Introductory Organic Chemistry - II
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Enols and Enolates: Intro

So now, let us move on to the next topic, which is Enols and Enolates. So, in this lecture, what we will do is we will do a little bit of recap of some of the concepts that we learned previously, and introduce you to some new concepts of Enols and Enolates.

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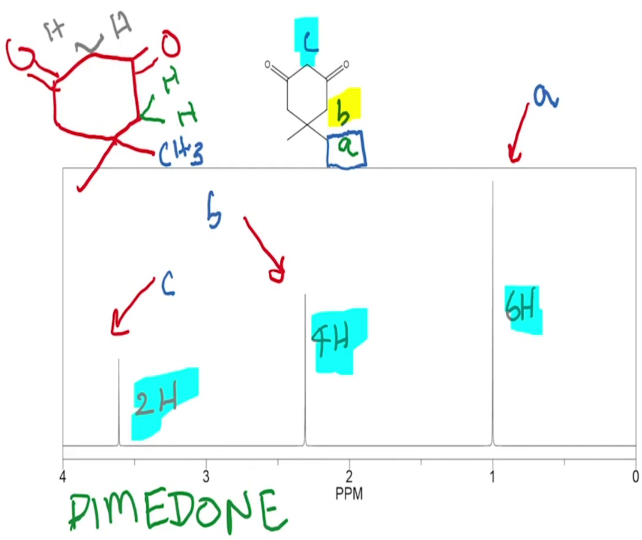

So, to begin with, let us start with an experiment. So, the experiment that we want to conduct is an NMR experiment. So, as many of you already have some exposure to NMR. In that, you may not know all the details about the instrumentation and so on, but what you know is that it is a reflection of the number of distinct protons that you would expect to see. So, therefore, if in a molecule, you have three different kinds of protons, then you should see three signals. So, with that information, we should be able to look at this NMR spectrum and understand it.

So, this is a theoretical NMR spectrum that I have obtained from ChemDraw. And so here, what do you expect to see is that you expect to see there are three kinds of protons, so let me just draw out this structure for you in its full structural formula, so that you understand this, so there is a cyclohexane ring, and then this is a ketone.

And let us start with this hydrogen. So, this is a CH_3. So, this, I am labelling it as 'a' and the CH_3 is identical to this because you have a plane of symmetry in the molecule. So, therefore, 'a' would be one kind of signal that you would expect. The next proton that we are interested in is the CH_2 and not only the CH_2 is equivalent to each other, but they are also equivalent to these CH_2's over here.

And therefore, I have labelled it as ‘b’. And so, you can take some time and draw out the structure and make sure that what I am saying is correct. But you have two planes of symmetry in this molecule. And so therefore, you can imagine that they would be similar. But the last signal, last distinct set of protons is this over here, which is basically two protons signal, which would correspond to the two hydrogens alpha to the carbonyl, which I am labelling it as ‘c’.

So, therefore, although this molecule has many hydrogens, so it has 6 + 4 + 2 = 12 hydrogens, you will still see only three signals in the molecule, one corresponding to 6 hydrogens, which is for a, and one corresponding to 4 hydrogens, which is for b, and one corresponding to 2 hydrogens, which is a c. So, this is the NMR spectrum that I would expect from this molecule. And this molecule, by the way, is called as Dimedone. It is a very interesting molecule. It is quite widely used for various synthetic and as well as analytical applications. So, this is the spectrum that I would see.

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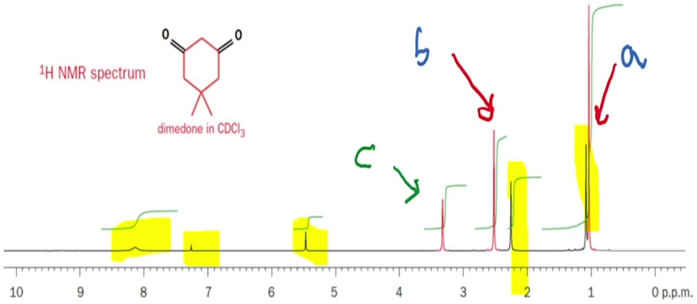

But now, when I go and record the Proton NMR spectrum, what I see is that I do see these three peaks, that is a, b, and c, as I have listed here, but we also see some additional peaks, so these additional peaks here are labelled in black. So, here are the additional peaks, which I am now highlighting, there is an extra peak here, there is an extra peak here, here, and here.

And so, just to be clear, the sample is clean, the compound is pure, it has only dimedone on it, so this is not a reflection of an impurity. So, therefore, the majority of the compound is still Dimedone and this is recorded in deuterated chloroform, but it seems like there is an additional peak that is being produced.

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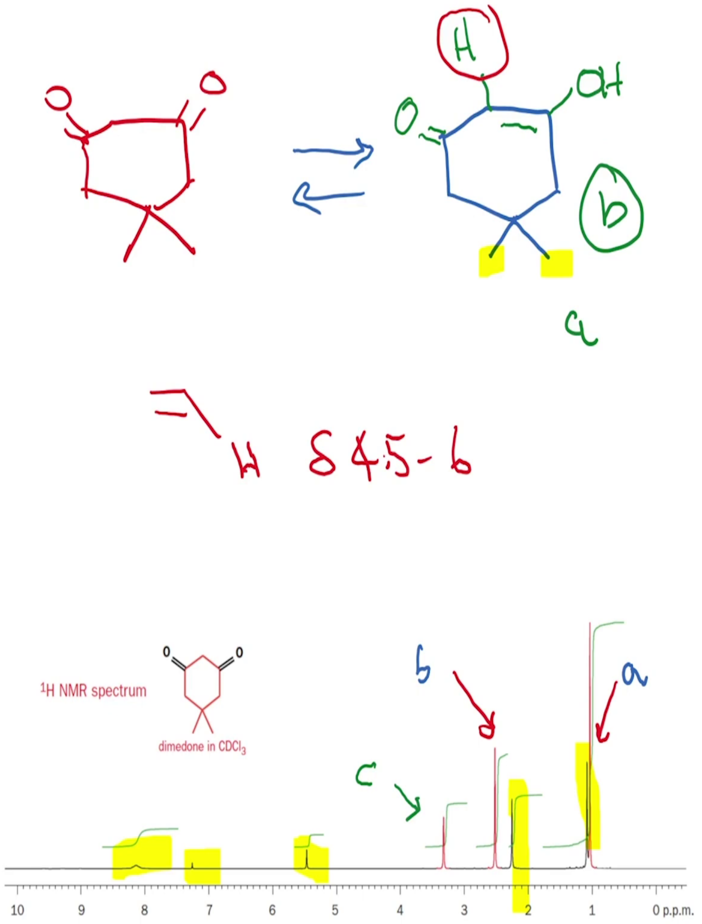

So, in order to understand this, let me just draw out one possibility is that if you have dimedone whose structures as shown here. Now, it is possible that, since, this is a keto form, it is possible that you could have what is known as enolization that can occur. So, this is a phenomenon that you guys have already studied in maybe 12 standard or so, but this is a possibility.

So, if it forms an enol, so, the structure of the compound will look something like this. So, you have C double bond O, OH and this hydrogen. Now, what is apparent from the NMR spectrum is that if it is an equilibrium between these two structures as shown here, then the methyl groups which are over here are quite far away from the enol and therefore, you would see only a small shift in the NMR spectrum.

So, if I go back to the NMR spectrum and look at it, you will see that this black peak that is being formed is quite close to a, and so, you can expect that It is going to be the six methyl groups. Now, coming to b. So, that is the a and now coming to b what we will see is that b is substantially closer to the enol and whatever changes that occur in the structure are going to be reflected more closely.

And so, you do see that, the b protons are quite distinct from the a. And there are further aspects of this NMR spectrum which I will not discuss at this point, but you will see that these two protons, which are next to it are going to be different from the other two and so on. But one more piece of important evidence is the production of this new hydrogen, which from our past experience of olefins, so if I just take a regular olefin.

This shows somewhere between 4.5 and 6 depending on what are the other functional groups that are present. And indeed, when we look at the spectrum of dimedone, we see a peak here at 5.5. So together, what it suggests is that there is a small but significant amount of the enol that is being produced.

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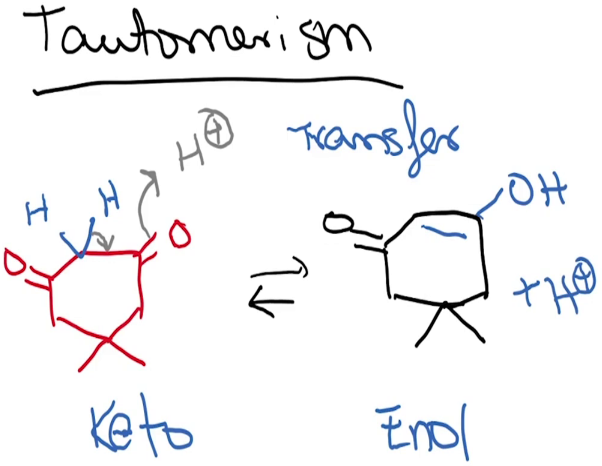

So, this phenomenon is known as Tautomerism. Alright, and this is again, something that you have studied previously, I am just recapping. So, in this Tautomerism, what happens is that, if I draw an arrow pushing mechanism, then it is going to look like this. And the important protons here, I am going to just draw them out so that it is easy for us to understand these two CH's.

And what is happening is that this carbon hydrogen bond breaks, and it goes now, and these electrons form a bond between carbon and carbon, and this goes and picks up a proton. So, if this happens, then you get a structure such as this, where you have, the main skeleton of the molecule remains the same, the C double bond O also remains the same, but you have a new carbon-carbon bond between these two carbons, and then you have an OH that is formed, which is the enol form.

And, of course, this enol can again, pick up O or H plus and form the ketones back. And so, the important aspects here are, this is called the keto form. And this is called the enol form. So, what you need to know is that this is a phenomenon where there is only a transfer of H^+, and there is no change in the pH. So, it picks up a proton. And if you see here in this process, it gives up a proton. So therefore, there is no change in pH of the medium. So, if I start with neutral water, I mean, neutral compound, I am just going to get neutral compound back.

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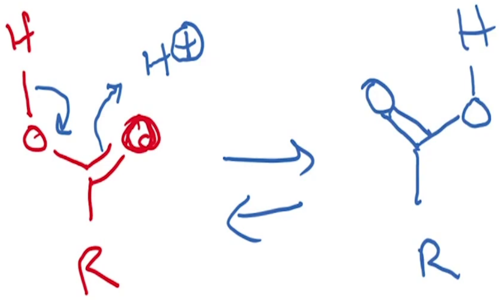

So, this is, again, we want to draw an analogy with the carboxylic acid. So, in a carboxylic acid, we are very familiar with writing these structures. And let us imagine that these two oxygens are different, then, you could think about the same process, which is now reacting with an H^+ and forming this and it is going to be in equilibrium with the other Tautomer, although normally we do not think about this manner, but indeed, the conversion of one carboxylic acid to the other form is a Tautomerism process.

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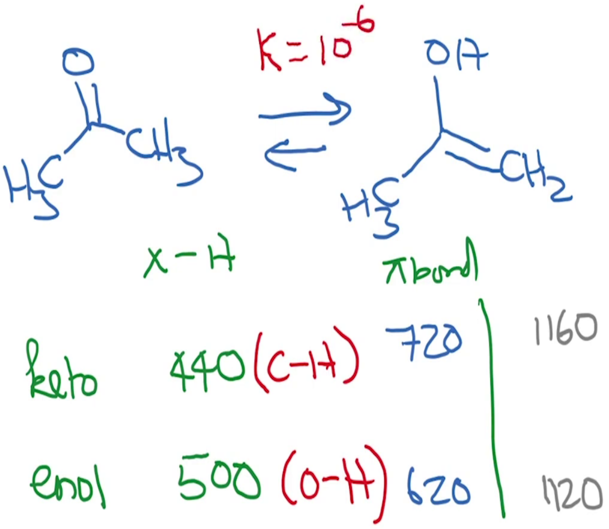

But the reality is that if we now move on to regular aldehydes, and ketones, so I have myself recorded NMR spectra of many aldehydes and ketones, and so have many of my colleagues in my lab. And invariably we almost never ever see a peak for the enol. So, if I take a regular ketone such as acetone and record the NMR spectrum. Although I just told you that it is possible that it will form the enol. But, when we record the NMR spectrum, we almost never see the enol form being prevalent.

And so, one of the reasons for this is that, if you look at the stability of these species, I am just going to draw some bond strengths over here. And so, just bear with me, this is the keto form, and this is the enol form. So, the bond that we are looking at is between X and H. And for the keto form, this is 440. Whereas for the enol form, it is 500. So, this is the bond strength of the carbon hydrogen bond as shown here, and this is between oxygen and hydrogen.

Now, if I look at the π bond, the pi bond strength of the C=O versus the C=C. And so, for the keto form, it is 720 kilojoules per mole, whereas, for the enol form, it is 620 kilojoules per mole. Okay, so now, what we can do is, if we can consider the sum of these two, so, that we can compare how much of energy we are losing or gaining in the process. So, if I sum these two values, then I should get the overall bond strengths.

So, in the case of the keto form, this would be the pi bond strength and for the Keto form it is C=O and for the Enol form it is C=C, and this is something that we have already studied. And now, if I add these two values, here I get 1160 kilojoules per mole, whereas, here I get 1120 kilojoules per mole. So, therefore, the enol is slightly less stable by about 40 kilojoules per mole compared to the Keto form.

So, the equilibrium constant that we usually find here is in the range of 10^{-6}. So, what is the equilibrium constant of 10^{-6} mean?

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$$A \rightleftharpoons B$$

$$10^{-6} \qquad \%B \qquad \frac{1}{10^{5}}$$

$$\boxed{0.01\%}$$

So, if I have to take to components A and B, A in an equilibrium with B, if the equilibrium constant is 10^{-6}, that means that the percentage of B that is going to be produced would be, basically it is a one part in 10^{5}, which would be 0.01 percent. So, it is a really, really small number.

And in terms of NMR spectra, we usually, observe impurities, or components of mixture, which are in excess of 1 to 2 percent. So, sometimes you do not see components which are less than 1 percent. Many times, you do not see this. So, therefore, clearly by NMR, you will not be able to detect the enol but the Enol is produced, and there is experimental evidence for this.

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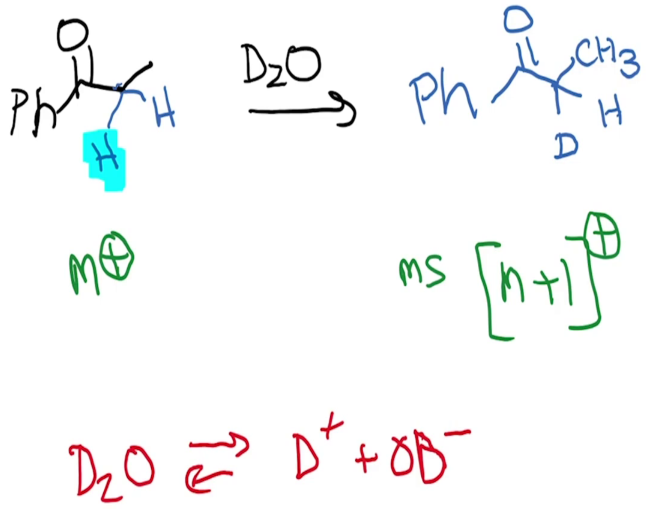

And I am going to share with you this experiment that has been done. So, the experiment that has been done is fairly straightforward. So, what we do is, we take, this compound this ketone PhC=OCH$_2$CH$_3$ and dissolve this in D$_2$O And what we know is that D$_2$O is much like, H$_2$O is going to be in equilibrium with D$^+$ and OD$^-$. And so, this much like water, the amount of the D$^+$ and OD$^-$ is going to be so low, but yet it is present in solution.

And so, therefore, when we do an experiment in D$_2$O it becomes a good source of D$^+$ and OD$^-$. So, when I dissolve this compound in D$_2$O, and record the NMR spectrum, so, D$_2$O is a very good solvent to carry out these NMR experiments because that is useful from the standpoint of minimizing the signal due to solvent.

And so, deuterium is the NMR silent so if a proton is replaced by deuterium, you do not see a signal for it in the NMR spectrum. So, what we find is that when you do this experiment, you see that gradually the signal that is corresponding to the carbon-hydrogen bond disappears. So, one of these hydrogen signals disappears.

And then after you do the experiment, you take the molecule and measure the mass spec, you know the mass spec shows that there is a peak, which is M$^+$ over here, it becomes (M+1)$^+$. So, this means that, you know the compound has picked up an additional, mass unit. And so now based on these two data points, what we can propose is that one of these protons is going to be replaced by a deuterium.

And so, we look at the mechanism and all that shortly. But this is one of the conclusions that one could make from this experiment. And that is that, I know when I add a ketone to D_2O, I do end up with a deuterated ketone as the product.

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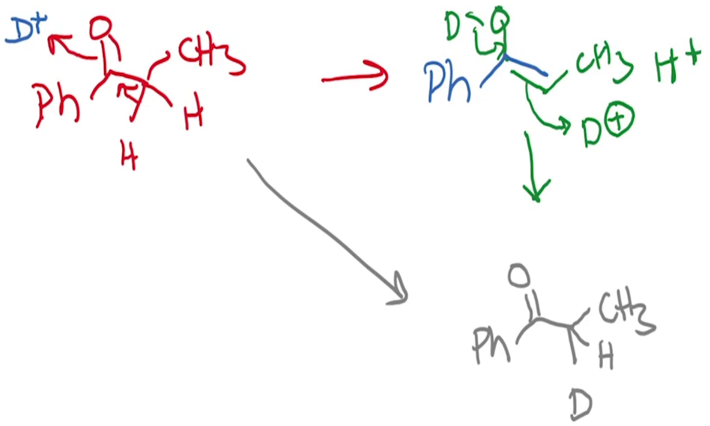

Now, so if you think about it, what can happen is that you have this compound $PhC{=}OCH_2CH_3$. And now, as we sort of looked at in the previous case, if there is small amount of D^+ that is present in solution, so, that is going to be floating around. And keep in mind that this is a D_2O, and we know the bottles of D_2O that we get are 99.98 percent of D_2O, really high amount of D_2O.

So, it is unlikely that there is going to be even a small amount of H_2O present. And so, therefore, this, you can assume that it is almost 100 percent D_2O in this reaction conditions. And so, under these conditions, if it is lost, then you can think about this kind of a scenario, wherein you produce Ph, C, O, and then deuterium. And so, there is a new double bond that is formed and there CH_3 over here. And so, you can imagine that this could be one of the components of the mixture.

And now, when this compound actually equilibrates you can also think about D^+ that is floating around in solution and keep in mind that this forward process actually produces another mole of one equivalent of H^+ and because H^+ is produced in such a small quantity, it is unlikely that the H^+ will compete with D^+ for the next step. So, you will see here that when this comes back, just surely by numbers, D^+ is present in much larger quantity compared to H^+.

And so, you will end up with $PhC{=}OCHDCH_3$ and now, instead of hydrogen, you have deuterium. And so, the other hydrogen remains intact, if you look at it. So, this is how this compound gets converted to the deuterated version. And in NMR timescales and the NMR experiment, we will not be able to observe the enol because, the Enol itself does not have a significant population for us to look at it, but you will observe that the compound on the left gets gradually deuterated to form the compound on the right. And, the signal due to hydrogen is going to go down slowly and it is going to produce this compound.

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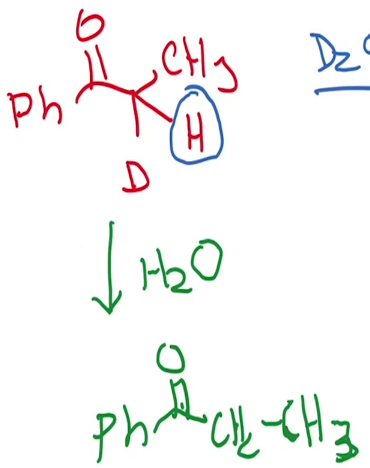

Now, another experiment that can be done as a follow up is if you take this compound and this product and I am going to draw it separately in the next slide, so if I start with this compound and now let us say I make this compound separately and I start with this compound and I expose this to D_2O. Now, what we observe is that this signal due to this hydrogen gradually disappears and you would end up producing the di-deuterated compound.

And this is something that is very interesting. So, you will get this compound. And so, what it tells you is that, if there is enough time given then this intermediary compound that we see on NMR can get converted to the di-deuterated compound. Interestingly, if I start with this compound, or even with this compound, and I add an H_2O, instead of D_2O and I allow the solution to sit for a while, and then I remove the water and I record the NMR spectrum, then I get back, $PhC=OCH_2\,CH_3$.

So, what these series of experiments tell me is that, Enol is being produced, but on the NMR experiment, we are unable to detect it. And second thing is that the production of the Enol is a reversible process. And so, once you form the enol, the enol can revert back. And further evidence for the reversibility is obtained when you take a deuterated compound, which we think is the product and add water to it, and we get back the starting material.

So, this is a very nice example of how you can demonstrate the principle of chemical equilibrium in the process. But together, keep in mind that this is a reversible process. And we do detect this in the NMR as an intermediate, although we do not detect it NMR, but we can infer its production by this NMR experiment.

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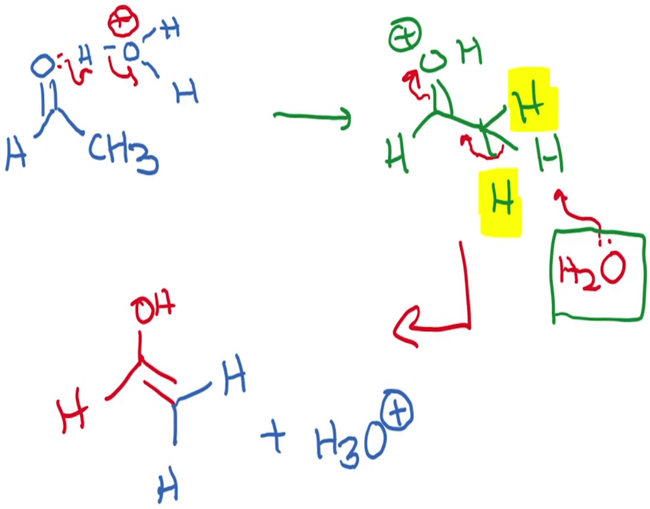

Alright, so let us now discuss a little bit about catalysing this reaction. So, enolization as a process can be catalysed by acids and bases. So, as you saw in the previous lecture, the first step of the enolization involves picking up of proton. So, similarly, we shall assume that the proton was generated in the medium. And so, that can be one assumption. And, usually in water, there is a very small amount of H^+ and OH^- that is available.

But you could also accelerate the process by adding in a small amount of H^+. So, let us say we add a drop of H^+. And so it is going to form hydronium ion. And, as you know hydronium ion’s structure is like this, and it has a positive charge on the oxygen. So, now this lone pair on this oxygen can pick up this proton and produce the corresponding protonated carbonyl.

So, it will be $HC=OH^+$, and you have your three hydrogens in the alpha position, and this is the aldehyde. So, you may notice that we have switched to an aldehyde in this example. But now, clearly there is water that is present as the medium, and water can now come in here, and this carbonyl is activated enough that it can allow for this H^+ to be picked up. And it is going to give you the product, which is the Enol, so, $OHCH=CH_2$.

And so, if we write them out, they are these two hydrogens here. And if you notice, the by product that is formed is H_3O^+, which can then go back and catalyse the reaction. So, if you want the Enol to be produced, then all you need to do is to add a small amount of H^+ in the reaction medium and that can convert the Keto to the enol form. Now, we like this mechanism a little better, because it shows that the water is attacking a keto form and producing the enol rather than just a spontaneous loss of H^+ as we have discussed previously.

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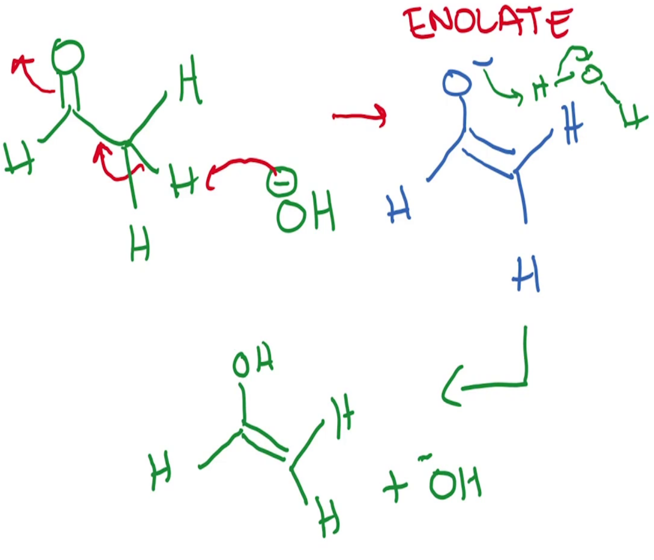

Now, a similar thing can also happen with a base. So, let me just quickly write that out. So, you have an aldehyde. And now if you have OH^- ; OH^- attacks here, and you can move this over here and produce the enolate directly. So, you have O minus, there is a double bond here, there is a hydrogen here and H, H. So, this can be produced and this is called the enolate.

And we will come back to this later in the lecture. So, it is called the enolate. Now, again, this enolate can react with the hydrogen of water. So, you will get H-O-H if it picks up this hydrogen, then you are regenerating the base and you are producing a enol. So, this is the Enol and then you get hydroxide ion being kicked out. And this hydroxide ion can go back and react with another mole of aldehyde and form a Enol. So, the keto-enol tautomerism can be promoted significantly by adding a small amount of acid or a small amount of a base.

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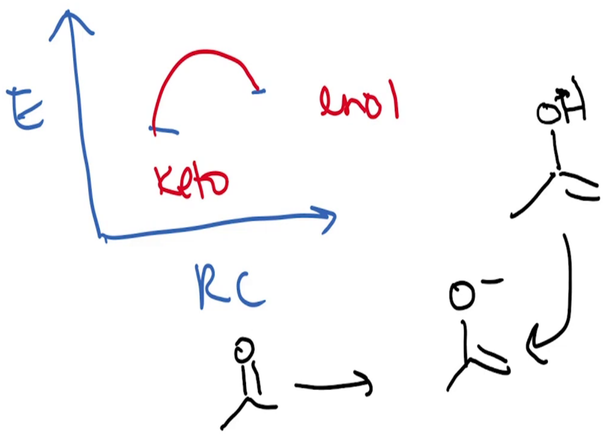

Now, with this background, now, let us talk a little bit about the stability of this keto and enol forms, so, as we discussed, if I draw out an energy profile. The keto form is a little bit more stable than the enol form. So, this is the keto and this is the enol and so there must be a small barrier that you need to overcome to get from the keto to the enol form.

Now, both the keto form and the enol form, produce the enolate that is both this, the ketone gives you the Enolate, and the enol also gives you the Enolate, that is if I have to draw it, here, the enol also gives you the enolate. So, but now, since the keto and enol are going to give you the same intermediate, we can make some judgments about which compound is more acidic.

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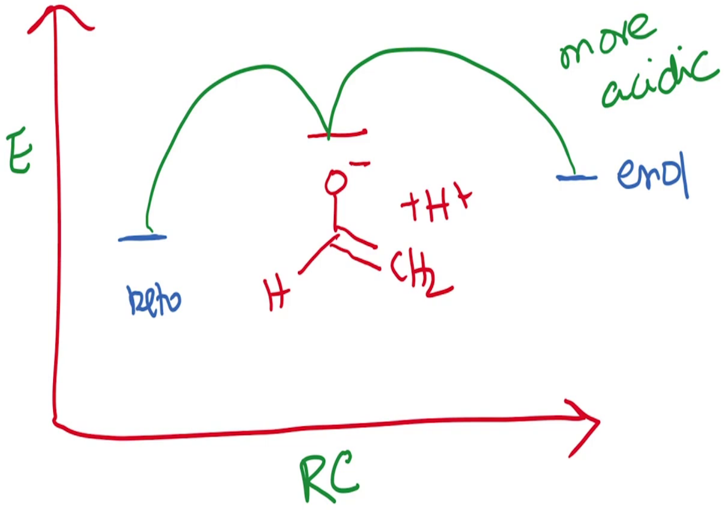

Now, let me just redraw this energy profile in the next slide. So, that we understand this better. So, what I am going to do is I am just going to assume that the enolate is over here, $O^-CH=CH_2$ and then we also have H^+ that is going to be formed. And now, let us assume that the keto form is more stable than the enolate. So, the keto is here. And we already know that the enol is more unstable compared to the keto.

So, the enol is going to be here. So, this is going to give you the enolate, this is also going to give you the enolate and therefore, if you look at this structure over here, now, we can assume that we can reliably deduce that the enol is more acidic. So, between the keto and enol, because the enol is inherently more unstable, the reaction of the enol to give you the enolate is going to be more facile. And therefore, the enol is going to be more acidic compared to the keto form. Now, let us compare the stability of the enolate with few other non-functional groups.

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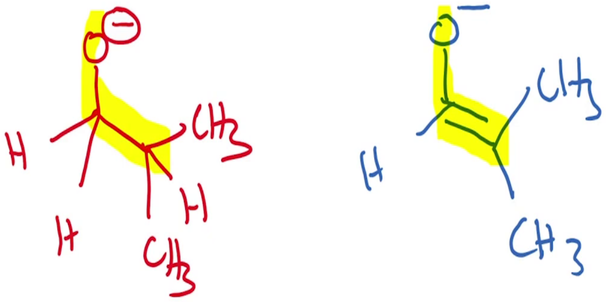

So, the first functional group that we want to compare it with is the alkoxide. So, if I draw out the alkoxide, it is over here $^-OCH_2CH(CH_3)_2$ versus the corresponding enolate which is ^-O $CH{=}C(CH_3)_2$. So, if you notice the difference between these two compounds is this CH_2 over here and this system is a conjugated system.

And therefore, the enolate is more delocalized compared to the alkoxide and therefore, one would expect that the enolate would be more acidic or the enol would be more acidic compared to a regular alcohol. So, with that, in the next lecture, we will move on to understanding the molecular orbital picture of this system.