Course on Stereochemistry
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Mod06 Lecture 24
Conformational Analysis of Substituted Cyclohexanes

Okay, welcome back last time we have we have done the analysis of flipping that how the energy changes and we have identified the conformers that are present in cyclohexane, the just to repeat it again that there are basically two conformers is present in cyclohexane the chair form and the twist boat form in the (())(0:48) okay boat form, because it lies in an energy maxima that is not a conformer, okay and we also know why the boat form is unstable, because mainly because of the presence of two eclipsed butane units in the boat form okay.

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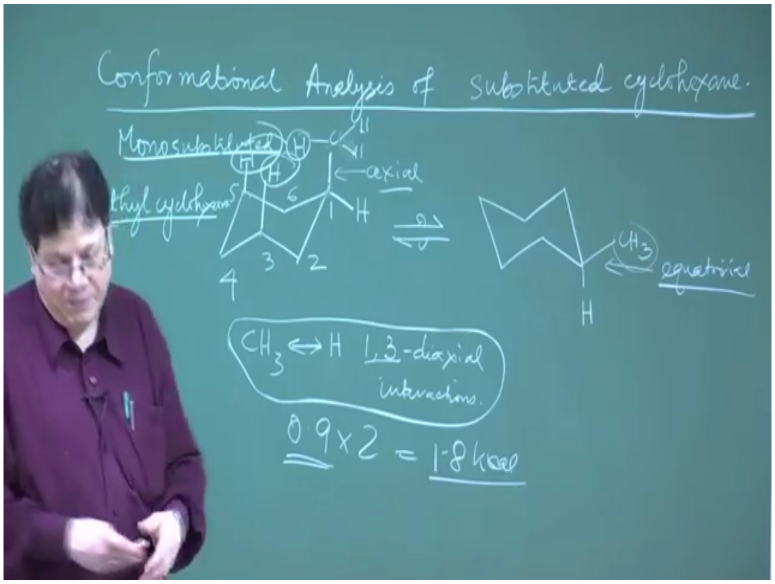

Now we will come to cyclohexane when we substitute it, substitute one of the hydrogens with a say suppose an alkene (())(1:16) group. So we will come to the mono-substituted cyclohexane. So how the energy changes and which position the substituent will occupy whether it will occupy the axial or the equatorial position, so that will we see. So let us take the simplest of all that is the methyl cyclohexane. Now methyl cyclohexane, so first write the chair form of cyclohexane and now you put the methyl group. Now you have the two you have options okay, you can put the methyl in the axial position and the hydrogen in the equatorial position or vice versa. Suppose I put the methyl in the axial position and then you know that just by flipping what happens? It goes into the mirror image chair form and by flipping the methyl becomes equatorial, but it remains beta.

So now there will be an equilibration between these two. Now these two flip forms are number longer as no longer having the same energy. Why? In cyclohexane these are hydrogen, so there is no difference between the chair form (())(2:39). Now have the methyl group, here it is axial and here it is equatorial, okay. So they are there will be a difference in energy between these two. So the question is which one is preferred? Now there is a rule of thumb in cyclohexane chair form that if you try to put a substituent that substituent wants to take the equatorial orientation, okay that is a rule of thumb, but not always it may not be true I give you also a question but general rule of thumb, it follows generally that the substituent if it is a mono-substituted system, the substituent enters to occupy in an equatorial position. The question is why, okay.

Now there are various explanations you can actually tackle this question in in basically two ways, one is that in the axial methyl form suppose this is the one position, 2 again I number it 4, 5, 6 there are these axial hydrogens at C5 and C3 remember methyl is I am writing it CH3, but actually it has got these hydrogens here. So these hydrogens and that hydrogen. So these 3 hydrogens now are within the (())(4:13), so there will be interaction between these methyl and these hydrogens which are at C3 and C5 between the axial hydrogens at C3 and C5.

So they will be methyl hydrogen interactions, but this has got a name, this is called 1, 3-diaxail interactions, okay. It is 1, 3 in both the cases this 1, 3 is the relationship between these two hydrogens note that we will not call this as 1, 5. This is also 1, 3. Basically if I say these two carbons are in a 1, 3 relation. So it is always 1, 3-diaxial interactions do not call it 1,5-diaxail interactions. This is 1, 3-diaxail interaction; this is also 1, 3-diaxail interaction, okay. So there are two 1, 3-diaxail interactions that are present in the axial conformer of methyl cyclohexane okay, we always draw the chair form, because the chair form is the more stable conformer. So it is the form that is present we are not considering the boat or the twist conformer we will consider directly the chair forms okay. We will come back later on with some examples of molecule which are force to adopt a twist boat conformation, okay but that will come later, right now the simple once where they exist only in the chair form okay.

The question is there are two chair forms possible, in one there is axial methyl and the other is equatorial. They are inter-convertible by flipping; however the energy say that because of this 1,3-diaxail into methyl hydrogen interactions, this form has higher energy than this one and people have given a value for these 1, 3-diaxial interaction and that is 1,3 for each 1,3 diaxial interaction that accomps (())(6:16) about 0.9 kilo calorie per mol. So now this molecule will have at energy which is extra above the which is more than this one, because in this case, those diaxial interactions are not present, because this is occupying an equatorial position. So the energy difference is 1.8 kilo calorie based on the presence of two 1, 3-diaxail interactions.

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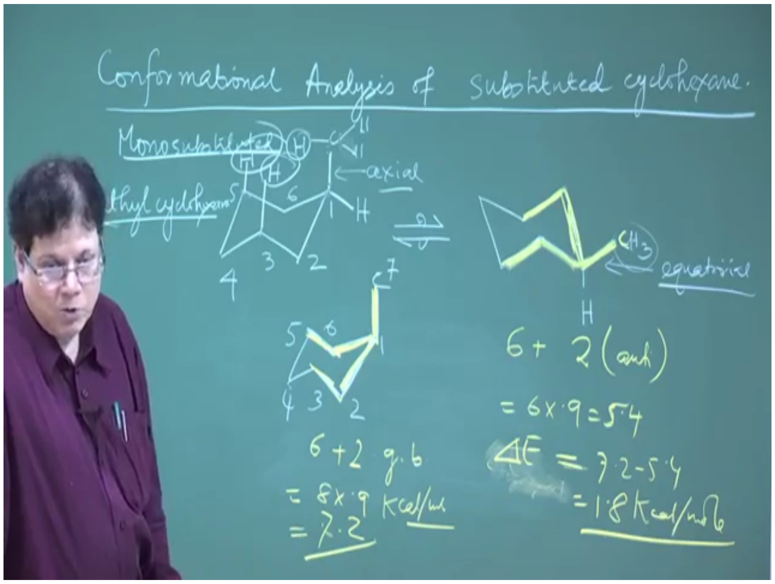

This is one way of looking at the problem another way is the way we looked at the energy of the cyclohexane chair you can also do the same dissection of the molecule and dissect it into n butane units okay. So when you have when you had this cyclohexane chair form, so we know that I can dissect it into 6 butane units and those 6 butane units where in the gauche conformation and accordingly we calculate in the energy 6 into 0.9 that is 5.4 kilo calorie per mol. Once I put a carbon extra carbon now a methyl, I introduce two extra butane units see earlier the butane units where this see you 1,2,3,4 then 2,3,4,5, 3,4,5,6 like that, but now as we have put an extra 1, suppose this is a C7 carbon, so now you have 2 extra butane units, one is 6,7,1,2 and 3, 7,1,2,3 and the other is 7, 1, 6, 5 okay, I can show you with the model that this is my cyclohexane chair and as I put this methyl, as I put this extra carbon, so now I have when I looked through this bond, I have again another set of carbon-carbon bonds, which are in the staggered form, okay and the dihedral angle between this, in this form when the methyl is axial is 60 degree.

So this new butane unit, one is this one and the other is on the other side that means you have to rotate it and the other is you look from this is the carbon, the other is you look from this and that carbon. So you get another extra set of butane unit that can be shown here in the in this that the extra butane unit is this one and the other one is this. So these are the two extra butane units. Now the question is what is the status of these butane units? These extra butane units, so it has already 6 gauche butane interactions that was inbuilt in the chair form and now we have two extra. So these two, the question is this two are in which form, actually the dihedral angle between this and that is 60 degree, I just shown it in the model, but you can also roughly guess it, because this is not anti, because the anti will go down the they are not anti and they are not in eclipsed position.

So the natural logical conclusion is that the dihedral angle is 60 degree between this and that and between this and that, okay. So we have 2 extra butane units and these two are in the all are gauche butane units. So the total energy, it becomes 8 into 0.9 kilo calorie per mol and here again you have extra butane unit here, because you have this carbon here. So now the extra butane units are one is this and the other is this, so these are the extra butane units and from just diagram you can now make out what is the status of this butane units.

So this is now anti to this one and this is now anti to this one. So these two extra butane units are, now in anti-butane conformation, okay. So you have 6 in built in the cyclohexane 6 gauche butane units plus two, but these two now are in the anti-form. The anti-form does not generate any extra energy, because that is our starting reference point; the anti-butane unit is the zero point energy, okay. So that does not give you any extra energy. So you have 6 into 0.9, so again 5.4 that means methyl cyclohexane has the same energy has the cyclohexane, you do not incorporate any additional interaction into the system. So this is 5.4, this is 7.2, so now the difference becomes again 1.8. So the difference delta E of between axial methyl He delta E between the axial and the equatorial is equal to 7.2 minus 5.4 that is equal to 1.8 kilo calorie per mol.

So you can explain it, in two way the either you go but for this 1, 3-diaxial interaction that gives the same value when 9 into 2, 1.8 otherwise if you are extremely thoro you can rely on this actually this is a better approach you better identify the extra butane units, try to find out what is their status, whether they are in the anti or the eclipsed or in the gauche form and then accordingly you calculate the relation, okay.

So now we are we can say that methyl cyclohexane will be will remain mostly in the equatorial form, okay. This has now been what worked out (())(12:31) actually how much is the percentage of the equatorial in the equatorial form in methyl cyclohexane, okay, but we can say just we do not know the number. So we will say that they, it is mostly remains in the equatorial form, 1.8 kilo calorie is quite a difference it is at least 90 percent of that will be in the equatorial form, okay the rest possibly in the axial form.

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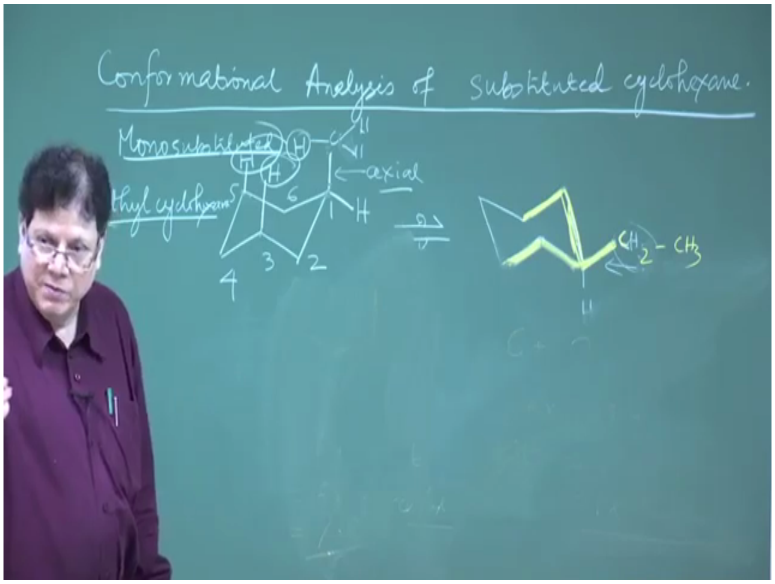

So that is for the methyl cyclohexane we will not go beyond this, just I will have a that if you were asked that there is a another carbon here say ethyl, then you know you can go by the number of butane units that you have, now introduce a butane unit 1, 2, 3, 4. So number of butane units as you put more carbons, the number of butane units keep on increasing. So in your analysis we should always try to find out the number of butane units extra and then see whether they are in the which form whether in the gauche form or in the eclipsed form or in the anti-form and then accordingly you can calculate the energy, okay.

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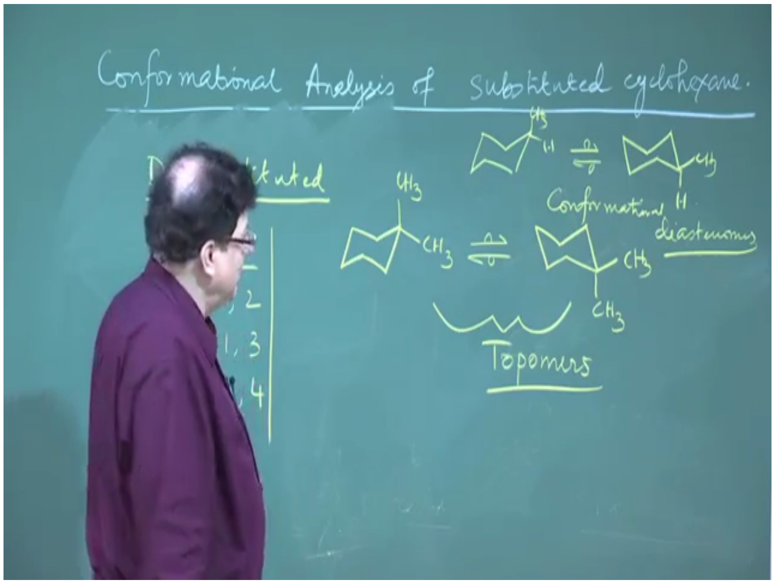

Now the next is if you have a di-substituted system if you have a disubstituted cyclohexane system okay. Now disubstituted can be various types, 1, 1, 1,2, 1,3, and 1,4 okay. So these are the kind of di-substitution you have. Now the 1, 1 the first the simplest one is that you have both as the msethyls both the substituents are at the same carbon and both are methyl. Now in that case see you do not have any choice, one methyl has to in the axial and the other methyl has to be in equatorial and now you this, what happens? It goes into the mirror image chair form, but the energy actually the molecule remains the same. Now again one methyl is axial another methyl is equatorial, okay. So there is no energy difference. Now these are what are known as topomers, another (())(15:00).

Topomers that means in flipping you are getting the same compound, so that is in that is they are known as topomers, but that happens when they are same loops (())(15:12) okay. I just remind you that if you have only one methyl, these two compounds are different, because this was; they are not topomers, okay. They are conformational isomers and they are basically they are conformational isomers. They are not topomers they are not identical here, they are different that means see this is a very tricky issue now, because what is our definition of stereo isomers that molecules which are same constitution, but they are they are different, same constitution same molecular formula, but different molecules. They are stereo isomers okay and stereo isomers have been divided into two enantiomers and diastereomers, okay. Mirror image isomers are called enantiomers okay, but diastereomers are they are not mirror images of each other okay.

So in stick sense (())(16:17) what are these then they have the same constitution everything, but the geometry this position of the methyl at this carbon at this carbon okay. So they are diastereomers, but the difference in the conventional diastereomers and between these diastereomers is that these diastereomers are inter-convertible very quickly okay, by just rotation you can come from one diastereomers and go to the other diastereomers. So they are called conformational diastereomers. They are diastereomers defiantly, because they are not mirror images of each other, although but they are different, they look different, but would because of the inter conversion they are called conformational diastereomers okay, but here they are topomers, even if you flip, it is a same thing, so that is a topomers and there is no question of which one predominates okay.

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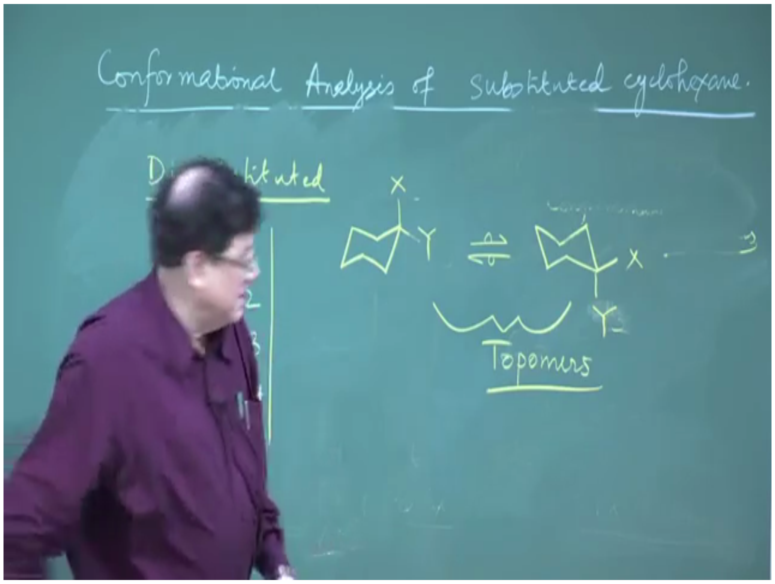
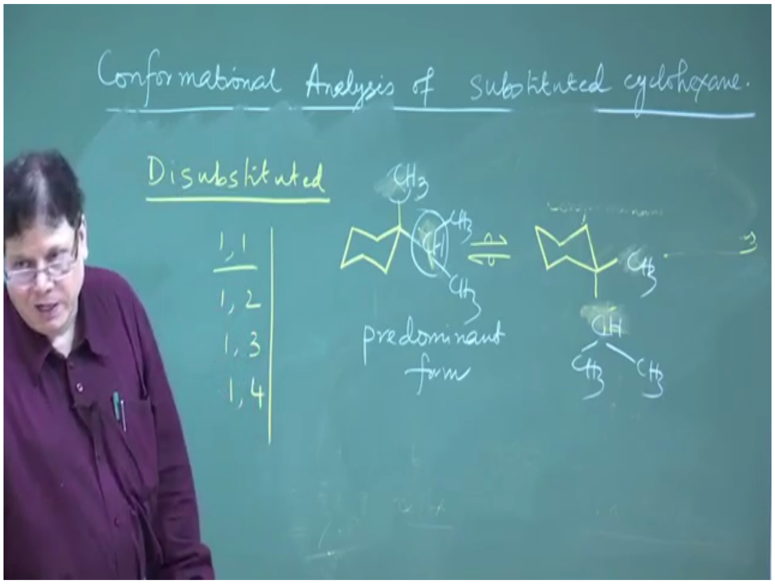
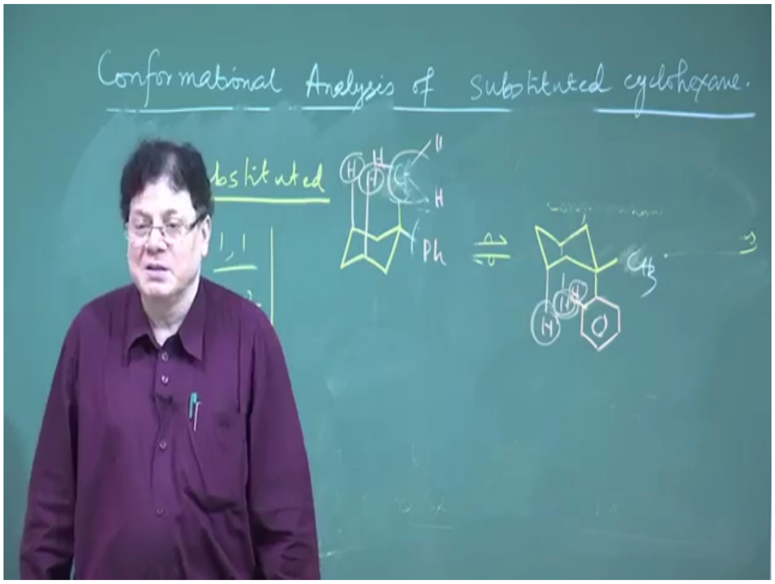




Conformational Analysis of substituted cyclohexane.

Disubstituted

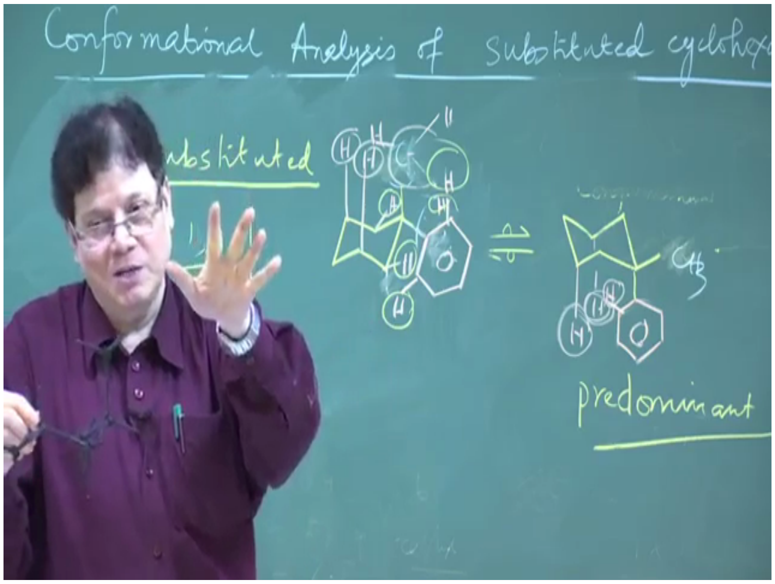
1,1
1,2
1,3
1,4



Conformational Analysis of substituted cyclohexane.

bstituted

1,1



It is a simple is a single compound that exist for the 1,1 dimethyl cyclohexane; however now if you suppose you have a methyl and suppose I just in general, suppose you have x and y. Now if you flip, so x will be here and y will be there. They are different now, because in this case y was occupying alpha equatorial position. Now this is alpha axial okay and x is just the opposite vice versa which opposite for the x. So now they are no longer topomers okay, so I have to erase that. Now they are no longer topomers they are again conformational diastereomers. They are not same. They are stereo isomers; however they are inter-convertibility make them conformational diastereomers okay.

Now which one will predominate between these two that depends on the relative size of x and y. so again the rule of thumb the bulkier group first if there is a one substituent than their substituent tries to go occupy go and occupy the equatorial position. If that is if there are two groups, now the bulkier group will try to occupy the equatorial position, okay and the less bulkier group try to occupy the axial position. So if you have a competition between a methyl and suppose verses isopropyl. So I can say that this is now methyl and this is isopropyl. So which one predominates I can say that this one will be predominant form, okay. Now sometimes it becomes little tricky to compare the steric bulk of the two groups, sometimes it becomes tricky, in which case? Suppose instead of isopropyl suppose now it is a competition between methyl and phenyl.

So this is a phenyl group and this is a phenyl group, okay. Now apparently phenyl is a larger group than methyl C6H5 and this is only CH3. So at first side you might say that okay this is the one the form which should predominate and not this one okay; however there is certain issues here. The issue is that see when methyl is occupying this position, I told you about the 1, 3-diaxail interaction. So there is two 1, 3-diaxial interactions between the methyl and hydrogen. When phenyl is occupying the axial position then you have again 1, 3-diaxail interaction between the phenyl and these axial hydrogens. The question is which (())(20:48) 1, 3-diaxial interaction is more, okay again if you just look phenyl and consider is steric bulk then you will say that okay, this has to be larger than the methyl hydrogen, 1,3-diaxail interaction; however there is a difference between phenyl and methyl what is the difference?

The methyl is tetrahedral carbon okay. So methyl has this 3 hydrogens, see if it had the option of putting all the hydrogens towards this side then it would have done that to avoid the 1, 3-diaxail interaction, but it does not have that option, because they the tetrahedral nature of the carbon compiles (())(21:31) that one of the hydrogen has to be on this side, okay. So that is the characteristics of the tetrahedral carbon sp3 hydrogens, but phenyl what happens the phenyl is a ring or sp2 carbons, okay.

Now there is a big difference that now here also the even if the methyl rotates one of the hydrogen will always be towards the left side. There is no conformation available for the methyl where all the 3 hydrogens are away from the one this diaxial, but phenyl what it can do? If it is in this plane then these hydrogen will now start heating these hydrogens, but if the phenyl is in orthogonal position like this then what happens? One hydrogen goes on this direction another hydrogen goes behind the plane of (())(22:27) and then the hydrogens are away from the diaxial hydrogens. So because of this rotation, so what I am saying if it is methyl, so you do not have any option, one of the hydrogen has to face this side of the ring and the other two hydrogens are (())(22:42), but if it is phenyl I do not have phenyl ring here, but if it is a flat carbon making a flat ring, so the ring has the option now either to place it this either to have it this orientation or that orientation.

If it has this orientation then the hydrogens point towards this hydrogen. If it occupies this orientation then this orientation then this 1,3-diaxial interaction is gone (())(23:06), because the hydrogen is one is in this direction another is in this direction, okay. So that means this 1,3-

diaxial hydrogen is no longer is important if it is a phenyl a flat ring, okay which can avoid this 1,3-diaxial interaction. On the other hand if the phenyl is occupying the equatorial position then what it cannot avoid is the these equatorial hydrogens, now start heating the hydrogens that are here, interesting now. So now when you put the phenyl in the equatorial position. In the equatorial position then this equatorial hydrogens are now having a steric repulsion with the ortho-hydrogens of the phenyl.

So contrary to the 1,3-diaxail interaction that we were thinking it does not when you have the phenyl that phenyl , in the equatorial position suffers interaction with this equatorial hydrogens and that makes it less stable than the axial. So there are two reasons means in the methyl just to summarize what happens that in the phenyl methyl case, the predominant form is this one. Why, because the 1, 3-diaxail interaction is reduced in this case, because the phenyl adapts an orientation where the hydrogens are away from the actual hydrogens that is number 1, so the hydrogens that is number one. So that fevers (())(24:56) the axial conformation and the equatorial the equatorial one is less preferred.

Now it suffers from strain from these hydrogens, oaky and if you think that okay, I put them in order to minimize this repulsion, I put the methyl , this phenyl in such a position that it is like this, in the plane of the board, but then how the problem is this hydrogen is heating the methyl hydrogen. So it does not have much choice. So what I am saying when the phenyl is on this side. So if it occupies this type of plane then these ortho-hydrogens start heating the equatorial hydrogens and if the phenyl adapts this conformation then the ortho-hydrogen starts heating these hydrogens the methyl hydrogens. So it has no escape (())(25:48) okay. So that makes it less stable.

So there are two reasons, first phenyl does not have this 1,3-diaxail interaction and the equatorial one on the contrary have this ortho-hydrogens heating either the methyl or this equatorial two equatorial adjacent hydrogens, so that makes it less stable. So here this is the predominant one. So I thought this is an interesting example, so otherwise if it not aromatic ring if it is between only alkil (())(26:17) groups then the bulkier alkyl group will always occupy the preferentially the equatorial position, okay. So thank you.