

# Pericyclic Reactions and Organic Photochemistry

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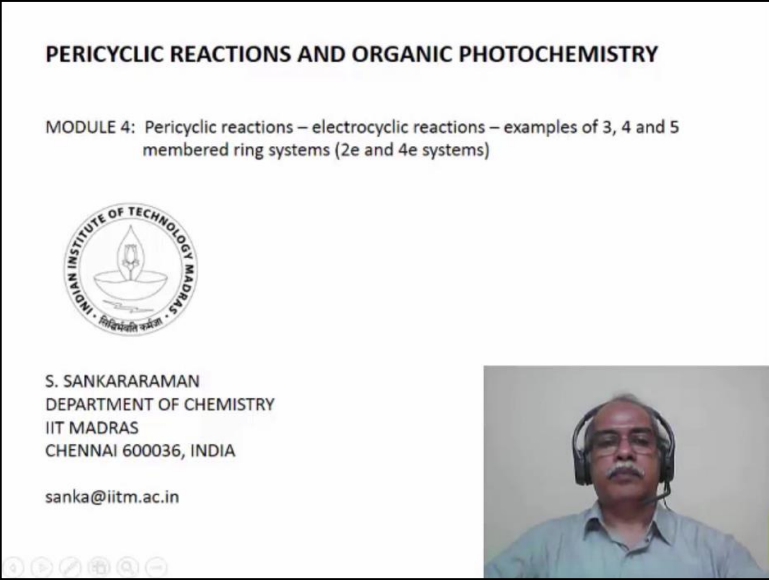
Indian Institute of Technology, Madras

Module No. #01

Lecture No. #04

## Pericyclic Reactions – Electrocyclic Reactions – Examples of 3, 4 and 5 Membered Ring Systems (2e and 4e Systems)

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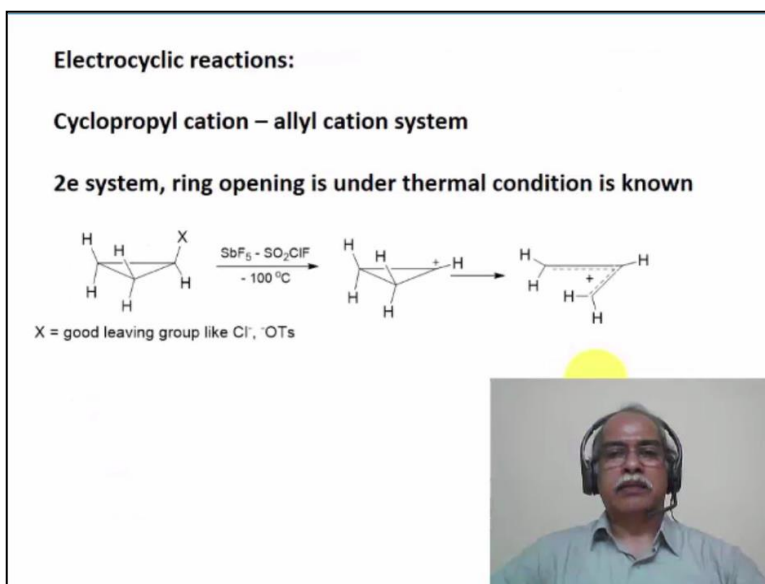


The image shows a presentation slide with the following content:

- PERICYCLIC REACTIONS AND ORGANIC PHOTOCHEMISTRY**
- MODULE 4: Pericyclic reactions – electrocyclic reactions – examples of 3, 4 and 5 membered ring systems (2e and 4e systems)
- The logo of the Indian Institute of Technology Madras, featuring a lamp and the motto "विद्यया ऽमृतमश्नुते".
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- A small video inset in the bottom right corner shows the speaker, S. Sankararaman, wearing a headset.

Hello, welcome to the course on pericyclic reactions and organic photo chemistry. We are now in module number four. We will continue with the electrocyclic reaction. In this particular module, we will consider the examples from 3, 4, and 5 membered ring systems, consisting of two electrons and four electrons, in terms of the electron count, that undergoes electrocyclic ring opening and ring closing reaction.

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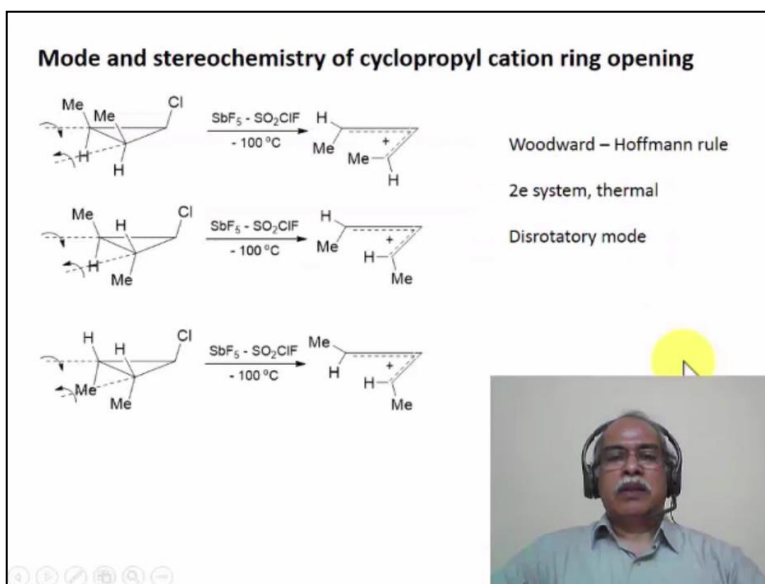


Let us start with, the smallest system, two electron system. This is an example of a cyclopropyl cation, undergoing a ring opening reaction, to allyl cation. So, if you take a cyclopropyl halide, or a cyclopropyl tosylate, with a good ionizing group, which is a CX bond, in this particular case. And, put it in a medium, which is a highly ionizing medium, like the antimony pentafluoride and this sulfonyl chloride, fluorochloride type of a solvent.

The beauty of this solvent is that, it is non-nucleophilic in nature, but at the same time, it is highly ionizing medium. So, under these conditions, the CX bond essentially ionizes, to produce a cyclopropyl cation. Now, in the cyclopropyl cation essentially, the sigma bond is the one, that is undergoing the reaction. So, the two sigma electrons are involved, in the course of the reaction.

The opening of the cyclopropyl cation, which releases the strain energy, associated with the cyclopropyl system to the allyl cation, is the pericyclic pathway, that we are talking about. So, the last step namely, the cyclopropyl cation undergoing the ring opening reaction, to give the allyl cation, is the pericyclic step. And, let us see, if this is a concerted process or not.

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Now, if you take specific stereo isomers of the cyclopropyl chloride, this particular case it is 2,3-dimethyl cyclopropyl chloride. This is isomer. The Trans isomer is what, we are considering. This is an all Cis isomer. This is a TRANS-TRANS isomer, in terms of the relative orientation of the two methyl groups, and the chlorine. And, this is the Cis, anti-kind of a stereo isomer, is what is being present in this particular system.

Now, what happens in these systems is, when they are ionized in the presence of this ionizing medium, namely antimony pentafluoride under the solvent, which is  $\text{SO}_2\text{ClF}$  at low temperature, one could follow these reactions by NMR spectroscopy. What the NMR spectroscopy tells us is that, the ionization is highly stereo selective in nature. The reaction proceeds, by the inward twisting of this carbon-carbon bond, like the arrow it is shown here. And, this corresponds to the disrotatory mode of ring opening reaction.

So, disrotatory mode of ring opening reaction, essentially pushed the two methyl groups interior position, like it is shown in this particular structure. So, the methyl group on this side, essentially moves inward. And, the methyl group on this side, also essentially moves inward. So, the two methyl groups, essentially end up the inside of the Pi framework, as it is shown in this particular structure.

If you take the Trans dimethyl derivative, again the inward motion is, what is indicated by the arrow. The twisting of the two carbon-carbon bond, which leads to the cleavage of this particular carbon-carbon bond, resulting in the formation of a diastereo isomer of the allyl cation, that was originally generated for the other diastereo isomer. Now, in the third example, where the chlorine

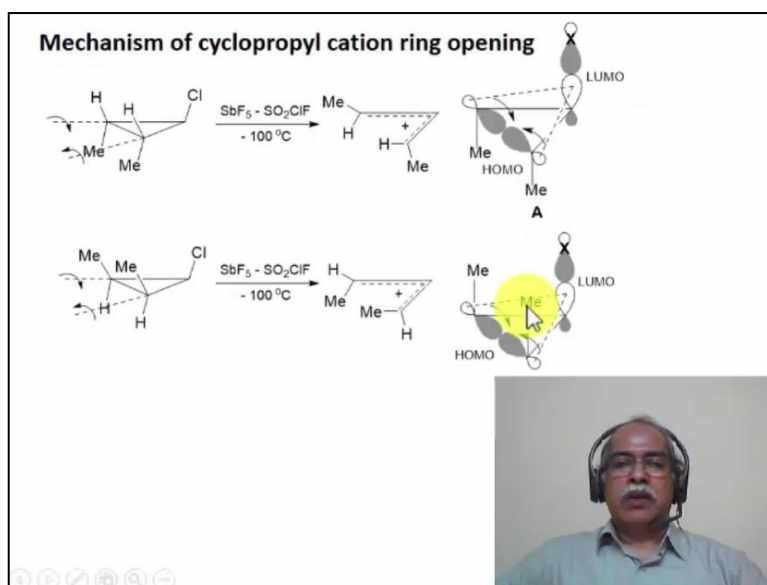
and the two methyls are Trans with respect to each other. And, the two methyls are Cis with respect to each other.

The inward twisting motion, essentially brings the two methyl groups, to the exterior of the Pi framework. So, this and this are essentially the two structures, which are diastereomeric structures. Here, the two methyls are in the interior of the Pi framework, whereas these two methyls are exterior of the Pi framework. So, what it tells is essentially, this reaction proceeds by following the Woodward-Hoffman rule, in the sense that, this is a two electrons system. So, it is actually a  $4N + 2$  electrons system, where N is equal to zero.

Under thermal condition, the disrotatory mode is the allowed mode, and strictly follows the disrotatory mode of ring opening, in this particular instance. One can ask the question, why only the inward motion is allowed, in this particular case. Why not the outward motion, which is also a disrotatory motion. In other words, this is clockwise, and this is anticlockwise. We can have it, the other way around.

This could be the anticlockwise, and this could be the clockwise direction twisting. Exactly in opposite direction, is what it needs to twist. So, it can be either inward motion or outward motion. Outward twisting of this two carbon-carbon bond, is what we are talking about.

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There is a reason behind this, which could be explained by the HOMO-LUMO interaction, in the Transition state. Now, consider this picture here, which tells you that, the carbon-carbon bond HOMO is depicted here. And, the carbon X bond, which is a LUMO, in other words, the breaking of this particular bond, is what is going to lead to the carbonium ion. So, the LUMO of

this particular CX bond, and the HOMO of the CC bond, interacts during the course of the bond breaking. In other words, as the bond is breaking between the carbon and the X-group, this orbital will essentially develop.

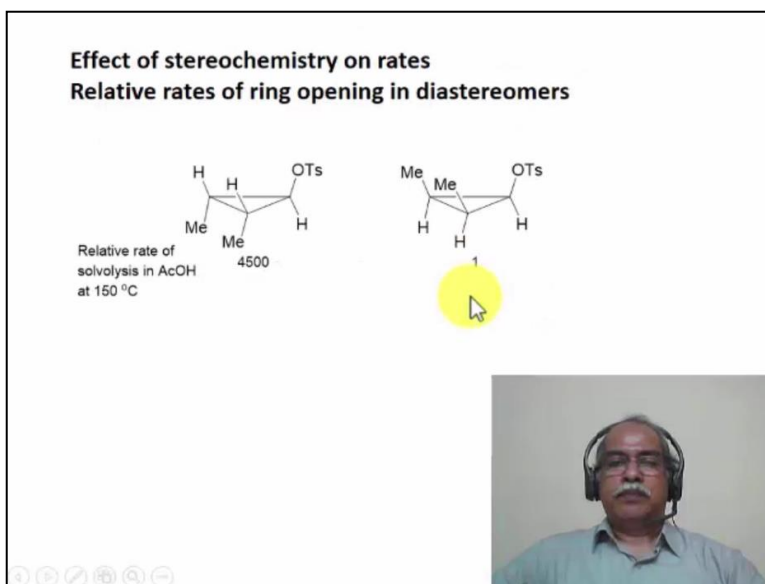
And similarly, when the carbon-carbon bond is breaking, this orbital, and this orbital, will tend to undergo the interaction. And, this would be a bonding type of an interaction. Because, the orbital lobe having the same algebraic sign, is what is interacting in this particular case. So, only in the inward motion, this orbital, the back lobe of this particular orbital, and the back lobe of this particular orbital, is going to interact with this developing lobe, of this particular orbital. Because, it leads to a bonding type of an interaction, that will be the stable system.

Suppose, if it were to be an outside, outward twisting of the motion, it will be this, the wrong algebraic sign lobes are, what is going to interact with this one, resulting in an antibonding kind of an interaction. So, the bonding type of an interaction, the Transition state is much more stable of lower energy, compared to an anti-bonding type of an interaction. That is the reason, this molecule essentially undergoes ring opening reaction, by the inward twisting of the two carbon-carbon bond, resulting in the disrotatory motion ring opening reaction.

So, if one were to consider the relative rates of these two compounds reacting, in this particular instance if you look at, the inward twisting, brings the two methyl groups, outside the Pi framework. In other words, there is a release of the steric interaction, between the two methyl groups is released, during the course of the ring opening reaction, by putting the two methyl groups, as far away as possible.

Whereas, in this particular case, the twisting motion brings the two methyl groups closer together, to the interior of the Pi framework. So, this particular molecule should react at a much slower rate, compared to this particular molecule. In other words, the diastereo isomer, the all Cis diastereo isomer should react, slower than the Cis-Trans isomers. Cis-dimethyl and the Trans-chloro isomer, should react faster, compare to this particular isomer.

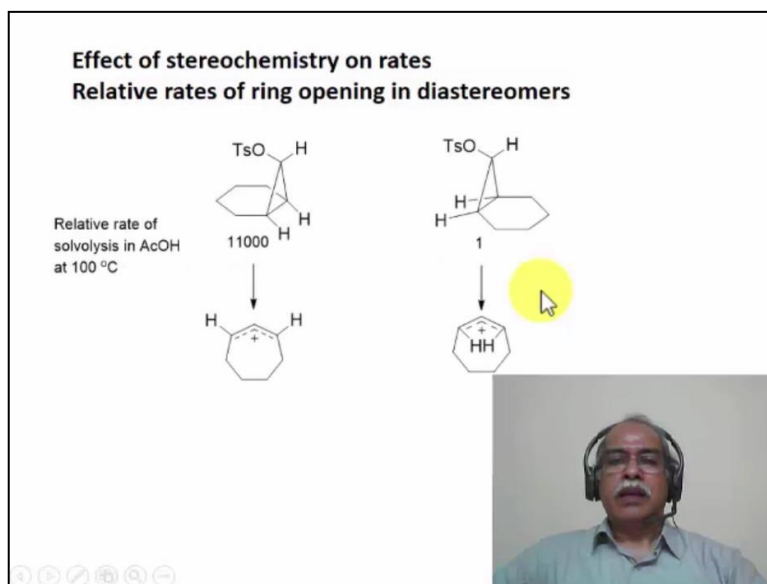
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And indeed, this is, what is seen here. We can see here, the all Cis isomer, the relative rate of solvolysis in acidic acid at 150 degree, if it is one, then the relative rate of the Trans isomer, with respect to the tosyl, the two methyl groups are Trans, that interacts, that reacts much faster, 4500 times faster reacting, compare to the all Cis isomer. Essentially because, in this particular case, the cyclopropyl cation, essentially will undergo ring opening reaction, to give the propyl cation with the two-methyl group, outside of the Pi framework. In other words, the steric hindrance will be released, in this particular case.

Here, the steric hindrance will be enhanced, during the course of the Transition state. Because, the two methyl groups will be moving inward, with respect to each other.

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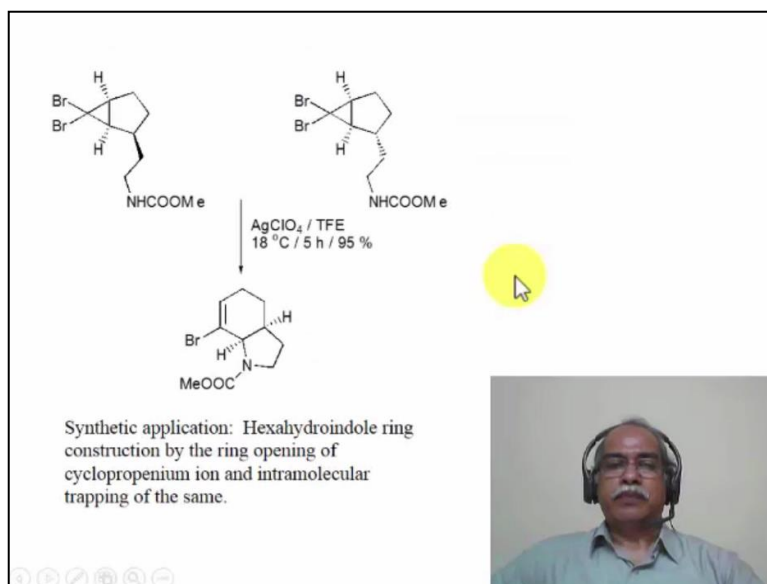


Now, if you consider the bicyclic system of this kind, this is also a cyclopropyl tosylate. In this particular case, the rate enhancement is even much higher. This particular isomer, where we have all Cis isomer of the molecule, undergoes the reaction, 11,000 times faster, compared to the Trans kind of a system, that you have. I am talking about the stereochemistry of the tosylate, and these two carbon-carbon bonds, to be Trans with respect to each other.

We can call this as an endo isomer, and this as an exo isomer, in terms of the tosylate being exo, with respect to the bi-molecular framework, whereas the tosylate being endo, with respect to the bio. The endo isomer reacts, 11,000 times faster than the ion, because of the reason that, during the course of the ring opening reaction, the two Hydrogen will be pushed outside the ring system.

Whereas, in this particular isomer, which is an exo isomer, because of the inward motion, the two Hydrogen will be pushed interior to the cyclic system. This is relatively an unstable structure, compared to this particular structure, where the two Hydrogens are outside of the Pi framework, as well as the ring structure. So, this is much more favored in terms of the rate of the reaction being much faster, compared to the rate of the, other diastereo isomer.

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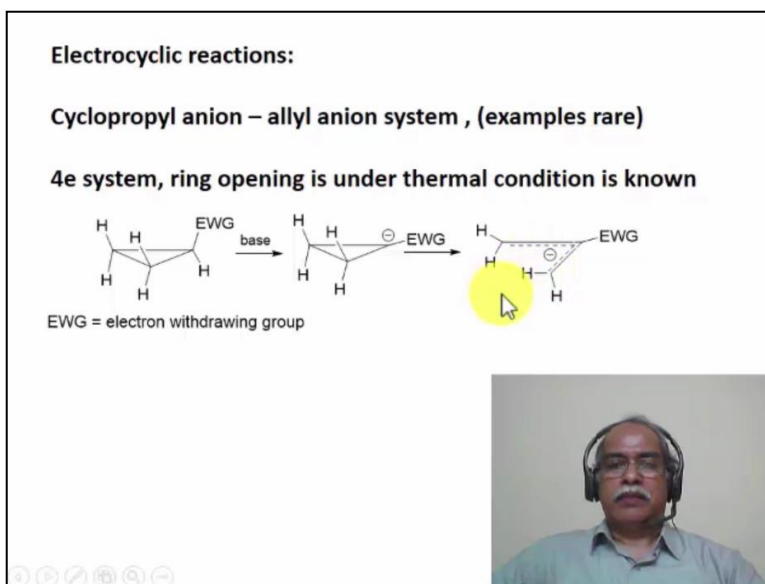


And, here is an example of a cyclopropyl cation being generated, by taking this gem dibromo derivative. This is involved in a total synthesis of a natural product, which is shown here, for example. This gem dibromo cyclopropyl derivative, undergoes reaction with silver perchlorate. Silver is a halophilic atom. Silver ion is a halophilic ion. So, it essentially ionizes a carbon bromine bond, and generates a cyclopropyl cation, that results in the cleavage of the cyclopropyl cation to the allyl cation.

The allyl cation, so generated, is trapped by the lone pair of electrons, on this particular nitrogen. So, intramolecular trapping of the allyl cation, results in the formation of this used bicyclic system, which is the hexahydro indole ring system, is what is being generated. As a synthetic application, the cyclopropyl cation ring opening, and an intramolecular trapping of the cyclopropyl cation, is illustrated in this particular example.

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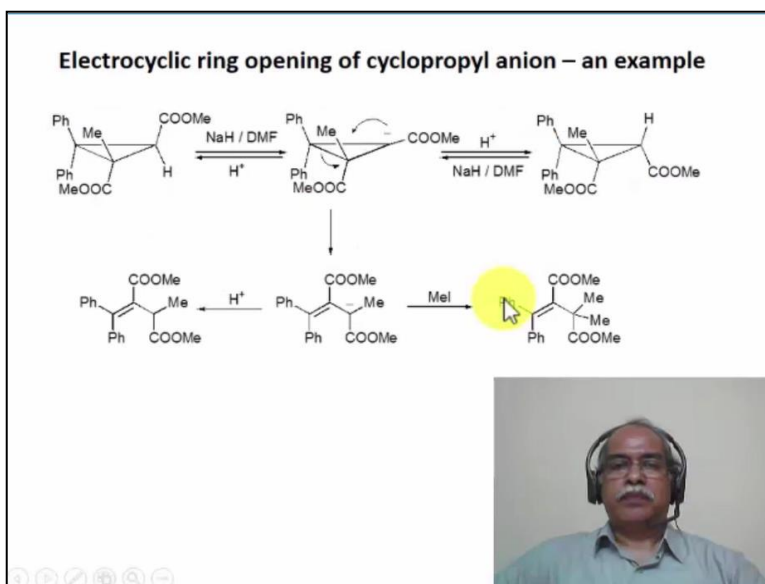




Now, when it comes to the cyclopropyl anion, undergoing ring opening, to give the allyl anion system, there are not many examples. The examples are quite rare. In this particular case, what happens is, if you have an electron withdrawing functional group on the cyclopropyl ring system, you can use a base, and abstract this particular Hydrogen, which is an acidic Hydrogen. Once the acidic Hydrogen is abstracted, the carbanion is generated.

Now, the carbanion can undergo, for example, a ring opening reaction, to give an allyl anion. In other words, a cyclopropyl anion undergoing a ring opening reaction, to give an allyl anion system, is a four-electron system. And, the ring opening under thermal condition, is known with a few examples, which will be illustrated in the next slide.

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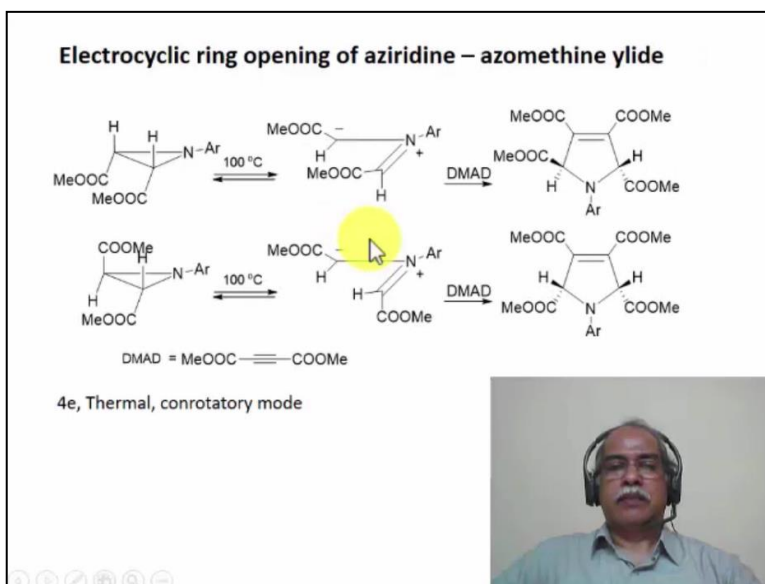


Now, if you take this particular diester, for example, this is the only Hydrogen, that is acidic in this molecule. So, when it is treated with sodium hydride as a base in DMF solvent, the corresponding anion is generated, which is a cyclopropyl anion. The cyclopropyl anion, undergoes ring opening, as it is shown in this particular case. And, the resulting carbanion is essentially stabilized, by the other ester group, in this particular instance.

Now, this allyl anion can be either methylated, to give this dem-dimethyl derivative, or the allyl anion can be protonated, to give the corresponding protonated species, which is shown on the left-hand side. This process of ring opening is essentially the, a pericyclic step of this particular reaction. So, this being a four-electron system. This is a four-electron system, under thermal condition. It will undergo a conrotatory process.

Unfortunately, the stereochemistry information is not available, in this particular instance. For the reason that, this is a symmetrical molecule, with two identical phenyl substituents being present here, in this carbon atom. So, one cannot say for sure, whether this is a conrotatory or disrotatory process. But, in all likelihood, this particular step is a pericyclic step, involving four electron system, undergoing a conrotatory process of ring opening, under thermal conditions.

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Now, the most illustrious example is, the ring opening of the aziridine. There are two electrons on the nitrogen, which is a lone pair of electron on the nitrogen. And, this is getting participated in this particular reaction. Aziridines, upon heating, or upon photolysis, can undergo ring opening reaction, to give the azomethine ylide, which is a 1,3-dipolar substance in this structure, that is indicated in the, in between the two structures, that are shown here.

So, the intermediate structure essentially is an azomethine ylide structure, which is trapped by means of dimethyl acetylene dicarboxylic acid. This is a 1,3-dipole. And, this is a 1,3-dipolarophile. So, this is the 1,3-dipolar cycloaddition reaction, is what, we are talking about. We will consider the part of the 1,3-dipolar cycloaddition part, at a much later stage. For the time being, let us concentrate on, the ring opening reaction of the aziridine to the azomethine ylide.

Now, if you consider the Cis isomer of the diester of the azomethine ylide, and heating to 100 degrees for example, you should undergo essentially a conrotatory process. The conrotatory process should bring, one of the ester group outside, the other ester group to the interior of the system, as it is shown. So, this process of the aziridine, going through the azomethine ylide, is a pericyclic step.

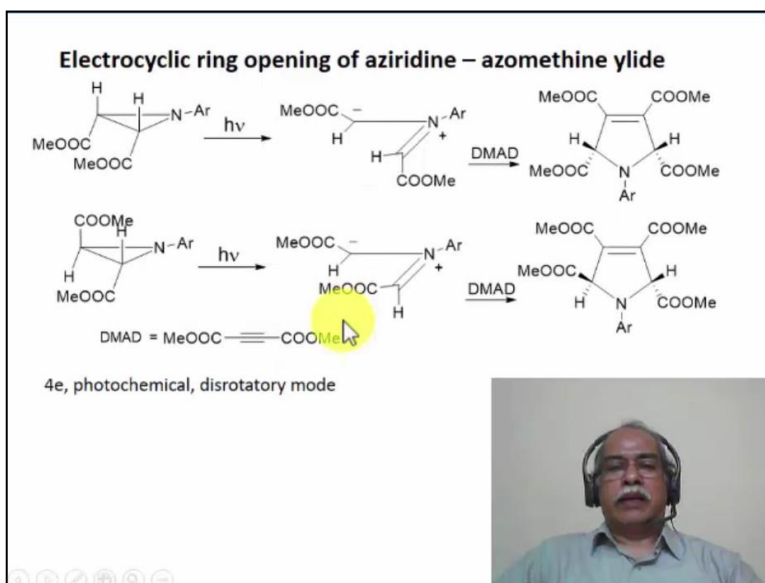
And, this essentially is a conrotatory process, resulting in the formation of the diastereo isomer, that is shown here. On the other hand, if the Trans diester is taken, and if it is pyrolyzed at 100 degrees, for example, the conrotatory process essentially brings, the two-ester functional group, away from each other. In other words, this is the other diastereo isomer of the azomethine ylide, that is being generated.

The azomethine ylide stereochemistry is inferred from, the stereochemistry of the pyrrolidine ring, that is being generated after the cycloaddition reaction, with dimethyl acetylene dicarboxylate. So, these are examples, good examples of ring opening reaction of a four-electron system, of a three-membered ring opening reaction, which is an aziridine ring, undergoing ring opening, to give the azomethine ylide.

These reactions, were extensively investigated by Huisgen. And hence, these are sometimes called Huisgen reaction, also. We will see this. We will come back to this, when we consider the 1,3-dipolar cycloaddition reaction, in terms of explaining the stereochemistry of the pyrrolidine ring system, that is being generated. The relative stereochemistry at these two carbons, the two esters, for example.

We will discuss these things, when it comes to the stereochemistry aspects of the 1,3-dipolar cycloaddition reaction. Now, if the conrotatory process is taking place, under the thermal condition, what about photochemical condition.

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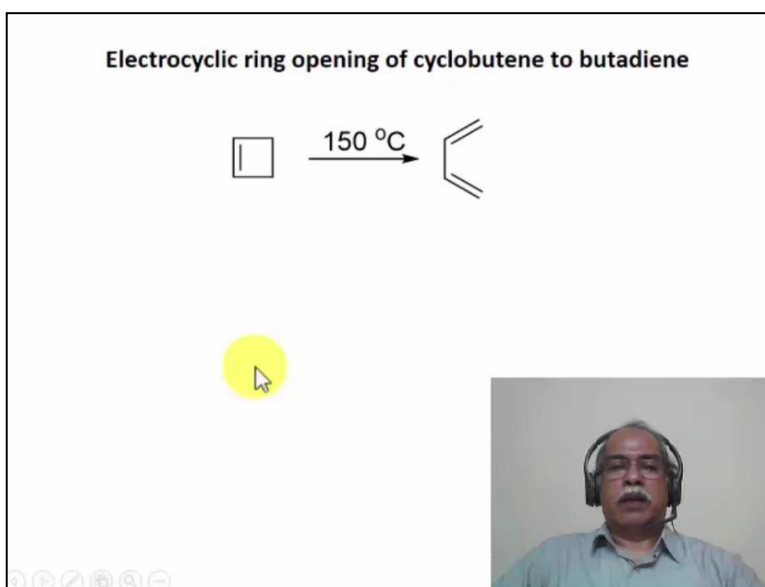


The aziridine is also susceptible to ring opening reaction, under photochemical condition. The photochemistry is done by irradiating the aziridine ring, in the suitable wavelength of UV light. It results in the formation of the ring open the product, by a disrotatory mode. You can see clearly, the two ester groups are far away from each other, and the exterior of the pi framework. Whereas, in this particular diastereomer, one of the ester group is pointing inside, the other ester group is pointing outside, with respect to the pi framework, that we are discussing in the azomethine ylide structure.

So, the photochemical disrotatory mode of ring opening, essentially gives the opposite stereo isomers, compared with the thermal ring opening, which is the conrotatory mode of ring opening reaction. In this case, the Cis isomer gives, the in and out kind of an ester functional group. Whereas, the Trans isomer gives out-out kind of a stereo isomer of the two-ester functional group. On the other hand, if you consider the photochemical ring opening reaction, you get exactly the opposite stereochemistry.

Because, the rotatory mode of ring opening is different, in the case of photochemical, compared to the thermal ring opening reaction.

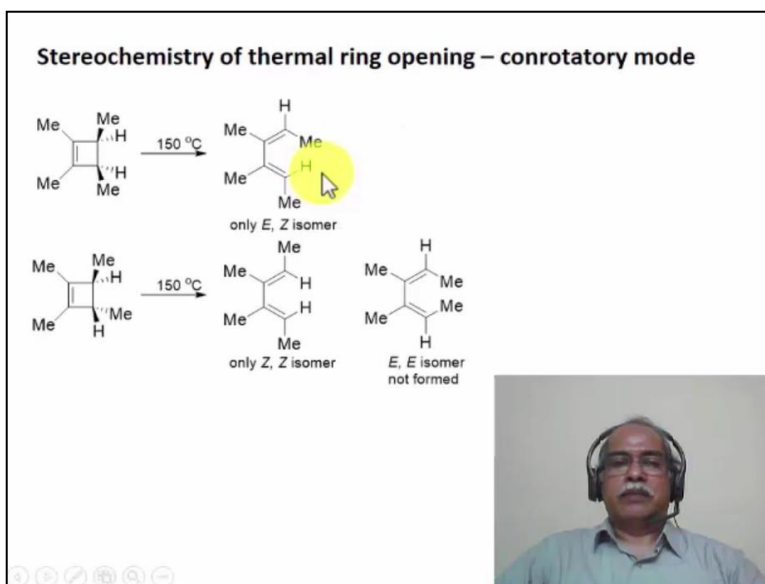
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Now, let us finally come to the carbon-based system. The carbon-based system, the simplest system, is the ring opening of a cyclobutene molecule to butadiene, under thermal condition. The small ring compounds such as, the cyclobutene is highly strained, because of the ring strain associated with a small ring. So, under thermal condition, it is thermodynamically favorable to undergo this ring opening reaction, to give the butadiene.

In fact, butadiene cannot be taken back to the cyclobutene, under thermal condition. Because, the forward direction reaction is a thermodynamically feasible reaction. The reverse reaction is not a thermodynamically feasible reaction. So, it never takes place under thermal condition. We will see, how the reverse reaction can be pushed, by means of a photochemical reaction, in a few minutes.

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Now, these are examples of the ring opening reaction of the cyclobutene derivatives, where the stereochemistry can be very clearly illustrated, conforming to the conrotatory ring opening process of the cyclobutene. Now, if you take the 3,4-dimethyl Cis isomers, of the 3,4-dimethyl cyclobutene, the conrotatory ring opening reaction will give you, only the ZE isomer, in terms of the stereochemistry of this molecule, here.

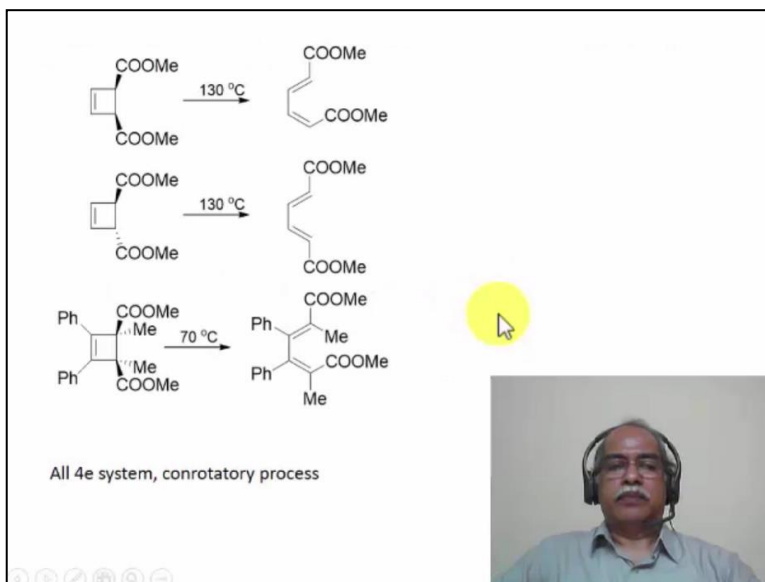
This is the Z isomer. And, this is the E isomer, in terms of the two-methyl group being Cis with respect to each other, and the two-methyl group being Trans with respect to each other. And, this is the ZE isomer stereochemistry, is what, we are referring to. On the other hand, if we take the 3,4-dimethyl derivatives, which is a Trans isomer, which is a diastereo isomer of the Cis isomer, under the same reaction condition.

The conrotatory process gives the ZZ isomer. The two methyl groups are Cis here. Similarly, these two methyl groups are also Cis. So, the opposite diastereo isomer is, what is being formed. In this particular case, the ring opening reaction essentially take place, by twisting motion in one direction, namely the clockwise direction, in this particular instance. The anticlockwise direction twisting motion, would have given the EE isomer.

This is not formed at all, for the simple reason that, when you do the anticlockwise motion, twisting motion, the two-methyl group will come very close to each other in the Transition state. You can see here, already in the product, the two methyl groups are essentially EE isomers, puts these two-methyl group to the interior core of the Pi framework. This is a sterically more hindered Transition state, to reach this particular product, compared to the product, where the two methyl groups are further away from each other.

So, only the ZZ isomer is formed, under thermodynamically stable condition. The EE isomer, which is a thermodynamically unstable system, is not formed during the course of this reaction.

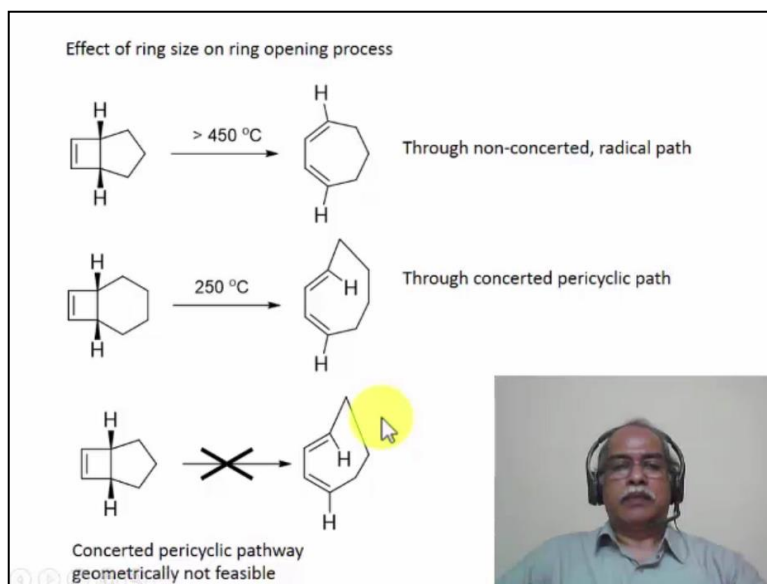
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Now, these are some more examples of the diester derivatives of the cyclobutene. In other words, 3,4-dicarbomethoxy ester derivatives of the cyclobutene. The Cis isomer essentially gives you ZE kind of a stereo isomer of the cyclobutene undergoing the ring opening, to give the butadiene derivative. The Trans isomer, on the other hand, for example, gives the EE isomer of this particular derivative.

This is one more example of the ring opening, under conrotatory process of a cyclobutene derivative, which is taking place at much lower temperature, compared to the earlier example, probably because of the release of the steric hindrance, as well as the ring strain in this particular molecule, to go to this particular product.

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Now, if the cyclobutene is fused in the form of a bicyclic system, as it is shown here, depending upon the ring size of the fusion, the reaction can either proceed by a concerted pathway, or by a non-concerted pathway. If you compare, this 2,3,0-bicyclic system, this particular molecule, that is shown here, this undergoes ring opening reaction, at extremely high temperatures, greater than 450 degrees.

And, this is essentially proceeding through a non-concerted radical path way, to give this particular product. Because, this is not a product, one would expect, based on the Woodward-Hoffmann rule. What happens is, if the Woodward-Hoffmann rule were to be followed, the last reaction, shown in the bottom should have proceeded, this particular case. But, the Woodward-Hoffmann rule essentially tells you that, this reaction has to proceed by a conrotatory process. Because, it is a four-electron system.

Two PI, two sigma, is the four-electron system, that we are talking about. That would end up putting the, one of the Hydrogen in the interior. In other words, this double bond is a Trans double bond. In a small ring size of this, ring compound of this kind, the Trans double bond is not particularly stable.

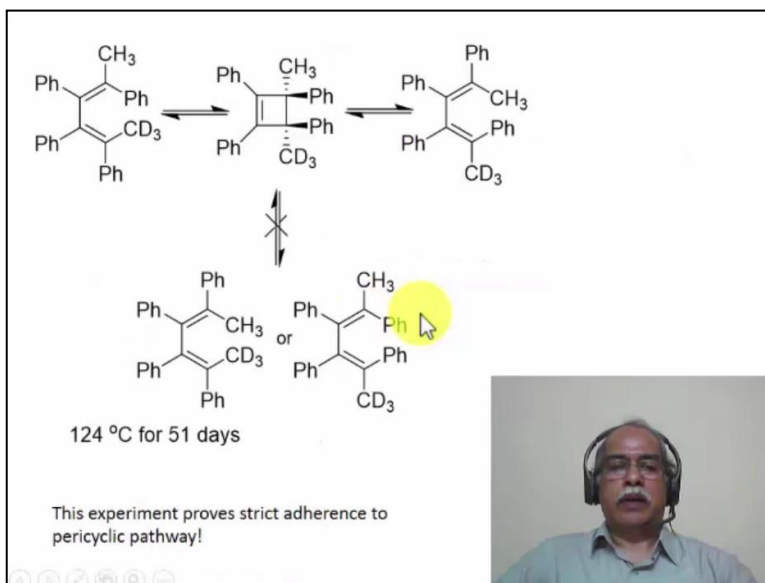
So, this reaction does not proceed in a concerted fashion, which will be forced to do so, by means of a conrotatory process, to give this particular product. On the other hand, slightly a larger ring system with one more carbon being present, this is a 6+2 8 ring, eight membered ring system. Whereas, this is a seven-membered ring system. In a seven membered, or a six-membered ring system, to accommodate a Trans double bond, is almost impossible.



Whereas, in an eight-membered ring system, accommodating a Trans double bond, is quite feasible. So, this reaction essentially proceeds through a concerted pathway, to give this particular product. So, the reason that, this molecule does not react at 250 degree, rather reacts only around 450 degree centi-degrees. At 250-degree C, if the concerted pathway has to proceed, it will give an unstable structure of this kind, which is not feasible.

So, the reaction does not proceed. On the other hand, at a very high temperatures, a non-concerted pathway essentially leads to the formation of a diradical, by breaking of this particular cyclobutene bond, to give a diradical species. And, subsequent rearrangement is what, leads to the formation of this particular product. On the other hand, this will undergo a concerted pathway, at a much lower temperature of 250 degrees, to give the product, where the Trans double bond can be easily accommodated, on a larger ring system like an eight-membered ring system.

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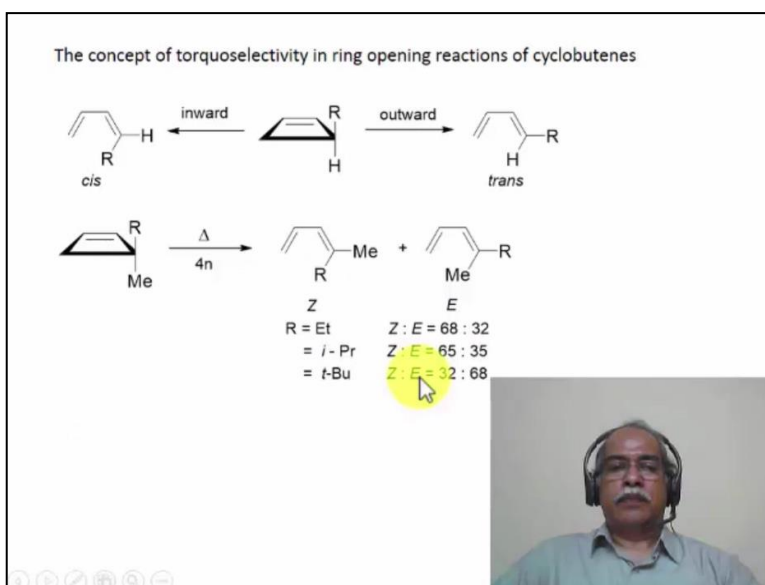
Now, this example is a beautiful example, which illustrates that, the 4N electron system of the cyclobutene undergoing the electrocyclic ring opening reaction, strictly adheres to the Woodward-Hoffmann rule. The experiment is carried out like this. You take this diastereoisomer of this particular molecule, where the two phenyls are Cis with respect to each other. And, the methyl and the CD3 are Cis with respect to each other. Under thermality condition, around 125 degrees, it is heated.

Upon heating, it essentially undergoes electrocyclic ring opening reaction, in a conrotatory process, to give either this or this, depending upon, whether it is a clockwise direction twisting, or anticlockwise direction twisting, to give either of this two molecule. Where, either the phenyl and CD3 are interior, or the CH3 and phenyl are interior, with respect to each other in terms of the diastereo isomer, that are being produced.

In no circumstances, these two molecules are produced, under these reaction condition. Even, when the reaction is carried out, for a very prolonged period of time of 51 days, for example. During this 51 days, this equilibrium would have gone back and forth, millions of times. Under these conditions, these two products are not formed. Because, these two products are essentially arising out of the disrotatory ring opening of this molecule.

So, disrotatory ring opening is not allowed by Woodward-Hoffmann rule. And, a dis-allowed process is completely forbidden. And it is, this reaction is strictly adhering to the pericyclic pathway is illustrated by the fact that, heating this for about 51 days, does not even produce trace amounts of these molecules, which are the anti-Woodward-Hoffmann rule kind of a product.

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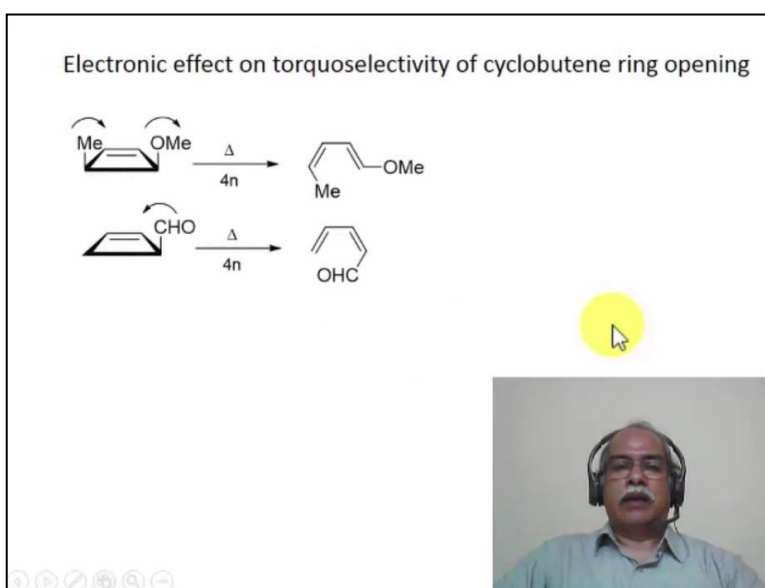


Now, we are talking about, in this particular slide, the possibility of an inward motion, or an outward motion. Remember, in the conrotatory or the disrotatory process, there are two possible modes of reaction. In the conrotatory process, the two bonds have to be twisted in the same direction. The same direction could be, either clockwise direction, or anticlockwise direction. So, when a three-substituted derivative of the cyclobutene is taken.

By the inward motion, the R group can, for example, come interior to the Pi system, like it is shown here, to give the Cis product, or by an outward motion, which is pushing the R group outside of the Pi framework, the Trans isomer can be obtained. Whether, the R will come to the interior or exterior, would depend upon the bulkiness of the R group. If it is strictly an alkyl group, like ethyl isopropyl, and tertiary butyl.

The tertiary butyl group prefers to be in the exteriors. So, predominantly, the exterior motion, outward motion of the tertiary butyl group is, what is being preferred in this particular case, when the R group is in the three position, like it is shown here.

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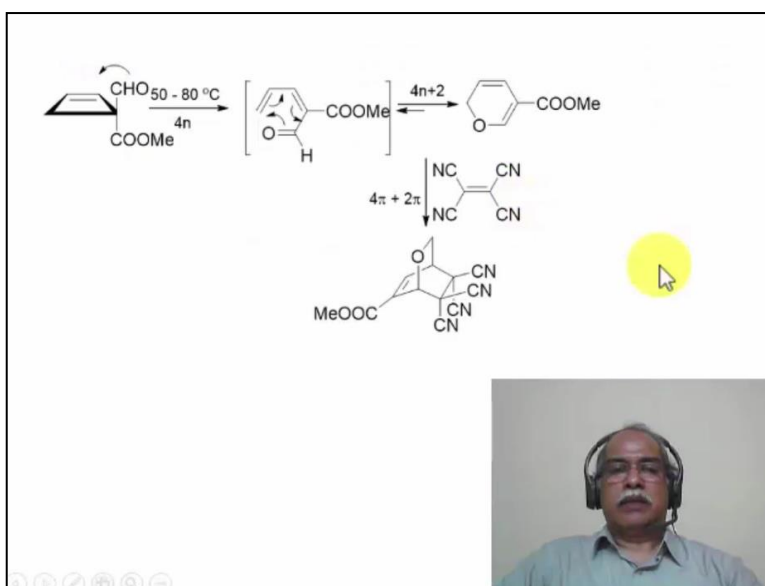
On the other hand, if you have an electronically biased functional group, like the electron donating methoxy group, or an electron withdrawing formyl group, aldehyde group, like this one, for example. The selectivity towards, either the clockwise twisting, or anticlockwise twisting, completely depends upon the kind of functional group, that you have. This is called the electronic effect on torquoselectivity.

Torquoselectivity is essentially the twisting motion selectivity, either in the clockwise direction twisting motion, or in the anticlockwise direction twisting motion. And, the term torquoselectivity was coined by ken houk. Through some theoretical calculation, he was able to show that, whenever you have an electron donating methoxy kind of a group, it is always twisted outward, to give this particular isomer.

Whereas, when you have an electron withdrawing functional group, the ester, or the carbonyl functional group of this kind, it is always push to interior to the Pi system, to give the isomer, that is shown in this.

So, the torquoselectivity essentially refers to, the preferential twisting of the carbon-carbon bond, say, either in the clockwise direction, or in the anticlockwise direction, under thermal condition, in a conrotatory process. Both of them are conrotatory, please bear in mind. Except, this is a clockwise direction conrotatory, whereas this is an anticlockwise direction conrotatory. And, that is what is meant by the torquoselectivity, in this particular case.

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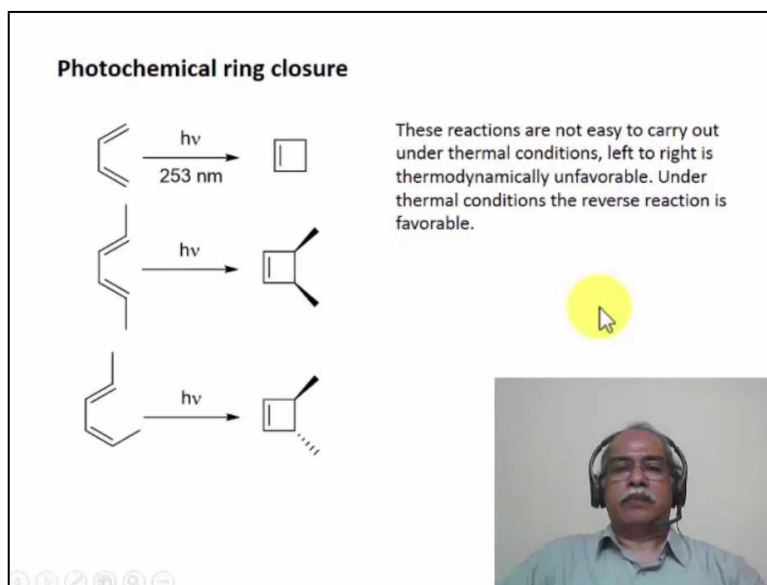
This is further illustrated, in this example, where you have a formyl group, as well as an ester functional group. The selectivity, torquoselectivity, essentially push the formyl group, aldehyde group, to the interior. And, the ester group is pushed exterior, for the reason that, this is sterically bulky, as well as, this is a stronger electron withdrawing functional group, compared with the ester functional group.

So, for both the factors, are in favor of pushing the formyl group interior, aldehyde group to the interior. Once it is pushed interior, you have a 6 Pi electron cyclization is what is taking place, for example. So, this conjugated aldehyde essentially undergoes electrocyclic ring closing reaction, to give this dihydro pyrene derivative, which is this particular derivative.

This is a diene. It can undergo diels alder reaction, with the tetracyanoethylene. This is not stable by itself. It will revert back to the starting material, in this particular aldehyde is, what is in

equilibrium, with this ring closed system. If you want to trap this diene unit, you can use tetracyanoethylene, and trap it in the form of a cycloadduct, which is shown in this particular case. So, this is also illustrating the torquoselectivity, in terms of the aldehyde functional group being pushed inside, and the ester functional group being pushed outside, by an outward motion by the arrow that is, twisting motion of the arrow is shown, in this particular slide, very clearly.

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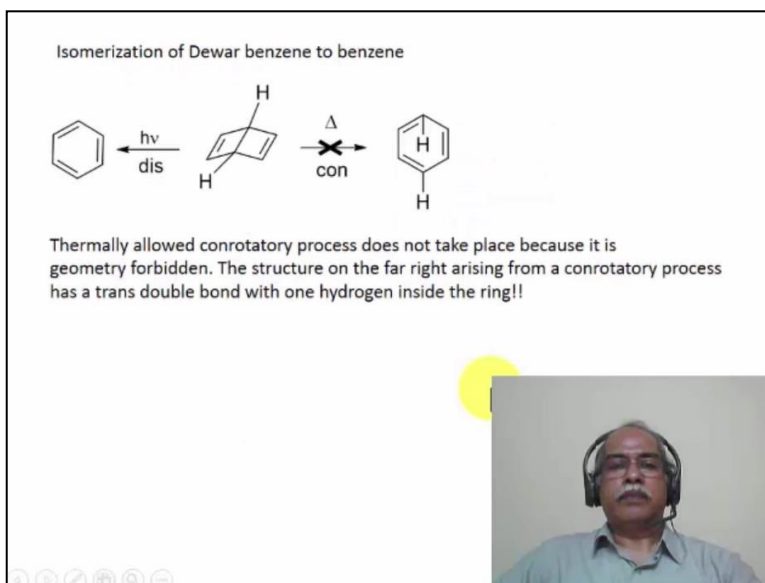
Now, let us come to the photochemical ring opening and ring closing reactions. These are examples, where you have a cyclobutene formation, from the open chain butadiene kind of a system. Remember, this reaction in the forward direction, is not easy to do under thermal condition. Because, the reverse reaction is thermodynamically favorable. So, what is done is, by selecting a wavelength, where the butadiene alone absorbs, for example.

This can be excited to the higher excited state. And, the reaction can proceed, from the higher excited state, to the ring closing product, which is the cyclobutene as a product. Although, it is thermodynamically unstable, photochemical reactions can essentially result in the formation of thermodynamically unstable system. Because, they come from the excited state of the molecule. This two examples essentially illustrate that, these reaction adheres to the Woodward-Hoffmann rule, by the disrotatory ring closing mode of the reaction.

The disrotatory mode of ring closing reaction of this *Z*, sorry, *EE* isomer of the dimethyl butadiene, will give you the 3,4-*CIS* dimethyl cyclobutene as the product. Whereas, the *ZE* isomer of the dimethyl butadiene molecule will give you, the 3,4-*TRANS* dimethyl cyclobutene as a molecule, by a disrotatory process. So, all you have to do is, imagine a disrotatory process of

the two carbon atoms of this, the terminal carbon atoms, resulting in the formation of the Trans isomer, from here, and the Cis isomer from this particular molecule.

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Here is a classical example, which appears like, the Woodward-Hoffmann rule is violated, but it is not truly violated. The question is, dewar benzene is an unstable compound. It can easily, should be possible for it to undergo a electrocyclic ring opening reaction, to go to benzene. But, the problem is, whether it will undergo electrocyclic ring opening under thermal conditions, or photochemical condition, is what, is being discussed here.

The thermally allowed process does not take place, for the simple reason that, if the thermal process were to take place, the conrotatory motion has to take place. Because, it is a four-electron system. Two sigma and two Pi electron is, what is supposed to take place, during the electrocyclic ring opening of the cyclobutene, to give benzene. However, the conrotatory electrocyclic ring opening reaction will put, one of the Hydrogen, the interior of the ring system. This is not benzene.

This is an absurd structure. This is a non-existing structure, where there is a Trans double bond within the benzene structure, which is not possible. Geometrically, it is not a feasible process. However, under photochemical condition, the disrotatory process will bring both the Hydrogens, to the exterior of the Pi system. And, benzene indeed will be formed, by the photochemical reaction of the dewar benzene. The central structure is dewar benzene.

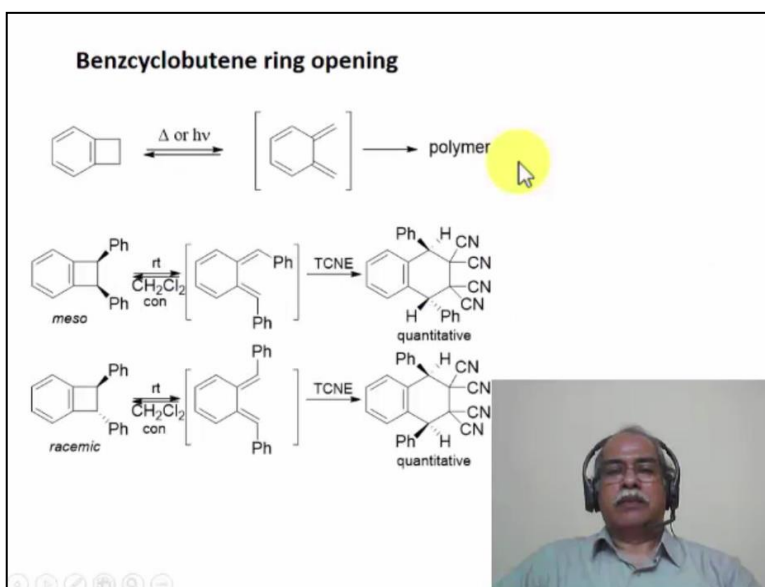
And, the left-hand side structure is benzene. Whereas, the right-hand side structure is Trans benzene, which is a non-existing compound. So, the structure on the far right, arising from the

conrotatory processes, as a Trans double bond, with the one Hydrogen inside the ring. So, this is not a feasible structure.

That is one of the reasons, the dewar benzene molecule is extraordinarily stabled thermal condition, surprisingly stabled thermal condition. In spite of the fact that, its ring opening to give the benzene molecule should be thermodynamically feasible, because of the aromaticity gain, gain in the aromaticity energy, for example. But, however, that is not taking place. Because, it is violating the Woodward-Hoffmann rule.

On the other hand, under photochemical condition, it confirms to the Woodward-Hoffmann rule, to produced benzene. So, photochemically, it is much more easy to do the isomerization of dewar benzene to benzene. Thermally, it is not easy to build conversion of the dewar benzene, to the benzene molecule. Because, it does not produce benzene at all, under the thermal condition.

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If the cyclobutene is fast up, part of a fuse to ring system, like the benzocyclobutene. Benzocyclobutene, under both thermal condition, as well as under photochemical condition, can undergo ring opening reaction, by breaking of this particular carbon-carbon bond of the cyclobutene, resulting in the formation of an intermediate, what is known as the quinodimethide derivative.

This is a ortho quinodimethide, which is a highly reactive substance, for example. When it is left on its own, it will either go back to the starting material, or most likely it will undergo

polymerization reaction. Because, it is a cross conjugated polyene system, prone to undergo polymerization reaction.

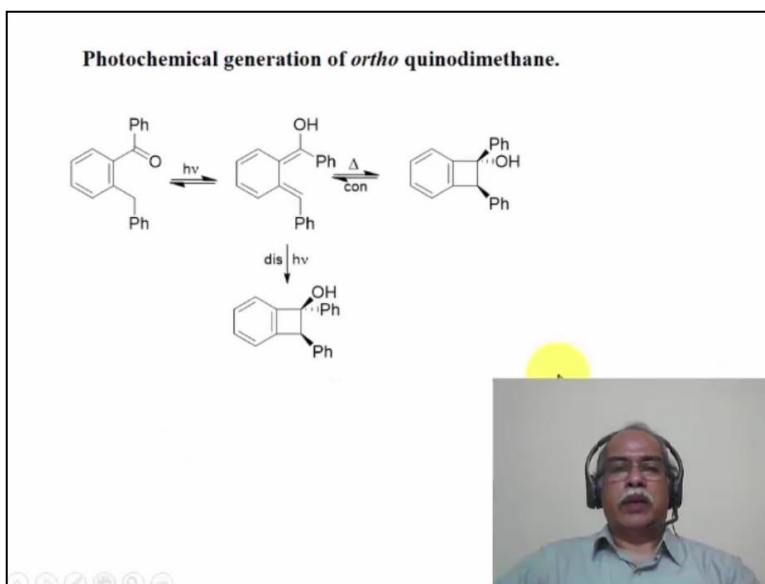
So, in the absence of any trapping agent, it is not possible to decide on the stereochemistry of this ring opening or ring closing reaction. So, that is carried out, using this two diastereo isomer. This is the meso isomer. In other words, this is diphenyl isomer of the benzcyclobutene. This is a Trans diphenyl isomer of the, racemic isomer of the benzcyclobutene. Under thermal condition, it undergoes conrotatory ring opening, to give this particular diastereo isomer, which is a diphenyl substituted ortho quinodimethide molecule.

This is trapped by tetracyanoethylene, to give this particular product in quantitatively. On the other hand, the Trans isomer gives the opposite diastereo isomer of the ring opened product, again by a conrotatory process, to give this. And, under thermal condition, it is trapped by tetracyanoethylene. So, the second step, what you are seeing using TCNE, which is tetracyanoethylene, is essentially the diels alder reaction between this diene and the dienophile, which is a tetracyanoethylene.

The first step is a electrocyclic ring opening reaction, proceeding through conrotatory ring opening reaction. The second step is the diels alder reaction of the diene and the dienophile, to give this adduct, which is the diels alder adduct. So, these are examples of benzcyclobutene, undergoing ring opening reaction.

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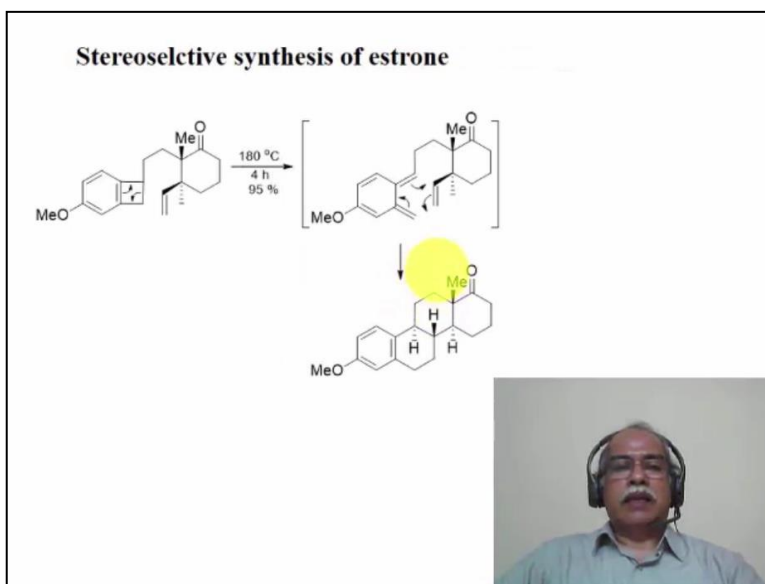


Benzcyclobutene can be produced also, by photochemical reaction. This is the famous Norrish type two, kind of a Hydrogen abstraction reaction. When aromatic ketones are excited to higher excited state, particularly in the triplet state, the oxygen becomes highly Hydrogenphilic, and abstracts the Hydrogen from, for example, alpha, beta, gamma position. The gamma Hydrogen abstraction results, in the formation of the ortho quinodimethide derivative, of this kind.

The ortho quinodimethide derivative, under the thermal condition, under room temperature condition, or under the conditions of the photolysis, for example, temperature of the photolysis, it undergoes the electrocyclic ring closure reaction, to give the conrotatory process, to give this particular diastereo isomer of the, where the two phenyl groups are Cis with respect to each other, in terms of the stereochemistry. On the other hand, under photochemical condition, it undergoes a disrotatory ring closing reaction, to give the benzcyclobutene derivative.

In this particular case, benzcyclobutanol derivative is, what is being formed. These highly stereoselectivity of this, high stereoselectivity of this reaction, essentially confirms to the Woodward-Hoffmann rule, in terms of the four-electron system, undergoing a conrotatory process, under thermal condition. And, in disrotatory process, under photochemical condition, to give the respective diastereo isomers of the ring closed, benzcyclobutene product.

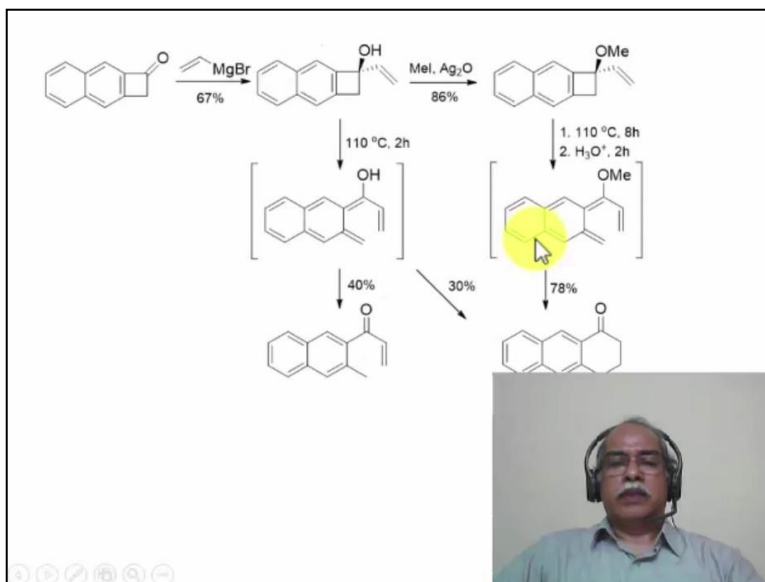
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It is a classical example of, synthesis of a steroidal molecule called estrone. Estrone is a naturally occurring steroid in our body. This is essentially produced by generating an ortho quinodimethide, by the benzcyclobutene ring opening reaction, followed by trapping of the molecule, trapping of the ortho quinodimethide, intramolecularly, using a built-in dienophile, which is this vinylic carbon that we have, vinylic substituent, that we have, here.

So, a 4 + 2 cycloaddition reaction essentially produces this ring, b ring of the steroid, for example, is produced by the thermal 4+2 cycloaddition process. So, the first step is an electrocyclic ring opening reaction of the benzcyclobutene, to give the ortho quinodimethide. The second step is a cycloaddition, by intra molecular trapping of the ortho quinodimethide with the vinyl substituent, that is present in the system.

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In this particular example, the benzocyclobutene derivative is generated from the benzocyclobutanone derivative, by addition of a vinyl magnesium bromide, for example. A vinyl magnesium bromide addition to this ketone, gives this treachery alcohol, which is methylated using methyl iodide, in the presence of the silver oxide, to give the corresponding methoxy derivative.

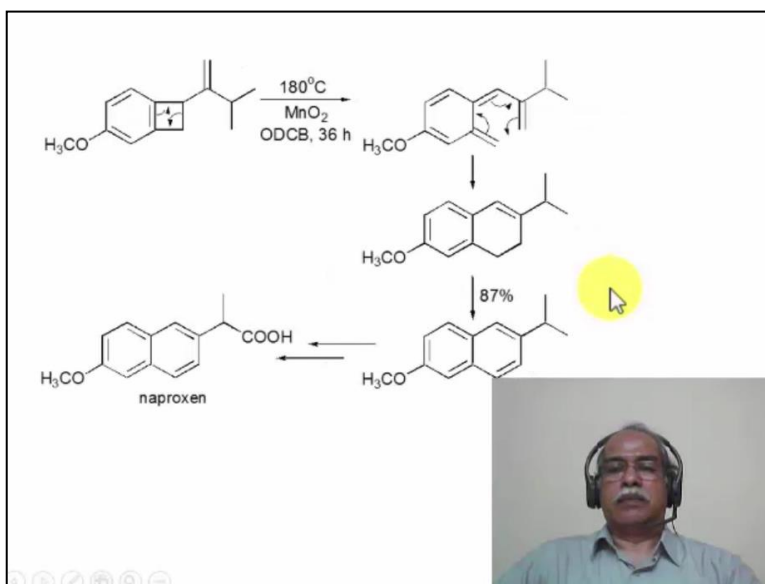
Heating of the methoxy derivative, gives the ring opening product, which is this triene product. A electrocyclic ring opening reaction will give you, the ortho quinodimethide derivative. But then, you have a vinyl group, attached to it. So, that vinyl group will now part of the triene system. Triene system, undergoes the electrocyclic ring closing reaction, to give the corresponding hexadiene, cyclohexadiene derivative.

The cyclohexadiene derivative will have, this methoxy as a enolic methoxy derivative. And, that is hydrolyzed under eco specific condition, to give the corresponding ketone. On the other hand, this enol, for example, essentially undergo keto-enol-tautomerism, to give the ketone, without the methylation, for example, when you do the ring opening of the cyclobutanol derivative, benzocyclobutene derivative, for example.

It gives the enolic structure, which undergoes essentially keto-enol-tautomerism, to give this particular product. So, these are all examples of benzocyclobutene, undergoing ring opening reaction, to give the corresponding ring open the product, which are subsequently manipulated to undergo, either diels alder addition reaction, or electrocyclic ring, further electrocyclic ring closing reaction.

The second step is a six-electron ring closing reaction, in this particular case. And, that will have its own Woodward-Hoffmann rule, in terms of being a six electron, thermal electrocyclic reaction would be a disrotatory process. But, the stereo chemical information is not possible, in this particular case. Because, this does not have any stereo centers, associated with the system.

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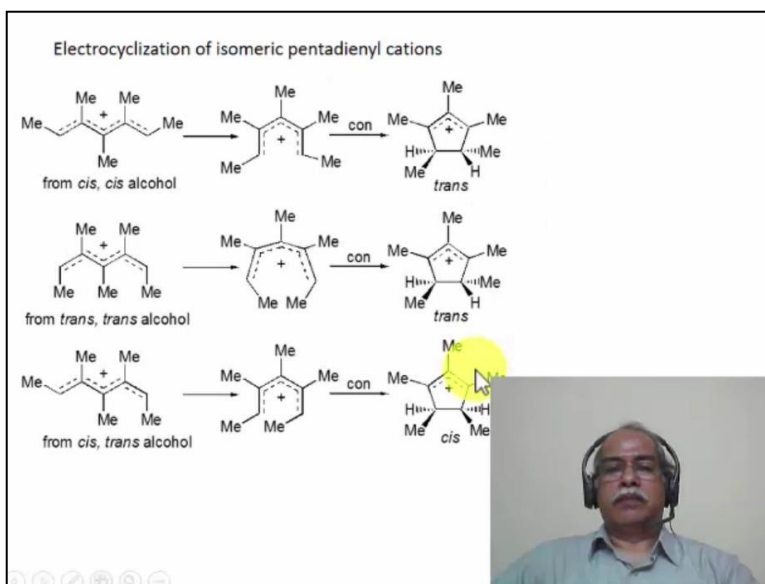


It is another example of a built-in vinyl cyclobutene derivative. The manganese dioxide comes at a later stage. So, do not worry about manganese dioxide, in this process. This is a thermal ring opening reaction of the cyclobutene, to give this hexatriene unit. Hexatriene unit undergoes electrocyclic ring closing reaction, by a disrotatory process, to give the corresponding dihydro aromatic derivative.

This is a dihydro naphthalene derivative. In fact, the oxidation of the dihydro naphthalene derivative is, what requires the manganese dioxide. Ortho dichlorobenzene is used as a solvent. ODCB is ortho dichlorobenzene, which is used as a high boiling solvent. The manganese dioxide gets involved, in the dehydrogenation of the dihydro derivative of this naphthalene derivative, to give the corresponding naphthalene derivative.

This derivative is useful for naproxen, which is a painkiller, commercially available painkiller. Oxidation of one of the methyl groups to the carboxylic acid, will essentially produce the naproxen molecule, from this particular molecule. So, this is towards the naproxen synthesis is, what is illustrated by means of a electrocyclic ring opening, followed by a electrocyclic ring closing, and aromatization reaction, leading to the formation of a naphthalene derivative.

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So far, we have been looking at four membered ring system. Let us move on to five membered ring system. Ring opening and ring closing reactions of pentadienyl cations, for example, to give cyclopentenyl cation. Now, if you consider the alcohol, corresponding to this position here. In other words, I will put a hydroxy functional group in the central carbon here, and take the alcohol with the pentadienyl alcohol, for example.

And, the pentadienyl alcohol, when it is treated with a strong acid like sulphuric acid, or magic acid, it undergoes dehydration, to give this pentadienyl cation. The pentadienyl cation, in this particular case is CIS-CIS isomer. The two methyl groups are Cis here. And, the two methyl groups are also CIS, in this particular case. If you follow the cursor movement, you will see the Cis relationship between the two methyls here, and the two methyls over here.

So, it is a CIS-CIS alcohol. It is rewritten in a way, such that, the one and five positions are close together. So that, it can undergo a cyclization reaction. So, the pentadienyl cation essentially undergoes a ring closing reaction, to give cyclopentenyl cation. In doing so, it is undergoing a conrotatory process. The conrotatory process will put, one of the methyl group in the top, and other in the bottom.

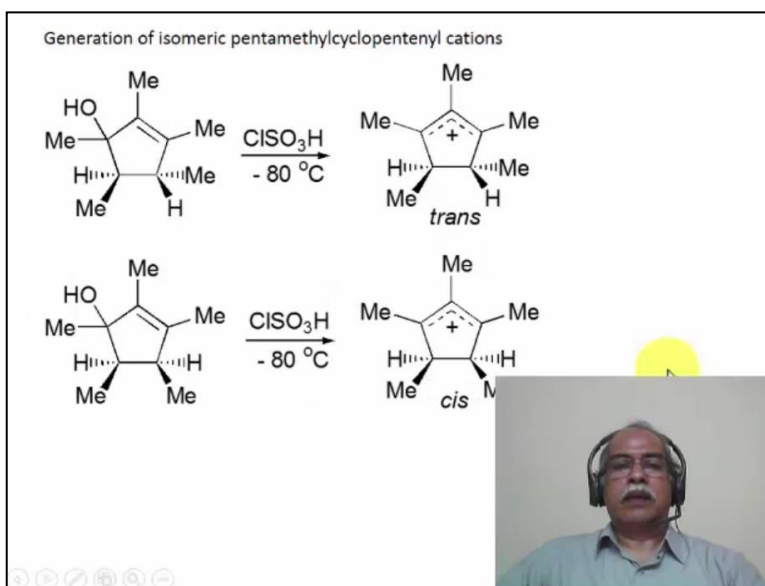
In other words, the Trans dimethyl derivative is, what is going to be obtained in this case. All of these intermediates are characterized by ((lorenz meijer)) (40:39) proton NMR spectroscopy. Because, this ionization of the alcohol to the pentadienyl cation, can be carried out at a very low temperature, using chloro-sulfonic acid kind of a very strong acids, at low temperatures. If you take the TRANS-TRANS isomer of the corresponding pentadienyl cation, this is TRANS, this is also TRANS, with the two methyl being Trans here, and the two methyl being Trans here.

That results in the formation of the pentadienyl cation, which is shown here. Conrotatory process, now gives the Trans isomer of the derivative, that is shown here. On the other hand, if you take the CIS-TRANS isomer, then it gives essentially. This is the pentadienyl cation, which is the TRANS-CIS isomer, is the stereochemistry. All of them are diastereo isomers, with respect to each other, in terms of the stereochemical relationship.

In this particular case, the Cis dimethyl derivative is, what all you have to do is, imagine a conrotatory process of ring closing, between carbon number one and carbon number five, across these two carbons, resulting in the formation of a pentadienyl cation. In this particular case, conrotatory process will bring, both the methyl groups above the plane of this, if you do the conrotatory process in a clockwise direction.

Similarly, if you do a conrotatory process in the clockwise direction, the two methyls will be anti-with respect to each other, in the other two cases.

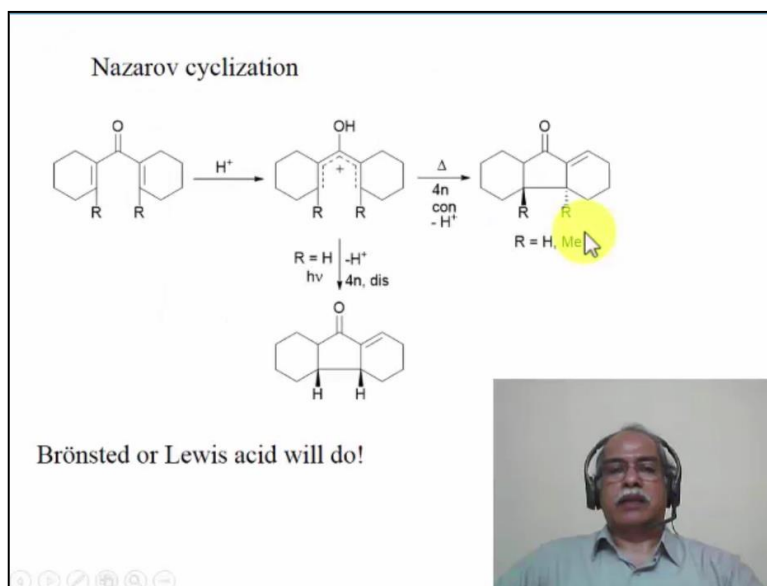
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And, this is how the pentadienyl cations were characterized. How do we know, the stereochemistry as TRANS, CIS, and so on, for this cyclopentenyl cation? They were independently generated, using chloro sulfonic acid, at very low temperature. And, comparing the NMR spectrum of the CIS, and Trans isomer, that was obtained during this reaction, versus the reaction, that is shown here, for example.

The identical NMR spectral features, of the Trans and Cis isomers from here to this particular reaction, is confirming the stereochemistry of the cyclopentenyl cation, as far as the stereochemistry of this reactions are concerned. .

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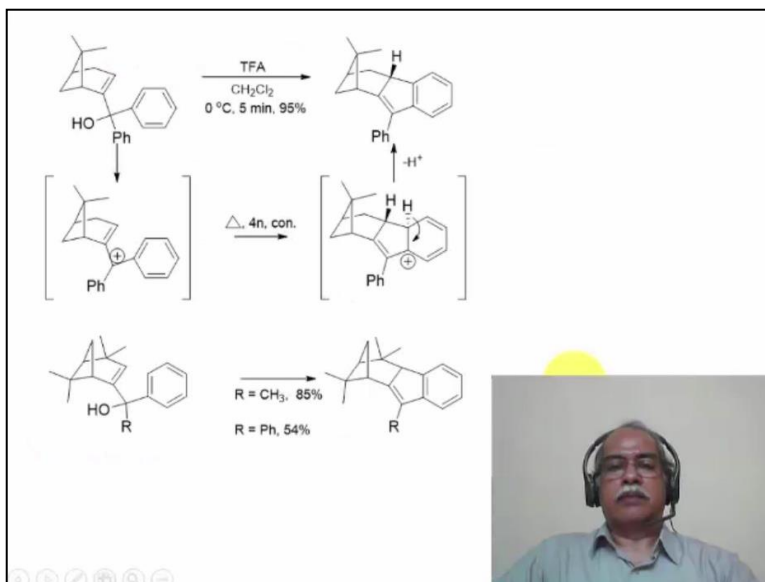
Now, pentadienyl cation undergoing cyclization, to give cyclopentenyl cation is called, sometime called nazarov cyclization. Nazarov cyclization can be triggered, either by a bronsted acid, or a lewis acid. In this particular example, the bronsted acid is given, protonic source is given. So, what happens here is, this cross conjugated ketone, essentially is protonated on the oxygen, to give the protonated ketone. The protonated ketone is nothing but a pentadienyl cation.

The pentadienyl cation, now undergoes reaction between, carbon number one and carbon number five, in terms of the electrocyclic ring closing reaction. This is a 4 electron electrocyclic ring closing reaction. Under thermal condition, it will undergo the, a 4N process will undergo the conrotatory process. And going so, it will give you a cyclopentenyl cation. The cyclopentenyl cation loses a proton, followed by keto enol tautomerism, to give this corresponding ketone.

So, the deprotonation takes place from the alpha position, which is this particular position. And, as a result, a double bond is generated here. The same reaction is carried out, under photochemical condition. The stereochemistry here reveals that, this is a conrotatory process. If you do a conrotatory process, to ring close this two carbons here, the two R will end up Trans, with respect to each other, if it is a conrotatory process.

If it is a disrotatory process, the two R groups will end up CIS, with respect to each other. That has been shown, when R is equal to Hydrogen, under photochemical condition, to give this particular product of stereochemistry being CIS, with respect to each other, corresponding to a disrotatory process, in this case.

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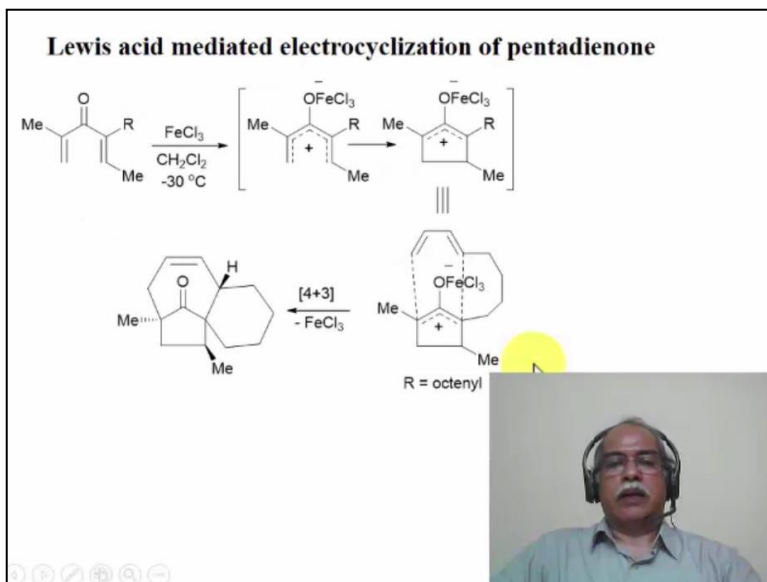
These are some more examples of pentadienyl cation, undergoing cyclopentenyl cations, syc cationic system. This alcohol is ionized in TFA at low temperatures, zero degree centigrade for example, that produces a cation here. That cation is in conjugation with these two double bonds, which are the pentadienyl cation. So, the pentadienyl cation undergoes a ring closing reaction at this stage, followed by loss of a proton from this position.

Initially, protonated water generates the carbonium ion. So, deprotonation results in the formation of the deprotonation, from this particular Hydrogen is being removed, to give this aromatic system back. And, this is a molecule, that is being produced. The mechanism is shown here. Initially, a carbonium ion is produced.

A carbonium ion is undergoing the electrocyclic closing reaction, under a conrotatory process, to give this molecule. This is undergoing a deprotonation reaction, essentially to lead to a neutral product, which is this particular product. This is a camphor kind of a derivative, is what is being taken here. To give the same kind of a electrocyclic ring closing reaction, to give the, cyclopentadienyl cation undergoing cyclization, to give cyclopentenyl cation, which deprotonates to give the cyclopentane derivative, as a final product in this particular case.

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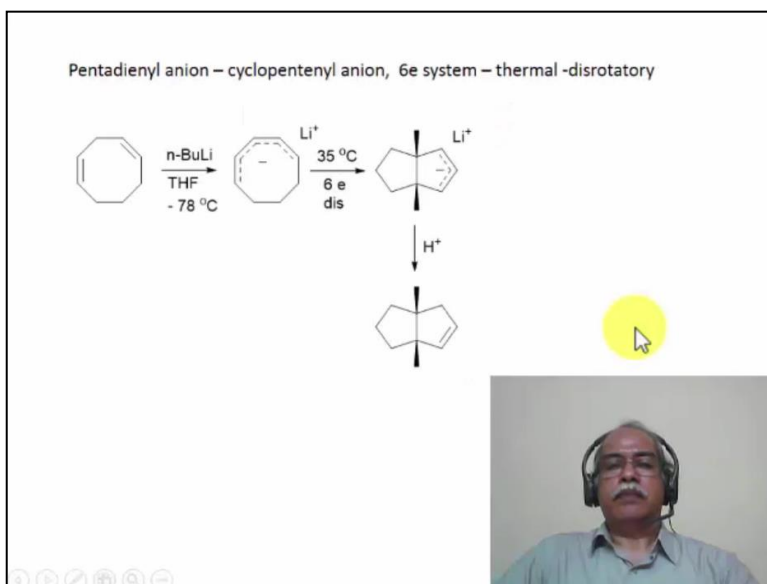




The Nazarov cyclization intermediate, namely the pentadienyl cation, undergoes a cyclopentenyl cation, in terms of the ring closing reaction. The pentacyclopentenyl cation can be trapped by a 3+4 cycloaddition reaction, if you have a built-in diene here. If the R group is this long chain built-in diene group, which is the butadiene group, then it can undergo a 4+3 cycloaddition reaction, to give the bridged bicyclic derivative of this kind.

The bridged bicyclic derivative is a result of the 4+3 cycloaddition reaction, followed by the loss of the ferric chloride, to give the neutral product, which is the ketonic product, in this particular instance.

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Finally, we come to the example of a pentadienyl anion, undergoing reaction, to give cyclopentenyl anion. This will be a six-electron system. If you consider a 1,2,3,4 - 1,4 diene of this kind. This is an octadiene. It is an octa-1, 4-diene, is what is being shown, in this particular slide. Upon treatment with butyllithium, the most acidic Hydrogen, of course is this Hydrogen. Because, this is an diallelic kind of a carbon. Methylene is diallelic in nature.

So, that would be the most acidic Hydrogen. So, that deprotonation, essentially gives a carbon ion here. That carbon ion is essentially delocalized, across this five carbon atoms. This is the pentadienyl anion, that we are talking about. The pentadienyl anion, undergoes the six electron disrotatory ring closing reaction, across the carbon number one, and carbon number five, to give the fused bicyclic system of this kind.

A fused bicyclic system, upon protonation, essentially give you, this is a cyclopentenyl anion. The cyclopentenyl anion on protonation, gives the cyclopentane. So, this is an example of a six electrons pentadienyl anion, undergoing a cyclopentenyl anion. Under the thermal condition, this follows a disrotatory pathway, conforming to the Woodward Hoffmann rule.

So, what we have seen in this particular module is, the various systems involving the, either a two electron or a four-electron system, involving a three-membered, four membered, five membered ring systems, to undergo the electrocyclic ring closing reaction. Each one of them conforming to the Woodward Hoffmann rule. As dictated by the Woodward Hoffmann rule, the corresponding stereochemistry aspect is being illustrated, in many of this example. Thank you very much, for your kind attention.