Mechanisms in Organic Chemistry
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Lecture-17
Deviation from Linear Free Energy Relationships

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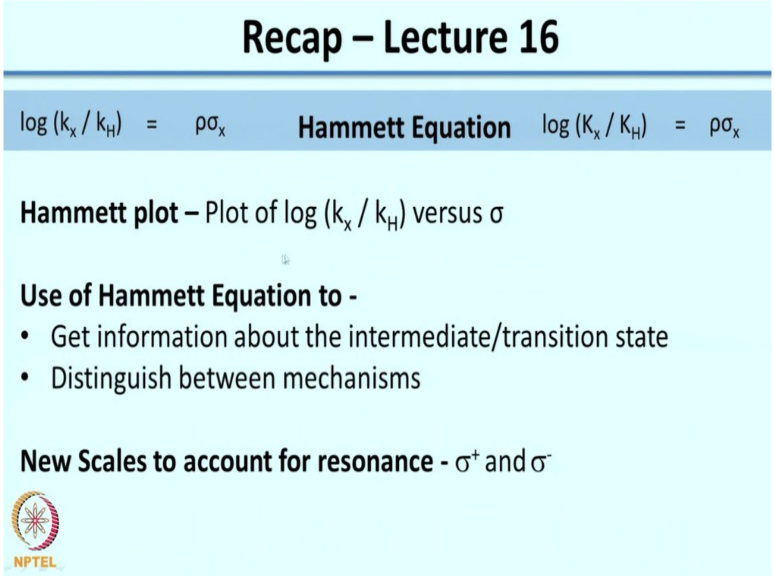

Recap – Lecture 16

$\log (k_X / k_H) = \rho\sigma_X$ **Hammett Equation** $\log (K_X / K_H) = \rho\sigma_X$

Hammett plot – Plot of $\log (k_X / k_H)$ versus σ

Use of Hammett Equation to -

- Get information about the intermediate/transition state
- Distinguish between mechanisms

New Scales to account for resonance - σ^+ and σ^-

Over the last couple lectures we were looking at how we can use the Hammett equation as well as the Hammett plot for a particular reaction to figure out the nature of the intermediate or the transition state in a particular reaction and we had seen examples where the Hammett equation could be used to get information about the intermediate and the transition state. And we had also seen how we could use the Hammett equation to distinguish between mechanisms.

We also saw that in reactions which involve conjugation of a positive or negative charge with the aromatic ring, there is a need to introduce two new scales and I had introduced you to the σ^+ as well as the σ^- scales.

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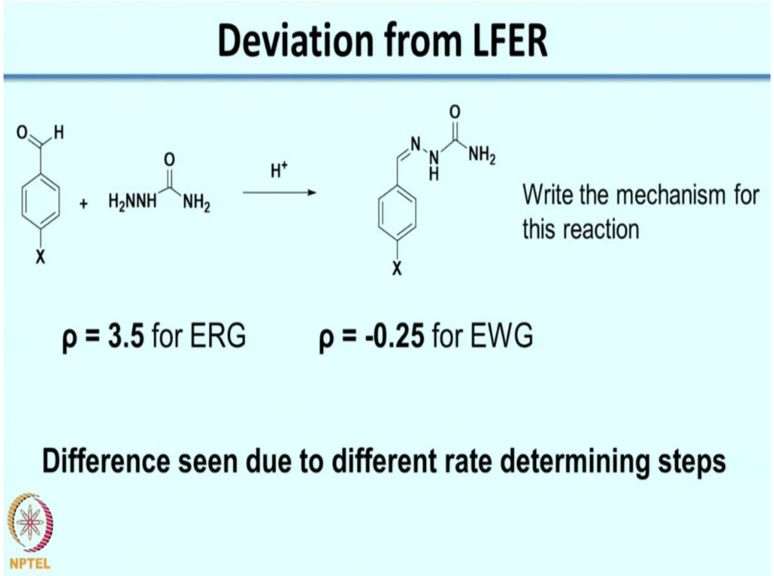

Deviation from LFER

Write the mechanism for this reaction

$\rho = 3.5$ for ERG $\rho = -0.25$ for EWG

Difference seen due to different rate determining steps

So, before leaving in the last lecture, I had asked you a question. I had asked you to think about why for this particular reaction, which is formation of a semi-carbazone two different rho values are observed? So, for electron releasing groups you have a rho value of 3.5 and for electron withdrawing groups you have a rho of -0.25. So, the first thing always would be to write the mechanism for the reaction.

One hint I can give you is that, in this case the difference is seen due to different rate determining steps. So, for those of you who have the mechanism written down and in front of you, what I would like you to do is now look at the mechanism carefully and identify whether rate determining steps could change depending on the substituent. So, it might happen that for an electron withdrawing group, one step is rate determining whereas for an electron releasing group it is a different step that is rate determining.

So, for those of you that have the mechanism in front of you, press the pause button and try to figure out these two rate meaning steps. So, if you are trying to write the mechanism for this and you were having trouble let us walk through the mechanism.

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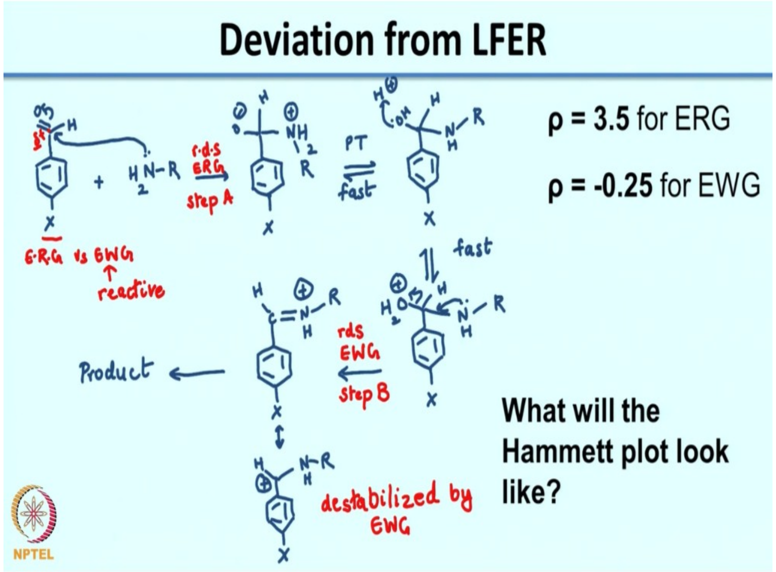

Deviation from LFER

ρ = 3.5 for ERG

ρ = -0.25 for EWG

What will the Hammett plot look like?

So, you start with the aldehyde and you have a substituent at this position. So, this is the aldehyde and it is reacting with; so you have a large group here but I will just place this, put this as R. So I am not writing the rest of the molecule. So, in the first step what will happen is you will have attack of the NH_2 lone pair and what this would generate would be an intermediate as shown here.

So, this would be the intermediate that is generated and then you have all this proton transfer and it will give you; so it will give you this neutral molecule. Now once you have this, you can again have protonation to give you, we are just converting this to a better leaving group and then you can have water leaving to give you this charged intermediate. And once you have this charged intermediate, again it can lose a proton to give you the product.

So, this is the mechanism for this reaction. Now in these, in this mechanism these steps occur pretty quickly. So this would be a fast step, this would also be fast. So, the two steps that would go relatively slowly would be this step let us call it step A and then this step, let us call it step B. Now let us look at the situation when you have X as an electron releasing group and X as an electron withdrawing group and I will let you think about this first before I tell you the answer.

So, if you have an electron withdrawing group, which of these steps will go slower? will it be step A or step B? So, look carefully at both these steps and try to rationalize which step will go slower if you have an electron withdrawing group. Similarly, if you have an electron releasing group, which of these steps would go slower? So, if you want to spend more time thinking about it you can press the pause button in the video and think about it.

So, what you would see is, for an electron withdrawing group, what happens is your reactant here has an electrophilic center here, δ+ where the NH_2 lone pair attacks. Now if you have an electron withdrawing group, what it would do is it would increase the electrophilicity at that carbon. In the case of the intermediate, because you have this zwitter-ionic kind of intermediate, there will not be much of a difference between an electron releasing or an electron withdrawing group but the reactant, there would be an effect if you have electron releasing versus electron withdrawing.

So, now a question to you is, in which case will the reactivity be more or in which case we will the electrophilicity be increased? In the case of the electron withdrawing group. So, in the case of an electron withdrawing group because you are now pulling electrons from the carbon what happens is you increase the electrophilicity or the δ+. So electron withdrawing group would be more reactive.

Now whereas if you have an electron releasing group what it does is, it decreases the δ+ at this center and because it decreases the δ+ the reaction would be slower. So, step A would be slower for an electron releasing group. So we will call this RDS for electron releasing group. Now let us look at step B. Now what is happening in step B? You are generating an intermediate here which has a positive charge.

So, if I were to write the resonance structure for this, it would be, so it would be a carbocation, which is now in conjugation with the ring. All right? So, now in this case what happens is, when you have an electron releasing group it will stabilize this carbocation and the reaction will go quickly. Whereas if you have an electron withdrawing group it will destabilize this intermediate and the reaction will go slowly.

So, essentially this step would be, so this is destabilized by electronwithdrawing group. So, this would be rate determining step for electron withdrawing group. Now that you have both of this information can you now figure out why the rho value is different for an electron releasing group and an electron withdrawing group? So, when you think of an electron releasing group you only think of step one.

So, if you look at step one, in the case of step one, the lesser electron releasing the group is, the faster will be the reaction rate. So, now again think about the scale that we were talking about earlier. As the group becomes more and more electron withdrawing, the rate increases. So you have a positive slope and the value is given by 3.5. Whereas what happens is, for an electron withdrawing group what happens is that, step B becomes the rate determining step.

And in the case of step B, as the group becomes less electron withdrawing, or in other words more releasing, the rate increases and you have a negative slope. So, this is a very interesting example where you have a fine equilibrium such that depending on the substituent, you can change the rate determining step from Step A to step B. So, now I have another question for you .Now that you know the values for ERG and EWG what will the Hammett plot look like?

So, can you go ahead and draw a plot of log (K_X/K_H) versus σ for this particular reaction? And you have all the information in front of you. So it is simple mathematics. So you have log (K_X/K_H) versus σ, where rho is 3.5 for electron releasing group and -0.25 for electron withdrawing group. So, you can go ahead and do this exercise.

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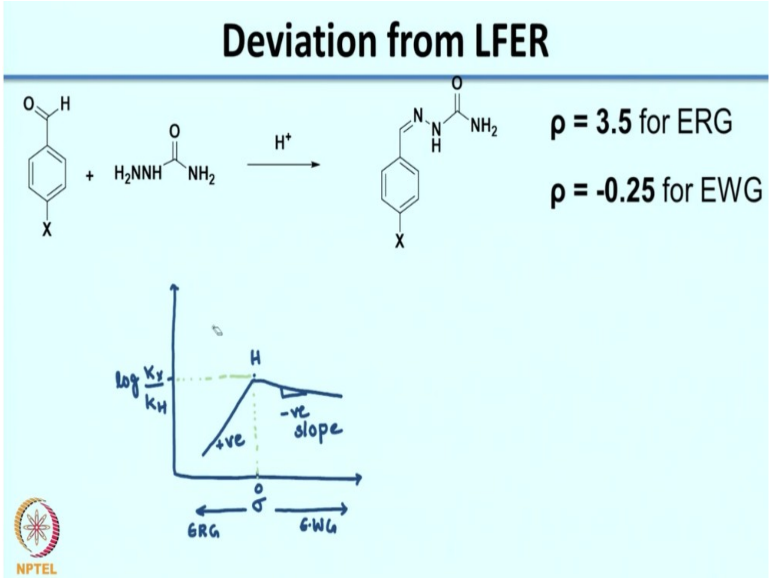

Deviation from LFER

ρ = 3.5 for ERG

ρ = -0.25 for EWG

So, now if we try to draw the Hammett plot, so you have log (K_X/K_H) and on your X-axis you have σ. Let us take this as the point where you have 00. So your hydrogen would be somewhere here. So as before, σ greater than 0 you have electron withdrawing groups, σ less than 0 you have electron releasing groups and σ 0 is hydrogen. So, what you see is you have a positive slope for electron releasing group.

So electron releasing groups are; so we are talking about this quadrant now and you have a positive slope, so it will be and a slope of 3.5 which is pretty large, so it will be like this. So, for electron withdrawing groups you have a negative slope and the value is not much. I will just delete this hydrogen. So you have a slope which looks like this. So, another thing you can see is that, electron withdrawing groups do not have as much as an effect on the reaction rate as the electron releasing group.

So, in this case you have a negative slope and in this case you have a positive slope. Remember, since hydrogen will have to be 0 you cannot have anything with a negative slope coming in this quadrant which is to the left and top of hydrogen which is this area. So you cannot have anything coming there. So, this is one illustration where there can be deviation from linear free energy relationships and here it is because the mechanism is same but the rate determining step changes.

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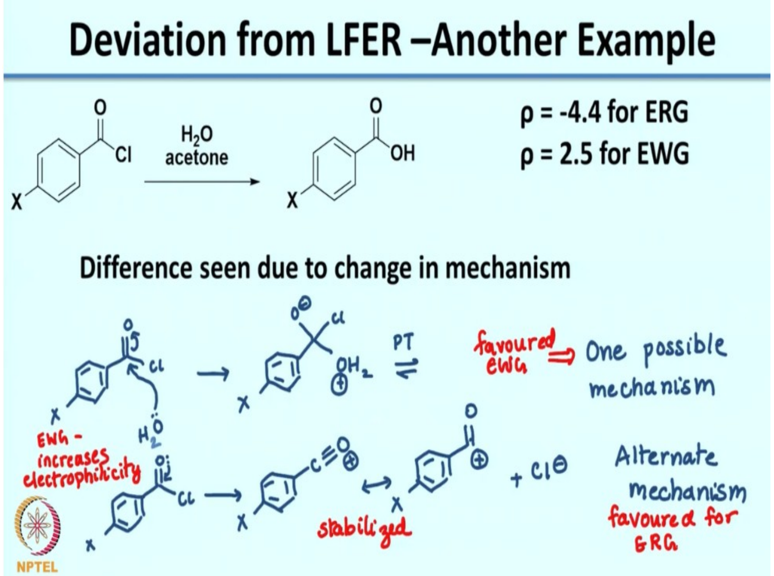

Deviation from LFER –Another Example

ρ = -4.4 for ERG

ρ = 2.5 for EWG

Difference seen due to change in mechanism

Let us look at another interesting example. So in this reaction, you have an acid chloride getting converted to a carboxylic acid and here again what you see is you have different rho values for electron releasing groups and electron withdrawing groups. So, now the question here is why do you see different rho values depending on the nature of the substituent? Here I will give you a hint. It is not because the rate determining step changes. But it is because the mechanism itself completely changes if you have an electron withdrawing group or an electron releasing group.

So what I would like you to do is I would like you to think about this and see what could be the mechanism for each of these reactions where you have an electron releasing group as a substituent or an electron withdrawing group as a substituent. So go ahead and you can write these out on your sheet of paper. So, let us think of possible mechanisms. One mechanism could be, where you have; so you have an electrophilic center at the C here and then if I attack water here and then you have subsequent steps of proton transfer etc would be faster.

So, I am not going to write the rest of the mechanism you can do that yourself as a homework.

So this is one possible mechanism. What would be another possible mechanism? Another possible mechanism could be; so you can imagine this giving you; you can either imagine it coming like this to give you or you can think of it. So, this is an alternate mechanism. So, now let us carefully look at each of these mechanisms.

So, if you have X as an electron withdrawing group, what would be possible? So if you have X as an electron withdrawing group the electrophilicity here would increase and so this would end up being more reactive. So, an electron withdrawing group, so just as we had seen in the earlier case an electron withdrawing group increases electrophilicity. Whereas if I have an electron releasing group, so, since you are not talking about a very strong nucleophile here if you have an electron releasing group it would be not as reactive as when you have an electron withdrawing group.

So, you can say that this mechanism favoured for electron withdrawing groups. Now if you have an electron releasing group, what it would do is it would stabilize this intermediate. So, it would stabilize this intermediate, which is why the alternate mechanism would be favoured for electron releasing groups. So, now that we have these two alternate mechanisms, can you rationalize why you have a rho of -4.4 electron releasing group and rho of 2.5 for electron withdrawing group?

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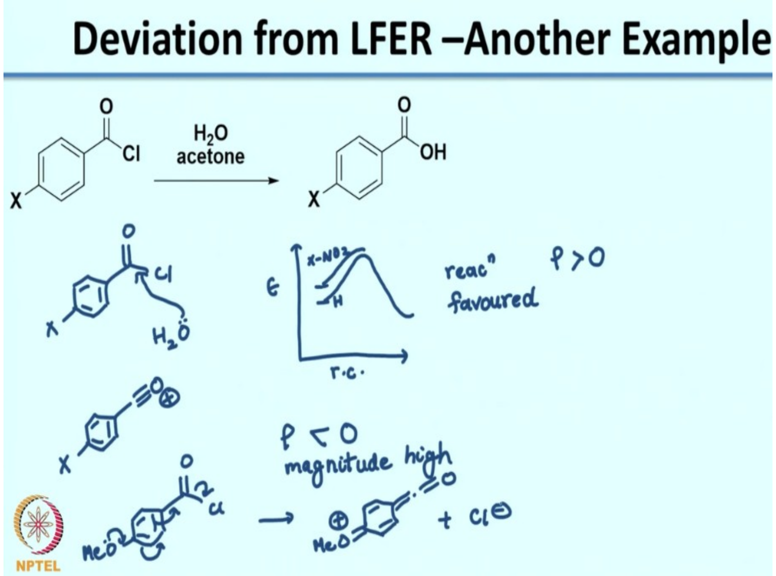

Deviation from LFER –Another Example

So, in the case of an electron withdrawing group, we are talking about the mechanism where you have water attacking. So, again as I told you earlier, if you have the energy versus reaction coordinate diagram for this, what you would see is that, if this is hydrogen, if you have an electron withdrawing group, what happens in this case is that the energy of the reactant or the electrophilicity is increased. It is more reactive and the effect on the transition state is not much.

So let us say X is equal to NO$_2$. So what you see is the reaction is favoured and which is why you get a rho which is greater than 0. In the case of an electron releasing group what you have is you have an intermediate which looks like this. Now here if you have electron releasing groups, this will highly stabilize this intermediate and which is why so you see that the value of rho is less than 0 and the magnitude is also very high because you have direct conjugation with the aromatic ring.

One can also imagine a scenario, say you have an electron releasing substituent such as OMe, with your acid chloride. You can also think of a situation where you actually generate a ketene like intermediate. Alright? So, now that you know how this reaction varies depending on nature of the substituent, can you go ahead and sketch out what the Hammett plot will look like? You can pause the video and go ahead and sketch out the Hammett plot.

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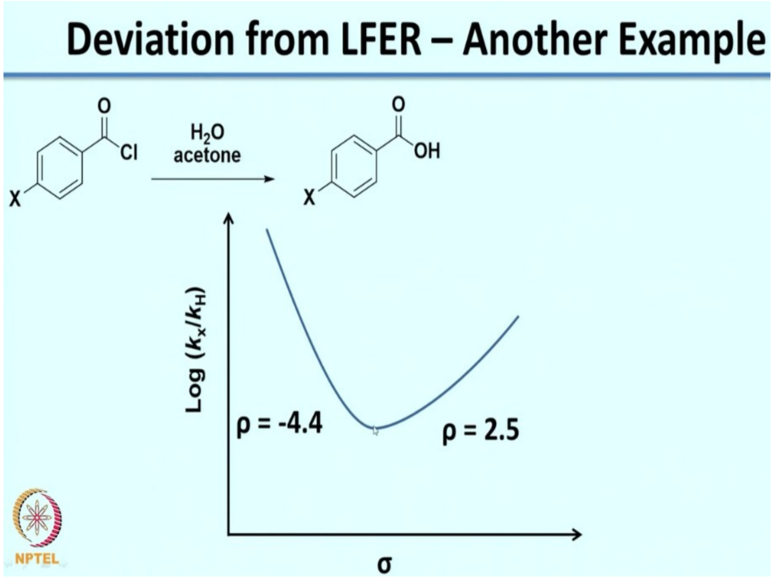

Deviation from LFER – Another Example

So, what you would see is, let us say this is the point where you have your 00 of hydrogen. In this case, you have a negative slope for electron releasing groups which is why here, where you have electron releasing groups, remember, on the left side of your X-axis you have a negative slope and you have a positive slope for electron withdrawing groups. So, on the right side what you have is you have a positive slope. So this is what your Hammett plot will look like.

So now we have seen two examples for deviation from linear free energy relationships. One is where the rate determining step changes, but the mechanism remains the same and the other example is where the mechanism can switch depending on the substituent on the aromatic ring.

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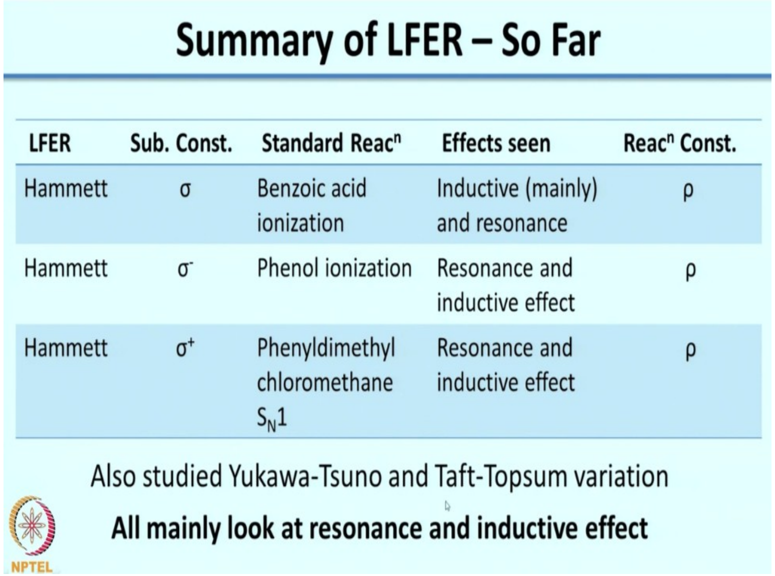

Summary of LFER – So Far

LFER	Sub. Const.	Standard Reac^n	Effects seen	Reac^n Const.
Hammett	σ	Benzoic acid ionization	Inductive (mainly) and resonance	ρ
Hammett	σ^-	Phenol ionization	Resonance and inductive effect	ρ
Hammett	σ^+	Phenyldimethyl chloromethane S_N1	Resonance and inductive effect	ρ

Also studied Yukawa-Tsuno and Taft-Topsum variation

All mainly look at resonance and inductive effect

So, to summarize what we have seen so far with LFER, we have seen the Hammett correlation to give you substituent constants σ, σ^- and σ^+. Now in all these cases you have a standard reaction or a basis reaction which gives you the X- axis of your Hammett plot. So, this basic reaction is benzoic acid ionization or dissociation for the σ scale and the effect seen is inductive mainly, but we have also seen a resonance contribution when we compare the σ values.

And if you were to use this to determine how the intermediate looks for an unknown or new reaction, the correlation factor is rho which is also called as the reaction constant. For reactions which involve conjugation of the positive or negative charge with the aromatic ring, two new scales have been introduced. One is the σ^- scale. In this case the standard reaction or the basic reaction is phenol ionization because the phenoxide ion is in conjugation with the aromatic ring.

Here the effect seen is resonance effect mainly and you also see a small inductive effect. And here again the reaction constant is rho and the third one that we saw is the σ^+ scale. In this case the standard reaction is dissociation of the Phenyl dimethyl chloromethane similar to what you see in an S_N1 reaction. Here again predominantly the effect is resonance because you have the positive charge in conjugation with the aromatic ring.

And here again the reaction constant is rho. We also looked at variations of the Hammett equation in terms of the Yukawa-Tsuno equation and the Taft Topsum equation. Now all of these mainly look at resonance and inductive effects. So, in the next class what we will do is we will look at correlations which can give you information about sterics in a particular reaction. So, thank you and see you in the next lecture.