# Molecular Rearrangements and Reactive Intermediates in Organic Synthesis

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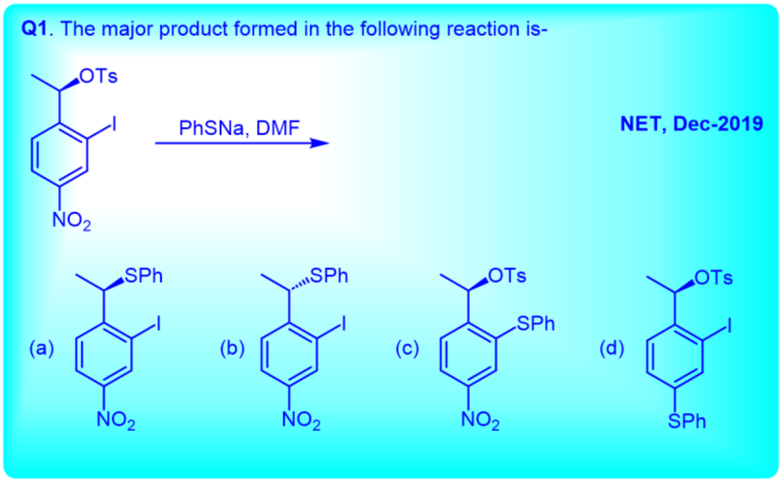
## Lecture 60: Tutorial 5

Welcome back to this NPTEL online certification course in reactive intermediates and the molecular rearrangement. So, our last couple of class, I am trying to solve several problems from the NET, GATE and the JAM exams. So, in the today's class, I am going to solve some problem from the organo-sulfur and organo-silicon chemistry. So, the first problem what we can see here, it has started with this particular compound and you have a -OTs group using PhSNa and DMF. So, if you have seen, I think, I already discussed the organo-sulfur reagents are very good nucleophile and of course, if you have a Na if you have SPh- then that is, it will be even better nucleophile this is going to take part in a $S_N2$ reaction.

So, back side attack is going to take part. So that, it is going to generate you the corresponding product where you can write -SPh. So, this will be the corresponding product. If you see among this option this cannot be the correct answer.

So, this is going to be the correct option here the option B.



**Q1**. The major product formed in the following reaction is-

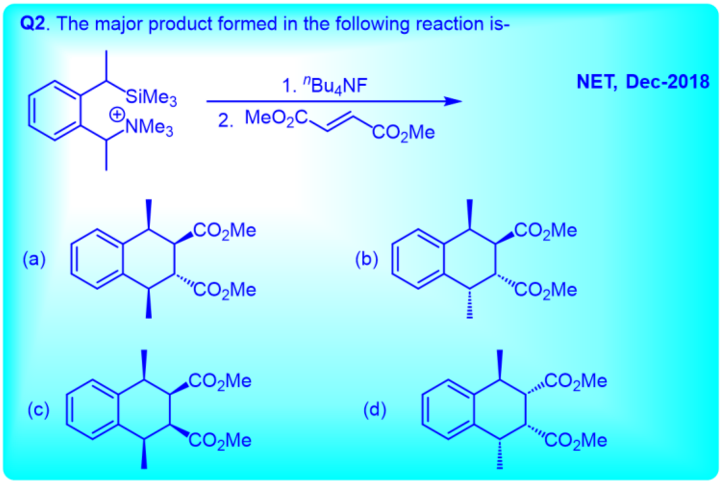
**NET, Dec-2019**

Ans. b

So, let us move to the next problem here. The major product formed in the following reaction is. So, what is going to happen, if you start with this compound and treat with $Bu_4NF$. So, if you use the TBAF then what is going to happen here? If you remember we talked about that the $F^-$ is going to attack to the Si through a pentavalent, through it will form a pentavalent compound at the beginning and then that will allow cleavage of the C-Si bond to generate a corresponding carbanion and now you have a leaving group here $^+NMe_3$.

What is going to happen this can dearomatize the ring to get rid of this $-NMe_3$ to generate this. So, this generate some sort of a diene species are here of course, we can see a diene here with 2 -Me group in the terminal position a symmetrical one. Now, if you react it with this so, you can see this is a diene and this is clearly a dienophile. Once you have a diene dienophile it will going to take part in a [4+2] cycloaddition. So, it will take part in a [4+2] cycloaddition and if it is a [4+2], what is going to be the product instead of writing that, I think can write this way. So, you will have a 6-member ring here and they are facing in the same side this -Me, they are approaching to the same phase.

So, these two-ester group are trans to each other. So, that will also reflect in the product. So, this is going to be your answer here. Now, if you look into all the different answers here, I think this has to be correct here that is not correct here also that is not correct and here they put both the ester on the same side, but we started with the trans. So, this is going to be the right answer the option A.



**Q2**. The major product formed in the following reaction is-

Ans. a

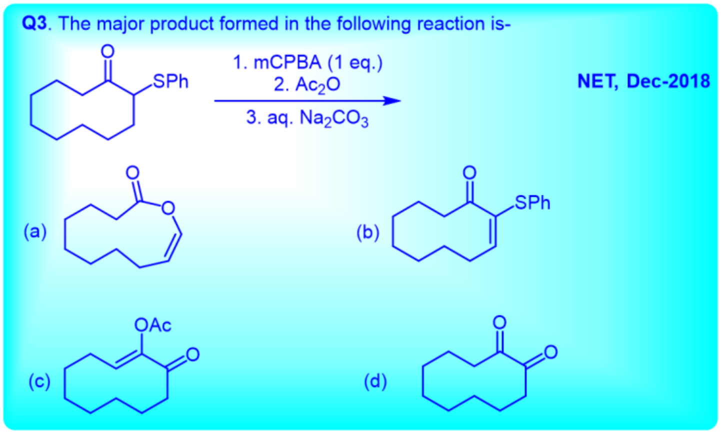
So, going to the next problem, here what will be, I think, we talk about this is a very important reaction. Once you have this -SPh group, we treat with mCPBA. What is going to happen? It is going to oxidize to the corresponding sulfide to a sulfoxide.

So, you will get a -SOPh. Now, we treat with $Ac_2O$. So, it can I think if you remember the Pummerer rearrangement, I talked about in the class.

So, once you have this, let me not take care of everything, I am just going to draw this for simplifying the problem you have. So, we can write SO, as if you remember $S^+$-$O^-$, I already discussed in the class that the S-O have an O is more electronegative, it can take the electron density towards the O. So, you will see more electron density on the O and now you have $Ac_2O$ which will be nothing, but $CH_3COOCOCH_3$. So, this $O^-$ can attack here to get rid of this in CH3COO$^-$ to form. I am not drawing the entire part, that is why I am writing like that.

So, I hope you have no problem with that again I think sulfur is a + and this can now allow you and you have this -OAc$^-$ which can come back to take this H and allow you get rid of the OAc to generate some sort of a thiol species and again you have $Ac_2O$ in the medium so that means you have acetate, this can attack here and if you remember once you have this species, there will be a protonation & another acetate and I think you are going for aq. $Na_2CO_3$. So, the $H_2O$ can attack here to take you to some species like this. and that can finally, form the corresponding diketo compound.

So, you end up forming a corresponding 1,2-dicarbonyl compound. So, if you look into all the options, so, you can see here the product will be 1,2-dicarbonyl compound, this is not the correct option, B is not correct, C is not correct, the D is the correct option because you can see there is 2 different carbonyl compound 2, there is 1,2-dicarbonyl compound. So, I think, I already talked about this the Pummerer rearrangement in the class, I talk about the mechanism. So, please practice you will be expecting more problems in the exam.



**Q3**. The major product formed in the following reaction is-

1. mCPBA (1 eq.)
2. $Ac_2O$
3. aq. $Na_2CO_3$

**NET, Dec-2018**

Ans. d

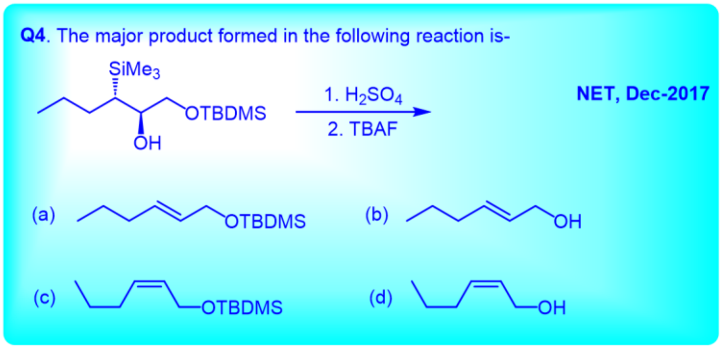
So, what will be the major product formed in the following reaction? If you remember, we talked about this reaction and once you have this, if you remember the starting material for this reaction, this is the Peterson olefination problem.

So, clearly if you understand that this has started forming by the reaction of a carbanion from the α to the Si with any reaction with the corresponding aldehyde, correct? That reaction, actually generate this silanol and once you have this, you treated with $H_2SO_4$ and TBAF. So, what is going to happen if you treat with $H_2O$ suppose in this compound? So, I talk about the beta effect of Si, if you forgot then you should definitely go back. So, they are trans. So, you have a $CH_2$ and then -OTBDMS. So, now you have a $H_2SO_4$ that can protonate this as well as you have a σ bond between C-O that will have a σ* orbital here. So, this can get electron density from the C-Si sigma.

So, C-Si σ bond electron density to the C-Si σ* orbital. So, this can make the C-Si bond weaker. So, $H_2O$ now can attack here, Si forms a double bond between the C-C get rid of the water. So, that will allow you through anti-elimination happening here, that can allow you to generate a double bond which is trans. Now, you have this -OTBDMS and you treated with TBAF.

So, again this is a -TBDMS. So, you have a Si which is having a dimethyl and a t-Bu group here. So, with O, that is the -OTBDMS, I am telling this in several classes. So, what is going to happen you have a $F^-$ is going to attack here. Again, you can see its formation of a pentavalent Si and then there will be cleavage of the Si-O bond to end up generating the corresponding alcohol. So, you will be generating corresponding allylic alcohol.

So, let us look into all the options your -OTBDMS cannot be survived. So, option A is not correct, option B is correct because you can see the allylic alcohol is forming neither C or D is correct. So, B is the correct option.



**Q4**. The major product formed in the following reaction is-

**NET, Dec-2017**

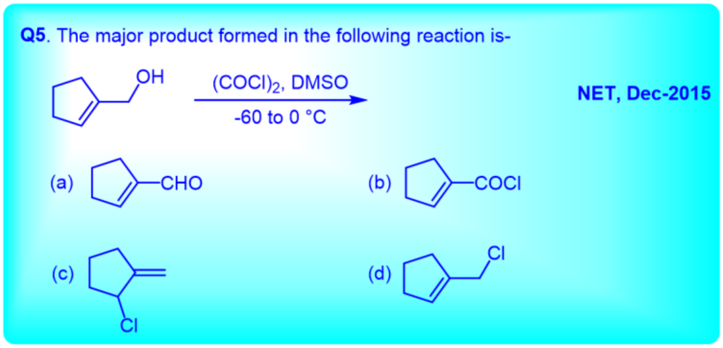
Ans. b

So, let us go to the next problem here. So, what they are asking, you have this allylic alcohol you treat with the $(COCl)_2$ and DMSO.

So, if you remember with activated DMSO we are talking about an oxidation reaction of the allylic alcohol, but what you have $(COCl)_2$ and DMSO. If you remember some reaction at -60° that is Swern oxidation, I already discussed in the class. So, if you remember in Swern oxidation, we can consider DMSO as a + and -. So, this can react with $(COCl)_2$. So, what is going to happen here? This $O^-$ can attack here.

This will come back to get rid of Cl, and S has a + charge here then what is going to happen you have a $Cl^-$ which can attack here then you will be forming a $CO_2$ and a CO. So, what are you getting out? You are getting out $-CO_2$, -CO to generate this activated species. This sulfonium is going to react with your alcohol here, that is the next step of this reaction. So, alcohol is coming and attacking getting rid of the $Cl^-$, but the problem happened after the next step, if you remember the mechanism your base has to come and deprotonate to form the ylide that can able to abstract the α to the alcohol H and form the corresponding aldehyde. But because you do not have that, now this becomes an activating agent and you have a $Cl^-$ in the medium, this can come and go for $S_N2$ reaction.

So, instead of going for an alcohol oxidation, you will end up generating a corresponding allylic chloride. So, you generate corresponding allylic chloride as a product. So, now if you look into this cannot be the answer neither the B or C, so the D is going to be the correct option here. So, if you remember if you do not have a base in the Swern oxidation you end up generating corresponding allyl chloride.



**Q5**. The major product formed in the following reaction is-

NET, Dec-2015

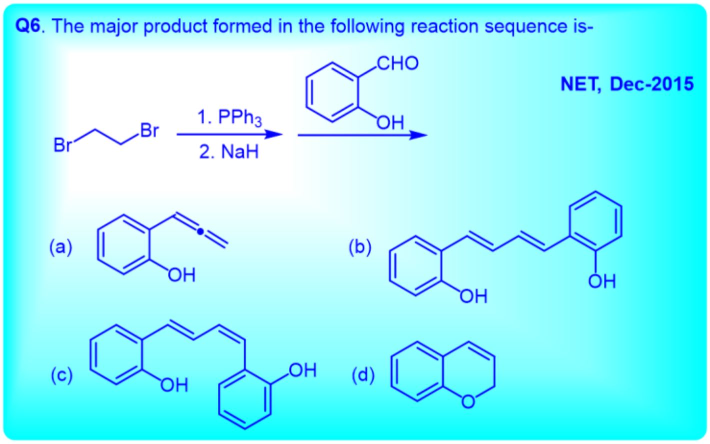
Ans. d

So, what will be the product in this reaction? First thing, you use this alkyl halide, you use $PPh_3$.

So, if you use $PPh_3$, alkyl chloride, you remember these are very good nucleophile. They can go for a $S_N2$ reaction to form this compound called $PPh_3^+Br^-$. You see NaH, so they can able to abstract this acidic H to generate a P ylide and now you are taking this ylide and reacting with a benzaldehyde. So, if you remember in this reaction what is going to happen, it is going to generate an olefin here and again these are unstabilized ylide. If you react with the unstabilized ylide then you end up generating this compound here.

I think, I already talked about this. You know the mechanism of this because if you remember you have ylide then it will come and form some sort of a bond like this you have P-O bond and then you will be able to form a double bond and a $PPh_3$=O as a byproduct. So, this can form the oxo-phosphonate in intermediate and it will cleave it and go. So, that is why you end up forming a *Z*-olefin as if you remember an unstabilized P ylide react with the corresponding aldehyde to form a corresponding *Z*-olefin. So, you end up a *Z*-olefin, you have a OH here you have base in the medium.

So, this can able to go for a $S_N2$ reaction that will generate you to this product. So, now if you look into all the different answer this cannot be correct neither B or C, D is going to be the correct option here. So, first there is a Wittig olefination and then there is an internal cyclization through a $S_N2$ reaction of O.


**Q6**. The major product formed in the following reaction sequence is-

**NET, Dec-2015**

Ans. d

So, moving to the next problem what we are learning here in this reaction you have α, β-unsaturated carbonyl compound, you are treating with this sulfoxide. So, you have that. So, you have a sulfoxide here and then you have a NaH. So, that can able to generate sulfoxonium, if you remember I talk about in the previous class, this will generate a stabilized sulfoxonium ylide.

You have a NaH, this condition can generate this corresponding sulfoxonium ylide which is a stabilized ylide. So, stabilized ylide will go for a 1,4 addition that means this $CH_2$ - can go for a 1,4 addition here.

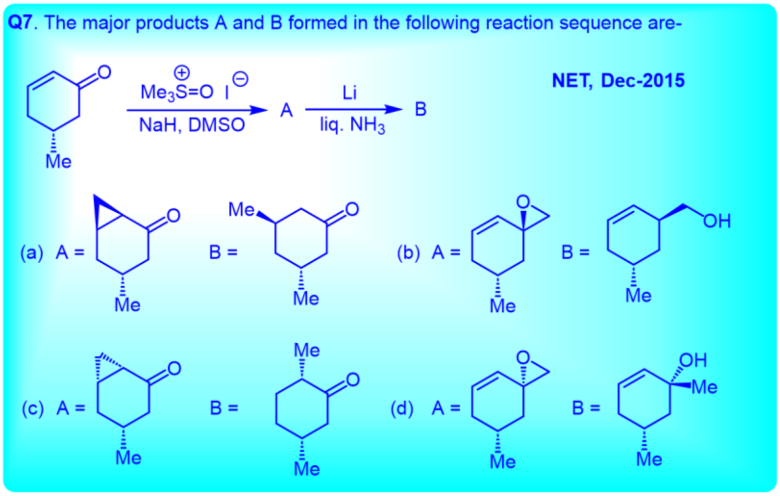
What is going to happen if it will go for 1,4-addition, we will come back to the stereochemistry in a minute. $CH_2$ and then $SO^+$, this will come back and going to react here to get rid of this. You have to remember that there is a -Me group here. So, this will try to avoid the steric to generate a product like this, there is a cyclopropane going to form, but in the opposite direction. And, then we can clearly explain this type of reactivity from this transition state. So, you can think about this is the corresponding carbonyl.

Now, you have the -Me group which is in this position. Let me see the -Me group is one C apart. So, you can have a -Me group here 3 hydrogen of the methyl group, it could be above or below. So, if you have a -Me group below then so, I have drawn above. Let me draw it below, according to the stereochemistry here. So, I think it is fine whatever I am doing, I am just trying to explain you if you have a -Me group in this space then the cyclopropane, the nucleophile is approaching this sulfoxonium ylide, cannot happen in this space, due to steric. So, it has to happen from the opposite space.

That means, the corresponding cyclopropane going to form the other phase. That means, you will be end up forming this particular product not the other one, where the cyclopropane is in the same side of the -Me. So, we got that answer now if you look into all the different answers this one seems correct neither this one, not this one either. So, now if you look into the next answer what is going to happen, you give single electron reduction, reason the Li and liq. $NH_3$.

Li and liq. $NH_3$ do the ring rupturing of the cyclopropane. So, to generate a -Me group here. So, you will be forming a carbonyl group that is going to cleave the cyclopropane to form this compound. Again, whatever mechanism this is happening, this can happen either through first reduction of the carbonyl forming a $O^{\cdot}$. Formation of $O^-$ and a $C^{\cdot}$ that can come back here and form a radical form a $CH_2^{\cdot}$ here and that can take another electron to make a $CH_3$ and then finally, this can come back to the corresponding carbonyl.

So, that way it will end up forming this.



**Q7**. The major products A and B formed in the following reaction sequence are-

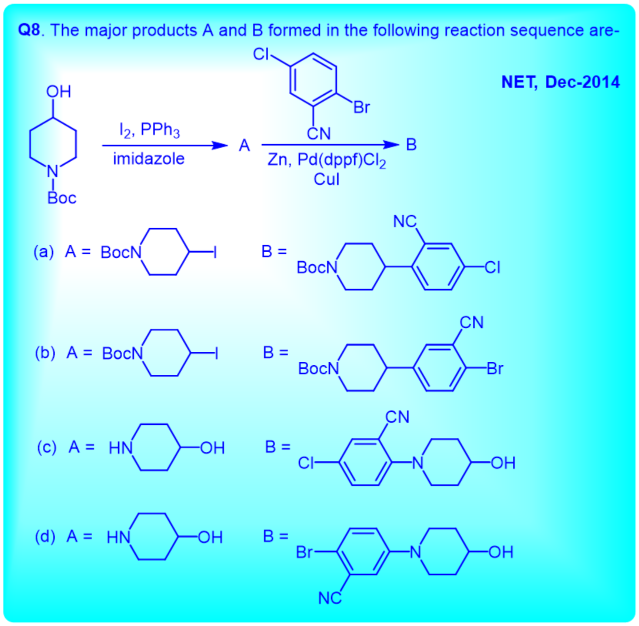
**NET, Dec-2015**

Ans. a

The next problem here you have an alcohol here, a secondary alcohol you treated it with $I_2$ and $PPh_3$ with a base. If you remember this reaction, I cover in the class, is the Appel reaction. So, what is happening here you have alcohol and you have a $PPh_3$ with $I_2$. So, $PPh_3$ can react with $I_2$ to form $PPh_3I^+$ and $I^-$. This $I^-$ can able to take this H to form $O^-$, that can attack here to get rid of this to form this $-OPPh_3+$.

Now you have an $I^-$ which come back, attack here and get to the corresponding. So, you will be replacing this alcohol by I and now once you treat. So, you have this corresponding Zn reagent and then using Zn, Pd(dppf)$cl_2$ and you have a corresponding aryl bromide. The Zn can able to make corresponding Zn iodide here and now it can able to go for a Negishi coupling. You have aryl bromide and you have a Pd(dppf)$cl_2$. I think, I already discussed this in the class that this can go for a Negishi coupling to include the corresponding product, Br will be replaced here.

So, you will be end up forming a product where one aryl ring will be introduced here, where you will have a CN and then you have a Cl here. So, if you look into all the options, this is the correct option in every case. So, among options A and B have a correct option for A, but here only in case of B you see the correct option because the CN will be in the next to that Br. So, this is nothing but Appel reaction and a Negishi coupling to get to the corresponding.



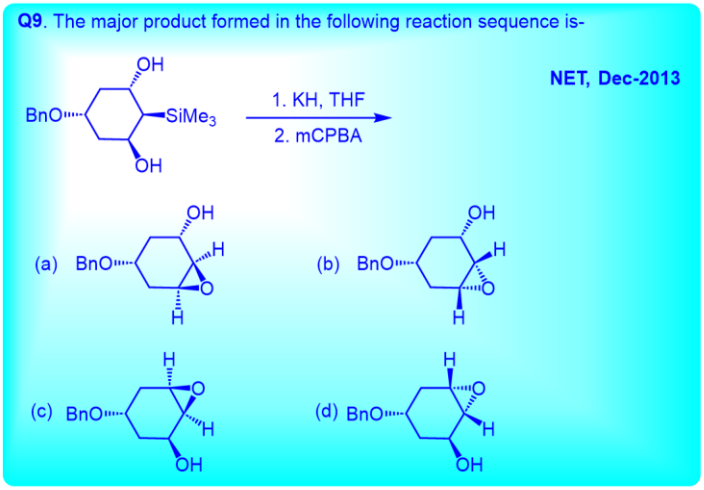
**Q8**. The major products A and B formed in the following reaction sequence are-

**NET, Dec-2014**

Ans. b

So, what is the major product in this reaction? Again, you are using a KH and you have a Si and you have an OH, they are in the vicinal C. So, what is going to happen, the KH become corresponding $O^-$ form O-Si bond then they are going to take part in a syn-elimination.

I think, if you remember in the Peterson olefination, there is a syn versus anti and this is going to go for a syn-elimination and that will end up forming the corresponding olefin. So, you will be able to form this corresponding olefin from there. So, it means you have a double bond here, you will have an OH and you have an O-benzyl. Now you treat with mCPBA, what is going to happen? If you have an olefin here, it is going to go for an epoxidation. Now you have an OH group here which can act as a directing group, remember directing group epoxidation that means the epoxy will be forming in the same side.



**Q9**. The major product formed in the following reaction sequence is-

**NET, Dec-2013**

1. KH, THF
2. mCPBA

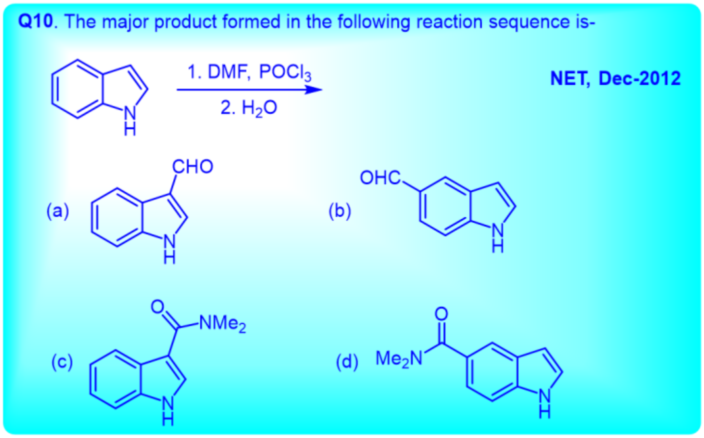
Ans. b

So, let us go to this particular problem here. So, here we are talking about again a reaction of an indole, you have DMF and $POCl_3$. So, what are you going to get the product? So, I think, this is a very important reaction, I talked in the class, is a Vilsmeier-Haack reaction. So, in the Vilsmeier-Haack reaction what is the reactive intermediate? Let us try to go through the mechanism again. You have this N, N-dimethyl formamide and you have this $POCl_3$. So, what is going to happen? You can think about this reacting to the O, getting rid of the Cl, then formation of this iminium species with $OPOCl_2$ and then you have a $Cl^-$ which is going to come back and attack here and this is going to generate with a Cl and with $OPOCl_2$.

So, this is getting a better leaving group. So, this N lone pair is going to come back to get rid of this and it will go to generate. So, this is the reactive intermediate in the Vilsmeier-Haack reaction. Now, if you have an electron rich species like indole which can react and can track an electrophile at the C-3 position. So, they can come and attack here to neutralize the charge on the N. Let me draw that, it is going to form this species and you can see there is a + on the N.

Now this H will be accepted to form so indole will come back and now you have a Cl. So, N lone pair can give electron density to get rid of Cl that can form the corresponding iminium. which is going to hydrolyze corresponding N, N-diaminum and the iminium can be hydrolyzed to the corresponding aldehyde. So, you end up generating this corresponding aldehyde in the C-3 position. So, please practice the Vilsmeier-Haack reaction, there are multiple problem that comes in the exam using the Vilsmeier-Haack reaction.

So, once you have this active intermediate, it is now going to take for a Friedel-craft type reaction to get to the corresponding product. So, this will be the correct option A not the B or C or D. So, again thank you so much, I think, this is the answer here you can see.



**Q10**. The major product formed in the following reaction sequence is-

**NET, Dec-2012**

Ans. a

Again, thank you so much for coming to the class and I hope, you have enjoyed the problems in the S and the Si chemistry.

I am going to see you guys in the next class.

Thank you.