Introduction to Organic Chemistry II
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Lecture 29
Reactions of Carboxylic Acid and Its Derivatives

Hello. So, we are discussing the reaction of carboxylic acids and their derivatives and really, the reactions as well as, if I try to cover each and every reaction, it is going to be a huge syllabus in itself. So, we are going to do some particular reactions. And we were discussing reactions of acids, wherein we have seen how acids react with $SOCl_2$ to form acid chlorides, we have formed anhydrides, we have also formed esters. You can even form an amide, starting from an acid. But here is one more reaction that it does to form ester and this is a very particular reaction. It is a reaction of diazomethane.

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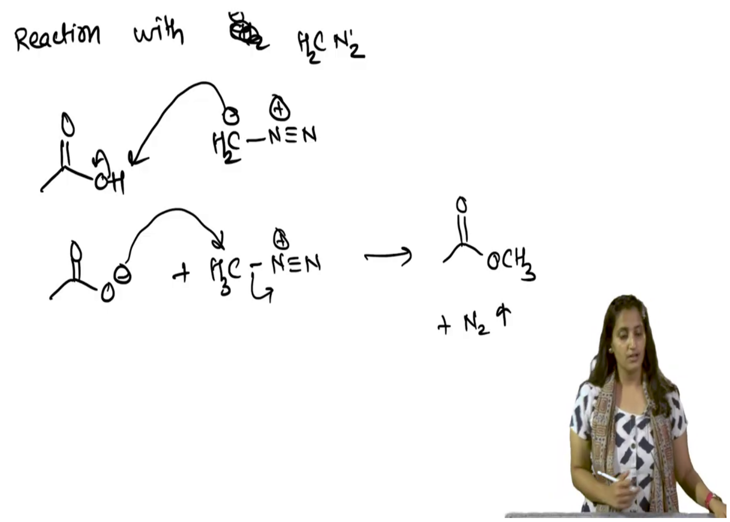

The first reaction that we are going to cover today is reaction with diazomethane. And diazomethane is a very wonderful compound because it gives a nice, clean reaction. Let me draw the structure of diazomethane. So, you have $CH_2^- N^+{\equiv}N$. So, overall it is a neutral molecule but there is a carbon having a negative charge, nitrogen having a positive charge and this is used to form esters in particular methyl esters from carboxylic acids.

So, we can take a carboxylic acid. Now, remember that carbon with a negative charge is a very, very good base. You have a very good acid. The first reaction that always, always happens is, acid-base reaction. What are we going to form? We are going to form the corresponding acetate.

So, I started from acetic acid. So, we have an acetate and you have CH3 $N^+\equiv N$. Now, what do we know about this molecule? This is a wonderful reagent for an S_N2 reaction. Why? Because that nitrogen is a very, very good leaving group, because it is going to leave as a gas, it is a very stable leaving group, and you have the methyl which is the perfect starting material for an S_N2, or alkyl for an S_N2 reaction.

And thus, what we see next, is this S_N2 reaction. So, what we form here is a methyl ester and N_2 as the leaving group. Very, very clean leaving group, almost results into very good yield of the methyl ester. Although, reacting the diazomethane is not a very easy reaction because it requires very impeccable conditions as well. It is an explosive kind of a reaction if it is not done in the right manner.

You can also do the same reaction for phenols and alcohols also, by the way. We started from a carboxylic acid, you can form ethers using this, you can form, if you start from a phenol, you are going to get the corresponding ether. That is one reaction that we wanted to do.

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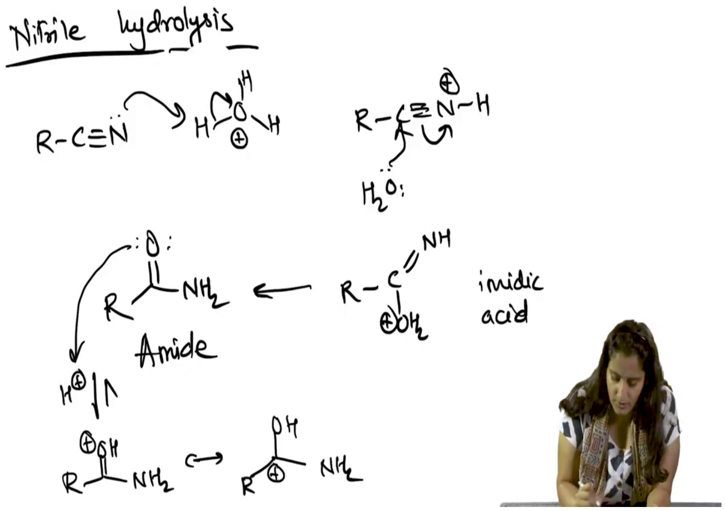

The second reaction that I want to discuss today is nitrile hydrolysis. So, remember we have been saying that how nitriles will be covered in this particular chapter? So, now, the way to form a nitrile is reacting with CN^- as a nucleophile so if you have RX and cyanide as a nucleophile, it is going to do a very nice nucleophilic reaction, substitution reaction. And you very often form good yield of the nitrile.

But nitriles can also get hydrolyzed. So, in the case of acid hydrolysis as well as base hydrolysis, both ways, they are going to end up carboxylic acid. So, let us do a reaction wherein we try to do an acidic condition hydrolysis, so we have $RC\equiv N$ and we have H^+ and H_2O so it is basically H_3O^+. And we are going to start doing the reaction. So, instead of writing it this way, let me write it in the correct manner.

Now, in a first step, you are an acid, you have a very good hetero atom in the molecule which can get protonated. The very first step is always protonation. It is the fastest step that can happen. And that is what happens. So, you have a protonated cyanide or nitrile to begin with and then, water is going to attack, and water is going to attack on this carbon opening this up. So, what do we have? So, now this is nothing but an imidic acid.

Instead of that NH if there was an oxygen, you would have called this into a carboxylic acid. So, this is very similar to that and this is an imidic acid. And that imidic acid is, remember, it is a keto-enol kind of a tautomerism happening. And what is that going to reorganize into, is an amide. So, you can try writing this mechanism from here to here. It is a simple keto-enol tautomerism.

In the first step, you need to deprotonate this OH_2^+, then protonate the amine, NH, form, reform the C=O and then deprotonate it again. So, it is a very simple keto-enol tautomerism reaction happening here, and we form the amide. So, the way we form carboxylic acid, starting from a nitrile, we have go through the amide and amides can then later hydrolyze to form carboxylic acid molecule and it is not very easy to hydrolyze an amide, as we had discussed the other day because amides are one of the stronger bonds and it is very difficult to hydrolyze it.

Although, under reaction conditions, so for example, if you do this reaction in a reflux conditions, it can do the hydrolysis. Base catalyze hydrolysis is even more difficult. Acid catalyze hydrolysis is comparatively easier for amides. So, let us go ahead and do that. In the first step, this is going to attack forming this.

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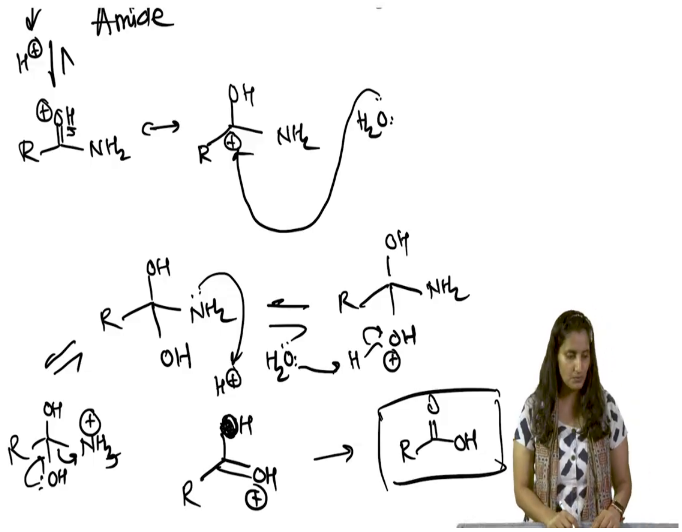

What next? So, this has a resonance structure but you have a water molecule that can come in, attack here. What do we form? Water also acts as the base. We are almost there because I can start seeing the blocks of the acid that we wish to form right there. In the next step, you have to make this NH_2 into a better leaving group by protonating it, forming, NH_3^+ and as it leaves, it forms the corresponding carboxylic acid.

That is the reaction of cyanide hydrolysis or a nitrile hydrolysis. We start from a cyano, we end up with a carboxylic acid. And that is why, we wanted to push the nitrile group in this chapter only because most of the reactions that they do are very similar to the carboxylic acid derivatives. And because the first step is going to be protonation, and then attack on the carbon to form a tetrahedral intermediate. So, that is what most of this mechanism is all about.

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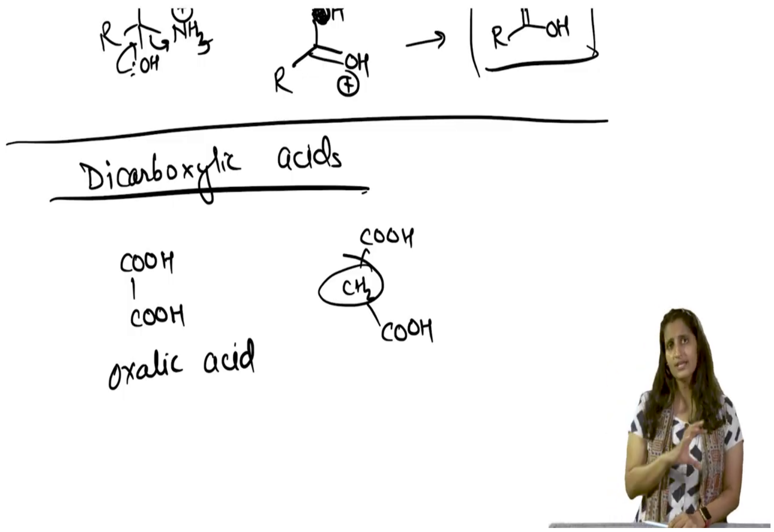

Okay, let us go ahead and let us look at the next chapter in this particular week which is Dicarboxylic acids? Now, dicarboxylic acids meaning, having two COOH groups. And in fact, you can have more than two. But we are going to restrict ourselves into two COOH groups.

The reason why we wanted to cover this is, because it is there in the BSc syllabus but there is not a big need to cover it very, very separately because, remember, that there are two COOH groups. If they are too far away from each other, that is, more than 5 or 6 members, or 6 carbons away from each other, they are going to behave as individual carboxylic acid functionalities. They are not going to affect each other's presence because of that.

Although, if they are very close to each other, so like in the case of oxalic acid or maleic acid, succinic acid, they are going to show a separate kind of reactivity, but there are only two or three different reactions that we need to think about. Having said that, dicarboxylic acids are important in most biological processes as well as in industrial processes. So, they are a part of, or they are required in order to manufacture various dyes, various chemicals, various paints and pigments, they are really important from that aspect, and there is a lot of commercial application for these molecules.

So, we know oxalic acid, for example, the simplest dicarboxylic acid. So, oxalic acid is, you might have used it as a way in analytical chemistry to figure out the exact molarity of NaOH solution. But it is also used as a bleaching agent and it is used very often in paint and pigment industry.

Then, we have malonic acid for example, here and malonic acid, we are going to cover it in the case of malonic acid ester synthesis. It is a very important part or, way to synthesize various other molecules. You have succinic acid which has, instead of one carbon here, now, we have two carbons in between, CH_2's in between and that will get you succinic acid, 4 carbon dicarboxylic acid and it is going to be used in various important chemicals, it is one of the starting materials.

So, what do we need to study about the reactivity of these dicarboxylic acids? The first thing, because of the presence of that other COOH, the acidity of this COOH increases a little bit, because that other COOH is going to pull inductively electrons away, so it is going to pull away the electrons inductively. Your conjugate base becomes much more stable. So, they are a little more acidic than the corresponding acids.

Regarding the reactivity, remember that having two COOH very close to each other, they are tend to undergo either cyclization reactions or they are tend to undergo decarboxylation reactions wherein, you end up getting rid of one of the carboxylic acid functionalities. So, there are various ways to really look at these reactions but I am not going to go over a lot of them. Just a little bit for us to get acquainted with.

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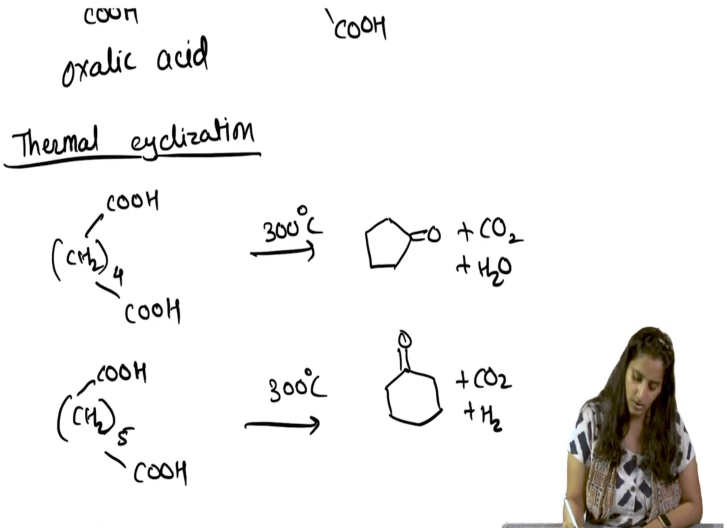

So, the first one I am going to talk about is thermal cyclization. Now, this is true for when we can make either 5-membered ring or a 6-membered ring. So, in order to make a 5-membered ring, we are going to start from a 6-carbon dicarboxylic acid. So, there are a total of 6 carbons here.

These are thermal cyclization reactions so as you heat these molecules, what is going to happen is that they are going to undergo de-carboxylation reaction to form the corresponding. So, in this case, we are forming a cyclopentanone. Similarly, you can form a cyclohexanone if we start from a 7-carbon dicarboxylic acid. Same thing, 300 degrees, you end up forming cyclohexanone molecule.

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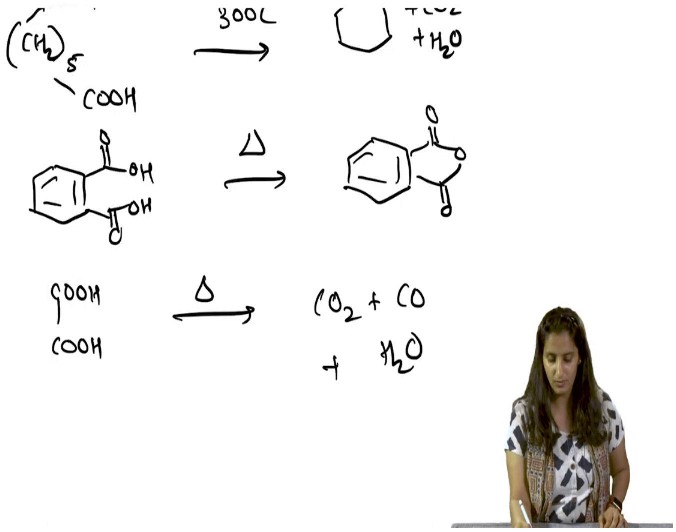

You do not need to go over the mechanism although if you want to write it down, it should not be a very difficult mechanism to write it. So, I am not going to cover it. We will not be asking questions on this. But if you want to try writing the mechanism for these reactions, try writing them.

Now, you had enough carbons in these two to form that cyclic ring, 5 or 6-memebered stable cyclic rings. If you have more than that, anyway the two carboxylic acids are going to behave as separate carboxylic acid entities and they will not show you this thermal cyclization. If you have less than that, sometimes you end up forming an anhydride.

So, for example, here, for this one, when it is heated, it is going to form the corresponding anhydride. And for very, very small ones, so like, for example, carboxylic acids, like oxalic acid, and if I heat it, what is going to happen is that it is simply going to decarboxylate, giving off carbon dioxide, carbon monoxide and water.

So, that is how these dicarboxylic acids react. One more reaction of dicarboxylic acid is the Dieckmann condensation and for Dieckmann condensation we are covering it in the next few chapters. It is again a cyclization reaction. I will just write it down, or putting a note here that when you go over Dieckmann condensation, I think it is in week 7, it is a name reaction, do remember that is starts from the esters of a dicarboxylic acids, so it starts with the diesters. And it forms a cyclized end product. So, I will not go over that right now. We will look at it in Week 7. But, that is all about the carboxylic acid and their derivatives.