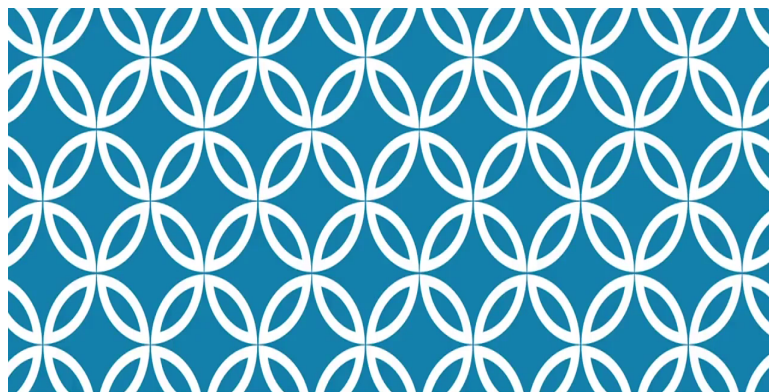


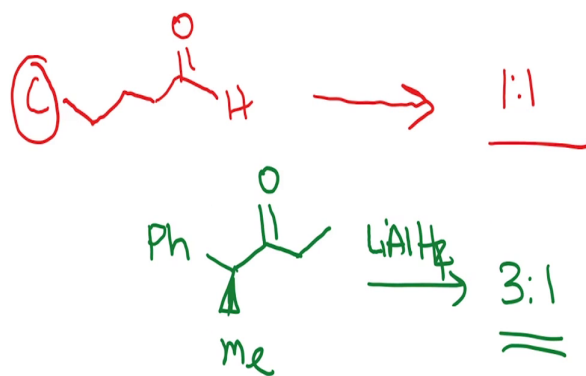
Introductory Organic Chemistry II
Professor Doctor Harinath Chakrapani
Indian Institute of Science Education and Research, Pune
Module 03
Lecture 22
Addition Reactions on Carbonyl functional group

(Refer Slide Time: 00:16)



PRINCIPLES OF ORGANIC CHEMISTRY
II

Harinath Chakrapani

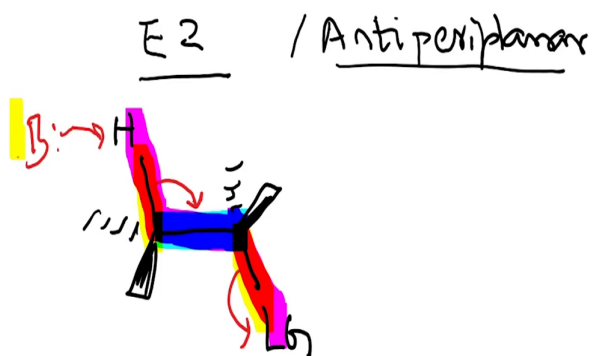


So, in the last lecture, we were trying to understand what various modes of addition to carbonyl compounds were. And, we looked at for example, Enantiotopic faces and how we named them and how they are quite precise in describing the mode of attack and so on. So, the important point to note there, in the previous lecture was that when you had a Chiral center, so, you also have not just Enantiotopic faces, but you also have Diastereotopic faces.

And so, the important point is that when the carbonyl group was quite far away from the Chiral center, you know there was literally no effect of addition; that means, you got a 1 : 1 mixture of the two products that could be formed due to two possible modes of attack. Whereas, when the chiral center was close enough to the compound that is when you had the example that we looked at was this, when you have this compound, and you do LAH reduction, you ended up with a 3 : 1 mixture.

So, in order to understand this, I am going to now provide you a theoretical framework that helps us reason this out. So, a lot of things in chemistry are first observed experimentally and then a theoretical framework is developed.

(Refer Slide Time: 02:01)



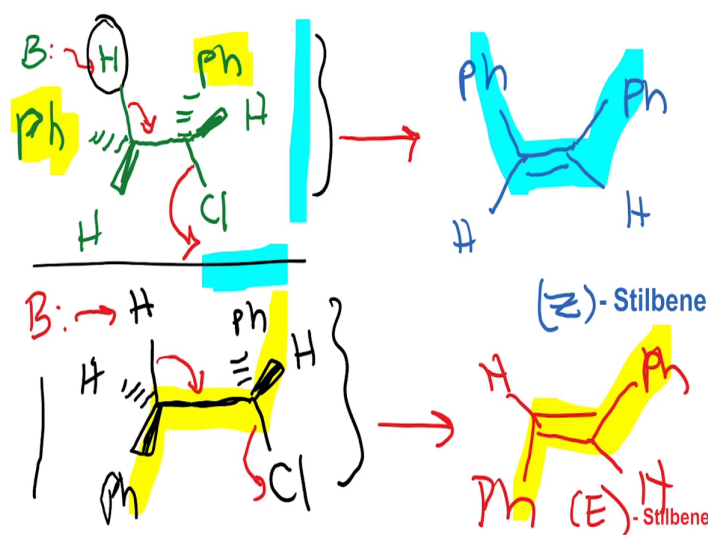
So, now, in order to understand this, let us go back and look at another example of something that we have already studied, which is Elimination reactions. So, in E2 elimination reactions, we have encountered the situation where you know this elimination occurs with the anti-periplanar transition state. So, anti-periplanar configuration or anti-periplanar geometry is in place.

So, what this means is that, you have the leaving group here and hydrogen over here, and the other groups are in this kind of orientation, and what happens is that, this bond starts to break and you have a new double bond that is being formed and this bond starts to break. So, you have this kind of an arrangement.

And of course, just to be complete, the base is attacking here, and then you have the formation of the double bond and the leaving group leaving. So what this anti-periplanar means is that, when you draw a plane that encompasses, or that has this, this and this, they are all in the same plane. So, this is what we mean by anti-periplanar relationship. So, this is something that you have already studied previously.

Now, when I want to use this information, for explaining the distribution of products, then what I would need to do is I am just going to take an example that helps you sort of reason this out.

(Refer Slide Time: 03:47)



So, the example here is the following. So, when we start with this particular alkyl halide, so you have hydrogen here, and hydrogen, phenyl. And there is another hydrogen here, and there is a phenyl. So, this is an elimination reaction that happens in the presence of a base to give you Stilbene. So, let us now look at this elimination from this configuration or conformer, and it attacks here and now, this is lost and chloride is eliminated and you get the following product.

So, the following product is basically the way we draw out the product is this phenyl ring, and these phenyl rings are actually on the same plane. So, you would end up with the following cis-isomer or Z-isomer. Now, I can always do some rotation of this bond. And if I do the rotation of the bond, then we will keep this carbon to be constant.

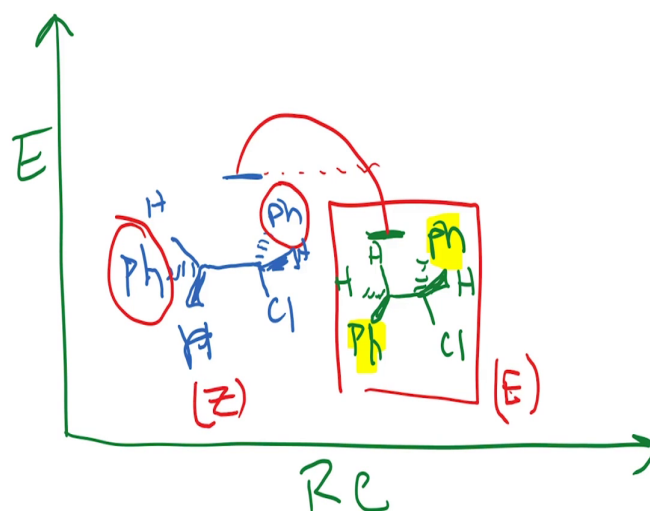
And we actually rotate this carbon over here. So now if I do that, let me just draw this out the way it is drawn. So, we have phenyl, hydrogen, Cl, and this is the carbon-carbon bond. And now, when I do the rotation, I am going to move this hydrogen further down, and the phenyl ring is going to be over here. So, this hydrogen goes here and this hydrogen goes here. So, this conformation, and you will notice that this is just a carbon-carbon bond rotation.

And so, there is nothing magical in this, it can happen very nicely at room temperature. So, now, if a base attacks it in this particular conformation, you still can undergo elimination, the only thing is that it is going to give you the E product. So, just to recap, we are just taking this starting material, and we are treating it with a non-nucleophilic base, maybe Potassium tertiary-Butoxide, or something like that. And we are just looking at the products that could be formed.

So, from this conformation, if we start from this conformation, we end up with a Z isomer. And if we start with this compound, we end up with the E product. So, now, one would be very tempted to say that this conformation is more stable, and therefore, the population of this conformation is higher, and it would give the E product, because we know that the E product is going to be the major product of this reaction.

So, I will repeat, it is very tempting for us to say that the E product is formed, which is formed from this conformation, this conformation is going to have a higher population when compared with this conformation. So, that kind of an explanation would certainly help us reason out or help us rationalize the result. However, what is important here is that the barrier for conversion of this conformer, the conformer that is leading to the Z product, and the conformation that is leading to the E product, that barrier is extremely low.

(Refer Slide Time: 07:56)



So, now I am just going to draw the two, I am just going to draw an energy profile, which describes this process. So, this is the energy and this is the reaction coordinate, E and R.C. So, now, this is one of the conformations and this is the other conformation. Now, let me just redraw this so that it is easy for us to understand this, I am just going to draw it a little smaller. So, here is the hydrogen, hydrogen, phenyl ring, the Cl is here, the hydrogen is here, and phenyl is over here.

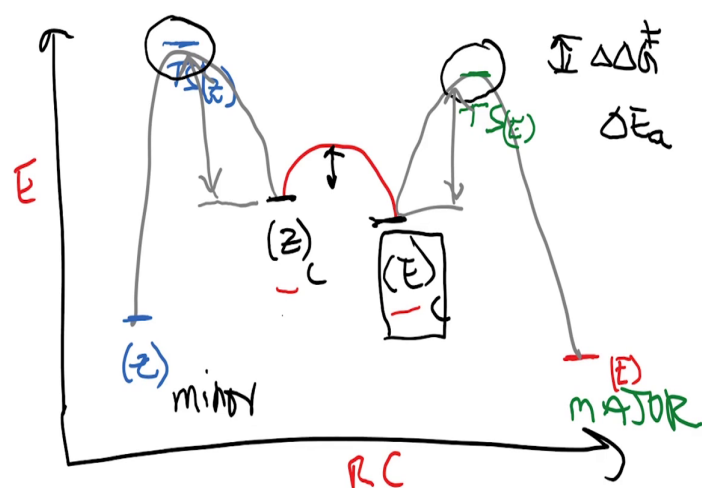
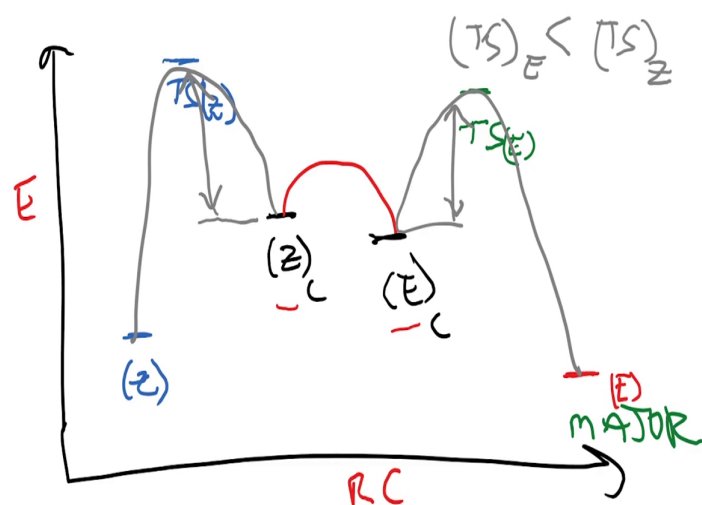
So, as you will see, here, the two phenyl rings are quite far away from each other. And so, that must give this conformation a little bit of higher stability compared to the other conformation. Now, let me just draw this a little further away. So that we can draw the other conformation nicely out. So, this is let us say, the other conformation, where the back carbon remains the same.

So, you have the phenyl ring. So, this is the carbon, and this is the hydrogen, and this is the Cl. So, this back carbon or the carbon on the right remains the same, but now in the other carbon, what we have is we have hydrogen and this is also hydrogen. And this is the phenyl ring. So, notice that the two rings are close to each other.

And therefore, this is of a higher energy. This conformation would be of higher energy compared to the other. Now, what we know from various experiments and theoretical calculations is that the barrier to conversion is not very large. So, people have estimated this to be somewhere between 10 to 15 kilojoules per mole, which is easily accessible at room temperature.

So, even if you go to a slightly lower temperature, you might slow those down. But it is really something that is going to be happening very rapidly. So, the argument that we make, that one would make saying that this conformation is of a higher population is not something that would hold good. So, we have to now develop an argument or theoretical framework that helps us understand the outcome. So, now going forward, this is going to be the E conformer. And this is going to be the Z conformer.

(Refer Slide Time: 11:06)



So, let me just redraw this energy profile again. So, just to recap, what we have agreed is that the difference between the Z conformer and the E conformer is real, that is E conformer, is definitely more stable, or the conformer that is leading to the E product is more stable, but this barrier is going to be so low that it is going to freely interconvert. So, now given this, how are we going to explain any difference in the product formation?

So, the way we would do this is now to propose or suggest that the product, you know that is going to be formed, which is the E olefin. We already know that the E olefin is going to be more stable compared to the Z olefin. And how do we find that out? You may recall that, if

you do a hydrogenation reaction on the Z olefin, and the E olefin, they are going to give you the same product, which is the alkyne.

And now, if you measure the heat of hydrogenation, the E olefin liberates less energy, which means that it is more stable when compared to the Z olefin, so that is how we experimentally determine that the E olefin is more stable. You can also do it by combustion analysis. So, by measuring the heat of combustion, you would get the same result. So, there are several thermodynamic parameters, which suggests that the E olefin is more stable.

So, therefore, now coming back to this picture, what we need to understand here is that the difference in the product distribution would be a reflection of the rate at which the product is going to be formed. So, if E is the major product that is being formed, then the rate at which E is being formed is substantially higher than the rate at which the Z is being formed.

So, in order for the rate to be higher, what we can propose is that the transition state leading to the formation of the E product is lower in energy, when compared to the transition state leading to the formation of the Z product. So, given that the rate of formation of the E is substantially higher than the rate of formation of Z, this may be reasonable to propose.

And now, if I draw out an energy profile, what emerges is that you are going to have a transition state that is of lower energy when compared to the Z. So, therefore, what we can sort of understand from this is that the transition state of E, has lower energy, or is more stable compared to the transient state of Z, or the way to understand this is that the barrier to the formation of E is substantially lower than the barrier to the formation of the Z product.

So, this is something that we may want to sort of look at again. So, I am just going to repeat this part a little bit, so that we can understand this a little better. So, when we consider reactions where there is going to be a competition, so here is a competition between the formation of the Z product and the E product. So, we know that the Z is the minor product, and the E is the major product.

So, what we tempted to do is to say that the conformation that leads to the formation of the E product is substantially higher in population compared to the conformation that is leading to the Z product. But that is not going to help us explain the result, because this barrier is extremely low. So, like we discussed, it is about 10 to 12 kilojoules per mole.

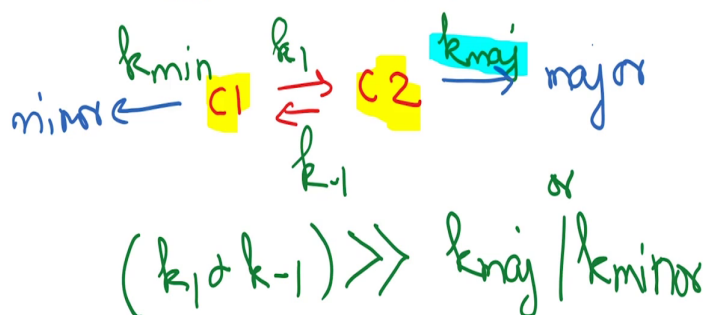
And that is easily accessible at room temperature. So, what may be more likely is that the transition state or the barrier to the formation of the E product is lower than the barrier that is encountered to form the Z product. So, this difference, that is the $\Delta\Delta G^\ddagger$, or ΔE_a , activation energy is something that is going to play a role in determining the product ratio in the reaction of interest. So, this principle is known as the Curtin-Hammett principle, I am just going to redraw over here.

(Refer Slide Time: 16:11)

Curtin Hammett



Curtin Hammett



So, the Curtin-Hammett principle says that when you have a reaction with multiple conformations in play, the more reactive conformation is going to produce the major product, so that means that the more reactive conformation, which is the E conformation, which is

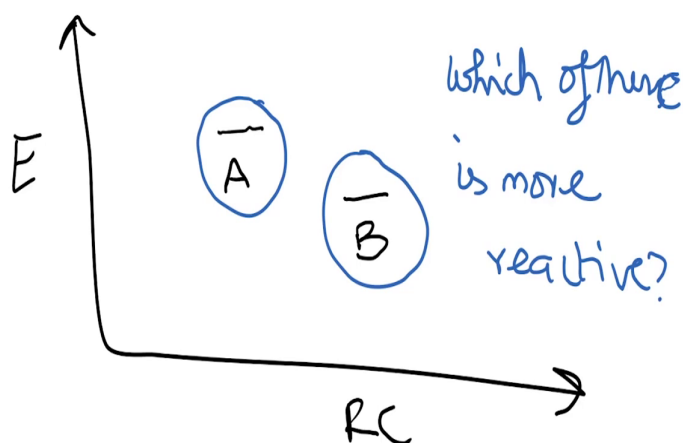
going to give E is more reactive than the conformation, that is going to give you the Z product, and therefore, you get the E product as the major product.

So, this helps us develop the framework to understand the difference in the carbonyl chemistry example that we looked at. So, I am just going to summarize this by drawing some rate constants over here. So, when you have conformation 1, in equilibrium with conformation 2, and conformation 2 gives you the major product. And conformation 1 gives you the minor product. Now, we can describe each of these processes using rate constants.

So, let us call this as k_1 , k_{-1} , which is the reverse of the C2 going to form C1, and let us call this as k_{major} . And this is called the k_{minor} . So, what we can understand from this is that k_1 and k_{-1} are much faster compared to k_{major} or k_{minor} .

So, therefore, what is important is that this conformation interconverting from here to here is going to be a really fast process. And so, the product distribution is dictated by the value of k_{major} , which is going to be, higher the value, the more of the major product that is going to be formed. So, with this background, now, we need to start looking at the formation of the two products when we add Lithium Aluminium Hydride to that carbonyl compound.

(Refer Slide Time: 18:48)

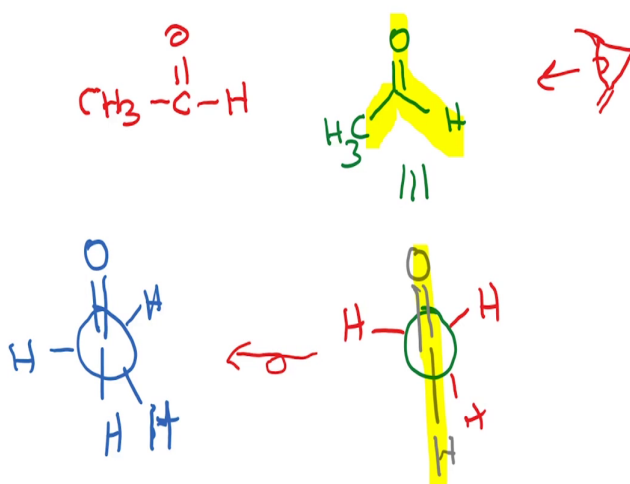


So, now, we understood that based on the Curtin-Hammett principle, that differences in major and minor products is likely due to differences in reactivity between conformers. And so, therefore, in the carbonyl example that we are looking at, so, there might be two states A and B. And now one of them may be more reactive and the other one might be less reactive. So,

therefore, what we need to now understand is to figure out how we can reason this out these differences in the reactivity.

I mean, there are probably multiple conformations that can exist, but our interest is in trying to understand two of these, because we learn very soon that the addition is going to happen through one side or the other. And so, in order to understand this, the question that we have to ask us, which of these is more reactive. So, like we mentioned earlier, we do not care about the population of this conformation because they are just going to be quite rapidly interconverting.

(Refer Slide Time: 20:20)

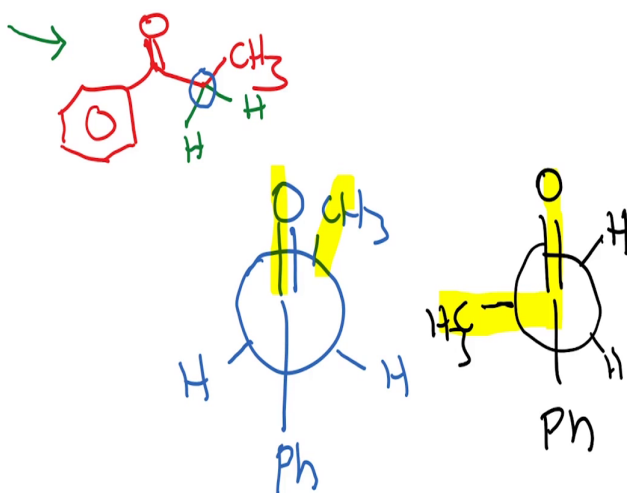


So, before we go forward with understanding the stability, let us understand some stereochemistry or how to represent molecules. So, let us start with acetaldehyde, CH₃CHO. And so, if I look at it from here, so these are my eyes and look at it from here, then it is going to look something like this. So, the C=O is over here, hydrogen is over here, and the CH₃ is here.

And if I have to draw this in the form of a Newman projection, and if I look at it, from the side that I have drawn, so I have the back carbon is with CH₃, the front carbon is C=O, and then there is a hydrogen, in the back carbon as CH₃. So, this could be one conformation. Now, if I do a rotation, we are going to get another conformation, which is the C=O is here, again, in the front. And maybe this time the hydrogen is going to be here, here, here.

So, in your free time, you can practice the various rotations around this carbon-carbon bond. So, just to repeat, so this is the carbon-carbon bond. And if we look at it from here, this is the front, the front carbon is $\text{HC}=\text{O}$, which I am showing over here. And then the back carbon is the CH_3 , which is shown here. So, you need to start getting familiar with this kind of notation.

(Refer Slide Time: 22:12)

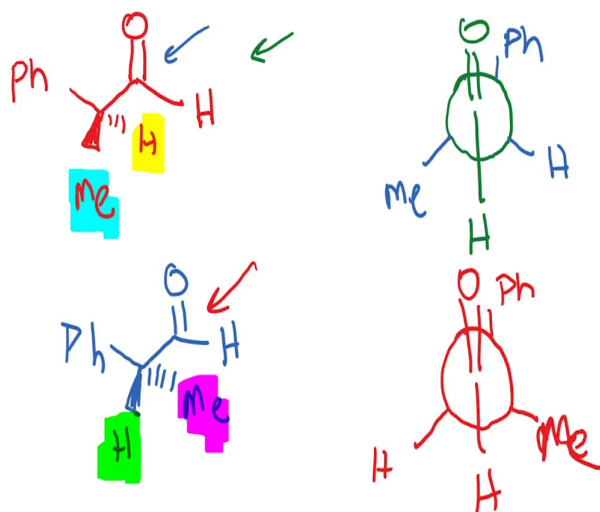


Now, let us take another example, we can take an example of maybe Acetophenone, so that we can draw a little bit more complicated molecule over here. So, Acetophenone is over here. Now, if I am going to look at it from this side over here, then the way this molecule is going to look like is there are two hydrogens sitting here. And so, the way it is going to look like is, this is the carbon that I am using to draw the back carbon, and $\text{C}=\text{O}$ is here, Ph is below.

And now, you have the possibility of the two hydrogens, which can be, you know two hydrogens are here and the CH_3 is behind. So, if I have to draw this molecule using this Newman projection method, it is going to look like this. And now you can always do rotations, draw out other conformations.

So, you have a $\text{C}=\text{O}$, Ph. Now your CH_3 can be perpendicular to the carbonyl. And so, this is 90 degrees over here. And so, this can be perpendicular to the carbonyl, it can be eclipsing, you can draw multiple conformations that are relevant to the carbonyl chemistry.

(Refer Slide Time: 23:53)



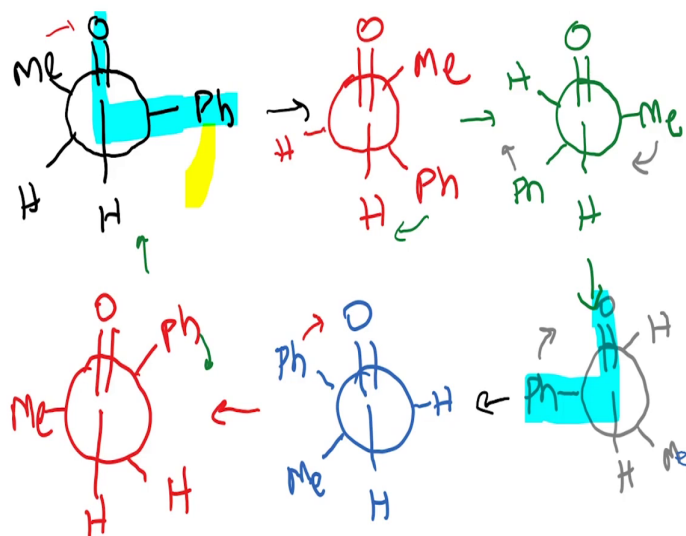
Now, with this background in mind, let us now look at one of the examples that we want to understand. So, let me just draw out this particular molecule, and then we can have a discussion about it. So, one of the methyl groups is here, hydrogen is here. And this is an aldehyde, C double bond O H. So, now what I want to do is I want to draw this, looking at it from this direction.

So, I have a C double bond O H. And now I am just going to be careful and label this in different colours. So, this hydrogen is going to be in yellow, and this methyl is going to be in blue. Now if I have to draw this out, if I am looking at it from here, the hydrogen is on my right. And the methyl is on my left and the phenyl ring is eclipsing the carbonyl compound. So, this is how I would draw this.

Now, let me take another example. Where I am just going to do simple swapping of the methyl and hydrogen, so that we get some practice. So, the methyl is over here, hydrogen is over here, and the phenyl ring is here. So, the way this conformation is drawn is that the C=O is up, H is here, the phenyl ring as you can see remains over here, and the green hydrogen, and the purple methyl group are going to be important.

And so, when I look at it from here, obviously the phenyl ring is eclipsing. But now the methyl group is on the right, and the hydrogen is on the left. So, this is something that you need to start getting familiar with in terms of drawing conformations.

(Refer Slide Time: 25:52)



Now, let us try to see if we can draw this in a slightly better way. I am just going to spend a little bit of time and draw all the conformations. And so, you need to be a little patient with me here. So, let me first draw one conformation of this molecule, $\text{HC}=\text{O}$. And let us say I am just going to draw one of the conformations where phenyl is here, hydrogen is here, and methyl is here.

Now, what I am going to do is I am just going to do a rotation, this phenyl ring moves down, and I am going to draw another conformation like this, so the carbonyl carbon remains intact. So, the phenyl moves down, the methyl moves from here to here, and then the hydrogen is now perpendicular to the carbonyl.

Now, I am going to draw one more conformation where I am doing more rotation over here. And here, the C double bond O is here, hydrogen is here. And now what I have done is, since the phenyl ring is moved here, the methyl now becomes perpendicular to the carbonyl and hydrogen is very close to the carbonyl.

Now, let me draw one more conformation, where we do one more rotation. So this time, the phenyl ring is now perpendicular and the methyl is down. So, remember that the methyl goes down here, and then the hydrogen moves up close to the carbonyl. We have a couple of more rotations to do before we get back to the original compound. And so, let us do that.

So, this again, do one more round of rotation. And so, here is a $\text{HC}=\text{O}$. And now, when we look at this, what we want to do is again, we just want to rotate the phenyl ring in this

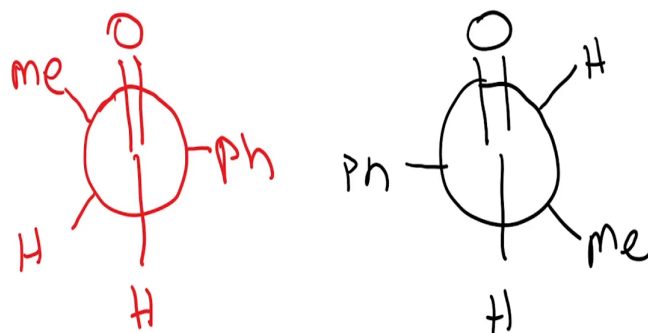
clockwise direction. So, when we do that, what we end up getting is the following conformation, let me just erase this arrow a little bit so that I can squeeze in one more conformation over here. So, here is the C double bond O. And when I do a rotation of the phenyl, then the phenyl ends up here and the hydrogen is now perpendicular to the carbonyl and methyl is over here.

And the last conformation is with the phenyl ring moving further, be one more round of rotation and it is going to give you the HC=O. And so the phenyl ends up here, the hydrogen is over here, and methyl is now perpendicular. So, I can draw out six important conformations and just one more, just to be clear, if I just do one more round of rotation, I get from here to here, in this direction, so we went on an entire circle.

So, in order to develop this model further, we need to understand that there are some conformations that are going to be important. And how do we understand these important conformations, we try to look at models that can help us with explaining the result. So, as far as we are concerned, the important conformations are the ones wherein the largest group is perpendicular to the carbonyl.

So, the largest group being perpendicular to the carbonyl occurs in two of these conformations that we have looked at, so one is this and the other one is this. All other conformations that we have looked at now do not have the largest group perpendicular to the carbonyl. So, one important reason why we would want to sort of understand this is because these two conformations are more relevant in developing the model further.

(Refer Slide Time: 30:28)



So, I am just going to draw out these two conformations once again. So, that we understand this. So, in the model that we are now constructing, we wish to consider the two conformations wherein the largest group is perpendicular to the carbonyl. So, this is one of those conformations and the other conformation is over here. So, these are the two conformations that we are interested in.