Pericyclic Reactions and Organic Photochemistry

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Module No. #04
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Pericyclic Reactions – Sigmatropic rearrangements – Introduction and [1,3]-migrations

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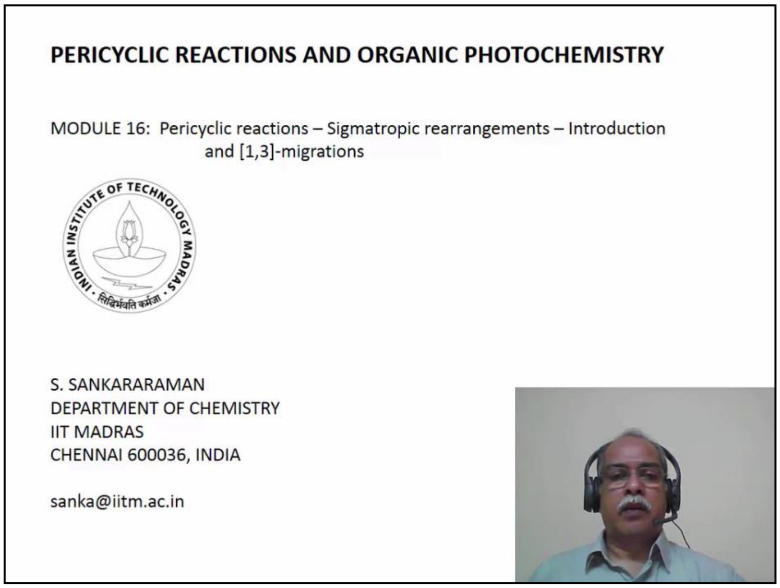

PERICYCLIC REACTIONS AND ORGANIC PHOTOCHEMISTRY

MODULE 16: Pericyclic reactions – Sigmatropic rearrangements – Introduction and [1,3]-migrations

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Hello, welcome to the online course on Pericyclic Reactions and Organic Photochemistry. We are in the fourth week of this program. We will have five modules in this week. And, in all the five modules, we will consider a very important reaction called the Sigmatropic Rearrangement reaction.

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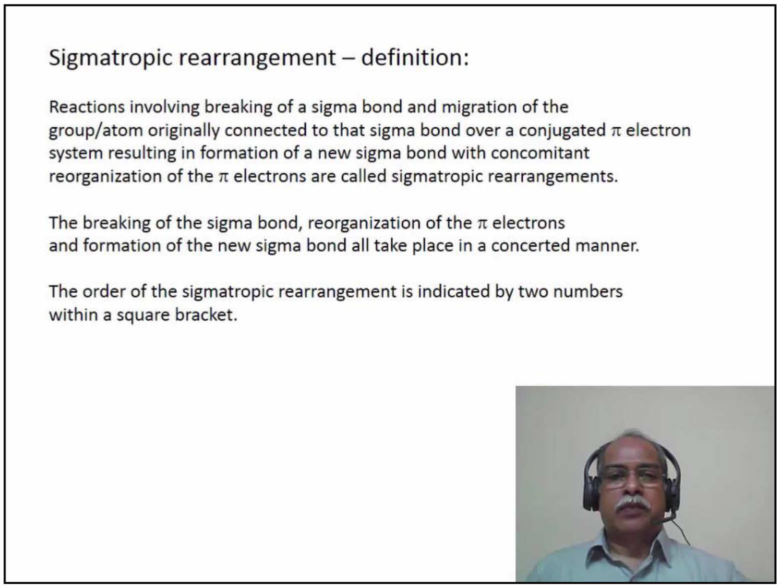

Sigmatropic rearrangement – definition:

Reactions involving breaking of a sigma bond and migration of the group/atom originally connected to that sigma bond over a conjugated π electron system resulting in formation of a new sigma bond with concomitant reorganization of the π electrons are called sigmatropic rearrangements.

The breaking of the sigma bond, reorganization of the π electrons and formation of the new sigma bond all take place in a concerted manner.

The order of the sigmatropic rearrangement is indicated by two numbers within a square bracket.

Now, Sigmatropic rearrangement reactions are defined as reactions, involving a breaking of a Sigma bond, with the migration of a group or atom, that is originally connected to the Sigma bond over a conjugated PI system, resulting in the formation of a new Sigma bond, with concomitant reorganization of the PI electrons. This may be difficult to follow, without an example. We will straight away go into an example, in the next slide.

What is important here is, that the breaking of the Sigma bond, and the reorganization of the PI cloud, everything takes place simultaneously, in a concerted manner. The order of the Sigmatropic rearrangement, is indicated by two numbers, within a square bracket.

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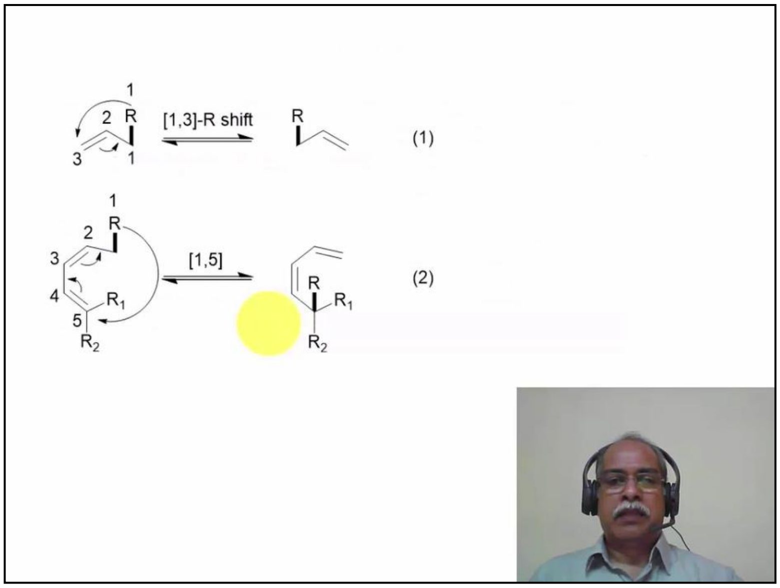

Now, let us take this example, shown in equation number-1. Equation number-1. It is a simple Allyl system, to which a functional group or an alkyl group is connected, which is the R-Group. The thick bond, that is shown here is the bond, that is going to break. And, with the breakage of this bond, the R-Group migrates to the third position. In other words, the numbering starts from the bond breaking, during the course of the Sigmatropic rearrangement. If the Carbon-R bond is breaking, then the numbering starts from 1 and 1.

And, the migration takes the R-Group to position 3. So, it is a [1,3]-R shift. Let us say for example, if the R is a Hydrogen, then it will be a [1,3]-Hydrogen shift. If R is a Methyl group, then it will be a [1,3]-Methyl shift. If R is a generally an Alkyl group, then it will be [1,3]-Alkyl shift, is what, we are referring to. During the course of the migration of the R-Group to the third position, that PI bond automatically reorganizes, so that the overall process is a concerted process, without involvement of any kind of a radical species or any intermediate species.

The same analogy can be extended to a [1,5]-Shift. This is a Butadienyl system, to which a Carbon-R-Group is attached. This Carbon is a saturated Carbon, SP3 Carbon. The group is now migrating to position number-5. So, it is a [1,5]-Sigmatropic rearrangement.

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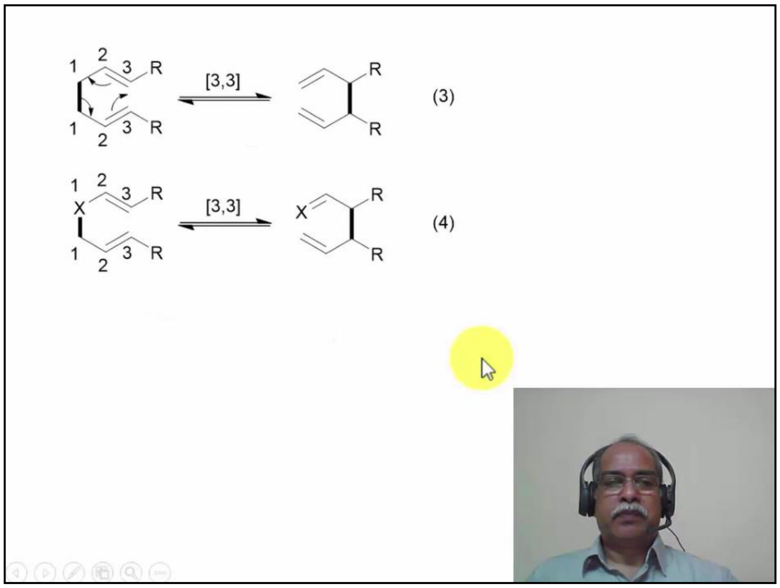

Now, these are two special class of Sigmatropic rearrangement, where the thick bond that is shown here, is migrating. And, during the course of the migration, a new bond is formed between Carbon number-3 and 3. These are called [3,3]-Sigmatropic rearrangement. There is a special name for this reaction. It is called the Cope rearrangement. Now, the second example that is shown in equation number-four, is nothing but an Oxygen Analog, or a Hetero Atom Analogue.

It could be, oxygen or Nitrogen. And, if it is an oxygen, FX is equal to oxygen, then the [3,3]-Sigmatropic rearrangement of this type is called Claisen rearrangement. Claisen rearrangement is nothing but, a Vinyl-Allyl-Ether undergoing a rearrangement, to give Gamma-Delta unsaturated Carbonyl compound. So, these are the generic examples of [3,3]-Sigmatropic rearrangement.

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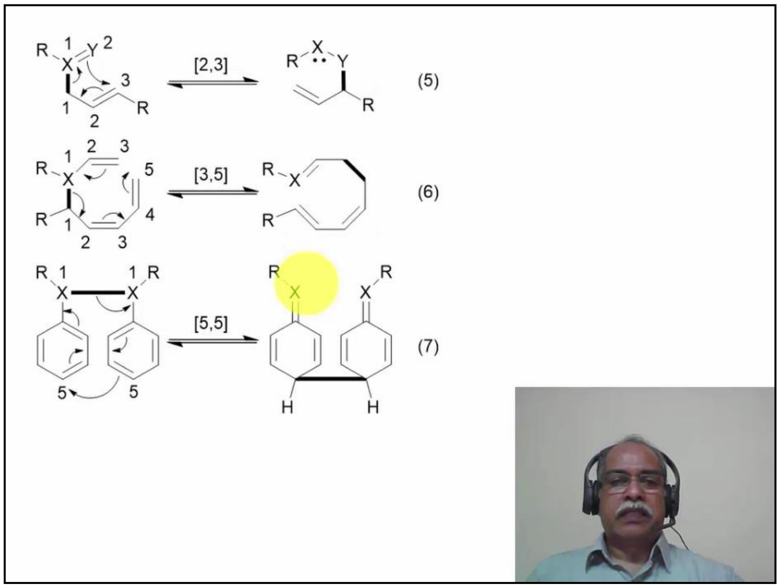

Let us look into further classification of the Sigmatropic rearrangement. In the equation number-five, an example of a [2,3]-Sigmatropic rearrangement, is shown. Here, the X and Y atoms can be, either Carbon atom, or it could be Hetero atom. In such a case, the Carbon X bond cleaves, and the new bond is formed between Y and the third position. So, if you number the Carbon X bond as 1 and 1, then it comes to 1,2,3 here. 1 and 2, and the 2 and 3, are connected. So, it is called [2,3]-Sigmatropic rearrangement

Here is an extended example of the same reaction. This is a [3,5]-Sigmatropic rearrangement. We can see here; the Carbon X bond is being broken. And, if that is a broken bond, then the numbering starts from 1,2,3,4,5 on the lower side, 1,2,3 on the upper side. The new bond is formed between 3 and 5, as you can see here, this is a new bond, that is formed. So, it is a [3,5]-Sigmatropic rearrangement. This rearrangement is known as Benzidine rearrangement, when X group is Nitrogen or NH, for example.

The NH-NH bond in Benzidine is broken, under strongly acidic conditions, due to protonation. Under these condition, the para positions are connected by a Sigma bond, through a transition state of this type, where the two benzene rings are parallel to each other, for example. And, the

[5,5]-Carbon, is what is attached during the Sigmatropic rearrangement, and that is corresponding to the [5,5]-Sigmatropic rearrangement.

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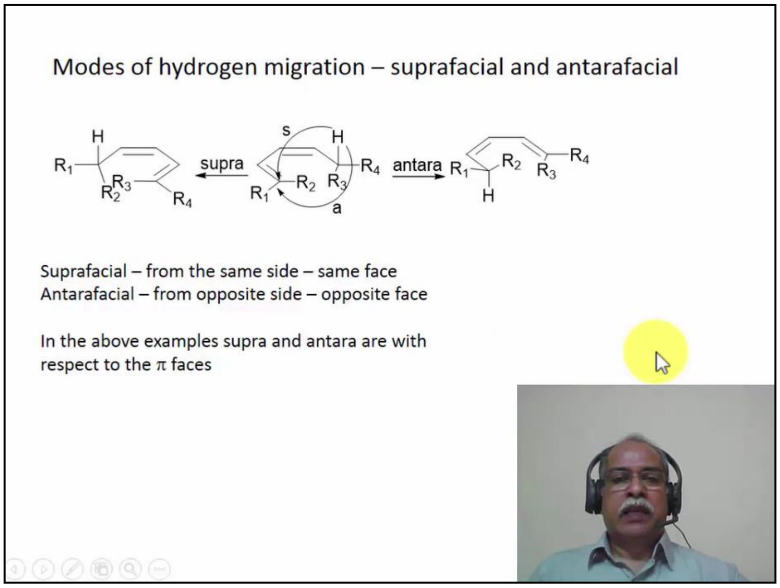

Modes of hydrogen migration – suprafacial and antarafacial

Suprafacial – from the same side – same face
Antarafacial – from opposite side – opposite face

In the above examples supra and antara are with respect to the π faces

Now, let us see, what are the modes by which, the Hydrogen migration can take place. Let us take the example of this particular PI framework, where one can expect a [1,5]-Sigmatropic migration to take place. It is a Hydrogen atom, that is going to migrate from this position to the position, where R3 and R4 groups are attached, with a concomitant rearrangement of the PI bonds, to be corresponding adjacent position. Now, in doing so, the Hydrogen can migrate from the top face to the top face of the PI framework.

This is called the Suprafacial mode. In other words, Suprafacial essentially needs from the same side, or from the same face. Now, we are talking about the PI face. Hydrogen does not have, any Suprafacial or Antarafacial migration. But, with respect to the PI face, it can either migrate the same position, from the top face to the top face, or from the top face, it can go to the bottom face also. Such a migration would be called an Antarafacial migration.

So, if a Suprafacial migration takes place, this would be the configuration of the resulting chiral center, that is generated. If an Antarafacial migration takes place, this would be the configuration of the resulting migration center, that is taking place. In the above example, Supra and Antara are with respect to the PI faces only. Because, Hydrogen does not have, any Suprafacial or Antarafacial modes of migration.

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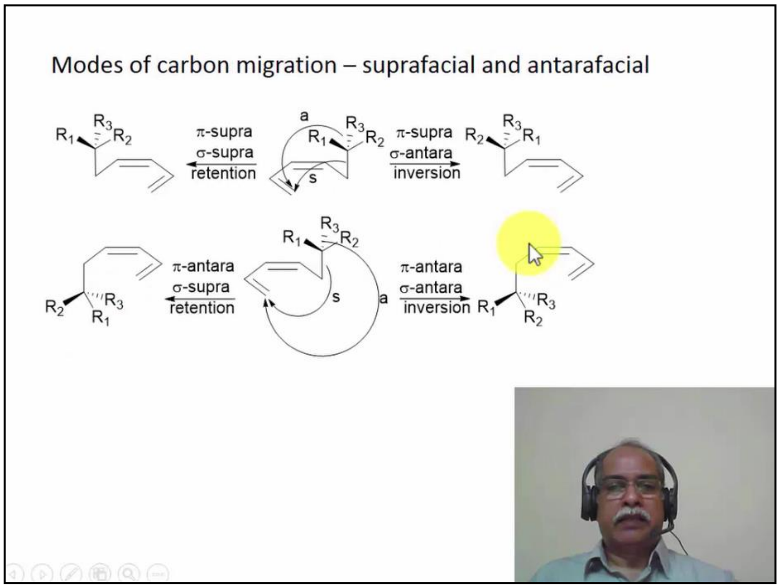

Modes of carbon migration – suprafacial and antarafacial

On the other hand, if you consider Carbon, Carbon can have Suprafacial or Antarafacial migration, depending upon, whether the migration takes place from the breaking of the Carbon-Carbon bond, which is shifted on to this position, or breaking of the Carbon-Carbon bond, with the inversion of configuration, in an Antarafacial manner. Now, let us take this particular example. Where it is with respect to the PI face Suprafacial, and with respect to Sigma face also Suprafacial.

This is equivalent to, breaking this bond, carrying this R1, R2, and R3 groups, and migrating it with intact to the other position from the top face itself, such that, the R2, R1, and R3 groups are, let us say, having the same configuration in the starting point, as well as in the end point. On the other hand, if the R-Group were the invert, and migrate in this position. In other words, the lobe on this Carbon, is going to interact with the backside lobe of the Carbon, which is undergoing the migration.

Such a migration, would result in the inversion of stereochemistry. Because, it is equivalent to an SN2 type of an attack, to the rear side of this particular Carbon. So, you can see here, the configuration here, R1, R2, R3, are in the anticlockwise direction, whereas R1, R2, R3, are in the clockwise direction, in this particular manner. So, whenever a Sigmatropic rearrangement takes place in an Antarafacial manner, with respect to the Sigma bond that is being broken, then the inversion of stereochemistry is what is expected, in this case.

In the top example, with respect to the PI system, it is Suprafacial. With respect to the Sigma system, Sigma in the sense, the Carbon-Carbon bond, that we referring to as a Sigma system. With respect to that, the Sigma Suprafacial on the left-hand side, Sigma Antarafacial on the right-hand side. Now, let us take the bottom example. Similarly, one can have with respect to the PI Antarafacial-PI Antarafacial. In other words, the migration takes place in an Antarafacial manner, with respect to the PI framework.

This Carbon-Carbon bond, is above the PI system. Now, if it migrates to, below the PI system. In other words, underneath the PI system. Then, it would correspond to an Antarafacial migration, with respect to the PI system. On the other hand, you can also have Antarafacial migration, with respect to the PI system, but a Suprafacial migration with respect to the Sigma.

In other words, this bond is broken. And, it comes and attaches itself, in this manner. You can also, in principle, you can have an Antarafacial-Antarafacial migration. But, in practice, such migrations are sterically very cumbersome. So, they do not take place in this manner, at all.

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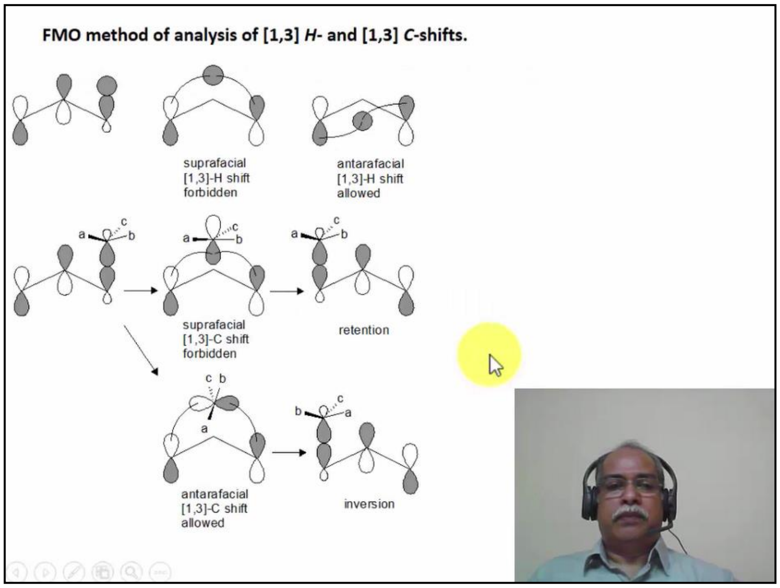

FMO method of analysis of [1,3] *H*- and [1,3] *C*-shifts.

Now, let us use the Frontier Molecular Orbital methods of analysis, for describing the [1,3]-Hydrogen shift, and [1,3]-Carbon shift. Now, if you look at this diagram, this essentially is a Sigma bond, connected to a Carbon-Hydrogen bond, is what is represented. Hydrogen, remember, is a one-S electron. So, it is approximated to be a spherical density of electron, in this position. And, this is a PI system, representing the Lumo of the PI system, and the Homo of the CH bond. When the migration takes place, the Hydrogen can migrate in a Suprafacial manner, to this position.

And, that would essentially end up in an antibonding kind of an interaction, in the Thermal migration. So, a Thermal Suprafacial [1,3]-Hydrogen shift would be a forbidden process, under thermal condition. On the other hand, if the Hydrogen migrates in an Antarafacial manner, as it is shown here. To start with, it is a bonding interaction. To end up also, it is with the bonding interaction. So, an Antarafacial [1,3]-Hydrogen migration, under thermal condition, is an allowed process.

However, imagine a one-S electron density, overlapping between Carbon number-1 and Carbon number-3, in an Antarafacial manner, this would be a geometry forbidden process. So, although a Woodward-Hoffmann says that, the Antarafacial [1,3]-Hydrogen shift is an allowed process, it is seldom observed, because of the fact that, the one-S Hydrogen orbital cannot overlap. It is not big enough to overlap, for example, with the 1-position and the 3-position of the Carbon framework.

On the other hand, if you consider a Sigmatropic migration of a Carbon-Carbon bond, the Carbon which is migrating, has three substituents, A, B, C, in an anticlockwise direction configuration, in this manner. When it undergoes a Suprafacial migration, the configuration is retained. In other words, the [1,3]-Suprafacial shift retains a configuration. However, if you look at the diagram carefully, this is a Suprafacial shift, but at the end of the interaction, that you see here, this is a antibonding kind of an interaction.

So, this shift is essentially a forbidden shift, as far as the Thermal migration is concerned. On the other hand, if you consider an Antarafacial migration, in other words, this lobe here, essentially interacts from the backside of this Carbon-Carbon bond, something like an SN2 kind of a process. So, the lobe of the Carbon essentially, overlaps with the [1,3]-positions of this PI framework, resulting in an Antarafacial migration, with the inversion of stereochemistry, at the migrating center.

This is an allowed process, with an inversion of stereochemistry. So, a [1,3]-Carbon shift is allowed, under the conditions of inversion of stereochemistry, under thermal condition.

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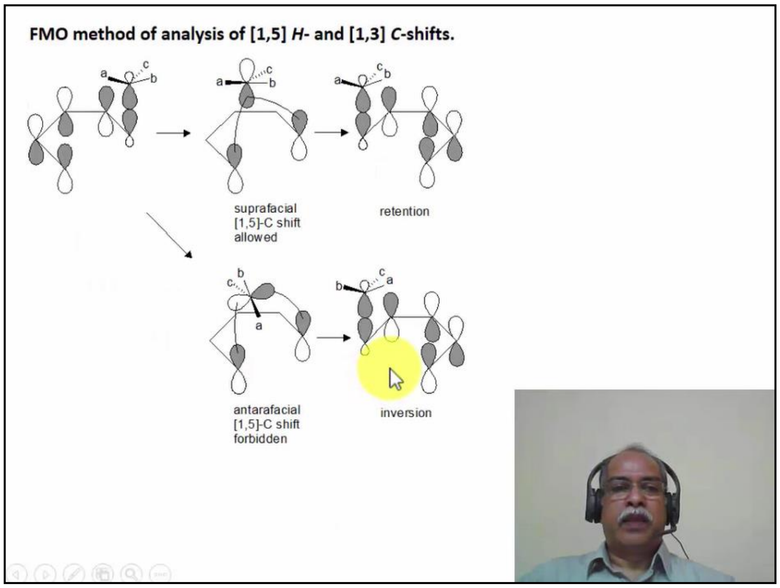

FMO method of analysis of [1,5] *H*- and [1,3] *C*-shifts.

One can extend the same analysis, to a [1,5]-Hydrogen, and a [1,5]-Carbon shift. In the case of a [1,5]-Hydrogen shift, it is easily allowed. Because, it is a larger framework, and it is a Suprafacial migration also. So, a [1,5]-Suprafacial migration, of both the Carbon, as well as Hydrogen, are allowed under thermal condition. However, the Antarafacial migration is a forbidden process, as in the case of the migration, leading to an antibonding type of an interaction, in the transition state of this rearrangement.

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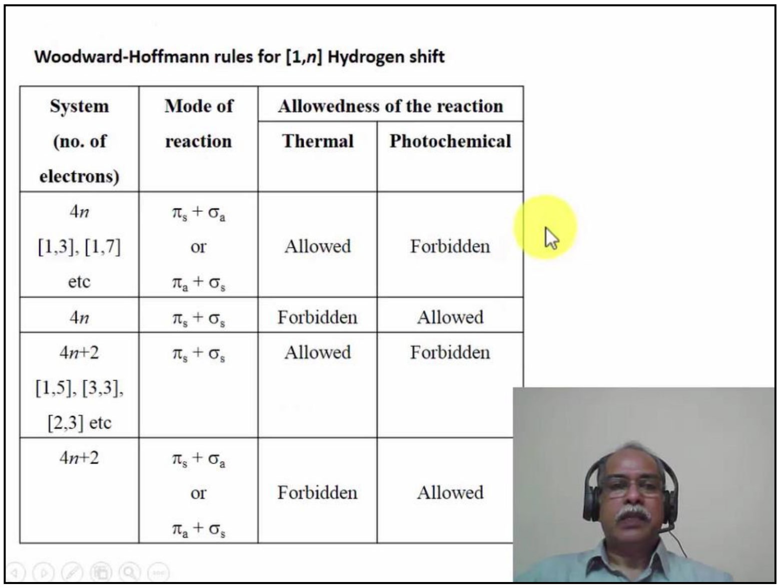

Woodward-Hoffmann rules for [1,*n*] Hydrogen shift

System (no. of electrons)	Mode of reaction	Allowedness of the reaction	
		Thermal	Photochemical
4*n* [1,3], [1,7] etc	$\pi_s + \sigma_a$ or $\pi_a + \sigma_s$	Allowed	Forbidden
4*n*	$\pi_s + \sigma_s$	Forbidden	Allowed
4*n*+2 [1,5], [3,3], [2,3] etc	$\pi_s + \sigma_s$	Allowed	Forbidden
4*n*+2	$\pi_s + \sigma_a$ or $\pi_a + \sigma_s$	Forbidden	Allowed

To summarize, the Woodward-Hoffmann rule for, 1N-Hydrogen shift. 1N-Hydrogen shift, because, this Hydrogen is a migrating group. There is no stereochemistry, involved here. So, if you consider a 4N electron system, in other words, systems involving 4N electrons, as in the case of [1,3], [1,7]. In the case of [1,3], it will be one PI bond, and one Sigma bond. So, 2+2, 4 electrons are involved. In a [1,7]-Shifted, it will be a Triene, and a CC bond.

The Triene will have 6 electrons, and the CC bond 2 electrons, totally 8 electrons will be involved in the reaction. So, it is overall a 4N system. In the 4N system, under thermal conditions, at least one of the component has to be an Antarafacial component, for it to be thermally allowed. If both of them are Suprafacial, then it is a forbidden process, under the thermal condition. Under photochemical condition, it is a complimentary nature of the Woodward-Hoffmann rule, is reflected here.

When one of the component is an Antarafacial component, it is forbidden. When both the components are Suprafacial, then it is an allowed process. Now, the 4N+2 electron system, as in the case of the [1,5]-Sigmatropic rearrangement, or a [3,3]-Sigmatropic rearrangement, both the components have to be Suprafacial in nature, for it to be allowed under the thermal condition. Whereas, if one of the component is an Antarafacial component, it becomes forbidden, under thermal condition. Of course, under photochemical condition, the opposite is true.

When both the systems are Suprafacial with respect to each other, then it is forbidden. When one of the component is Antarafacial, then it is allowed for a 4N+2 kind of a system involving, let us say for example, [2,3]-Rearrangement, or [1,5]-Rearrangement, or [3,3]-Rearrangement, and so on.

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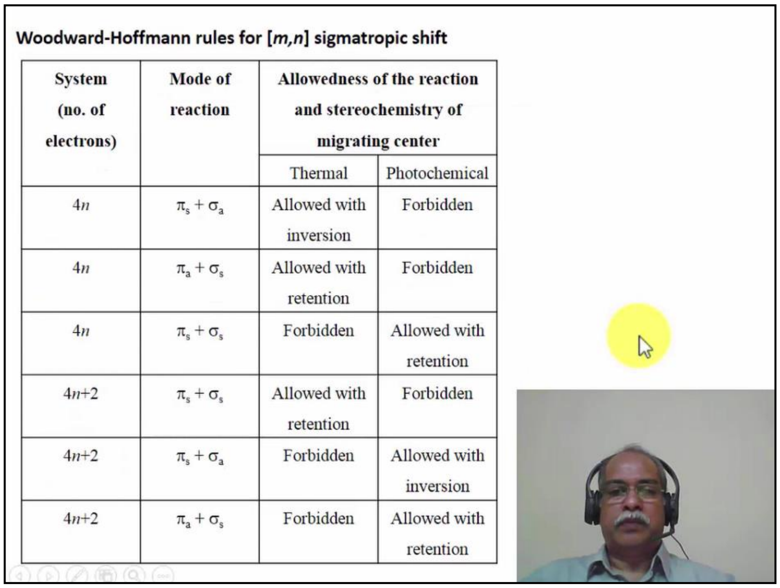

Woodward-Hoffmann rules for [*m*,*n*] sigmatropic shift

System (no. of electrons)	Mode of reaction	Allowedness of the reaction and stereochemistry of migrating center	
		Thermal	Photochemical
4*n*	$\pi_s + \sigma_a$	Allowed with inversion	Forbidden
4*n*	$\pi_a + \sigma_s$	Allowed with retention	Forbidden
4*n*	$\pi_s + \sigma_s$	Forbidden	Allowed with retention
4*n*+2	$\pi_s + \sigma_s$	Allowed with retention	Forbidden
4*n*+2	$\pi_s + \sigma_a$	Forbidden	Allowed with inversion
4*n*+2	$\pi_a + \sigma_s$	Forbidden	Allowed with retention

When Carbon is involved in the Sigmatropic migration, wherever you have an Antarafacial component of the Carbon, whether it is allowed or disallowed, that is one thing, that one need to worry about. When it is allowed, it will undergo inversion at the Carbon center, that is extremely important, for example. So, wherever, when you have a Sigma Antarafacial allowed process taking place, it has to happen with the inversion of stereochemistry of the Carbon, that is undergoing the migration.

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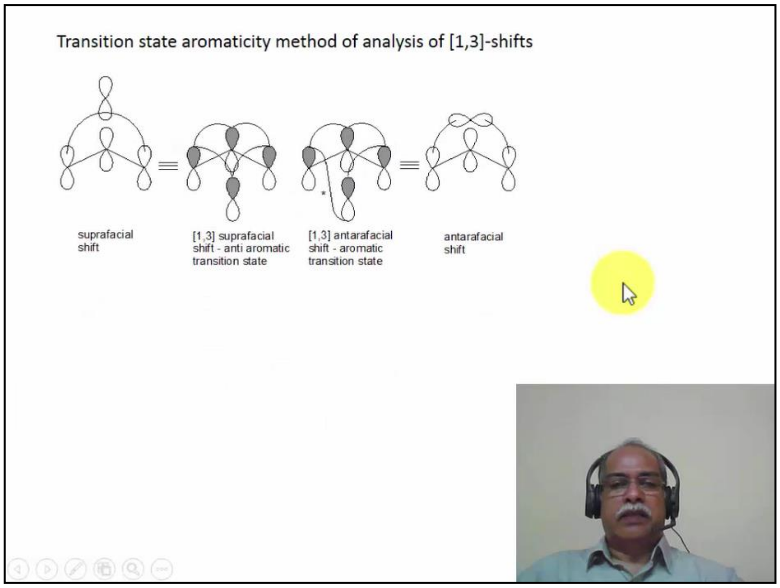

Transition state aromaticity method of analysis of [1,3]-shifts

We will see some examples of this kind of [3,3]-Sigmatropic rearrangement, and understand it very clearly, with respect to the inversion of stereochemistry, during the course of the Antarafacial migration. One can also use transition state aromaticity method, for the analysis of [1,3]-Shifts, if you consider a [1,3]-Shift of this type, it is a Suprafacial shift. So, the overlap is a continuous overlap of the 4 electrons, that are involved here, resulting in a Huckel type of a transition state, which is antiaromatic transition state.

So, antiaromatic transition state, in an Antarafacial manner would be a, this is a [1,3]-Suprafacial shift, for example, resulting in an antiaromatic transition state. So, it would be a forbidden transition state. On the other hand, if it is an Antarafacial migration, that will be a 4N electron system, Mobius kind of a system. And, such a Mobius kind of a transition state, will be an allowed process. Because, it would be an aromatic transition state. So, Antarafacial shift is allowed under thermal condition. Whereas, Suprafacial shift is forbidden under the thermal condition.

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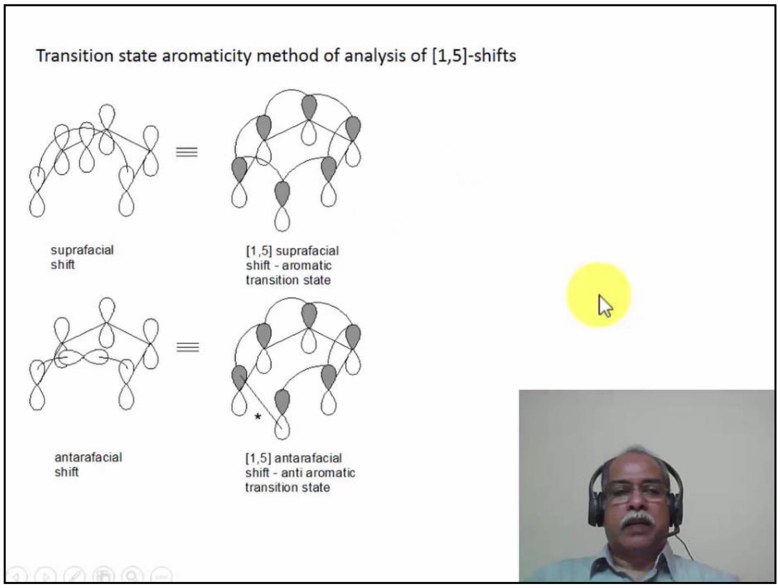

Transition state aromaticity method of analysis of [1,5]-shifts

Exactly, opposite is true, for the case of the [1,5]-Shifts, if it is a [1,5]-Suprafacial shift, for example. It is a cyclic 6 electron transition state, which is a Huckel kind of a transition state. So, it is aromatic. Whereas, one of them is Antarafacial, then the nodal point comes into picture. So, this would be essentially a Mobius kind of a twisted cyclic transition state, is what is seen here. And, that corresponds to an antiaromatic transition state. So, it will be a forbidden transition state.

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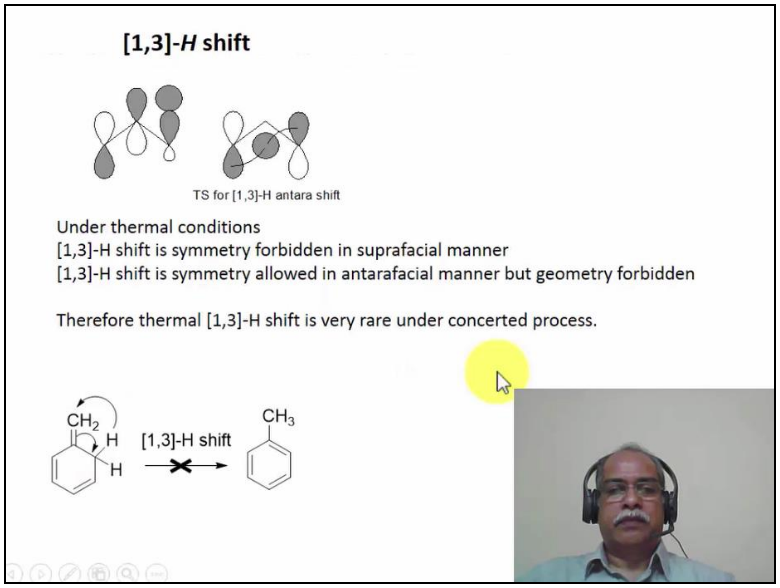

[1,3]-*H* shift

Under thermal conditions
[1,3]-H shift is symmetry forbidden in suprafacial manner
[1,3]-H shift is symmetry allowed in antarafacial manner but geometry forbidden

Therefore thermal [1,3]-H shift is very rare under concerted process.

Now, let us take the example of [1,3]-Shift, in a more detailed manner. This is a [1,3]-Shift. And, this is essentially the transition state for the [1,3]-Antarafacial migration. Under thermal condition, [1,3]-Shift is symmetry forbidden, in a Suprafacial manner. However, [1,3]-Shift is symmetry allowed, under Antarafacial manner, but geometry forbidden. As i already mentioned, the one-S electron density is very small, and it is unable to overlap between Carbon number-1 and the Carbon number-3, in an Antarafacial manner.

So, as a result of it, although Woodward-Hoffmann rule allows under the Antarafacial manner, the migration, geometry is forbidding the reaction. Because, effective overlap between Carbon number-1 and 3 in an Antarafacial migration, by a one-S electron density of the Hydrogen, is nearly impossible. So, such reactions do not take place. So, although the concerted processes is a symmetry allowed process under Antarafacial migration, it is rarely seen to occur, in this particular case.

Such an example is exemplified. Such a process, which is a geometry forbidden is exemplified, using this particular example. What you see on the right left hand side, this structure, is nothing but a Tautomer of Toluene. So, one would expect the Hydrogen migration to this particular Carbon, through a [1,3]-Shift. In other words, this is a Carbon-Hydrogen bond, that is breaking. So, this would be 1 and 1, 1, 2, 3. So, this a [1,3]-Hydrogen shift, is what is expected here, to go to Toluene.

In spite of the fact that, this is a stable structure thermodynamically, in comparison to Toluene structure. Toluene is stable, because of the gain of aromaticity energy, the delocalization energy. Such a thermal [1,3]-Shift, does not take place quite readily, as illustrated by the example, that is shown here.

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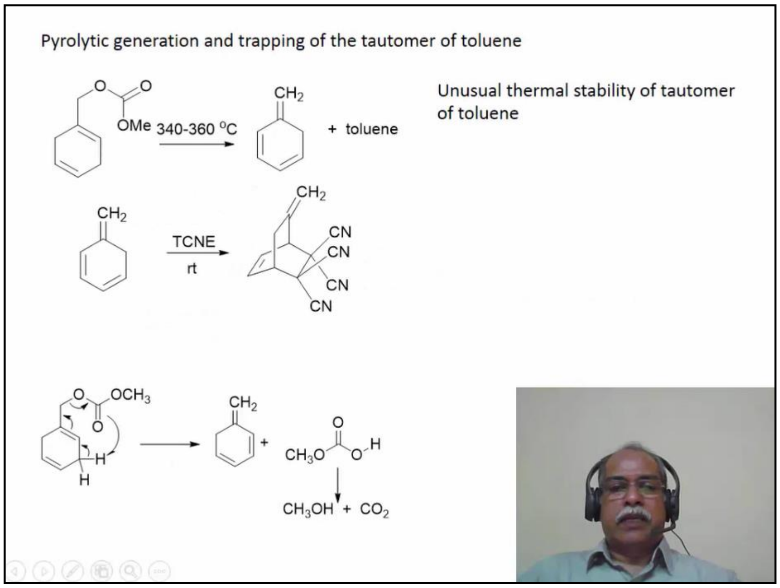

Pyrolytic generation and trapping of the tautomer of toluene

Unusual thermal stability of tautomer of toluene

When this Carbonate is pyrolyzed, the pyrolysis essentially leads to the Tautomer of Toluene, along with small quantities of Toluene, of course. How is the Tautomer of Toluene formed, from this Carbonate? The mechanism is shown here. This oxygen, essentially picks up this Hydrogen, with simultaneous migration, and loss of the Carbonic acid, which is decomposing to Carbon dioxide and Methanol, resulting in the formation of the Tautomer of the Toluene.

The Tautomer of the Toluene, under this condition, is reasonably stable. Because, it does not readily isomerize to Toluene. So, in the presence of something like Tetracyanoethylene, this Diene can be trapped by a Diels-Alder reaction, to give the Diels-Alder adduct. So, this example, essentially illustrate the fact that, in spite of the fact, the Toluene is a more stable, thermodynamically stable product. It does not get formed, under the reaction condition.

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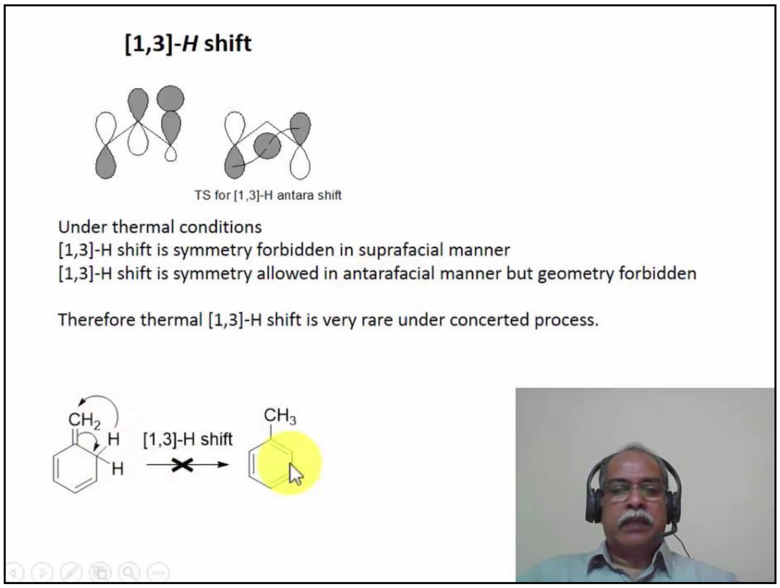

[1,3]-*H* shift

TS for [1,3]-H antara shift

Under thermal conditions
[1,3]-H shift is symmetry forbidden in suprafacial manner
[1,3]-H shift is symmetry allowed in antarafacial manner but geometry forbidden

Therefore thermal [1,3]-H shift is very rare under concerted process.

For the reason that, this particular reaction is geometry forbidden reaction. In other words, the [1,3]-Shift under the Antarafacial migration condition, does not take place quite readily, because of the fact, this geometry is an unfavorable geometry, for the overlap of the one-S Hydrogen, with the 1 and 3 position of the Allylic system, that is shown here.

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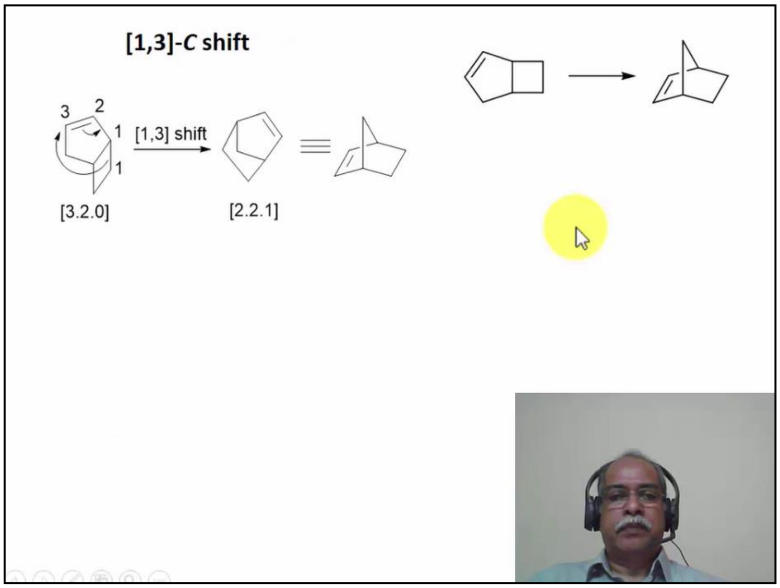

[1,3]-*C* shift

The most common [1,3]-Carbon shifts are, the shifts of this particular Carbon-Carbon bond, in a 3,2,0-Bicyclic system. This is a 1,2,3,1,2. So, it is a 3,2,0-Bicyclic system. In other words, it is a fused bicyclic system, is what we are talking about. A fusion of a 4-Membered ring, with a 5-Membered ring, with a double bond. So, this is a Cyclopentane, is what we are talking about.

The rearrangement of that particular skeleton, to 2,2,1-Bicyclic system. In other words, this reaction, where you are fused bicyclic system, undergoes a bridged rearrangement, to go to the bridged bicyclic system, corresponds to a [1,3]-Carbon shift of this kind. So, you can see here, when you break this Carbon-Carbon bond, and shift this bond over here, this Methylene becomes the bridging Methylene. So, as a result of that, you get the 2,2,1-Bicyclic system.

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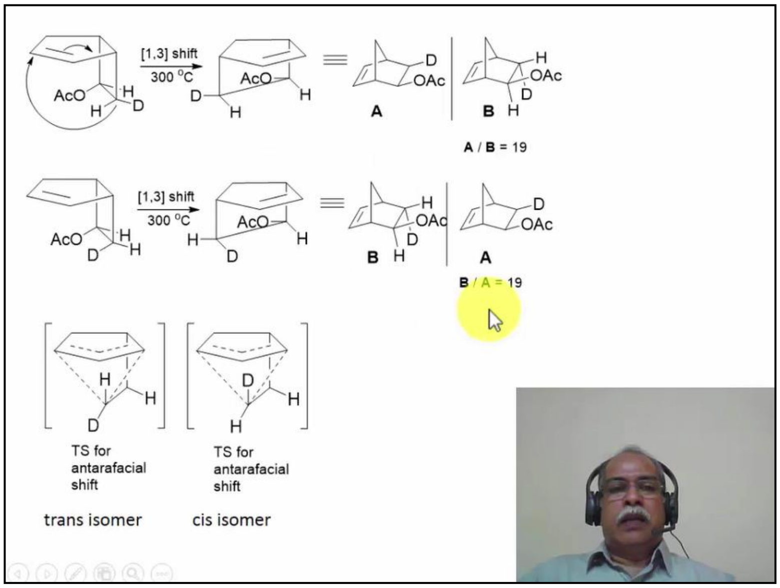

These are beautiful examples, which will illustrate not only the feasibility of the [1,3]-Shifts in an Antarafacial manner, the stereochemistry also revealing its nature in terms of the Antarafacial migration, resulting in the inversion of stereochemistry. If you look at the stereochemistry of this Carbon-Carbon bond, the Deuterium and the Acetate are, Trans with respect to each other. And, if this Carbon-Carbon bond is broken, and if it migrates to this position, this is the product, that one would get.

In doing so, this is a [1,3]-migration, under thermal condition, and it has to undergo an Antarafacial kind of a shift. If you see the transition state here, the Hydrogen is pointing inwards to the PI system, and the Deuterium is pointing outside the PI system. And, during the course of the migration, the inversion will take place. And, such an inversion, brings the Acetate and the Deuterium, Cis with respect to each other.

So, the Trans stereochemistry of the starting material, and the Cis stereochemistry of the product between the Acetate and the Deuterium, very clearly tells us, there is an inversion that has taken place, with the migrating Carbon, which is this particular Carbon, indicated by the cursor. And, the migration essentially leads to the formation of the Exo-Deutero Acetate, as it is shown. So, product A is actually the Woodward-Hoffmann allowed product. Product B, where the inversion has not taken place, for example, is formed in minor quantities.

That is a Woodward-Hoffmann disallowed process, or forbidden process, occurring in a very, very small amount. Perhaps, through a radical type of a non-concerted reaction mechanism, may be operating under this condition, to a very small extent. We can see here, the A, B ratio is close to 19.

So, A is the predominant product, not an exclusive product, which is a Woodward-Hoffmann rule allowed product. If you take the opposite diastereo isomer, where the Acetate and the Deuterium are Cis already, with respect to each other. Under these conditions, the inversion take place. The Acetate and the Deuterium becomes Trans, and the bridged bicyclic system, which is the product. So, you can see here, the Acetate and the Deuterium are Trans with respect to each. This is a Woodward-Hoffmann allowed product.

This is a Woodward-Hoffmann disallowed product, for example, where inversion of stereochemistry has not taken place. So, the ratio essentially tells us that, the Woodward-Hoffmann allowed process is the most preferred pathway, in this particular system. Now, in the transition state geometry for the Trans isomer is shown here, which brings the Hydrogen interior to the PI system.

Whereas, for the transition state for the deuterated Cis isomer, brings the Deuterium into the interior of the PI system. Suppose, if there were to be a Methyl group here, instead of a Hydrogen, and the Methyl group would come interior to this, that would be highly sterically hindered, for example. So, such a reaction will be much slower reaction, compared to a reaction, where you have a Deuterium or a Hydrogen, that is being present, Cis to the Acetate functional group.

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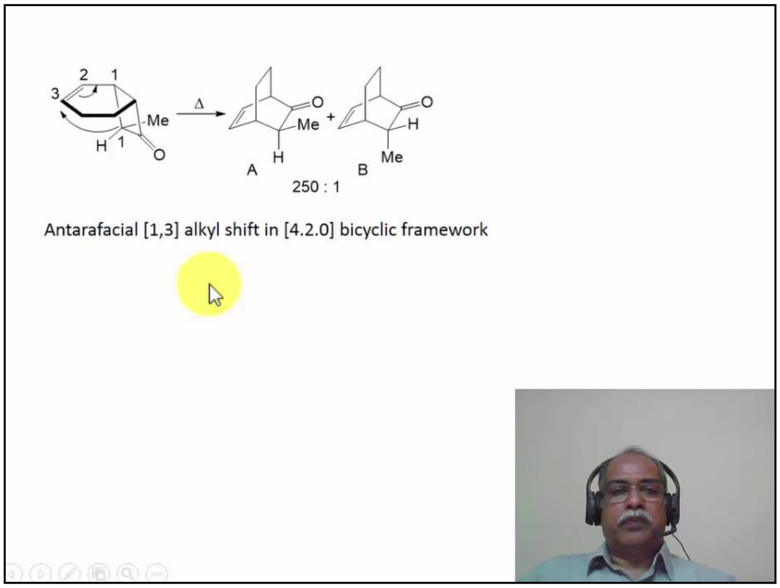

Antarafacial [1,3] alkyl shift in [4.2.0] bicyclic framework

Now, here is an example of a [1,3]-Alkyl shift, that is taking place in a 6-Membered ring, fused to the, in other words, it is a 4,2,0-Bicyclic system, is what we are. Fused bicyclic system, undergoing a [1,3]-Alkyl shift. We can follow the [1,3]-Alkyl shift, by the number. This is the bond, that is being broken. So, it is migrating to this position, leading to a 2,2,2-Bicyclic system.

In fact, this reaction is a much more facile reaction, faster reaction, compared to the 2,2,1-Bicyclic system. And, this is a Woodward-Hoffmann rule allowed product, which is formed in 250:1 ratio. This is a forbidden product, formed in extremely small amounts, in this particular case.

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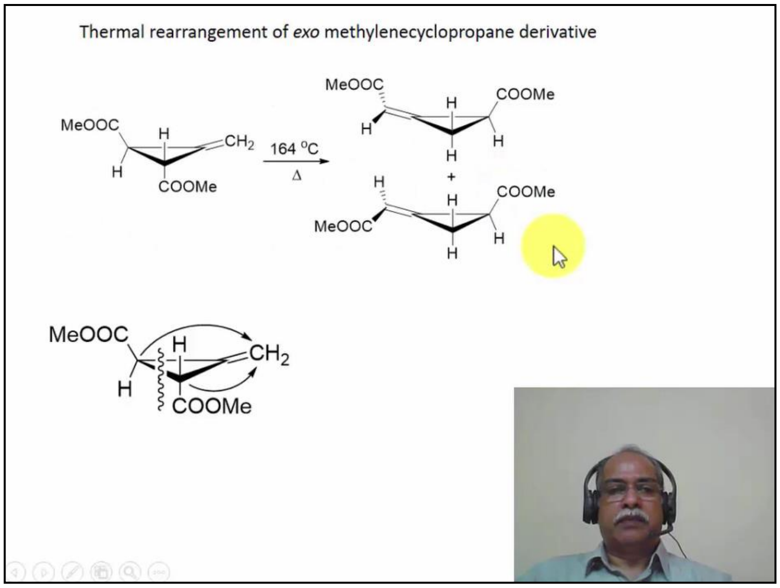

Thermal rearrangement of *exo* methylenecyclopropane derivative

Here is an interesting example of an Exo-Methylenecyclopropane derivative, undergoing the Sigmatropic rearrangement. This is a Carbon-Carbon bond, which is undergoing the migration. The Carbon-Carbon bond that is broken, is this particular bond. When this bond breaks, either this Carbon can migrate over here, or this Carbon can migrate over here. Depending upon, which Carbon is migrating, with the inversion of stereochemistry at that particular center, either of this product can be, formation can be explained.

So, go through this example very carefully, and figure out, which one of this Carbon migration leads to this product, and which one of the Carbon migration leads to this particular product, between the two Carbons, that are shown here. The necessary condition is, that during the course of the migration, the inversion of the stereochemistry of the migrating Carbon should take place, to lead the corresponding product. And, the resulting other Carbon, will essentially become the Exo-Methylene Carbon, with the specified stereochemistry, that is shown in this particular case.

So, the process is described here, mechanistically. This Carbon-Carbon bond is broken. The wavy line essentially shows, that is a breaking bond. That is, this Carbon-Carbon bond. So, either this Carbon can migrate over here, or this Carbon can migrate over here, in the Exo-Methylenecyclopropane derivative, that is discussed in this slide.

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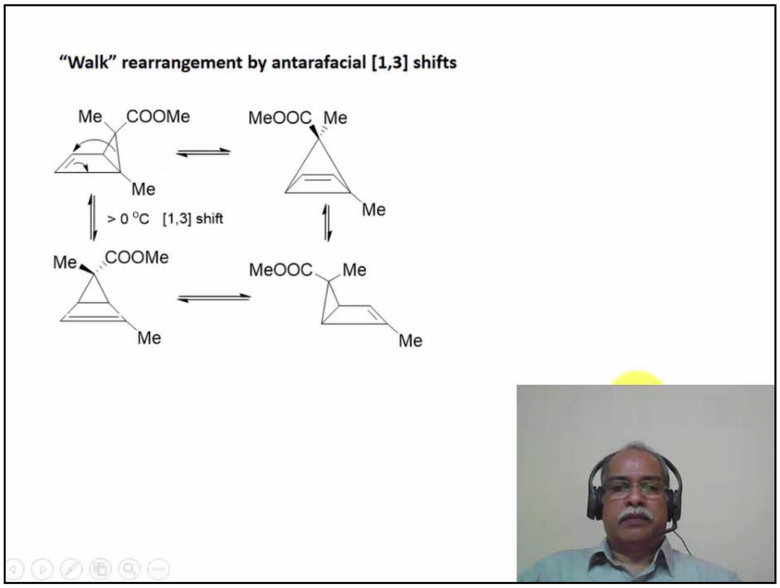

“Walk” rearrangement by antarafacial [1,3] shifts

Walk around the ring rearrangement, is a very common phenomenon. In the case of the Sigmatropic rearrangement, the reaction is essentially that, this particular Carbon is walking around the ring, if you see it carefully. Let us say for example, this Carbon is migrating over here, by breaking this Carbon-Carbon bond, that will result in the formation of this. Or, if this Carbon-Carbon bond is broken, and it is migrating over here, that is, this Carbon migrating over this, that is also [1,3]-Sigmatropic rearrangement, that would give this particular product.

So essentially, what is happening is, this particular Carbon, which is the Cyclopropyl Carbon here, essentially migrating to the various positions of this 4-Membered ring, resulting in these four structures, which are equilibrating structures, for example, with respect to each other. In each one of this migration, it is a [1,3]-Carbon shift, that is taking place. If you look at carefully, the Methyl group is interior to the PI system here, interior to the 4-Membered ring system and the, or in other words, it is Endo to the 4-Membered ring system.

And, the Methoxy Carbonyl functional group, the Ester functional group, is Exo to the PI system. And, it remains Exo, throughout the course of the migration, irrespective of which Carbon it gets attached, it is Exo with respect to the Ester functional group, and Endo with respect to the Methyl group. So, whenever an Antarafacial migration is taking place, the Endo group remains Endo, and the Exo group remains Exo, during the course of the migration, which corresponds to the inversion of stereochemistry, which i will clarify in a few slides later, by a diagram.

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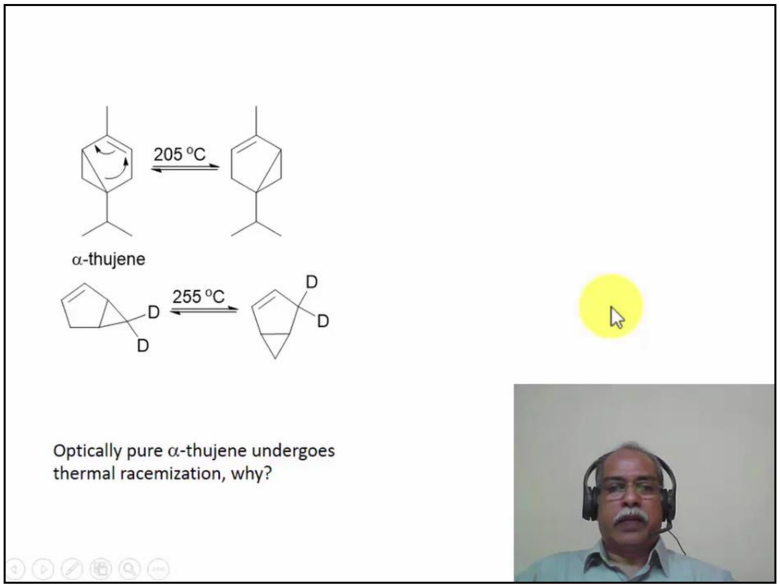

Optically pure α-thujene undergoes thermal racemization, why?

Now, this is a structure of a Thujene. This is Alpha-Thujene, naturally occurring compound. This occurs in an optically pure form, for example. When you take an optically pure form of Alpha-Thujene, and pyrolyze it at 205 degree centigrade, it undergoes [1,3]-Sigmatropic rearrangement. What is the rearrangement? This Carbon-Carbon bond migrates over here, with the concomitant migration of the PI system over here, with the formation of a new Carbon-Carbon bond, resulting in the formation of Alpha-Thujene. In other words, this is a degenerate rearrangement.

Alpha-Thujene, if you take the plus isomer, it will produce the minus isomer. Alternatively, if you take the minus isomer, it produces the plus isomer. So, during the course of a migration, essentially Alpha-Thujene undergoes thermal racemization process. Why is it undergoing a thermal racemization process? Because, the rearranged product is an optical isomer of the starting material, because of the inversion of stereochemistry, that has to take place during the course of the migration. So, these two are optical anti-force, with respect to each other. So, essentially this is a reaction, which can go back and forth.

Because, there is no difference in the energy between, the forward reaction and the backward reaction. Because, it is a degenerate rearrangement. Therefore, the plus isomer and the minus isomer, will be equally populated, at certain point of the rearrangement, because of the equilibrium process, that is taking place. This is the very similar example. A Vinyl Cyclopropane is what is undergoing rearrangement, to give this particular product, by the migration of the Carbon-Carbon bond, over here, with the concomitant migration of this Carbon-Carbon PI bond, in this particular case.

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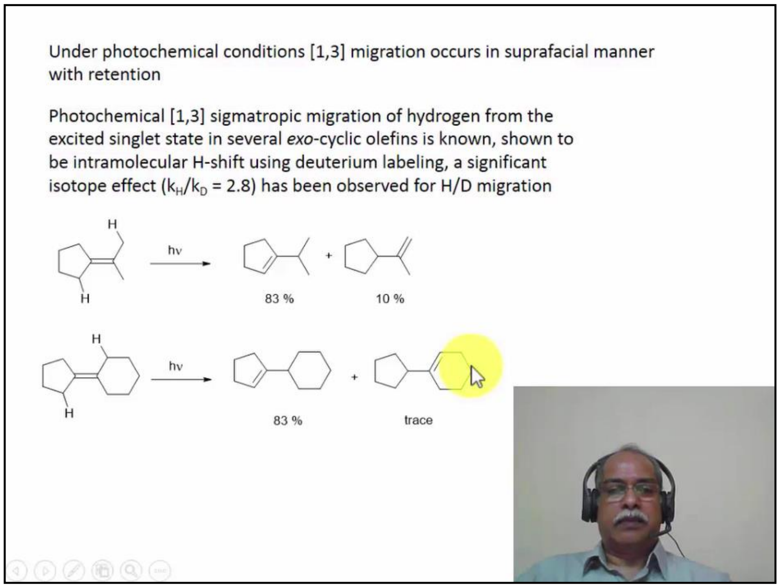

Under photochemical conditions [1,3] migration occurs in suprafacial manner with retention

Photochemical [1,3] sigmatropic migration of hydrogen from the excited singlet state in several *exo*-cyclic olefins is known, shown to be intramolecular H-shift using deuterium labeling, a significant isotope effect ($k_H/k_D = 2.8$) has been observed for H/D migration

Under photochemical conditions, the [1,3]-Hydrogen migration is a Suprafacial migration. So, it readily takes place, unlike the Thermal migration, which is geometrically forbidden. So, the photochemical [1,3]-Sigmatropic rearrangement examples are given here. The Exo-Methylene Cyclopentene, Cyclohexene, undergo the [1,3]-Sigmatropic migration, through a Suprafacial manner of migration. And, by using the Deuterium labelled compound, it has been shown that, there is a significant primary kinetic isotope effect.

In other words, the Hydrogen substituted compounds, reacts 2.8 times faster than, the Deuterium substituted reaction. This is a primary kinetic isotope effect, which corresponds to the, they have Carbon-Hydrogen or the Carbon-Deuterium bond breaking, during the course of the transition state. So, there is a direct evidence to show that, it is the single step reaction, involving the Hydrogen-Deuterium migration, as the case may be, which has the kinetic isotope effect, indicating that, in the transition state, the Carbon-Hydrogen or Carbon-Deuterium bond is breaking, in this case.

So, what is happening in this reaction? This hydrogen, which is the allylic hydrogen, migrates to this position, with the concomitant migration of the double bond. Or, this hydrogen here, migrates to this position, with the concomitant double bond migration to the ring side, for example. The migration of this particular hydrogen, to give the Cyclopentene derivative, occurs in a more predominant manner, compared to the exomethylene hydrogen migrating to this position, to give this particular product.

Similarly, in the case of the Cyclopentadienylidine, Cyclohexene, for example, the Hydrogen migration from the Cyclopentane, to give the Cyclopentene derivative, is occurring in a more predominant manner, compared to the Cyclohexane-Hydrogen, migrating to this position, to give this secondary product. So, this product is arising from the migration of this particular Hydrogen. Whereas, this product is arising from the migration of this particular Hydrogen. The two types of Hydrogens, that are shown in this molecule, very clearly.

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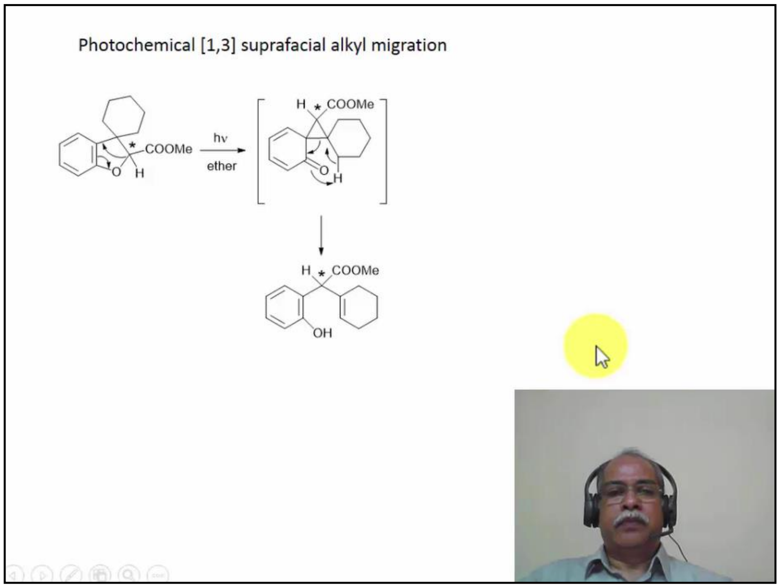

Photochemical [1,3] suprafacial alkyl migration

The [1,3]-Suprafacial Alkyl migration example, is given here. This is a Spiro cyclic derivative, where the starred position is a chiral center. And, that is supposed to undergo migration, with an inversion of stereochemistry, for example. So, the migration takes. This is like for example, the Carbon migrates to this position, with the concomitant formation of a Carbon-Oxygen double bond, resulting in the formation of this particular intermediate.

And, then the Keto–Enol tautomerism essentially results in the formation of the phenolic compound, which is this particular product, which is the final product. Important point is, this particular center, which has certain stereochemistry, will be inverted during the course of the migration. So, this would be having the opposite stereochemistry, in comparison to the stereochemistry, that is shown here. Sorry, this is a Photochemical migration.

So, this will be a Suprafacial migration, with a retention of stereochemistry, i am sorry. The inversion of stereochemistry takes place, only in the Antarafacial migration, which is a Thermal migration. This is an example of a Photochemical migration. So, that is with a retention of stereochemistry, it should take place.

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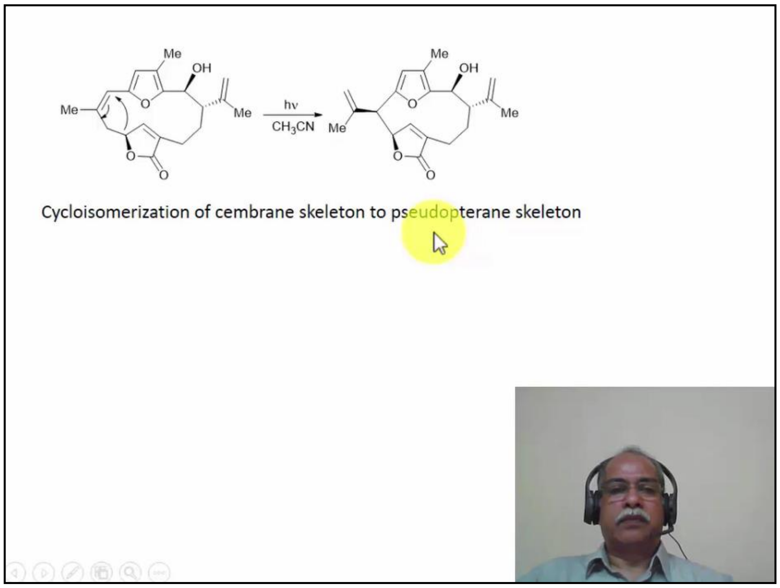

Cycloisomerization of cembrane skeleton to pseudopterane skeleton

This is a cyclo-isomerization of one particular Terpenoid skeleton, to another Terpenoid skeleton. And, the Cembrane skeleton, is this particular skeleton. And, Pseudopterane skeleton, is this particular skeleton. The migration is very clearly shown, to be breaking of this Carbon-Carbon bond, with the migration over here, resulting in the formation of an Exomethylene compound, which is this particular. Under photochemical condition, this is a Suprafacial [1,3]-migration, is what is taking place, resulting in the formation of this particular product.

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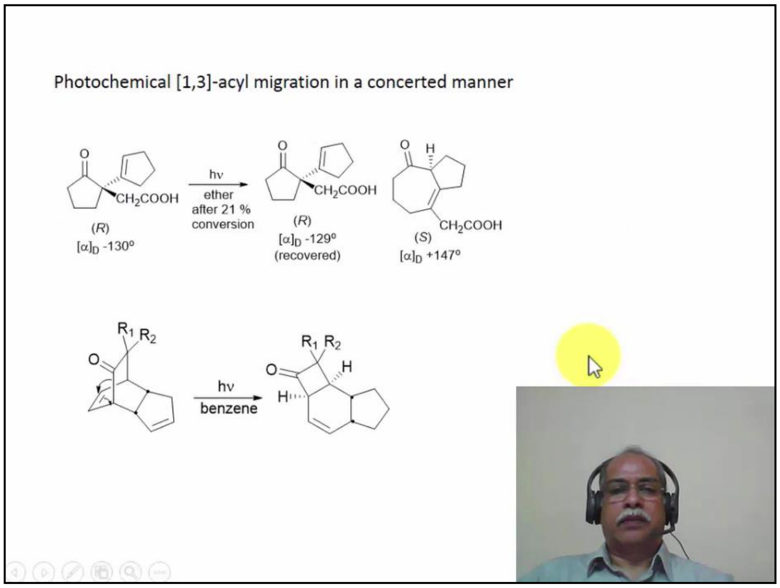
Photochemical [1,3]-acyl migration in a concerted manner

Now, the fact that, the [1,3]-Suprafacial migration, results in the retention of stereochemistry, is very clearly illustrated, by taking a optically pure isomer of this particular molecule. The R configuration of this is evident, from the structure here. The migration of the Acyl group, to this position. In other words, the Carbon-Carbon bond that is broken, is this bond. This has to migrate over here, with the concomitant migration of this.

A ring expansion, is what is taking place. A 5-Membered ring, when the Acyl Carbon migrates over here, it adds its 2 extra Carbon, so it becomes a 7-Membered ring. So, a fused 7-Membered ring, is what is being formed, during the course of the migration. In doing so, this chiral center over here is, retain its stereochemistry, in terms of the migration being a Suprafacial migration. So, if the Acyl migration were to be a simple Carbon-Carbon bond breaking, and a reattachment over here, in a stepwise manner, you would expect racemization process to take place.

So, when the reaction is carried out, under very low conversions of 21% conversion, the starting material that is recovered had essentially, the same optical rotation as the starting material, which was taken originally. In other words, the starting material does not undergo racemization by a simple Carbon-Carbon. You can imagine, this Carbon-Carbon bond to be broken, to give an Acyl radical, by an Alpha fragmentation, which is Norrish-1 process.

Then, the Norrish-1 process produces a diradical. The diradical recombine here. If that were to take place, racemization would have taken place. If it is a concerted [1,3]-migration, followed by the ring expansion, then the product that is formed, is going to be this particular product. And, the resulting unreacted starting material, essentially has the same optical rotation, ruling out the possibility of a stepwise mechanism, in this particular instance.

Here is another Acyl migration, where the 2,2,2-Bicyclic system, undergoes Acyl migration, to give the fused bicyclic system, in this particular case. Another example of a Photochemical [1,3]-Sigmatropic rearrangement, in this case.

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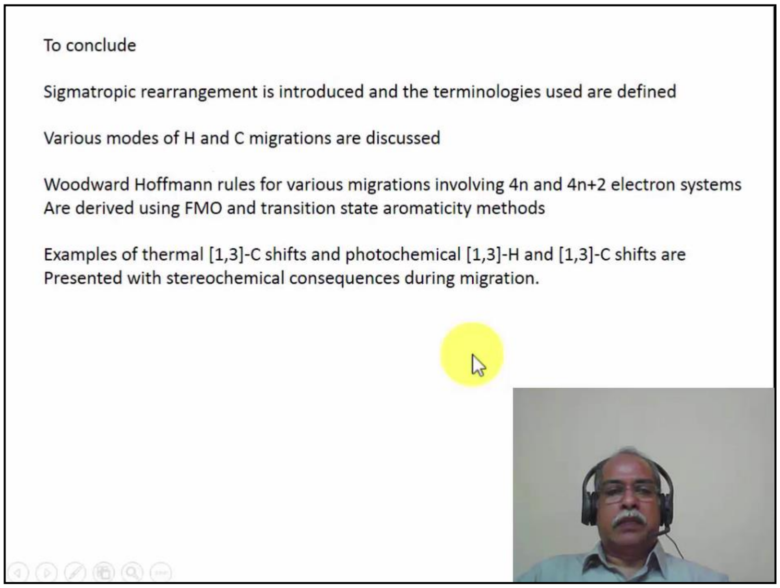

To conclude

Sigmatropic rearrangement is introduced and the terminologies used are defined

Various modes of H and C migrations are discussed

Woodward Hoffmann rules for various migrations involving 4n and 4n+2 electron systems
Are derived using FMO and transition state aromaticity methods

Examples of thermal [1,3]-C shifts and photochemical [1,3]-H and [1,3]-C shifts are
Presented with stereochemical consequences during migration.

So, let us conclude, this particular module. What we have seen is the, Sigmatropic rearrangement is introduced, in this particular module. And, the terminologies used, are defined in this module. Various modes of Carbon and Hydrogen migration, are discussed. Woodward-Hoffmann rules were derived, using the Frontier Molecular Orbital method, as well as the Transition State Aromaticity Method, for the 4N, and 4N+2 electron involving systems, which undergo the Sigmatropic migration.

Several examples of the Thermal [1,3]-Carbon shift, and the Photochemical [1,3]-Hydrogen as well as the Carbon shift, with the consequential stereochemical aspects of the migration, is also discussed here. Wherever, there is an Antarafacial migration, it invokes an inversion of stereochemistry of the migrating center. Wherever, there is a Suprafacial migration taking place, there is a retention of stereochemistry.

Both the points are illustrated with suitable examples, in the Thermal migration of the [1,3]-Carbon Thermal migration, and the [1,3]-Carbon Photochemical migration, with a retention of stereochemistry, in this particular module. Thank you very much, for your kind attention. I hope, you enjoyed this particular lecture.