**Transcriber's Name Angela**

# Pericyclic Reactions and Organic Photochemistry

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## Module No. #03
## Lecture No. #15
## Pericyclic Reactions – Cycloaddition reactions – Tutorial Session 2

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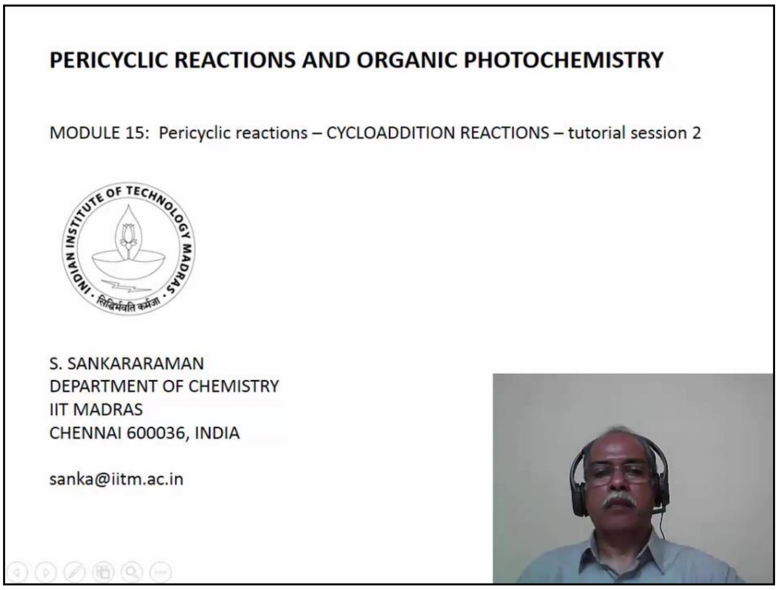

PERICYCLIC REACTIONS AND ORGANIC PHOTOCHEMISTRY

MODULE 15: Pericyclic reactions – CYCLOADDITION REACTIONS – tutorial session 2

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Hello, welcome to the tutorial Session Two. In Tutorial One, we consider the Electrocyclic reaction. In this tutorial, we will consider certain problems concerning the Cycloaddition reaction. Now, in the Pericyclic reaction, there are large number of problems, that one can come across, with respect to assignments. And the final examination, and so on. So, this kind of tutorial sessions are going to be extremely useful to follow, so that you can do well in your final examination, as well as in the assignment problems.

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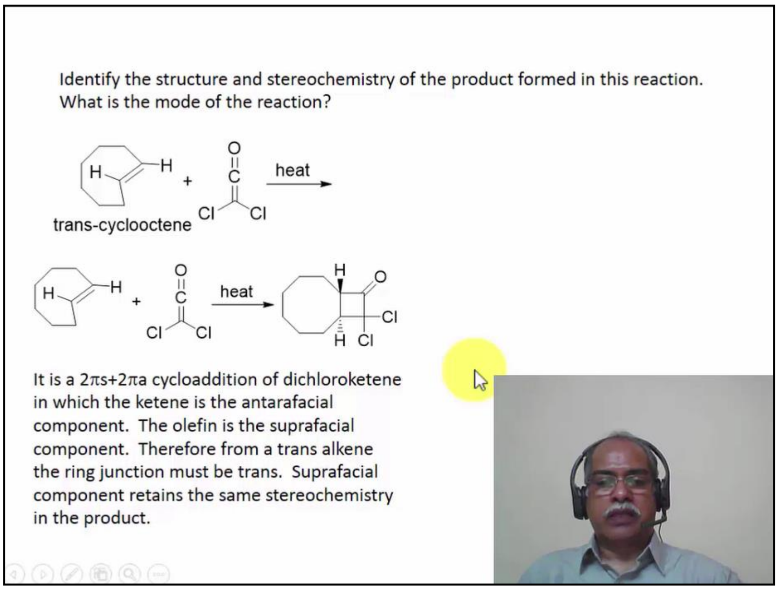

Identify the structure and stereochemistry of the product formed in this reaction. What is the mode of the reaction?

It is a $2\pi s+2\pi a$ cycloaddition of dichloroketene in which the ketene is the antarafacial component. The olefin is the suprafacial component. Therefore from a trans alkene the ring junction must be trans. Suprafacial component retains the same stereochemistry in the product.

Let us start with problem number one. The question is, identify the structure and stereochemistry of the product formed in this reaction. What is the mode of the reaction. This is the question. Now, this is Trans Cyclooctene, undergoing a Cycloaddition reaction with Ketene. In this particular case, Dichloro Ketene, under thermal condition. Please recall, the Dichloro Ketene Cycloaddition reaction with Olefins. It undergoes a Suprafacial-Antarafacial 2PI-2PI Cycloaddition reaction.

Therefore, the answer is that, the reaction involves the Trans Cyclooctene as a Suprafacial component, and the Dichloro Ketene as the Antarafacial component, resulting in the formation of the Dichloro Cyclobutanone derivative, which is this particular derivative. Please note that, the stereochemistry is Trans in the Olefin, and that retains its stereochemistry as Trans in the final product also, indicating that the Suprafacial component is actually the Olefin component, in this particular case. And, the Ketene component is a Antarafacial component, as far as the Suprafacial-Antarafacial components of the Cycloaddition partners are concerned.

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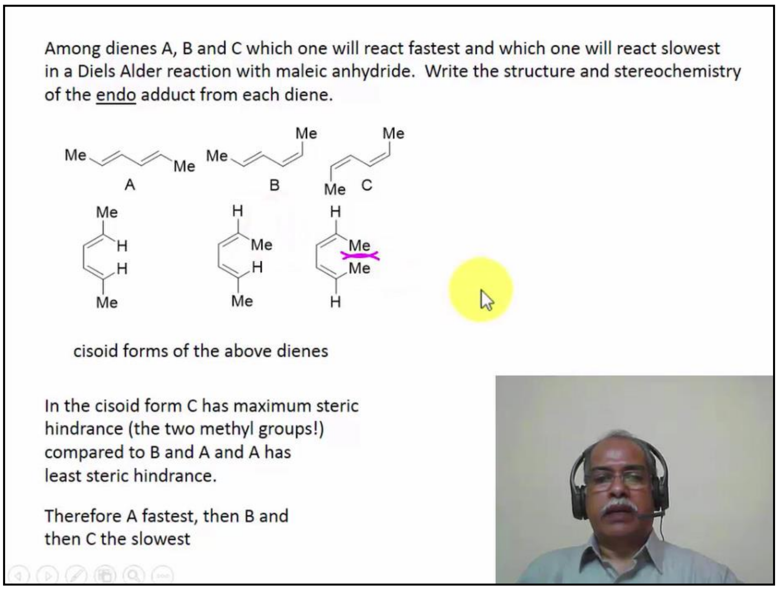

Among dienes A, B and C which one will react fastest and which one will react slowest in a Diels Alder reaction with maleic anhydride. Write the structure and stereochemistry of the endo adduct from each diene.

cisoid forms of the above dienes

In the cisoid form C has maximum steric hindrance (the two methyl groups!) compared to B and A and A has least steric hindrance.

Therefore A fastest, then B and then C the slowest

Now, let us consider problem number two. There are three structures of the Diene A, B, C are given here. There are all diastereo isomers, in terms of the stereochemistry of the double bond, that is given. Now, among the Dienes A, B, C, the question is, which one will react faster, and which one will react the slowest, in a Diels-Alder reaction with Maleic Anhydride. Now, write the structure of the product, and the stereochemistry of the, specifically the Endo adduct arising from the, each one of the Diene. Now, these are all written in the Transoid form.

So, one should transform the Transoid form into the Cisoid form, which is shown here. Now, if you look at the stereochemistry of this double bond, this is E, and that is retained as E. And, this bond is now a Transoid bond, and that is made into a Cisoid bond. Then again, the Trans stereochemistry of this double bond is retained as Trans. In other words, by simply twisting this Carbon-carbon bond alone, we come to this structure, retaining the relative stereochemistry of these two double bonds as Trans, with respect to each other. So, please do not make a mistake of changing the Cis into Trans, and so on.

You are merely changing the Transoid into a Cisoid, that is all, it is done, in this particular transformation. Similarly, B is converted in the Cisoid form, which is this form. And, C is converted into the Cisoid form, in this form. If you consider all the Cisoid forms, in the molecule C, where the two double bonds are Cis with respect to each other. In the Cisoid form, that brings the two Methyl close proximity, with respect to each other. So, the two Methyls are sterically hindered, in the C form. So, it would not like exist in this particular confirmation, predominantly it will exist in the Transoid confirmation.

So, from the reactivity point of view, this will be the least reactive, because the concentration of the Cisoid form, is going to be bare minimum in this particular case, because of the steric hindrance that is involved in the. It is not only steric hindrance, that it is involved in the Cisoid confirmation of the C molecule, in the transition state also, these two Methyl groups will be in close proximity with steric hindrance, with respect to each other. Therefore, the fastest reacting one is the one, where the two Methyls are further apart from each other. The slowest reacting is one is, where the two Methyl groups as in close proximity to each other. This will have an intermediate reactivity of this kind.

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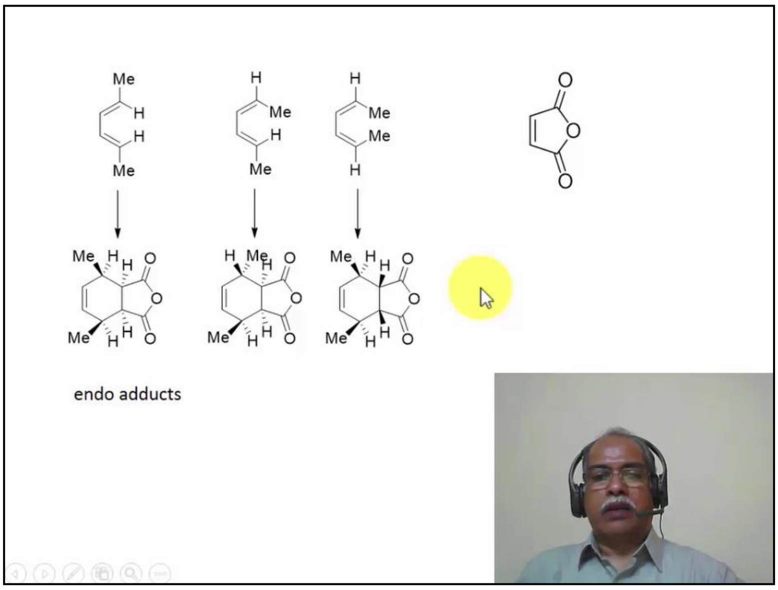

endo adducts

Now, in order to ascertain the stereochemistry of the Endo adduct, one has to carefully consider the relative orientation of the Maleic Anhydride. This two Hydrogens to be Cis. So, this two Hydrogens are Cis, in all the adducts. Only the relative stereochemistry of the Endo comes from the fact that, the Endo addition product would involve the, this Hydrogen pointing out, and this Hydrogen also pointing out, in the Endo stereochemistry. So, this Hydrogen, and this Hydrogen, of the Cycloaddition partners, should remain a Cis for the Endo adduct.

So, in this particular case, this is pointing out, and this also is pointing out, in the Endo approach is taking place. That would put, this stereochemistry of this two Hydrogens, Cis with respect to each other. Now, in this particular case, the Methyl is pointing out here, the Hydrogen will be pointing out in the Endo adduct. Similarly, the Methyl and the Hydrogen are Cis with respect to each other. Finally, the Methyl and the Hydrogen are again, Cis with respect to each other, in a different fashion, in this particular case.

Because, the two Methyl groups are interior to the system, in this particular case, so the Endo adduct. There are two things, that one need to worry about. The relative stereochemistry at these two junctions, which is governed by the stereochemistry of the Diene. The relative stereochemistry at these two junctions, which is governed by the Cis stereochemistry of the

Dienophile. And, the relative stereochemistry between Carbon 1 and 2, and Carbon 3 and 4, which is governed by the Endo approach of this.

So, one need to write the Endo approach properly, and see which are the Hydrogen, which are Cis with respect to each other, which are the Hydrogens, Trans with respect to each other, in the transition state of this particular molecule. You can see here; the two Methyl groups are Cis in the final product, because they are pointing out, in this particular case. Here, one Methyl is inside, and the other Methyl is outside, that would result in the Trans stereochemistry of the 1,4-Junctions, here.

Here again, the two Methyl groups are Cis in pointing interiors, so they remain as Cis, in the final product also as Cis, in this particular case. So, these are the Endo adducts structures, arising out of the 3C. You will consider carefully the transition state, that is resulting from the Endo approach, then you will be able to figure out the relative stereochemistry of all the three isomers, which are diastereo isomers with respect to each other.

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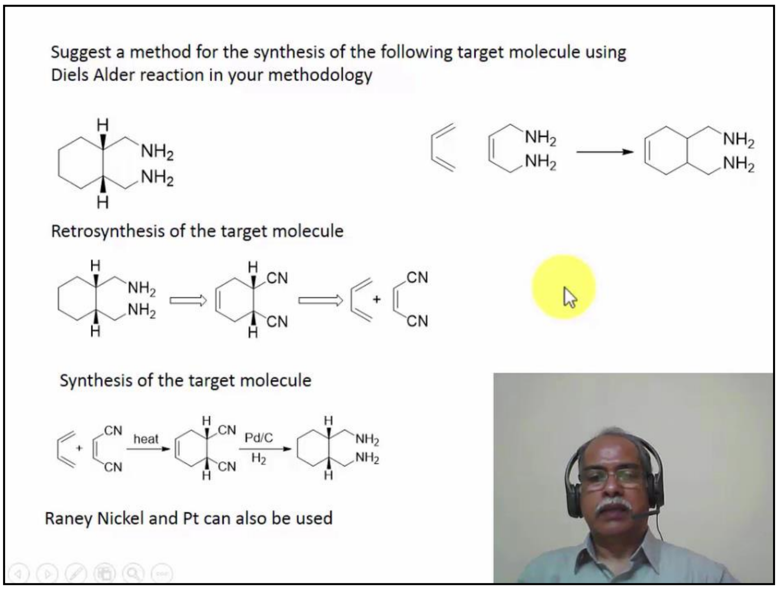

Suggest a method for the synthesis of the following target molecule using Diels Alder reaction in your methodology

Retrosynthesis of the target molecule

Synthesis of the target molecule

Raney Nickel and Pt can also be used

Now, the third question has to deal with the synthetic methodology, involving a Diels-Alder reaction. The question is, suggest a suitable method for the synthesis of the following target molecule, using Diels-Alder reaction in your synthetic methodology. Diels-Alder reaction, remember, gives a 4+2 Cycloaddition product, which is a 6-Membered ring. So, this 6-Membered ring has to be generated by a Diels-Alder reaction. However, Diels-Alder reaction gives you a Cyclohexene derivative, not a Cyclohexane derivative.

that means, after the Diels-Alder reaction, some other chemical reactions have been performed, to saturate the double bond into a saturated molecule, which is a Cyclohexane molecule. So, now if you do a retro synthetic analysis, if you form this ring by a Diels-Alder reaction, this would be the precursor Diels-Alder adduct, that one needs to consider. this on Hydrogenation, would give you the double bond to be saturated, as a saturated Carbon here. simultaneously, the cyano functional group can also be Hydrogenated, to give the primary Amine, which is in the target molecule, for example.

This can be a Diels-Alder adduct, arising out of Butadiene and Dicyanoethylene, as the Dienophile, for example. The Diels-Alder adduct is essentially a Cis adduct. So, you need to have a Cis isomer of the Dicyanoethylene, to form the Cis isomer of the product, that is shown here. So, the actual reaction is, take Butadiene, Dicyanoethylene, heat it. You will produce a Cis isomer of this particular derivative, when you do Hydrogenation using Palladium Carbon on Palladium Charcoal and Hydrogen, or Nickel and Hydrogen.

You simultaneously, saturate the double bond to unsaturated system, and saturate the C-Triple bond-N also, to the primary Amine. So, Platinum, Nickel can also be used for this particular reaction. Now, we cannot do a retrosynthetic analysis, in this particular manner. For example, if you take a Diaminoethylene of this kind, in principle, the Diels-Alder adduct would be formed directly, with the Cis stereo chemistry, if you start with the Cis isomer. However, this is not a very good Dienophile, unlike the Dienophile, which is a Di-Cyano substituted Dienophile.

Remember, in Diels-Alder reaction, the Diene is usually electron rich, and the Dienophile is electron poor. So, we were deliberately avoided using this Di-Amino derivative as the Diels-Alder Dienophile, instead the precursor, which is the mast form of the primary Amine, which is a cyano functional group, which is an electron withdrawing functional group, is used as the Dienophile substituent in the Dienophile, in this particular case. So, this would be a wrong answer, although in principle, this reaction can take place. In reality, this is not a very reactive Dienophile.

So, the reaction is not a very easy reaction to perform, with the primary Amine being present. And so on, so forth. It is not easier to perform the reaction with the Dicyanoethylene, rather than this Dimethyl Amino Methyl Ethylene, in this particular instance. So, one has to be careful, when you do the retro synthetic analysis, to make sure the Diene and Dienophiles are complementary in nature, in terms of their electronic character.

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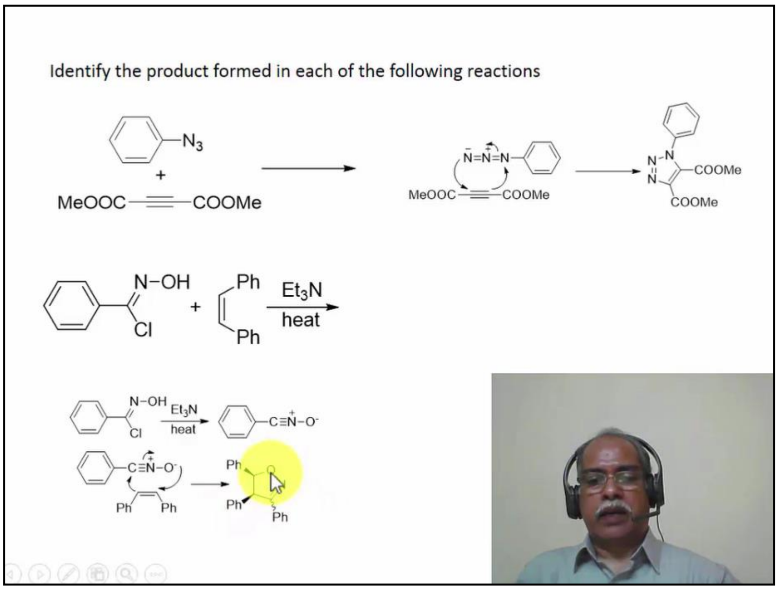

Identify the product formed in each of the following reactions

The question is fairly simple here. This is a fourth question. Identify, the product formed in each of the following reactions. The first reaction shown is Phenyl Azide and Dimethyl-Acetylene-Dicarboxylic acid. Remember, Phenyl Azide is a 1,3-Dipolar component, of a 1,3-Dipolar Cycloaddition reaction. This is a 1,3-Dipole component of the 1,3-Dipolar Cycloaddition reaction. The reaction essentially involves the Cycloaddition of the Azide to the Alkene, to give the Triazole as the molecules.

So, the final product is N-Phenyl Triazole, with this two Ester functional group substituted arising from the Dipolarophile, which is Dimethyl-Acetylene-Dicarboxylic acid. The second reaction is, this is an Alpha Chloro Aldoxime. And, its reaction with Cis Diphenyl Ethene, in the presence of Triethylamine. Remember, this is a precursor for making the Nitrile Oxide. By the elimination of HCL, one can form the Nitrile Oxide. In the presence of Triethylamine, the elimination of HCL, will result in the formation of the Nitrile Oxide.

So, it is a Nitrile Oxide Cycloaddition reaction, with Cis-Stilbene as the starting material. So, the first reaction is the Alpha Chloro Aldoxime, undergoes elimination to give Nitrile Oxide. The Nitrile Oxide undergoes, Cycloaddition reaction with Cis-Stilbene. What is important is, the Cis stereochemistry of the two Phenyl units. Because, this is a Suprafacial-Suprafacial Cycloaddition reaction. With respect to the third Phenyl group, a mixture of diastereo isomer is definitely will be formed in this reaction, as this is not going to be a highly stereo controlled reaction, of this kind.

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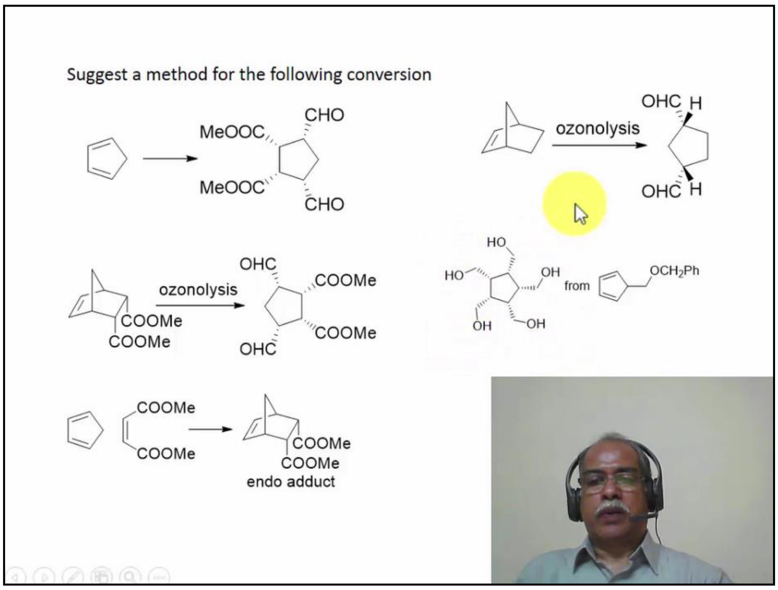

Suggest a method for the following conversion

Now, this is a very interesting question. Suggest a method for the following conversion. In other words, you have to take Cyclopentadiene, react it with whatever molecule, that is necessary to form this particular product. Now, a clue can be given to solve this problem. If you take a Norbornene kind of a 2,2,1-Bicyclic system, and do the ozonolysis, the 1,3-Dialdehyde can be obtained. The 1,3-Dialdehyde will be a Cis Dialdehyde. Because, this Carbon-carbon bond, and this Carbon-carbon bond, are pointing in the same direction, resulting in the Cis stereo chemistry of the Dialdehyde.

So, if you look at this target molecule, this two Dialdehydes are Cis with respect to each other. So, all one needs to know is, what kind of a starting material that one needs to take, in order to do a Diels-Alder reaction, to bring this component, that will undergo ozonolysis, to give the Dialdehyde. You take this example. Suppose, if you take this particular molecule, and do the ozonolysis, this is the component, that will be forming, during the course of the ozonolysis. The Carbon-carbon bond, this Carbon-carbon bond, and the Ester Carbon-carbon bonds, are Cis with respect to each other.

So, all the four Carbonyl functional group, will be Cis with respect to each other. So, now the question is, how does one get this as a Diels-Alder adduct. This is a clearly a Diels-Alder reaction, between Cyclopentadiene and Dimethyl maleate as the starting material. So, if you take Dimethyl maleate as a starting material, and react it with the Cyclopentadiene, the Endo adduct is going to be the predominant adduct. This is an Endo adduct. The Endo adduct is important, because, that would put this Carbon-carbon bond, and this Carbon-carbon bond, Cis with respect to each other. The Exo adduct will have exactly the opposite stereochemistry of the two Esters, being Trans with respect to the two Dialdehyde.

So, this is the first reaction. Once this reaction is over, ozonolysis will essentially give you, the aldehyde diester kind of a molecule. One can use this molecule, this strategy, in an analogous manner, to synthesize this particular molecule. In other words, All-Cis-Penta-Hydroxymethyl-Cyclopentane as the target molecule, starting from this as the Diels-Alder Diene component. So, one please think about this problem very carefully, and try to identify the starting materials, that are necessary. One of the starting material is given, as this molecule. The other starting materials, you consider carefully, and see, if you can arrive at the synthesis of this particular molecule.

I am not going to solve this molecule, this problem. This problem is an assignment, that is given to you. So, try to solve this problem carefully, using the same kind of a strategy, that is shown for this. For example, if you take this molecule, and reduce it with Lithium aluminium hydride, you will get four Hydroxymethyl functional group. So, you need to think about the fifth Hydroxymethyl functional group, coming from the already existing Hydroxymethyl derivative, that is shown here. So, it is not a very difficult problem. Once you understand the concept of this particular problem, to be able to solve this problem, very carefully.

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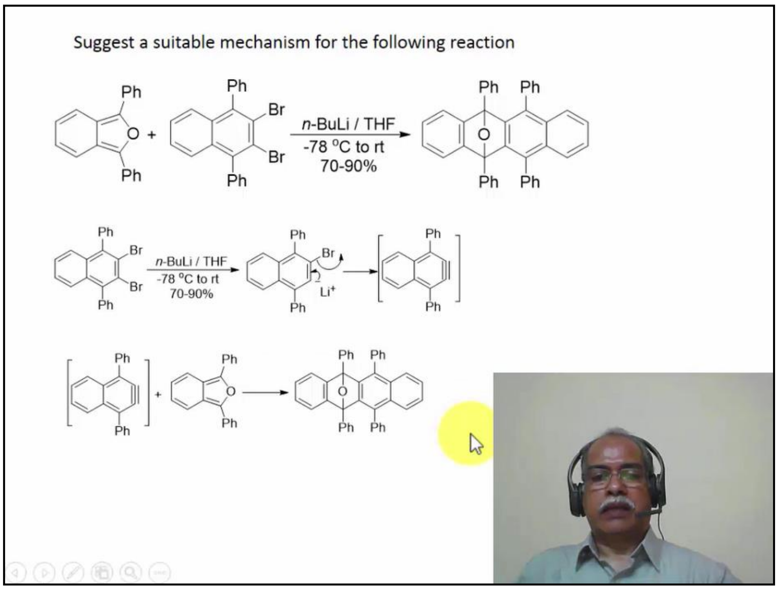

Suggest a suitable mechanism for the following reaction

Now, this problem has to deal with a mechanistic aspect of the Diels-Alder reaction. Suggest a suitable mechanism for the following reaction. Now, this Dibromo derivative, when you treat it with Butyllithium, first it will undergo a Bromine-Lithium exchange, Metal Halogen exchange reaction, resulting in the formation of a Lithium derivative, which will undergo Lithium-Bromide elimination, to give the corresponding Benzyne derivative. So, the initial reaction is the Dibromo derivative, undergoes lithiation, followed by elimination of Bromine, to give a Benzyne.

Once the Benzyne is formed, this is a Diene, Benzyne is a Dienophile. So, this Diene, and this Dienophile, will essentially undergo Diels-Alder reaction. So, the Diels-Alder reaction between these two components, is what is going to give this Oxa-Bridged bicyclic system of this kind. This is the Oxa-Bridged Tetraphenyl substituted Tetracene derivative, is what is given as the final product, which arises from the 4PI-2PI Cycloaddition reaction, that is shown in the last stage of the set of equations, that are shown here.

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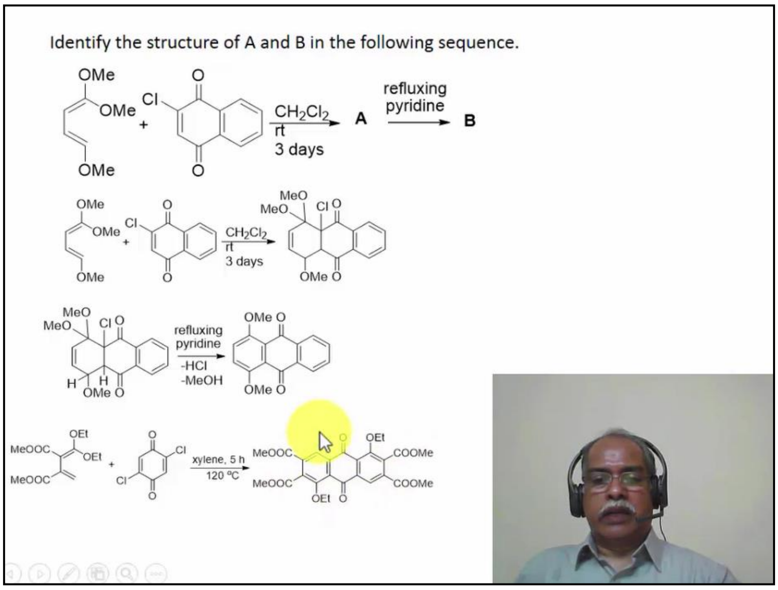


Identify the structure of A and B in the following sequence.

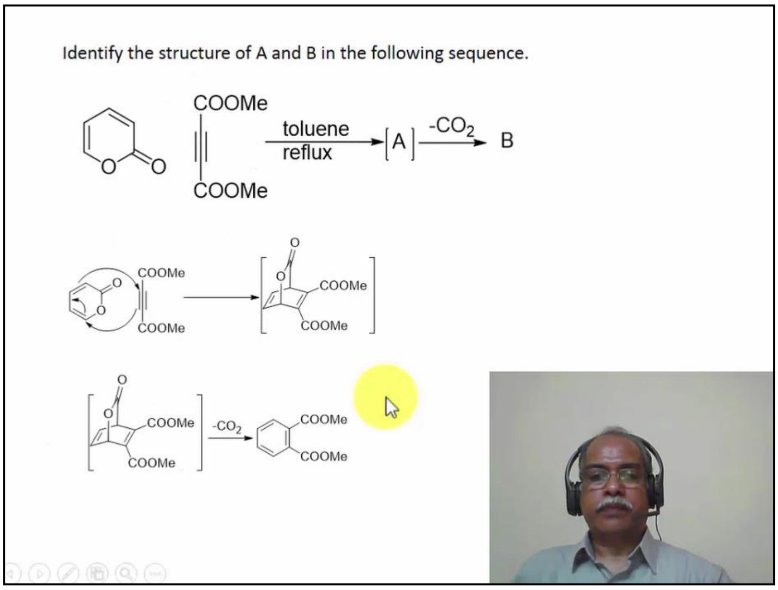
Here is a problem, where you need to identify, what are the products A and B formed, during the course of this reaction. You can see here, this is a Diene, and this is a Dienophile. So, initially one can think of a Diels-Alder reaction, between these two components. It takes place at room temperature in three days, to produce A. So, A should be the Diels-Alder product. Then, A is refluxed in pyridine. In other words, this refluxed with a base. So, it undergoes some kind of an elimination reaction, probably to give B. Because, there is halogen in this molecule. So, what is the first reaction. The reaction is Diene and a Dienophile, undergoing a Diels-Alder reaction, to give this

Do not worry about the stereochemistry of the product, because you are going to do elimination of this system. Only stereochemistry, that you need to worry about is, this Chlorine and the Hydrogen, that is present here, should be Cis with respect to each other. And, the Methoxy and the Hydrogen, that is being present here, should be probably Trans with respect to each other, if it were to be a Exo adduct, and Cis with respect to each other with, if is an Endo adduct. So, let us not worry about the stereochemistry of this, although stereochemistry is easy to predict, in this particular case.

Now, this compound, when it is refluxed with Pyridine, undergoes elimination of the Hydrochloric acid, HCL is eliminated. Simultaneously, a molecule of Methanol is also eliminated, resulting in the formation of the aromatic system, which is the Anthraquinone derivative, that is shown here.

So, the structure of A is this, with the Halogen. And, the structure of B is this one, which is an Anthraquinone derivative, in this particular case. Similarly, this reaction is also known, where you have a Dicarboxylic acid derivative of the Ketene Acetal, that is shown here, undergoing a Diels-Alder reaction. This is a double Diels-Alder reaction, involving a Diels-Alder reaction, two equivalence of this is used.

One equivalent is consumed on the one side of the Benzoquinone, the other equivalent is consumed on the other side of the Benzoquinone. Then, finally loss of Hydrochloric acid, two units of Hydrochloric acid, and two units of Ethyl alcohol, is resulting in the formation of this particular product, which is the Anthraquinone derivative. So, this is an extension of the example, that is shown here. One can perform, with this as a Diene, and the Dichloro Benzoquinone as a Dienophile. A double Diels-Alder reaction, a double elimination of Hydrochloric acid, and double elimination of Ethanol, is what is going to lead to the formation, of this particular product. (Refer Slide Time: 17:41)


Identify the structure of A and B in the following sequence.

Now, again another question, identify the structure of A and B, is what is given here. The answer is also shown in this particular slide. The structure A is this particular structure, which is an intermediate, is a reactive intermediate, because of the fact that, it has an angle strain associated with this Carbonyl SP2 Carbon, present in the system. It cannot accommodate 120-degree angle, which is the SP two angle.

Now, initially a Diels-Alder reaction with Alpha Pyrone and the Dimethyl-Acetylene-Dicarboxylate, results in the formation of this bicyclic derivative. A bicyclic derivative, under the reaction condition is unstable. It loses Carbon dioxide, to form Dimethyl Phthalate as the product. So, essentially one goes from Alpha Pyrone to a Benzenoid derivative, by loss of Carbon dioxide, during the course of the synthesis of Dimethyl Phthalates as the product, in this particular instance.

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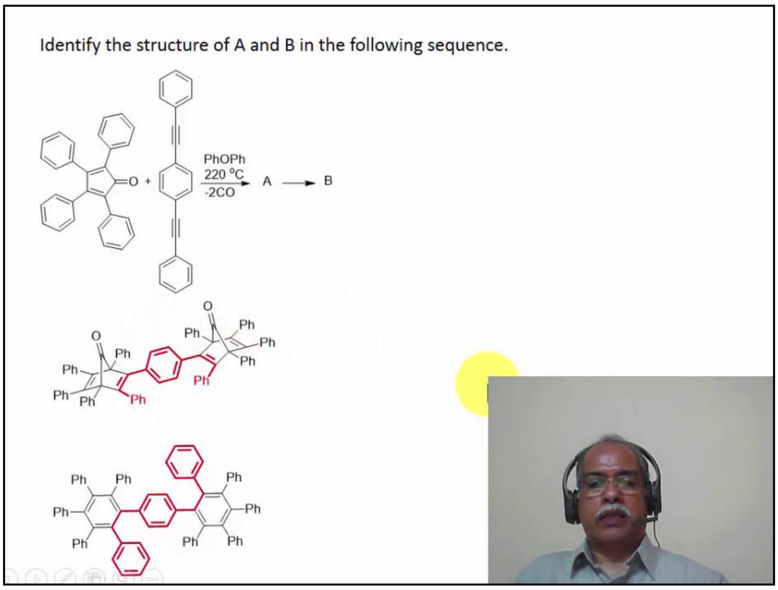

Identify the structure of A and B in the following sequence.

This is an example, which has already been discussed earlier. Identify the structure of A and B in the following sequence. So, this is a Tetracyclone. In other words, Tetra Phenyl Cyclopentadienone. It is undergoing a Diels-Alder reaction, with this Di-Acetylenic molecule. In other words, two units of this can undergo, one unit can undergo Diels-Alder reaction here, another unit can undergo Diels-Alder reaction here, with the loss of Carbon monoxide, as indicated in this particular case, for example. So, the initially formed adduct A, would be a reactive intermediate, which is this particular intermediate.

It is not necessary that, this should survive under the reaction condition. This would undergo a loss of Carbon monoxide, to give this particular product. The Di-Acetylene molecular unit is shown in the red, so that you can understand. Originally, this was a triple bond. This was also a triple bond. It has undergone aromatization, by loss of Carbon monoxide, two times from this adduct, to give this particular product. So, A could be this, and B could be this. It is not necessary that; both the triple bond will simultaneously undergo Diels-Alder reaction. It could be used a stepwise reaction

Initially, this one undergoing a Diels-Alder reaction, that eliminates the Carbon monoxide, to give this unit. And the second acetylene, then undergoes the Diels-Alder reaction, with the loss of Carbon monoxide, to give this particular unit. One can also write a stepwise mechanism, involving two concerted 4PI-2PI Cycloaddition reaction, rather than involving one concerted 4PI-2PI Cycloaddition reaction, taking place twice, in this particular instance. I hope this problem-solving session was useful to you. You are able to understand, certain basic concepts once again, and apply it in the problem-solving session, as discussed in this particular module. Thank you very much, for your kind attention.