Molecular Rearrangements and Reactive Intermediates in Organic Synthesis

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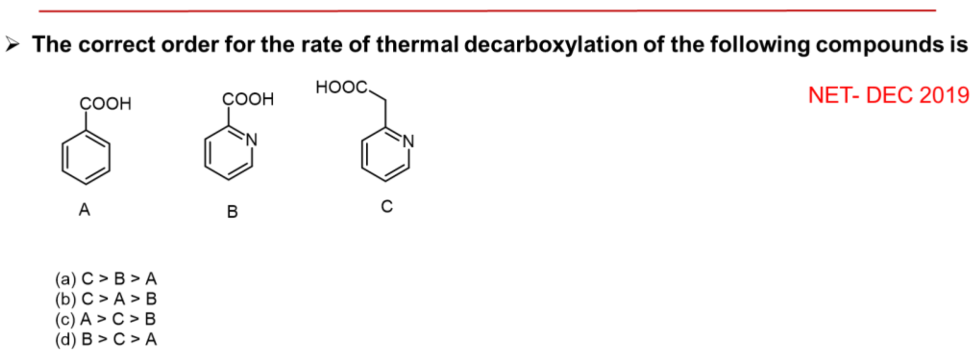
Lecture 01: Tutorial 1

Welcome back to this NPTEL online certification course in molecular arrangement and reactive intermediates. I talk about several different topic in this course if you remember I started talking about carbocation, carbanion, carbene in nitrogen chemistry followed by some of the benzene chemistry organolithium, organomagnesium, organometallic chemistry and the phosphorus, sulfur, silicon. So, the p-block element and also about the organoboron chemistry. So, in the in the following classes, so I will think there will be 5 or 6 classes. So, I am going to talk about some of the question answer which came in the different type of NET GATE and JAM exam. Because that can also make sure that you understand the material. I covered and also help you to prepare for such competitive exam. So, let's start with some of the questions.

So, first question came in the NET exam. So, you can see if the question which is saying give the correct order for the rate of thermal decarboxylation of the following compound. So, this is given as A, B and C. And now they are asking the thermal decarboxylation reaction so that means what we are talking that you will have this corresponding carboxylic acid which going to get out from here So once the carboxylic acid is going to get out what you are end up generating a corresponding carbanion So from here if you see is the CO_2 is getting out you are generating a and once from here the CO_2 will Let us write the mechanism I think if you have not followed try to understand how the decarboxylation reaction happens.

So, generally if you see the decarboxylation reaction happens by you need to use some sort of a base that will form the minus. Now you can come back here and so this can allow you to get minus CO_2 and you generate So, here you are going to form. So, this is you can see this is next to pyridine and here you are generating it is also pyridine, but so now, we have to compare them. So, that means, for predict the correct order for the rate of decarboxylation, you have to understand the rate of decarboxylation depends on the stability of this after the decarboxylation once you form this corresponding carbanion you have to understand the stability so if you try to compare them one of the important factors here once you have this type of benzylic carbanion vs this allyl carbanion what are the effect which is important here. So, you can clearly see in this particular compound we can able to draw the resonance structure.

We can able to clearly draw the resonance structure, but here we can see clearly the only effect is the -I effect and then here you do not have that. So, what we are seeing the resonance effect. Resonance will be again, the Resonance will have a better the more stronger effect compared to the the Inductive effect. So, that is why you can see the C will be decarboxylative much faster compared to B compared to A. So, the correct order will be the A is C greater than B greater than



- **The correct order for the rate of thermal decarboxylation of the following compounds is**

NET- DEC 2019

(a) C > B > A
(b) C > A > B
(c) A > C > B
(d) B > C > A

Moving to the next questions again I think the question which is asked if you have the epoxide and you treat it with BF3.

OEt₂ If you remember I talk in the class that BF3.OEt₂ adduct is a actually is a Lewis acid correct. So, now if you take a Lewis acid and again this question came in the NET 2019. So, what will be the product if you remember I think we talk about this thing in the class that once you have a epoxide and you take a Lewis acid It is going to form a plus and then that is going to open the epoxide to generate a It will be able to generate some sort of a species like that where there will be plus and there will be O with a Lewis acid. so in this particular substrates if you again the Lewis acid is a BF_3 going to bind here.

And if the epoxide going to open up, there is a two different possibility it can either open up through this way. So, that means, let me try to draw them. So, here you can clearly see that these are the methyl. Now it can open up a epoxide this way to form a plus and O with Lewis acid or it can able to from the other one where it can form a plus here and methyl. Now the question comes if you try to compare it you can see this is a tertiary carbocation this is a secondary carbocation. So, if you learn about the stability of carbocation we always talk about the tertiary will be more stable because of the number of hyperconjugations.

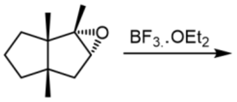
So, here then this will be the the corresponding intermediate which is going to form, one that is going to form the formation happen. So, this is the proton from here which is going to be So, now, you are forming a plus charge, there once you are forming a plus charge we cannot draw them like up and down we should not draw them I think we should draw like a straight line here So, let me draw them. So, what I was trying to show you that. So, here you have a methyl correct plus and you have once you form a carbocation now you kind of lost the corresponding stereochemistry. So, you have the O with a LA.

So, now you can see that. So, there will be a proton going to be proton abstraction going to happen because to neutralize the positive charge. So, this can give electron density the sigma bond of carbon hydrogen can be give electron density here. So, that can form this and then it is going to end up forming and now what is going to happen you can think about this as some sort of a enolate. So, this can come back and take a proton.

So, if you see there is a two methyl here now both are in the same side will not be a favorable structure. So, that is why when the protonation will be happen the protonation will be happen from the top phase. So, that the product which is going to form which will be trans. So that means, if you see that then we end up to a product here this is the one which is the answer a. The other answer if you try to see this is not even possible, clearly there is no possibility of that particular methyl to be migrate there.

So, what they are saying that there is a possibility that saying if this methyl going to migrate here to form the carbocation here. Then there is a possibility they are saying if it is going through formation of carbocation like a methyl is migrating here to so these are not the correct answer, the correct answer will be a here.

NET- DEC 2019



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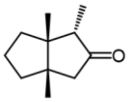

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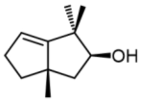

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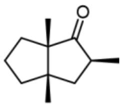

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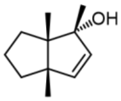


In this question predict the major product A and B formed in the following reaction so we talk about this dithione chemistry if you remember we talk about how do you form this How do you form this corresponding dithione from this -SH and then you have here you are using this corresponding formaldehyde. Now, once if you remember in the class in sulfur chemistry. I mentioned that clearly there once you use So, these are the protons are the acidic proton here. So, once you use a base like BuLi they can able to form the corresponding carbanion here.

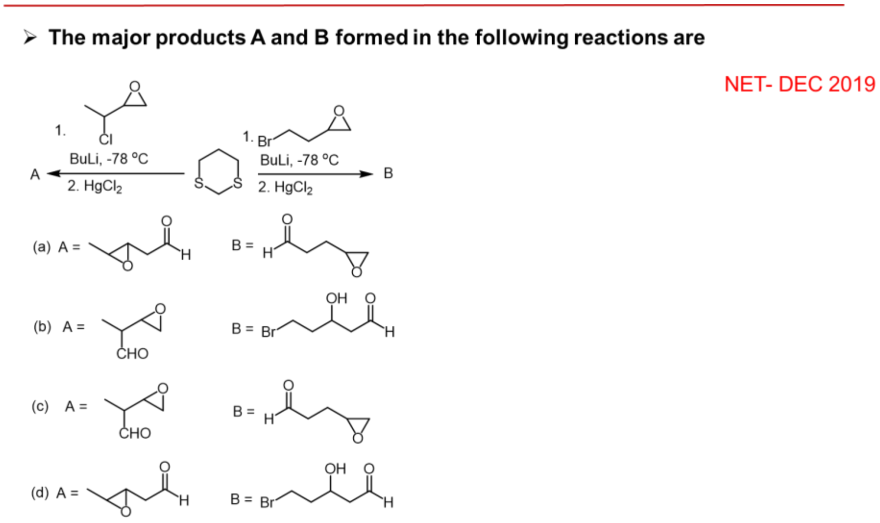
So, that carbanion can able to participate in a SN2 reaction also I talk about that and also it can take part in a epoxide opening and other reaction as well. So, here what is happening in first reaction you can see here you have a primary alkyl halide and you have a corresponding epoxide. So, here I think you can see these compounds can take part in the SN2 substrate and this is a very good SN2. is the corresponding bromide primary alkyl bromide it will take part in a SN2 reaction. So, if it is go for SN2 what will happen here? So, let me try to use a erasure.

So, let's try to see the product going to form. So, what is going to happen it is going to take part in the SN2 reaction and then what they are doing they are treating with $HgCl_2$. If you remember we use $HgCl_2$ to remove the dithione and get back to the corresponding aldehyde. So, if this will happening then you will be getting back to the So, this will be your product in this. So, B will be this is the B.

So, let us look for the products where the B is given. You can see B is given here this is the product we are asking. So, in this option number-a and option number-c this is the B is given. So, let us try to solve the answer for A. So, here you have a epoxide versus a secondary chloride.

Again you see the chloride is not a better living group not good for SN2. That's why this corresponding carbanion will be taking part opening of the epoxide. So, once this opening of epoxide going to happen, what is going to happen there is a chloride here and you open up the epoxide formation of the O minus and you have this corresponding So, Now you can see clearly this O minus will be taking part in another SN2 to get rid of the chlorine here which is going to form this compound and after that once you use $HgCl_2$ you remember $HgCl_2$ going to deprotonate this dithione and from the corresponding aldehyde. So, that means, you can end up forming this corresponding aldehyde here. So, you can see this is the structure we are finding and in the option number-d, and option number-a, having this structure which you are getting in the product.

So, now if you see option number-a, having both the correct answer for A and B. So, option-a will be the correct answer.



➢ **The major products A and B formed in the following reactions are**

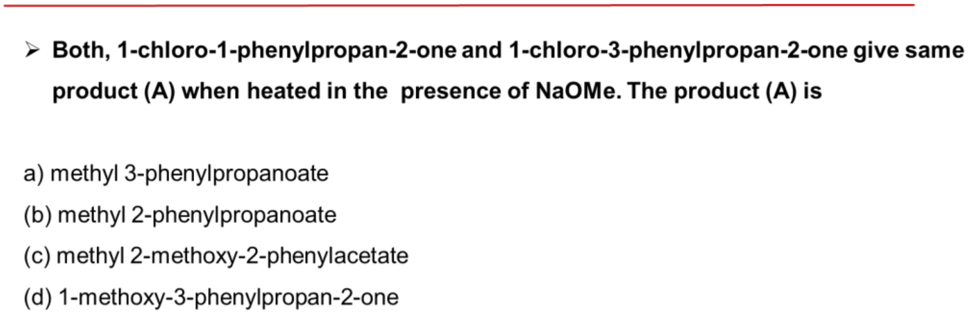
NET- DEC 2019

So, let's go to the next problem. So, here I think the problem is given that we start with 1-chloro-1-phenylpropane-2-one. So, let's try to draw them.

So, we are talking about propane-2-one. So, this is a propane and there is a 2-poison carbonyl, we are talking about 1-chloro-1-phenyl vs we are talking about a 1-chloro-3-phenyl. So, now, they are saying if you treat them with a sodium methoxide you end up giving same product A. So, what will happen if you treat with sodium methoxide here. If you remember I talk about a reaction using α-halo so these are α-halo carbonyl compound if you remember α-halo carbonyl compound treated with a base Now I am talking about a carbanion chemistry so in the carbanion chemistry you have learned this can take this proton form a carbanion it can attack here to get rid of chlorine to form this So, this can give you to the very important rearrangement reaction called Favorskii rearrangement.

So, you will be forming this intermediate now if you treat here also sodium methoxide what will happen? This is going to abstract this proton next to the chlorine this will be more acidic proton sorry this is going to take the proton next to the phenyl and then it is going to attack here because chlorine has been a very good living group. So, it is going to form the very similar intermediate here. So, you can see both are forming very similar intermediate. Now, what is the next step of the Favorskii reaction? The sodium methoxide is going to the -OMe minus going to attack here to the cyclopropane This can come back is going to form the corresponding ester there with a CH_2 minus Ph which can take a proton to get to the corresponding product. So, that's why both of these going to end up forming this same intermediate for the Favorskii and then end up forming the product same product So, now we have to find out the name for this compound.

So, it is a methyl 3-phenylpropanoate. So, if you see this is actually is a propionate correct if you give carbon number 1,2, and 3. So, this is a 3-phenyl, but of course So, this is a methyl propionate. So, that means, a methyl 3-phenyl propionate will be the correct answer it cannot be methyl 2-phenyl because the phenyl will be in the terminal position not in the internal position.



- **Both, 1-chloro-1-phenylpropan-2-one and 1-chloro-3-phenylpropan-2-one give same product (A) when heated in the presence of NaOMe. The product (A) is**

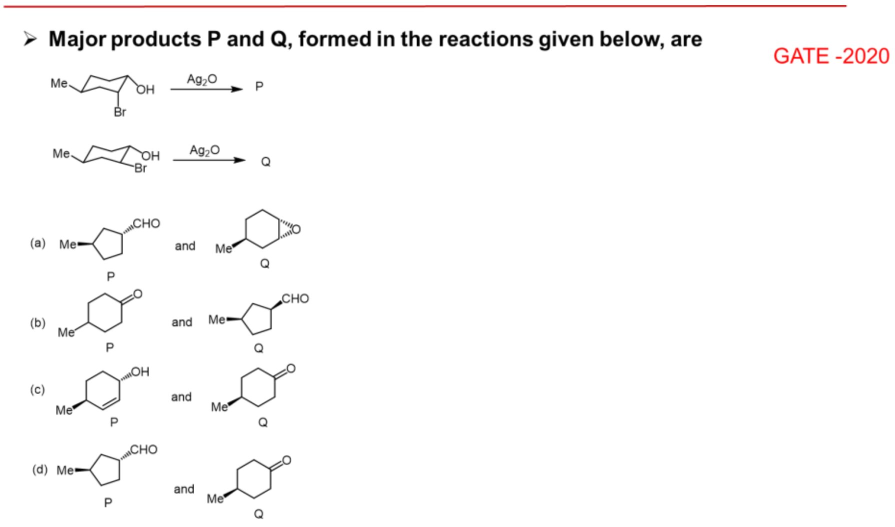
a) methyl 3-phenylpropanoate
(b) methyl 2-phenylpropanoate
(c) methyl 2-methoxy-2-phenylacetate
(d) 1-methoxy-3-phenylpropan-2-one

What is the major product P and Q from the reaction given below again this came in the GATE exam So what you are happening here you have given two different compound here and you are treating with the corresponding silver oxide so now we try to learn about this chemistry what is happening here. You have this methyl in the equitorial position bromine in the axial position Now if you treat with silver what is going to happen silver with the secondary bromide is slowly started forming a bond with the silver and bromine and this carbon bromine bond going to get weak and it is slowly going to develop a carbocationic character.

So, if that is happening then if you remember that generally if you have a carbocation formation happening here then So, then to stabilize that this is the sigma bond can give electron density. So, that means what is going to happen here if you forming a corresponding carbocation, forming a carbocation here then this is the bond which is the anti-periplanar to this. So, they can the CH going to this can end up forming you to the corresponding cyclohexanone So, we clearly understand this will be the product if you start with the So, this will be the product here first one and let's try to show this will be the P. So, you can understand P will be this one. Now let's try to figure out that what will be the structure for the Q.

Now the question comes once so this bromine was in the axial now question come in the same substrate if the bromine will be in the equitorial what will happen? Again you can think about here also the silver is going to form a bond here correct. Now for the and then that is going to generate some sort of a δ+ character. So, if you see that these are the bonds like these carbon-carbon bonds and these carbon-bromine bonds are anti-periplanar to each other. So, what will happen here this sigma bond electron density will be given here to allow this carbon bromine bond to get out that can end up formation of and think about this bond is going to attach here Here it will going to it is going to form a OH with a positive charge and we have a methyl here, so this will end up forming a 5-member ring with a methyl group. And again you can see clearly that the methyl is up and you have a corresponding CHO which is going to form here So, this will be your actually axial bond here.

So, let me just go back and fix it. So, what is going to happen? Once you form this one, now you can clearly see that this bond going to give electron density to this anti bonding orbital of this carbon bromine bond. So, this can allow formation of this compound here. So, this will happen in the same side, but here there will be a positive charge here on this carbon and this can able to. So, this oxygen lone pair can give a electron density can convert to the corresponding aldehyde. So, you can see this will be the correct answer for the Q.



➢ **Major products P and Q, formed in the reactions given below, are**

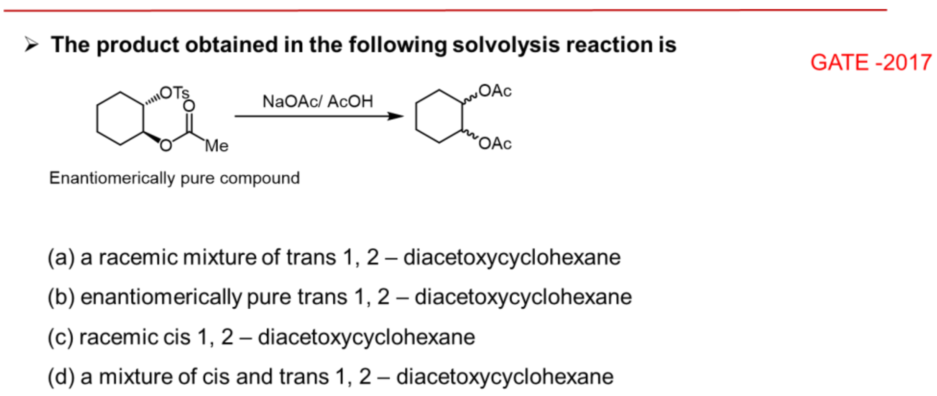
GATE -2020

The product obtained in the following solvolysis reaction again came in the GATE exam So, you started with the enantiomerically pure compounds and they are asking that if you treat sodium acetate and acetic acid you end up forming a two acetyl group here. There are four option one they are saying a racemic mixture of trans 1,2-diacetoxycyclohexane or enantiomerically pure trans or the racemic cis or a mixture of cis and trans. So, what will be the what will be the correct answer here? So, let's try to draw them first we are talking about a 1, 2-disubstituted. Now, if you think about drawing them like both of them are. So, you have a -OTs here and then you have a -OAc here Now, you can think about from there once they are in the both are in the equatorial they cannot do anything any reactivity here you cannot, but once you go for a ring flip again you will be seeing that So, now your -OAc will be here and you will have your -OTs.

So, we can also we can switch them also I think that way it will be better we can write -OTs here and that can help us to understand the question even better. you have -OTs here and then you have a O acetate. So, now, once they are in the di-axial position of course, that will not be the more stable one. So, you will see the equilibrium will be always in this side. ok But once there axial position now you can expect some sort of a neighboring group participation.

Now this oxygen lone pair can attack here to get rid of the -OTs group. Once that is happening so you started with a enantiomerically pure compound. So, it is a trans and now you can see here that let me try to draw the next step. So, you are forming some sort of oxonium here, sometime it is very difficult to deal with this. I think I can try to redraw them shapes are not looking great so now if you think about there is a formation of oxonium and so both of this oxygen is getting rid of the the -OTs gr. Now if you try to think about this one what is the structure actually this is both of them are up and there is a plus on the oxygen. So, now, if you think about this particular intermediate which is forming here after the NGP happening now you can clearly see that this particular intermediate this particular double bond kind of on the two on the on actually this both the oxygen actually sharing these charges. So, you can think about this can have a sigma plane which is passing through this Now, if the nucleophile can attack suppose now what is going to happen you have a sodium acetate correct. Now, if you have a sodium acetate attacking from this side and this side suppose it is attacking from A from this side attacking from here is B you end up forming a compound let's try to draw them if this is the A then what is happening there is SN2 happening. So, both cases you are seeing SN2 then you will be So, this is via A and once you are attacking via B.

So, what we are seeing that at the end what you are forming A and B they are enantiomer to each other. So, actually there is a 50-50 probability attacking from the either side that is why you end up forming a racemic mixture of the trans compound. So, the option one will be the correct answer



➢ **The product obtained in the following solvolysis reaction is**

GATE -2017

Enantiomerically pure compound

(a) a racemic mixture of trans 1, 2 – diacetoxycyclohexane

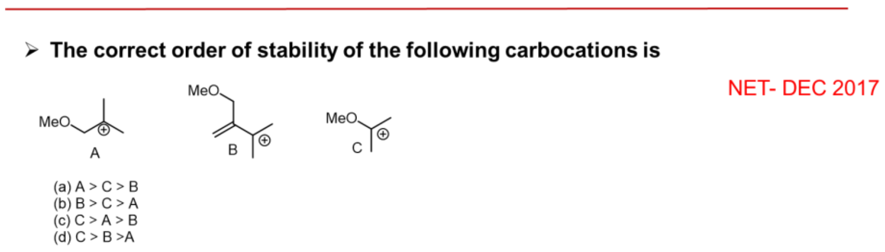
(b) enantiomerically pure trans 1, 2 – diacetoxycyclohexane

(c) racemic cis 1, 2 – diacetoxycyclohexane

(d) a mixture of cis and trans 1, 2 – diacetoxycyclohexane

Correct order for the stability of the following carbocation is again here we are talking about stability of A vs B vs C. Now let's try to understand what is that. So, these are talking about the carbocation correct.

Now if you talk about this particular carbocation there are -CH_3, -CH_3 and there is a -CH_2. So, there are total 8 hyperconjugation can be. So, there are that many CH bonds are there that that can take part here you have only 6 proton can take part in the hyperconjugation and then here you have a 6. So, if you look into that then you might be thinking that A will be more stable on the basis of hyperconjugation, but you are missing something else that there is a oxygen o-methoxy. So, that non-bonding orbital can be donate to the empty P-orbital here So, this non-bonding orbital donation is going to stabilize this one way more compared to this hyperconjugation. And then there is one more effect in the B which is this is a allylic. So, these are called allylic carbocation. If you have allylic carbocation this can be resonance stabilized as well. So, you can try to draw them like this that it can come here to go stabilization So, there is a resonance stabilization for B, in case of in case of C you are seeing the very important stabilizing factor is the non-bonding electron is given to vacant p-orbital So, that is why the C will be way more stable compared to B and compared to A which has only the hyperconjugation. So, that is why the answer will be d.



- **The correct order of stability of the following carbocations is**

NET- DEC 2017

(a) A > C > B
(b) B > C > A
(c) C > A > B
(d) C > B >A

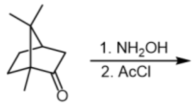
Major product in the following reaction is Once you see a carbonyl compound NH_2O is acetyl chloride you can think about the Beckmann fragmentation or Beckmann rearrangement. So, now, what is going to happen here let's try to see from the product we can clearly understand there is a CN here and CN formation happen only from the Beckmann fragmentation. That means first thing is and again if you remember the Beckmann fragmentation only happen at the time when you have a stable carbocation formation possibility. So, first thing formation of the reaction of hydroxylamine with the ketone will generate the N-OH which will react with the acetyl chloride to form -OAc. So, now you can see there is generally what you are seeing here that if there is a possibility of a carbocation generation which is stabilized then it will go for that route instead of the Beckmann rearrangement.

So, that is why this bond going to get cleaved to get rid of the OAc that will generate the corresponding CN and a carbocation here and of course, I think we missed the methyl group here. So, there is a methyl here. So, means you are generating a corresponding tertiary carbocation. So, after that what is going to happen there will be a proton abstraction going to happen from here to neutralize the corresponding carbocation that will end up you to this product. So, if you try to give them a numbering here if you have this methyl is 1, 2, 3 and then 4 and 5.

So, this is the 5 and then this is the 4, 3, 2 and 1. So, this will be the your correct structure So, here the option-a will be the correct structure not the option-b or the option-c because here one of the things you might be thinking sir why not happening from the methyl because if it is happening from the methyl you will be generating here a tri-substituted olefin correct, but here you will be generating a exocyclic one with a just a olefin which will be a disubstituted one. the here it is a terminal in this side there will be only H here. So, and then there will be two substitution in this side correct. So, here I think this will be way more stabilized one compared to this one that is why this will go for hydrogen abstraction from the internal position

- **Major product in the following reaction is**

NET- DEC 2017



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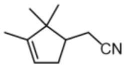

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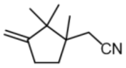

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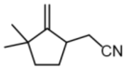

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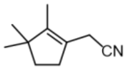

For the four reaction given below the rates of the reaction will vary. So, they have given the order they have actually arrange them in the highest vs the lowest.

So, if you compare between 1 and 2 and then compare between 3 and 4. Let's try to compare between 1 and 2. So, if you see from the starting material to product it is clearly understandable that some sort of a nucleophilic attack happening from the O minus some sort of a nucleophilic aromatic substitution type reaction happening for formation of and formation of a species like this and then what is going to happen this is going to come back and it is going to break this carbon nitrogen bond. Once it is going to break the carbon nitrogen bond it is going to get you to the corresponding product. So, now you can clearly understand if this is the reaction it is happening then this negative charge going to be more stabilized if there is a nitro group(-NO_2) there.

So, that is why the one will be reacting faster compared to 2 that was correct. Let us try to understand about 3 and 4. 3 and 4 there is a different type of reaction is given I think we have learned about some sort of a non classical carbocation when I talk about that carbocation that part I talk about this And also I talk about very similar example during that time now they are taking there is a aromatic group with a nitro here Which will be electron withdrawing and you have -OTs. So, what is happening again the once you have a olefin here the π-density they can give electron to this corresponding σ*-orbital to get rid of the. So, the -OTs can be out from here and now after the OTs is gone it is as you use the π-cloud.

So, that can the π-bond. So, that can able to generate. So, there is could be a bond between here and here, there will be plus charge here or could be a possibility that it can form a bond between these and these carbon and form a positive charge there. So, generally people write this as a 3 center 2 electron bond. So, you can write a $\delta+$ here you can think about the positive charge is actually around this 3 carbon . So, now if there is a positive charge here if you have a aromatic ring with a nitro group that positive charge will be destabilized So, that is why if you do not have the nitro group then that will be then that will be reacting faster compared to one with the nitro group.

So, despite having the nitro group this will be reacting slower. So, that means, in this case of this particular reaction of compound 4 will be faster compared to the 3. So, we have to look for the option the 4 greater than 3. So, the d will be the correct option here.

- **For the four reactions given below, the rates of the reactions will vary as**

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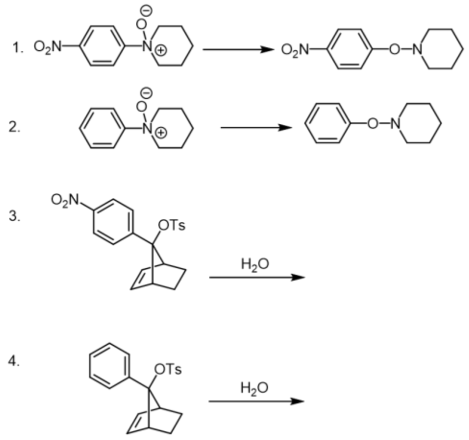

(a) 1 > 2 and 3 > 4
(b) 2 > 1 and 3 > 4
(c) 2 > 1 and 4 > 3
(d) 1 > 2 and 4 > 3

Correct order for the rate constant for the following reaction it will be very similar I think here what is happening you can see the nitrogen is attacking here going for some sort of ipso substitution here for that you can understand that the Z.

So, they are giving three different group here CF_3, CH_3 vs OCH_3. So, of course, what you want here you want some sort of electron withdrawing group. So, that once the nucleophile going to attack that will generate anion here that anion can be stabilized. So, for that you want Z equal to electron withdrawing group that means, $-CF_3$ will be reacting faster compared to the $-CH_3$ and compared to the $-OCH_3$. So, this will be the order for this reaction. So, you can see the option will be the correct option it is very similar to the previous problem.

- **The correct order of the rate constants for the following series of reactions (Z = $CF_3/CH_3/OCH_3$) is**

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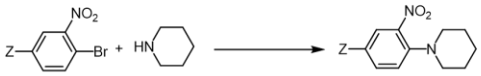
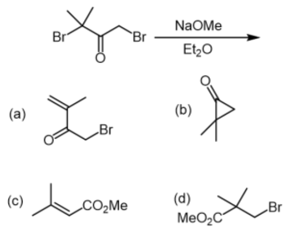


(a) $CF_3 > CH_3 > OCH_3$
(b) $CF_3 > OCH_3 > CH_3$
(c) $OCH_3 > CF_3 > CH_3$
(c) $CH_3 > OCH_3 > CF_3$

The major product formed in the following reaction. So, here we can see these are a α-halo carbonyl compound, but there is two different halogens you treat with sodium methoxide. So, we we know that this could be a problem for the Favorskii rearrangement. So, what is going to happen here now you can see one side there is no proton other side there is a sodium methoxide can able to generate this carbanion which can attack here to form this sort of intermediate let's try to draw the intermediate here. So, we will form the corresponding cyclopropane where one side we have a dimethyl and one side we will have a Br. So, sodium methoxide going to open up here, there is a Br here so you can see this is going to come back here and this is going to generate one negative charge next to the methyl This will be generating a minus we allow the elimination to happen to get to the corresponding product. So, if you look for the this is the c will be the correct option here.

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

NET- DEC 2015



So, thank you so much and I hope you guys have learnt some of the problems of this carbocation and the carbanion chemistry and thank you so much and I hope you will come back to the next class. Thank you.