Mechanisms in Organic Chemistry
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Lecture-31
Checking for Common Intermediates

So welcome back. In the last class we had looked at how you can trap intermediates other than carbocations, carbanions and radicals using suitable trapping agents. So we had looked at the example of the benzyne intermediate and how you can trap that using the diels-alder reaction. We had also seen how trapping reagents can be used to understand biology.

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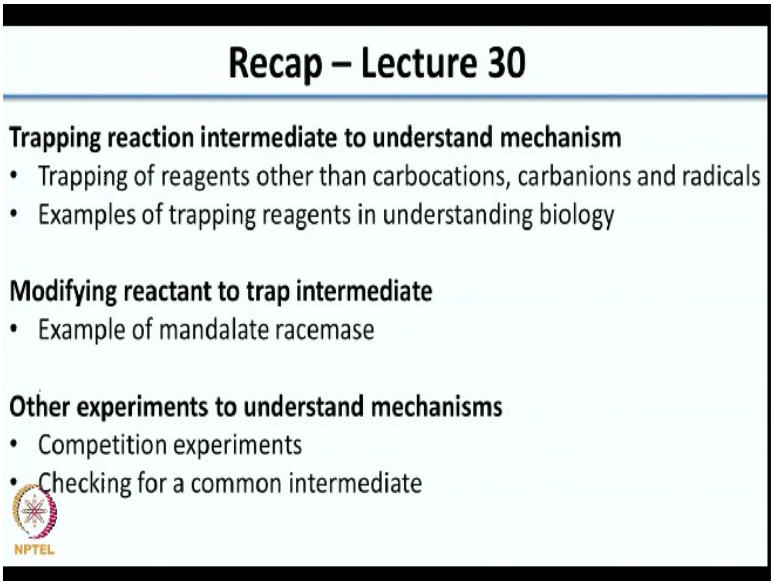

Then a slight modification we had seen is how you can modify the reactant to trap a particular intermediate. So we had seen again an example of biology where to understand the mechanism of mandelate racemase a model substrate was chosen so that you could trap the intermediate and towards the end we had looked at other experiments to understand mechanism. So we had seen what are called as competition experiments where you add 2 traps

so that once you form the intermediate it can be trapped by 2 reagents and depending on the ratio of products you get an idea about what the nature of the intermediate is and the last example we had seen is where you start with 2 reactants which could lead to the same intermediate, so that

you get a single product from different reactants. So this is an indirect way to tell you that the same intermediate was formed from both reactants.

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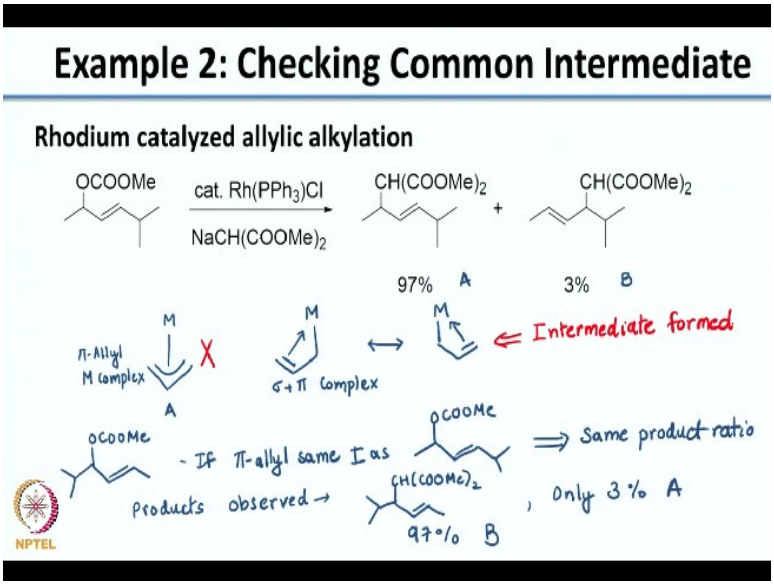

And we had seen an example of this. Before leaving I had shown you this example where we had seen how the rhodium catalyzed allylic alkylation reaction was carried out and it led to 2 products in the ratio of 97% and 3%. Now if you look at this reagent, the reagent used is a rhodium reagent and there are 2 possible ways in which the rhodium can interact with this double bond. One way is where you have what is called as a π complex.

So you can imagine you have 3 carbon centers here and a single double bond which you can think of as multiple resonance structures. So the average structure would be complexing with your metal which is rhodium here. So this is called as a π-allyl complex. Now the other possible intermediate is, so this is possibility A. Possibility B is you can think of a sigma bond between the metal and this allylic ligand and you can also see the pi bond interacting favorably.

So this is a σ + π complex and of course you can have 2 resonance structures for this where you can also think of the other resonance structures. So in this case what you had sees you have a vinylogous carbonate here. So once you have the carbonate group leaving your allylic molecule can form a complex with your rhodium. So this ligand can form either a pi allyl complex or a σ + π allyl complex.

Now which of these is actually forming? Let us try to understand. So what are seen is with this particular reactant you get a mixture of 97:3. So here what is finally adding to the metal carbon bond is the diester shown here. So now what if I change the substrate? So what if I change the substrate? So that I use this particular substrate. So here I have, so what is the difference between the earlier substrate and this substrate?

You see here that now the isopropyl group and the methyl group have been switched. So now we have switched the isopropyl and the methyl group. Now once you switch these group what I want you to think about is if it forms the π-allyl complex what would be the product that you get and if it forms a σ + π complex what would be the product that you get?

So if you assume case one, that it forms the π-allyl complex, it would essentially indicate an intermediate which would be identical to the earlier one. So if π-allyl complex. So if you have the same intermediate as the earlier example it would indicate same product ratio. Correct? Because both of these would give you the same intermediate. Now what is actually observed is the products observed are.

So is seen is in this case you get the exactly reverse ratio, you get 97% of this product which was only 3% in the earlier case. So let us call this product B. So you get 97% of product B and only 3% A. So the very fact that the product ratio is completely reversed, what does that indicate? That indicates that both of these actually do not form a common intermediate. So here we are seeing the opposite to the earlier example we had seen in the previous class where you were getting the same product ratio. Here you see the exact reverse product ratio.

So what this indicates is that the intermediate is not a π-allyl complex, but a σ + π complex. So shown here is a very nice example where by switching the substituents on the reactant you get completely different product ratios and indirectly it tells you what is the intermediate that is being formed. So we saw 2 different examples of how you use the common intermediate concept to figure out the nature of the reaction intermediate.

Now we will move on to other experiments. One very commonly used experiment is what is called as a cross over experiment and this is usually used for rearrangement reactions. So say you have a reaction A B which leads to C D. So you essentially have A B forming C D.

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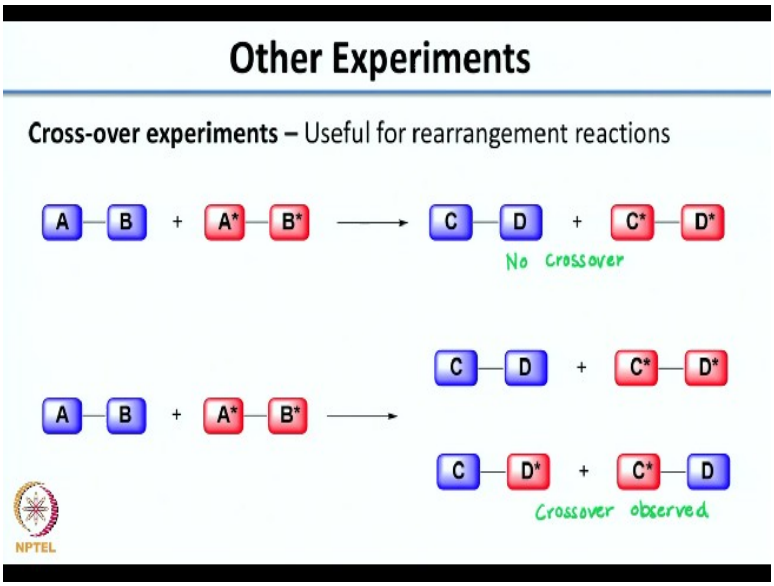

What is done is a very similar competing reactant is put A* B*. Now if the reaction is an intramolecular reaction, so intramolecular means A and B are rearranging within themselves to give the product which is C D, what you would see is the products observed would be only. One corresponding to the rearrangement of A B and the other corresponding to the rearrangement of the second starting material.

So essentially you start with a mixture of reactants and you get a mixture of products each coming from the intramolecular reaction. There is another scenario. Now suppose instead of the intramolecular reaction what you have this you have A B dissociating to give intermediate either cations or anions or radicals. Then what you see is you will see a possible mix of 4 products. So if you assume this A B bond and A* B* bond is breaking,

they can be put together in any possible way. So if you put them together in any possible way there are 4 combinations you can get. One would be the original two, which is C D and C* D*. The other is you have 1 component coming from A and the other component coming from A * B *. So you have C D* or C* D. I have color-coded it. So that it is easier for you to understand and this case what you see is you see that a cross-over has happened.

You can see the cross over here with the different colors. So crossover has happened means that A B or A* B* have actually disintegrated to give you intermediates which can then recombine to give you all possible combinations. So this experiment is called a crossover experiment and what you observe in this case, the result is called as no crossover because you see that each individual reactant gives you the product corresponding to that.

Whereas in this case what you see is crossover is observed. So this method as I said is used very commonly for rearrangement reactions. So we will look at 2 examples where the mechanism has been determined using these experiments.

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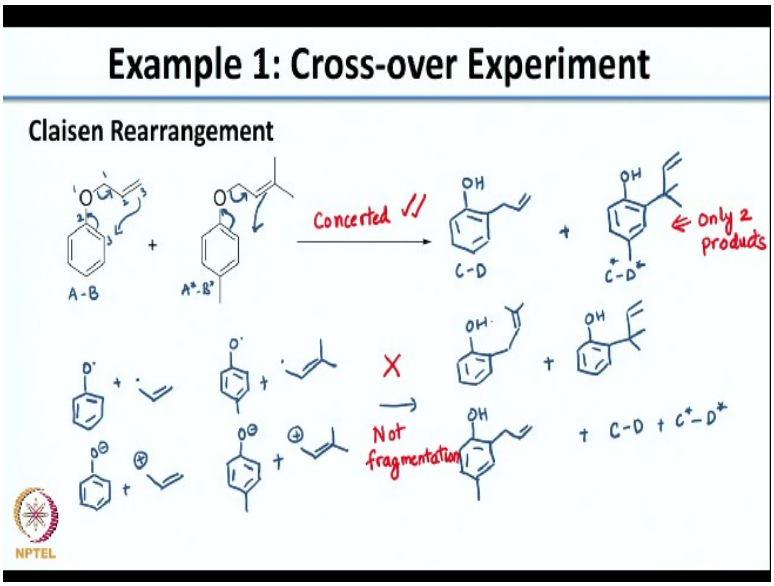

The first example is the Claisen rearrangement. We had seen this reaction when we had studied isotope labeling several classes ago. So you know what the mechanism of this reaction is and we had actually written down multiple possible mechanisms. Now let us write what the product would be of this reaction mixture. As you see there are 2 reactants here, I want you to write the products assuming that there is no crossover.

So go ahead press the pause button on the video and write the products for this reaction. So if you assume a concerted process what you have is you have a [3,3] sigmatropic rearrangement. So you can draw the arrows any possible way. So you have this sigma bond cleaving. So the

product that you get. So this is your A B system and this is your A* B* system. So the product that you get, so if it is an intra molecular rearrangement would be,

and of course this would tautomerize to give you the corresponding phenol. Now this is product C D and what is the product C* D*? That product would be I am going to directly write the phenolic form. I will just show you the arrow push here. So you have this new bond forming these pi electrons migrating this sigma bond breaking. So the product you get would be. So this is the product that you will get.

So this is your C* D*. Now had this gone through any intermediate. So this could be one could think of this fragmenting to give say a radical. So say a radical you could also think of polar intermediates and again we had seen this earlier. So this should be just like revision for you. Similarly A* B* can also disintegrate to give you and again I am writing the corresponding polar intermediates.

So had these intermediates formed you would have seen other products as well right? So what are the products that you would have seen? You could have seen, you would have seen this product. You could have also seen the rearranged version of this. So you could have seen or you would have seen. So each of these could have recombined. So here where you have the para methyl you could have seen the plane allylic substituent.

So all of these different products would have been possible had it fragmented plus you would have seen C D + C* D*. But only 2 products are actually observed when you do this reaction. So what that indicates is that the reaction goes via the concerted pathway and not by any of the fragmentation pathways. So this is a very nice illustration of how you can use the crossover experiment to figure out the nature of the mechanism.

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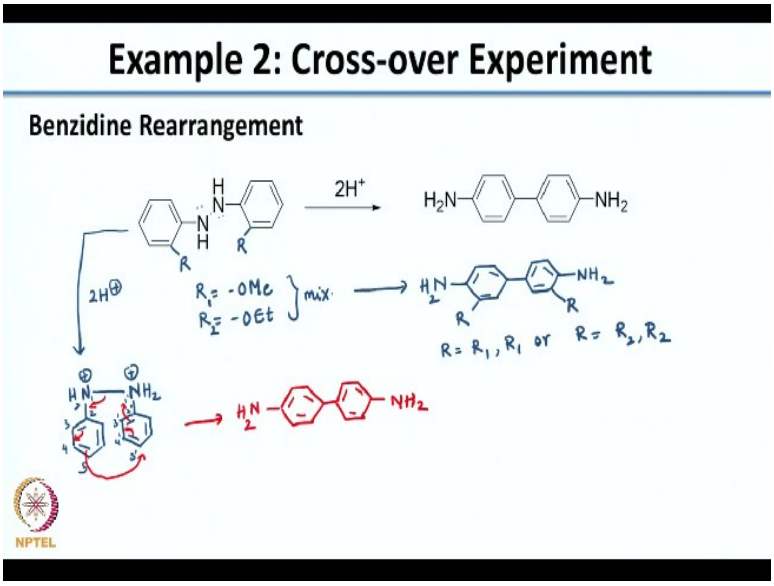

We will look at one more example. This is again a rearrangement reaction. So this is called the benzidine rearrangement and what I would like you to do is I would like you to think of the mechanism of this reaction and to give you a hint what was seen was that when you do the reaction. So I am putting this as R. So you can take R as OMe. You can take R as OEt. So when you have a mixture of these you get only 2 products and the 2 products correspond to.

So these are the 2 products formed. So let us call this R_1 and R_2. The 2 products formed are. So what is seen is that you have either the product where both the R groups are methoxy or both the R groups are epoxy. You do not see any crossover. So here again you have an example where it goes via and intramolecular rearrangement and not a fragmentation. So now that I have given you this information can you try to write the mechanism for this reaction?

You can press the pause button and work it out in your notebook. So let us see if your mechanism is correct. The first step would be protonation. Now where will it protonate? You have the lone pairs on the nitrogen. So it will protonate here and I will write it in a different fashion to make it easier for you to visualize the mechanism. So in the earlier case we had seen what is called as a [3,3] sigmatropic shift, here what you observe is a [5,5] sigmatropic shift.

So what you can see is you can imagine. So if I call this 1, 2, 3, 4, 5 and 1' 2' 3' 4' 5'. So just like we did the [3,3] sigmatropic shift you can do a [5,5] sigmatropic shift to give you in one pot. So

you have these electrons coming here. So you can have this sigma bond breaking, rearrangement of the pi electrons, formation of a new sigma bond and again rearrangement of these pi electrons to give you the product.

And this happens in one step which is why you do not see crossover. So the crossover beautifully supports this [5,5] sigmatropic shift. So this is again a very nice illustration of how you can use crossover to determine whether you have an intramolecular reaction or you have a fragmentation take place. So to summarize we looked at a lot of experiments that can be used to determine the nature of the intermediate.

So we looked at isotope labeling, we looked at trapping. Before that we looked at kinetic isotope effects and we looked at linear free energy relationships. Now we will move on to another very important topic when you think of reaction mechanisms and that is catalysis. I am sure you have heard of what the term a catalysts means. So when you think of a catalyst what is the picture that you get in your mind?

So what does a catalyst? it is an English word also. So when you think of the catalyst what is it that immediately comes to your mind just write that on a sheet of paper. So if you have your notebook next to you just put 3 points as to what you think of when you think of the term catalyst for an organic reaction. So if you have done this exercise I want you to do another exercise. In the second week of this class we had learned how to write reaction coordinate diagrams.

So what I want you to do is, I want you to draw the reaction coordinate diagram for a reaction of A going to B and I want you to draw another reaction coordinate diagram of what you think you will see when you do the same reaction in the presence of a catalyst. So I want you to show how the reaction coordinate diagram will change. So go ahead and do both of these activities. Alright. I hope you did that. As I told you earlier these activities help you improve your learning. Rather than just watching me solve these for you.

If you solve this yourself you end up learning a lot more. So let us see what a catalyst actually means.

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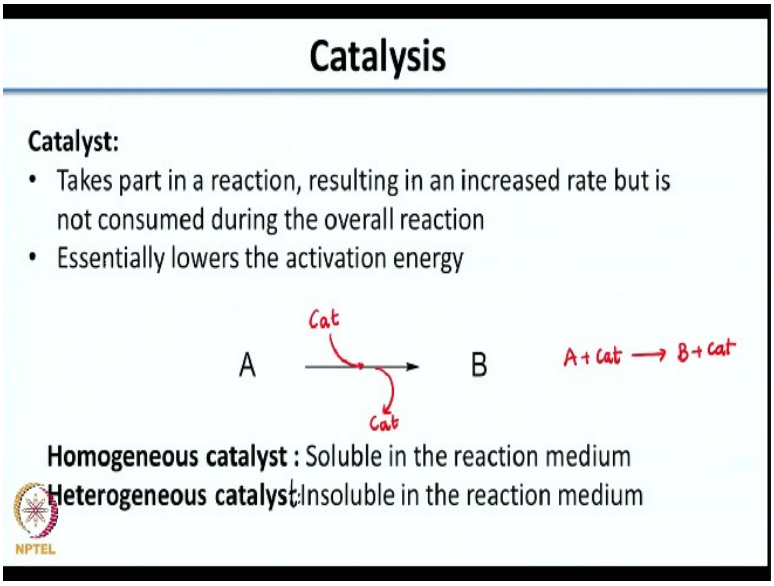

So catalyst is a molecule or a compound that takes part in a reaction and due to its participation you observe an increased reaction rate. But this catalyst is not consumed during the overall reaction. In other words what a catalyst does is it lowers the activation energy for the reaction. So if I have a reaction of A going to B, what a catalyst does is, it will come into the reaction, increase the reaction rate and once the reaction is done it will go back.

So you can also write it as A + catalyst giving you B + catalyst. So this is another way of writing the overall reaction. Now catalysts can be classified depending on how soluble they are in the reaction medium. A homogeneous catalyst is one which is soluble in the reaction medium. So whenever you have a reaction where the catalyst dissolves in the reaction medium that is a homogeneous catalyst.

A heterogeneous catalyst is insoluble in the reaction medium. There is a t missing here. So the heterogeneous catalyst is insoluble in the reaction medium. So this goes with the definition of the word catalyst. Now what I had asked you to do is, I had asked you to draw a reaction coordinate diagram and I wanted you to show on that reaction coordinate diagram what the catalyst does to that diagram. So in the earlier slide I had told you that a catalyst lowers the activation energy of the reaction.

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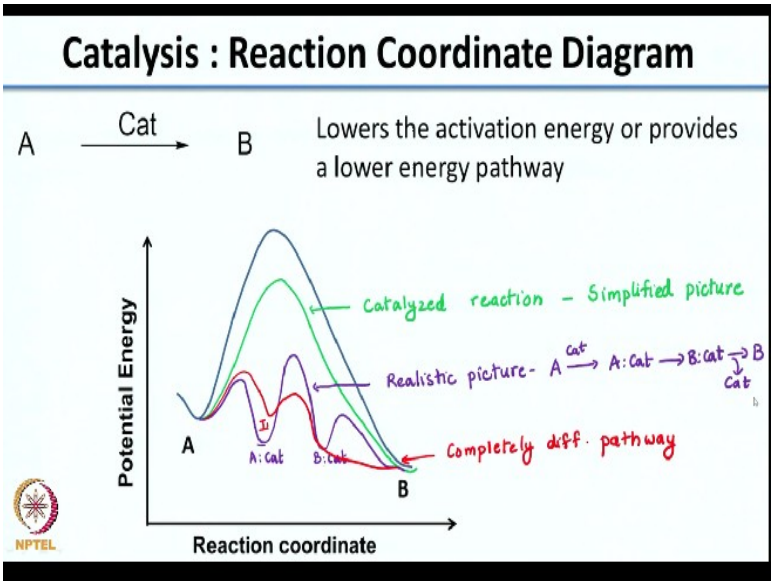

So if I go from a reactant A to the product B, what a catalyst does is, it lowers the activation energy. A lot of books sometimes indicate this as a process like this. So they would say that this is the catalyzed reaction and some of you might have also drawn this in your reaction coordinate diagram. So this is a very simplified picture. In reality what you see is the catalyst complexes with the reactant to give you a catalyst reactant complex.

And this would further convert to a product which is again bound to the catalyst and finally you get the product B. Now what you seen is the overall activation energy of the process has been reduced. So this is a more realistic picture. Now here how you can represent it is you can represent it as A going to in the presence of catalyst and A catalyst complex which will give you the B catalyst complex which finally gives you B.

And then you again you lose the catalyst. So the cycle is repeated again. So this is what you actually see when the catalysis takes place and not the overly simplified picture that was shown early and in terms of activation energy what you can see is that you have an overall lowering of activation energy. There is also another pathway where you can think of a completely different pathway taking place to give you your product.

So what this is is, let us say it forms I1. So this is the third possibility where a. So this is a totally different reaction coordinate. It is not complexing with the reactant. It is probably complexing but forming a completely different intermediate and using a different pathway to lead to the product. So these are the multiple possibilities of reactions taking place in the presence of a catalyst.

So now what we will do is we will take a deeper look into the reaction coordinate diagrams in the next class. So before that what I want you to do is, I want you to look very closely at the realistic picture that we saw shown in purple where you have the A reactant forming the A catalyst complex which then goes to the B catalyst complex and finally to B.

So I want you to redraw this and practice this because in the next class we are going to look at multiple scenarios and draw reaction coordinate diagrams for different cases where you can have different affinities of the catalyst with the reactant. So thank you and I will see you in the next class.