Hello everyone

I am Dr. Mayuri Naik working as an Assistant Professor in Parvatibai Chowgule College of Arts & Science, Autonomous, Margao - Goa.

I teach subject chemistry for second year B.Sc. students of semester 3.

The module which I'll be discussing now, it is from physical chemistry and organic chemistry paper, having paper code CHC103 and it's from Section B, that is organic chemistry.

The name of the module is Comparative study of acyl derivatives towards nucleophilic substitution reaction and the module number is 08.

This module is from unit 1, that is, Carboxylic acids and their derivatives.

Outline of the module:
In this module, I'll be discussing different acyl derivatives, Nucleophilic acyl substitution reaction, Comparative study of acyl derivatives towards nucleophilic substitution reaction, Examples and Summary.

Learning outcomes:
At the end of this module, the students will be able to:
Understand the reactivity of different acyl derivatives towards nucleophilic substitution reaction.
Identify the product of nucleophilic acyl substitution reaction
Apply the mechanism of nucleophilic acyl substitution reaction to more acyl derivatives
And analyze the reactivity order of acyl derivatives.

So what are acyl derivatives?
For this, we know that the structure of carboxylic acid is **RCOOH**. That means there is a presence of carbonyl, the carbon of which is attached to **R** group on one side and **OH** group on the other side.

So **OH** I have marked in red because by replacing this **OH** group by any other group, you can get its derivative.

So when **OH** is replaced by **X**, which can be fluoride, chloride, bromide or iodide, we get acid halide.

When **OH** is replaced by **OCOR’** group, we get Acid anhydride.

When **OH** is replaced by **OR’** group, we get Ester

and when **OH** is replaced by $\mathbf{NH_2}$ group, we get Amide.

R and **R’** group can be Alkyl or Aryl group.

Nucleophilic acyl substitution reaction: In this reaction, acyl substrate is to be treated with nucleophile wherein we get **RCONu** that is, the nucleophile replaces **Y** group and we get a new substituted product.

Let us see the structure of acid derivative.

We've already seen different derivatives in which they are different with respect to **Y** group whereas carbonyl group is common in all the derivatives.

Carbonyl carbon being less electronegative, carries a partial positive charge and oxygen being more electronegative, carries a partial negative charge.

The double bond which is there between carbon and oxygen, out of these two bonds, one is σ (sigma) bond and one is π (pi) bond.

Carbon carbon is sp^2 hybridized and all the three bond angles are 120°.

The reactivity of carbonyl depends on two factors that is electronic factor and steric factor.

This is the mechanism of nucleophilic acyl substitution reaction.

It takes place in two steps: step 1 is Addition and step 2 is Elimination.

In step 1, nucleophile attacks on carbonyl carbon and the π bond breaks and this π electrons move on oxygen. As a result, we get intermediate which is now tetrahedral and the acyl substrate was trigonal.

This tetrahedral intermediate then undergoes step 2 that is elimination, in which the negative charge on oxygen it returns back to form carbonyl and **Y** group leaves, giving rise to the product in which now nucleophile is attached to the carbonyl.

This is the order of reactivity of different acid derivative towards nucleophilic substitution reaction.

According to this order, acid chlorides are most reactive followed by acid anhydride, further, esters are less reactive and finally amides are least reactive.

So why this order is like this? So we have to see the basicity of the leaving group which I have marked in red colour.

Here, we have to remember that the weaker the base, the better the leaving group.

So let us see the basic strength and leaving ability of leaving group.

From chloride to NH_2^- ion, the basicity goes on increasing. As a result, from NH_2^- to Cl^-, the leaving ability increases. This is because chloride is very weak base and hence it is very good leaving group.

However, as we move on and reach to NH_2^-, it is the strongest base and hence is bad leaving group.

As a result, acid chlorides react faster than the other derivatives and amide reacts very slowly.

The hydrolysis of acid derivative is one of the example of nucleophilic acyl substitution reaction.

So when hydrolysis of acid chloride is carried out by adding water to it, the reaction occurs at 20°C to give carboxylic acid as the product and the reaction takes place quite fast.

The same reaction when is carried out by using acid anhydride, it occurs at 20°C, however, the rate of the reaction is slow.

This shows that acid anhydride is slower in reactivity than acid chloride.

Further, ester can also be hydrolyzed, however acid or base catalyst has to be added in the reaction and the reaction is required to be heated because the rate of the reaction is very slow.

And finally, when amides are hydrolyzed, in addition to acid or base catalyst, prolonged heating is required to get the product because the rate is exceedingly slow.

So this tells us that, the order for the hydrolysis reaction of these four derivatives is like this:
Acid chlorides are highly reactive and undergoes hydrolysis reaction at a very fast rate followed by acid anhydride wherein the rate decreases, further with respect to ester, the rate further decreases and finally amides are least reactive and hence undergoes this hydrolysis reaction at a very slow rate.

Then why the hydrolysis of acid chloride is fastest?

This can be explained based on two effects: one is inductive effect -I effect and the second one is resonance effect that is +R effect.

So in inductive effect, the **Y** group which is attached to carbonyl, it pulls the electrons of sigma bond towards itself. This is because of the electronegativity of **Y** group.

So more the -I effect, the electrophilicity of carbonyl carbon will increase and leaving group ability of **Y** will also increase making the carbonyl compound more reactive whereas in case of resonance effect that is +R effect, the lone pair of electrons which is present on **Y** gets delocalized over the adjacent carbonyl group.

As a result, the electrophilicity of carbonyl carbon decreases and the leaving group ability also decreases, making the carbonyl compound less reactive.

So if we see these four acyl derivatives, with respect to these two effects, in acid chloride, chloride ion being most electronegative, it will pull the electrons towards itself strongly, making carbonyl carbon more reactive and hence it reacts at a faster rate.

As we go down, the -I effect goes on decreasing and in amides it is very less because nitrogen being less electronegative, it cannot pull the electrons that strongly, as a result, it undergoes reaction at a slower rate whereas +R effect is maximum in amides because the lone pair which is of electron which is present or nitrogen can be easily delocalized over the adjacent carbonyl group, as a result the amides undergo this nucleophilic substitution reaction slowly.

But as we go towards up direction, that is towards acid chloride, in acid chloride the resonance effect is less. So it goes on decreasing from amides to acid chloride. So more the -I effect, more is the reactivity of acyl derivatives and more the +R effect less is the reactivity of acyl derivatives towards nucleophilic substitution reaction.

These are some of the examples of nucleophilic substitution reaction.

You can predict the major product in each of these examples.

In summary, we have seen different acyl derivatives like acid chloride, anhydride, ester and amide.

We have also seen nucleophilic substitution reaction of acyl derivatives and its mechanism.

Comparative study of different acyl derivatives towards nucleophilic substitution reaction.

And finally, the reasons for the observed reactivity order.

These are the references which you can refer for this particular module.

Thank you.