Course on Stereochemistry
Prof. Amit Basak
Department of Chemistry
Indian Institute of Technology Kharagpur
Mod07 Lecture 31
Conformation and Reactivity (Conted.)

Okay, let us continue with the sub topic of stereochemistry, which is conformation and reactivity. Now earlier we have done what is called the static stereochemistry we have done the conformational energy conformational analysis of various conformations and how the energy are varies with that and which type of molecule will prefer, one conformation of over with the other and the reason for such type of preference that we have discussed. Now in the dynamic stereochemistry, the first thing that was , very relevant was the Curtin-hammett principle, because in dynamic stereochemistry, now you have conformation conformational flexibility, so one conformer goes to the other conformer and it may so happen that one conformer leads to one compound and the other conformer leads to another compound.

So the question is what will be the ratio of the two products? These products ratio according to Curtin-hammett principle, if the conformational flexibility barrier is low that means it is happening at a very rapid rate as compared to the rate of the reaction, then what happens? The ratio of the two products is not dependent on the population of the conformers in the ground state, it depends on the difference in the free energies of the respective transition states for the two processes, okay and we have given some examples; however as I said the Curtin-hammett principle usually what happens that the more stable conformer gives the major product that means the conformer, which is more populated is giving the major product. So that people might say that the formation of the major product was due to the greater population of the starting conformer.

Now to really prove it the best way is to if I can show that the least the less stable conformer that means the, less populated conformer giving the major product and yesterday, I have given an example of bicyclic as a bicyclic compounds where alkylation is happening from a less populated conformer. So that really proves experimental proof for the Curtin-hammett principle.

Now we will elaborate on this Curtin-hammett principle, but we will a last time you remember that I told you about, the preference of certain conformers, to have axial axially oriented groups like, in case of 1,3-cyclohexane diol where hydrogen bond plays a key role in forming the diaxial conformation. Then dihalo system 1,2-dihalo system, in order to reduce the repulsion between the two halogens negatively charged halogens then the molecule also, takes a conformer where the halogen groups are axial, okay and we have also seen that there is a effect call the alkyl ketone effect.

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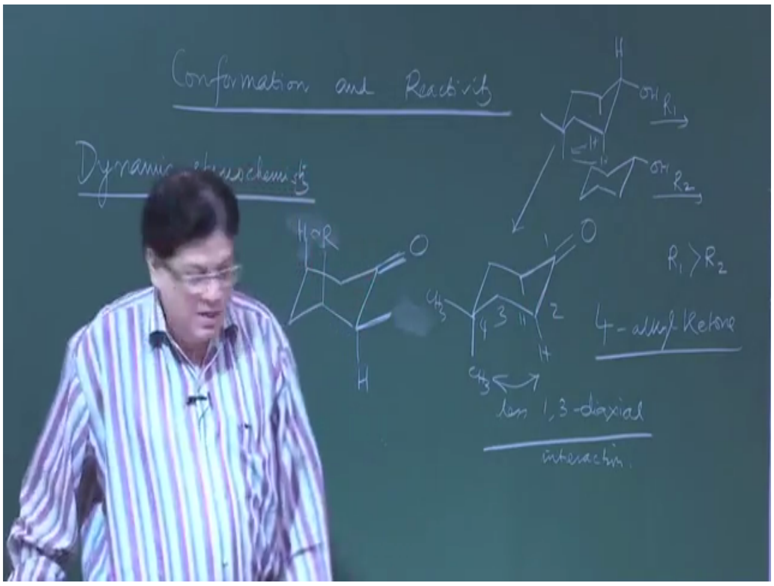

We have seen the two alkyl ketone effect, the 3 alkyl ketone effect and I told you briefly about the 4 alkyl ketone effect, I will just tell something about the 4 alkyl ketone effect. the alkyl ketone effects arise, because of the presence of the ketone in the cyclohexane system the presence of the ketone what it does? It immediately affects the it affects the hydrogens in the equatorial position. This bond is nothing now almost eclipsed through this carbonyl. In addition to that you have now if you have a group here, there is only one hydrogen at the axial position in 1, 3 relationship where the 1, 3-diaxail interaction takes place. So by putting this carbonyl, first of all you are incorporating this eclipsing interactions and you are reducing one 1, 3-diaxial interaction. So what happens here that there is a substantial amount of the, if it group is R then there is a substantial amount of these going into the axial orientation and this effect is called 2 alkyl ketone effect, because it is in the two position with respect to the carbonyl.

If there is a R here, then also because of the reduction of 1 diaxial 1, 3-diaxail hydrogen. This conformer will also the present in substantial amount, in greater amount as compared to a cyclohexane system. So this is what is called the 3 alkyl ketone effect and there is also, this was done by (())(5:20), he shown that there is also 4 alkyl ketone effect that is also present, although this is quite removed from this, but it is due to the fact that, because of the flatness of these two the carbonyl and 2 carbons, the flatness of this ring. So these hydrogens are little bit bent towards this direction. So if that happens then what happens?

So if you have a methyl here and the methyl here. So this methyls suffers less 1,3-diaxail less 1,3-diaxil interaction as compared to a cyclohexane system, okay. So how do you know that it suffers from less interaction? the experiment to do is that you take dimethyl cyclohexanol and you take cyclohexanol. So 1 this is 4, 4-dimethyl cyclohexanol and this is cyclohexanol.

Now if you oxidize it, you will see the rate of oxidation, suppose this is R1 and the rate of oxidation this is R2, you will see that R1 is greater than R2. This is because that in this oxidation, you are realizing the 1, 3-diaxail interaction suffered by this axial methyl. If it is in the alcohol form then there is these are in the normal 1,3-diaxail mode, but as soon as oxidation takes place, so there is a release of the this steric strain, that 1,3-diaxail interaction. So this undergoes oxidation faster oxidized product is this, but this undergoes oxidities oxidation slower, okay.

So this is what you that means, this is giving some stability to the you to the system, okay and the stability arises due these two hydrogens being bent away from the methyl. So thus reducing the 1, 3-doiaxail interaction. This is what is called the 4 alkyl ketone effect, because you have 1,2,3,4, so this is 4 alkyl ketone effect. So I thought just complete the whole thing, because I said one about two alkyl ketone effects, 3 alkyl ketone effect quite elaborately. So I should say about something about 4 alkyl ketone effects and why does it originate that is a important thing, because of the bending of this CH axial hydrogens, okay.

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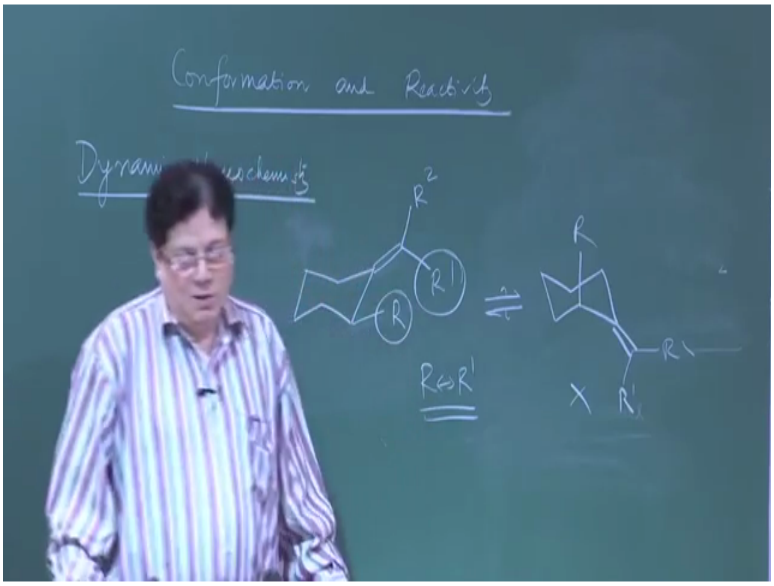

Similarly, yesterday also I again told another, kind of system where there is significant amount of axial substituent and that happens; in very similar system like the cyclohexanone only think that you have a double bond here, exocyclic double bond with substituents R1, R2 and R1. So here what happens? Now if there is a group here, so that is now undergoing steric compression with this R1. So as a result, this undergoes flipping and you get this R as axial. So now there is no steric compression between the R1 and R2. So R-R1 that one is there, okay. So that is now gone that is not present. So there is significant amount of this axial conformer and this is what is called A 1, 3-strain**,** okay. Now because this is 1, this is 2, this is 3, so that is the origin of the name how it originates.

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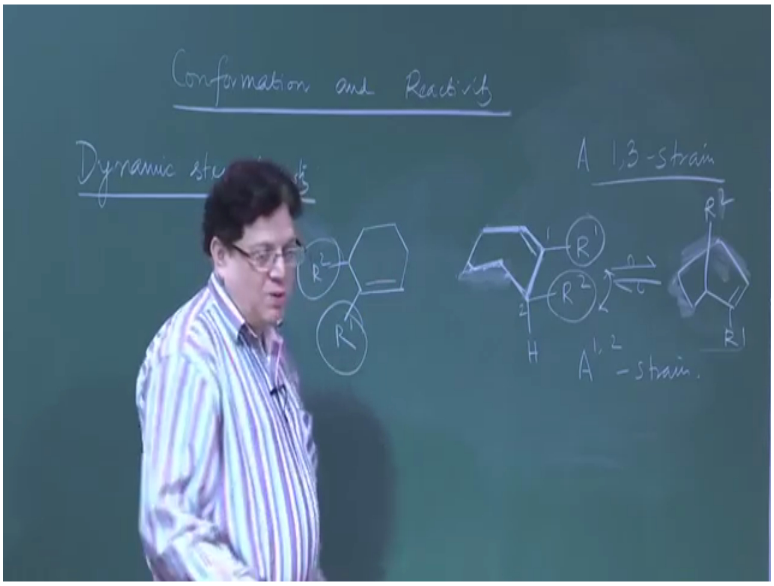

Now instead of there is another one that is called A 1, 2-strain. If the double bond happens to be in the, inside of the ring. So if the double bond happens to be a cyclo that means you are talking about a cyclohexene, okay and in cyclohexene, there is if there is a there will be an interaction between these two groups and this interaction apart 2 with R1 will depend upon whether R2 is axial or in the equatorial conformation; however orientation. Now the question is we have not done the how the this cyclohexene looks like we have done the cyclohexane, but just to let you know that cyclohexene exist as a conformer, which looks like this, sorry. It is somewhat like this. So it is a it is what happens here that one carbon, these see basically, this is a double bond so, this carbon this carbon that carbon and this carbon, these are in the plane, how many (())(10:49) 1,2,3,4 sorry 5, 6,7, it. So this is the cyclohexene. So these 4 carbons are in the plane and then one carbon, it goes above the plane another carbon goes below the plane, okay.

Now if you have the substituent here and the substituent there. This is call the equatorial pseudo equatorial you can call, this is not perfectly equatorial like the cyclohexane and this is a axial position, okay. So if it, first of all this is not a planer system. This is a kind of what is called a half chair type of conformation and in the conformation, you must clarify that 4 carbon atoms are in the plane, 1,2,3,4 and this goes the down and this goes up. So this is in the plane of this, because of the double bond sp2 nature, okay that has to be.

Now this R2 is in the equatorial orientation. If it is in the equatorial orientation, it suffers from, now steric compression with R, because there is lot of kind of, they are very close to each other. So that flips and it takes a conformation where, let see to how to draw it. So it takes a conformation, where so a conformation is 1,2,3,4,5,6,7 up to is 7, so something like this that is the flipped form and the R1 goes to the top a R2 goes to the top sorry and this is the R1,

So this is the flipped form of the cyclohexane. So again I start from the beginning that if you have, this disubstituted cyclohexene system by the way cyclohexene is a non-planar system. If this R2 is in the equatorial position or a pseudo-equatorial position to be précised then there is steric compression between R1 and R2. If you flip it then R2 goes into the axial position like this. So it is oriented upwards and if it does that then this interaction is gone. So this kind of strain, so called A 1, 2-strain. So A 1, 2-strain is, because this is 1 carbon and you can say this is two, because they are adjacent to each other. So that is called A 1, 2-starin. Now there are many reactions which are controlled stereo chemically by this a 1, 2-strain, I can show you in the model whatever I was telling you that in the in the, this is the cyclohexene**.** This is the double bond and then you have these 4 carbon atoms in the plane as I now saying. So one carbon goes down one carbon goes down, another carbon goes up, okay. This is the system.

Now what happens? This is the pseudo equatorial substituent on my left and this is a substituent attached to the (())(14:17) carbon, okay. So you see now their dihedral angle is not zero degree, not 60 degree also, but they have a much, they have quite in the eclipsing interactions zone and in that zone there will be steric repulsion between this and that and there will be bond of position strain also. So that makes it little unstable.

So in order to avoid this type of strain what this molecule will do? This will undergo flipping, so you see the flipping what happens? The up carbon goes down and the bottom carbon goes up, earlier this was up and this was down. Now this is down, this is up, but what happens this is a substituent, which is now pointing upwards that is, it is axial, okay. So this axial orientation, now avoids the steric compression that it was suffering when it was in the equatorial position, so this is what is the genesis of A 1, 2-strain, okay.

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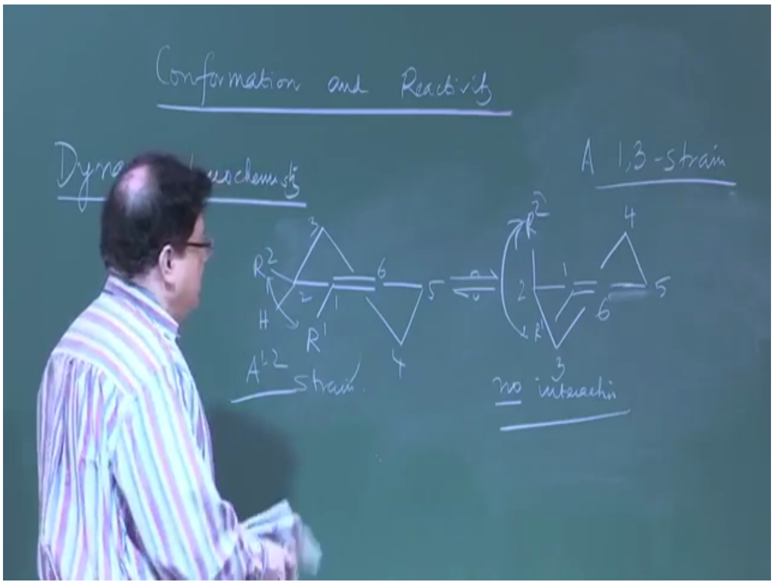

So you also know little bit about the cyclohexene, geometry. Now you can actually write a cyclohexene. There are two ways of writing, one is the way I have writurn another is that the way I have you in the model if you now write a perspective formula from the model. So this is what is happening. So this is the seen arrow. So this is the substituent, I was talking to you and these are the, this is the R2 and this is the hydrogen, okay. So when it flips, so it goes into the this will go down. So now the chair will half chair will look like, sorry this, okay. So if I number it, 1 say 2,3 correct numbering should be 1, this is 1,2,3 something like that I am not following the (())(16:27) system, just a rough numbering 1,2, because I want to show the allylic 1,2-strain. The vicinal strain, so 1, 2, 3, 4, 5,6.

So now it will be one, this will be 1, so this is 2 that is note out 2. This is 3, that has gone, now this is 4, this is 5 and this is 6, okay. Now where is this R1 R2 the R2 is pointing to this side and R1 still here? So now this interaction is less. There is no interaction practically no interaction between R1 and R2, but here is there is A 1, 2-strain, okay. This is the other way to write the cyclohexane, okay whichever is convenient for you, do that, okay, but we mostly we will later on we will use this type of conformer, in in describing certain reactions, okay. So that is again some kind of static stereochemistry that we talked about that how the preferential conformation is dictated by, these kind of stains. So we have seen different kinds of strains. So these are the addition ones, okay.

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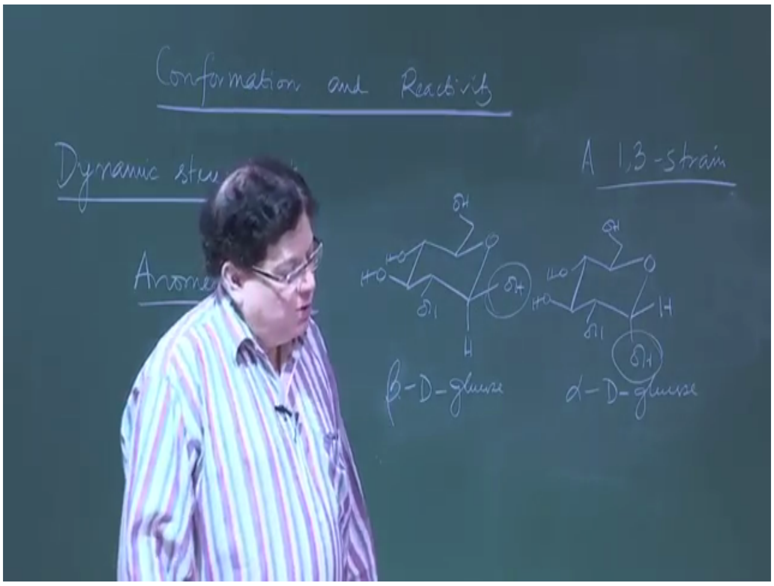

There is one more important strain that is they are just a second let me try to (())(18:01) that okay. So let us see, there one another effect like this allylic effect is there. There is this ketone effect is three. There is another effect which also tries to put the substituent in a axial position preferentially and that is called anomeric effect. Now anomeric effect actually the name comes from the sugar chemistry where you know the glucose has the number one carbon of glucose is also called anomeric carbon. So let me write the glucose structure, two forms of glucose are there. This is the alpha-D glucose and there is this beta-D. This is the beta, sorry this is the beta-D glucose and the other one is alpha-D glucose, alpha is when the OH is axial, other groups remain at the same orientation. So this is the alpha-D glucose.

Now in water solution you know that this is the predominant one. It exists as a 2 is to 1 mixture of the alpha and beta D glucose 2 is to 1 mixture of beta, beta is 2 and alpha is 1. So if you take pure alpha then this undergoes muto rotation and ultimately it creates a mixture where this is 2 and that is 1 or if you take beta put it in a solution amphoteric character with amphoteric character base (())(19:57) both acid and base character then it undergoes mutarotation and ultimately the equilibrium value is reached where this is present , in a 2 is to 1 ratio, okay. So that is understandable this OH is equatorial and this OH is axial. So we know that the groups tend to be tend to assume the equatorial position preferentially, so that is okay, but the moment this was made into way mean, say the methyl glucoside.

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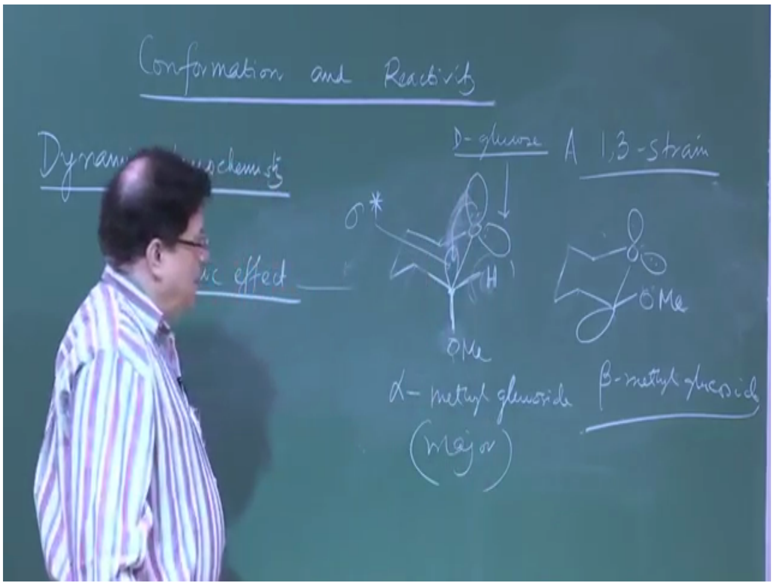

So this is the alpha methyl glucoside and this is the beta methyl glucoside. Now between these, so if you want to do, this glucoside formation with methanol and take glucose whether it is alpha or beta, because they will always be equilibrating into this via mutarotation into a 2 is to 1 form.

So we expect that if I take glucose, D-glucose and do this glycosylation, the methylene this methyl glycosylation ((())(21:19) then I expect that, this should be formed in major amount and this should be formed in minor amount, but in the contrary, actually this was formed in the major amount this was found to be major amount and so what happens when it is glucose, it was Oh the as expected the OH assume preferentially the equatorial position, but when you convert the OH into OMe or OCoCH3 and or OCoCH3 then what happens?

The preference for the axial orientation increases and that is what is called, because this is happening at the anomeric carbon and this is what is called the anomeric effect. The anomeric effect is the effect, in which the axial orientation is preferred over the equatorial orientation, okay. Now this happens then this happens only when you have oxygen here. If you remove the oxygen, then this was more stable than this one, but if you have the oxygen here then this thing happens. Now what about the other groups, later on people found that this is a very general effect? It is you do not need these groups. So if you have an oxygen and then the next carbon is a stereo genic carbon and you put OMe at the axial and OMe at the equatorial, which one is more stable? It was found that the axial was more stable than the equatorial and why is that.

The explanation there are many explanations, one explanation is the what is call the dipole, because in this case, the dipole the polarities in this direction and the C-OMe also in this direction. So there will be repulsion between these dipoles. So which is minimized in case of the axial methoxy, but there is another which is little better approach to explain this preference for the axial orientation and that is what is said is that, see oxygen has two lone pairs. One is pointing towards the axial position and the other is pointing towards the equatorial position.

Now if you have the OMe attached in the axial position. So you have a carbon-oxygen bond. Now oxygen orbital and carbon orbital are combining with each other. So they form a they can form an anti-bonding orbital, which is has a bigger lobe at the back side and that is empty. So now this oxygen lone pair in the axial position and this empty sigma star, they are in lateral position. So there is a possibility that this oxygen now, overlaps with this empty anti-bonding sigma star the carbon oxygen sigma star orbital. Thus stabilizing the system, which is not possible in case of the equatorial isomer, because the anti-bonding orbital will be on this side. So there will be no interaction.

So now you have this interaction, which is stabilizing the axial isomer. So the I think that is a better way of explaining the anomeric effect. So this is another new, chemistry that you have learned to this anomeric effect, that is whenever you have a system in which hetero atom like oxygen is present in a ring, then the next adjacent carbon and tries to adapt a orientation in which the electronegative group.

Now this is an electronegative group that has to be important. It does not happen with a alkyl group, it happens with only with electronegative group, and the electronegative group tends to occupy preferentially the axial position and that is the anomeric effect and this is quite important in explaining the product formation or the dynamic stereochemistry in sugar molecules, okay. Thank you.