chiral center but they are different because the iupac definition says that they should be non-enantiomorphic. One pair of enantiomorphic ligands, other two should be different from this and they should be non-enantiomorphic. So that satisfies this one. So this is what is class 3 and this is class 2.

So, the question is first of all select a pilot atom. The rule for selecting pilot atom is that the pilot atom cannot be selected from the set of enantiomorphic ligands. For molecules belonging to class 2 that means this one so sorry the molecule belonging to class 2 between the remaining 2 ligands the one having chirality center is considered to be the pilot atom.

That is why I have selected this as the pilot atom and for class 3 between the non-enantiomorphic chiral ligands the one with higher CIP priority that means one if B has a higher priority than D then D will represent the pilot atom. If D has higher priority over B then B will represent, then D will represent the pilot atom. Let us just do one and that will clarify that how it solves the reflection invariance problem.

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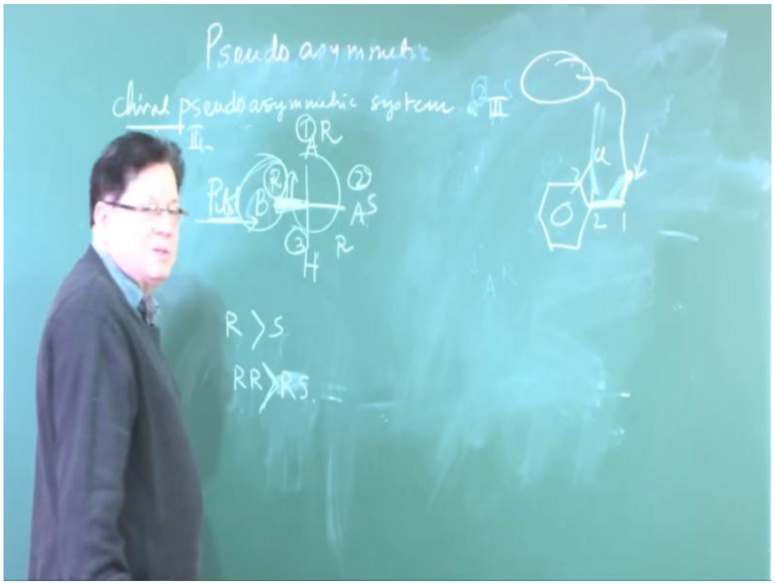

So, this is your pilot atom. Now pilot atom has a configuration R. So when you do the preference order of these 3 ligands obviously hydrogen is the num, the least priority. Here you are not giving any priority to the pilot atom, you are just giving priority to the other 3 and other 3 priority especially for the chiral ligands the priority will depend on the relationship with the pilot atom like here it is AR so we have a RR system.

And here we have a RA system. So we know that the rule is R precedes S that we know. Similarly, RR precedes SS or RR precedes RS. So those rules are there. So let us do that so here because this is RR so that gets one. This is RS that gets 2 and this is 3. So now the configuration now you look from the side of the pilot atom. Now this concept has come from the absolute configuration of planar chirality.

Remember planar chirality has something like this, there is another plane here and suppose there is a chlorine here. So the atom which is closest to the carbon first of all the amongst these 2 rings this is the, this substitution is giving the chirality. So amongst, so you take the atom which is closest to the planarity that of the chiral ring of the ring which is having a planar chirality.

So, that is your pilot atom and then you have 1, 2, 3 and then you to see from the side of the pilot atom. So the same concept you apply here. You look from the side of the pilot atom and see side of the pilot atom because it is Fischer projection. So this is the beta side. So you are looking from the side of the pilot atom and the configuration becomes 1, 2, 3. So that becomes now R configuration.

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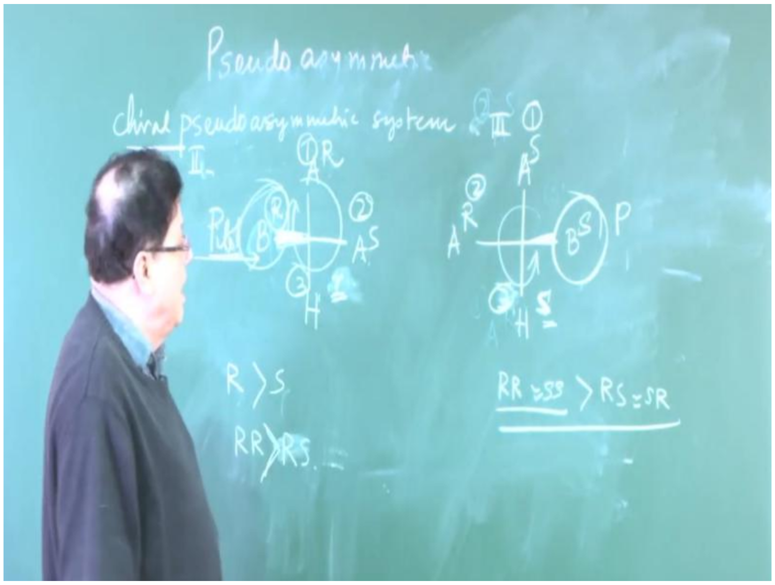

If you take the mirror image, if you take the mirror image then what will happen? This will be your BS this will be your AS and this will be your hydrogen and this will be your AR. Now here what happens here see there what is the rule like precedes unlike, that means, RR basically is SS, they are like both same. So they precede RS or SR. So that is the, that is always inbuilt in the iupac in the CIP rules.

So, now if you want to do the preference, find preference then what will happen this will be 4 sorry 1st find the pilot atom. This is the pilot atom. The chiral non-enantiomorphic ligand is the pilot atom and then this is beta that is okay. Now this is SS and SR, so that will be now 1, that will be now 2 and that will be 3. This is basically the like precedes the unlike combination.

And then this becomes your 1 that is 2 that is 3. So now that becomes S configuration. You still remain keep the smaller small s, this is better small r and this is small s. But you see by applying of this pilot atom system or pilot atom, applying the pilot atom rule you can convert it you can make this reflection variant.

There are many examples we will try to solve it in the last lecture we will solve whatever remaining problems are there, we will solve that. At that time we will take more of these pseudoasymmetric problems and then solve it. So the again I repeat what actually is has been first what I said what is a pseudoasymmetric carbon.

A carbon which is sometimes asymmetric sometimes not, it is not a real it depends on the configuration of the enantiomorphic ligands, pair of enantiomorphic ligands that are present and then the definition of pseudoasymmetric carbon that I have also given to you by what is given by iupac and then the interesting phenomena that in a pseudoasymmetric system applying the present CIP rules.

It becomes the reflection invariant the RS configuration. On the other hand the EZ configuration becomes reflection variant which is kind of contradictory to the normal behavior of the asymmetric carbons or the EZ double bonds. And then finally we showed that how one can solve this reflection variance or invariance problem by adopting what is called a pilot atom.

And then based on the configuration of the pilot atom you assign the sequence of the remaining ligands maintaining the fact that the like systems are, like systems precedes over unlike systems, like in this case it was RR like systems precedes over unlike. In this case it was SS which is preceding over SR unlike.

So, by applying this simple pilot concept, pilot atom concept which is nothing different because in planar chirality that has been done and but and in planar chirality also it is the molecule is viewed from the side of the pilot atom here also the same thing you view from the side of the pilot atom and see what is the sequence of 1, 2, 3 and that will give you the absolute configuration and that really solves the reflection variance invariance problem. Thank you very much.