Mechanisms in Organic Chemistry
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Lecture-34
Specific Catalysis

So, welcome back. In the last class we were looking at acid based equilibrium and if you consider this as a genetic reaction for acid base equilibrium, you have to acids here HA and BH^+ which is the conjugate acid of the space.

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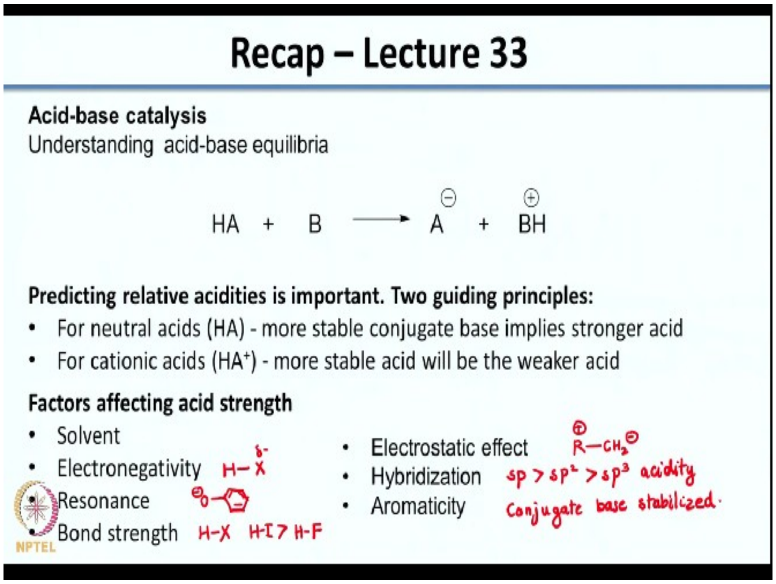

Recap – Lecture 33

Acid-base catalysis
Understanding acid-base equilibria

$$HA + B \longrightarrow \overset{\ominus}{A} + \overset{\oplus}{BH}$$

Predicting relative acidities is important. Two guiding principles:

- For neutral acids (HA) - more stable conjugate base implies stronger acid
- For cationic acids (HA^+) - more stable acid will be the weaker acid

Factors affecting acid strength

- Solvent
- Electronegativity $H-\overset{\delta-}{X}$
- Resonance
- Bond strength H-X H-I > H-F
- Electrostatic effect $\overset{\oplus}{R}-CH_2^{\ominus}$
- Hybridization $sp > sp^2 > sp^3$ acidity
- Aromaticity Conjugate base stabilized.

So, I told you understanding the related acidities of both of these is very important. So, to predict the relative acidities, there are 2 guiding principles you can use. For neutral acids more stable conjugate base implies stronger acid, for cationic acids more stable acid would be the weaker acid and then we had looked at all of these factors which affect acid strength. We had looked at solvent. a solvent which is solvates the ion more,

so, in the case of a neutral acid, if the ion is more solvated, that means you have a better acid, whereas for a charged acid, if the acid is more solvated, it would be a weaker acid. Then we had looked at electronegativity, where if you have the acid HX. So, greater the electronegativity of X better would be the acidity. Then we had looked at examples as to where resonance plays an important role in increasing the acidity.

So, if you have a conjugate base, which can be stabilized by resonance, then you see an improvement in acidity. We had also looked at bond strength, so within a group, so within a group what you see is as the bond strength decreases the acidity increases. So, if you compare HX, where X are halides, what you would see is HI would be greater than HF and I told you that you can use this to compare only when you have atoms within a particular group.

Then we had looked at electrostatic effect where if you have your conjugate base, say you have. So, if you have a positively charged species here, let us say R^+ that would stabilize this conjugate base. Then we had looked at hybridization, where sp would be more acidic than sp^2 would be more acidic than sp^3 and the last thing we have seen is stabilization due to aromaticity, which leads to improvement of acidity.

So, if the conjugate base is stabilized by aromaticity you see an increase in acidity or lowering of pK_a. So, we had looked at all of these factors in the previous class. So now what we look at is the catalyst by acids and bases.

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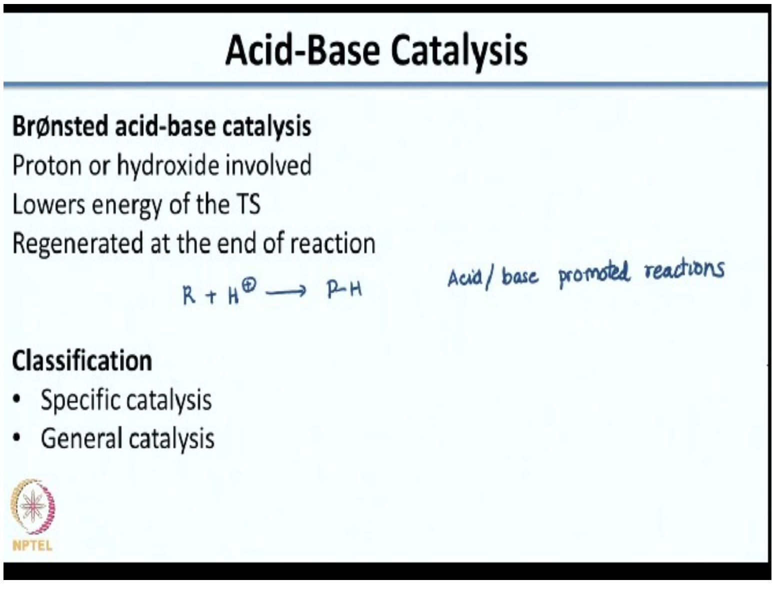

Acid-Base Catalysis

Brønsted acid-base catalysis

Proton or hydroxide involved

Lowers energy of the TS

Regenerated at the end of reaction

$R + H^{\oplus} \longrightarrow R\text{-}H$

Acid / base promoted reactions

Classification

- Specific catalysis
- General catalysis

We would be looking mainly at Bronsted acid base catalysis. So Bronsted acid base catalysis means you have a proton or a hydroxide. So, proton generally in the form of H_3O^+ or the protonated solvent that you were working with that is what would be important and the hydroxide. And here what happens is the proton or hydroxide due to interaction with the reactant lowers the energy of the transition state for the reaction

and thereby you have an accelerated reaction. So it acts as a catalyst. And of course, at the end of the reaction your proton or hydroxide is regenerated. What you would observe is, so, these are called Bronsted acid catalyzed reactions. What you would see is there will also be examples where you will have the acid or base being consumed. So, if you have your reactant + say H^+, when you get back your product you do not get back your H^+, it is in some form incorporated in the product.

So, in these cases these reactions are called acid or base promoted reactions. They cannot be called catalyzed because your acid or base is not regenerated at the end. So, for classification, they are classified as specific catalysis and general catalysis. So, what do each of these terms mean? Let us look at each of them in a little detail.

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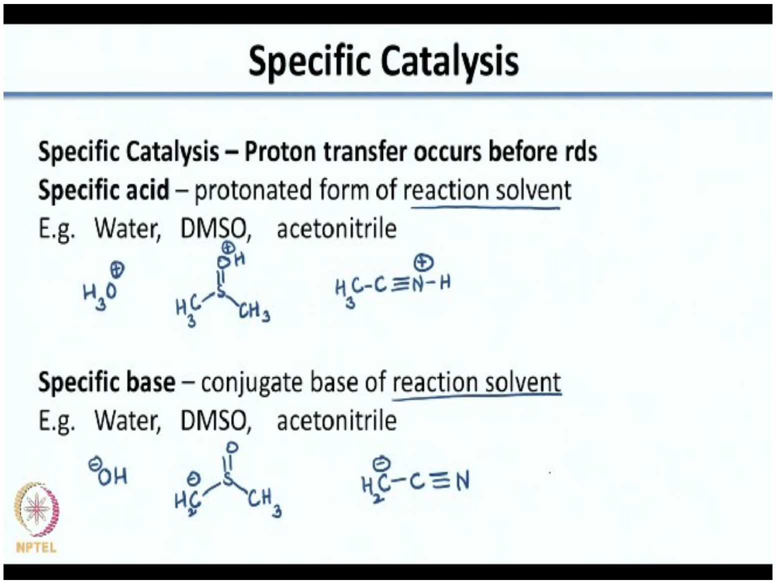

Specific Catalysis

Specific Catalysis – Proton transfer occurs before rds

Specific acid – protonated form of reaction solvent

E.g. Water, DMSO, acetonitrile

Specific base – conjugate base of reaction solvent

E.g. Water, DMSO, acetonitrile

So, the first is specific catalysis. Now many people get confused with the term specific and general. What you need to remember is in specific analysis proton transfer occurs before the rate determining step. So proton transfer is not involved in the rate determining step. Proton transfer occurs before the rate determining step. So, in other words the proton transfer is very very fast. Ok? Now, what exactly is a specific acid?

Specific acid the term itself means protonated form of reaction solvent. So, it does not matter what acid you are adding in the reaction. You are only talking about protonated solvent as the factor which improves or which shows up in the reaction kinetics equation. So, what do you mean by protonated form of reaction solvent? If you are looking at water as your reaction solvent, the protonated form would be of course H_3O^+. That is a specific acid.

If you are looking at doing a reaction in DMSO. This is the structure of DMSO. This protonated form is your specific acid. If you are talking about doing a reaction in acetonitrile, this is your specific acid. So again, I want to emphasize is, specific acid is the protonated form of the reaction solvent. You can add any other acid in the reaction, you can add some small amount of acidic acid, it does not matter. What matters is only the protonated form of the reaction solvent. It is very very specific to only the protonated form of the solvent.

Again, specific base is the conjugate base of the reaction solvent. Not any other external base that you are adding. So if you consider water, the conjugate base would be OH^-, if you are looking at DMSO the conjugate base would be this carbanion here. If you are looking at acetonitrile, this is the base that you are talking about. So these are all the specific bases that you are talking about when you do the reaction in these particular solvents.

Now let us try to get a deeper understanding of what it means that no other concentration of acid or base has an impact on the reaction rate. And it is only the protonated form of the reaction solvent.

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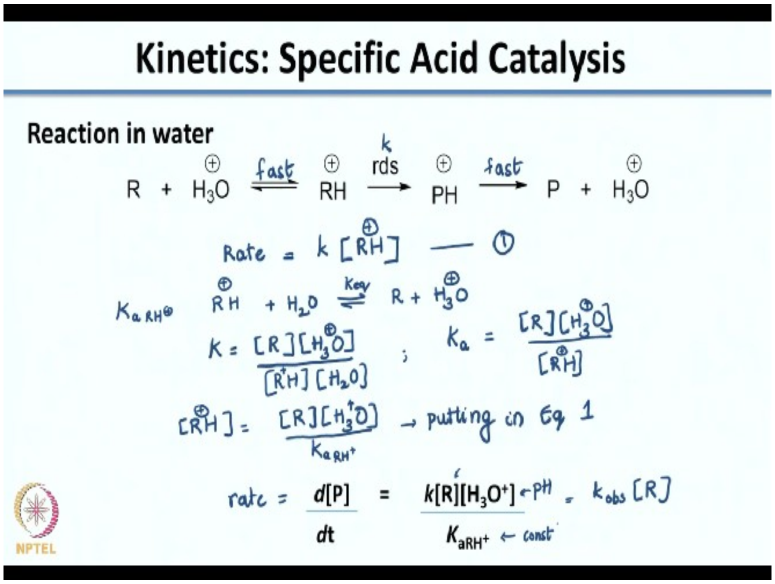

Kinetics: Specific Acid Catalysis

Reaction in water

$$R + \overset{\oplus}{H_3O} \underset{}{\overset{fast}{\rightleftharpoons}} \overset{\oplus}{RH} \xrightarrow[]{\overset{k}{rds}} \overset{\oplus}{PH} \xrightarrow{fast} P + \overset{\oplus}{H_3O}$$

$$Rate = k\,[\overset{\oplus}{RH}] \quad — \quad ①$$

$$K_{a\,RH^{\oplus}} \qquad \overset{\oplus}{RH} + H_2O \overset{K_{eq}}{\rightleftharpoons} R + \overset{\oplus}{H_3O}$$

$$K = \frac{[R][\overset{\oplus}{H_3O}]}{[\overset{+}{R}H][H_2O]} \;;\quad K_a = \frac{[R][\overset{\oplus}{H_3O}]}{[\overset{\oplus}{RH}]}$$

$$[\overset{\oplus}{RH}] = \frac{[R][\overset{+}{H_3O}]}{K_{a\,RH^+}} \rightarrow \text{putting in Eq 1}$$

$$rate = \frac{d[P]}{dt} = \frac{k[R][H_3O^+] \leftarrow pH}{K_{aRH^+} \leftarrow const} = k_{obs}\,[R]$$

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So to keep it simple, let us look at a reaction in water. I have just chosen water for simplicity. You can choose any other solvent and it will boil down to the same kinetic expression. So let us give this reaction, so you have your reactant being interacting with the protonated form of water, which is your specific acid. So you have H_3O^+ giving you the protonated reactant. The next step conversion of the reactant to the product is your rate determining step.

So this is a slow step, and the protonation takes place fast. And all these steps are also fast. So this is a typical expression that you would see for specific acid catalysis. I repeat, for specific acid catalysis, proton transfer is fast. So it occurs before the rate determining step alright? And the reaction rate only depends on the protonated solvent. In this case it would be H_3O^+ . Now, let us derive the kinetic expression for this.

So if you remember when we were studying kinetics, we were looking at rate laws. So when we were looking at rate laws we had done derivation of rate laws for complex reactions. So let us try to derive the rate law for this. So in this case, to simplify it, we will just start from the rate determining step. So the rate for the reaction would be given by *k* which is the rate constant for this process into concentration of RH^+ right?

So based on what we had studied for rate laws, this is the rate expression. Now what we usually do is we move back and try to express RH^+ in terms of R and H_3O^+. So I will give you a hint. I will give you the final expression. So this is what the rate *d*[P] by *d*t, the rate expression is given by this, where in the numerator you have the rate constant *k*, which is this [R] [H_3O^+]

and in the denominator the term that you have is the acid dissociation constant of RH^+ alright? So with this information I want you to look at your screen carefully and try to derive this from this form that is given here. So will I asked you to press the pause button and do this derivation yourself before you start working it out with me. As I have told you again and again, the best way to learn is to practice yourself.

Once you practice you can check your answers by comparing with me. While practicing you also come to know what the mistakes it is that you are making. So, go ahead and try to work out this derivation. So, you can check your answers now. So by definition the dissociation constant Ka of RH^+ deals with this equation. So, you are looking at RH^+ + water giving you R + H_3O^+ right? And this would be the K equilibrium for this process.

So, now, the K equilibrium for this process is given by [R] [H_3O^+] / [RH^+] we had done this and I had told you if you take water on the left side, what you get would be the Ka or dissociation constant would be given by [R] [H_3O^+] /[RH^+]. So, in other words, if I work to write RH^+ in terms of these, it would be [RH^+] = [R] [H_3O^+] /K_{aRH+} right?

So, now, if I plug in this value of RH^+ in this equation, let us call this equation 1, you would get rate is equal to *d*[P]/ *d*t = *k* [R][H_3O^+]/$K_{a\ RH+}$. So, now, we have derived the rate law for this reaction, which is catalyzed by an acid in which the proton transfer step is fast and occurs before the rate determining step. So, what do you see here now? When you look at the rate law, the acid dissociation constant is a constant for the particular acid RH^+.

Concentration of R is your reactant. So, what you would see is you do not have any term corresponding to the acid. So, what you have is essentially you can say this, say this is *k* observed it only depends on concentration of the protonated solvent which is H_3O^+ here. Now, one might argue like what if I add a small amount of acetic acid to this? If I add acetic acid you would say that instead of H_3O^+ maybe I will have the acetic acid there.

And it would be something different. So based on the definition of specific acid catalysis in this case you have specific acid catalysis because the rate only depends on concentration of H^+, which in turn depends on the pH of the reaction medium. So to maintain the pH of the reaction medium you essentially are maintaining the reaction rate.

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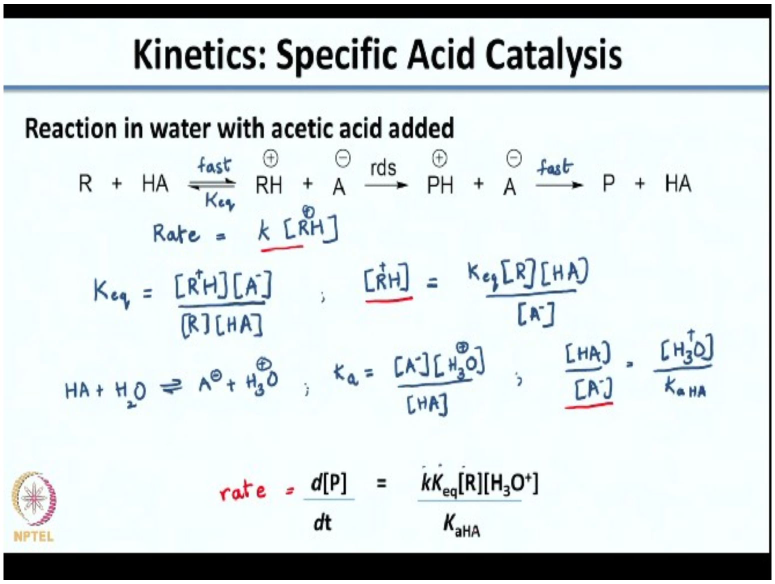

Kinetics: Specific Acid Catalysis

Reaction in water with acetic acid added

$$R + HA \underset{K_{eq}}{\overset{fast}{\rightleftharpoons}} \overset{\oplus}{RH} + \overset{\ominus}{A} \xrightarrow{rds} \overset{\oplus}{PH} + \overset{\ominus}{A} \xrightarrow{fast} P + HA$$

$$Rate = \underline{k} [\overset{\oplus}{RH}]$$

$$K_{eq} = \frac{[R^+H][A^-]}{[R][HA]} \; ; \quad \underline{[\overset{+}{R}H]} = \frac{K_{eq}[R][HA]}{[A^-]}$$

$$HA + H_2O \rightleftharpoons A^{\ominus} + H_3\overset{\oplus}{O} \; ; \quad K_a = \frac{[A^-][H_3\overset{\oplus}{O}]}{[HA]} \; ; \quad \frac{[HA]}{\underline{[A^-]}} = \frac{[H_3\overset{+}{O}]}{K_{aHA}}$$

$$rate = \frac{d[P]}{dt} = \frac{kK_{eq}[R][H_3O^+]}{K_{aHA}}$$

So now if you argue with me that I am adding now a little acetic acid. So now we have added an additional term, which is HA right? So if you are adding acetic acid, the question is, now will this still follow specific acid catalysis? So now you need to remember that this step is again fast. All of these are fast. So, what we have is based on the original definition, you have proton transfer occurring before the rate determining step.

So by definition, they should follow specific acid catalysis. But now let us mathematically derive to see, is it true? So like before, you would write the rate would be given by k [RH^+], because that is what is involved in the rate determining step, right? A^- is just a byproduct of the first reaction, so it does not show up. So you have the rate determined by concentration of RH^+.

Now, let us see if we can write RH^+ in terms of R and HA. Remember, you also have water in the medium, so it is not just the HA disintegrating to H^+ and A^-. It is slightly more involved than that. So, you need to introduce water here. So, this is the final expression, where you can talk about the rate in terms of the first equilibrium which is this. So this is K equilibrium and the dissociation constant of the acid HA.

So, again, let us try to derive this. I will ask you to derive this first yourself. So, what I want you to do is I want you to press the pause button on the screen and try to derive this expression yourself. So, let us see if you have the answer. So, here again, let us first try to write it in terms of the equilibrium constant. So the equilibrium constant for the reaction Kequilibrium is given by $[RH^+]$ $[A^-]/[R]$ $[HA]$. Correct?

So, in terms of this what you would have is you will have $[RH^+] = K_{equilibrium}$ $[R]$ $[HA]/[A^-]$. So, that takes care of these 2 terms. And this we have already. Now, we would like to write $[HA]/[A^-]$, this ratio is determined by the acid dissociation of HA, so K_{aHA}, so, the equation that you are looking at is HA + water giving you $A^- + H_3O^+$ right? This is what gives you the acid dissociation of the acid HA.

So, now, the K_a value is given by $[A^-]$ $[H_3O^+]/[HA]$. Remember the concentration of water is included in the term K_a. So, now that you have this term, what you get is you get the ratio of $[HA]/[A^-] = [H_3O^+]/K_{aHA}$. So if I plug in the value of $[RH^+]$ and this $[HA]/[A^-]$ into this equation, what I will get is the final equation that you have here. So here you can substitute for K equilibrium $[R]$ and $[HA]/[A^-]$ is given by $[H_3O^+]/ K_{aHA}$.

Now, what do you observe here? What do you observe here again is despite the fact that you have added an external base, here again it reduces to the earlier form where you have k observed into R. So it essentially depends again on the pH of the reaction and what was your reaction solvent? Water and protonated form of water is H_3O^+. So we have mathematically derived here that the specific acid catalysis is seen whenever you have a reaction where the proton transfer occurs quickly before the rate determining step.

So now that you have an understanding of specific acid catalysis, what I want you to do is, I want you to do the same derivation for specific base catalysis

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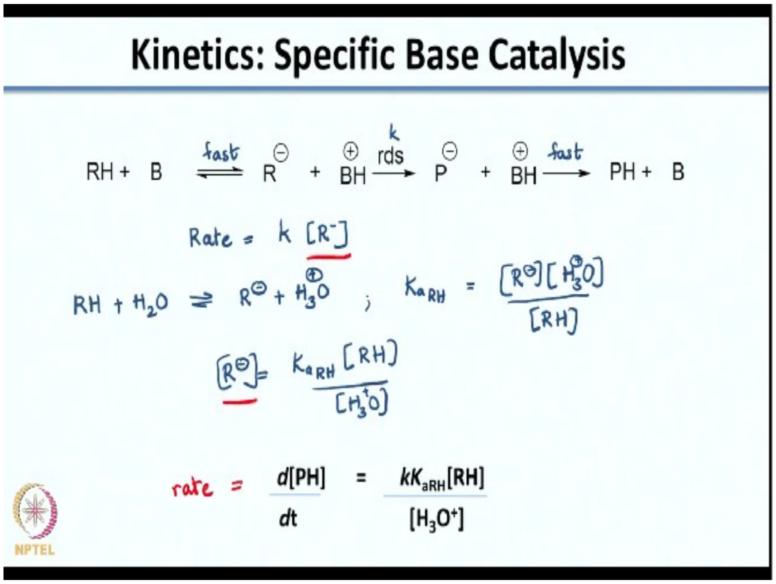

Kinetics: Specific Base Catalysis

$$RH + B \overset{fast}{\rightleftharpoons} \overset{\ominus}{R} + \overset{\oplus}{BH} \overset{k}{\xrightarrow{rds}} \overset{\ominus}{P} + \overset{\oplus}{BH} \xrightarrow{fast} PH + B$$

$$Rate = k\,\underline{[R^-]}$$

$$RH + H_2O \rightleftharpoons R^{\ominus} + H_3\overset{\oplus}{O} \;;\quad K_{aRH} = \frac{[R^{\ominus}][H_3\overset{\oplus}{O}]}{[RH]}$$

$$\underline{\boxed{[R^{\ominus}]}} = \frac{K_{aRH}[RH]}{[H_3\overset{+}{O}]}$$

$$rate = \frac{d[PH]}{dt} = \frac{kK_{aRH}[RH]}{[H_3O^+]}$$

and here again, what we would be looking at is we would be looking at the rate will be given as this is *k*, here again the base would be protonate much faster as compared to the rate determining step. So, the rate is given by *k* $[R^-]$ alright? And now you can write $[R^-]$ in terms of the base and just like we had done for the previous slide, where we had added acetic acid in water, here again we have added a base in water.

So, this is what your final expression will come like. So, we are again writing it in terms of acid dissociation constant of RH into concentration of RH and H_3O^+. So, you can go ahead and derive this quickly. Now that we have seen the earlier example, this derivation must be quite quick for you to do. So, we will quickly go ahead and do this derivation. So, here, what you have is the rate of formation of the product is given by this expression.

So, when you look at the dissociation of RH, you are looking at RH + water giving you R^- + H_3O^+. correct? So, now, Ka of RH would be given by R^- concentration into H_3O^+ concentration. And in the denominator, you have RH, water as I said is included in this. So now, you can write R^-, so $R^- = K_{aRH}$ into RH divided by H_3O^+. So, you plug it into the equation above. So, if you plug this value into this equation, you will get the final equation for the rate.

So, here again, you would see that the rate does not depend at all on the concentration of the base. So we have seen how by deriving the rate law, again, we are connecting to a concept we had learned earlier, which is the deriving rate laws for reactions. So when we derive these rate laws, what we see is that when you have specific acid or specific base catalysis where proton transfer occurs quickly, before the rate determining step, you do not see a dependence on concentration of the acid or base.

The kinetics depends only on specific acid or specific base, which is the protonated solvent. Ok? So now if you look at, so if you have understood this concept, I will ask you to just make a very simple plot. So what will the plot of k_{observed} versus concentration of HA, where HA is the acid that you are adding say in water, which is the solvent. So what will this plot look for when you are doing specific acid catalysis. Alright? I will repeat the question is there on your screen.

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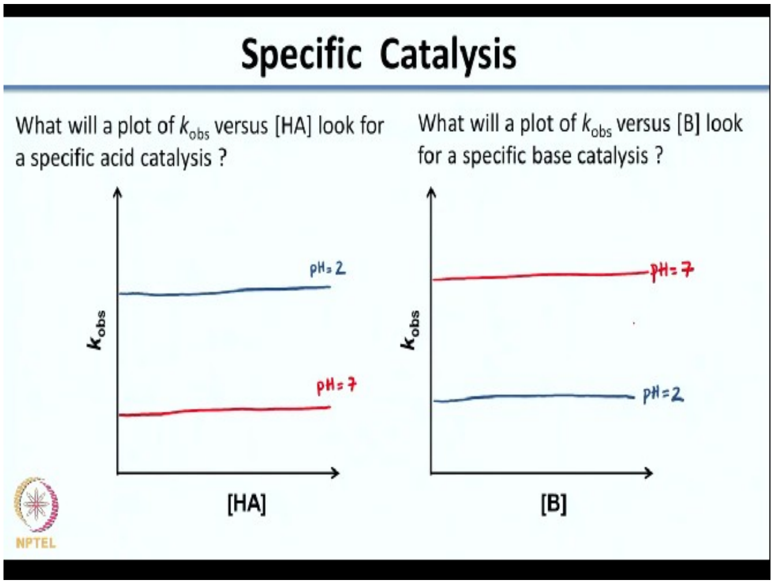

Specific Catalysis

What will a plot of k_{obs} versus [HA] look for a specific acid catalysis ?

What will a plot of k_{obs} versus [B] look for a specific base catalysis ?

So you can press that pause button and write what the plot will look like in your notebooks. So let us see if you have this answer correct. So if you have let us say, a k_{observed} value, what you would see is that the plot would be a straight line, as I told you, it does not depend on concentration of HA, so this would be a straight line. So let us say this is the plot at pH = 2. Now, if I do the same reaction at pH = 6 or 7, ok, let us say I am doing the same reaction at a pH = 7.

What will happen to this plot? I want you to think about it. So I want you to draw the plot when I do the same reaction, but now I am varying the pH, I have the pH at 7, what will the plot look like? Again it will be a straight line because it does not vary on concentration of HA, but now will the k_{observed} be higher or lower at pH 7, pH 7 means right. If you are doing say the reaction in water, the concentration of protonated solvent which is H_3O^+

In pH 7 would be greater or less than pH 2? pH 7 is less acidic, right compared to pH 2 I mean, has a lower concentration of H_3O^+ right compared to pH 2? pH 2 is more acidic. So what will happen is you will have a lower k_{observed} value. But again it will still be a straight line. So this would be at pH 7 alright. Now I want you to think, what will the plot of k_{observed} versus B look for a specific base catalysis. So we have already looked at specific acid catalysis, here now we are plotting k_{observed} versus B. What will this look like?

So again, let us start with pH 2 and pH 7. Now that we have this example on the left, you can go ahead and draw it for 2 pHs pH 2 and pH 7. So, what you would see is at pH 2, in this case, you will have a lower rate, if you remember the expression, in this case, the H_3O^+ concentration was in your denominator, and we are looking at a base catalyzed reaction. So having an excess concentration of H^+ will not help you.

So the k_{observed} will be lower at pH 2, again, just by the definition, specific base catalysis what that tells us that it was be a straight line. It will not vary with the concentration of B, and what you would see is it will be higher at a higher pH. Alright? So you see a complete switch here, where when you are doing specific base catalysis, the k_{observed} value is higher at a higher pH.

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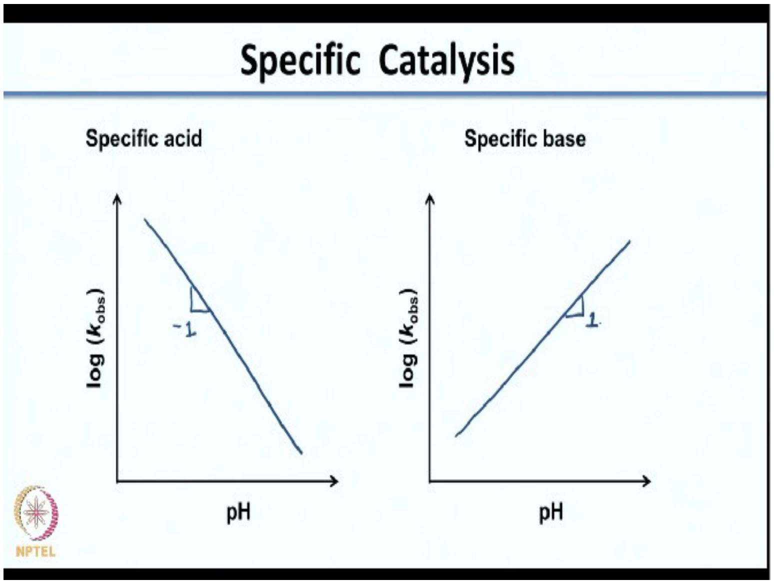

Specific Catalysis

The last thing that I want you to think of before we end this class is, in the case of specific acid catalysis how do you think the log of k_{observed} will vary with pH. Alright? So remember, now on your X axis, you have pH and not concentration of the acid HA. So I want you to think how it will change with the pH. For specific acid catalysis we saw in the previous slide, that for lower pH, you have a higher k_{observed}. And for higher pH you a lower k_{observed}.

So what you would see is as the pH increases, this value will come down alright? And if you look at the specific base catalysis, you would see the exact opposite trend. What you would see is that as the pH increases, the k_{observed} value will increase. And what you would see is this will have a slope of –1 and this will have a slope of 1 alright? So we will stop here. And in the next class, we will look at the general acid and basic analysis and we will look at reactions where you can actually see the specific acid catalysis and specific base catalysis. Thank you and see you in the next class.