Introductory Organic Chemistry - II
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Lecture 46
Conjugate Additions: 1,2-addition and 1, 4-addition

So, welcome back. So, in the next lecture, we are going to look at very closely three important reactions. First reaction is a conjugate addition, which I think several of you might have already been exposed to. And the second reaction we want to look at is enolate alkylation. And this we have been passing we have looked at it in some examples, but we will look at a few more examples. And lastly, we will look at acylation reactions. So, let us start with the first reaction, which is the conjugate addition.

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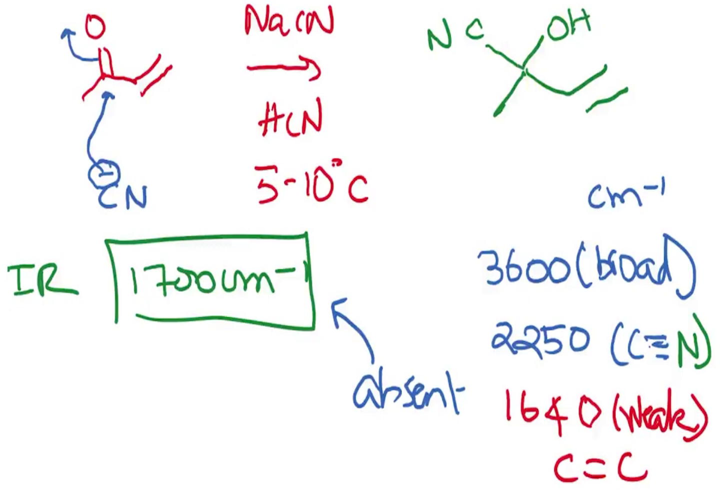

So, I will start with this example or a reaction that has been conducted. So, when we take a carbonyl compound typically and react it with sodium cyanide, we have looked at this in several examples. And the conditions I am going to use are NaCN, HCN and I maintain the temperature between 5 and 10 degrees centigrade. So, you know, we already know quite well, that cyanide can attack and open this up and eventually you produce the cyanohydrin as the product.

So, as expected, if I look at the infrared spectrum of this compound, I see peak around 1700 cm^{-1} which corresponds to the carbonyl compound and when I record the infrared spectrum of the product, I see a peak at 3600 cm^{-1} which is broad and this is basically corresponding to the OH stretching frequency. And I also see a peak at 2250 cm^{-1} all of these are in centimetre inverse and this corresponds to the $C\equiv N$. So, this we also looked at prior in the class.

And lastly, I see a peak at around 1640 cm^{-1} which is a quite a weak signal that corresponds to the $C=C$. And most importantly, this stretching frequency that I see here is absent. So, all of these data show that or suggests that this is the product, they are consistent with the formation of this product.

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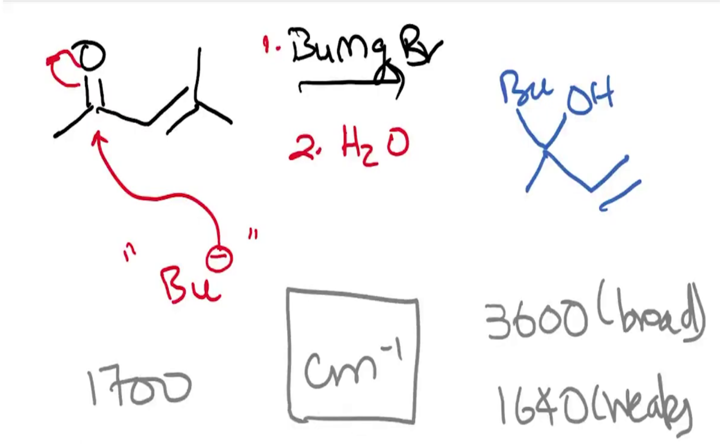

Now, I will give you one more example. So, we take $C=O$ and react it with Butyl magnesium bromide, so there is a Grignard reagent which we have looked at previously and the second step is basically addition of water and again the similar mechanism is proposed. So, you have Bu$^-$ in principle, it attacks here and produces the addition product and you would expect $CH_3C(OH)(Bu)CH=CH_2$.

And again, if I measure the IR or if I record the IR spectrum of this, I see a signal at 3600 cm^{-1} and then 1640 cm^{-1} which is a weak signal and this is broad, right and no signal at 1700 cm^{-1} which is expected for the ketone. So all of these values are in centimetre inverse. So, this works very well and this is consistent with whatever you have studied so far, or you have discussed so far.

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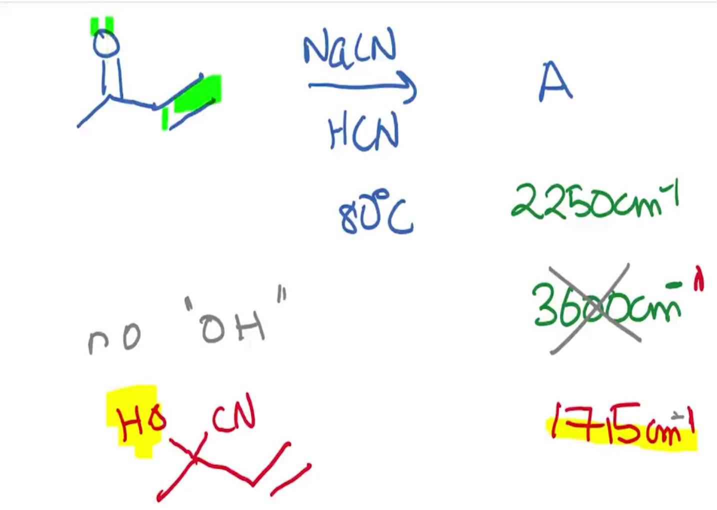

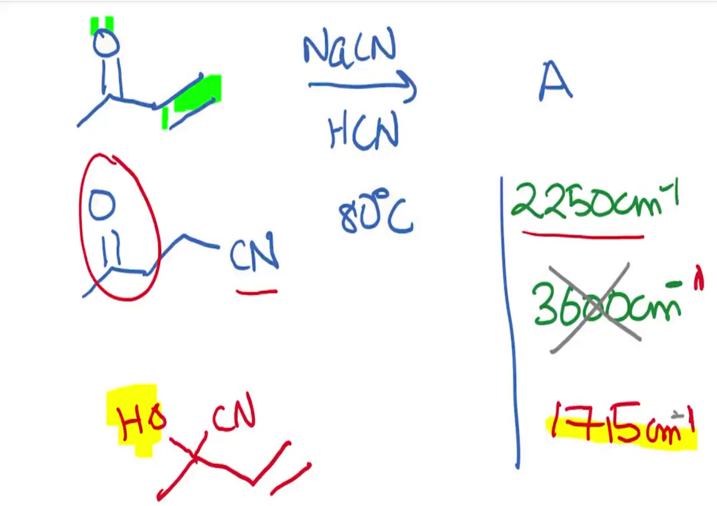

But you know if there is a change in conditions a little bit. So, the conditions I am going to use for the first reaction, the cyanohydrin formation reaction, is if I start this reaction at instead of 5 to 10 degrees centigrade, I started at 80 degrees centigrade, so I just put it in RB flask and just heat it up to 80 degrees. Now I get this product A. And this product has a signal at 2250 cm^{-1}. And it does not have a peak at 3600, this is absent but it instead it has a peak at 1715 cm^{-1}.

So, now, what this IR spectrum data suggests is that there is no OH functional group because the OH functional group is very, very characteristic and you will see a very broad signal at 3600 cm^{-1}. And in fact, sometimes if you don't dry your sample properly you also end up getting a peak for water but sometimes you do misinterpret the spectrum but if you dry your sample appropriately and properly then you should not see a signal for water under those circumstances.

So, now, the question is what is this product. So, looking at the data, it seems like you know clearly the cyanohydrin is not an option because the OH peak is not being seen and you see a nice sharp peak at 1715 cm^{-1} which shows that the carbonyl compound is still present. But another clue that we get is that the weak absorption at 1640 cm^{-1} is absent. So, it seems like this double bond has gone, the carbonyl remains intact and the cyanide has been added.

So, based on this data we can suggest, I mean of course we can look at other data as well. But just for the purpose of this experiment, we just suggest that we have only let us assume that we only have an IR spectrum to work with, otherwise you know we would use things like NMR and Mass Spec and many other tools to study the reaction or to identify the product.

So, based on this one can propose that C=O remains intact and this is the product. Now, is this product consistent with the structure? So the C≡N is still here, the carbonyl is still there, and there is no hydroxyl group so you don't expect a peak at 3600 cm^{-1}. So, this is not a single example of this.

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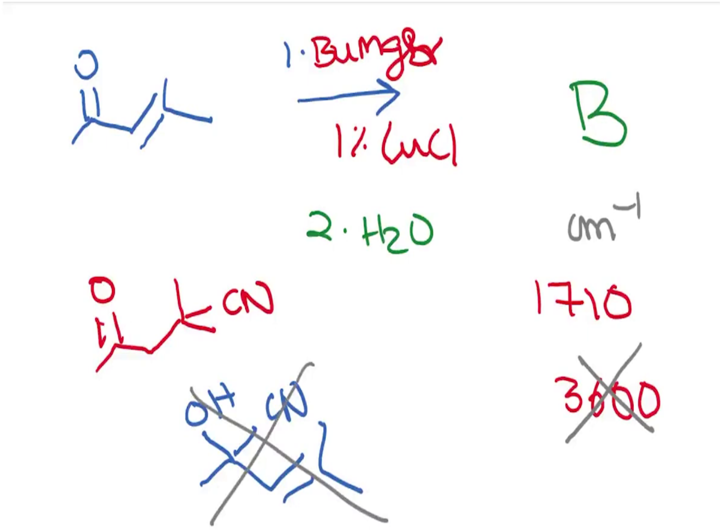

So, let us look at the linear addition. Now, we are going to change the conditions a little bit just like we increase the temperature in the case of the sodium cyanide reaction, what we will do is we will add butyl magnesium bromide, but the difference here is we will add a 1% of copper chloride and the second condition remains the same which is basically work up with the water. Now I get this product B. Now, let us look at the characteristic signals of product B.

So, here again I see signal at 1710 cm^{-1} and 3600 cm^{-1} is basically gone. And just to be clear, you know the C=C weak signal is also absent. So, based on this observation, keep in mind we will get to this later, but the only difference in conditions is the addition of 1% CuCl. And the product that is proposed is $CH_3C{=}OCH_2C(CN)(CH_3)_2$. So, as opposed to the original product that we would get which is this. So therefore, you know this compound is not formed under these conditions, but it is compound B that is produced. Now before we get into some details, let us look at the arrow pushing mechanism.

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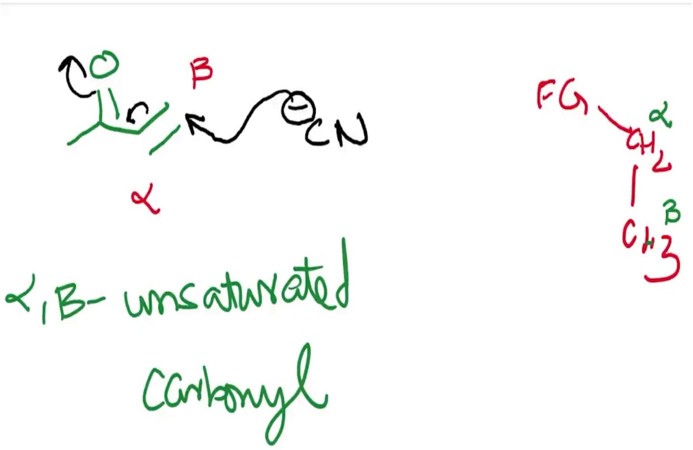

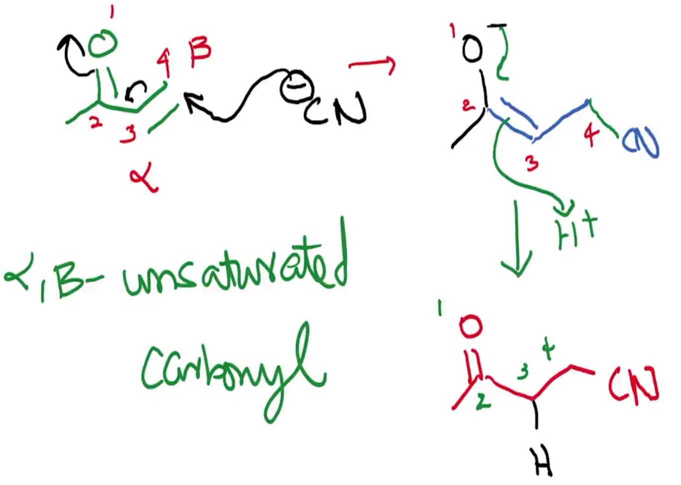

The arrow pushing mechanism is as follows. So, I start with C double bond O and this α, β-unsaturated. So, by the way, this is called as the alpha position, this is called the beta position. So, whenever you have functional group, which is attached to a carbon, let us say this is CH_2, this is CH_3. This is referred to as the alpha position, this is beta and then you have gamma delta and so on, if you have a longer carbon chain.

So, these are important positions because they you know, they sort of play a role, sometimes they are better at accepting electrons or accepting radical or reacting as a radical and so on. So, in this case, this is an α, β-unsaturated carbonyl compound, so these are important compounds, very important synthetic intermediates, we will look at it not just here, but throughout the next few years that you will be studying chemistry.

So, now coming back to the arrow pushing mechanism, so we have CN^- that attacks on this here, and then this moves here, and this move here. So, the product that is produced, the intermediate that is produced is this. So, let me just number this so that it is easy for us to follow, we follow the same system 1, 2, 3 and 4. So, let us draw out the skeleton first. There is a new bond between 1, 2, 3 and 4. So there is a new bond between carbon 2 and carbon 3. So new bond between carbon 2 and carbon 3, and then there is a bond between carbon 4 and CN and rest of the molecule remains the same.

Now, if this picks up proton, basically from water, then you have, it is like an enolate, it picks up this proton, and the product that is formed is $CH_3C{=}OCHCH_2CN$ and there is your new hydrogen is produced and the numbering is 1, 2, 3, 4. So this is the formal arrow pushing mechanisms, I would urge you to draw this out for the similar mechanism for the 1, 2-addition as well.

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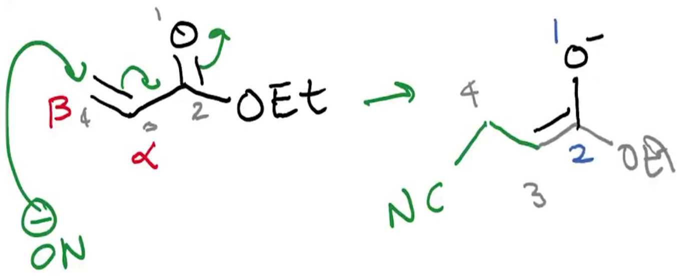

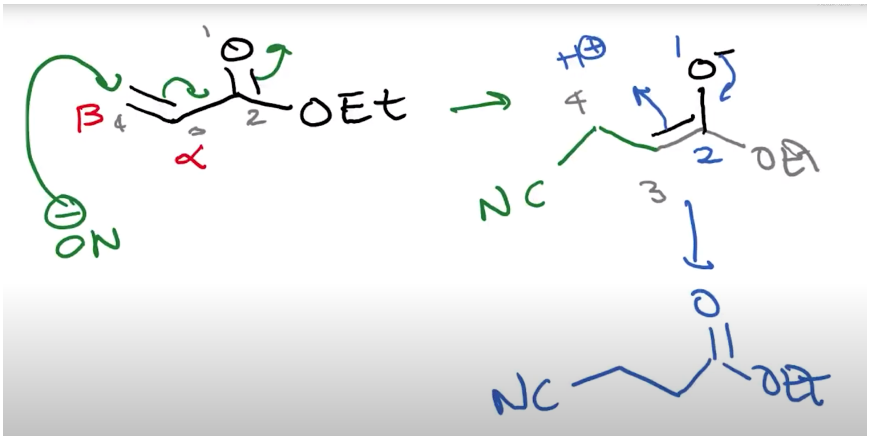

Now, with that, let us look at some examples. I am not going to go into an exhaustive set of examples but I am just going to give you 2 or 3 examples. So, the first example is I can also start with α, β-unsaturated ester, so this is the alpha position, this the beta position. And now the reaction of cyanide under certain conditions can occur and you get the corresponding cyno derivative, so let us keep the same numbering 1, 2, 3, 4, so this is carbon 4, 3 this is 2, and this is 1. Now here is your OEt, O minus that is the enolate and here is carbon 2, this is oxygen 1. So, this is going to be your intermediate which then picks up a proton to give you $CNCH_2CH_2C{=}OOEt$. So, this is possible.

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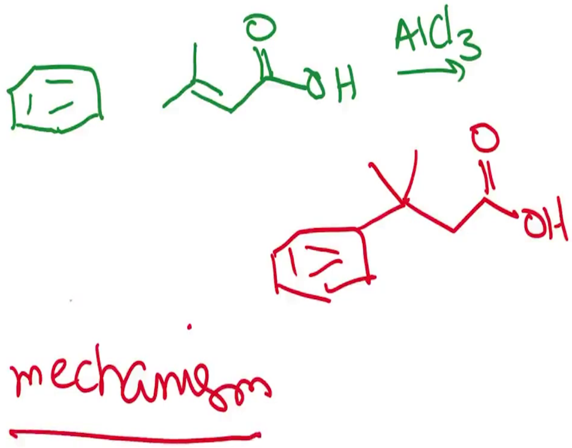

You can also have the reaction of different kinds of nucleophiles we will look into that a little bit later, but the interesting reaction that I would point you out to is the reaction of benzene, so which we have looked at quiet in detail in the earlier part of the semester, but let us say you start with this type of a compound and you add $AlCl_3$ so if you recall, this is the Friedel crafts reaction and the product that is formed is this. So, draw out the arrow pushing mechanism for this you know when you get time and get yourself familiar with this whole reaction.

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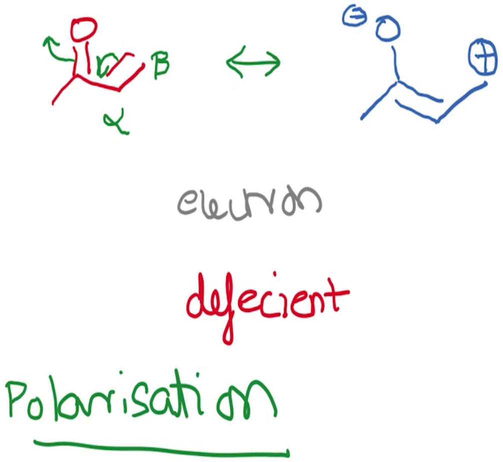

Now, let us try and understand some of the aspects of reactivity of these conjugated olefins or conjugated carbonyl compounds or these α, β-unsaturated carbonyls. So, the first sort of important aspect in the reactivity of or the structure of these compounds is that, you know, what we normally look at is basically since there is conjugation, we can look at resonance forms. So, if we were able to draw out, this resonance form, which is the enolate form. So, you have O minus and then you have a full-fledged positive charge on carbon.

So, one could argue that this carbon over here is going to be electron deficient, so this is an electron deficient centre. Therefore, it is not unreasonable to expect that this carbon is actually a reactive centre. So, let us just revise that this is called the alpha position and this is called the beta position. So, there is a fair amount of polarization that occurs and this is going to contribute to the unique reactivity of these types of compounds. Now, can we detect this polarization through spectroscopy.

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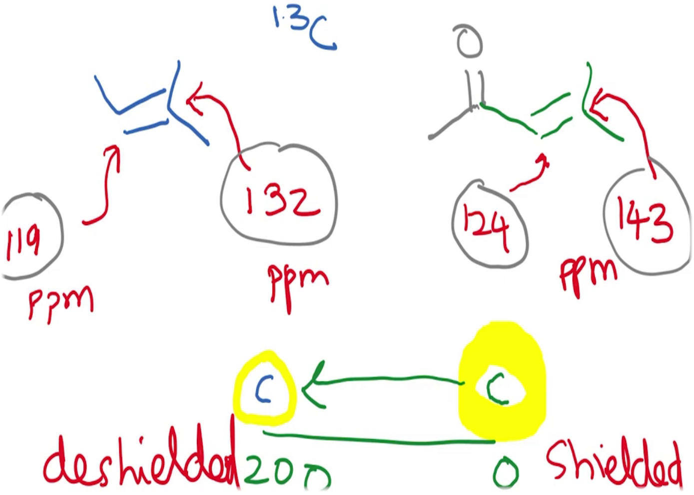

electron

defecient

Polarisation

So, one of the important spectroscopic tools is NMR. So, here if I for example, just take a traditional olefin such as this then the C-13 NMR spectrum of this shows that you know this over here appears at 119 ppm and this carbon over here shows up at 132 ppm. So, these are all values in ppm. Now, so just to sort of put this data in perspective. Normally, if I take a functional group and if I keep adding electron withdrawing groups, the electron cloud around the nucleus sort of goes down and once the electron cloud goes down, let us say I take the values of 0 to 200. So, the more electron deficient it is, the higher the ppm values.

So, therefore if I take a carbon, which has some, this is only a very rough analogy to show, so if I take this is the electron cloud around this carbon, then as the values go up, one of the indications not the only indication, but one of the indications is that the electron cloud around this is less. So, as and when you add more electron withdrawing groups, the values of the chemical shift goes up. And this is also called as deshielded. So, this is more shielded. And this is deshielded. So, this is also another terminology that is frequently used, nevertheless coming back to these compounds.

So now, if we look at the same sort of framework, but the only difference here is I am adding a C=O instead of a methyl group, I am adding a carbonyl compound. So, this carbon over here shows up at 143 whereas, this carbon over here shows up at 124, so these values are ppm again. So, you see here that, you know, if I compare 119 and 124, I see that there is an increase or a shift towards the more de-shielded region. Similarly, if I take this carbon 132 and 143 there is a substantial de-shielding that is going on. So, this spectroscopic data, again supports that the resonance form that we looked at in the previous slide, it shows that, you know, it sort of suggests that this kind of an electron deficient carbon is actually present.

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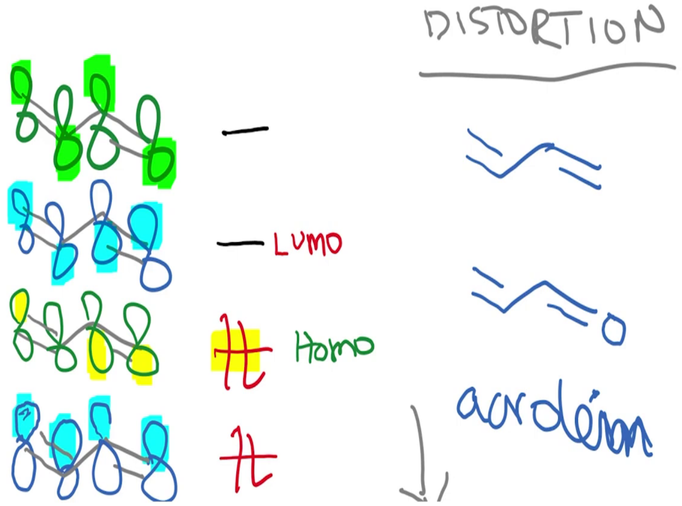
Chap22



Now, you know, we will spend a little bit of time and look at molecular orbitals, of course, you will realize that, it is going to take a little bit of time to draw these out. But nevertheless, we will try and draw them out. I would urge you to look at the textbook in, there's a chapter on this, this is chapter 22 in Clayden. which talks about conjugate addition, you may also look up other chapters, other textbooks that we have in the list but Clayden is a really nice book.

So, I am going to try and draw this all-in-one slide, which is going to be quite challenging, but let me nevertheless give it a shot. So, the reference set of molecular orbitals that we are looking at is actually 1, 3-butadiene. So, 1, 3-butadiene as the following structure. Now, so if we just want to draw all of them over here. So, this is my framework for 1, 3-butadiene. Now, I am going to draw out some orbitals, but they are going to be, the size of these orbitals are not accurate.

And so there may be some differences because of my drawing. But I would again urge you to look at the text to get the correct number or the size. So, this is the first set of orbitals. Now, if all of them are the same sign then this is going to lead to the most favourable, you know, sort of overlap. The second situation is that, you know, two of them are going to have the same sign and the other two, for example, are going to be overlapping, and then there is a nodal point, and then there is, these two that are going to overlap.

So, this is the second level. The third level is, you are going to have these two sort of the same sign, and this is going to give the opposite sign. So, that leads to the empty orbital, you know, because there are only 4 electrons in butadiene. And the last one is where, you know, all of them are mismatched, so there is no sort of overlap. So, this is here, this is here, this is here. So, it's fairly straightforward to draw out.

And now, just to recall, this is the lowest unoccupied molecular orbital, and this is the highest occupied molecular orbital. So, now what I am going to do is I am just going to draw similarly, the sort of picture for acrolein. And acrolein maybe I should just draw it out on the next page. So, this is for 1,3-butadiene. And if instead of the carbon, if I have an oxygen, this is called as acrolein. So, let me just draw out the acrolein in the next page.

But suffice to say is that because of the higher electronegativity, you know, by the oxygen, there's going to be, the levels are going to go down. Compared to this, the levels are going to go down. Second thing is that what you can expect from previous discussion is that there is going to be a fair amount of distortion and asymmetry because of the presence of the oxygen.

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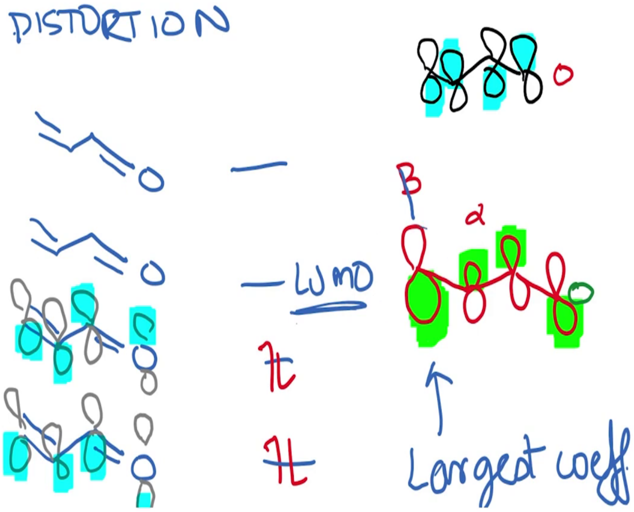

Now, so if I draw out the levels for acrolein. Again, I am just going draw this out in the following manner. So, that it is easy for us to follow it. And then we will draw out the orbitals. So now, again, like I mentioned, these are, each of them is one energy level. And, you know, you have 2 electrons here, 2 electrons here, and then that's a water. So, keep in mind that when we are looking at the molecular orbital picture, we always look at the pi-bonds here because they are the most reactive.

So now, coming to this, coming back to this MO picture, so we have a lobe over here, and then over here, over here and then over here. So again, I am not drawing this to scale, but the 2 important features of this, I will just tell you shortly, but this is here, here, here and here. So, here all of them are going to be favourable overlap. And as you know, the second one is going to be, two bonds are going to be favourable overlap.

Now, coming to the third, which is the LUMO, which is the Lowest Unoccupied Molecular Orbital, the picture looks something like this. The slightly smaller lobe over here, there's a slightly smaller lobe over here, and then there's a lobe for the oxygen. Now, we need not worry about how these orbitals have been calculated. But the important point here is that you know, you are going to have the largest coefficient is going to be at this beta-position. This is the orbital with the largest coefficient.

So, what this means is that LUMO, which is the lowest unoccupied molecular orbital has the beta carbon as the lobe or the orbital which has the largest coefficient. And lastly, to complete the diagram, we have the last orbital to look at. And here again, we are just going to draw out the orbital and show you the signs, the sizes of these orbitals are going to be something that you need to look up and find out for yourself.

So, this is the, they are all the opposite sign. And so that completes the molecular orbital picture for us. So, there are several important points here. Number 1, there is distortion. So, some lobes are going to be larger and some molecule orbitals are going to be smaller. Number 2 is that there is an indication of polarization because of the electronegative oxygen. And the third point is that the LUMO, which is in this case, because it is an electron acceptor, the LUMO becomes one of the most important orbitals to look at. And the LUMO has the largest lobe on the β-carbon.

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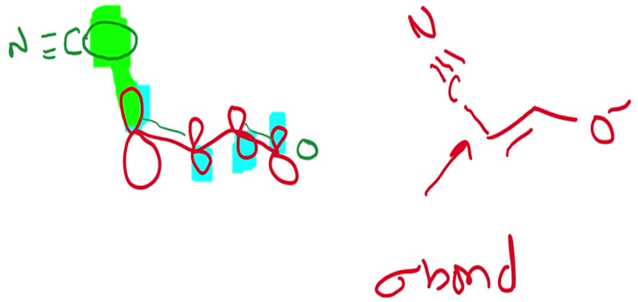

So now, this sort of helps us understand, you know, this reactivity in terms of orbitals as well. So now, if I am looking at this picture again with oxygen over here. Now, here is your double bond and here is the C=O. Now, this is the as we discussed, this is the LUMO where you have you know, this kind of an arrangement. And now, if for example, the nucleophile, say, C≡N has its electron cloud in this manner, and obviously, it has to orient itself in the correct way, but it can attack here, and once it adds the electrons to the slope, then you know there's going to be a moment over here and you form the enolate.

So, this is the new bond, $C{\equiv}NCH{=}CHO^-$. So therefore, this is the new sigma bond that is formed and this pi bond is actually going to be broken. This carbon-carbon pi-bond is also going to be broken and you generate the enolate. So, this sort of gives us the perspective about how these reactions can actually occur. And it provides a framework for us to understand you know, the reactivity of α, β-unsaturated carbonyl compounds. In the next lecture, we will look at how to explain some of the observations that we have seen in terms of why one product is formed over the other.