Introductory Organic Chemistry - II
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Lecture 47
Conjugate Additions: Kinetic vs Thermodynamic Products

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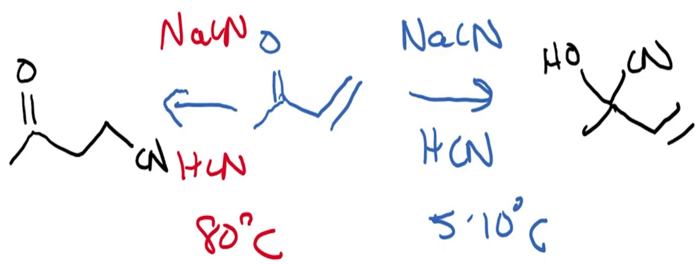

Now, we will spend some time and understand the difference between 1, 2-addition and conjugate addition and how the reaction conditions can actually dictate the outcome of the reaction. So, now let us go back to the first reaction that we sort of looked at the beginning of this lecture. So, you start with this compound and when you add NaCN, HCN at somewhere between 5 and 10 degrees centigrade versus the similar reaction conditions that is NaCN, HCN, the only difference is we do this reaction at 80 degrees centigrade.

So, the product that is formed in the first case is the cyanohydrin. And the product that is formed in the second case is the addition to olefin. So, now the question that we are all trying to understand here is these are experimental facts and they are very well established and the question that we are trying to address here is how do we explain this result. Now, you know, so I would urge all of you to pay a little bit of attention over here, so that we can see if everybody understands this concept.

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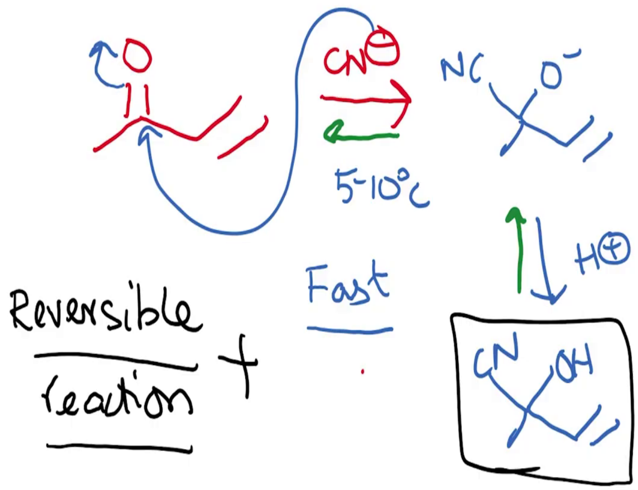

So, what is proposed is that when you start with this type of a carbonyl compound and when you add a CN^- you know, so we have looked at already the formation of cyanohydrin. So, you can produce this kind of an intermediate which can then pick up a proton and give you the product. Now, at 5 to 10 degrees centigrade, this is the dominant path, that means that you do not see the other product being formed. We also know that if you take cyanohydrins and dissolve them in just an organic solvent, we also know that this can go back that is you can get back this compound and cyanide.

So, this is something that we already know from our previous discussions. And so, therefore the formation of cyanohydrin is a reversible reaction which means that it is going to be in equilibrium. So, as in when you add cyanide, you are going to find this product and then you work up the reaction and you will be getting this as the product. And now, when you dissolve this in an organic solvent it is possible that you will get some of the starting material back and cyanide back.

So, therefore what we can understand or what we can suggest is that this the first step here is a fast given the outcome of this reaction we can suggest that the first step is a fast reaction. However, it is also a reversible reaction. So, I guess we have already written it over here. So, it is a reversible reaction and it is a fast reaction. So, this helps us understand what happens at somewhere between 5 and 10 degrees.

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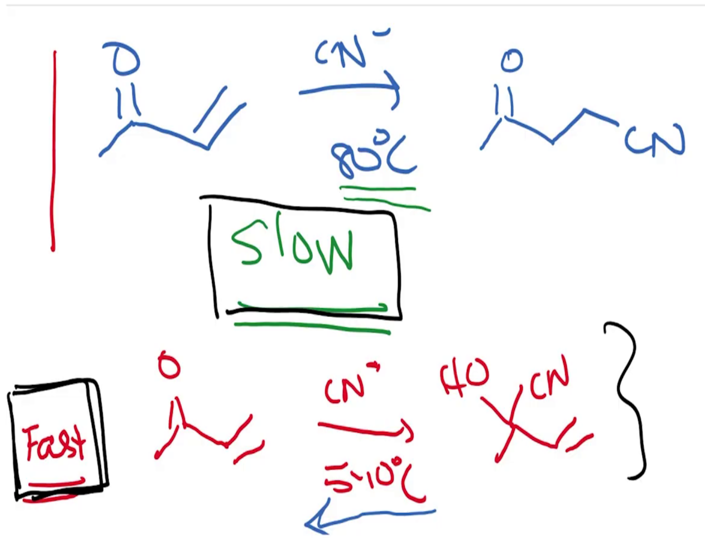

And we also know that it is reversible. Now, the importance of reversibility will come now, because at 80 degrees centigrade when we carry out this reaction. So, now the product that is formed is actually the conjugate addition product. Now, what we can suggest is that, based on the observation that this must be a slow reaction because at somewhere between 5 and 10 degrees centigrade you do not observe this product, but you need a higher temperature which likely means that you need a larger fraction of molecules which have enough energy to get over the barrier to form this product.

So, I will now just quickly summarize. So, what we are suggesting is that at 5 degrees or low temperatures, somewhere between 5 and 10 degrees centigrade this reaction gives you $CH_3C(CN)(OH)CH{=}CH_2$. So, this is the fast reaction, compared with this because the conjugate addition does not occur at 5 to 10 degrees centigrade. So, therefore the conjugate addition must be a slow reaction. Now, the slow and fast is again going to be a relative term.

So, the formation of the cyanohydrin must be a fast step. Now, why is the equilibrium important, because even at 80 degrees centigrade, this fast reaction will be the dominant reaction. So, it is not that the reaction is not going to occur at 80 degrees centigrade, this reaction will occur at 80 degrees centigrade. The only suggestion here is that it is going to be a reversible process. Now, I will just go through quickly the energy profile, so that you will understand this process better.

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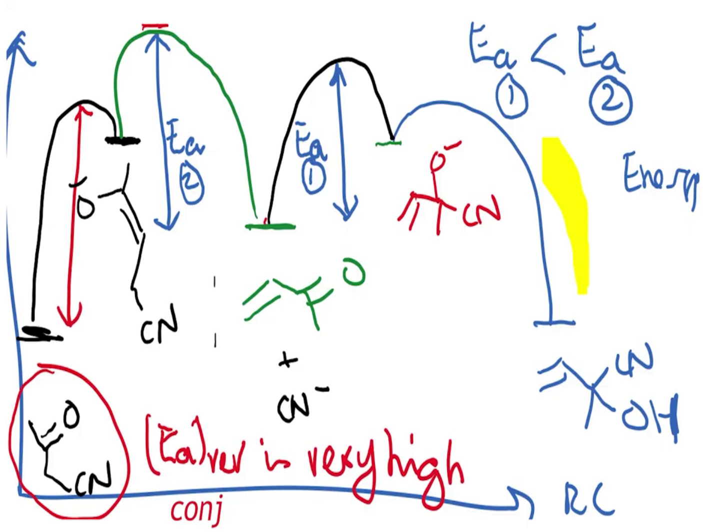

So, the y-axis is energy and the x-axis is the reaction coordinate. So, what we can look at is, let us start with this compound over here, this is the starting material. And now, what we are suggesting is that the first step of this reaction must have some barrier and you get CH_2=CHCO$^-$(CN) (CH_3). And then subsequently, this is going to give you the product and I am just going to assume that it is an exothermic reaction.

And this is just a protonation step. So, therefore, this would give you CH_2=CHCOH(CN) (CH_3). So, let me just redraw this barrier so that it is a little bit more reasonable. Now, this is fairly straightforward. Now, the important point here is that the first step that is going to be that is reaction with cyanide can occur and there is enough energy that is at 5 to 10 degrees for this reaction to occur. Now, since the conjugate addition is the slow step, it is likely that the barrier for conjugate addition must be higher.

Now, again this is basic kinetics, slow reaction means that the barrier would be higher and the first reaction means the barrier will be lower. Again, we are comparing the same molecule reacting, that is, this molecule reacts with cyanide so all the reactants are identical. The only difference here is the products that are formed. So, it is likely that this barrier, that is Ea for the first reaction and this is the energy of activation for the second reaction. So, it is quite likely that Ea or it is obvious that Ea1 is lower than Ea2.

And this we can clearly reason out because at 5 to 10 degrees centigrade, there is no reaction or there is no conjugate addition that is actually happening. Now, this is the product that is going to be produced.

Now, so this is the conjugate addition product and then this is going to subsequently pick up a proton and give you the product. So, here is the initial intermediate enolate $CNCH_2C{=}CO^-(CH_3)$ and the final product is the conjugate addition product. So, now the important point here is that this Ea2 is going to be greater than Ea1. Now, here is the question of reversibility. So, when you look at a reversible reaction, what it means is that the barrier for the reverse reaction, that is the barrier for this reaction is going to be accessible at the temperature at which you are doing the reaction.

So, when we look at the formation of a cyanohydrin, we know that it is reversible. So, therefore, the barriers of the forward reaction as well as the reverse reaction are actually accessible at the temperature at which you do the reaction. Even more so, there are a larger fraction of molecules that can cross the barrier, even more so at 80 degrees centigrade, this reaction is going to be happening at a substantial rate.

However, in order to explain the formation, or this result, we have to invoke the concept that the last reaction which is the formation of this conjugate addition product is an irreversible reaction. So that means, that this barrier $[Ea]_{reversible}$ for conjugate addition is very high. So, I will just go through this once again, in a fresh slide so that you understand this better.

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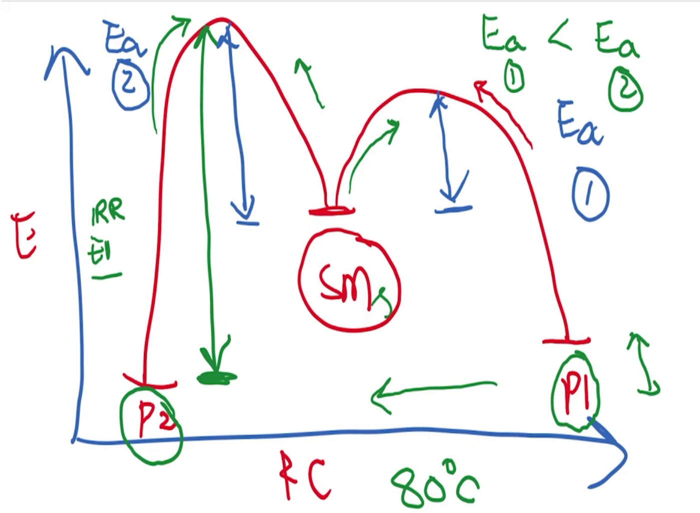

I am just going to remove all the structures and just explain to you what this concept is. So, I have a starting material, and I am just going to simplify this by drawing out two products. So, this is going to give me P1 and this is going to give P2. So, the way this is constructed is that this is Ea1 and this is Ea2. So, the first concept here is that Ea1 is less than Ea2. What this tells me is that the formation of P1 is substantially faster when compared to the formation of P2. And the second concept is that the formation of P1 is reversible.

And this helps us understand why a particular product is actually not formed at higher temperatures. So, just to be clear here, if Ea1 is less than Ea2, no matter what the temperature is the product 1 is going to be formed much faster than P2, there is absolutely no doubt about this. That is if this barrier is lower than this barrier, P1 is always going to be formed faster than P2.

But since P1 formation is a reversible reaction, that means that this barrier is accessible at the temperatures at which we are doing this reaction or as a larger fraction of molecules have enough energy to cross this barrier, it goes back to forming the starting material. And then since there are a fraction of molecules, for example, at 5 to 10 degrees, the largest fraction of molecules can only go back this way, this goes back here and forms P1 but at 80 degrees centigrade, this is a reversible reaction that means that this goes this way, gives you back the starting materials and then the starting materials can cross this barrier and give you P2.

Now, the only way in which we can explain this reaction or one of the ways in which we can explain the formation of these products is that the reverse reaction that is the reaction of P2 going back to starting materials has an extremely high barrier. So, if we look at this, this is the barrier that we are looking at and this barrier is inaccessible at 80 degrees centigrade. And therefore, this reaction is an irreversible reaction. And this helps us explain the distribution of products at two different temperatures.

So, the 1, 2-addition product is actually formed much faster, when compared to the 1, 4-addition product, but since the 1, 2-addition product is actually less stable, so if you see the, there is a difference in the energies of these two. And P2 is definitely more stable than P1. And since the 1, 2-addition product is actually a reversible reaction, this reverses and goes back to producing the starting materials and then the starting materials that have a larger fraction of or a fairly large fraction of molecules which can actually cross this barrier and give you P2.

But now, once they form P2, they do not have enough energy, P2 does not have enough energy to come back to the starting materials and therefore, this reaction goes in this direction at 80 degrees centigrade. So, this is a very important concept that all of you have to understand.

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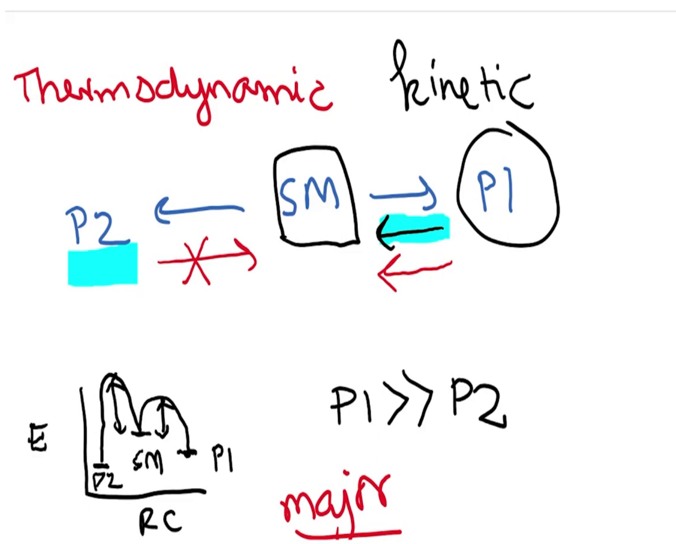

Now, I am going to use some terminologies here for us to put in perspective. So, when you have this kind of a situation where you have a starting material and giving you P1 and starting material giving you P2 and let us say the formation of P1 is much faster than the formation of P2. These types of products are called kinetic products that means that the outcome of the reaction is dictated exclusively by the rate of formation of the product and the major product that is produced is actually the kinetic product.

So, if you recall, if I look at the barrier's energy versus reaction coordinate, I have this and I am going to give you this product and this is P1, this is the starting material and the formation of P1 is substantially lower in energy compared to the formation of P2. So, therefore, this compound that is product 1 is called the kinetic product.

Now, P2 is invariably never formed if P1, if this does not reverse. So, if this is an irreversible reaction that is if there is a competition between the formation of P1 and P2 even if you go to higher temperatures P1 is only going to be the major product unless it is a reversible reaction. So, if it is a reversible reaction that means if this reaction can also go in this direction, then the starting materials are formed again and they are going to give you back P2.

And this kind of a product is called the Thermodynamic product. And this thermodynamic product is usually fairly more stable compared to the kinetic product. So, I will repeat here, when you have a competition between two different products the formation of two different products, the one which has the lower barrier will always be formed at a higher rate or to put it in a different way the major product that is formed, the interpretation from that result is that the barrier towards the formation of that product is lower.

And there may be a minor product that is formed which is P2 at lower temperatures and the formation of P2 is always going to be slower compared to P1. So, now when I increase the temperature, what is going to happen is that our larger fraction of molecules has higher energy. And now, when a larger fraction of molecules has higher energy, P1 is still going to be the major product, which means P1 is going to be formed much faster when compared to P2.

However, if the formation of P1 is reversible, then this reverse reaction can occur, give you back the starting materials and those can again react and give you up P2. Now, if P2 is an irreversible reaction that means the reverse reaction does not occur. Then P2 ends up becoming the major product and P1 is called the kinetic product and P2 is called the thermodynamic product.