Pericyclic Reactions and Organic Photochemistry

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Pericyclic Reactions – Cycloaddition Reactions – Introduction and Woodward Hoffman rules – 2π+2π cycloadditions

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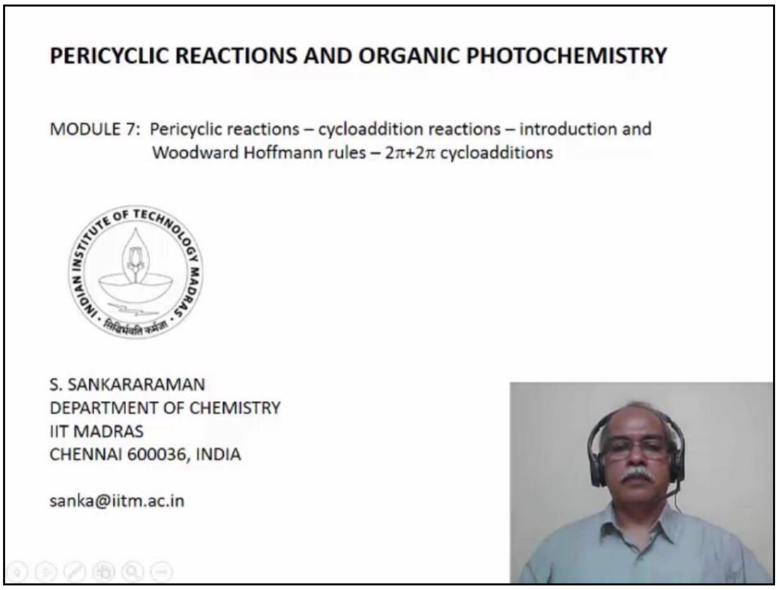

PERICYCLIC REACTIONS AND ORGANIC PHOTOCHEMISTRY

MODULE 7: Pericyclic reactions – cycloaddition reactions – introduction and
Woodward Hoffmann rules – 2π+2π cycloadditions

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Hello, welcome back to the course on pericyclic reactions and organic photochemistry. We are in module seven of the course, now. In this module, we will start with cycloaddition reactions. Cycloaddition reactions are extremely important reactions, because they are ring forming reactions. They are very widely used in organic Synthesis.

We will see in a few modules, how the cycloaddition reactions are useful in organic Synthesis. In this module, we will introduce the cycloaddition reactions, derive the Woodward-Hoffmann rules for the cycloaddition reaction, and also consider some 2+2 cycloaddition reactions, which are the simplest of cycloaddition reactions, one can think of.

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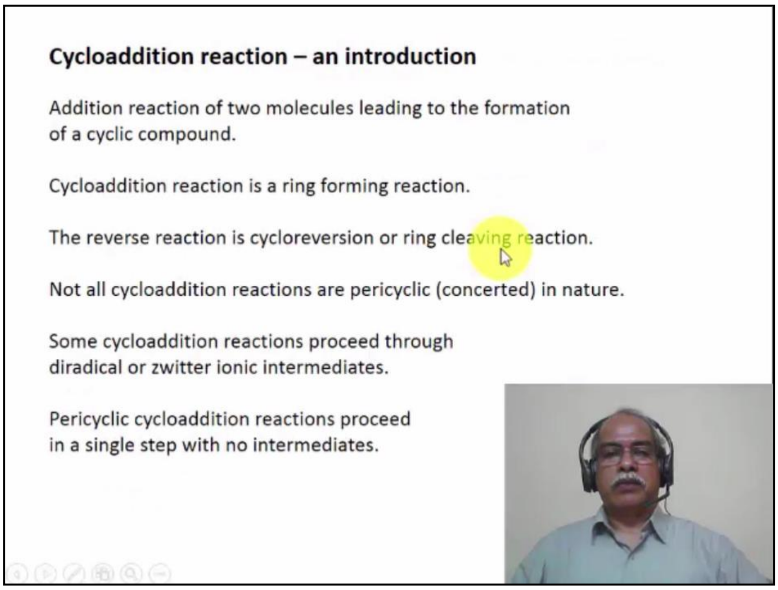

Cycloaddition reaction – an introduction

Addition reaction of two molecules leading to the formation of a cyclic compound.

Cycloaddition reaction is a ring forming reaction.

The reverse reaction is cycloreversion or ring cleaving reaction.

Not all cycloaddition reactions are pericyclic (concerted) in nature.

Some cycloaddition reactions proceed through diradical or zwitter ionic intermediates.

Pericyclic cycloaddition reactions proceed in a single step with no intermediates.

By definition, addition reactions of two molecules leading to the formation of a cyclic compound is called a cycloaddition reaction. Cycloaddition reactions are essentially ring forming reactions. So, they are very useful in formation of rings of various sizes. The reverse reaction is known as cyclo-reversion, or the ring cleaving reaction. Some of these reactions are reversible. They do undergo cyclo-reversion.

One must understand that, when we are dealing with pericyclic reaction, you should be in a position to distinguish those cycloaddition reactions, which are pericyclic, concerted in nature, and those, which are not pericyclic, and non-concerted in nature. Not all cycloaddition reactions are pericyclic or concerted in nature. This is something one can see very clearly, in the next two slides, by various examples.

Some cycloaddition reactions are essentially proceeds through diradical intermediate, or ionic intermediate, which are known as the zwitter ionic intermediate. Pericyclic cycloaddition reactions are essentially those reactions, which proceed in a single step with no intermediate, which is the basic definition of any pericyclic reaction.

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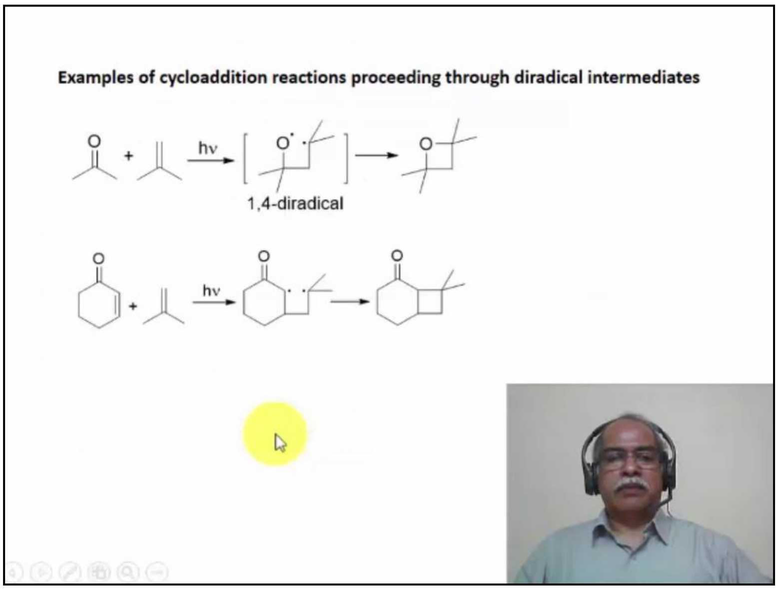

Examples of cycloaddition reactions proceeding through diradical intermediates

Now, take this example. The first example is, what is known as the Paterno-Buechi reaction. This is a cycloaddition reaction of a Ketone with Olefin, to give a Oxetane, as the product. This is truly a cycloaddition reaction, because it is giving a cyclic product at the end. However, this reaction is known to go through, the one four diradical, that is shown as an intermediate, in this case. So, that makes this, a non-pericyclic cycloaddition reaction.

Similarly, the cycloaddition reaction of an Enone to a Olefin, to give the Cyclobutene is known. This reaction is also known, to undergo via the formation of the 1 4 diradical species, that is shown here as an intermediate. So, these are reactions, which proceed through, some kind of an intermediate. So, they make them disqualified from the pericyclic pathway. They are not pericyclic cycloaddition reactions.

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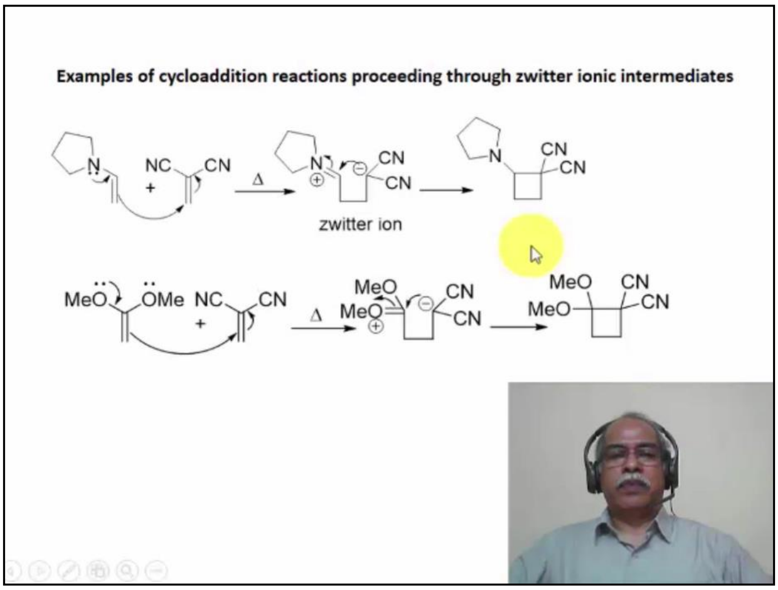

Examples of cycloaddition reactions proceeding through zwitter ionic intermediates

Now, when the two components are highly biased, in terms of their electronic nature, one being extremely electron rich, the other one being extremely electron poor in nature, they can undergo cycloaddition reaction, through the formation of ionic intermediates of this type. Take the example of this particular enamine, which is nothing but N-Vinylpyrrolidone, for example. And, Dicyanoethylene, as the other component. The cycloaddition reaction essentially gives you the Cyclobutene derivative, but not in a single step, but in a stepwise process, involving the formation of a zwitter ion.

Why is this zwitter ion formed, in this particular case. Because, the zwitter ion is particularly stable, because of the stabilization of the positive charge, by the Nitrogen lone pair, and the stabilization of the negative charge, by the two electrons withdrawing Cyano functional group, in this particular. This is an active methylene kind of an anion, is what is generated in this particular system. Instead of having an enamine, one can have enol ether. This is a Ketene Acetal, is what the structure represents. Ketene C, double bond C, double bond O.

This is a Acetal of the particular carbonyl functional group, in the Ketene. So, this is called Ketene Acetal. Ketene Acetal also undergo cycloaddition reaction, with Dicyanoethylene, through the formation of the zwitter ionic intermediate, which are 1,4-di-ionic substances. This intermediate essentially collapses, to give the Cyclobutene derivative, that is shown here. So, these are examples of non-pericyclic, non-concerted, cycloaddition reactions.

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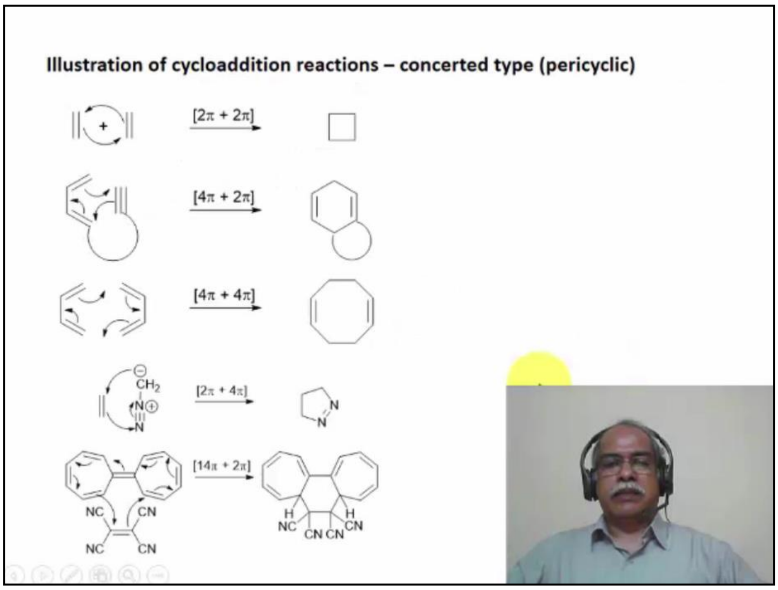
Illustration of cycloaddition reactions – concerted type (pericyclic)

Now, when it comes to pericyclic type cycloaddition reaction, they can be classified depending upon the number of electrons, that are involved in the cycloaddition step. For example, 2+2 cycloaddition reaction to form of, two Ethylene molecules to form a Cyclobutene is a very well-known reaction. The designation that is given is, 2 PI + 2 PI. Because, there are 2 PI electrons involved, in the each of these Acetylenes. So, the 4 PI electron system is, what is responsible for the formation of the Cyclobutene formation.

This is an intramolecular cycloaddition reaction. Both the components of the cycloaddition reactions, are built-in within the molecule, connected by a loop of, let us say, carbon atoms, in this particular case. Here is the Butadiene molecule, undergoing a cycloaddition reaction with an Acetylene, to form a bicyclic derivative. Because, this is already connected by a loop. This is an intramolecular system. This should essentially give you a bicyclic compound of this kind. Note that, this is a 4 PI electron system. All the 4 PI electrons, are involved in the cycloaddition process.

However, the Acetylene, which is also a 4 PI electron system, only 2 PI’s electrons of the Acetylene are actually involved. The remaining 2 PI are intact in the product, you can see here. So, this is actually a 4 PI +2 PI, 4 PI components is a Diene, 2 PI components is the Dienophile, which is this Acetylene unit. In this particular case. When two Butadiene units undergo face-to-face cycloaddition reaction of this type, then it is called the 4 PI- 4 PI cycloaddition reaction.

4 PI- 5 PI cycloaddition reaction of two Butadiene molecules, essentially gives you Cycloocta-1,5-Diene as the product. Now, here is an interesting example of Diazomethane adding to an Olefin to give, the Pyrazolidine kind of a structure, heterocyclic compound, is what is being formed here. Here, the diazomethane essentially is a 4 PI electron component,

and the Ethylene is 2 PI electron components. The 2 PI electrons of the Nitrogen, emerged in a double bond, and the two electrons from the CH2 minus, essentially contributes to the overall four electron system of the Diazomethane.

This is an example of a 1,3-Dipolar cycloaddition reaction. One can always write the structure, in the form of a 1,3-Dipolar structure. This is a dipolar structure, that is written. And, it forms a five-membered ring, heterocyclic. Various types of 1,3-Dipoles essentially give you, various types of heterocyclic compound. These are important class of cycloaddition reaction, to Synthesize heterocyclic system. Finally, let us come to the largest cycloaddition reaction, that is known, for example. This is Hepta Fulvalene, as the molecule. This is a fourteen-electron system.

Overall, if you count all the electrons in this Hepta Fulvalene molecule, there are 14 electrons. And, this is a two-electron system. So, it is a 14 PI +2 PI cycloaddition reaction. You can see here, all the fourteen electrons are involved in the cycloaddition reaction, by the product structure, that is given here. And for the time being, let us not worry about the stereochemistry of the two Hydrogen, in this particular system.

This is a 14 PI +2 PI cycloaddition reaction. 14 electrons of the Hepta Fulvalene, as well as two electrons of the Cyanoethylene, react together to form this particular cycloadduct. So, these are some generic examples, or the illustration of cycloaddition reactions of various kinds, that we will encounter in this course.

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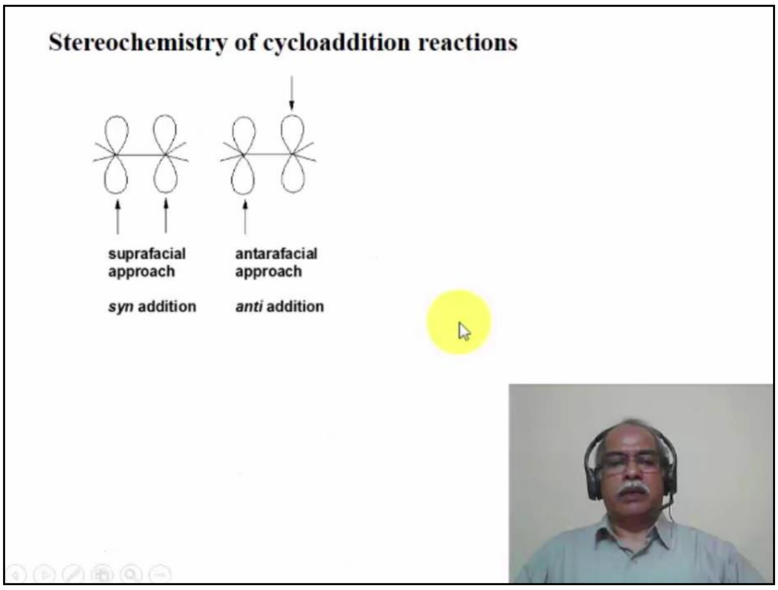

Stereochemistry of cycloaddition reactions

If it is a simple addition reaction, when the two addition adding atoms, let us say, two Bromine atoms are adding to an Ethylene, then you would call it as an Syn addition. And, if the two bromines are adding from opposite face of the PI system, then you would call it as an

Anti-addition. In the cycloaddition terminology, the addition taking equivalent to a Syn addition is called Suprafacial addition. In other words, the two components are adding to the lobes of the PI system, from the same side of the PI system.

If you consider the plane or a PI system, the top face and the bottom face can be distinguished. If the both the components are adding from the same side of the lobes of the PI electron system, then it is called Suprafacial. On the other hand, if one of them is approaching from the bottom, the other one is approaching from the top, then it would be an Antarafacial kind of a cycloaddition reaction. We will see some examples of, what is a Suprafacial addition, and what is an Antarafacial addition, in a few minutes.

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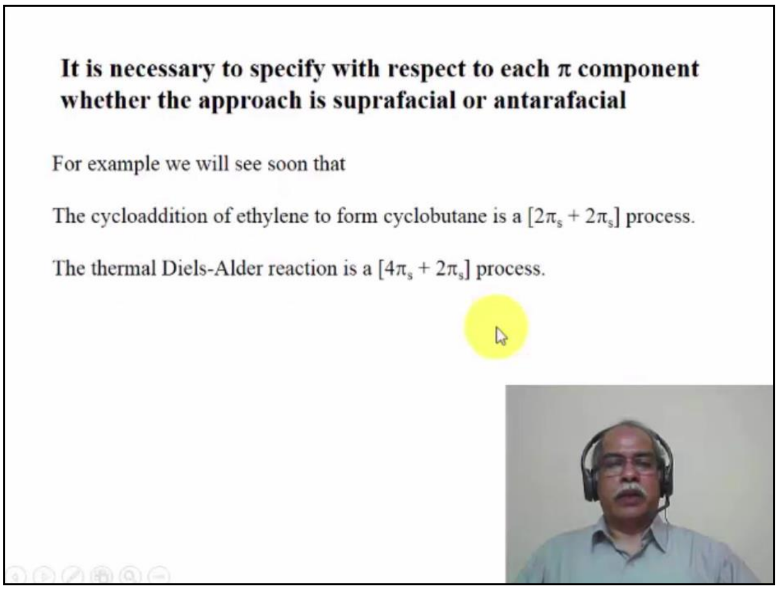

It is necessary to specify with respect to each π component whether the approach is suprafacial or antarafacial

For example we will see soon that

The cycloaddition of ethylene to form cyclobutane is a $[2\pi_s + 2\pi_s]$ process.

The thermal Diels-Alder reaction is a $[4\pi_s + 2\pi_s]$ process.

It is not only necessary, how many PI electrons are involved in the cycloaddition components, it is also necessary with respect to each of the component, whether it is a Suprafacial or Antarafacial. This has to be specified, in order to completely, in order to complete the definition of the cycloaddition reaction, for example. We will see very soon that, the cycloaddition of Ethylene to form Cyclobutene, is a 2 PI Suprafacial, 2 PI Suprafacial process.

In other words, both the Olefins are adding to each other in a Suprafacial-Suprafacial manner. A thermal diels alder reaction is a 4 PI Suprafacial and 2 PI Suprafacial process. In other words, the Diene and the Dienophile approach face-to-face, with respect to each other. And, in each of the component, the addition is a Suprafacial manner addition, is what is taking place. So, this kind of a complete description of a cycloaddition reaction, not only gives you the number of PI electrons, and the number of components involved, it also very clearly tells you, what is the nature of overlap between the molecular orbitals of the components, whether they are Suprafacial, Antarafacial, with respect to each other.

Now, the cycloaddition of Ethylene to form Cyclobutene, is a Suprafacial-Suprafacial process, is only under photo chemical condition. Whereas, this is under thermal condition. This is the based on the Woodward-Hoffmann rule, that we will be deriving very soon for the cycloaddition reaction.

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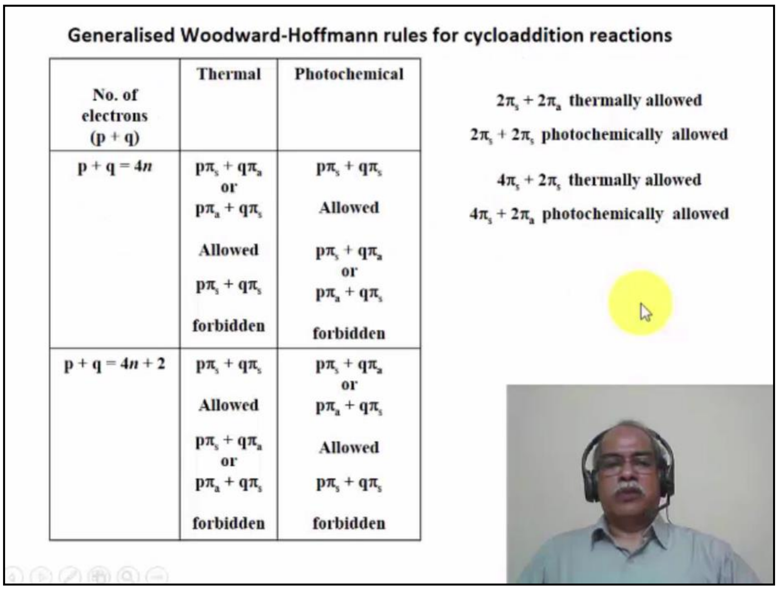

Generalised Woodward-Hoffmann rules for cycloaddition reactions

No. of electrons (p + q)	Thermal	Photochemical
$p + q = 4n$	$p\pi_s + q\pi_a$ or $p\pi_a + q\pi_s$ Allowed $p\pi_s + q\pi_s$ forbidden	$p\pi_s + q\pi_s$ Allowed $p\pi_s + q\pi_a$ or $p\pi_a + q\pi_s$ forbidden
$p + q = 4n + 2$	$p\pi_s + q\pi_s$ Allowed $p\pi_s + q\pi_a$ or $p\pi_a + q\pi_s$ forbidden	$p\pi_s + q\pi_a$ or $p\pi_a + q\pi_s$ Allowed $p\pi_s + q\pi_s$ forbidden

$2\pi_s + 2\pi_a$ thermally allowed

$2\pi_s + 2\pi_s$ photochemically allowed

$4\pi_s + 2\pi_s$ thermally allowed

$4\pi_s + 2\pi_a$ photochemically allowed

Now, before we derive the Woodward-Hoffmann rule, the generalized Woodward-Hoffmann rule is given here. The number of electrons, let us say for example, there are two components, that are involved in the cycloaddition process. If you take 2+2 cycloaddition reaction, then P + Q will be 4. So, 2 PI + 2 PI, corresponding to four-electron system. Or you can have a 4 PI + 4 PI, corresponding to an eight-electron system.

All of them are 4N electron system. On the other hand, you can have a 4n +2 electron system. 4 +2, or 6+4, for example, these are all 4N +2 kind of an electron system. Now, under thermal condition, under photochemical condition, the Woodward-Hoffmann rule allowedness, as well as the forbiddingness of the reactions, are very clearly defined, in this particular table. For a 4N electron system, to undergo a thermal addition, one of the component has to be, at least the Antarafacial component.

If both of them are Suprafacial component, it is not an allowed process, it is a forbidden process. However, under photochemical condition, both the components are Suprafacial with respect to each other, then only it is allowed. If one of the component happens to be an Antarafacial component, then it will be a forbidden process.

We will use the various methods of analyzing the pericyclic reactions, for the cycloaddition reactions also, and derive this Woodward-Hoffmann rule. Now, once the Woodward-Hoffmann rule for the 4N electron systems are defined, defining the 4N +2 electron system is not difficult. Because, they are complementary to each other.

What is good for the allowedness under thermal condition, will be a forbidden process in the case of the 4N +2 system. For example, here, one of the component is an Antarafacial component, when it is in the 4n +2 kind of a system, that is a forbidden process. Whereas, here, it is an allowed process.

What you need to remember essentially to follow this lecture is that, the 2 PI Suprafacial-2 PI Antarafacial is a thermally allowed process, whether it will take place or not, we will see in a few minutes. The 2 PI Suprafacial-2 PI Suprafacial, where both the components are Suprafacial with respect to each other, is a photo chemically allowed process.

The 4 PI Suprafacial and 2 PI Suprafacial is a thermally allowed process. This is the diels alder reaction, that we are talking about. Similarly, the photo chemical diels alder reaction, one of the component has to be Antarafacial, the 2 PI component, or the 4 PI component, has to be Antarafacial, with respect to each other.

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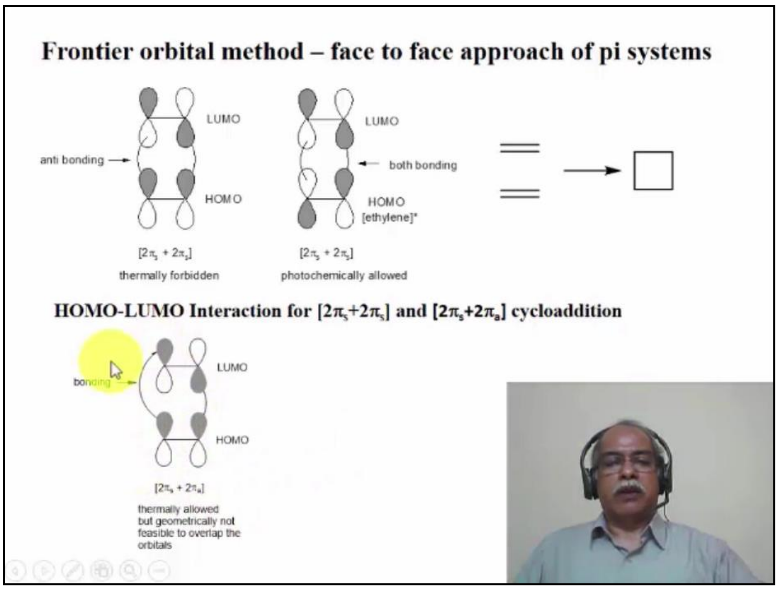

Frontier orbital method – face to face approach of pi systems

$[2\pi_s + 2\pi_s]$
thermally forbidden

$[2\pi_s + 2\pi_s]$
photochemically allowed

HOMO-LUMO Interaction for $[2\pi_s+2\pi_s]$ and $[2\pi_s+2\pi_a]$ cycloaddition

$[2\pi_s + 2\pi_a]$
thermally allowed
but geometrically not
feasible to overlap the
orbitals

Now, let us say for example, the frontier orbital method usage, for the derivation of the Woodward-Hoffmann rule. Let us look at it. If two Ethylene units are coming parallel to each other, like a sandwich for example, it can form a Cyclobutene. Under these condition, the overlap of the orbital is shown, in this particular case. This is the highest occupied molecular orbital of one of the Ethylene, and this is the lowest unoccupied molecular orbital of another Ethylene.

And, essentially the orbital interaction, if you see, these two lobes are interacting with this two lobes, during the course of the reaction, in the transition state. In other words, with respect to this PI system, it is Suprafacial. Because, the two lobes are on the same side of the PI system. Similarly, these two lobes are also on the same side of the PI system. So, both the components are Suprafacial and Suprafacial with respect to each other.

However, in the ground state, the Homo-Lumo interaction essentially leads to an antibonding kind of an interaction, which is shown by the overlap of this molecular orbital lobe, with this molecular orbital lobe. Such an antibonding interaction will cause energy. And, as a result of that, we can say that, this is a thermally forbidden reaction.

However, under photochemical condition, you are promoting, one electron from the ground state to the excited state, so the Homo of the Ethylene, actually is similar to the Lumo of the Ethylene. Because, this is an excited state Ethylene, we are talking about. In the ground state Ethylene, you have a Homo with two electrons. In the excited state Ethylene, you have the highest occupied molecular orbital with one electron, and the lowest ground state molecular orbital with one electron, each.

So, the Homo of the Ethylene is essentially having, the same symmetry of the Lumo of the Ethylene. So, this is the ground state Lumo. And, this is the excited state Homo of the Ethylene molecule. Here again, the bonding is Suprafacial with respect to this Ethylene, and Suprafacial with respect to this Ethylene, also. You can see here; this overlap is a bonding type of an interaction. This overlap is also a bonding type of an interaction.

So, this is a perfect combination of overlap, with the bonding interaction of both the lobes, in forming the Sigma bond of the Cyclobutene. And hence, this is a photo chemically allowed process. Because, one of the Ethylene has to be in the excited state, electronically excited state. It is possible to have one of the Ethylene in the electronically excited state, only under photo chemical conditions.

The Homo-Lumo interaction is essentially, 2 PI Suprafacial-2 PI Suprafacial, and 2 PI Suprafacial and 2 PI Antarafacial, cycloaddition reaction. That is, this picture corresponds to the homo-lumo interaction, being a 2 PI Suprafacial with respect to one component, and 2 PI Antarafacial with respect to another component. The top picture shows you, the 2 PI Suprafacial-Suprafacial overlap. The bottom figure, if you look at, this is Suprafacial with respect to one of the component here.

And, it is Antarafacial with respect to the other Olefinic component. For example, this lobe and the opposite side lobe is what is interacting with this. Although, geometrically, it is not feasible for this lobe to interact with this lobe, when the two molecules are approaching parallelly, conceptually one can think of this, to be a Antarafacial kind of an overlap, with respect to this Ethylene, Suprafacial kind of an overlap, with respect to this Ethylene.

With the parallel approach, it is thermally allowed process, but geometrically not feasible to overlap the orbitals, in this particular manner. Going from the bottom to the top of the orbital, is not possible in terms of the overlap. So, geometrically, this is not an allowed process, although Woodward-Hoffmann rule wise you would say that, this is an allowed process.

This is the, problem is that, this two Olefins are approaching parallel with respect to each other, the Suprafacial-Suprafacial is the most convenient way of overlapping. Suprafacial Antarafacial overlap is not a convenient way. Because, it is a geometrically, this orbital is far away from this orbital, so overlap will not be possible.

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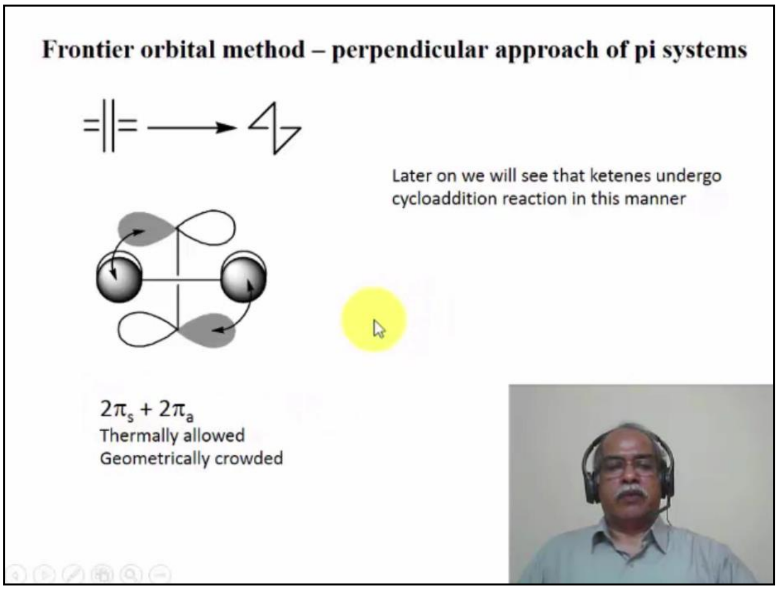

Frontier orbital method – perpendicular approach of pi systems

Later on we will see that ketenes undergo cycloaddition reaction in this manner

$2\pi_s + 2\pi_a$

Thermally allowed

Geometrically crowded

So, what if the two ethylene’s are approaching perpendicular to each other, instead of parallel to each other. That will give you a twisted Cyclobutene, as the product, in this case. And, this is an orbital pictorial representation of the perpendicular approach. This is the horizontal Ethylene. And, this is a vertical Ethylene. And, the disposition of the PI bonds are very clearly shown here.

Now, with respect to the horizontal Olefin, if you look at, this top lobe of the molecular orbital, and this top lobe of this molecular orbital, is what is interacting. If you look at the vertical Olefin, the orbital interaction is between this lobe and this lobe, and this lobe and this lobe. So, with respect to the vertical Olefin, it is Antarafacial, very clearly. Because, this lobe and this lobe, are not on the same side of the plane, of the Ethylene.

This is in opposite side. So, with respect to the vertical Olefin, this is an Antarafacial process. With respect to horizontal Olefin, it is a Suprafacial process. Although, this looks like geometrically feasible, this is geometrically highly crowded, because of the Hydrogens will pope, with respect to each other. These Hydrogens will essentially, come in the way of this Sigma bond, here.

So, although it is a thermally allowed process, but geometrically, it never happens because of the fact that, it is a highly, geometrically, crowded system, is what we have, in this particular system. However, we will see that, later on. Ketenes do undergo cycloaddition reaction, in this manner. The 2 PI Suprafacial-2 PI Antarafacial is the mode of cycloaddition for ketenes.

Ketenes are special cases. Because, the central carbon atoms is an SP carbon, without any substituents being present there. So, that will not have any kind of a steric interaction, when it undergoes a Suprafacial-Antarafacial kind of an overlap, which we will see in a few modules, later.

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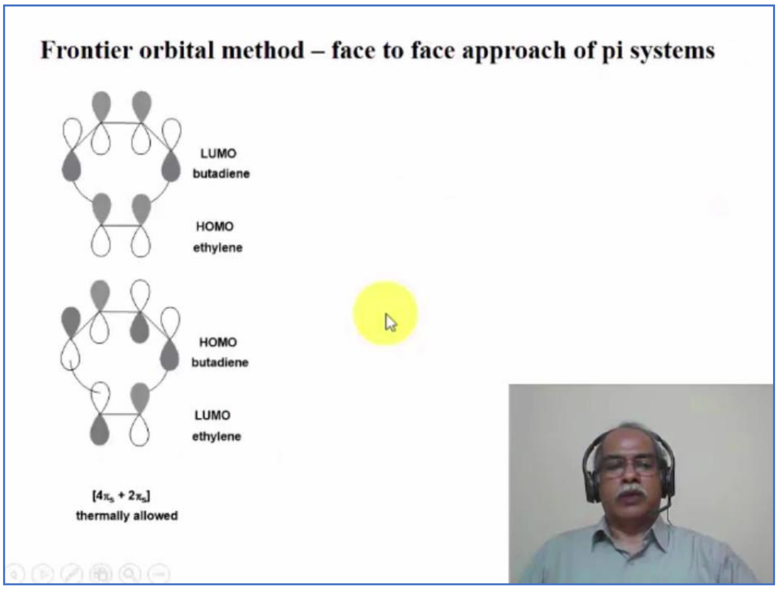

Frontier orbital method – face to face approach of pi systems

$[4\pi_s + 2\pi_s]$
thermally allowed

Now, what happens to a 4 PI-2 PI cycloaddition reaction. This is the Homo of Ethylene, and Lumo of Butadiene. Or, you can take Homo of Butadiene, and Lumo of Ethylene, it does not matter, in this particular case. Both these overlaps are iso-energetic in nature. We will see it in a few minutes. And, this is a thermally allowed process, you can see here. Suprafacial with respect to the Diene, because this lobe and this lobe is interacting.

Suprafacial with respect to Dienophile also, because the same side lobes are interacting with the Butadiene unit. Same is the picture here. This is Suprafacial with respect to the Diene. This lobe and this lobe are interacting. Whereas, this is also Suprafacial with respect to the Dienophile Ethylene, where the two lobes on the same side are interacting.

You can see, such an interaction essentially leads to bond formation, bonding type of an interaction, is what we have. So, the coefficients of the algebraic sign of the coefficients, are essentially same between the overlapping orbital, which will lead to a Sigma bond formation. And, hence, this kind of a face-to-face approach, with a Suprafacial-Suprafacial overlap for a 4 PI electron-2 PI electron system, is a thermally allowed process.

On the other hand, if you take the photochemical process, one of the component has to be in the excited state. The Homo of the Butadiene is in the excited state Butadiene, is what is given here. The Homo of the ground state Butadiene, is a SI 2 or the PI 2, with the only one node here. Whereas, the Homo of the excited state Butadiene, should have two nodes. One node is present in this bond.

Another node is present in this bond here. Between bond one-two, there is one node, between bond three and four, there is another node, that is being, which we have seen this earlier, in the orbital pictures of the various polyene systems. Here, although, this is Suprafacial and Suprafacial, with respect to both the components, this leads to an antibonding character in the transition state.

So, this will be of higher energy in nature, compared to this kind of a molecule. So, a photochemical Suprafacial-Suprafacial overlap, is a photo chemically a forbidden process, according to the Woodward-Hoffmann rule. So, essentially a 2+2 is photochemically allowed, when both the components are Suprafacial. A 4+2 is allowed thermal conditions, when both of them are under Suprafacial mode.

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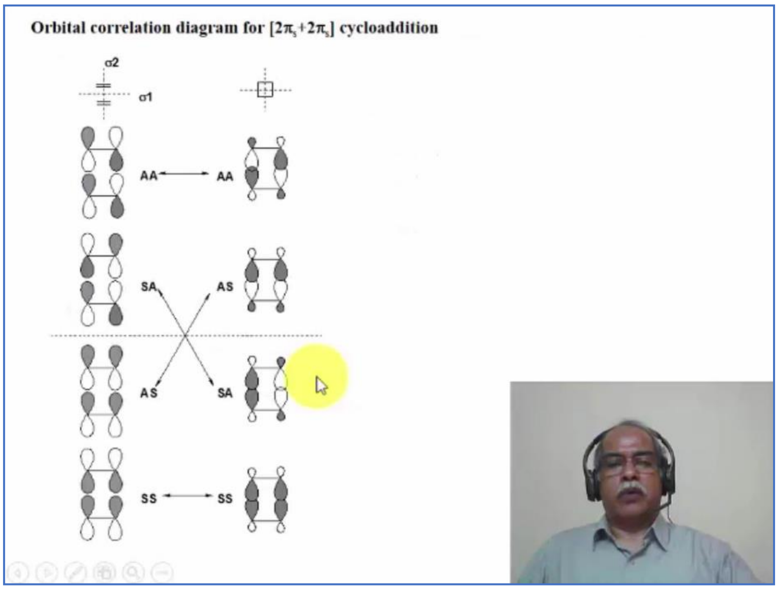

Orbital correlation diagram for $[2\pi_s+2\pi_s]$ cycloaddition

We can use the orbital correlation method, to arrive at the same conclusion, as we arrived in the case of frontier molecular orbital method. This is a face-to-face approach of the two Ethylene molecules, to give a Cyclobutene molecule. There are two possible mirror planes, that one can consider as symmetry elements. Sigma one, which is a horizontal mirror plane, which bisects the newly formed Sigma bonds. And, the Sigma two is the vertical mirror plane, which bisects the PI bonds of the original Ethylene unit.

So, what we have done is, essentially arrange the interacting molecular orbitals. These are two Ethylene molecules interacting. In other words, the SI one and SI one of the Ethylene molecule, interacting in a symmetrical fashion. The SI one and SI one of the Ethylene molecule interacting in an anti-symmetrical manner. The SI two of the Ethylene molecule interacting in a symmetrical manner, and an anti-symmetrical manner.

This will be in the increasing order of energy, in terms of arranging the overlap of the various orbitals of the. And, this kind of an interaction, is what leads to the formation of the Sigma bond. So, you have a Sigma. You have another Sigma bond. You have a Sigma star, and another Sigma star kind of a system, is what we have. So, there are two Sigma bonds found. So, you will have two Sigma's and two Sigma stars.

And, these are the overlapping molecular orbitals of the starting points. And, these are the overlapping molecular orbitals of the endpoint. Now, all you have to do is, look at the symmetry properties, with respect to the Sigma one and Sigma two. With respect to Sigma one, which is a horizontal plane is symmetric. With respect to the vertical plane also, it is symmetric.

Here, with respect to the horizontal plane, it is antisymmetric, with respect to the vertical plane, it is symmetric, with respect to the horizontal plane, the third overlap is symmetric, the vertical plane, it is antisymmetric, and so on. The finally, the topmost interaction, which is the antisymmetric interaction of the two antibonding molecular orbitals of the Ethylene, essentially is antisymmetric, with respect to both vertical as well as the horizontal mirror plane.

In the case of the Sigma bond symmetry, this is, both are symmetric, with respect to vertical as well as horizontal plane. With respect to horizontal plane, it is symmetric. With respect to vertical plane, it is antisymmetric. Here, the horizontal plane is antisymmetric, and the vertical plane is symmetric, which you can see, very clearly. Here, both the vertical plane, as well as the horizontal planes, are antisymmetric with respect to each other.

So, these are all filled molecular orbitals. These are all also filled molecular orbitals. Whereas, these are antibonding molecular orbitals. This is also antibonding molecular orbitals, in terms of the orbital interaction. Now the symmetric correlation is very clear that, the symmetric-symmetric combination, correlates with the symmetric-symmetric combination, in the ground state.

However, this antisymmetric-symmetric combination, remember, this is with respect to Sigma one and Sigma two, that has to be very clearly specified. One should not confuse that, SA is same as AS. Because, the first alphabet corresponds to the horizontal plane, and the second alphabet corresponds to the vertical plane, for example. So, this antisymmetric-symmetric combination is correlated with, the antisymmetric-symmetric correlation, of this particular molecular orbital.

Similarly, the symmetric-antisymmetric combination is correlated here. Finally, the antisymmetric-antisymmetric combination is correlated in this manner. You can see very clearly, that the correlation is between the ground state and the excited state. Which means, this reaction has to proceed through an electronically excited state. In other words, this can be possible, only under photo chemical condition.

So, a Suprafacial-Suprafacial cycloaddition reaction of the 2 PI-2 PI type, is photochemically allowed, and thermally it is forbidden. That is the conclusion, that we arrive at.

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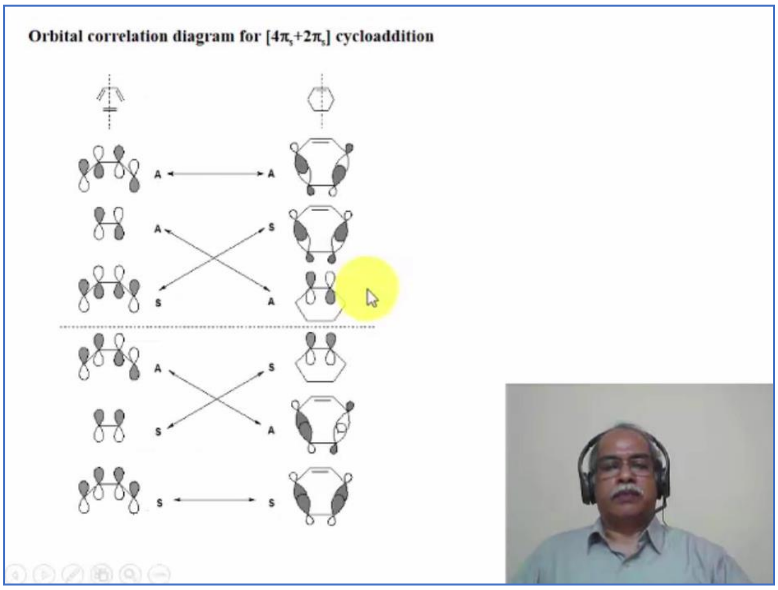

Orbital correlation diagram for $[4\pi_s+2\pi_s]$ cycloaddition

In the case of a diels alder reaction, we set up the PI molecular orbitals of the two-interacting component. The only symmetry element, that is present throughout the course of the reaction, is the vertical Sigma, which bisects the carbon number two and three of the Diene, and carbon number one and two of the Ethylene, for example. It also bisects in a symmetrical manner of the cyclohexane, that is being formed in this particular case.

Now, this is Butadiene SI 1. And, this is SI 1 of the Ethylene. This is SI 2 of Butadiene. This is SI 3 of Butadiene. And, this is SI 2 of Ethylene. And finally, SI 4 of the Butadiene. In the increasing order of energy, we have written the molecular orbitals of the Butadiene and the Ethylene, in the increasing order of energy. Here, remember, there are two Sigma bonds, that are formed, and one PI bond is also formed. So, you will have a Sigma 1, Sigma 2, PI, PI star, Sigma 1 star, and Sigma 2 star.

So, these are antibonding molecular orbitals, which are not filled. And, these are bonding molecular orbitals, which are filled with electrons. Now, clearly with respect to the vertical plane of symmetry, this is symmetric. This is also symmetric. Whereas, this is antisymmetric, and this is symmetric. This is antisymmetric. And finally, this is also antisymmetric. With respect to the vertical plane, this is symmetric.

This is antisymmetric. This is symmetric. This is antisymmetric, symmetric, and antisymmetric. So, when you want to correlate the symmetry properties of the left-hand side molecular orbitals, to the right-hand side molecular orbital, symmetry correlation is very clear, between the lowest energy orbitals to be symmetric, with respect to each other. And, this molecular orbital symmetry, correlates with this molecular orbital.

Again, filled molecular orbitals are correlated. There is no correlation, across the nonbonded level. That means, this reaction should proceed under thermal condition. So, a diels alder reaction, which is a 4 PI Suprafacial-2 PI Suprafacial addition reaction, is an allowed process, under the thermal conditions, and not under photochemical condition.

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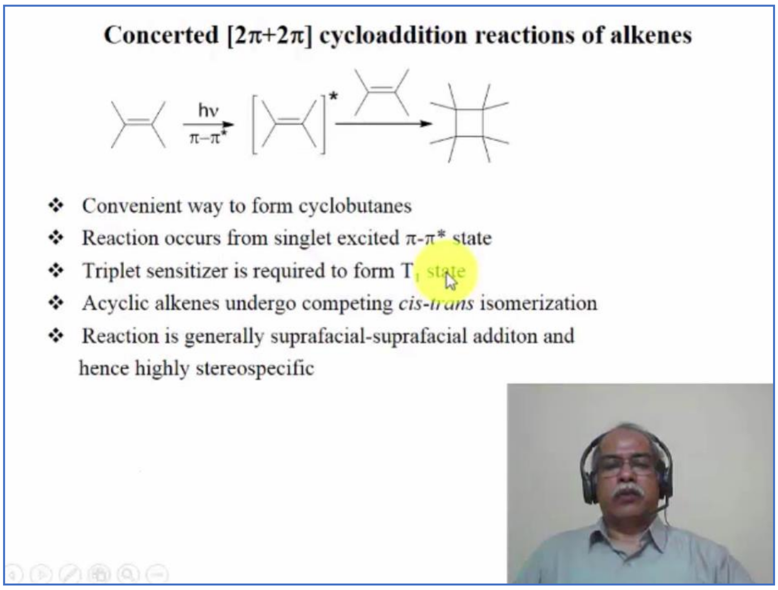

Concerted [2π+2π] cycloaddition reactions of alkenes

- ❖ Convenient way to form cyclobutanes
- ❖ Reaction occurs from singlet excited π-π* state
- ❖ Triplet sensitizer is required to form T_1 state
- ❖ Acyclic alkenes undergo competing *cis-trans* isomerization
- ❖ Reaction is generally suprafacial-suprafacial additon and hence highly stereospecific

Now, the 2 PI-2 PI cycloaddition reaction, we will consider first. These are reactions, which are concerted reaction. The convenient way to form Cyclobutene’s in an organic Synthesis. Quite often, this is used in the formation of caged compounds also, with Cyclobutene rings forming, during the course of the reaction. Reaction, generally occurs from the singlet excited state, PI to PI star state of the Olefin. Triplet sensitizer is required, to form the triplet state of the molecule. The reaction can also take place, from the triplet state.

We will consider this in more detail, when you consider the photochemistry component of this reaction. Acyclic alkenes undergo, competing Cis-Trans Isomerization. In other words, if this were to be a Trans-2-Butene, when you fertilize, it can also undergo Cis-2-Butene. We will see that in a few minutes. Reaction is generally Suprafacial-Suprafacial addition. And, it is highly stereospecific in nature, because of the fact that, you have Suprafacial-Suprafacial kind of an addition.

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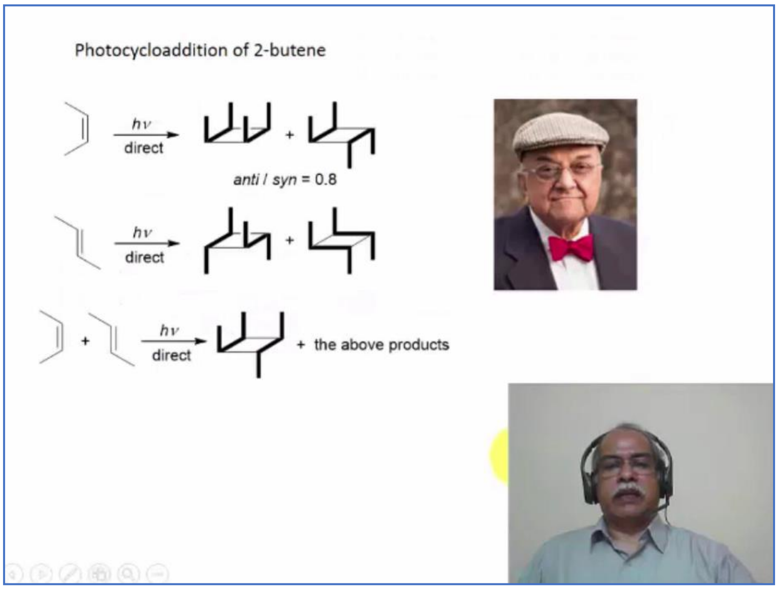

Photocycloaddition of 2-butene

Now, this gentleman here is Professor R Srinivasan, who worked in IBM. And, he was responsible for the investigation of the cycloaddition reactions, of Cis-2-Butene, Trans-2-Butene, and so on. What he found out was, when the reaction is carried out at low temperature, remember these are gaseous molecule, and they also absorbed in the vacuum ultraviolet region. So, these are extremely difficult experiments to do. In addition to that, there is a competing Cis-Trans Isomerization can also take place, under the photochemical condition.

So, the reactions were carried out the low conversion, so that the competing Cis-Trans Isomerization, is not a major problem, so that, one can figure out these stereo specificities of this reaction. So, the credit goes to Professor R Srinivasan, for enlightening us with the investigation of the two butene system, in this particular example.

So, if you take Cis-2-Butene under the low conversion, where the Cis-Trans Isomerization does not take place. In other words, the pure Cis-2-Butene undergoes the direct photolysis, to give two molecules, where the four methyl groups are Cis, with respect to each other.

Here the two methyl groups are Cis. And, this is Anti-Cis. So, this is Cis, Anti-Cis, is what we have. We will just call it as an Syn-Isomer here, and an Anti-Isomer here, in terms of the nomenclature, that we are talking about. So, this is formed in about 0.8 ratio. The Syn-Isomer is formed, slightly higher than the Anti-Isomer, for example. We can see here by following the thick line, the Cis-2-Butene component is approaching face-to-face. This is also approaching face-to-face, except that it is an anti-face-to-face kind of an approach, is what we have. Here is the Trans-2-Butene component. The Trans-2-Butene components are clearly given by the thick lines.

So, here a head to tail approach, is what is happening. Here, a head to head approach, is what is happening. Remember, these two are common products. These two structures are essentially identical structures, and their common product in this Cis, as well as the Trans Isomer. This is, these two Isomers are different in the Cis and Trans, with respect to each other. When a mixture of Cis and Trans are taken. Mixture is taken and photolyzed, for example.

In addition to these three products, that is product one, product two, and product three. In addition to all these three products, there is a unique product formed, which is a combination of the Cis and Trans Olefin, which is undergoing the cycloaddition reaction, in this manner. So, this essentially illustrates and confirms the stereo specificity of the cycloaddition reactions, proceeding through a Suprafacial-Suprafacial cycloaddition process, with a retention of stereo chemistry of the Olefin, which is shown in the thick lines, in the Cyclobutene that is being formed, in this particular case.

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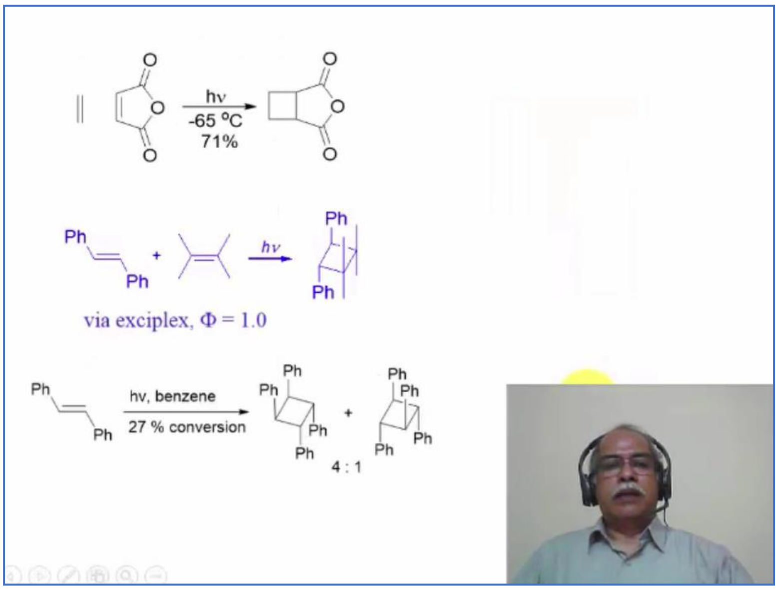

These are some more examples of the 2+2 cycloaddition reaction. Ethylene reacts with Maleic Anhydride, for example, at -61 degrees. Because, Ethylene is a gas. It needs to be condensed at a low temperature. Essentially, a 2+2 cycloaddition reaction is what is taking place, to give this particular product. Here is an interesting example of an Exciplex formation. Exciplex formation is nothing but, the excited state complex. In other words, if one Olefin is in the excited state, and it forms a complex with another Olefin, you call it as an Exciplex.

Exciplex are excited state complex, where the two components are different. One of the component is in the excited state, the other component is in the ground state. In this particular example, this molecule is excited. It goes to the excited state, and it forms a complex with the Tetra Methyl Ethylene, for example. And, the complex probably is a sandwich type of a complex.

It immediately undergoes cycloaddition reaction, to give the Cyclobutene formation, in this particular case. The quantum efficiency of exciplex formation is nearly one. And hence, the formation of this particular product, is also very efficient in this photochemical process. Now, the Trans-Stilbene can undergo Cis-Trans Isomerization, as well as it can undergo the cycloaddition process. In the cycloaddition process, you can see here, there is a 4:1 ratio of this Syn, Anti-Syn product is formed.

This is the Trans. This is another Trans molecule. Here, this is head to tail approach. Whereas, here is a head-to-head approach. In terms of the approach of the two molecules. Both the molecules are possible to obtain, from the Trans Isomer of the Stilbene molecule.

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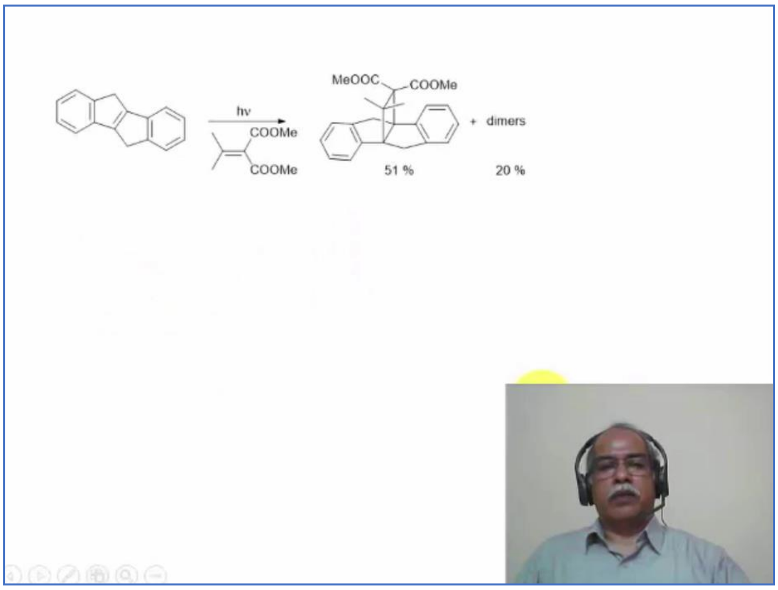

When the Trans Stilbene is tied up in the, this is also, we can consider to be a rigid form of a Trans Stilbene. If we consider this Benzene ring, connected to this Olefin and the other Benzene ring, except it is a fused form. Unlike this form, where we have a Benzene ring connected to a double bond, and connected to the Benzene ring. This is a conformationally flexible system. Whereas, this is a conformationally rigid system. In the rigid system, the central double bond undergoes C2 +2 cycloaddition reaction, with this particular diester, essentially giving this product, in about 51% yield. The dimers of the individual components are also formed, to extent of about 20% also, in this case.

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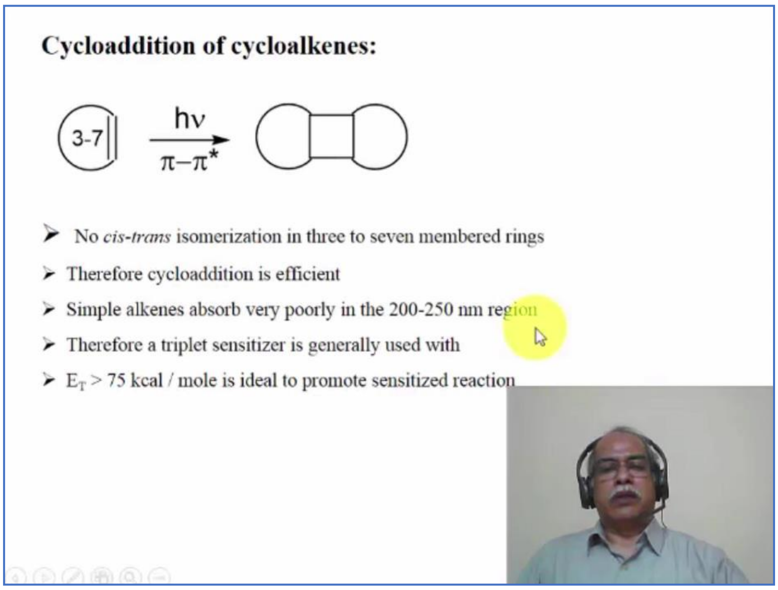

Cycloaddition of cycloalkenes:

- No *cis-trans* isomerization in three to seven membered rings
- Therefore cycloaddition is efficient
- Simple alkenes absorb very poorly in the 200-250 nm region
- Therefore a triplet sensitizer is generally used with
- $E_T > 75$ kcal / mole is ideal to promote sensitized reaction

Now, the Cis-Trans Isomerization is not a problem, when you have a Cycloalkene, particularly cycloalkanes of the smaller ring sizes, from 3 to 7. So, no Cis-Trans Isomerization competes with the cycloaddition process, in the case of cyclic Olefin. Therefore, cyclic cycloaddition is efficient. There is no energy wasting in the Cis-Trans process. Simpler alkenes absorb very poorly, in the 200 to 250 nanometer regions.

Therefore, a triplet sensitizer might be useful. Typically, triplet sensitizer with energy above 75 kilo calories per mole, is ideal to promote this kind of a reaction. In other words, sensitizers are essentially photo catalyst. They will absorb the light energy. And, Transfer that light energy to the Olefin. By themselves, they are very poor observers.

So, it helps to transfer the energy from one molecule to another molecule, to make them excited, to go to the excited state, for example. That is accomplished using a triplet sensitizer, provided the triplet sensitizer has a higher energy, than the triplet state of this particular molecule.

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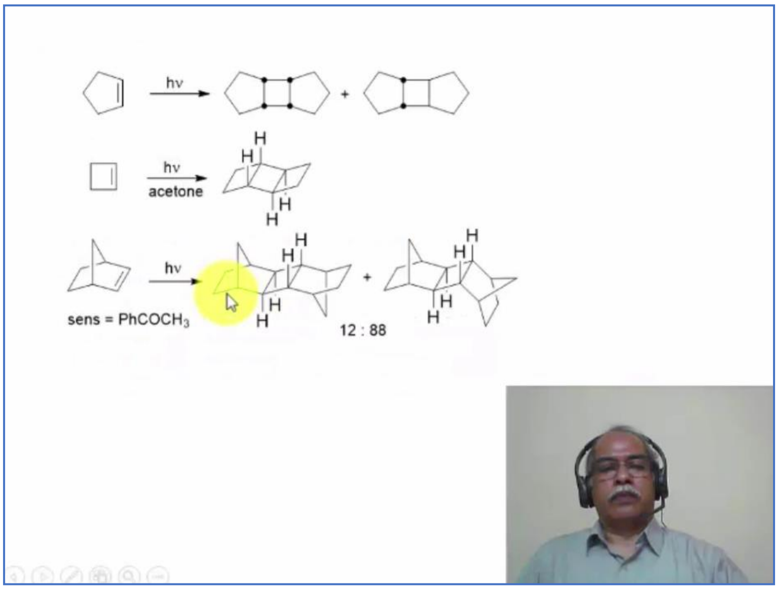

These are example of simple Olefinic system, undergoing 2+2 cycloaddition reaction. Cyclopentane, for example, undergo cycloaddition process, to give All-Cis Hydrogen. In other words, this is a Cis fused dimer of the Cyclopentane. This is a Cis, Anti-Cis kind of an Isomer of the. The thick dot, essentially indicates that, there are four Hydrogens. And, all the four Hydrogens are above the plane of the cyclo-butane ring, here. In this case, these two Hydrogens are above the plane of the cyclo-butane ring, and there are two Hydrogens here, which are below the plane of the Cyclo-Butane ring.

Cyclobutene, itself undergoes a cycloaddition process, 2+2 cycloaddition process, to give a ladderane kind of a system. A tricyclic system, is what is formed. Norbornene, for example, undergo sensitized, photo sensitized cycloaddition reaction. This is a triplet sensitizer, Acetophenone. So, it absorbs light energy, and then transfers it on to the Norbornene. Norbornene, then undergoes a cycloaddition process, to give two types of products, depending upon, how initially the two Olefins are oriented, with respect to each other.

You can see here for example, this is a head to tail kind of an orientation. Anti-orientation is what is taking place. Whereas here, you have a Syn orientation, with the two bridge is forming in the same direction, for example in this particular case.

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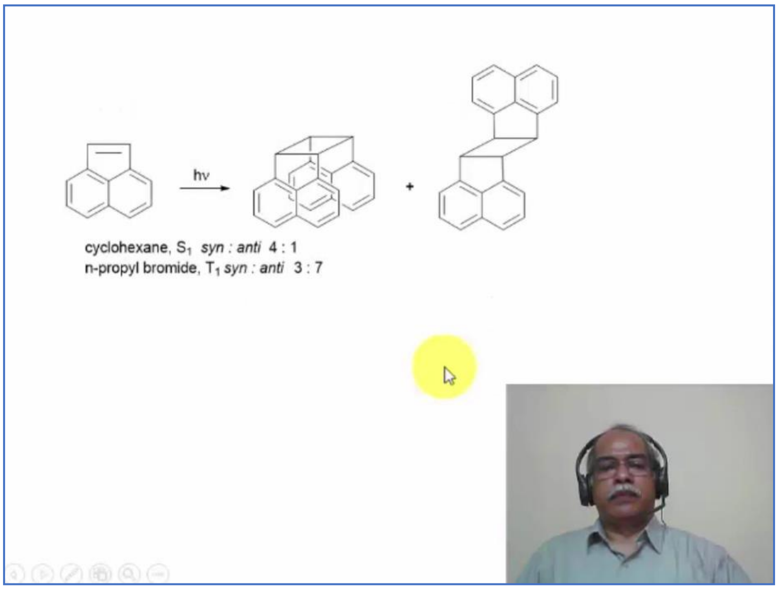

cyclohexane, S_1 *syn : anti* 4 : 1
n-propyl bromide, T_1 *syn : anti* 3 : 7

This is Acenaphthylene. Acenaphthylene undergoes cycloaddition process to give, head to head, or head to tail, kind of a Syn, and Anti-kind of an Isomer. And, depending upon, whether you have a singlet. Direct photolysis gives 4:1 ratio of this two products, probably forming through an excimer kind of a system, where the two Olefins are coming parallel with respect to each other, to form an excimer, and then collapses to give the Cyclobutene ring, here.

Alternatively, when it is carried out in N-Propyl Bromide, this reaction proceeds through a triplet state. Because, the heavy atom effect, crosses the inter system crossing to take place. We will discuss, all these things in detail, under the photochemistry topic, not under pericyclic topics. So, assume that, this reaction is proceeding. One is proceeding through a singlet state, the other one is proceeding through a triplet state. The ratios seem to depend upon the state in by which, the reaction is taking place, in these two cases.

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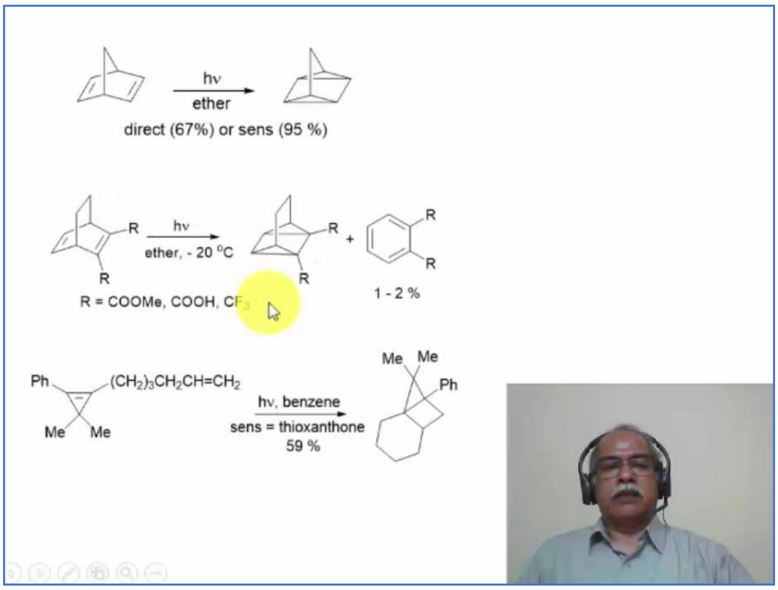

Here is an interesting example of an intramolecular 2+2 cycloaddition reaction. All of them are in fact, intramolecular 2+2 cycloaddition reaction. This molecule has a curvature, that is responsible for the intramolecular cycloaddition reaction. Norbornadiene undergoes 2+2 cycloaddition reaction, intramolecularly. In other words, this PI bonds are facing in this direction. The other PI bonds are facing in the other direction.

So, there is a possibility of an overlap of the lobes of the PI system, from this side to this side, essentially forming a Sigma bond. This is called Quadricyclane. This is a highly-strained system. This a high-energy molecule. This is not thermally stable. When you heat it, it goes back to the Norbornadiene, as the product. In this case, again, this is a larger system. This is a 2,2,1-bicyclic system, whereas, this is a 2,2,2-bicyclic system.

Here also, the Quadricyclane kind of a compound is formed readily, when the photolysis of this kind of molecule take place. Here is an intramolecular version of the 2+2 cycloaddition reaction. Cyclopropane is a very reactive molecule, in the excited state. It undergoes cycloaddition reaction, for example, to give the Cyclobutene. This is a newly formed Cyclobutene.

So, originally, you had a Cyclobutene here, with six carbon attachment, that is three plus three, six carbon. This is, how many methylene’s are there. There are three plus four methylene’s are there. 1,2,3,4. So, this is originally an Olefin, that is the terminal Olefin, of this Cyclopropyl derivatives. So, the Cyclopropane is still intact. This newly formed Cyclobutene is fused with a six-membered ring. The six-membered ring is arising, because of the long chain, which has the four carbon plus the two carbons of the Olefin, resulting in the formation of the six-membered ring. So, this intramolecular version of the cycloaddition reaction is what, we are referring to here.

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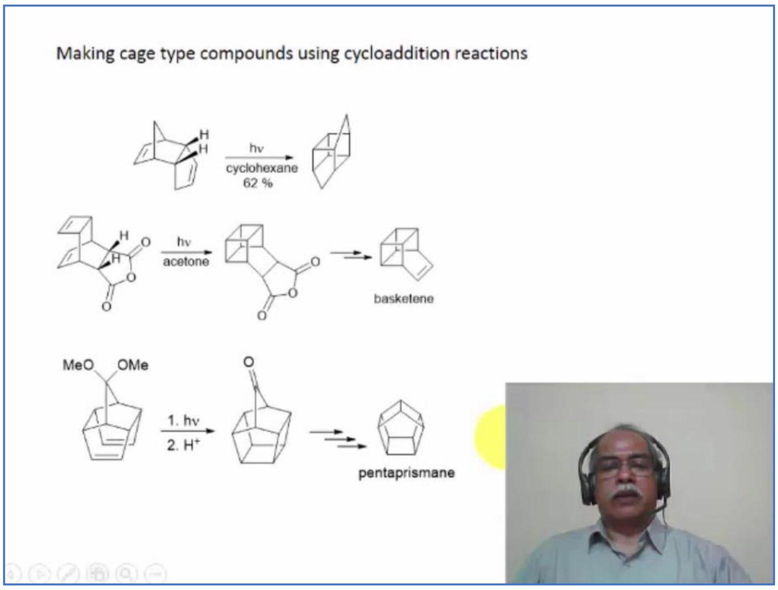

Making cage type compounds using cycloaddition reactions

These are some interesting examples of, how to make caged compounds, using cycloaddition process. Cage compounds representations are given here. This is Bis-Homo-Cubane. If this two methylene's are not present, then you would call it as Cubane. If you form a bond between, these two carbons here, and this two carbon, that would be Cubane. This is two carbons more than Cubane. So, it is called Bis-Homo-Cubane. Now, this is a dimer of Cyclopentadiene.

The dimer of cyclopentadiene is an Endo Isomer, is what is taken. These two Olefins are in close proximity, because of this curvature, that we talked about, in a few minutes back. The same is true, in this molecule also. This curvature causes, this PI bonds to come in close proximity to this PI bond. So, intramolecular 2+2 cycloaddition reaction is very facile. So, the newly formed Cyclobutene derivative, you can see here.

This is a newly formed Cyclobutene molecule, that is given here, by an intramolecular 2+2 cycloaddition process. Now, this is a molecule, which is formed by a cycloaddition reaction, which is a diels alder reaction, from Cyclooctatetraene and Maleic Anhydride. We will see that later. These 2 PI systems are facing parallel to each other.

This is a most convenient geometry of the molecule, to undergo a 2+2+2-Suprafacial-Suprafacial cycloaddition reaction. It does undergo 2 +2 cycloaddition reaction, to form the Cyclobutene, that is shown here. This Cyclobutene is formed by a 2+2 cycloaddition reaction. This molecule is hydrolyzed. And then, it is made undergo oxidative decarboxylation, using Letetra Acetate, to give, what is known as Basketene. This molecule is supposed to be a basket, where this is a handle, and this is the basket part of the molecule.

Now, Pentaprismane is an interesting molecule. This was Synthesized by Phil Eaton. And, this is essentially carried out by a face-to-face, 2 PI-2 PI cycloaddition reaction, of this particular Acetal of the Ketone, which is this particular Ketone. This Ketone is now decarbonylated, to give essentially the Pentaprismane molecule, after a few steps. So, the crucial step is the formation of the cage, by forming the Cyclobutene derivative, which is this particular Cyclobutene derivative. And, that essentially results in the Synthesis of the Pentaprismane.

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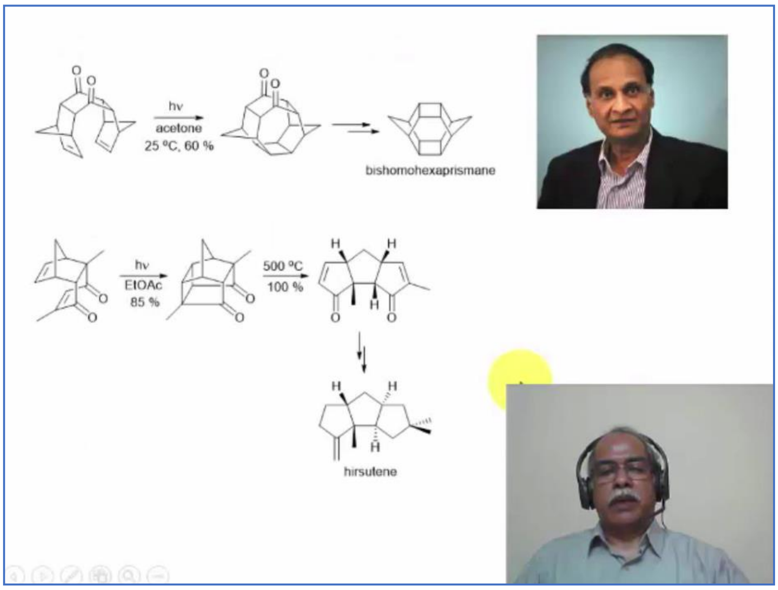

This is professor Mehta, who is the former director of the Indian Institute of Science in Bangalore. He has made several contributions in the, 2+2 cycloaddition reaction. And, he is responsible for the Synthesis of the Bis-Homo-Hexa-Prismane. Hexa-Prismane is a molecule, where you have a bond in between these two carbons, and these two-carbon, divide of these two methylene units, for example. However, that molecule could not be Synthesized. The Bis-Homo-Hexa-Prismane has been Synthesized.

This is essentially by a face-to-face, 2 PI,2 PI-cycloaddition reaction of this Olefinic compound, to give the Cyclobutene derivative. From here, the decarbonization followed by the cycloaddition here, essentially leads to the formation of this four-membered ring. So, this is a very elegant Synthesis of the Bis-Homo-Hexa-Prismane, that is given in this particular slide. Here is another example of Synthesis of Hirsutene.

Here is a cycloaddition adduct of a Cyclopentadiene with Benzoquinone molecule. This is a diels alder adduct of Cyclopentadiene with Quinone molecule, that puts these two double bonds in close proximity to each other. The face-to-face separation here, because of the curvature of this molecule, essentially because it is an Endo-adduct.

This comes in close proximity to this particular double bond, resulting in the formation of the 2+2 cycloaddition reaction. Now, the newly formed bonds are these vertical bonds, which is a Cyclobutene bonds. Now, if you cleave the horizontal bonds, in these bonds for example, the slanting bonds, you will essentially open up this molecule. So, to give a five-membered ring, five membered ring, and five membered ring fused system. And, these are all Cis fused five membered ring system. Essentially, this was converted to a natural terpin called Hirsutene. And, these reactions were carried out, in the laboratory of Professor Mehta.

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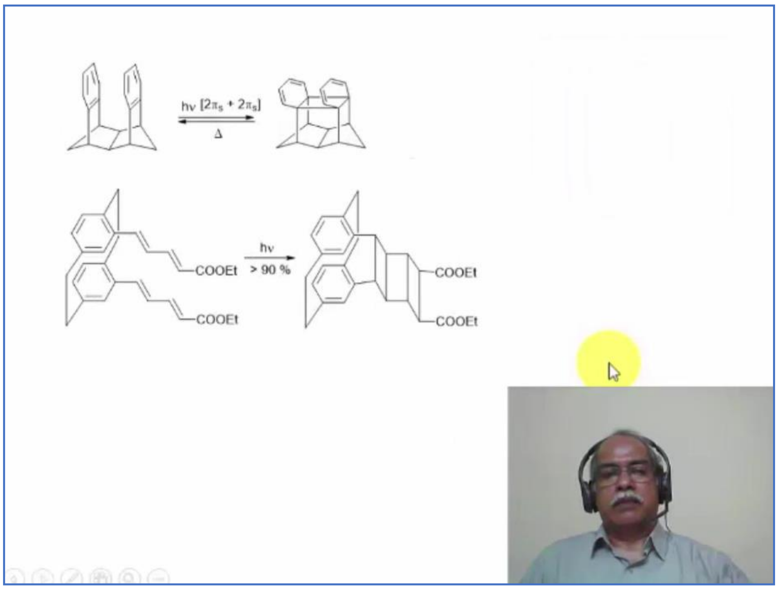

Finally, the last example of two Benzene units. Because of the rigid structure of this bicyclic system, the two Benzenes units are essentially face-to-face. Benzene, normally does not undergo 2+2 cycloaddition reaction. Because, it does not like to do aromaticity. However, this is a special case, where the two Benzene are coming face-to-face, within a short distance of about three angstroms, are so.

So, that photolysis of this molecule, essentially led to the formation of a 2+2 cycloaddition reaction. Interesting caged structure is what, is being formed here. Here, the 2+2 cycloaddition reaction is prompted by the spacer unit, which is a two-two Paracyclophane unit. The distance between the two to two Benzene rings, of the two-two Paracyclophane unit, is about 3.5 angstroms or so.

Anything, that is less than 4 angstroms separation, between two double bonds of this parallel double bonds, will undergo cycloaddition process, for example. So, the 3.5 angstroms separation spacer, is a very useful spacer. So, this Diene, essentially undergoes cycloaddition reaction with the Diene, which is parallel to this.

This is called the Pseudo-Geminal Isomer of the disubstituted Paracyclophane derivative. So, that gives an ladderane kind of a structure. 2+2 cycloaddition reaction, between this Diene and this Diene, essentially gives these four membered rings, resulting in the formation of a ladderane kind of a structure, in this particular case. Very interesting example of 2+2 cycloaddition reactions are shown here.

So, what we have seen in this module, is the definition of cycloaddition reaction, the various types of cycloaddition reactions, the analysis of the cycloaddition reactions, using a frontier molecular orbital method, for the 2+2, as well as 4+2, the orbital correlation method for the 2+2, and the 4+2. And then, we see a lot of examples of 2+2 cycloaddition reactions are intramolecular, as well intermolecular type. I hope you enjoyed this session. Thank you very much, for your attention.