Mechanisms in Organic Chemistry

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Lecture-13
The Hammett Equation

So welcome back in the last lecture, we had looked at methods to study reaction kinetics and specifically we had looked at how you can measure the concentration of the reactant or product over time. So, methods are dependent on the time scale of the reactions.

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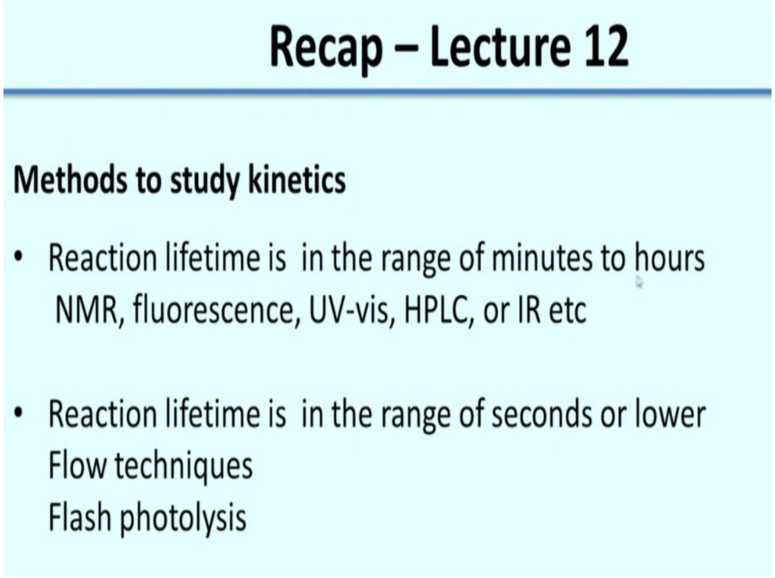

Recap – Lecture 12

Methods to study kinetics

- Reaction lifetime is in the range of minutes to hours
  NMR, fluorescence, UV-vis, HPLC, or IR etc
- Reaction lifetime is in the range of seconds or lower
  Flow techniques
  Flash photolysis

So, if the reaction lifetime is in the range of minutes to hours, you can use methods like spectroscopy, NMR spectroscopy, fluorescence spectroscopy etc. to figure out the concentration of the species over time. Now, if the reaction goes really really fast say you are looking at a reaction which has a lifetime of seconds or even lower than that we had looked at how you can use Flow techniques or Flash photolysis to study the reaction kinetics.

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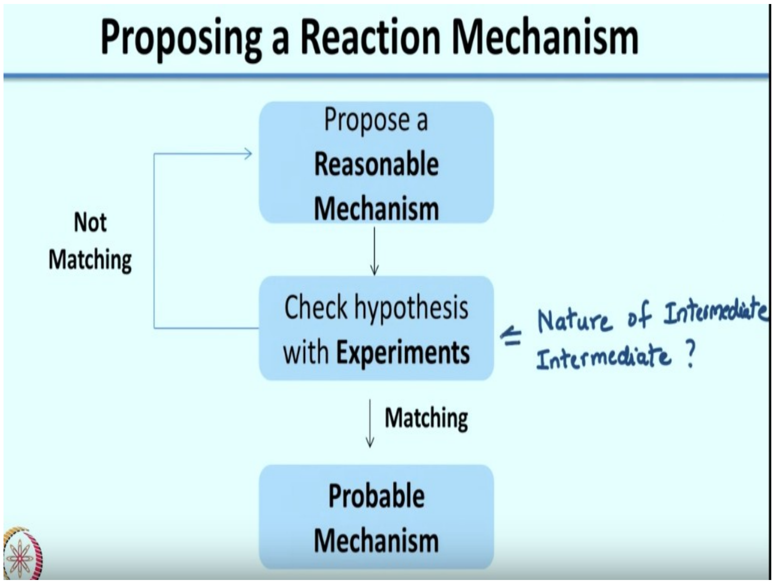

Proposing a Reaction Mechanism

Propose a **Reasonable Mechanism**

Check hypothesis with **Experiments** ⇇ Nature of Intermediate

Intermediate ?

Not Matching

Matching

Probable Mechanism

So, as I told you in the last class as well as the first class, in this course, we will be looking at proposing reasonable reaction mechanisms and checking the hypothesis using experiments. One set of experiments which we looked in the earlier lectures was how you could use kinetics to determine how the reaction takes place. So, kinetics as I showed you could be used to distinguish between multiple mechanisms and find out which is the reaction mechanism.

Another very important clue about a reaction is what is the nature of the intermediate? So an intermediate is very important because once you understand that it is a very solid clue as to how the reaction is taking place. Even for that matter, you can also do experiments to even see whether an intermediate exists or not. So, the next set of experiments that we would be looking at would be seeing how we can gather information about nature of the intermediate. So if you remember when we were talking about kinetics, I told you that it is very difficult to see the intermediate or measure it using spectroscopic techniques because they are very transient.

So, let us look at alternate methods where indirectly, you can get information about the nature of the intermediate. So, there are different types of intermediates. We had looked at them when we were looking at reaction mechanisms.

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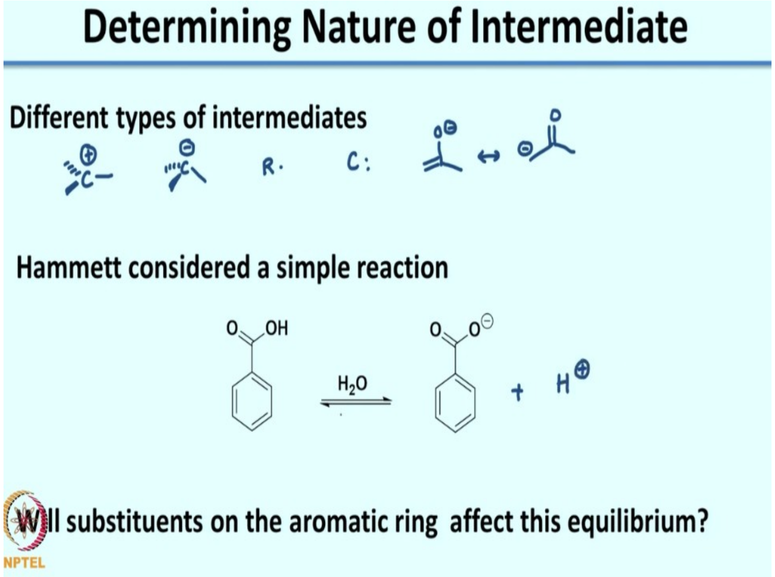

Determining Nature of Intermediate

Different types of intermediates

Hammett considered a simple reaction

Will substituents on the aromatic ring affect this equilibrium?

So, you can have charged intermediates. So in the charged intermediates, you can have carbocations, you can also have carbanions you can have radicals, you can also have carbene and nitrene intermediates. And also you have reactions where instead of carbon based intermediates you have other hetero atoms like the enolate which of course is the resonance structure of a carbanion. When you have reactions where you can have any of these intermediates or no intermediate for example, like the S_N2 reaction, it would be very useful to have methods for you to see what is the nature of the intermediate.

So to understand this Hammett considered a very simple reaction. So look, if you look at the reaction here the reaction is actually quite simple. If you have not identified this molecule this molecule is benzoic acid. Now benzoic acid, if you take in water can dissociate to give you the benzoate and anion and of course H_3O^+ not shown here. So benzoic acid when dissociates in water you get the benzoate anion and H^+. And let us say the equilibrium constant for this is given by K.

Again, remember capital K is what we use for equilibrium constants. So now what we need to see is will substituents on the aromatic ring affect this equilibrium.

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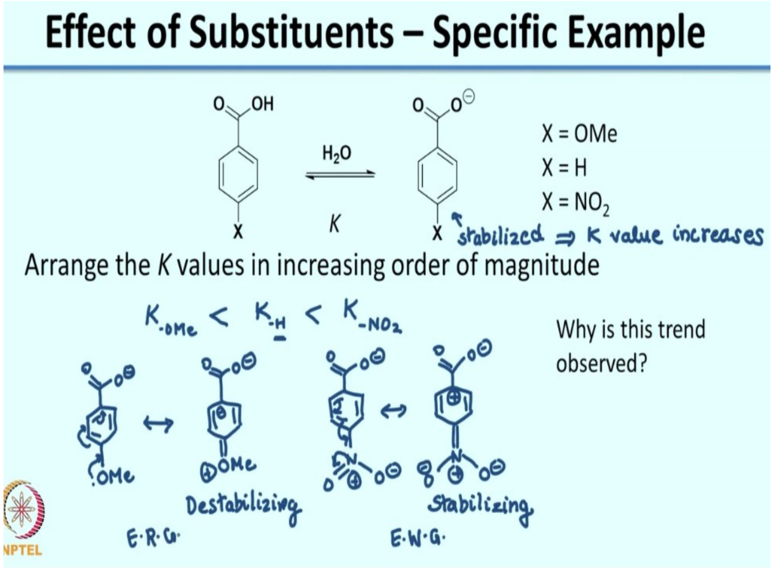

Effect of Substituents – Specific Example

X = OMe
X = H
X = NO_2

stabilized ⇒ K value increases

Arrange the *K* values in increasing order of magnitude

$K_{-OMe} < K_{-H} < K_{-NO_2}$

Why is this trend observed?

Destabilizing

Stabilizing

E·R·G·

E·W·G·

And to understand this I have a simple problem for you. So let us consider substituted benzoic acid where you have the substituent at the para position. And again, you are doing this reaction in water. So benzoic acid will dissociate to give you your benzoate. Now, let us consider 3 cases one where you have X as methoxy, which is OMe. The other case where X is not substituted. So you have a hydrogen. The third case is where you have X which is a nitro group.

Now, I want you to think about this problem for each of these molecules, there will be an equilibrium constant which will tell you the extent to which this benzoic acid is dissociated. So, greater the value of the equilibrium constant it indicates more of the benzoic acid is dissociated. So what I want you to do is I want you to arrange the K values in increasing order of magnitude. So, to do that you can think about this problem, press the pause button on your video and arrange the 3 substituents in increasing K value. So the trend that you would observe is. K for OMe would be less than K for the unsubstituted benzoic acid would be less than the K equilibrium for the nitro group.

So now the question is why do you observe this trend? So again, you can think about this. I am sure when you came up with the trend you would have a rationale as to why this particular trend is observed. So, I have O^- OMe, now I have lone pairs on this oxygen.

So, what I would get would be a resonance structure. So the resonance structure generates a negative charge at the carbon, which is close to your carboxylate ion. Now, let us look at the case of nitro group. So, in the case of the nitro group, I would write out the expanded structure of the nitro group. So, if I write out the expanded structure of the nitro group I can again write the resonance form where

So, now you have a positive charge at the carbon which is next to the carboxylate. So if I were to compare both of these structures, this is destabilizing and this is stabilizing. Therefore, when you have a nitro substituent, it pushes the equilibrium towards the right whereas when you have a OMe substituent because it is destabilizing, it is lower than the unsubstituted case, which is that of hydrogen. So what do you see in this case is that, when you have electron withdrawing groups so these are electron withdrawing groups.

versus electron releasing groups, electron withdrawing groups stabilize the benzoate which is why you see that the reaction works better when you have electron withdrawing groups.

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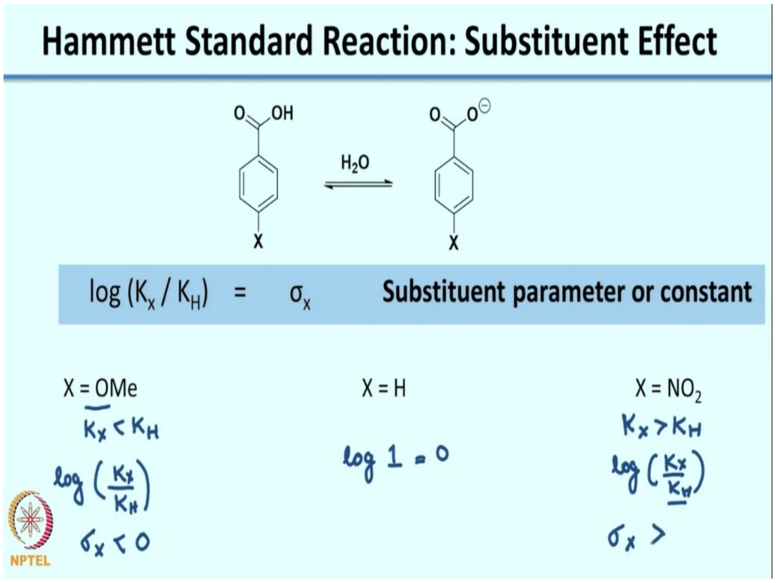

Hammett Standard Reaction: Substituent Effect

$\log (K_x / K_H) = \sigma_x$ **Substituent parameter or constant**

X = OMe
$K_x < K_H$
$\log \left(\frac{K_x}{K_H}\right)$
$\sigma_x < 0$

X = H
$\log 1 = 0$

X = NO_2
$K_x > K_H$
$\log \left(\frac{K_x}{K_H}\right)$
$\sigma_x >$

So now this concept was used for Hammett to come up with his standard reaction to study the substituent effect. So similar to the case that we just saw in the previous slide with two substituents and unsubstituted benzoic acid. What you would see is if you take this generic reaction where you have a substituent at the para position, so, when you have a substituent at the para position the log (K_X/K_H)of is given by σ_x. The σ is called as a substituent parameter or substituent constant. So, log of K_X where K corresponds to equilibrium constant for substituted benzoic acid and you divide that by K_H which corresponds to equilibrium constant for unsubstituted benzoic acid.

So now let us go back to the previous example that we had seen,if I were to compare these 3 and try to find out the substituent constant for each of these I would like I would have to do the log (K_{OMe} / KH) in this case. And in this case, it would be K_{Nitro} divided by K_H and of course in this case, it would be log of 1 so σ would be 0. In these two cases what would be the value of σ? Will it be greater than 0 or will it be less than 0.? So what I would like you to do is I would like you to think about this based on the concept we are done the previous slide will the σ value be greater than 0 or less than 0 for both of these substituents which is X is equal to OMe or X is equal to nitro.

So, as we had seen in the earlier case when you have X is equal to OMe you have K_X Which is less than K_H. So when you do log (K_X/K_H) since K_X is less than K_H what you end up getting would be a number which is less than 1 and so the σ value would be negative or less than 0. In this case you would have, log of 1 so that would be 0. In this case you have K_X greater than K_H So when you look at log (K_X/K_H) this value would be greater than 1 so your σ_x would be greater than 0.

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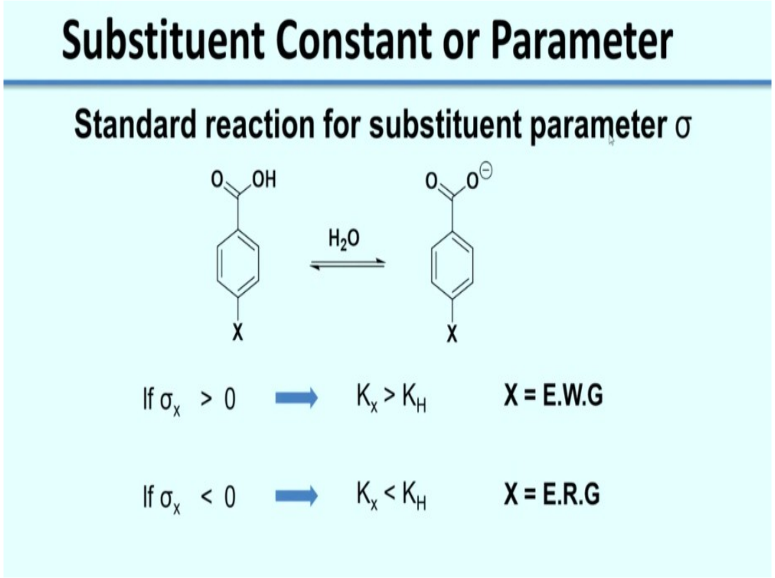

Substituent Constant or Parameter

Standard reaction for substituent parameter σ

If $\sigma_x > 0$ ➡ $K_x > K_H$ X = E.W.G

If $\sigma_x < 0$ ➡ $K_x < K_H$ X = E.R.G

So in general what one can do is one can generalize this, where one can say that σ_x would be greater than 0 for any case where you have K_X greater than K_H. that is a substituent which stabilizes your conjugate acid your benzoate anion. So whenever you have a substituent which stabilizes your benzoate anion on you would get σ_x greater than 0 and since your intermediate here is negatively charged and electron withdrawing group will stabilize your negatively charged intermediate.

Whereas if you have a substituent which destabilizes so K_X is actually less than K_H in that case the value of σ_x would be negative. And then what you would have is and typically an electron releasing group because you have a negatively charged intermediate and electron releasing group will destabilize this. So, this is the standard reaction used for determination of substituent parameter σ.

So if you look at any textbook on physical organic chemistry, you would find tables which give you the value of σ for multiple substituents and these values are obtained for this benzoic acid reaction. So this is the standard reaction for obtaining the substituent parameter σ. Not any other reaction.

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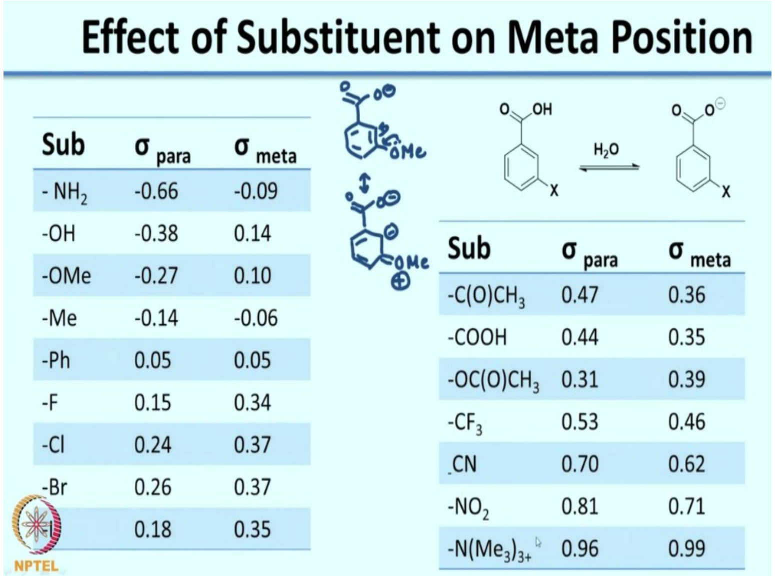

Effect of Substituent on Meta Position

Sub	σ para	σ meta
$-NH_2$	-0.66	-0.09
-OH	-0.38	0.14
-OMe	-0.27	0.10
-Me	-0.14	-0.06
-Ph	0.05	0.05
-F	0.15	0.34
-Cl	0.24	0.37
-Br	0.26	0.37
-I	0.18	0.35

Sub	σ para	σ meta
$-C(O)CH_3$	0.47	0.36
-COOH	0.44	0.35
$-OC(O)CH_3$	0.31	0.39
$-CF_3$	0.53	0.46
-CN	0.70	0.62
$-NO_2$	0.81	0.71
$-N(Me_3)_{3+}$	0.96	0.99

So having understood that, let us now look at the magnitude of some of these values so that you get a feel of how these σ values vary. So we will first look at the substituent at para position. Now when you have the substituent which is an amine, so the amine is an electron releasing group by resonance and what you see is it destabilizes quite a bit. So you have a negative value for σ para and the value is given by minus 0.66.

So based on this information, I want you to ignore the rest of the values for now, can you predict what the values would be for OH OMe and Me? You need not get actual values, but just the trend whether it would be comparable to this less than this or more than this? So you can think about it for a minute by pressing the pause button on your video. So what you would see is when you go from NH_2 to OH and this is something you would have also studied when you study electrophilic aromatic substitution.

NH_2 is the most activating group for an electrophilic aromatic substitution. So, the same Trend you see here when you go from NH_2 to OH the negative value decreases from - .66 to - .38 so what that indicates is that NH_2 is more destabilizing as compared to OH. Again when you go from OH to OMe the value again reduces from .38 to from -.38 to -.27, so again this is less destabilizing as compared to OH and Me which is not as electron releasing as these substituents, gives you a lesser negative value.

Now what do you would observe in the case of the aromatic substituent which is pH and the halogens is that you see a mix of the resonance effect as well as the inductive effect. So based on the resonance effect one would assume that the halogens would be releasing but based on the electronegativity of these atoms they behave as withdrawing groups. So what you see is a mix of these effects so you would not see a large negative or large positive value, what you see is values which range from .15, .24, .26 and .18 when you go from fluorine to iodine.

So, there is no trend as it is a mix of both of these effects. Now let us look at some more substituents. If I look at a keto substituent, which is C double bond OCH_3 this would behave as a withdrawing group and the value would be positive. So you have a value of .47. Now if you compare a ketone versus a carboxylic acid, the carboxylic acid will not be as withdrawing as the ketone which you can see comparing the value.

So, it is less positive as compared to the ketone. Now based on this, can you predict how the values of these other substituents would compare with the ketone and CF_3 and carboxylic aci, which I have given here? So you can press the pause button on your video and think about what the values could be. You need not get the actual values, but just the trend. So what you might have written is that if you have a carboxylic acid versus a nester.

So, OC OCH3 where you have the oxygen attached to the aromatic ring, it would be less withdrawing as compared to both of these substituents. So the value is less positive. Whereas when I compare it with CF_3, which is quite withdrawing it has a very large value. Now when I compare CF_3 with CN and NO_2 now in these cases with CN and NO_2, you can also use resonance as I had shown you in the previous case for withdrawing electrons from the aromatic ring and creating a positive charge on the carbon next to the carboxylate ion.

So, as you see these values are much higher. So you have a value of 0.7 and .81 and when you have a positive charge here, inductively, the value is the highest where it is 0.96. So looking at this you get a feel for how the substituent parameter will vary when you go from electron releasing to electron withdrawing substituents. For electron releasing substituents the value is negative whereas for electron-withdrawing substituents the value is positive.

So if you get confused what I would suggest you do is, just think of those two examples, which we did in the previous question where we just looked at methoxy and NO_2. So methoxy if you understand is a negative gives you a negative σ you can then extrapolate it to all electron releasing groups. Similarly, when you think of nitro group, if you are able to derive that the nitro will give you a positive σ value, you can then extend that to all electron withdrawing groups.

So now let us look at what happens when you have a substituent at the meta position. So now the effects would be different because when you have the para position and you write resonance structures you generate a charge at the carbon next to your carboxylate ion. Whereas here in the case of a meta substituent, I will take the case of OMe and if I were to write the resonance structure, so the resonance structure would put the rest would put the charge farther away from the carboxylate ion.

So the resonance effect is not as pronounced at the meta position, similar to what you see for electrophilic aromatic substitution or nucleophilic aromatic substitution. So the effect that you see is predominantly inductive in nature. So what you see now is when you compare σ_p versus σ_p, let us take the example of NH_2. you see that it is not as negative as it was in the case of para. So in the case of meta, it is an inductive effect and not a resonance effect, which is why the magnitude is lower.

Also, if you look at OH, here what you see is you see a complete reversal in effect where you actually see a positive σ value indicating that the effect that you are observing is only inductive and not resonance. Same thing can be seen at OMb with OMe, with Me you see a decrease in the value of σ similar to that of amine. For the other cases, for example, the halides, what you would see is that the inductive effect is now predominating here whereas here it was a mix of resonance and inductive effect, which is why the values were lower.

Here it is mainly the inductive effect and inductively, as you know, these are electronegative. So that is why you see that the value is greater than σ_p. Similarly, you can see for these substituents that the withdrawing effect has also reduced in the case of the ketone and the carboxylic acid. Whereas when you have the oxygen so similar to the case of OH and OMe here the inductive effect predominates, you see a greater increase in σ value for the meta substituent.

When you look at cyanide and nitro where resonance was also contributing a lot to stabilization of the carbox carboxylate ion, what you see here is that effect is reduced, so the value is lower and for NMe_3, so were majorly it was a inductive effect. You see an increase in the σ value. So these tables are available in any textbook on physical organic chemistry. And remember when you think about the substituent constant or substituent parameters σ it is only the benzoic acid reaction that you are thinking about.

So you need not think of any other reaction substituent parameter or substituent constant constant is only for the benzoic acid reaction.

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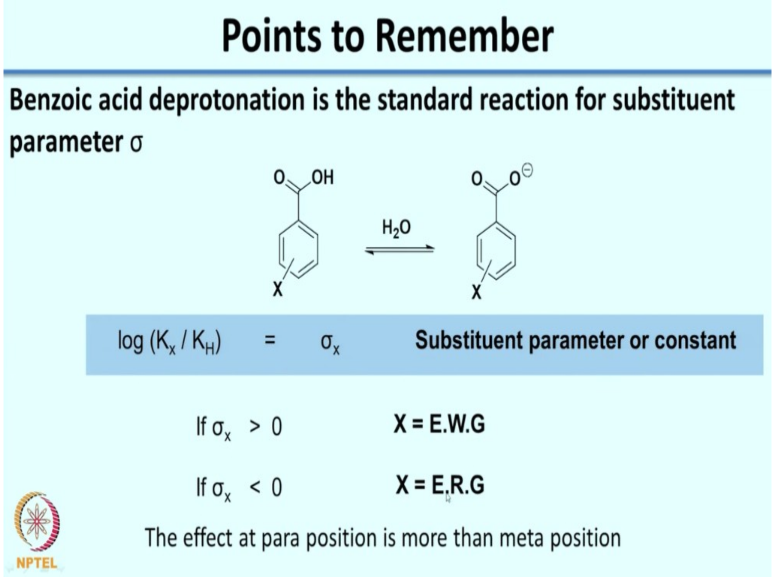

Points to Remember

Benzoic acid deprotonation is the standard reaction for substituent parameter σ

$\log (K_x / K_H) = \sigma_x$ **Substituent parameter or constant**

If $\sigma_x > 0$ **X = E.W.G**

If $\sigma_x < 0$ **X = E.R.G**

The effect at para position is more than meta position

The points to remember when you think about the substituent constant is that benzoic acid is the standard reaction And the substituent parameter or substituent constant σ_x is given by log (K_X / K_H) so this is determined for each substituent. So each substituent has its own σ_x value and depending on whether the substituent is meta or para, It has its σ_m or σ_p value.

If σ_x is positive or greater than 0, it stabilizes the benzoate anion in other words pushes the equilibrium to the right and typically that a scene for electron withdrawing groups. If σ is less than 0 that means it is destabilizing the benzoate ion and which indicates a shift of equilibrium to the left and this is typically seen for electron releasing groups and in general the effect at para position is more than meta position.

So what we will do in the next lecture is we will look at How we can use this substituent constant to understand how intermediates are in other reactions and how we can determine what the intermediates are in other reactions.