Mechanisms in Organic Chemistry

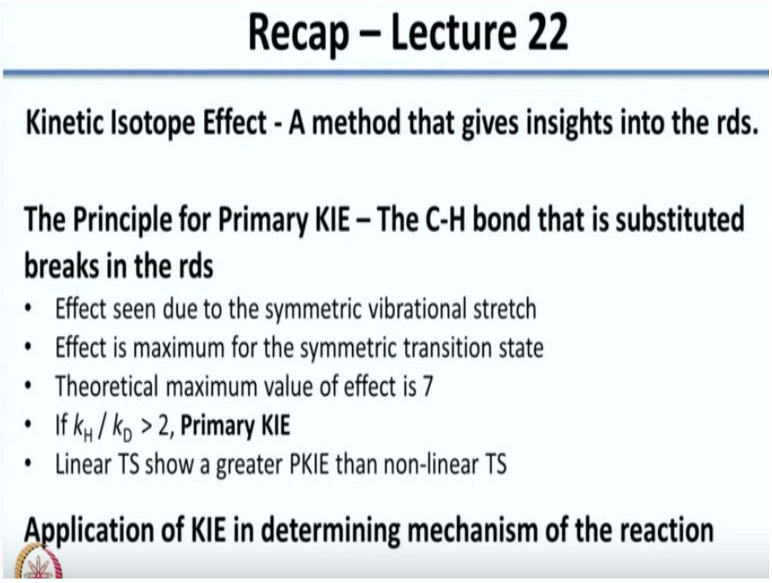
Prof. Nandita Madhavan
Department of Chemistry
Indian Institute of Technology-Bombay

Lecture - 23

Secondary Kinetic Isotope Effect: Part A

So welcome back. In the last lecture, we had looked at kinetic isotope effects.

(Refer Slide Time: 00:21)



Recap – Lecture 22

Kinetic Isotope Effect - A method that gives insights into the rds.

The Principle for Primary KIE – The C-H bond that is substituted breaks in the rds

- Effect seen due to the symmetric vibrational stretch
- Effect is maximum for the symmetric transition state
- Theoretical maximum value of effect is 7
- If $k_H / k_D > 2$, **Primary KIE**
- Linear TS show a greater PKIE than non-linear TS

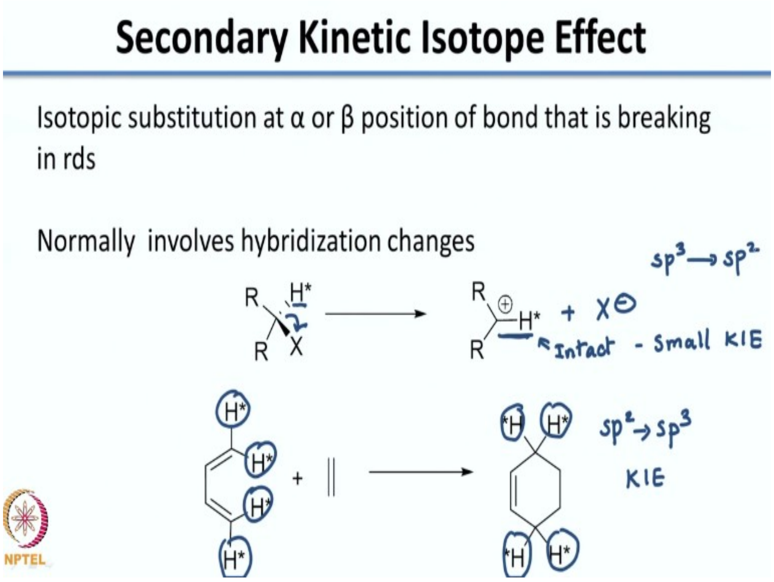
Application of KIE in determining mechanism of the reaction

Specifically we had looked at primary kinetic isotope effects. So this gives an insight into the rate determining step and whether the bond that you are making the substitution at is cleaved during the rate determining step. So the principle of primary kinetic isotope effect is that the C-H bond that is substituted breaks in the rate determining step. Effect is seen due to the symmetrical vibrational stretch.

Effect is maximum for a symmetric transition state. And the theoretical maximum value is 7. And we had also seen how if you have a k_H/k_D value greater than 2 it is called a primary kinetic isotope effect. And we also saw that a linear transition state shows a greater primary kinetic isotope effect than a nonlinear transition state.

And this is because in a linear transition state, the difference between the C-H and C-D zero point energies is very less as compared to the difference between the C-H and C-D zero point energies for a nonlinear transition state. And we had looked at the application of kinetic isotope effect in determining the mechanism of a reaction. So today what we will be doing is we will be looking at what is called as a secondary kinetic isotope effect.

(Refer Slide Time: 01:46)



Secondary Kinetic Isotope Effect

Isotopic substitution at α or β position of bond that is breaking in rds

Normally involves hybridization changes

So in the secondary kinetic isotope effect, the isotopic substitution occurs at an alpha or beta position of the bond that is breaking in the rate determining step. So we are not looking at the C-H bond that is actually breaking in the rate determining step, but we are looking at bonds that are at the positions which are alpha or beta to the C-H bond that is breaking.

So normally when you think of it, it usually involves hybridization changes. So if you look at it here, you have an example where you have the substitution at this hydrogen for an sp^3 reactant. Now once you have X leaving, what you generate is the carbocation and X-. Now when you see it here, the C-H bond is still intact. And if you remember the examples that we had done in the previous class, we had seen that in these cases, what you observe is a small kinetic isotope effect.

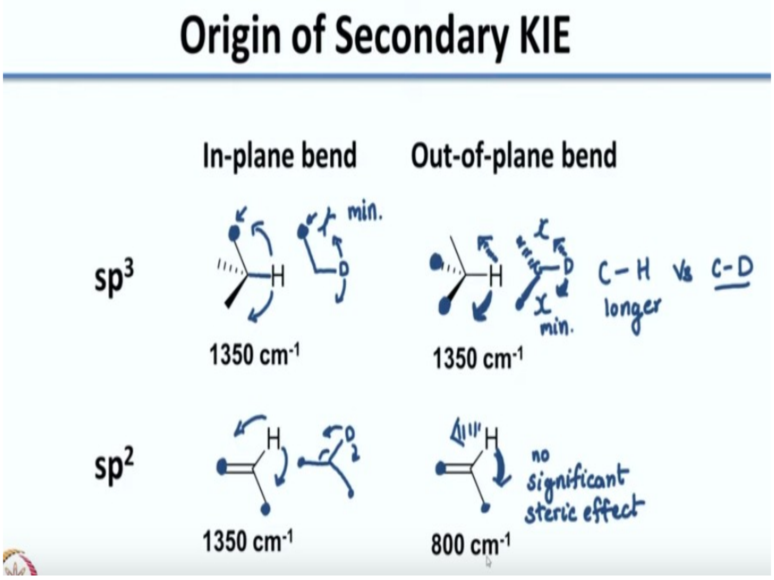
Some of you might be wondering although this bond is not breaking, why do you see a kinetic isotope effect at all? Because one would assume that okay this bond is not breaking. So it does not matter whether you put C-H or C-D. So the question is why do you see an effect at all. Another example is here, the second reaction you have hydrogens that are substituted and once, so this is a concerted process.

So in the product, you have the hydrogens with the bond still intact. But here you have a change from sp^2 to sp^3. So there is a hybridization change and what is observed is that this also leads to a kinetic isotope effect. So one thing which will be very obvious to you is that if you compare magnitude that is the value, the magnitude for primary kinetic isotope effect would be larger than a secondary kinetic isotope effect.

But then you still observe a kinetic isotope effect whenever there is a change in hybridization. So the first example, you had sp^3 going to sp^2. And in the second example, you had sp^2 going to sp^3. So now whatever we had studied in the previous lectures about the primary kinetic isotope effect, one thing you must understand by now is that, when you talk about kinetic isotope effects, the vibrational levels are very important.

So in order to understand now secondary kinetic isotope effects, also we should look at the vibrations that are involved.

(Refer Slide Time: 04:44)



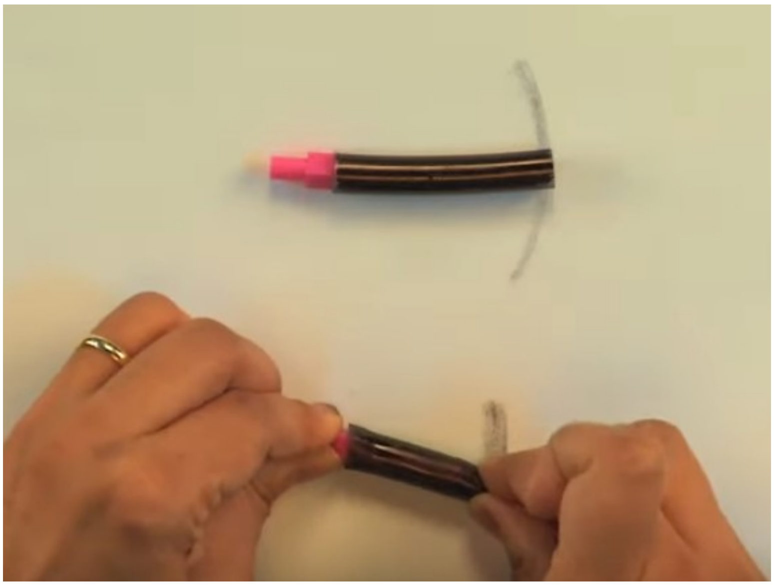
Origin of Secondary KIE

So now let us look at the origin of a secondary kinetic isotope effect. So, we will look at the vibrations that take place. Now since the bond is not breaking the stretching vibrations do not make as much of an impact as you had seen in the case of the primary kinetic isotope effect. But what plays a very important role is the bending vibrations.

So now to understand the bending vibration, first I would like to ask you a simple question. So if you compare the bond length of C-H versus C-D, which bond would be longer? So again I repeat the question. So if you were to compare the bond length of C-H versus C-D, which bond would be longer? So you can think about this question by pressing the pause button on your screen. Alright.

So when you compare C-H versus C-D, the C-H bond is longer than the C-D bond. So let us assume that this is your C-H bond and this is your C-D bond.

(Refer Slide Time: 05:54)



So the C-D bond is smaller than the C-H bond. Now when you think of bending, it involves movement of the bonds. So if you imagine a C-H bond and let us imagine that the bond is moving from left to right, like this.

So this is my C-H bond. Now, if I compare my C-D bond, so this is a smaller bond, I am going to do the same movement. Would you expect, so I have an arc that has come here. Would you expect this arc to be smaller or bigger? So now I have a smaller bond. And I am again going to bend it from left to right. So what do you think this arc will be? Will it be smaller or bigger? Let us find out.

So now I am going to move it from left to right. So when I compare both of these, what you would observe is that in the case of the C-H bond which is longer, it has greater freedom to move, right? Whereas, when I have a shorter C-D bond, it has lesser freedom to move, alright? So you can also try it in your homes by taking a small string.

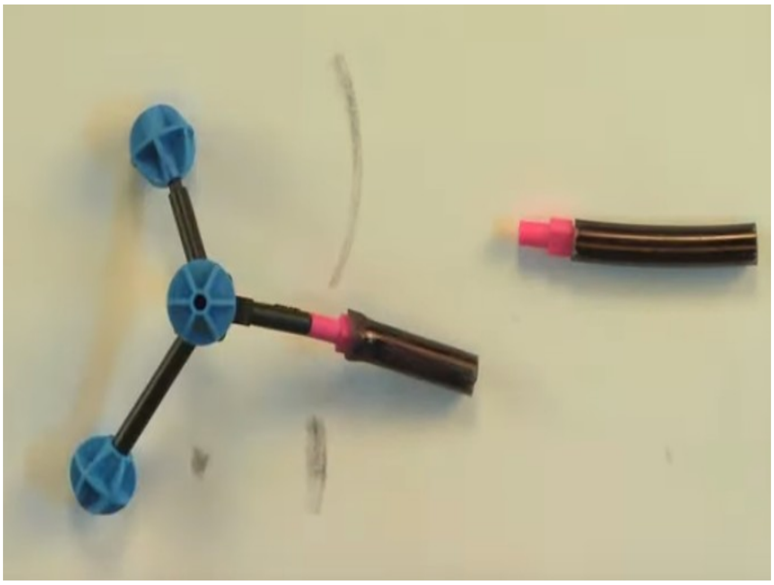
So you can cut the string in two different sizes, and then you can try holding the string on one side and seeing how much you can move, alright? So use two different strings and you can see how much the string moves. So what you see is there are different types of vibrations possible both for sp^3 as well as sp^2. So in the case of sp^3, there are two types of bending vibrations that are shown.

One is an in-plane bend and one is an out-of-plane bend. Similarly for sp^2, so if I draw arrows to show it. So in in-plane bend, you will have this C-H bond moving in the plane of your screen. In the out-of-plane bend, you can imagine this bond moving out of the plane. So you can imagine it moving perpendicular to the plane of your screen.

So I am using the dash and wedge that you usually see when you represent molecules and show their stereo chemistry. So what this means is, this is an out-of-plane bend, where the C-H bond is coming out of the plane of your screen and into the plane. And I mean going behind the back of your screen. Similarly, you can have in-plane bends for the sp^2 and you can have out-of-plane bend.

So in out-of-plane bends again I will show it with a dash. So I will show it with a dash and a wedge. So now let us think of the scenario where you have C-H versus C-D. So this is longer as compared to the C-D bond. So now we already saw just with the flexible bond which I had shown you earlier that when you compare C-H versus C-D C-H can move for, covers a larger area in doing so.

(Refer Slide Time: 09:56)



So let us try to understand the bending vibrations looking at the sp^3 carbons, okay. So in the sp^3 for those of you who have not seen, this is what the sp^3 looks like. It is a tetrahedral. So what I have here is I have these three atoms in a plane and then I have the wedge coming closer to me and the dash going away from me. So this is what the representation looks like when you draw the stereochemistry of the molecule.

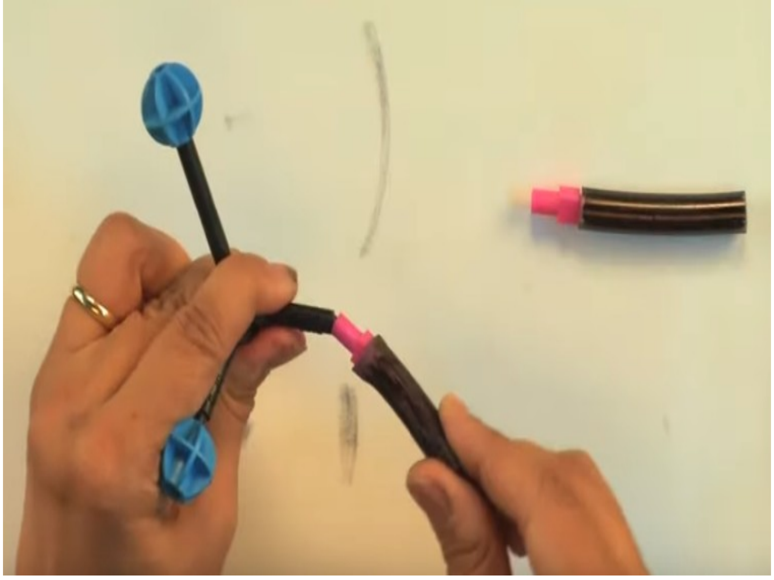
So now let us see what happens when you have C-H versus C-D bond. So let us first consider the case of in-plane vibrations. So when I consider the case of in-plane vibrations, so as I said I have these in plane so I move the bond like this. Now because the C-H bond is longer it covers a larger area. Remember the arc that we had shown here. Now that it covers a larger area what happens is the steric interaction that it faces with this atom here is more.

Now if I compare it with a C-D bond, so if I compare it with a C-D bond, again I am doing the in-plane bend. It covers a smaller area, remember the smaller arc. Now because it covers a smaller area, the steric interaction with this atom here is minimized, alright? So if we were to look at the first case shown here, which is the in-plane bend, I have this is my C-H bond and I am moving it in plane.

So you have interactions with this atom here, alright? So this interaction is minimized in a C-D bond, which is smaller. So when you compare a C-D bond, this bond length remains the same because we have not done any substitution here. What happens is, this movement is smaller. So this interaction, steric interaction is minimized, alright?

So now let us look at the out-of-plane bend.

(Refer Slide Time: 12:48)



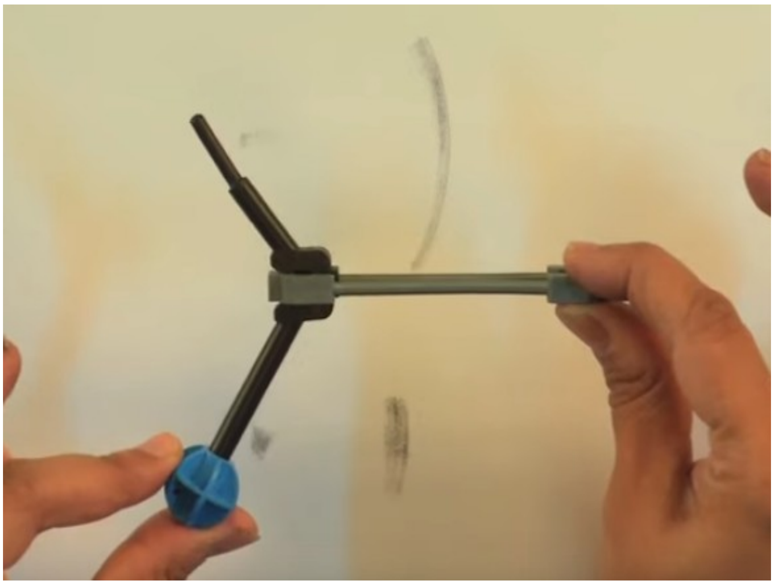
So in the case of an out-of-plane bend, now we will start with C-D. So in the case of an out-of-plane bend, what I will be doing here is I will be moving this up and down, okay? Remember, this one atom is closer to me and another one is behind me. Let us try to see it again. So I am moving this up and down. So let us see it from a different angle. Let us see it from this angle so that it is easier for you to see.

So this is how it is moving. So now when I have C-D, as you can see it moves less. Now if I compare that with C-H, it can actually move more, alright? And this case, what is happening? It is interacting with these two atoms here, alright? So when you compare the out-of-plane bend so when you have the case of C-H or C-D, there are these two atoms that they interact with.

And again in the case of C-D, since the bond is smaller, again this bond length does not change so this interaction is better because the sterics again here in both these cases this is minimized as compared to the case of the C-H, alright? So again to revise, in the case of sp^3, you can have an in-plane bend and out-of-plane bend and in both these cases, when the C-H bond moves, it meets some atoms.

And what is seen is that, so in every case what is seen is that, when you move the C-H bond it meets some atom and which is why so you have a wave number of 1350 cm^{-1}, alright? So, this is directly proportional to the energy that you are talking of the vibration. Now let us look at the case of sp^2. Now sp^2 is very interesting as compared to sp^3, because here what you have is you have all three atoms in one plane.

(Refer Slide Time: 15:28)



So you have all these atoms in one plane unlike the sp^3 where you also had atoms coming close to you and away from you. Here you have everything in one plane. So here let us see what happens when you have C-H versus C-D. So let us make the substitution. So this is our C-H bond and now we are looking at the in-plane bend. So we are looking at the plane of the molecule.

So the in-plane bend would be moving in the plane of the molecule. So in the in-plane bend, what you see is you have interaction with both of these atoms. So as it moves in the plane, it has interactions with both of these atoms. Again, we can draw it here. So in sp^2 you have the atoms in one plane. So you have the in-plane interactions with both the atoms. So here again in the case of C-D, this would be smaller.

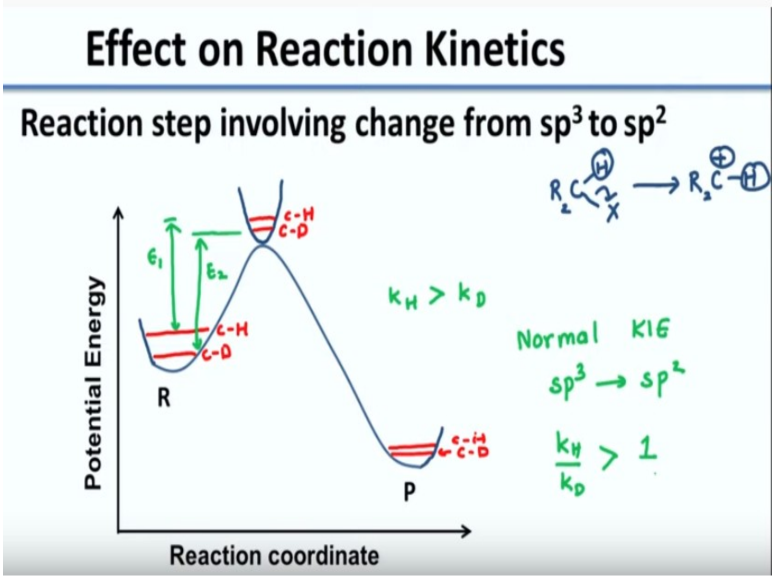
But remember in this case, since the atoms are farther apart the effect is not as pronounced as your C-H bond. So in this case, you have the C-D bonds again interacting with both these atoms. So here again let us look at the out-of-plane bend. So in the out-of-plane bend, if you have, so in the out of plane bend, what you have is this is the plane of the molecule. So you have the bond move up and down.

Now what is interesting in the case of your sp^2 is that there is nothing above or below the plane of the molecule. So if you were to look at it with a different view, so you have all of these in one plane, and I am moving this like this. What you see is as this moves, you have nothing in this region and you have nothing in this region. So there is no steric problem that you are talking about.

So in general the energy for this bending vibration is lower. So here again, if you replace a C-H bond with a C-D bond, what you would see is it would move lesser. So now let u look at what happens here. So here in the out of plane bend, there is no significant steric effect. So that is why if you compare both of these energies, you would see that the energy for the out-of-plane bend is actually lower than the in-plane bend for the sp^2 case.

So now that we have an idea about how the in-plane and out-of-plane bend works for sp^3 and sp^2, let us see what influence this has on the kinetic isotope effect because that is what we are trying to understand. We are trying to understand the secondary kinetic isotope effect.

(Refer Slide Time: 19:04)



Effect on Reaction Kinetics

Reaction step involving change from sp^3 to sp^2

So here let us look at the first case, where we are looking at a reaction step involving a change from sp^3 to sp^2. This is similar to the example that we had seen on the first slide, where you have and then this is an S_N1 like reaction. So you have a carbocation that is generated and let us say that we are making the substitution at this hydrogen.

So what happens in the case of sp^3 and what happens in the case of sp^2. So in the case of sp^3 if you remember the in-plane and out-of-plane bend in both of these cases, you have significant steric interaction. That is why both of them were 1350. So in the case of sp^3, in all these cases, whether you have your out-of-plane bend or you have your in-plane bend, what you see is you have steric interactions with all these three atoms.

So here if I compare C-D versus C-H, the vibrational levels, which one would be lower in energy? So again for sp^3 both in-plane so the net effect you see is a combination of in-plane and out-of-plane vibration. So for a sp^3, when you replace C-H versus C-D, which would be lower in energy. You can think about it and press the pause button on your video.

So all right, let us see if you are able to get this answer. So in the case of sp^3 what you notice is that the C-D and C-H energy difference is large because C-D has less destabilizing interactions as compared to C-H. Now your transition state would have a mix of sp^3 and sp^2 character. Now what happens in the case of sp^2? In the case of sp^2, if you remember what we had seen earlier in your in-plane bend, you still have some steric effect.

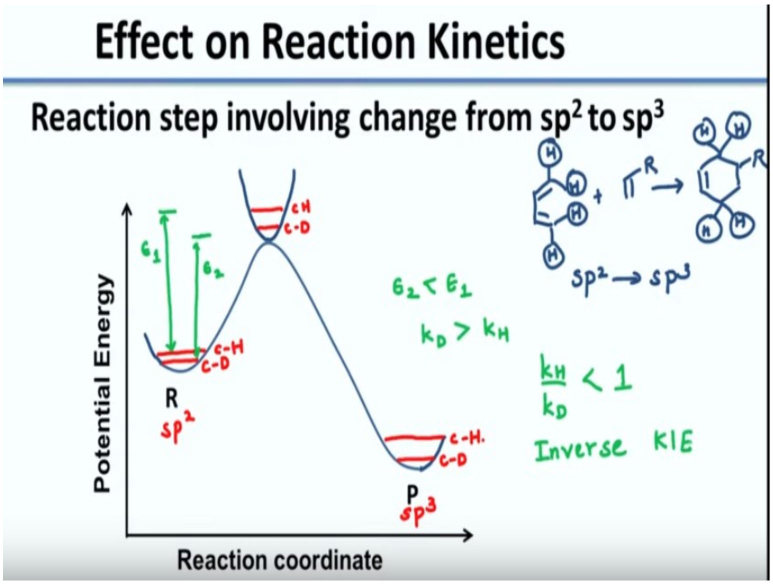
So C-D would be lower in energy than C-H. But in the out-of-plane bend since it is not meeting any atoms above and below, it does not matter whether you put a big bond, a small bond, a very small bond, so it does not matter. So C-H over C-D will not have a very large impact if you are talking about sp^2. So in the case of sp^2 the energy difference would be less; I will just extend this a little.

So now your transition state would be somewhere in between. So when you draw your transition state, so we are looking at the vibrational energy levels here. So this is what your transition state will look like. So now when you compare the activation energies, so if I compare the energy from C-H versus C-D, so this is E_1 this is E_2; again the same example that we had seen earlier.

So we are talking about climbing a mountain. If you are already at a higher power point and your destination is almost the same, then you have a smaller distance to travel. So what you would see is k_H would be greater than k_D. So typically, you would see what is called as a normal kinetic isotope effect, while going from sp^3 to sp^2. And that means the value would be k_H/k_D greater than 1 because k_H is greater than k_D.

And this value would be somewhere between 1 and 2, as I told you a much larger effect is seen in a primary kinetic isotope effect. So secondary kinetic isotope effect, magnitude is not large, but then you do see an effect. So in this case, you see k_H is greater than k_D. It is called a normal kinetic isotope effect.

(Refer Slide Time: 24:33)



Effect on Reaction Kinetics

Reaction step involving change from sp² to sp³

Now what happens when you go from sp^2 to sp^3. So the example that we had looked at earlier was the Diels-Alder reaction. So if you have let us say these are the hydrogens that we are substituting reacting with some sort of a dienophile. So the product you get is cyclohexene and then you have these hydrogens here in the R group here.

And if you are making substitutions here, so here again the bond is not breaking. We are going from sp^2 to sp^3. So now let us look at the vibrational levels again. So in this case now that you have understood the case of sp^3 to sp^2, this would be easier. Transition state energy level. So let us write all the vibrational energy level. So I would like you to do this exercise yourself.

Now that I have shown you the potential energy diagram, I want you to sketch that out in your notebook and draw the different vibrational levels for the reactant, the product and the transition state which would be somewhere between the reactant and the product. So go ahead, press the pause button on the video and work this out yourself.

So welcome back, let us see if you are able to do this. If you were not, you can also try to follow what I am doing. So here again, this is sp^2, this is sp^3. So in the case of sp^2, the difference in energy between C-D and C-H is not much. So if you did not understand this, you can go back, you can rewind back and look at the explanation for sp^3 to sp^2. And whereas in your product, you have a greater difference in energy.

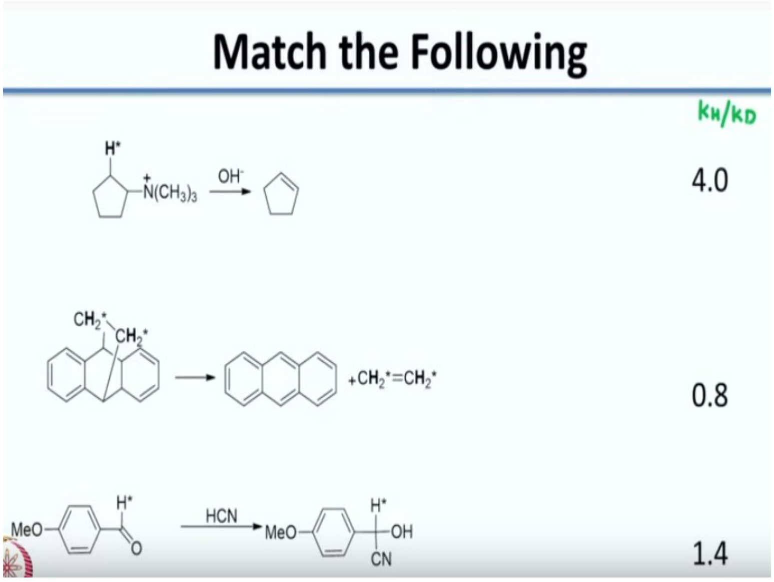
So you transition state now would be somewhere in between these two. So you would have an energy difference here. So now let us try to figure out the activation energies. So this is the case of C-H, this is E_1 case for C-D. This is E_2. Now in this case what is happening is you have a reverse scenario. So imagine again the mountain where you are starting from almost the same point.

But then one person has to climb a much higher peak as compared to the second person. So who will climb quicker? The person who has to climb the lower peak. So in this case, what you have is you have E_2 less than E_1 because C-D has to climb a lower peak as compared to C-H. So E_2 is less than E_1 which implies k_D is greater than k_H. So essentially what that means is k_H is greater than k_D is less than 1, alright?

So this is what is called as an inverse kinetic isotope effect. Why inverse because usually you would expect the C-H to be faster than C-D. But in this case, what you observe is it is the reverse. So it is called as an inverse kinetic isotope effect. So now we have understood the basis for the secondary kinetic isotope effects involving hybridization changes.

So sp^3 to sp^2 gives you a normal kinetic isotope effect that means k_H over k_D is greater than 1 and sp^2 to sp^3 gives you what is called as an inverse kinetic isotope effect, where k_H over k_D is actually less than 1.

(Refer Slide Time: 30:38)



Match the Following

k_H/k_D

4.0

0.8

1.4

So now to understand this further, so now let us see if you have understood this concept. So shown are some reactions on the left and some values on the right. So these are k_H over k_D values. So what I want you to do is look at the reactions, write their mechanisms and match the value on the right. So see if you can go ahead and do this exercise. We will come back in the next lecture where we will check if the answers that you have are correct. So thank you and see you in the next lecture.