Introductory Organic Chemistry II
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Module 08
Lecture 56
Rearrangements - Part 3

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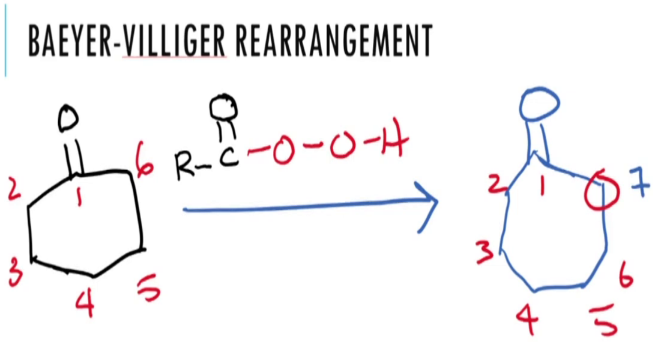

BAEYER-VILLIGER REARRANGEMENT

So, the next rearrangement that we will be considering is the Baeyer-Villiger Rearrangement. So, this is a very interesting reaction, you will see here that if you start from a ketone such as cyclohexanone you end up with a 7-membered ring, so, let me just number this so that it becomes clear, this is 1, 2, 3, 4, 5, and 6. So, if I keep this 1, then this becomes 2, 3, 4, 5, 6. And now we have a 7-membered ring with oxygen in it.

So, this is the reaction that we are going to consider now and this is called the Baeyer-Villiger Rearrangement. Let us look at the mechanism.

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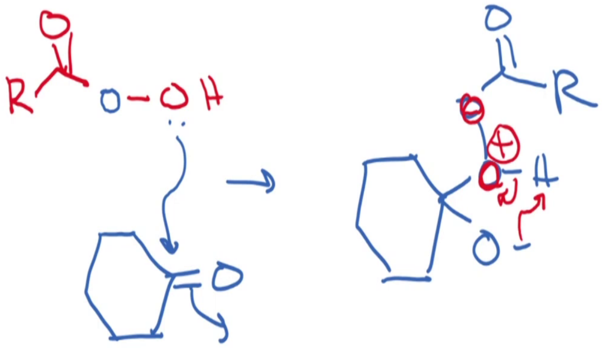

So, the important player here is the peracid. So, this is something which you have already studied during epoxidation reactions. So, this is the peroxy acid which basically is a, you have a peroxide which is attached to a carboxylic acid with an extra oxygen. And so, this is the major player in this reaction.

And when it reacts with a ketone, you have the attack of this and the formation of the tetrahedral intermediate and here is the tetrahedral intermediate that we are looking at. And let us just draw this in red, so that it becomes easy for us to follow this. Now, there is a positive charge on this oxygen and so which can be sort of transferred over here.

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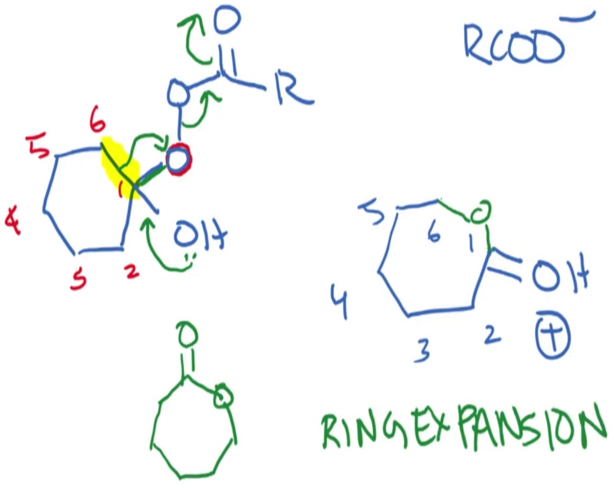

And the product that you get is the OH, O O C double bond O R. So, now the movement of these electrons here can occur. And here is the important aspect of this reaction, wherein this migrates, the form between this carbon-carbon bond attacks this oxygen, and you have an excellent leaving group in the form of a carboxylate ion.

And so, you can imagine that this leaves as carboxylate. So, let me just colour this oxygen in red, and then we will number the carbons, so this is 1, 2, 3, 4, 5, and 6. So in this reaction, what we are doing is between carbon-6, and carbon-1, this bond is breaking, and you have a new bond between carbon-6 and oxygen and the loss of carboxylate.

So, carboxylate I will write it here separately. And there is a new bond between this ketone, so I am just going to draw it exactly the way it is drawn. So, this is 1, 2, 3, 4, 5, 6 and 6 is now linked to oxygen. And let me just draw this a little better so that we can see the new bond. So, the new bond is basically like this to the oxygen and now the oxygen is connected to the carbon-1, already.

So, you see here that this is the bond between carbon-1 and oxygen and RCOO$^-$ is the product. So, if I redraw this, we would get 7-membered ring within oxygen in it. So, the Baeyer-Villiger reaction is a reaction where you have ring expansion. So, reaction that can occur and you see that it can convert a ketone to the ester or lactone.

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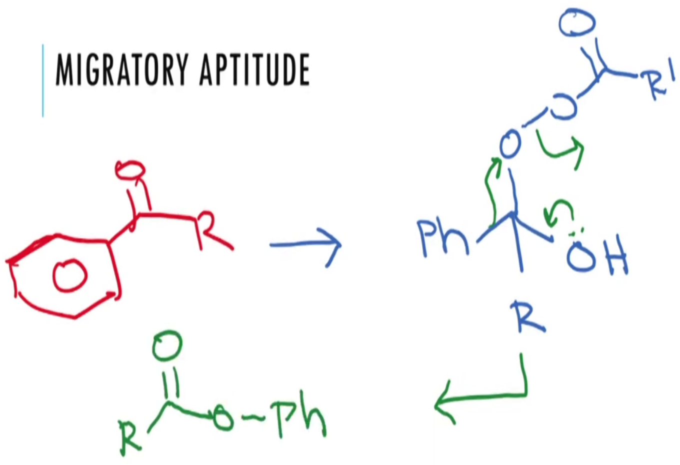
MIGRATORY APTITUDE



So, now we look at a concept called as Migratory Aptitude. So, the reason we are interested in this is because when you have a competition between two different groups migrating, then which group has a better or a higher propensity to migrate? So, there is no easy formula for this. So, we will have to reason it out, based on experimental data that we have.

So, we just looked at the Baeyer-Villiger oxidation. So, if you consider that, you have let us say you start with an asymmetrical ketone. So, in the example that we looked at it was cyclohexanone and so cyclohexanone is a symmetrical ketone. So, either carbon migrating is going to give you the same product.

But here, if you start with something like acetophenone or a ketone such as this and do the Baeyer-Villiger oxidation, you can have a situation where either one of them migrates that is you have the situation where either R group migrates, or you have the phenyl ring migrating. So, depending on which group migrates, you will have a different product that is formed.

So, let me just draw out the intermediate so that we can understand what I am talking about. So, you have this intermediate that we have seen, there is an oxygen, oxygen, C double bond O, let us say, R prime, and then you have OH. So, you have possibility one where this lone pair comes in here. And the phenyl ring actually migrates and kicks out the carboxylate. So, this gives you the green product, which is RCOOPh.

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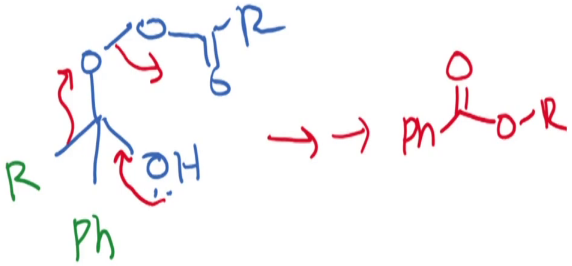

Now, you also have the second possibility of the R group migrating instead of the phenyl. And that would give you a different product. So now let us draw this out in red, so you have this, and maybe I should just draw this slightly differently, so that it is easy for us to understand, we will keep the phenyl here and R here. And so now, if this R migrates, then you have the loss of carboxylate.

And the product that you would get eventually after loss of a proton is PhCOOR. So clearly, the two products that are going to be formed are going to be different. So now this sets up a beautiful experiment for us to see wherein we just changed the R group and study which group migrates.

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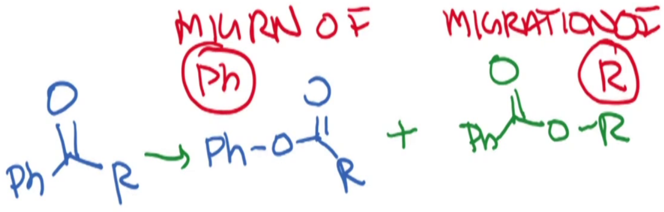

Me	90	0
Et	87	6
iPr	33	63
tBu	2	77

So, we start with this PhC=OR. And we would end up with a mixture of products, let us say. So, the first product as we discussed would be PhOC=OR, and just going to draw this into a little bit smaller size so that we can look at all the data in one page. So, the conditions are the same, you add a per acid.

And the second possibility is that you have PhC=OOR. So just to be clear, here is migration of the R group gives you this product, the migration of phenyl gives you this product. So that is important for us to understand. So, once I do this experiment, and now I can change R so I can make it into methyl, R as Me, then I do the reaction and I find out how much of these two products are being formed.

So, in this case, the percentage is 90, percentage is 0. Now, we do this with ethyl, that is R equals ethyl. And this is pretty much the same 87 and 6, and then we move to isopropyl. So here, the ratio changes and you get migration of R becoming more dominant. And the last case is tertiary butyl, where you get only 2 percent of this product and 77 percent of the migration of R.

So based on this data, what we could suggest is that there is clearly a difference in the migration. So that means that it is not equally likely that either group will migrate. And when a smaller group such as methyl or ethyl is present, then the phenyl migrates, and as the group size increases to isopropyl and tertiary butyl, then one of those two groups migrate.

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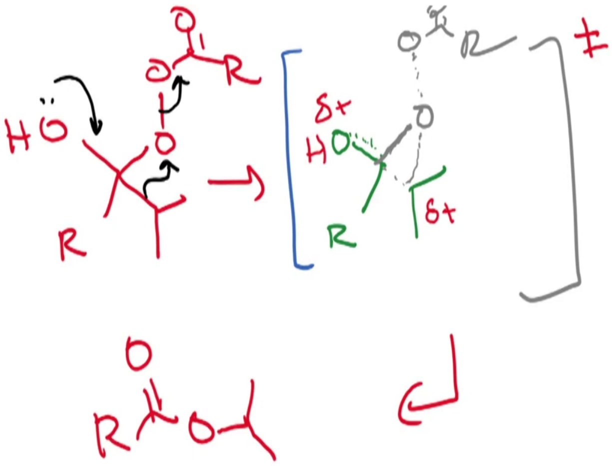

So, you might sort of get a clue here in that the stabilization of partial positive charge works better as the group size increases. So that is a tertiary carbocation is more stable than a secondary carbocation. And so, this might have some role to play in our understanding. So, see the transition state for this reaction is something that we need to look at. And so, the way we would draw this out is in the following manner.

So, you have OH, and you have, let us say you have an isopropyl group, which is what we are interested in. So, you have O, C double bond O, R. And now, this is the group that is going to migrate. So therefore, it is likely that you will have some sort of polarization that is going to happen between the carbon-oxygen bond, and you have clearly the OH coming in here.

And then this is being lost. So, if we were to draw the transition state for this reaction, it is going to look something like this. So, you have the oxygen bond, there is, this starts forming a small double bond, and then you have this R here. And the isopropyl bond is slightly broken. So, I will, again represent this by broken bond.

So, you have this bond being broken, and there is a bond between this bond and oxygen is intact, and this bond is going to break and so on. Now, there is a new bond that is being formed between this carbon and this oxygen. So, the transition state is much better drawn out in that textbook. So please do take a look at it.

So, one thing that becomes clear is that because this oxygen is going to get a full positive charge, so it is likely that there is some delta plus over here, but what is also suggestive, based on the migratory aptitude data that we have, that there must be some sort of a small positive charge that is being formed here, which can be stabilized by alkyl groups. So, as you increase the number of alkyl groups, the stabilization of that partial positive charge is going to go up.

So, this is one proposal that we can consider wherein you have a transition state like this. And this is going to contribute to the migratory aptitude. So, the product that you will eventually get is RC=OOCH$(CH_3)_2$ as shown here. So therefore, one way to understand this is that there is going to be some effect of changing the group, because the stabilization of the transition state that we envision, the stabilization is going to be different.

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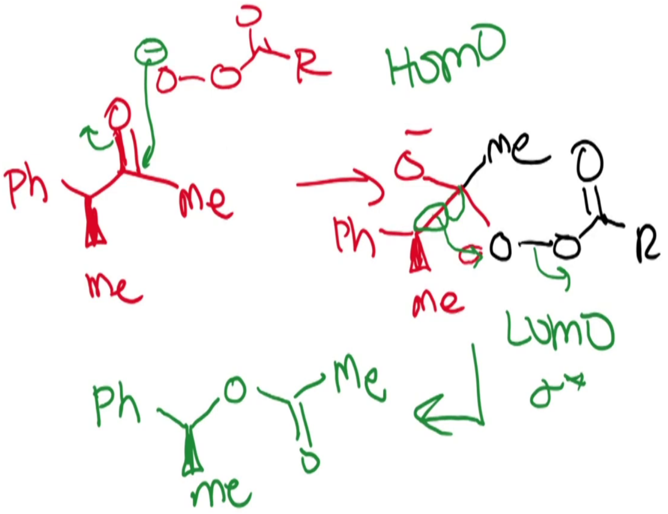

Now, let us look at some orbital aspects of this, and then we will move on to understanding the phenyl ring. So, if I start with, for example, this type of a compound Ph with a stereocenter Me, and then we have C double bond O Me. Now, the way we would understand this is that you have the C double bond O here.

And clearly, the attack of the peracid occurs over here. And you generate a tetrahedral intermediate, and the tetrahedral intermediate is going to look something like this. And the methyl group continues to be here. So now when you consider the movement of this group, so we would think that this oxygen over here, which is this oxygen, the antibonding orbital of this oxygen is going to be important.

So let me just redraw this in a slightly different way so that we can think about this in a much better orbital sense. So, let me put this as the oxygen. And here is the methyl group that is over here. So now, this is the antibonding orbital of oxygen. And this is the highest occupied molecular orbital. So, this is the LUMO, and this is the HOMO. And keep in mind that these have to align otherwise the migration is not going to occur.

So therefore, if this bond moves here and attacks here, this is going to kick this out. So, this is the σ^*. And so, the product that is going to form actually has a retention in stereochemistry, which means that Ph Me, and then you have the bond to the oxygen, and then you have C double bond O Me. And so, what this tells me is that the retention in stereochemistry also suggest that this is going to be very close to a concerted step.

So, this also helps us understand that there is no intermediate that is formed, that means that bond breaking and bond forming pretty much happen in a synchronous manner. Otherwise, if you had a carbocation like intermediate that is formed, then you might be able to explain, that could be one reason why you are getting a tertiary butyl better than isopropyl and so on. But that seems unlikely.

What is more likely is that the transition state that I described in the previous slide is in play. And the stabilization of the partial positive charge that happens there is going to be important.

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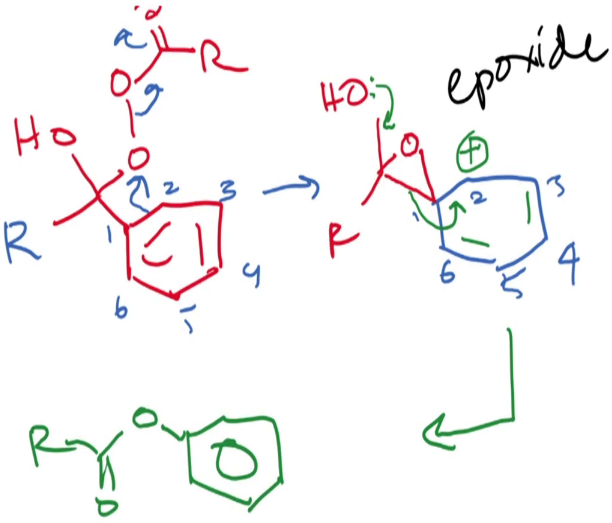

Now, let us move on to the migration of the phenyl ring. So, let us think about how that process is going to happen. So, I am just going to skip directly to the intermediate. By now we are quite familiar with this intermediate, which is the tetrahedral intermediate. And so, this is our phenyl ring. And so now, this attack, like our electrophilic aromatic substitution may occur and kicking this out as a form of a carboxylate.

And so, what would be expected is 1, 2, 3, 4, 5, 6-membered ring, this 6-membered ring remains intact. So, I am just going to draw it the way it is, here 1, 2, 3, 4, 5, and 6 and it is quite reasonable to expect that you will have a 3-membered ring that is going to be formed and this carbon 1, 2, this tetrahedral intermediate remains the same, so you have the rest of the molecule to be the same.

Now, you have a ring that is formed between this carbon-1, the original carbon which had the ketone and oxygen. So, this is the epoxide ring that can be an intermediate and you will have a full positive charge on this aromatic ring which is typical of an electrophilic aromatic substitution. And now, you have the situation where this lone pair can come in here.

And this bond can now migrate and restore aromaticity and give you the final product which is O C double bond O R. So, this is important for us to understand because the benzene ring plays an important role. The migratory aptitude of the benzene ring is quite good and it only is worse compared to a tertiary butyl group and it is comparable to isopropyl group.

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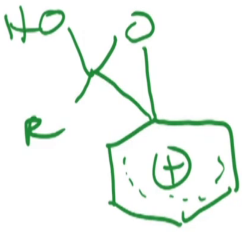

So, now, the important transition state or the intermediate that we want to look at is this with an oxygen and over here. So, this is OH, and this is R and so you have delocalization of this positive charge that can occur by the aromatic ring. So, this sort of puts the phenyl ring in perspective. So, the way we understand the migration of phenyl ring is through this kind of a process.

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$^{t}\mathrm{Bu} > \mathrm{Ph} > {}^{i}\mathrm{Pr} > \mathrm{Et} > \mathrm{Me}$

So, coming back to the data that we have, what we can suggest is that the migratory aptitude in the case of the Baeyer-Villiger reaction is tertiary butyl greater than phenyl greater than isopropyl greater than ethyl and greater than methyl. So, the phenyl and isopropyl can be sort of comparable in nature because 66 and 33.

So, these two can be similar to one another, whereas the ethyl and methyl clearly are inferior migrating groups when compared to phenyl and tertiary butyl. So, this sums up the migratory aptitude, and it is important that we understand this and also how to design an experiment that helps us put this migratory aptitude in perspective.