Mechanisms in Organic Chemistry

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Lecture-02
Writing Reaction Mechanisms: Arrow Pushing

So welcome to the second lecture on reaction mechanisms. So first we will just do a recap of what we did in the previous lecture. So in the previous lecture we looked at classification of organic reactions. So this was a very broad classification into polar, radical and concerted reactions.

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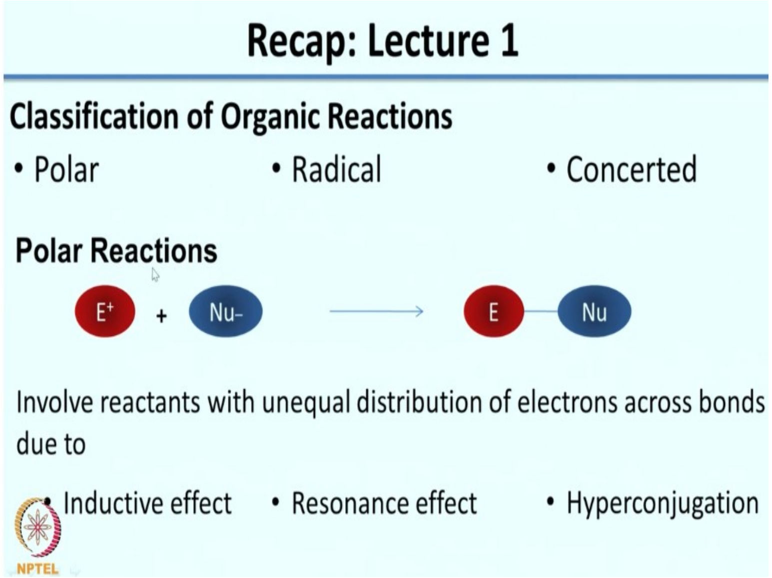

Recap: Lecture 1

Classification of Organic Reactions

- Polar
- Radical
- Concerted

Polar Reactions

Involve reactants with unequal distribution of electrons across bonds due to

- Inductive effect
- Resonance effect
- Hyperconjugation

And now after that what we did was we looked at how there is an unequal distribution of electrons across bonds in polar reactions. So in particular, we looked at the inductive effect and the resonance effect.

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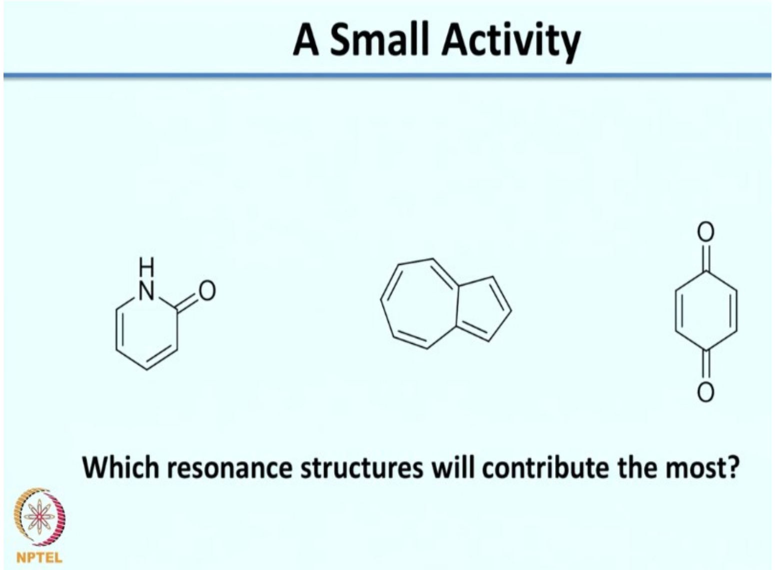

A Small Activity

Which resonance structures will contribute the most?

And if you remember before the class ended, I gave you a small activity to do as homework. So what I wanted you to do is for the structures given I wanted you to write the resonance structures and say which resonance structure would contribute the most. So if you remember what I told you is that the actual structure is actually a hybrid of all the resonance structures. But what happens is sometimes due to added stability of one particular structure it contributes more.

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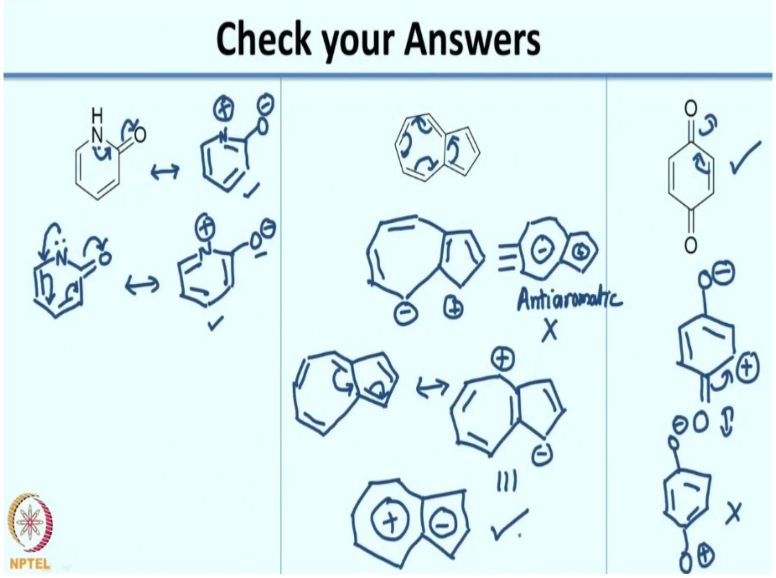

Check your Answers

So let us now see what the answers are to these problems which we had given. So the first example if I were to push electrons I had also taught you how to push electrons. So now there are these lone pairs on the nitrogen, so if I were to push electrons, I can push it this way and now because here I have too many electrons, I would push it again to the oxygen. So one resonance structure would be, so I have put a new pi bond here.

And because the electrons have come here, I have a negative charge on this oxygen and I have a positive charge on the nitrogen. I can also push the electrons in the other direction. So I will show you that as well and you can check this with your answers. So instead of pushing to the right if I push to the left, what I will get is. So once these electrons come here these pi bonds would move and again, I would get a resonance structure which would look like this where again I have a negative charge on the oxygen and a positive charge on the nitrogen. Now between all these structures, which structure would actually contribute the most? So what you would see here is in both of these structures I end up generating an aromatic center and I have a negative charge on oxygen which is an electronegative atom.

So this structures would also contribute despite the fact that there is a charge that is generated. So if I push electrons in this direction, let us first draw the skeleton structure, so I have a 5 membered ring and then I have a 7 membered ring, so now that I have pushed the electrons I am generating a positive charge here, a double bond here, the double bond there moves, the double bond here comes and then I have a negative charge here. Alright?

Now if you look at this structure will the structure be very stable? What you would see is in this structure because you have a positive charge here and a negative charge on the second ring you can equate it to a structure where you have a positive charge here and a negative charge here. Now if you remember the basic rules of aromaticity what it does is it makes both these rings anti-aromatic.

So this will not be a major contributing structure. Now let us try to push the electrons in the other direction. So if I push the electrons in the other direction, so again, let me draw the first problem again. So now what I am doing is instead of pushing the electrons out of the 5 membered ring, I am going to push the electrons into the 5 membered ring. So what I end up getting is I have these electrons move in. So the structure that I get would have a negative charge here and the positive charge here.

So again, I can equate this to a structure where I have a completely delocalized positive charge on the 7 membered ring and a delocalized negative charge on the 5 membered ring. So I can show this to be equivalent to, now in this case both of these rings gain aromaticity, so this would be a major contributing structure. Now let us look at the last example. Here if I were to push electrons I would get a structure.

This would be one structure and further I can again push electrons where, now here what happens in this structure is that I have a positive charge on oxygen which is an electronegative atom. So this is not a major contributing structure. So in this case the major contributing structure would actually be the neutral molecule. So this is actually an example of a non aromatic compound, whereas in this case you have an example of an aromatic compound.

So hopefully you were able to solve some of these problems. If not, you can ask our TAs or me in the discussion forum and we could help you out with writing these resonance structures. So now let us come back to contribution of unequal distribution of electrons in molecules. So we looked at inductive effect and we also looked at resonance effect. Now a third effect is hyperconjugation.

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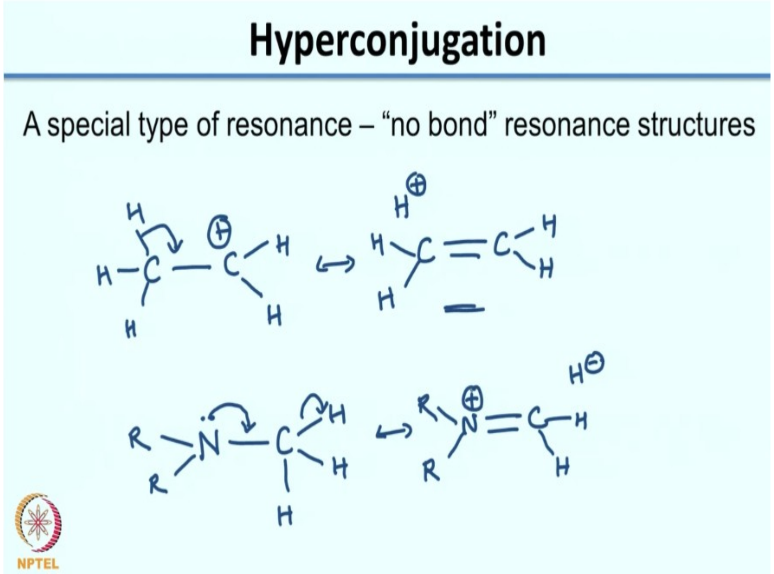

Hyperconjugation

A special type of resonance – “no bond” resonance structures

Hyperconjugation is a type of no bonded resonance structure. So an example would be, so if I were to write the structure now, I have hydrogen, hydrogen, hydrogen. So I am looking at this cation, so a no bonded resonance structure would look something like this where essentially I generate an H^+ and then I have a double bond here. This structure is called as a hyperconjugation structure.

And you would have come across this when you are looking at the stability of carbocations where the tertiary carbocation is more stable than the secondary carbocation which is more stable than the primary carbocation primarily because you can have more hyper conjugation structures for the tertiary carbocations. So these are what the hyperconjugation structures look like, which is essentially a form of no bonded resonance structures.

Now you must have seen these kind of structures where you generate an H^+. Can you also think of structures which are again an example of hyperconjugation, but here you actually get a negative charge on the hydrogen. So you can imagine the bond breaking such that the hydrogen tends to take the electrons. One such example would be, suppose I have a nitrogen and again I have a carbon center next to it.

Now I have the lone pairs on the nitrogen. If I push electrons, so now what I have done is I have generated a hyperconjugation structure. But in this case I have the hydrogen actually taking the electrons instead of giving the electrons like you saw in the previous case. So both of these are example of hyperconjugation structures. So now let us come to how to write reaction mechanisms. So that was one of the first learning outcomes for this course.

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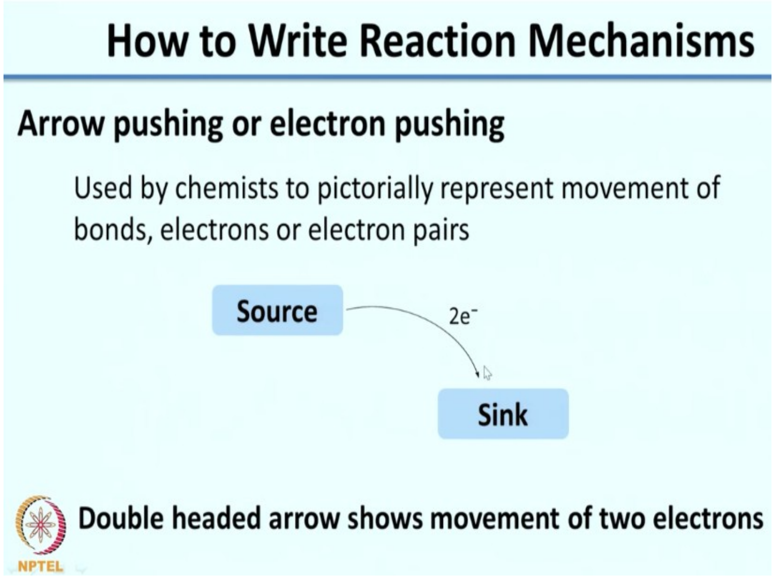

How to Write Reaction Mechanisms

Arrow pushing or electron pushing

Used by chemists to pictorially represent movement of bonds, electrons or electron pairs

Double headed arrow shows movement of two electrons

So now I already told you while you were writing resonance structures that you push arrows or electrons and the direction is usually from the source to the sink. And for 2 electrons you use a double headed arrow. So now what are the typical sources and sinks that you see when you write reaction mechanisms? So whenever you have a polar reaction typically you will have either charged intermediates or you would have intermediates where you would see a dispersion of charge, but there would be a polarity associated with the reaction.

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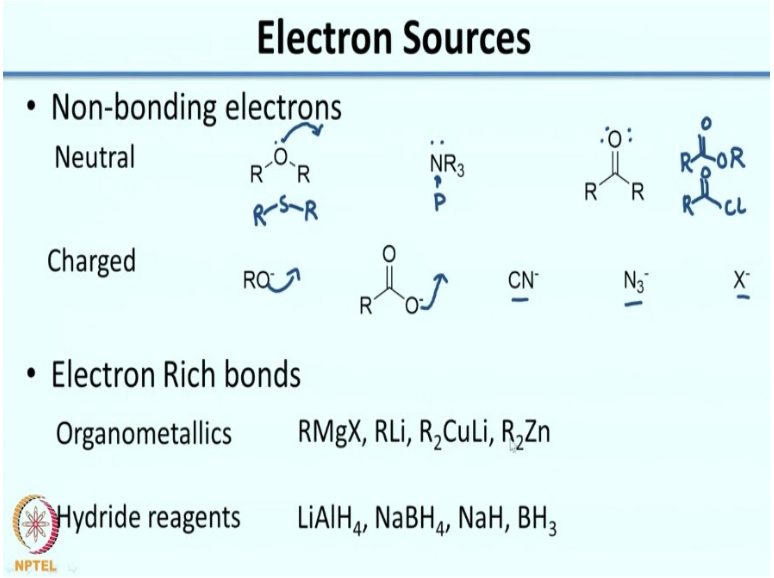

Electron Sources

- Non-bonding electrons

Neutral

Charged

CN^- N_3^- X^-

- Electron Rich bonds

Organometallics RMgX, RLi, R_2CuLi, R_2Zn

Hydride reagents $LiAlH_4$, $NaBH_4$, NaH, BH_3

So let us look at some electron sources. So you can have neutral sources of electrons. So in this case you have the oxygen lone pair, the nitrogen lone pair. All of these would be your electron source. So when you actually draw mechanisms you will be drawing such that this would be your source, your lone pair. Now instead of oxygen you can also think of sulfur, instead of nitrogen you can also think of phosphorus

and instead of a ketone you can also think of other acid derivatives, you can think of esters, you can think of acid chlorides. So in all these cases the lone pair would be an electron source. So when you push your arrows the source would be from the lone pair. The other example is when you have charged species. So these are your typical nucleophiles that you are used to, so you must have seen X^-, N^{3-}, CN^-.

Also you can think of RO^-, O^-, so in this case your electron source would be from the charged species. The other source of electrons is electron rich bonds. So an example would be organometallic species such as your Grignard reaction, organolithium reagents also R_2CuLi, R_2Zn. These are all examples of R where your R is actually electron rich. You can also have hydride reagents.

So these are sources of H^-, so you have $LiAlH_4$ (lithium aluminum hydride), sodium borohydride, sodium hydride and borane based reagents. So in all these cases these are sources of hydrides or H^-. Other electron sources are those that involve pi bonds. So your pi bonds are sources of electrons

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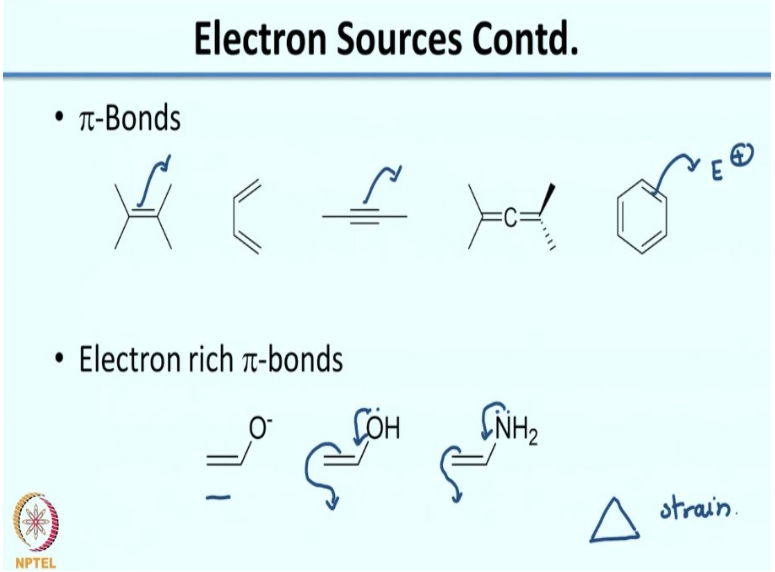

Electron Sources Contd.

- π-Bonds
- Electron rich π-bonds

and typically when you write mechanisms involving pi bonds where it is a source the arrow would be originating from the pi bond. Also if you have a triple bond that can also act as a source. Allenes, so where you have a carbon center with 2 double bonds on either side, they could be a source. You have also looked at aromatic reactions where your aromatic ring is actually a source of electrons and it grabs an electrophile in your electrophilic aromatic substitution reactions.

The other example is where you have electron rich pi bonds. So the example would be an enolate. So here you have a charge on the oxygen, you can also have neutral species like you can have the enol. So typically you have known pairs here and it has a carbon center that usually interacts with an electrophilic species. Similarly if you have a lone pair on the nitrogen, again, it would be the carbon center which would actually be interacting with an electrophilic species if it is a soft electrophilic species that you are looking at.

Some other examples which are not listed here, is if you have strained 3 membered rings, for example, so if you have cyclopropane, because of the strain this could again be a good source of electrons. Now let us look at what could be good sinks. So in this case you need things which would grab electrons just like you have money transactions. So with human beings rich people are not as nice as molecules,
but money transaction is what you would imagine when you talk about when you think of human being, so somebody with a lot of money would be giving money to someone who has no money. Similarly in this case we are talking about electron transactions, so species which have lot of electrons would be giving electrons to species that have less electrons or electron sinks. So species with empty orbitals just like we talked about human beings with empty pockets,

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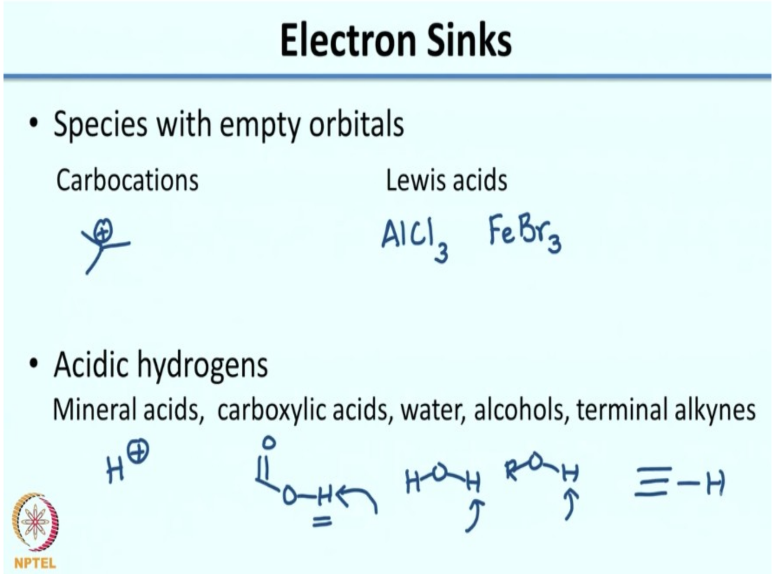

Electron Sinks

- Species with empty orbitals

Carbocations

Lewis acids

$AlCl_3$ $FeBr_3$

- Acidic hydrogens

Mineral acids, carboxylic acids, water, alcohols, terminal alkynes

these would be good candidates to take electrons. So you can think of carbocations, other examples are Lewis acids so you can have $AlCl_3$. So you can have Lewis acids, which are also good electron sinks, other sources are mineral acids, so these are sources of H^+, carboxylic acids.

So here again, you can think of a species which would grab the proton from the carboxylic acid, water, alcohols. So in all these cases now that we have sinks as you see the arrow is what is coming towards the sink, so you can have species that grab this hydrogen, grab the hydrogen from an alcohol and also terminal alkynes.

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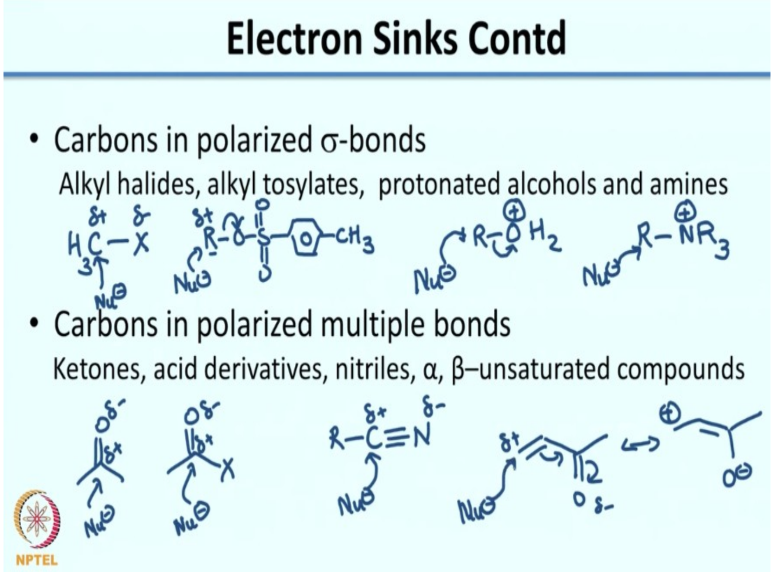

Electron Sinks Contd

- Carbons in polarized σ-bonds

  Alkyl halides, alkyl tosylates, protonated alcohols and amines

- Carbons in polarized multiple bonds

  Ketones, acid derivatives, nitriles, α, β–unsaturated compounds

So other examples of electron sinks are carbons in polarized bonds. So if you have alkyl halides, now you have a δ+ here and a δ- here. So this would be your electron sink and you can think of an electron rich species attacking your electron sink. Alkyl tosylates, so here you have a tosyl group. So here again you can think of a nucleophilic species interacting with the electron deficient R.

Another example is protonated alcohol. So if you have, now here you should remember that when I interact this with a nucleophile it will not interact with the positively charged oxygen species because as you see it will be violating the octet rule. So it would actually prefer to interact with the electron deficient carbon and you have an excellent leaving group in the water. Similarly, with protonated amines you can think of a nucleophile interacting here.

The other example is carbon in polarized multiple bonds, so you can think of ketones. So here again because oxygen is more electronegative than carbon, you have a δ- and a δ+ here. Instead of ketones you can also think of acid derivatives like esters, acid chlorides, amides, again in all these cases you have an electrophilic center at these carbons.

Other sources are nitriles, so here again you can imagine a nucleophile attacking this carbon because you have a δ+ and a δ-. Another example is alpha beta unsaturated compounds. So here I can actually draw a resonance structure. So what you end up having is a δ+ here and a δ- here. So, this is again a good sink where a nucleophile can add in. So you must have seen this when you would have studied like a Michael addition reaction.

So these are all examples of electrons sources and electron sinks. So now that you have a good idea about what could be sources of electrons and what could be sinks. We should now look at the entire picture and how you would actually write a reaction mechanism where you have all these molecules together and where you need to push electrons from a source to a sink to actually write the reaction mechanism.

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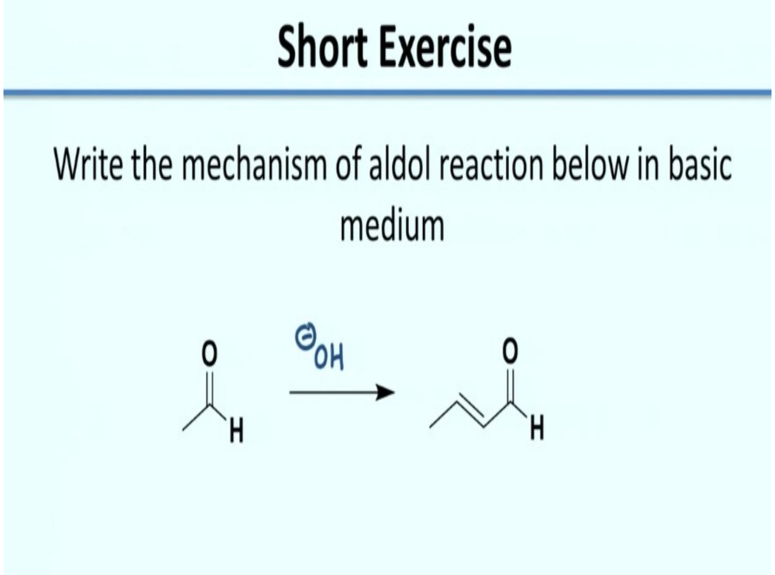

Short Exercise

Write the mechanism of aldol reaction below in basic medium

So as an exercise, what we would like you to do is to write the mechanism of the aldol reaction given below and in particular what I would like you to focus on is the reaction in a basic medium. The medium is very important when you write reaction mechanisms. So I would like you to press the pause button on your screen and try to write the mechanism of the aldol reaction in your notebooks.

So hopefully by now you have some basic mechanism for the aldol reaction. So you can check your answers. I will walk you through writing the mechanism for the aldol reaction in the basic medium.

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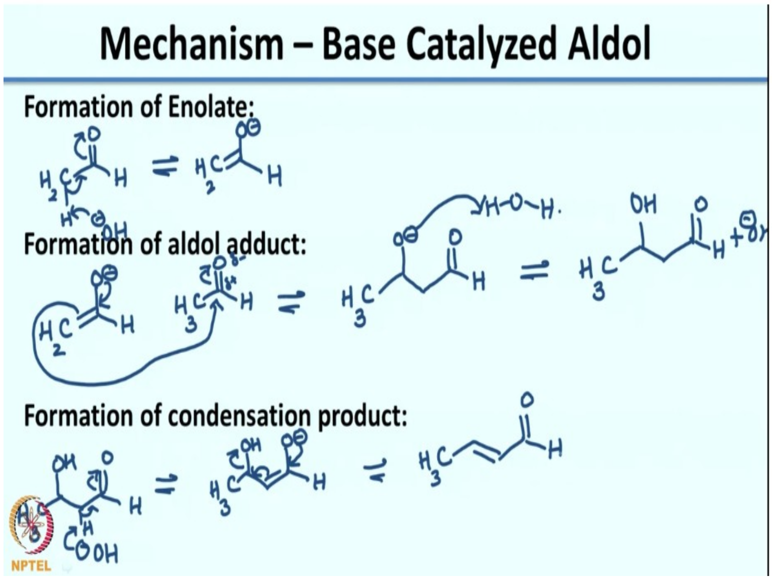

Mechanism – Base Catalyzed Aldol

Formation of Enolate:

Formation of aldol adduct:

Formation of condensation product:

So what we were looking at is the aldol reaction of acetaldehyde. So you have, now this hydrogen here is acidic. So in the presence of a base, the base food abstract a proton and generate an enolate. So the base would abstract a proton and generate an enolate. So this would be the first step of your reaction. So now in this case your electron source is your OH^- and your acidic proton is your sink.

Now the next step would be formation of the aldol adduct. So now you have a source, so in this case your source is the enolate and now it would interact with an electron sink which would be an other molecule of your aldehyde. So as I told you before you have a δ+ here and a δ- here. And again I had told you that when you have an enolate it is actually the carbon center which would act as the nucleophile.

So what you end up generating would be a species, so I am carefully following the arrows that I pushed. Now what you need to remember when you write these mechanisms is that the charge has to be always maintained. So if you remember in the first step, I started with an OH^- and an aldehyde so the net charge was negative, I generated an enolate which has a negative charge. In the second step I am reacting an enolate with a negative charge with the aldehyde.

So again, the net charge would be negative, so that this means that at least I am maintaining the charge balance. Now the next step would be abstraction of proton by this species. Now remember the medium we are using is basic, so there will not be free protons lying around. So the source for proton would actually be water plus OH^-. So now as you can see again the net charge is maintained.

So now the last step would be formation of the condensation product. So for that we start with the aldol adduct, which is now a neutral compound. Now my electron source would be OH^-, so it would grab a proton from here and I would end up generating the enolate. And the last step would be where these electrons would come out and it would kick out the OH^- to give you the final aldol condensation product. So this is the mechanism for the base catalyzed aldol reaction.

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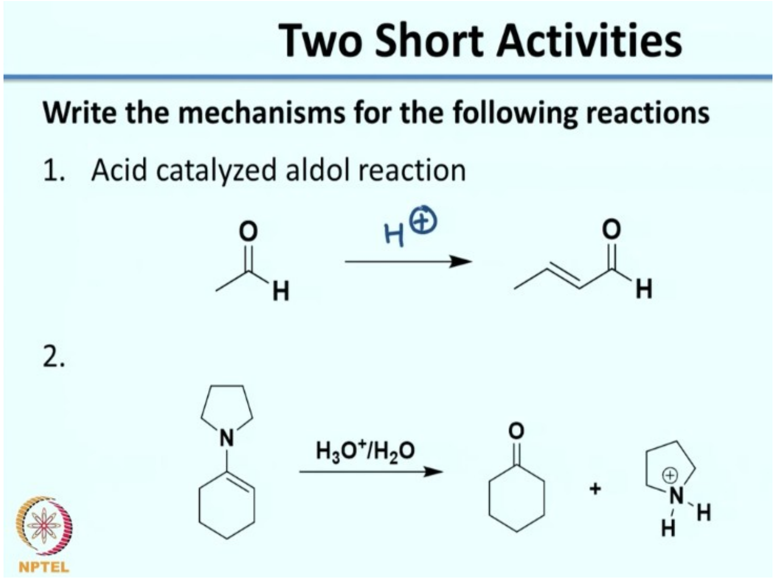

Two Short Activities

Write the mechanisms for the following reactions

1. Acid catalyzed aldol reaction

2.

So now what I would like you to do is I would like you to write the mechanisms for the following reactions as homework. The first reaction is the same aldol reaction that we saw earlier, but now the difference being that you are looking at this reaction in an acidic medium. And again the second reaction is also in an acidic medium. So as homework, what I would like you to do is I would like you to look at the mechanisms for both of these reactions.

So thank you. I will see you again in the next lecture where we will look at the answers to these two questions and we will also look at other mechanisms that you could work on.