Mechanisms in Organic Chemistry

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

Lecture-04
The Radical Reactions

So, welcome to the fourth lecture of this week on mechanisms. So just before we move on a recap of what we did in the previous lecture.

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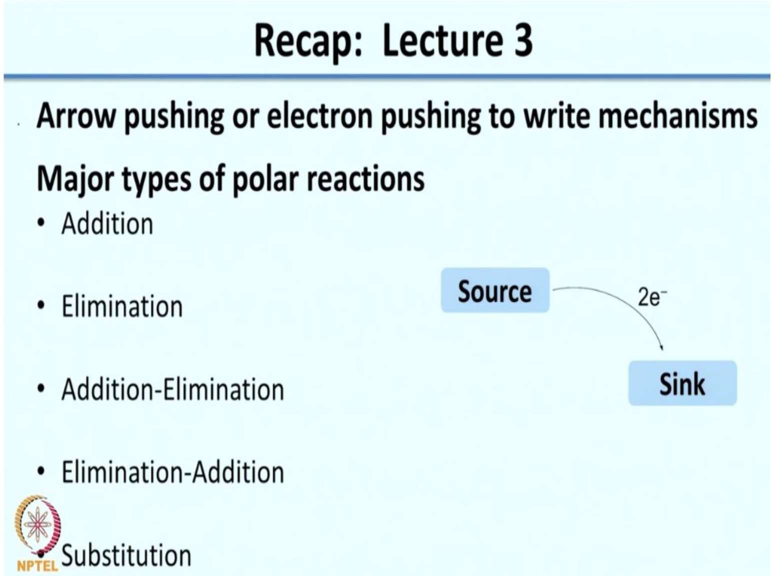

Recap: Lecture 3

Arrow pushing or electron pushing to write mechanisms

Major types of polar reactions

- Addition
- Elimination
- Addition-Elimination
- Elimination-Addition
- Substitution

So, in the previous lecture we looked at arrow pushing or electron pushing to write reaction mechanism and we also classified polar reactions and looked at the major types of reactions which could be seen under polar reaction. So, we looked at addition reactions, elimination reactions, addition-elimination, elimination-addition and substitution. So, the basic aim here was not to give you a big overview about all the different types of reactions under these sub classes.

But what I wanted to show you was the general mechanistic principle behind each of these. So, once you understand the basic mechanism it is easy for you to extend that to a broad set of different reactions. So, now in today's class the first thing that I like to do is go over the 3 homework problems which I had given you in the previous lecture. So, in the previous lecture, I had given you 3 problems on very similar looking compounds. I am not sure if you are familiar with this functional group, it is a hemiacetal.

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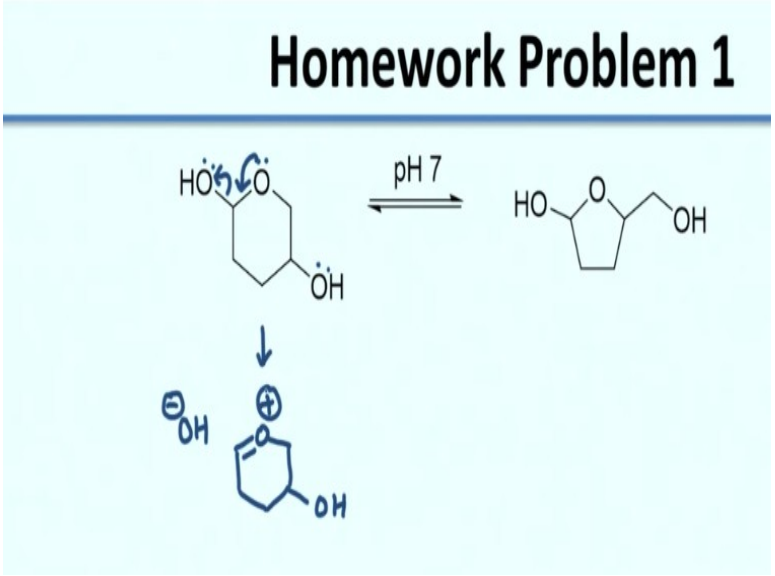

And the reactions shown where at different pH. So the first reaction was at neutral pH. So I hope you got a chance to work on this. Now if you look at this reaction remember the basic rules you need to think of is, think of the electron source and the electron sink. So, in this case for the electron source you have your lone pair on the oxygen, you also have two more lone pairs on the other two oxygens, so these would be great sources for your reaction to take place.

Now you need to decide which of these oxygens would actually initiate the reaction. So let us start systematically pushing arrows from each oxygen. Now if I push arrows from this oxygen what I would end up getting would be. Now after I get this species if you look at the product there is not much you can do beyond this point. So, now what you need to think of is probably this is not the path through which the reaction takes place. So, then what you can do is you go back and we will now think of which could be the other pathway that the reaction can take.

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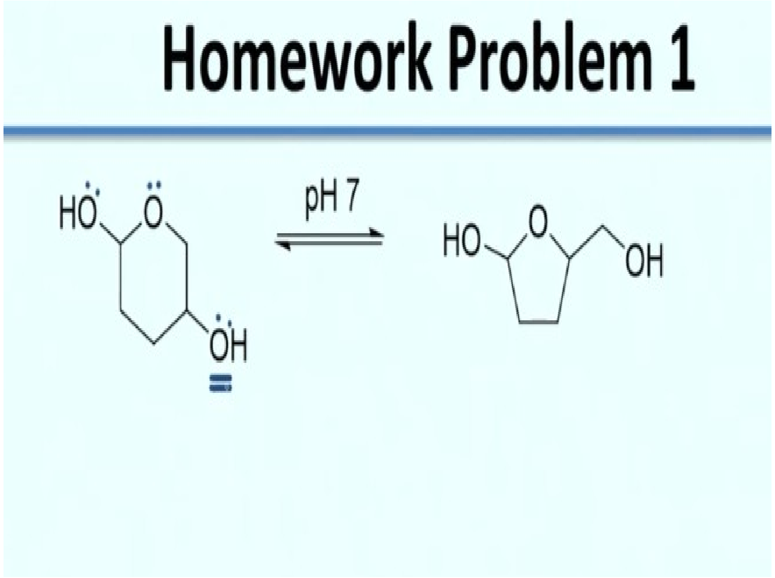

Homework Problem 1

So, if I consider this oxygen there is really nowhere, where it can go to give you a fruitful reaction. So this pathway also I am going to discard.

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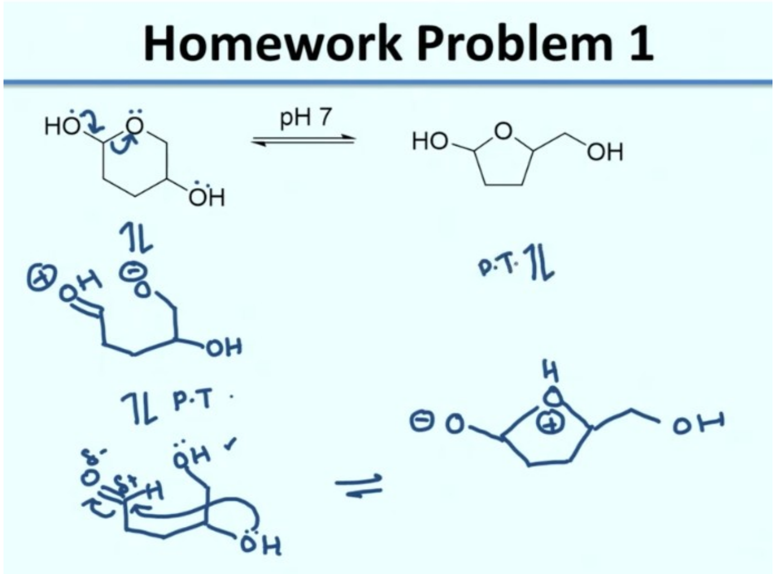

Homework Problem 1

So, now comes the third oxygen and let us see what happens when we push arrows from there. So, if we go from this oxygen, I will systematically write it so that the charge balance is maintained. So, I start from a neutral compound and I get a neutral intermediate. So this would be the species that I would get. So, then as I showed you the last time I can do proton transfer. So what I end up getting would be, so I would get another neutral species.

Now if you look at this molecule carefully, I have two alcohols and one aldehyde. So this would be my sink. Now if I choose this OH as a source, I get back my starting material. So I will not do that, instead I will use this lone pair as the source and I will push my electrons here. So, now what I end up getting is, so here again now you can do a proton transfer to give you the desired product. So, now you have seen that at neutral pH we have not added any acid or any base but we were able to systematically go from the starting material to the product.

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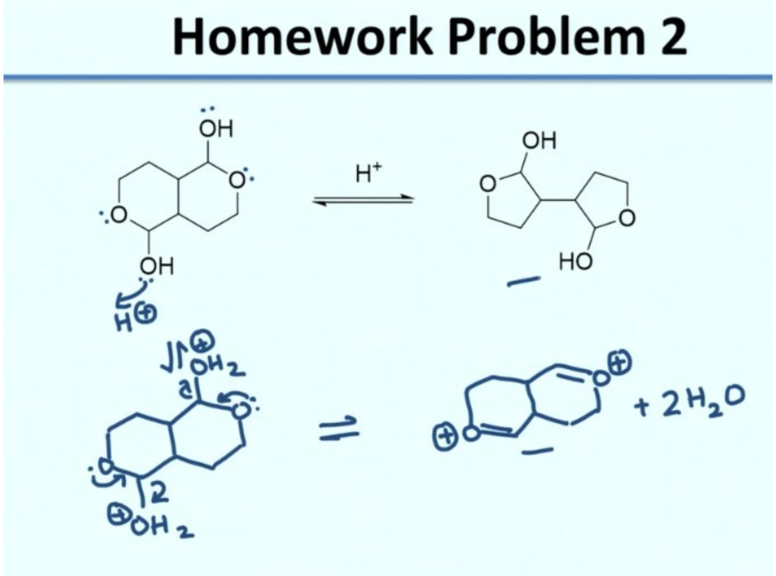

So, similarly now let us look at the next problem. Now in this problem, again you have 2 hemiacetals but here your medium is acidic, so you have H^+ in the medium. So, now here again let us look at all the sources that you have. The first thing would be protonation since you are doing this reaction in an acidic medium. So, now again one would be where, so here I am protonating this OH, so I can imagine a similar protonation happening on the other side.

So, once I do this protonation the next step you can think of would be, so now what you would end up getting. Now if you look at this and look at your product what you would see is, there is no way you can get from this intermediate to your product. So, now obviously you know that there is some problem here and probably this oxygen is not the source. So, now let us go back and now we will again look at the reaction mechanism if we use the other oxygen as the source.

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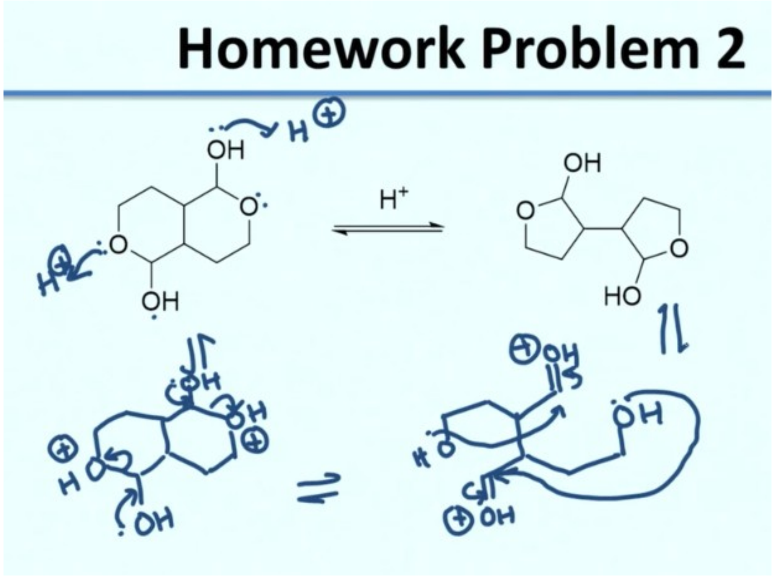

Homework Problem 2

So, if I use this oxygen as the source, now I have H^+ similarly I can think of another H^+ interacting with the oxygen. So, now what I end up getting would be, so the next step would be again you have a source right here, similarly. So, now you have opened up both these 6 membered rings, so now you have two free alcohols and a protonated aldehyde. So, now what would happen is you can imagine this oxygen interacting with the other aldehyde.

So, initially it was forming a 6 membered ring but now it is forming a 5 membered ring similarly you can imagine this oxygen interacting with this aldehyde. So, then the product that you get would be the desired product. So, now again you have seen even when you have multiple sources if you systematically identify the source and the sink, you will be able to figure out the mechanism.

Sometimes you might take one or two tries or sometimes you would be able to get it immediately. Now coming to the very last problem, here again you have a hemiacetal and you have OH^- here in a catalytic amount. So, what it tells you is here you do not have the OH^- acting as a nucleophile it is probably acting as a base.

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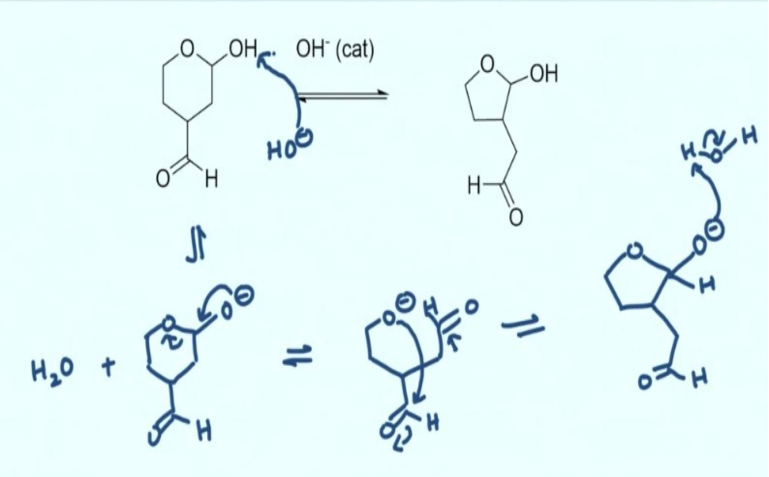
Homework Problem 3



So, what you can think is, so you can think of the OH^- deprotonating and what you would get is see you have O^- plus water. So, now you have a source here in your O^-, so it can come in here this bond will open. So, now that you have opened up this 6 membered ring. Now this O^- that you have has two options it has, it sees 2 electron sinks. Now if it goes to the aldehyde here you will get back your reactant but now.

So, now if your O^- goes to the other aldehyde, what you would end up getting would be and of course the next step would be. Now remember do not show H^+ here because your medium is basic. So now, so once you do that you will get your product. So, hopefully these three problems have illustrated at depending on the medium even if you have very similar looking substrates you can actually has very different mechanisms.

And in each of these substrates what you see is there were multiple sources and multiple sinks but with a very systematic approach we were able to write the mechanism for all these reactions. So, now what we will do is we will look at another class of reactions. So, radical reactions are different from polar reactions where you talk about single electron species called as radicals and to show the movement of single electrons what is used is a single headed arrow.

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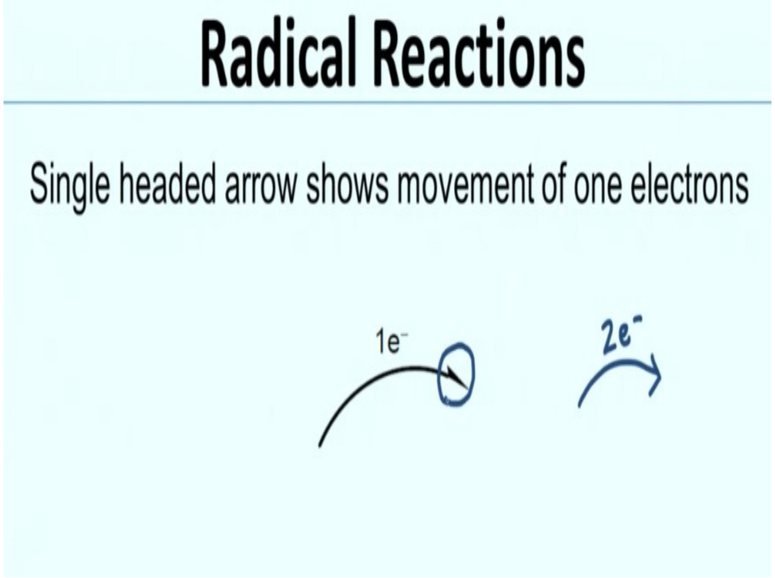

Radical Reactions

Single headed arrow shows movement of one electrons

So, as we saw earlier, for the polar reactions we used a double headed arrow. So double headed arrow indicates movement of two electrons. But a single headed arrow indicates the movement of one electron. So, radical reactions or radical species are very reactive, you can classify radical reactions very nicely.

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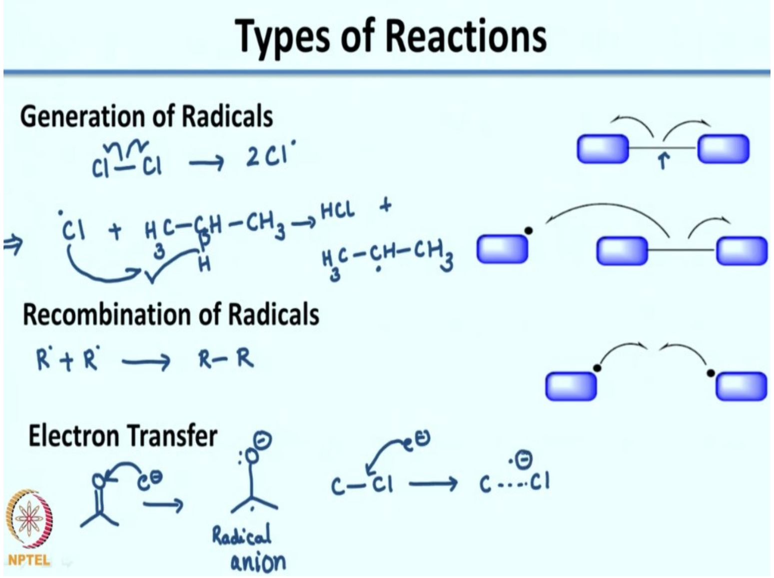

Types of Reactions

Generation of Radicals

$Cl-Cl \longrightarrow 2Cl^{\cdot}$

$Cl^{\cdot} + H_3C-CH(H)-CH_3 \longrightarrow HCl + H_3C-\dot{C}H-CH_3$

Recombination of Radicals

$R^{\cdot} + R^{\cdot} \longrightarrow R-R$

Electron Transfer

$C-Cl \xrightarrow{e^{\ominus}} C\cdots Cl^{\cdot\ominus}$

Typically, you have reactions involving generation of radical, so what you would see is you can have a bond, typically these are weak bonds. And the bond cleaves such that each partner takes one electron. This is called as a homolytic bond fission. So, common examples are suppose you have so you can have Cl_2, Br_2. And again, watch carefully I am using single headed arrows to show that the bond has cleaved homolytically.

So, then the species I would get would be $Cl^{\cdot}$ Now radicals can also be generated where you have an already formed radical which interacts with an intact bond leading to the hemolytic fission of that bond. So, what you can see is you can think of again now this $Cl^{\cdot+}$. So now to indicate it clearly what I will do is I will actually show you the hydrogen. So, now you can imagine this CH bond cleaving such that.

So, what I generate would be the other commonly observed things with radical is radicals as I said are very reactive. So, you can have reactions where you have two radicals quickly combining, so it can be $R^{\cdot} + R^{\cdot}$ give you. So, recombination of radicals typically is a termination of the reaction because you are in a way after this reaction takes place the radical species does not exist. So, the reactivity decreases whereas in the example that you had seen here what happened is you are still generating a new radical which can propagate the reaction forward.

The other case where you see radicals is electron transfer reactions, so these can be to pi bonds or sigma bonds. And typically, when you look at pi bonds you would have an electronegative atom attached to one of the ends of the pi bonds. So, this is one example, if you have an electron transfer taking place what you end up generating would be so called as a radical anion, you can also see it happen in the case of sigma bonds.

In this case the electron actually goes to an antibonding orbital. Now that is difficult to show. So, lot of times what you would see is it is shown as a dashed bond with a radical and a charge shown. So, this is a very generic representation of the basic types of reactions that you see with radicals. So, to give you a very specific example typically what you would see is when you have radical reactions they are initiated by cleavage of a bond.

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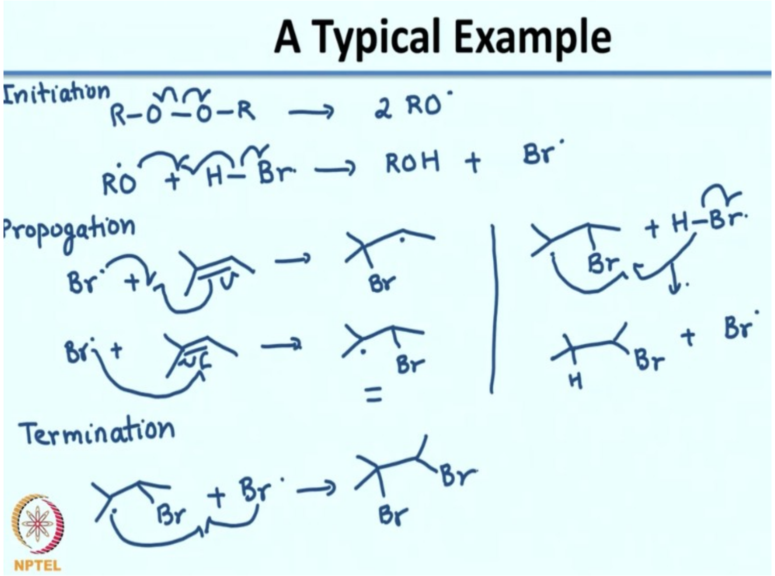

A Typical Example

that is very weak. So you would see a lot of times peroxides used as initiators, so this step would be called as the initiation. Again, remember I am showing this with single headed arrows so now what I get would be. So, now that the initiation step has occurred it would generate more radicals because RO$^{\cdot}$ is not the species that you want to interact. So you will have RO$^{\cdot}$ interact with another species let us say H-Br.

So, now what you have generated is, so now you have generated a new radical which is your reactive species. So, the next step would be propagation. So now let us see what happens when you have this species Br$^{\cdot}$. Let us say it is interacting with an alkene. So now there are multiple products that you can think of getting. See you can have one product where you have, the other product that is possible is I am going to draw this again, so that I can show you the arrows.

So, I can have the other carbon centre interact with the Br, so now what I would get would be. Now a lot of these radical reactions are governed by stability of the radical that is formed. Now when you look at these two intermediates that are formed, you must have studied this earlier, this would be a more stable intermediate. So, what you would see is especially in the case of Br and we will look at this later, the major product would be formed such that it gives you the more stable radical.

So, once you generate this, this is your propagation, so you have this radical, now a lot of times what can happen is once you have generated this radical you can also have unwanted termination reactions. So, now that you have seen this you have generated the two radicals, now once you generate the alkyl radical what you can have is. And now what you would end up getting would be, and now this $Br^{\cdot}$ can go on and react with another alkene.

So, the reaction will propagate in the way shown here. Now sometimes when you have radical reactions you can also see what is a termination reaction. So, in the termination reaction what will happen is once you have this intermediate it can interact with another Br radical to essentially give you this species. So, now the reactivity is lost because all your radical species are converted to neutral species.

So, this is an unwanted termination reaction, whereas with the propagation mode what you would see is you would have more and more of your alkenes getting brominated. Another commonly seen example is in photochemistry. So especially when you have groups such as the carbonyl group a C=C and N=N. So, what you see is in the presence of light you have excitation.

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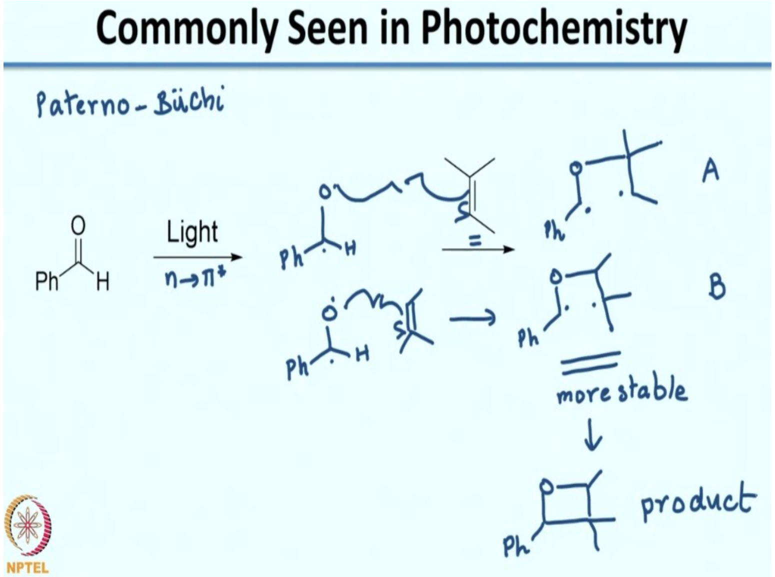

Commonly Seen in Photochemistry

Typically, in this case it would be an n to pi star excitation and you can think of this bi radical been generated. Now once you generate this bi radical similar to the examples at shown earlier you can draw mechanisms of this bi radical interacting with say another pi bond and this is a name reaction it is actually called the Paterno-Buchi reaction. It is okay if you do not remember the name for what I would like you to understand is the mechanism of the reaction.

And I would like you to think for a minute, so based on the example that I had shown in the previous slide you can press your pause button now and try to see what would be the product that you would get when you react this bi radical with the alkene that is shown here. So, there could be two possible products that you can get and one of them would be the major product.

So, what I would like you to do is I would like to spend some time write in your notebooks what are the two possible products and then think as to which would be the major product. So, hopefully you have done this exercise and I will walk you through this mechanism.

So, if you have this bi radical one thing that can happen is you can imagine that it could form another bi radical intermediate, this is one possibility. The other possibility is it can also form a bi radical intermediate, I will write it for you, where essentially, I have the regiochemistry changed. So, now I have intermediate A and intermediate B, again for those of you who were not able to get these two intermediates, I would like you to press the pause button again and look at these two carefully and figure out which would be more stable. Okay, so, what you would see is in this case because you are generating a tertiary radical it is more stable. And so, the product that you formed, so with radical chemistry you can rationalize formation of the product very nicely by actually looking at the stability of the radical intermediate that is formed.

So, it is extremely logical and you can in a very systematic way figure out what would be your product. So, now based on this what I would like you to work on is there are 2 reactions that are shown, both of these are photochemical, so it would involve generation of a radical as I had shown you earlier on this C=O.

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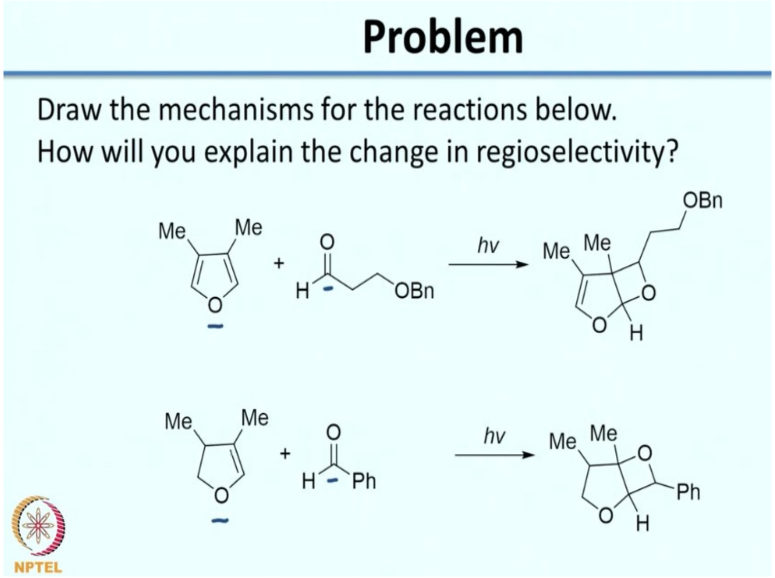

Problem

Draw the mechanisms for the reactions below.
How will you explain the change in regioselectivity?

So once you generate the bi radical again it can interact with a double bond to give you the two products that are shown. So, what I would like you to do is one I would like to draw the mechanism for both of these and once you draw the mechanism, I would like you to explain why you have a change in regioselectivity when you change the molecule from a furan to a dihydrofuran.

So, the difference between these two is in this case you have two double bonds whereas in this case you have only one double bond. So, I would like you to go ahead press a pause button and then try to solve both these problems and rationalize the regioselectivity. So, hopefully you have time to work out both of these problems, so now let us try to rationalize the regiochemistry.

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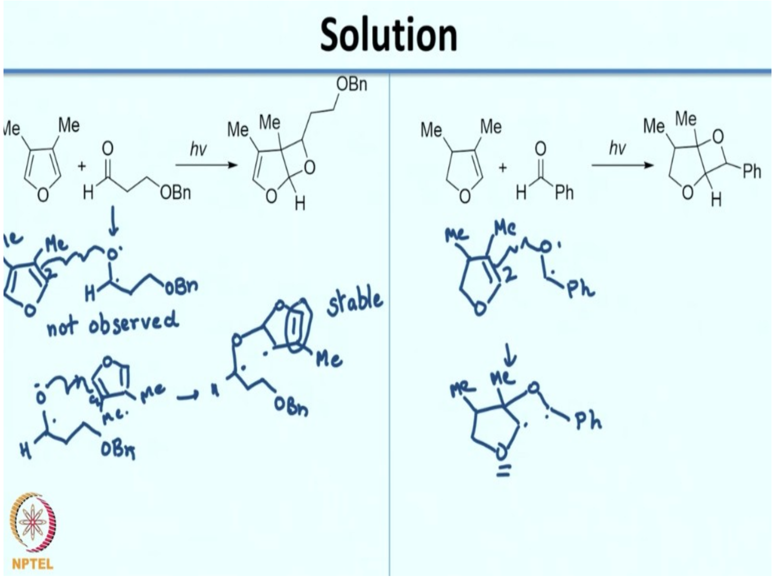

So, in one case what you have is, so you generate this bi radical and now it can interact with the furan. So, now what happens is based on the regiochemistry of the product shown what you would see is it does not prefer to interact such that you have, so this is not observed, right? So, what you observe is actually formation of the opposite regiochemistry. So, for the opposite regiochemistry I will just write it like this.

So you have, So, this is the bi radical intermediate that is formed. Now if you look at this intermediate what you would see is this radical is in conjugation with a double bond. So, you have an allyl radical which is highly stable. Now what happens in this cases once you generate the diradical and now you interact with dihydrofuran. So, the double bond is not there to make it look like an allylic radical intermediate.

So, now what happens is it actually prefers to form this product, sorry, so it, so it prefers to form this intermediate bi radical because in this case you have an oxygen atom right next to the radical which stabilizes this whereas in the earlier case you have a double bond which makes it allylic in nature. So, what you can see is a very small change in the starting material or the reactant has a pronounced effect on the regiochemistry of the product.

And this you can understand mechanistically by drawing the intermediate and seeing which gives you a more stable radical. So, with this I would like to summarize what we have done so far. We looked at drawing arrow pushing mechanisms or electron pushing for polar reactions.

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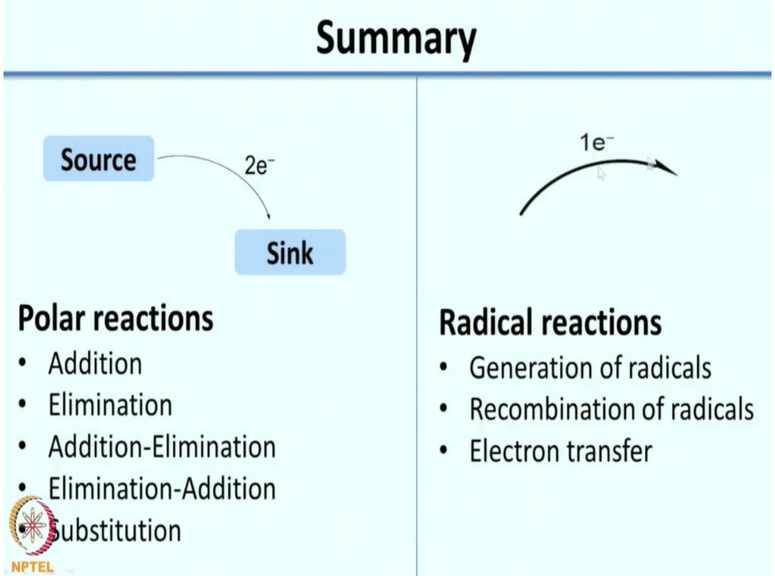

Summary

Polar reactions
- Addition
- Elimination
- Addition-Elimination
- Elimination-Addition
- Substitution

Radical reactions
- Generation of radicals
- Recombination of radicals
- Electron transfer

So, for polar reactions what you have is you have a source and a sink and you would show the electrons such that it originates from the source and the head goes to the sink. And we looked at different types of polar reactions we did not look at each of these in detail but we looked at the basic mechanism for each of them. We also looked at radical reactions involving one electron and you denote that with a single headed arrow.

And in radical reactions broadly what you see is there are reactions involving generation of radicals, recombination of radicals or electron transfer. So, this is a broad summary of how you can use arrow pushing to write reaction mechanism. So, the assignment will also give you a good practice as to how you can push arrows to write reaction mechanisms. So, thank you and what we will be doing next week is we would be looking at experiments to help you determine the reaction mechanisms.