Pericyclic Reactions and Organic Photochemistry

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Introduction – Pericyclic Reactions – Electrocyclic Reactions – Examples of 6 and Larger Ring Systems (6e and More)

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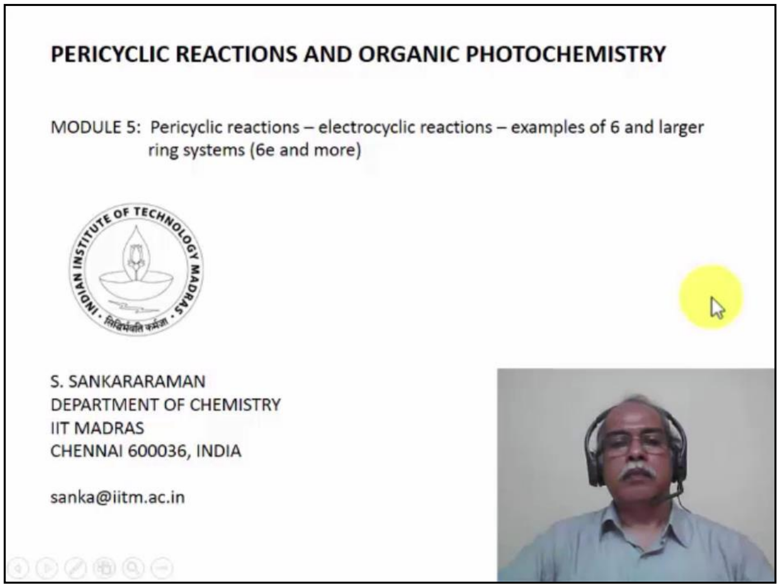

PERICYCLIC REACTIONS AND ORGANIC PHOTOCHEMISTRY

MODULE 5: Pericyclic reactions – electrocyclic reactions – examples of 6 and larger ring systems (6e and more)

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Hello, welcome to the online course on pericyclic reactions and organic photo chemistry. This is module five. We will continue with the electrocyclic reaction, in this module. In the earlier module, we saw smaller systems of four membered and five membered ring system. In this particular module, we will see examples of six and larger ring system, six or more electrons, involving electro cyclization reactions.

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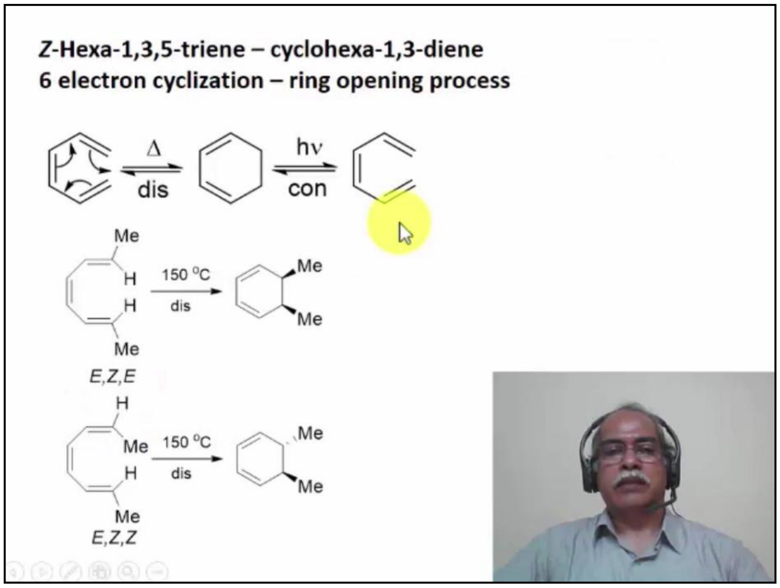

Z-Hexa-1,3,5-triene – cyclohexa-1,3-diene
6 electron cyclization – ring opening process

Now, the hexatriene itself can undergo electrocyclic ring opening and ring closing reaction, under suitable conditions of either, under thermal or under photochemical condition. So, the Z hexa-1,3,5-triene, this. Z 1,3,5-hexatriene undergoing an electrocyclic ring closing reaction, to give hexa-1,3-diene, which is this particular cyclohexa-1,3-diene, which is this molecule here. This can happen under thermal condition, under a disrotatory process, or under photochemical condition, conrotatory process, according to the Woodward-Hoffmann rule.

Because, this is a six-electron system. It has exactly the opposite mode of ring closing and ring opening reaction, under photochemical and thermal condition, in comparison to the four-electron system, which are butadiene, and cyclobutene system. These two example essentially illustrate, the confirmation of the disrotatory process, under thermal condition. This dimethyl substituted hexatriene, when it undergoes the ring closing reaction, it essentially gives the Cis dimethyl derivative, by means of a disrotatory process.

In this case, disrotatory process here, in the clockwise process, and anticlockwise twisting motion, essentially brings the two methyl to the top, to give the Cis isomer. On the other hand, if you take the E,Z,Z isomer of the hexatriene, dimethyl substituted hexatriene, this is a Trans double bond, so it is E. And, this is a Cis double bond, so it is Z, compared to E,E,Z - E,E,Z,Z. These are two diastereo isomers. The opposite diastereo isomer, essentially gives the Trans isomer, by means of a disrotatory process, in this particular instance.

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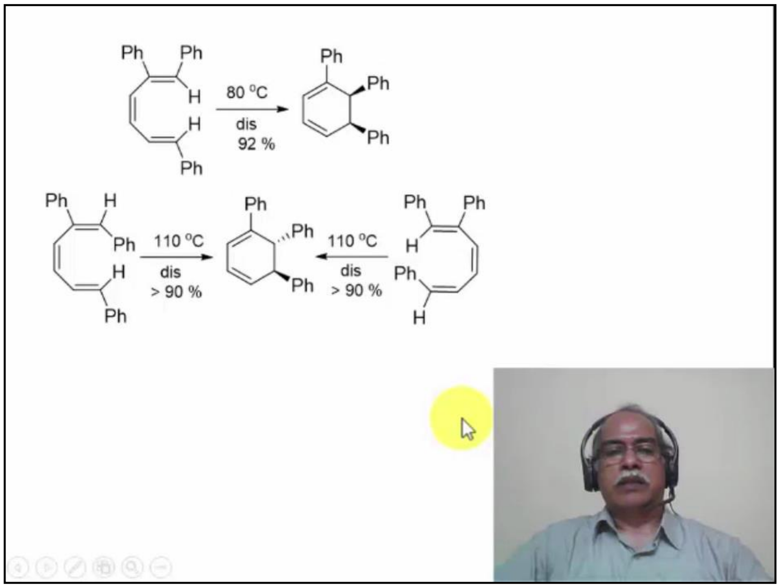

These are some more examples, of the electrocyclic ring closing reactions of the hexatriene molecule, undergoing electrocyclic ring closure, to give the cyclohexadiene kind of a system, confirm in to disrotatory process, in all cases. So, synthesis of the cyclohexadiene, from an open chain hexatriene is facilitated, by means of this thermal electrocyclic ring closing reaction.

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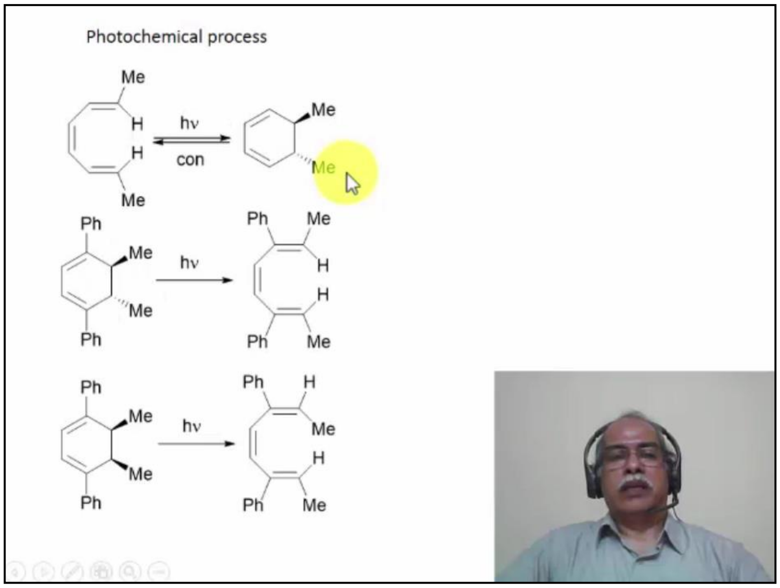

Photochemical process

Under photochemical condition, of course, it will have the opposite mode of stereochemistry. The conrotatory mode, is what will happen. In the case of the photochemical condition, one can either do the, ring closing reaction, or ring opening reaction, depending upon the choice of wavelength. The wavelength corresponding to the triene, if it is used, then the ring closing reaction will take place, like it is shown here. On the other hand, if the radiation corresponds to the cyclohexadiene unit, then the ring opening reaction can also be pushed towards, in this particular case, by photochemical reaction.

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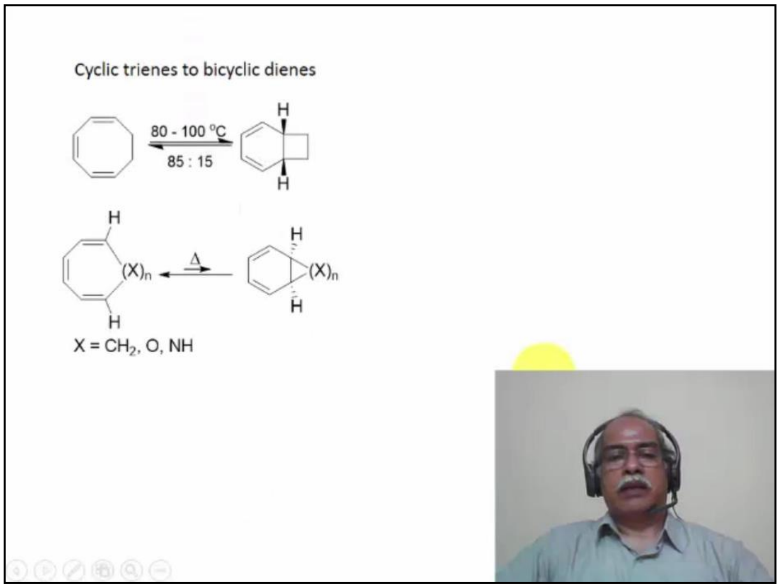

Cyclic trienes to bicyclic dienes

X = CH_2, O, NH

Cyclic trienes also undergo, electrocyclic ring opening, ring closing reaction, to give the bicyclic derivatives, which are the bicyclic dienes, for example. So, these are some of the examples of the electrocyclic ring closing of the cyclic triene, to give the bicyclic derivative, diene derivatives, in this particular case. Conforming once again, to the disrotatory mode of ring closing reaction, in this particular case.

This is an example of a hexa-cycloheptatriene, undergoing reaction, to give norcaradiene, or a oxetane, undergoing electro cyclization reaction, to give benzene oxide. if X is equal to oxygen, then this would correspond to oxetane derivative. The oxetane derivative, undergoes thermal electrocyclic ring closing reaction, to give the benzene oxide. Upwards the equilibrium, is far towards the hexatriene system, rather than the cyclohexadiene system, because of the strain, that is associated with the three-membered ring formation, in these cases.

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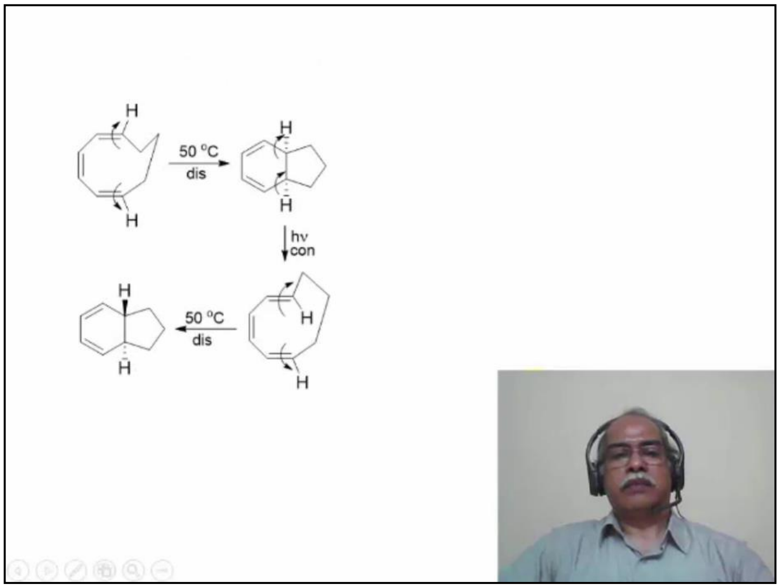

Here, some more examples of the electrocyclic ring closing of the hexatriene, cyclic hexatriene is given. This is a 10-membered ring system. The ten-membered ring system, essentially undergoes at room temperature, are close to room temperature, a disrotatory motion, to give the corresponding Cis fused derivative, which is, this bicyclic derivative.

This, under photochemical condition, will undergo conrotatory process, to give the opposite diastereo isomer, of what we started with. In this particular case, the two hydrogens are outside the PI frameworks. Whereas here, we have a Trans double bond with hydrogen interior, to the 10-membered ring system. This, under thermal condition, will give the thermodynamically more stable transfused ring system. This is a Cis fused ring system. This is thermodynamically unstable, compared to the transfused ring system of this type.

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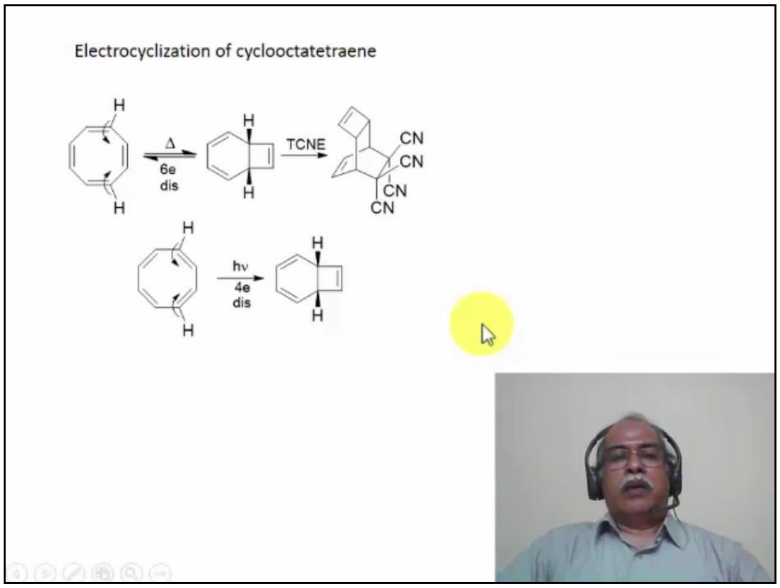
Electrocyclization of cyclooctatetraene

Now, in the case of a cyclooctatetraene, irrespective of, whether one uses the thermal condition or under photochemical condition, it always gives the Cis fused bicyclic derivative of this kind. For example, if you take the cyclooctatetraene, it can function either as a four-electron system, or a six-electron system, depending upon, how many electron system is involved in the electro cyclization. In this case, it behaves like a six-electron system, undergoes a disrotatory electro cyclic ring closing reaction, to give the Cis fused derivative.

The Cis fused derivative can be trapped with tetra ethylene, to give the corresponding TCNE adduct, which is the diels alder reaction of the diene and the dienophile. Let us not worry about the diels alder reaction, for the time being. However, the same cyclooctatetraene can behave like a four-electron system, under photochemical condition, to give the corresponding CIS, same product namely the Cis fused bicyclic system. It never gives, behaves like a four-electron system under thermal condition, or a six-electron system under the photochemical condition, to give the corresponding Trans isomer of this product.

What is the problem with the Trans isomer. If we consider the geometry of this molecule, the Cis fused derivative, with the two hydrogens and the cyclobutene derivative, fused to the six-membered ring, is perfectly normal for a geometry of a molecule. Whereas, if it one were to have a Trans geometry, the two transpositions have to be fused by a CH 2-CH 2 group here, for example, which is geometrically not feasible.

So, such a molecule cannot be produced from the cyclooctatetraene, either under thermal condition, or a photochemical condition. That is a reason, cyclooctatetraene, irrespective of whether it is undergoing a thermal electro cyclization, or photochemical electro cyclization, always produces the Cis fused derivative of the bicyclic derivative, which is the triene derivative, that is shown here. Because, this is geometrically not feasible to be formed, under any condition.

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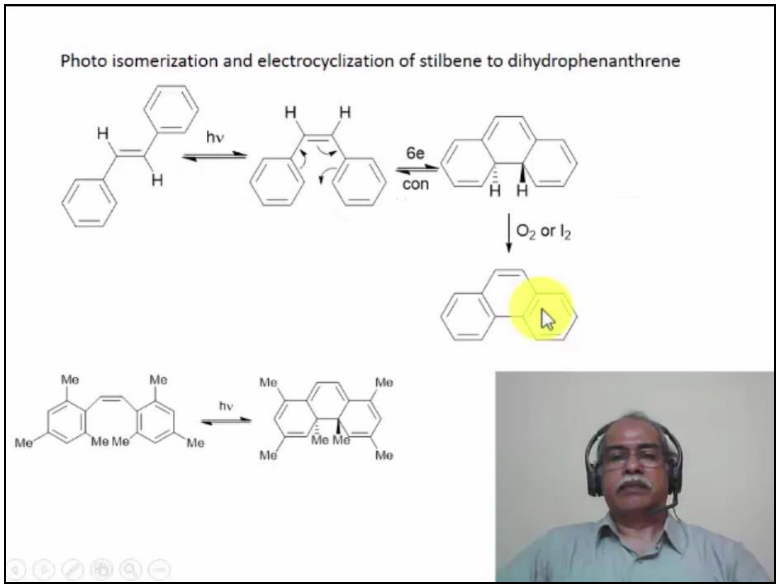

Photo isomerization and electrocyclization of stilbene to dihydrophenanthrene

These are examples of reactions of aromatic olefins, undergoing electro cyclization. This is Trans stilbene. Trans stilbene can undergo, Cis Trans isomerization, under photochemical condition. The Trans stilbene goes to the Cis stilbene. In the Cis stilbene, it has a favorable geometry of the cisoid triene configuration is available here. The cisoid triene configuration, essentially undergoes a six-electron cyclization, by means of a conrotatory mode of ring closing reaction, under photochemical condition.

And the, how do you know, it is a conrotatory process? The stereochemistry of the two hydrogen very clearly tells us that, it is a conrotatory process. If we consider this hydrogen here, and this hydrogen here, only a conrotatory process will push, one of the hydrogen down, and bring the other hydrogen up, to give the Trans dihydro aromatic derivative.

This is dihydrophenanthrene. Dihydro phenanthrene can be oxidized to phenanthrene, by means of either oxygen, or by means of an oxidizing agent like iodine, for example. So, this is essentially a method, for the synthesis of angularly fused aromatic system. And, this particular reaction is widely used in the synthesis of heliecenes, for example.

Now, if you take the example of ortho protected Cis stilbene derivative, as in the case of the dimesityl ethylene derivative, Cis isomer, the ring closing reaction, essentially gives you this dimethyl substituted dihydro derivative. And, this cannot be, for example, oxidize to the aromatic derivative. Because, there are no hydrogens in this position. So, it can either undergo back reaction to start this, to give the starting material, or it can stay in the product stage. And, if it can reversibly go back and forth, then it will constitute a photochromic system.

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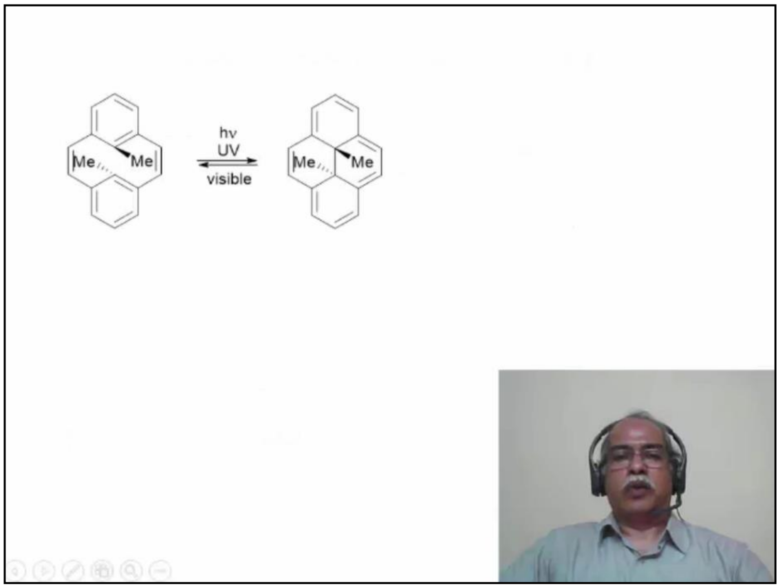

Photochromic systems are binary color systems, which the molecule of a particular color undergoes, electro cyclization reaction, or any other reaction, to give a different color. And, if these colors can be reversed, by means of thermal and photochemical reactions, then you have a photochromic system. Here is an example of a dimethyl substituted metacyclophane diene, undergoing an electro cyclic ring closing reaction.

If you consider this, to be a six-electron cyclization reaction, this would be constituted as a six-electron cyclization, under the photochemical condition, to take place under conrotatory modes of ring closing reaction, to give the Trans dimethyl derivatives. This Trans dimethyl-dihydropyrene is the molecule, that we are talking about here. Under visible light condition, this is a colored compound. Whereas, this is nearly a colorless compound.

So, under UV light condition, the forward reaction can be triggered. Under visible light condition, wavelength of 450 or more, the reverse reaction can be promoted, constituting a photochromic kind of a system.

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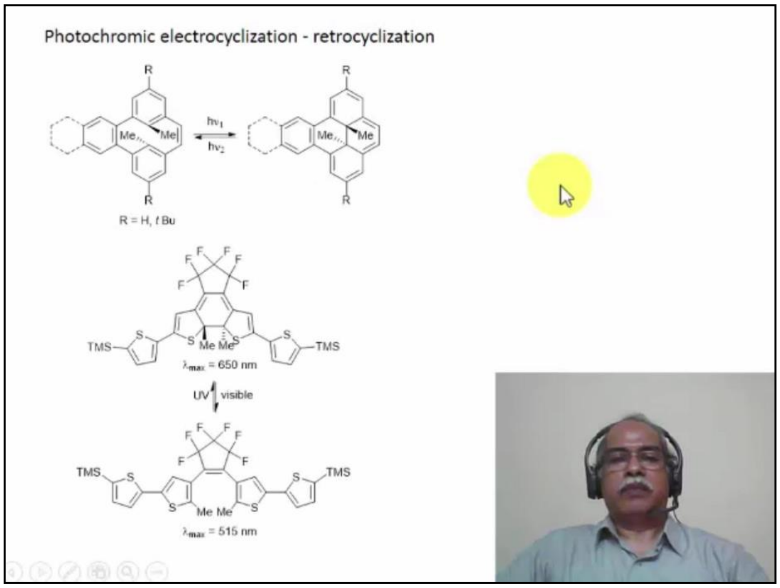

Photochromic electrocyclization - retrocyclization

Now, the larger systems are very well-known in the electro cyclization, retro cyclization, photochromic cells, for example. This particular example essentially illustrates, the six-electron cyclization, and ring opening ring closing reaction, essentially taking place, under UV light in the forward direction, and visible light in the reverse direction, for example. Because, this molecule is absorbing at a much longer wavelength of 650 nanometers, because of the conjugation, that it presents.

Whereas, this molecule is absorbing only 515 nanometers, for example. So, using suitable wavelength, one can promote, either the reverse reaction, or a forward reaction, as the case may be. These two compounds are differently colored. And, that is a reason, it is a photo chemic switching device kind of a thing, one can have. This is a largely, feel a larger. This is a dihydropyrene derivative. This is a large ring system fused dihydropyrene derivative. This is a more-fancy version of this molecule, that we talked about.

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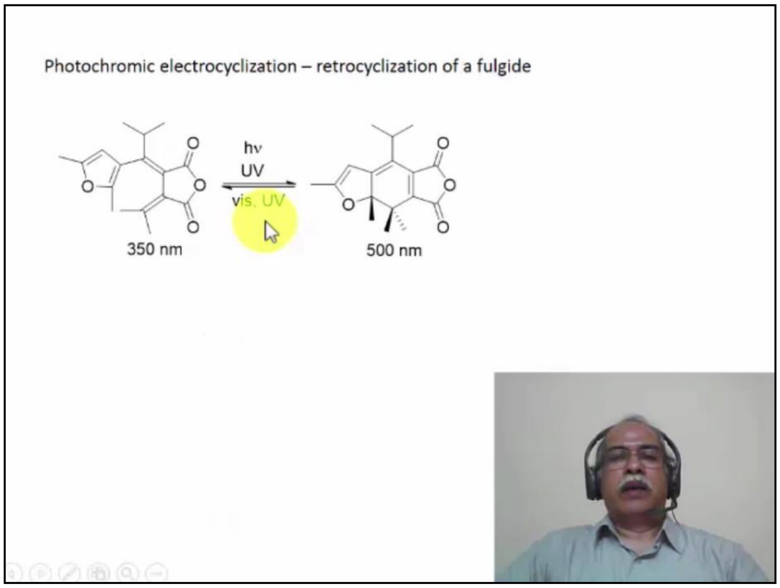

Photochromic electrocyclization – retrocyclization of a fulgide

Here is an example of, a six-electron cyclization of a full guide. Full guide is this, class of molecules, here. And, these have the gem dimethyl hexamethylene compound structure, is what is being present in the system. They undergo electro cyclic ring closing reaction, under UV light. Because, it absorbs in the UV light of 350 nanometers, whereas the ring closed system absorbs in the visible light.

So, one can promote the forward reaction by UV radiation, and the reverse reaction by means of a visible irradiation, for example. All of them are six-electron cyclization, in the forward direction, and six-electron retro cyclization, in the reverse direction.

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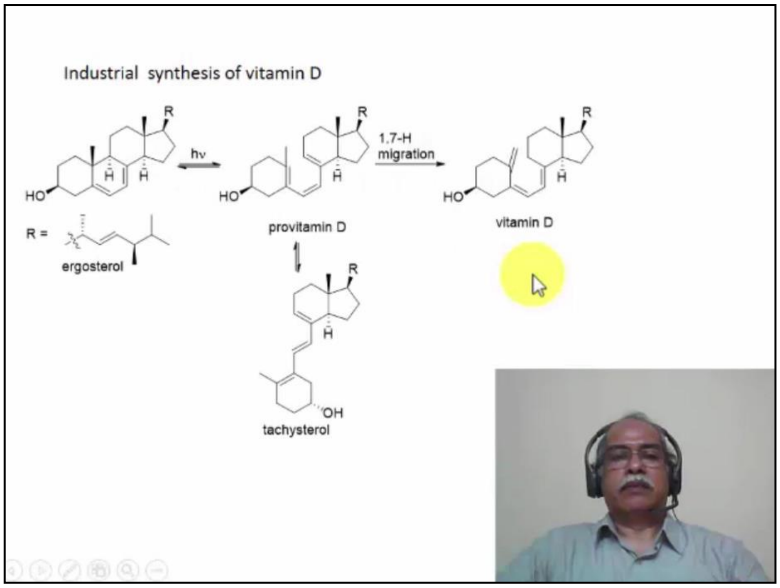

Industrial synthesis of vitamin D

Now, this is a very important synthesis of vitamin D. As you all know, for the synthesis of vitamin D, sunlight is absolutely essential. People, who lack exposure to sunlight, will have vitamin D deficiency. The chemistry behind is, as follows. Ergosterol is a steroidal molecule, that occurs in our skin, under the skin, for example. And, exposure to sunlight, essentially causes an electro cyclic ring opening reaction, to take place.

So, this is a six-electron electro cyclic ring opening reaction, to give this particular product. This is a methyl substituted hexatriene unit, is what we have. And, this is called the pro vitamin D. This is a molecule, that is necessary to be produced under photochemical condition, by exposure to light, such that, this molecule can further undergo a 1,7-hydrogen migration, which is actually a sigmatropic migration.

In other words, the hydrogen from the methyl group, essentially migrates to this position, over here. So, you can see here, this CH has become CH 2. And, this CH 3 has become CH 2, by a hydrogen migration. Why is it 1,7. Because, it is going from 1,2,3,4,5,6,7 carbons away from the, hydrogen is migrating, seven carbons away. That is why, it is a 1,7 migration.

The 1,7-migrated product is, what is known as the vitamin D. Vitamin D is absolutely an essential vitamin for our function. And, this is what is being done, on the industrial scale, for example, for the production of vitamin D. The pro vitamin D can also undergo Cis Trans isomerization, which is a menace. Because, the Cis Trans isomerization is a reversible process, and the 1,7-migration is an irreversible process.

The whole reaction can be pushed towards the formation of the vitamin D, by a reversible process of the Cis Trans isomerization, and the irreversible process of the 1,7-migration, of this. So, this is an industrially important process, as far as the photochemistry is concerned. The crucial step that is involved is, the electro cyclic ring opening of a hexadiene to a hexatriene, cyclohexadiene to a hexatriene unit, which is an electro cyclic ring opening reaction.

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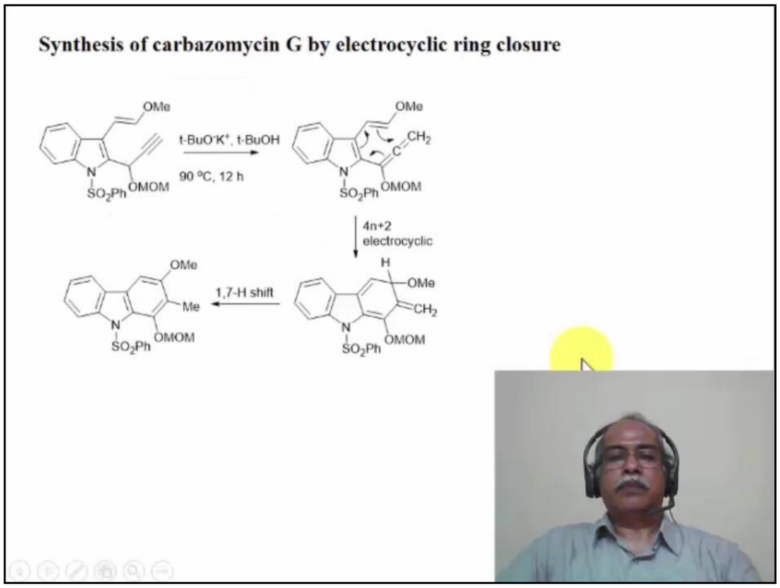

Synthesis of carbazomycin G by electrocyclic ring closure

Now, in this particular example, the synthesis of carbazomycin G, by electro cyclic ring closing reaction is, what is illustrated. If you take this molecule, this is a propargyl system. The propargyl system, on treatment with a strong base like potassium tert-butoxide, will rearrange to a allenyl system. So, this is an allenyl system, and this is a propargyl system. The allenyl system is essentially ready to undergo the electro cyclization, by a six-electron cyclization, as it is shown by the arrow, to produce this hexo methylene compound.

The tautomerism of this particular hydrogen, essentially results in the formation of an intermediate, which is used for carbazomycin G synthesis, by. The crucial step, of course is the electro cyclic ring closing reaction of the allenyl substituted hexatriene system, to give the hexo methylene cyclohexadiene system, which undergoes 1,7-hydrogen shift again, to give the corresponding aromatized system, which is a carbazole derivative.

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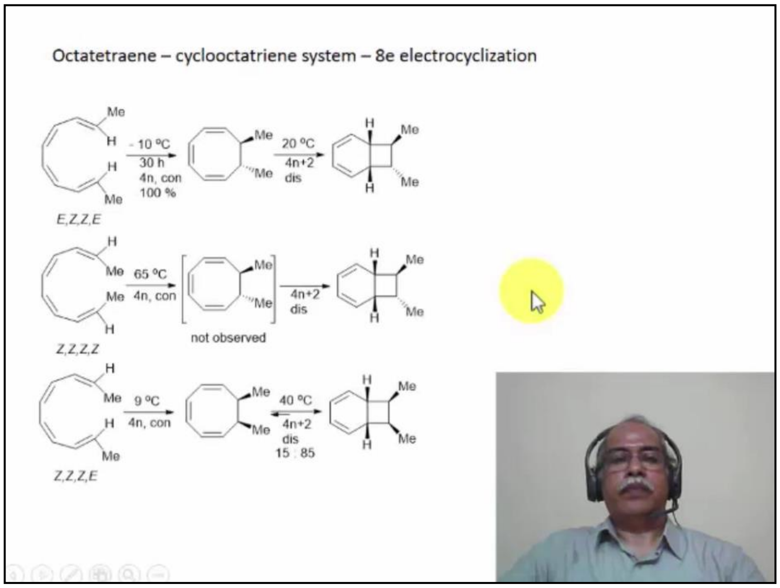

Octatetraene – cyclooctatriene system – 8e electrocyclization

These are larger system, where you have eight-electron cyclization taking place. All of these molecules are diastereo isomers. This is a E,Z,Z,E isomer, in terms of the stereo chemistry of the four-double bond. This is all Z isomer. This is a three Z and one E isomer, in terms of the stereo chemistry isomer of this thing. You can see these molecules, readily undergo electro cyclization, even at room temperatures, or below room temperature, for example, at -10.

This is undergoing an electro cyclic ring opening reaction. They do not stop at the first stage of an electro cyclic ring opening reaction. They go, all the way to the bicyclic system. So, let us look at it very carefully. The first step is an eight-electron electro cyclization reaction, to give a octa tetraene, undergoing an electro cyclization, to give cyclooctatriene kind of a system. This is a conrotatory process.

Because, it is a four-electron system. The conrotatory process of the E,Z,Z,E isomer, essentially gives the Trans dimethyl derivative. And, this molecule can further undergo electro cyclization, to give this bicyclic derivative, which is shown as the final product. In doing so, this will undergo a disrotatory ring closing reaction, putting the ring junction, Cis with respect to each other, the two hydrogen.

Now, if you take the other diastereo isomer of all Z isomer, this is not observed, although this is presumed to be the intermediate. The electro cyclization gives you, the Trans dimethyl derivative. The Trans dimethyl derivative, essentially undergoes the electro cyclization, to give the same product, as you saw in the earlier case, in terms of the stereo chemistry of the product.

On the other hand, if you take the Z,Z,E isomer, the intermediate is observed that, this Cis dimethyl derivative is known. The Cis dimethyl derivative, further undergo electro cyclic reaction, which is a six-electron cyclization, under disrotatory mode, under thermal condition, to give the all Cis isomer. This particular stereo chemistry is, what is observed.

So, the stereo chemical aspects are extremely important and interesting, to show that, this confirm to the Woodward-Hoffmann rule prediction, of initially an eight-electron system, which is a 4N electron system, undergoing conrotatory process to give an intermediate, which is a six-electron process. It is a 4N +2 electron system, undergoing a disrotatory process, to give a bicyclic system, as the final product, in all these cases.

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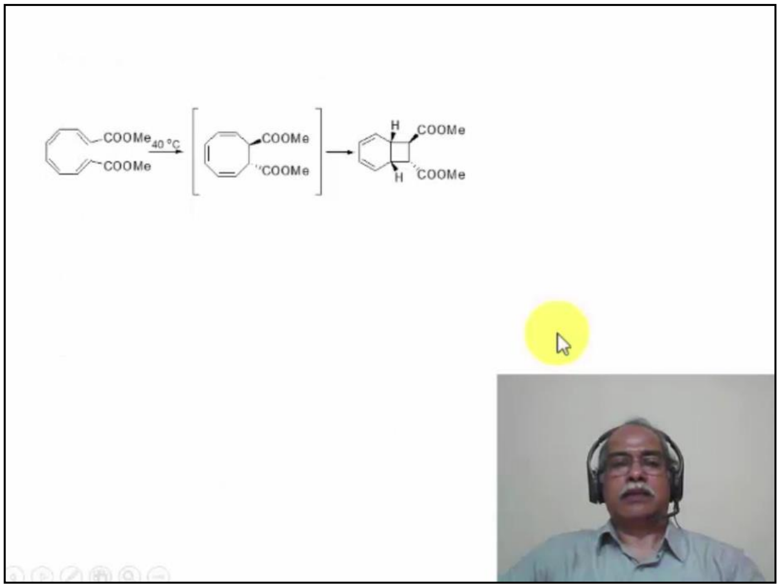

This is again, one more example of a diester substituted octa tetraene, undergoing electro cyclic ring closure, to give you cyclo-octatriene. Cyclo-octatriene essentially undergoes ring closing reaction, to give a bicyclic system of this kind, by initially a conrotatory process, followed by a disrotatory process, to give the bicyclic derivative.

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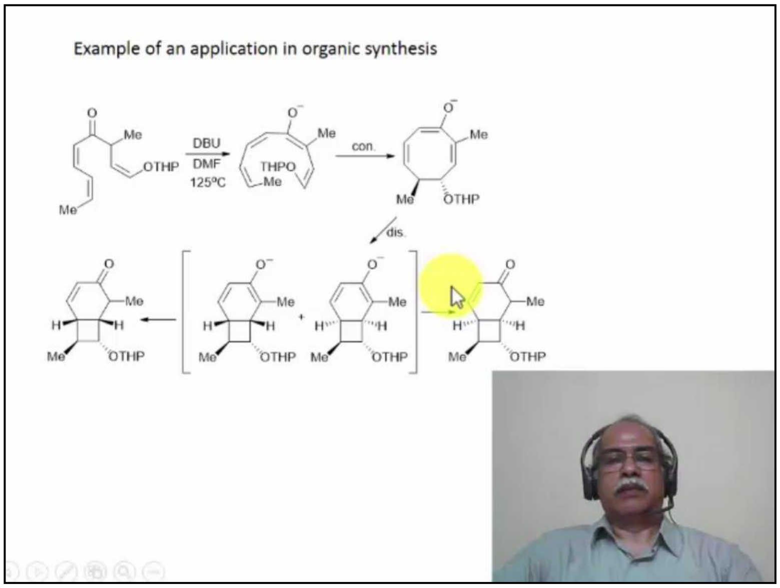

Example of an application in organic synthesis

Now, as an application to organic synthesis, these are terpenoid compounds, which have been generated by electrocyclic ring closing reaction. This is a starting material. The starting material has an enolizable hydrogen, which is this particular position, there is a hydrogen. So, when it is treated with diazabicylo-undec-ene as a base, the DBU as a base, the deprotonation occurs, to generate the enolate. Now, this is written in a sort of a cyclic fashion, such that, an electro cyclic ring closing reaction can take place.

If you look at the stereo chemistry of this double bond, this is CIS. Here again, this is Cis only. Stereo chemistry is retained, by rotating the bond, to bring in the, this kind of a cyclic transition state is favored, in this kind of a confirmation, rather than in this type of a confirmation. Similarly, this double bond is also a Cis double bond. It is retained as a Cis double bond, in this case also.

So, this is a octa tetraene system, which is undergoing an electro cyclization, to give the cyclooctatriene. Cyclooctatriene, further undergoes disrotatory process, to give the two diastereo isomer. The disrotatory process can be either inward or outward, depending upon the inward or outward motion. The stereo chemistry can be Cis here, with two hydrogens up, or Cis here, with two hydrogen down.

Essentially, upon protonation, it gives you the bicyclic ketone. So, synthesis of this bicyclic ketone, is essentially accomplished from an open chain tetraene molecule. The tetraene itself, is generated by enolate chemistry, in this particular instance, resulting in the formation of the final product, in this case.

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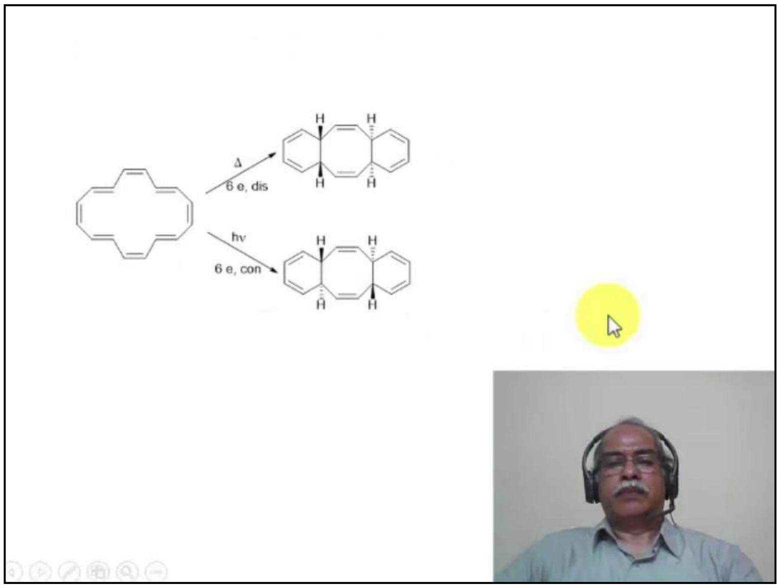

These are, some fancy examples of a larger ring system. But, the reaction itself, is a simple six-electron cyclization, if you look at it. This is behaving like a six-electron cyclization step, resulting in the formation of a fused tricyclic molecules, of this type. The disrotatory mode of ring closing, essentially gives the Cis, Anti-Cis kind of a fusion, here. Whereas, under photochemical condition, the conrotatory process gives you the Trans, Trans, Anti-Trans, kind of a stereochemistry, is what is being observed.

So, all you have to do is, draw the hydrogens here. And, follow the hydrogen for the disrotatory process. If you do the disrotatory process of the hydrogen, for example, the two hydrogen can be either pushed up or down depending upon, whether it is an inward motion or the outward motion of the disrotatory process, resulting in the stereo chemistry, which is Cis, Anti-Cis or if it is a conrotatory process, it will be Anti-Trans, Anti-Trans kind of a product, is what is being observed in this case.

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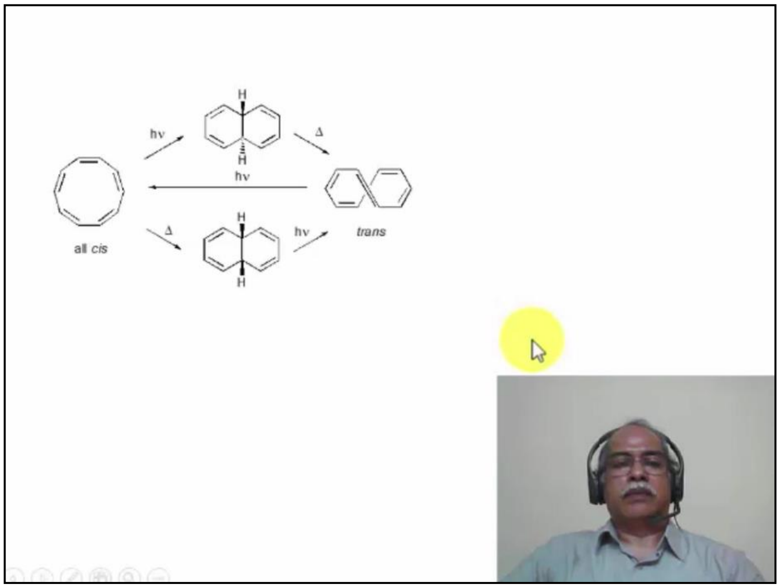

This is a 10-membered ring system. This is a DEC, CYCLO, DECANE, DECA, PENTAENE derivative. Cyclodecapentaene derivative is undergoing, either a thermal ring closing reaction, or a photochemical ring closing reaction. The ring closing takes place, across the carbon number one, and the carbon number six, for example, resulting in the formation of a fused bicyclic system of this. In doing so, this is undergoing a photochemical reaction.

If it is a photochemical reaction, occurring in the six-electron cyclization, occurring under photochemical condition, it will be a conrotatory process. The conrotatory process will bring, one of the hydrogen up, the other hydrogen down. So, it will have a transfusion. On the other hand, the thermal process will be a disrotatory process, that will give the Cis fused derivative, for example. And, this can be further, thermalize to give the Trans isomer.

Because, again the six-electron cyclization, under thermal condition, will be a disrotatory process, resulting in the formation of a Trans double bond, in this particular instance. And, the Trans isomer can also be converted with the CIS, all Cis isomer, by means of a photochemical. So, this is a fairly complex example. Nevertheless, the individual steps are simple enough to follow, as a disrotatory or a conrotatory process, resulting in the, either the Cis geometry fusion, or the Trans geometry fusion, in this particular case.

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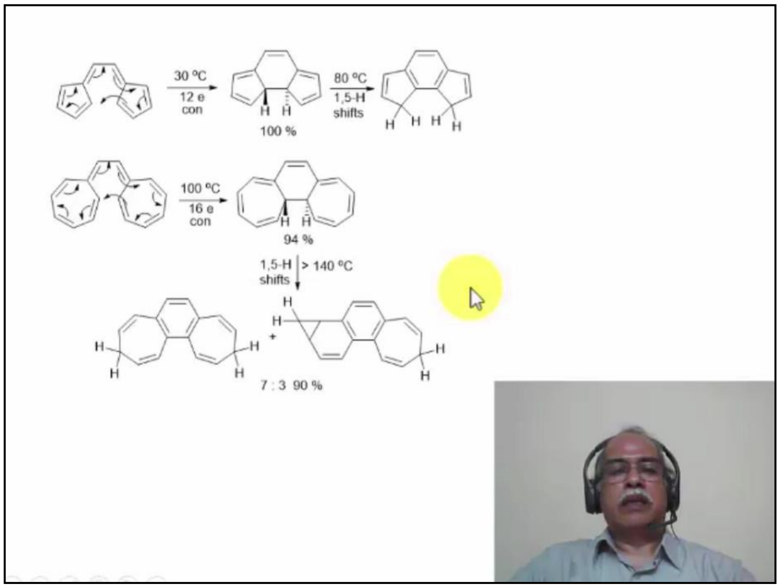

So, what we have seen in this module, is essentially larger system. Here is another example of a bis-fulvalene kind of a system. This is a twelve-electron system, undergoing electro cyclic ring closing reaction, to give the conrotatory process. This is a 4N electron system, under room temperature condition itself, this cross conjugated molecule is an extremely reactive molecule, undergoes electro cyclic ring closure, to give this.

Subsequently, it undergoes 1,5-hydrogen migration, to give thermodynamically more unstable aromatic system, rather than a dihydro aromatic system, of this kind. Similarly, in this case also, the molecule is a hepta-fulvalene kind of a molecule, is bridged hepta-fulvalene kind of a molecule, undergoes a sixteen-electron cyclization. If you count all the electrons here, this will be 6+6 twelve, 12+4 is 16 electrons cyclization.

In other words, all the electrons are involved in the cyclization. It is a 4N electron system, undergoing a conrotatory process, to give the corresponding transfused derivative here. The transfused derivative suffers, undergoes a 1,5-hydrogen migration, to give an aromatic system. So, this kind of a 1,5-hydrogen shift, from this position to the other positions, leading to the formation of the aromatic system, is driven by the fact that, you gain the aromaticity energy, in these particular cases.

So, what we have seen in this module, is larger six membered electro cyclization ring opening, ring closing reaction. Confirming into the Woodward-Hoffmann rules. And also, the larger electrocyclic ring systems of 8,10,12, and 16 electron system, is what we have seen, during the course of this particular lecture. Thank you very much, for your kind attention.