Pericyclic Reactions and Organic Photochemistry
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Module No. #04
Lecture No. #17
Pericyclic Reactions – Sigmatropic rearrangements continued… [1,5]-H and C migrations and Cope rearrangement.

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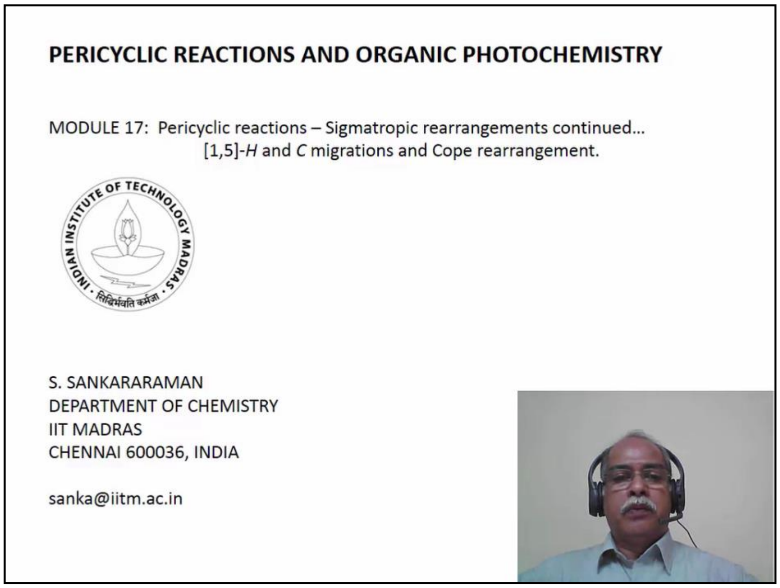

PERICYCLIC REACTIONS AND ORGANIC PHOTOCHEMISTRY

MODULE 17: Pericyclic reactions – Sigmatropic rearrangements continued…
[1,5]-*H* and *C* migrations and Cope rearrangement.

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Hello, welcome to Module Seventeen of the online course, on Pericyclic Reactions and Organic Photochemistry. We will continue with Sigmatropic rearrangement, and consider [1,5]-Hydrogen and [1,5]-Carbon migrations, as well as Cope rearrangement, which is a [3,3]-Sigmatropic rearrangement, in this particular module.

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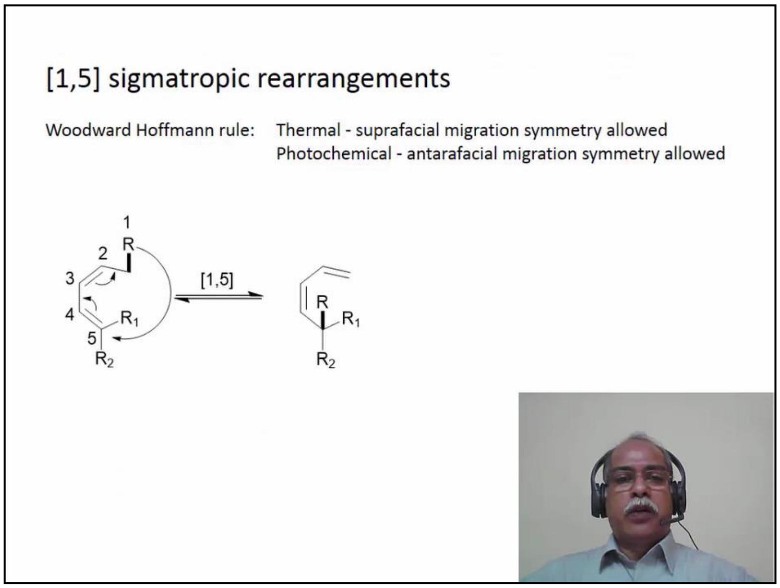

[1,5] sigmatropic rearrangements

Woodward Hoffmann rule: Thermal - suprafacial migration symmetry allowed
Photochemical - antarafacial migration symmetry allowed

In the last module, we consider the [1,3]-Shift. A similar analogy is drawn here, to illustrate the [1,5]-Shift, in the case of Sigmatropic rearrangement. If you consider the thick bond, which is a Carbon R1 bond, for example, the R group is migrating to this particular position. So, it is corresponding to a [1,5]-Carbon shift, if the R group is a Carbon. If R group is a Hydrogen, it would correspond to a [1,5]-Hydrogen shift.

Let us recall the Woodward-Hoffmann rule, for the [1,5]-Carbon and Hydrogen shift. Under thermal condition, Suprafacial migration is symmetry allowed, as well as geometry allowed. Photochemical migration is allowed, only if the Antarafacial migration is possible, in the case of the [1,5]-Sigmatropic rearrangement, under Photochemical condition. So, thermal [1,5]-Sigmatropic rearrangements, are quite common.

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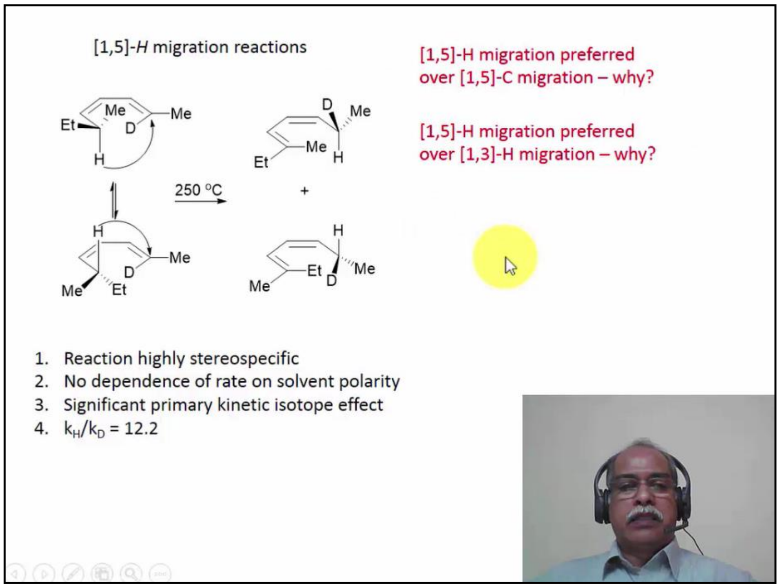

[1,5]-*H* migration reactions

[1,5]-H migration preferred over [1,5]-C migration – why?

[1,5]-H migration preferred over [1,3]-H migration – why?

1. Reaction highly stereospecific
2. No dependence of rate on solvent polarity
3. Significant primary kinetic isotope effect
4. $k_H/k_D = 12.2$

There are several examples, that are known here. Now, let us take for example, this example, where the migration of Hydrogen is illustrated, by this example. These two structures are essentially conformational isomers, because of the Carbon-Carbon bond rotation, that is taking place. This will be in rapid equilibrium, with respect to each other. So, in other words, they are conformers with respect to each other. In each of the conformer, the Hydrogen migration, is what is illustrated in this reaction. So, at 250°, the Hydrogen migration takes place in this thing.

When the Hydrogen migration takes place in a Suprafacial manner, with respect to the PI framework, this is a stereochemistry of the resulting chiral center, that is generated. And, this is a stereochemistry of the double bond, that is generated. You can see here, when the Hydrogen migrates, it is Suprafacial with respect to the PI framework, and it attaches itself from the bottom face from here, resulting in the attachment of the Carbon-Hydrogen bond in the bottom, and with the concomitant change in the hybridization of this particular Carbon, to an SP3 Carbon, as shown here.

From this conformer, if the Hydrogen is migrating, it is going to migrate from the top face, indicating, that the Hydrogen ends up in the top face, with the resultant stereochemistry of this chiral center, to be like this. And, the resulting stereochemistry of the Carbon-Carbon double bond that is formed, it to be like this. These two isomers are Diastereo isomers. the reaction is highly stereospecific in the sense that, Hydrogen migration is Suprafacial in both cases, resulting in the formation of either this, a mixture of these two products, where the stereochemistry here is defined as this, with the stereochemistry of the double bond, to be here.

In other words, the stereochemistry of the double bond, with this stereochemical double bond, and with this stereochemical, SP3 Carbon is not formed, in any of these reactions. There is no significant dependence of the rate on solvent polarity indicating that, you can rule out the possibility of ionic intermediates being formed, during the course of the reaction. This solvent effect is consistent with a concerted Hydrogen migration, involving no reactive intermediates, in this particular instance.

Significant primary Kinetic isotope effect is observed because, during the course of the transition state, the Carbon-Hydrogen bond, or the Carbon-Deuterium bond, as the case may be, depending upon the Deuterium substitution, in this particular molecule. A significant K_H/K_D, which is the primary Kinetic isotope effect of about 12.2 is observed, indicating that the rate determining step, which is a single step reaction, involving the Carbon-Hydrogen bond breaking is significant, in this particular case.

Now, [1,5] migration is preferred over, [1,5]-Carbon migration. Why is that? In other words, it is possible to migrate the Methyl group, or the Ethyl group, instead of Hydrogen. Now, typically a Carbon-Carbon bond breaking is more difficult, than a Carbon-Hydrogen bond breaking. It is of lower energy path way. So, only the Hydrogen migration takes place. Why is it that, [1,5]-Hydrogen migration take place, over [1,3]-Hydrogen migration. Remember, [1,3]-Hydrogen migration, although it is possible in this particular case, it has to take place in an Antarafacial manner.

Such an Antarafacial shift is although symmetry allowed, it is geometry forbidden. And, that is why, this reaction does not take place. So, the fact that, the Hydrogen bond is of lesser energy than Carbon-Carbon bond, explains why Hydrogen migration takes place, in preference to the Carbon migration. the fact that, [1,5] migration is a Suprafacial migration, and [1,3] migration is an Antarafacial migration, which is geometry forbidden. We will explain this particular question.

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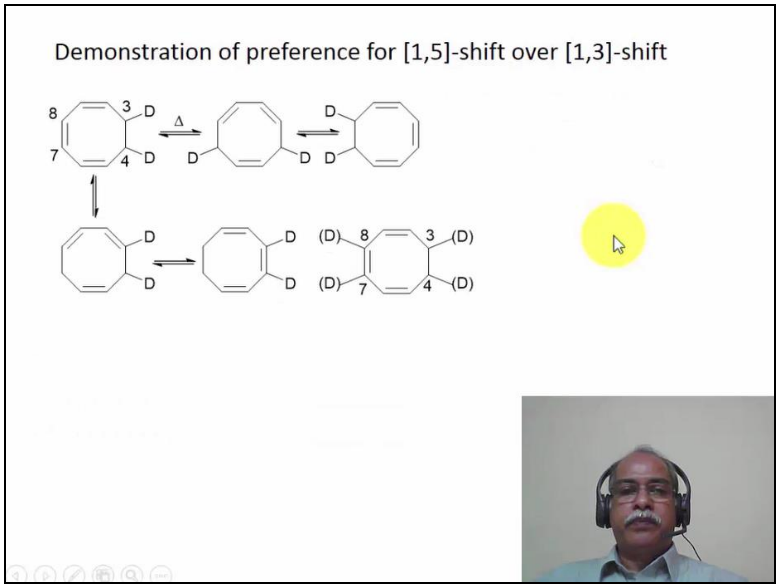

Demonstration of preference for [1,5]-shift over [1,3]-shift

Now, the preference of [1,5]-Shift over [1,3]-Shift is illustrated by this example. Initially, the [3,4]-Dideuterio substituted derivative is taken. And, this particular derivative was made to undergo thermolysis. In doing so, if the reaction were to be a [1,5]-Shift, the Deuterium in the 3 position, will migrate to 7 position. the Deuterium in the 4 position, with migrate to 8 position, which would correspond to [1,5] migration. If you consider this to be 1and 1, then it will be 2,3,4,5, the 7 position will be the 5th Carbon, from the Deuterium, point of attachment.

So, [1,5] migration will result in the 7 position, or 8 position. In fact, the [1,5] migration results in the formation of the 7 and 8 position Deuterium substituted derivative. In other words, during the course of the migration, the Deuterium scrambles only to position 3,4, which is starting point, and 8,7. And, none of the 1, 2, 5, 6 positions are never occupied by the Deuterium. So, the Deuterium scrambling is very specific, which is controlled by a [1,5]-Shift.

If the reaction were to proceed through a [1,3]-Shift, this Deuterium will end up in the 1 position here, and this Deuterium will end up in the 6 position, here. Such rearrangements are not taking place. So, this fact that, the Deuterium label is specifically located only in 3,4,7,8 position, and not in 1,2,5,6 position, clearly explains that this reaction proceeds through a [1,5]-Hydrogen shift, rather than a [1,3]-Hydrogen shift. Deuterium shift, in this particular case.

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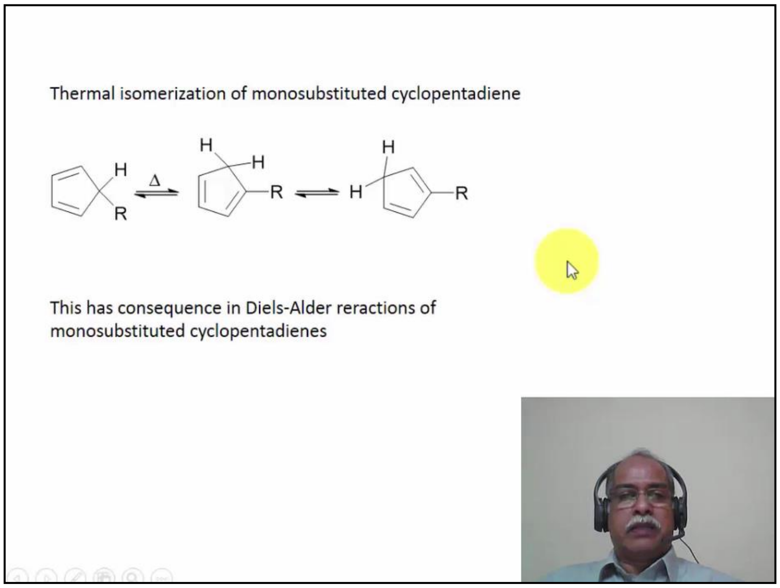
Thermal isomerization of monosubstituted cyclopentadiene

This has consequence in Diels-Alder reractions of monosubstituted cyclopentadienes

The Thermal isomerization of mono substituted Cyclopentene is very common. You can see here the example, that is shown here. This is a mono substituted Cyclopentadiene derivative. This Carbon-Hydrogen bond is undergoing the migration to this position. So, in the process of migration, another isomer of the Cyclopentadiene is produced. And, further migration will produce, another isomer of the Cyclopentadiene. the consequence of this migration is that, you have a mixture of Cyclopentadiene's in the, during the course of the migration, that is produced.

So, if one were to do the Thermal Diels-Alder reaction, with the mono substituted Cyclopentadiene, one has to be very careful, not to make this reaction take place simultaneously, during the course of the Diels-Alder reaction. Because, if this reaction takes place, each one of them will be a Diels-Alder Diene, resulting in an awful mixture of cycloadducts being formed, from each one of this Diene, during the course of the Diels-Alder reaction. So, Diels-Alder reaction with mono substituted Cyclopentadiene, are typically carried out at low temperature. If the reaction does not proceed at low temperature, then catalysis using Lewis acid as a way to go, with respect to carrying out the reaction, at a low temperature.

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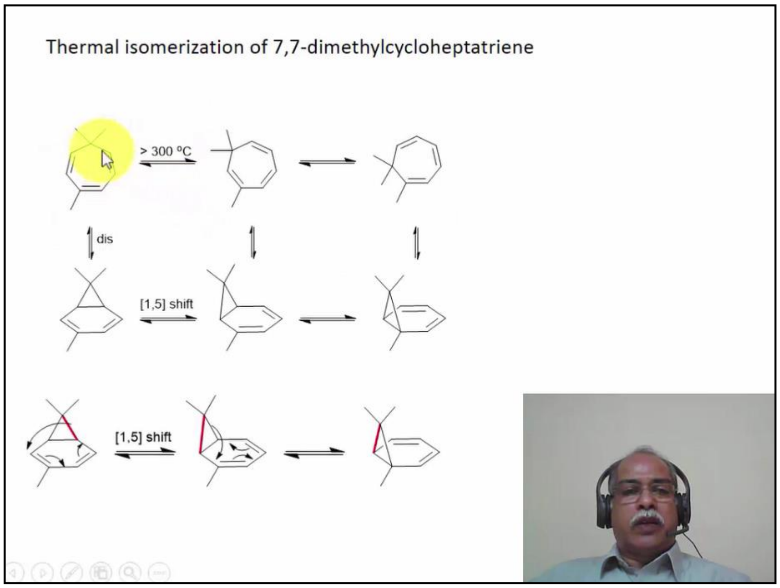


Thermal isomerization of 7,7-dimethylcycloheptatriene

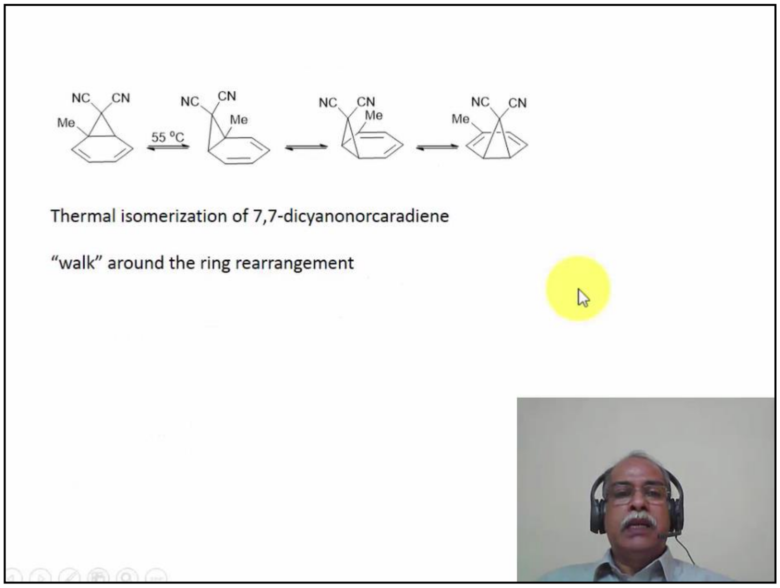
Now, here is a Thermal isomerization of [7,7]-Dimethyl Cycloheptatriene. This is the starting point, where you can see, the Methyl group is at this particular position, and the Gem-Dimethyl group is in this position. When, if the molecule is heated to 300°, the Methyl group seems to be migrating in terms of the relative position, between the Gem-Dimethyl Group Carbon, and the Methyl substituted Carbon, seems to be changing, with respect to each other. Here, it is two Carbons away. Here, it is one Carbon away. This is adjacent Carbon, with respect to the Gem-Dimethyl group, and the methyl substituted Carbon derivative.

How does this reaction take place? Imagine a ring closing reaction, involving this Cycloheptatriene, going to Norcaradiene structure. This is essentially a electrocyclic ring closing reaction, is what is taking place. And, this is an electrocyclic ring closing reaction, in a disrotatory manner, will essentially produce this particular compound. Once this compound is formed, this is a Vinyl Cyclopropyl derivative. This can undergo [1,5]-Carbon shift, for example. This Carbon-Carbon bond can be broken. And, it can be shifted over here, which would correspond to a [1,5]-Shift, going through this Butadiene unit here.

And, such a process for example, this Carbon-Carbon bond, is what is broken here. It migrates to this particular position. So, this will be 1 and 1. 1,2,3,4,5, so attachment at this position. This is essentially [1,2]-Shift, but we call it as a [1,5]-Shift, because of the Sigmatropic notation essentially tells you that, it is a [1,5]-Shift. After the migration of this particular, this Carbon-Carbon bond can be broken, and it can be migrated.

Once the migrated Carbon-Carbon structures are there, they can undergo electrocyclic ring opening reaction, in a reversible manner. To produce, that would explain the formation of this two products from the starting material, which is this particular starting material. Mechanistic elite is illustrated here. the red bond is the one, that is undergoing the breaking. And, that results in the formation of the new red bonds, between this Carbon and this Carbon, which corresponds to [1,5]-Shift, with the concomitant migration of the PI electrons.

Now, the Carbon-Carbon black bond is migrating, that would result in the formation of this particular product, resulting in the ring opening product, to give the isomerized product of [7,7]-Dimethyl Cycloheptatriene, in this case. So, there is a series of walk around the ring rearrangement that is taking place, in this particular [1,5]-Sigmatropic shift, followed by a electrocyclic ring opening reaction, to explain the formation of this products, in this particular case.



Thermal isomerization of 7,7-dicyanonorcaradiene

“walk” around the ring rearrangement

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In the case of [7,7]-Dicyanonorcaradiene, it remains in the Norcaradiene form, and does not remain in the Cycloheptatriene form, for example. So, the Thermal isomerization takes place at a lower temperature, in terms of the isomerization of the walking of the Gem-Dicyanomethyl group, for example. This particular Carbon bearing the Gem-Dicyano groups for example, essentially walks around the ring, in this manner, to give this particular product.

So, the Thermal isomerization reaction is of this type, is what is known as the “walk” around the ring rearrangement. Because, this Carbon is essentially walking over the ring, forming the various intermediates, that are shown in this particular example.

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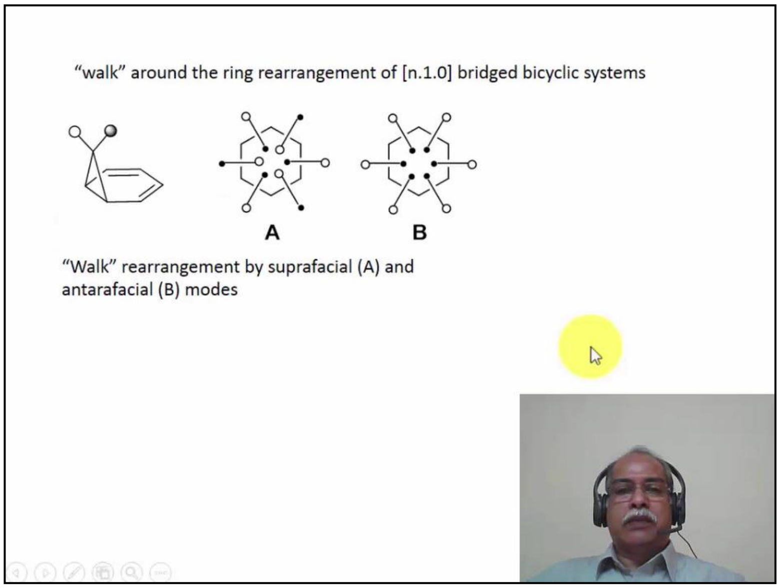

“walk” around the ring rearrangement of [n.1.0] bridged bicyclic systems

“Walk” rearrangement by suprafacial (A) and antarafacial (B) modes

The walkaround the rearrangement process, can be cartoonically represented, by this particular picture. Imagine that, there is a shaded substituent, which is this particular substituent. And, unshaded substituent, which is this particular substituent. With respect to the Butadiene unit, this shaded substituent is Endo, and the unshaded substituent is Exo, with respect to the PI framework, here. What is happening in the case of A, during the course of the walkaround rearrangement, if you look at the molecule from the top position, in other words, from the top of this Planar-5 framework, you would see this Carbon, which is must in this particular position.

And, the shaded and the unshaded Carbon, which is the shaded Carbon inside, let us say for example, this would be the Carbon. The unshaded Carbon outside, which is this particular Carbon. So, essentially, a view perpendicular from above the Cyclohexadiene ring, will show the molecule in this particular position. In the case of the Suprafacial migration, the inside and the outside group will be alternating, with respect to each other, during the course of the migration. For example, a [1,5]-Sigmatropic migration to bring this Carbon over here, would end up taking this shaded portion outside, and the unshaded substituent inside, if it were to be a Suprafacial migration.

If it is an Antarafacial migration, what remains inside, will always remain inside. What remains outside Exo, will always remain Exo, with respect to the PI framework. So, here is a situation, the structure A would correspond to a Suprafacial migration, where the shaded and the unshaded substituents, alternate the Exo and the Endo position, during the alternate migration. Whereas, if it is an Antarafacial type of a migration, the Exo substituent remains Exo, throughout the migration. And, the Endo substituent remains as Endo, throughout the migration.

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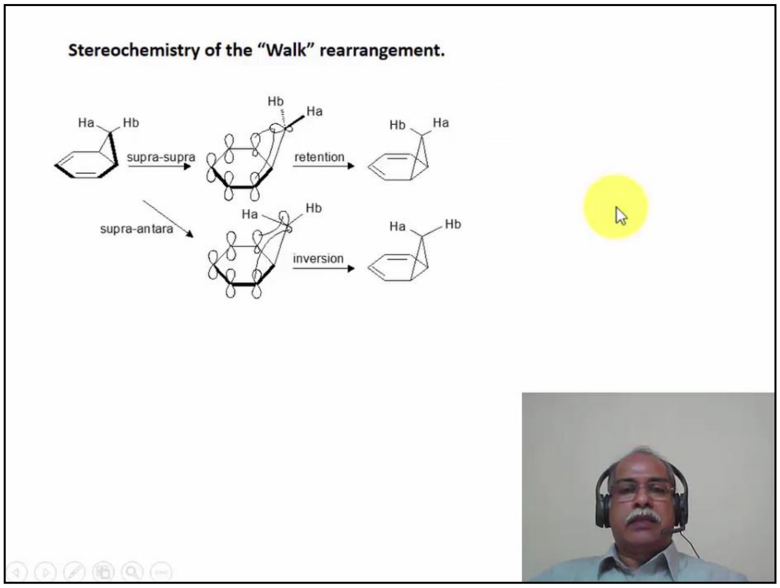

Stereochemistry of the “Walk” rearrangement.

Why does this take place, like this. This is explained, using the simple mechanistic scheme here. Consider a Suprafacial-Suprafacial migration, of this particular Carbon. Hydrogen-A is Endo Hydrogen-B is Exo, with respect to the PI framework, in this case. If there is a Suprafacial migration, that is taking place. That means, this bond, has to break. This Carbon-Carbon bond, has to break. And, once the bond is broken, this is a lobe, that is going to interact with both the Carbons, in a simultaneous manner. Because, it is a concerted process.

So, in doing so, it will bring the HB inside, and HA outside, resulting in the formation of HB to be, now the Endo substituent, and HA to be the Exo substituent. So, what was originally Endo, has become now Exo. What was originally Exo, has become Endo, as a result of a Suprafacial-Suprafacial, with a retention of stereochemistry, resulting here. If it were to be an Antarafacial migration, then the bond is broken here. And, the back-side lobe, is now going to attach itself to this particular position. So, as a result of that, inversion takes place. But then, the Endo substituent remains as Endo, the Exo substituent remains as Exo.

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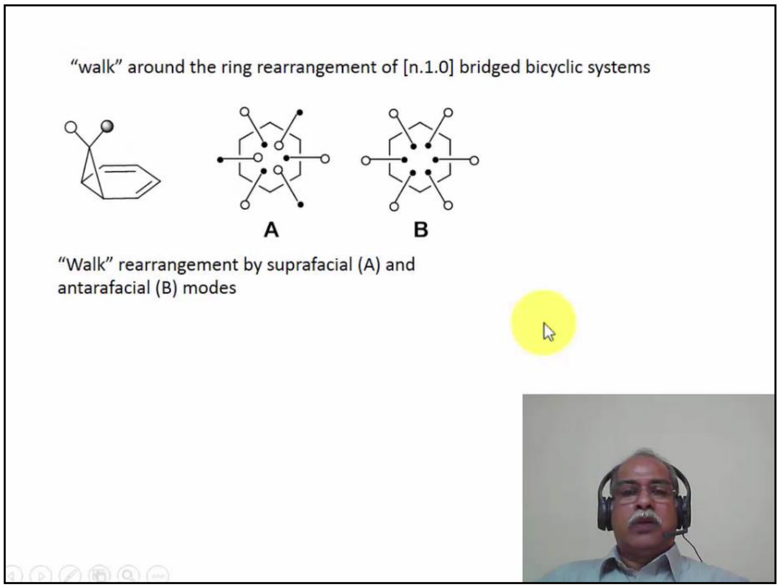

"walk" around the ring rearrangement of [n.1.0] bridged bicyclic systems

"Walk" rearrangement by suprafacial (A) and antarafacial (B) modes

So, in a walkaround rearrangement, if it is happening in a Suprafacial manner, the Exo-Endo substituent will alternate, during the course of the rearrangement, between the Exo and the Endo position. If it is an Antarafacial migration of the rearrangement, then what was remaining as Exo substituent, will remain Exo, throughout the migration. What was originally an Endo substituent, will remain as an Endo substituent, throughout the migration, which is explained by this mechanism of retention and inversion of stereochemistry.

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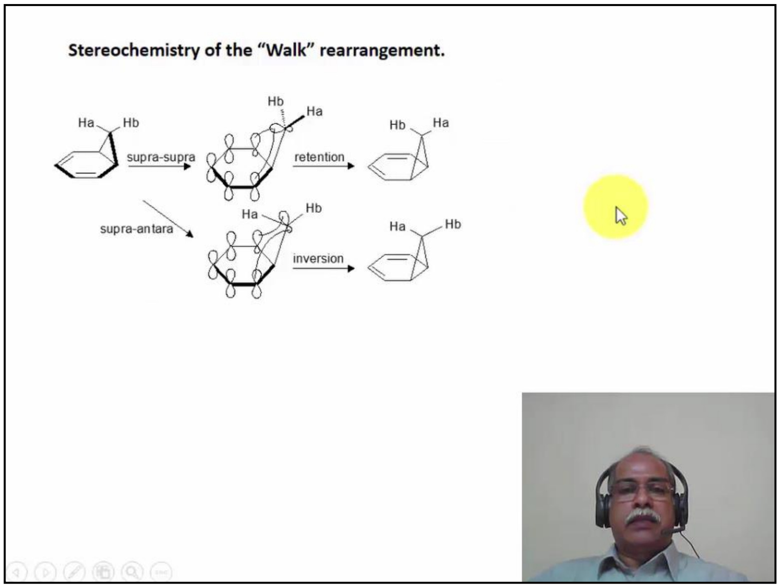

Stereochemistry of the "Walk" rearrangement.

In one case, the Suprafacial migration is taking place, the other ways, Antarafacial migration is taking place, with respect to the Sigma bond, that is being broken, in the course of a rearrangement.

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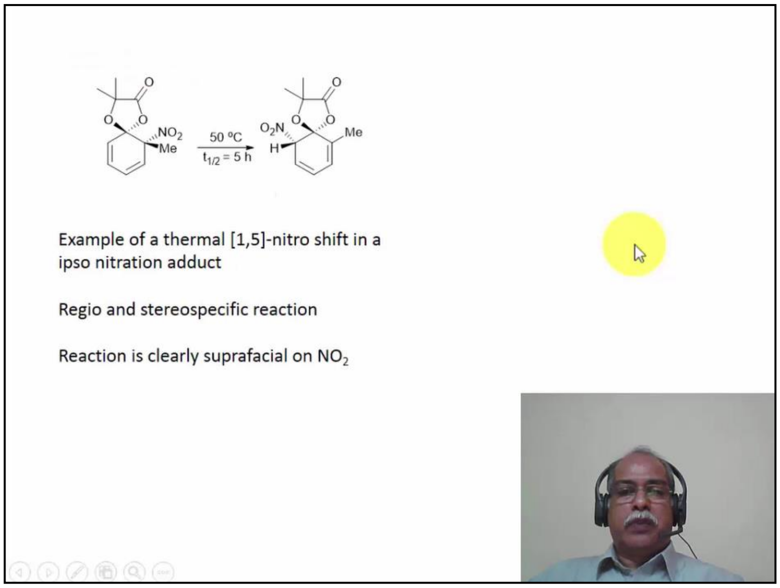

Example of a thermal [1,5]-nitro shift in a ipso nitration adduct

Regio and stereospecific reaction

Reaction is clearly suprafacial on NO_2

Here is a rare example of a migration of a Nitro group in a [1,5]-Shift. This is an Ipso nitration product. The Ipso nitration product has the Nitro group, attached to this particular Carbon. Remember, the stereochemistry of the Nitro is actually the, inside is the Nitro, and what is projecting in front of us, is the Methyl group. And, in during the course of the rearrangement, the Nitro remains Suprafacial migration, with respect to the PI framework.

So, it remains interior. And, the Hydrogen, which was originally here, now is pointing towards us, for example. So, this is a Regio specific, as well as the Stereo specific reaction. It is the Regio specific, because it is the [1,5] Nitro shift. It is a Suprafacial migration, and that is why the stereospecificity also gets into picture. The reaction is clearly Suprafacial, with respect to the NO2 migration, is what is illustrated in the example.

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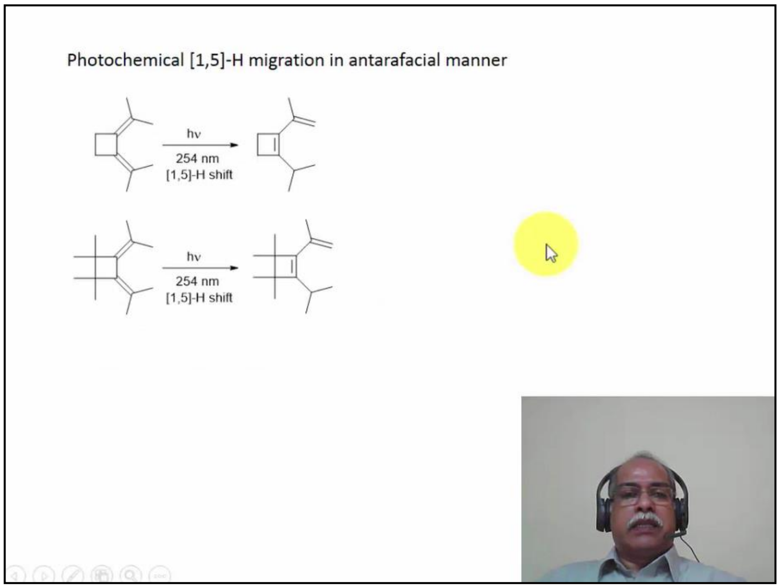

Photochemical [1,5]-H migration in antarafacial manner

Now, let us consider the Photochemical [1,5]-Hydrogen migration, in an Antarafacial manner. In these reactions, the 2PI systems are not planar, with respect to each other. Because of the steric hindrance between this two Methyl group, this PI will be pointing up, or this PI will be pointing down, or vice versa, as the case may be. That brings, the Hydrogen to be in a favorable position, for the Antarafacial shift.

Remember, it is a Photochemical reaction. [1,5] migration should be Antarafacial. So, the migration of this particular Hydrogen over here, results in the formation of this particular compound. And, the steric effect essentially, which leads to the non-planarity of the PI bond, is what is responsible for the fissile Antarafacial migration, in both cases.

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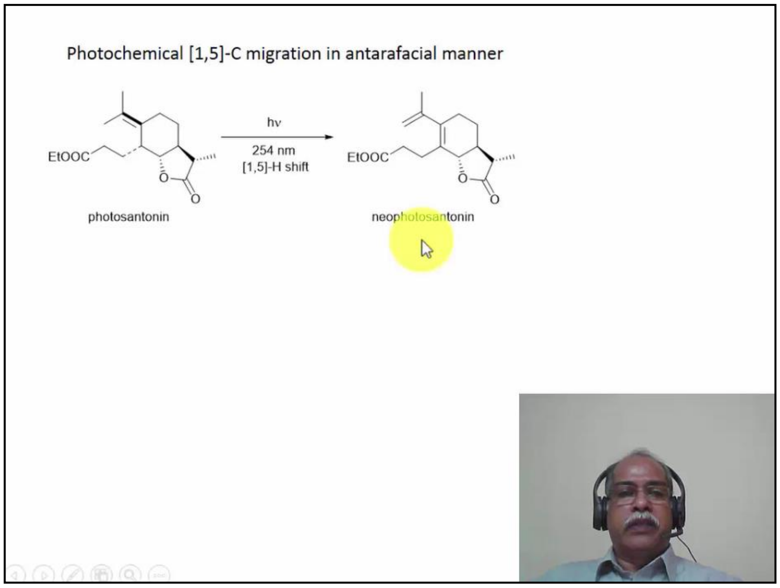

Photochemical [1,5]-C migration in antarafacial manner

These are two examples of Antarafacial Hydrogen migration. One can also have a Antarafacial Hydrogen migration. There is a double bond missing here, i am sorry. There should be a double bond here. The Hydrogen is migrating to this particular position, in an Antarafacial manner, resulting in the formation of this particular product, which is the migrated product. This isomerization of Photosantonin into Neophotosantonin, by a [1,5]-Hydrogen shift. Please, put a double bond over here, which is missing in this particular structure.

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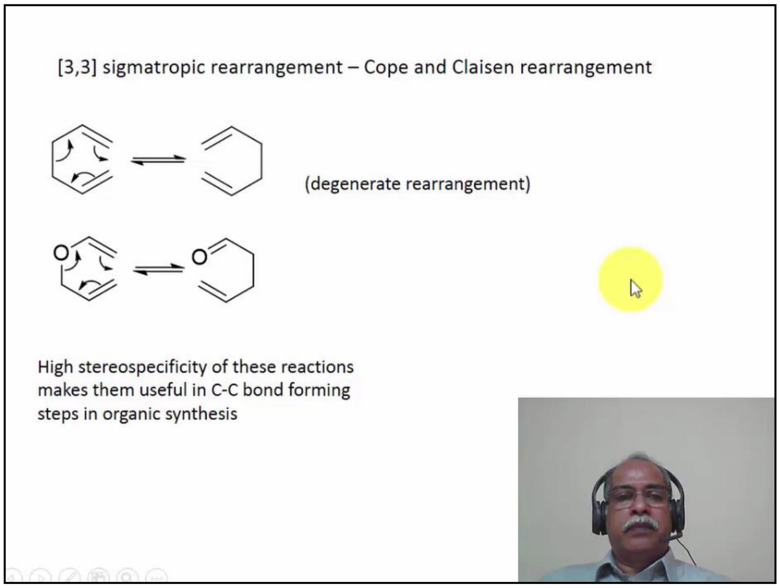

[3,3] sigmatropic rearrangement – Cope and Claisen rearrangement

(degenerate rearrangement)

High stereospecificity of these reactions makes them useful in C-C bond forming steps in organic synthesis

Now, let us move on to a very interesting [3,3]-Sigmatropic rearrangement, which is known as the Cope rearrangement, or Claisen rearrangement, as the case may be. This is a, rearrangement of [1,5]-Hexadiene into a [1,5]-Hexadiene. So, this is a degenerate rearrangement. Both the starting material and the product are essentially same. In the case of the Oxygen substituted Allyl-Vinyl Ether, resulting in the formation of an unsaturated Carbonyl bond.

This is not a degenerate rearrangement. This is also, not a reversible reaction. This is always proceeds in the forward direction only, and not in the reverse direction. These are examples of [3,3]-Sigmatropic rearrangement. If, this is a Carbon-Carbon bond, that is breaking here. Or, this is the Carbon-Oxygen bond, that is breaking here. With respect to the bond, that is being broken, this is 1,2,3,1,2,3. Similarly, this is 1,2,3,1,2,3, so, this is [3,3]-Sigmatropic rearrangement, of the degenerate type.

This is [3,3]-Sigmatropic rearrangement, of non-degenerate type. Please, remove this arrow, in the reverse direction. It proceeds, only in the forward direction. The importance of this reactions are, that they are highly stereospecific in nature. So, they are extremely useful, in Carbon-Carbon bond forming reaction steps, in organic synthesis. That is the beauty of this reactions, in organic synthesis.

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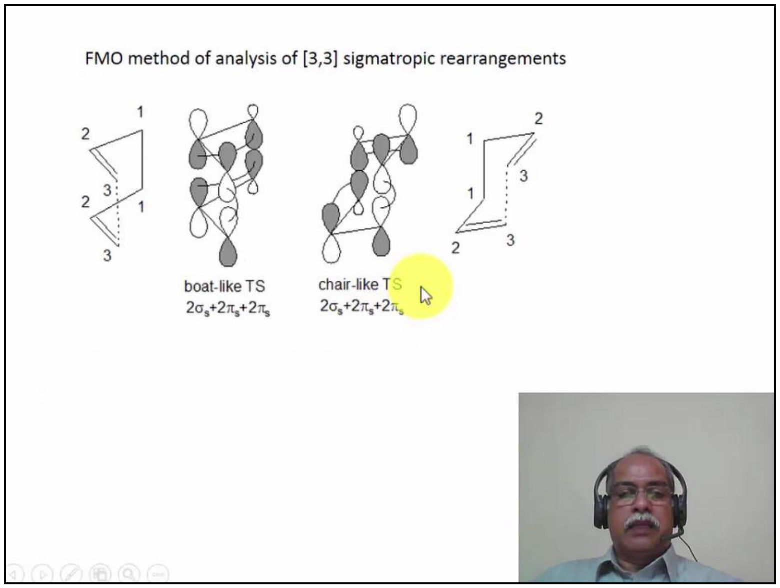

FMO method of analysis of [3,3] sigmatropic rearrangements

boat-like TS

$2\sigma_s+2\pi_s+2\pi_s$

chair-like TS

$2\sigma_s+2\pi_s+2\pi_s$

Now, the Frontier Molecular method of Analysis of [3,3]-Sigmatropic rearrangement, is shown here. Because, these reactions involve a 6-Membered cyclic transition state. One can model the 6-Membered cyclic transition state, as a boat type of a transition state, or a chair type of a transition state. The chair type of a transition state, is energetically about 2 to 3 kilocalories more favored, compared to the boat type of a transition state.

So, the reaction is often explained by the formation of the chair type of a transition state, resulting in the formation of a particular product, which can be explained, only from the chair like transition state, and not from the boat like transition state. In, both the transition state, of course, it is a Suprafacial migration, with respect to all the component. This is an original Sigma bond.

And, you can see here, this is the Allyl, this is the PI system, this is another PI system. With respect to the Sigma, it is Suprafacial. With respect to this PI system, it is Suprafacial. With respect to this PI system also, it is Suprafacial. So, it is the 2Sigma-Suprafacial, 2PI Antarafacial, and 2PI Antarafacial, kind of a migration, is what is taking place. In other words, it is Suprafacial in all the components, that are involved, during the course of the migration.

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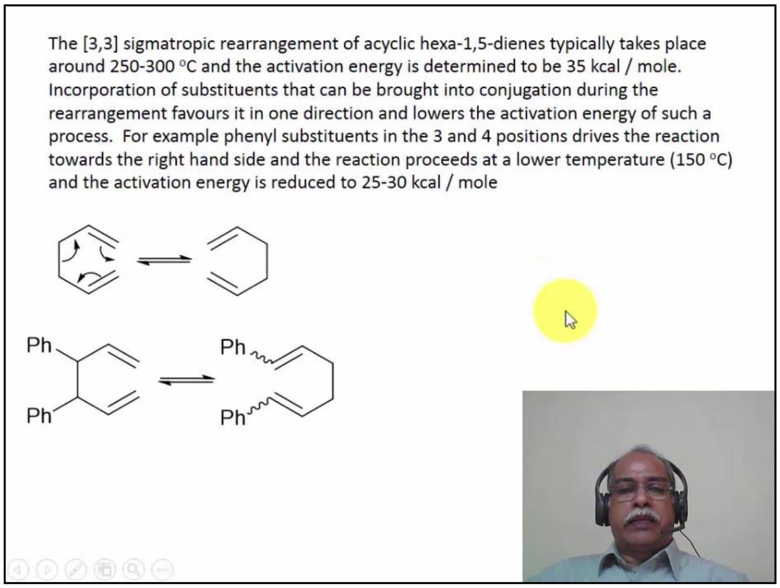

The [3,3] sigmatropic rearrangement of acyclic hexa-1,5-dienes typically takes place around 250-300 ^{o}C and the activation energy is determined to be 35 kcal / mole. Incorporation of substituents that can be brought into conjugation during the rearrangement favours it in one direction and lowers the activation energy of such a process. For example phenyl substituents in the 3 and 4 positions drives the reaction towards the right hand side and the reaction proceeds at a lower temperature (150 ^{o}C) and the activation energy is reduced to 25-30 kcal / mole

Now, the [3,3]-Sigmatropic shift of Acyclic [1,5]-Hexadiene, typically takes place around 250 to 300. This is a thermolysis, which is to be carried out. The activation barrier is estimated to be about 35 kilocalories per mole. The incorporation of substituent, that will bring the Olefins in conjugation, would favor this reaction. For example, if we consider this reaction, and this reaction, in this reaction, the reaction will proceed from left to right, very nicely.

And, the reverse reaction is probably not going to take place, under this condition, for the simple reason, that the Phenyl groups are not conjugated, in the starting material. But, in the product, the Phenyl groups are conjugated with the Olefin. So, the extra delocalization energy, that one need to enjoy in this particular structure, will promote this reaction from the left-hand side, to the right-hand side. So, when, such a facility exists, the activation energy comes down to about, 20 to 30 kilocalories per mole. And, the temperature of the reaction is also lowered, to about 150.

So, this particular unsubstituted Hexatriene, undergoes rearrangement around 300° or so. Whereas, the substituted Diphenyl derivative, undergoes rearrangement, at a much lower temperature of 150°. Of course, one cannot figure out, whether this reaction is taking place or not, without proper Deuterium substituent of something in the position, to indicate the rearrangement has taken place. Otherwise, this is a degenerate, non-distinguishable. Starting material is same as the product kind of a rearrangement, is what is depicted in this equation.

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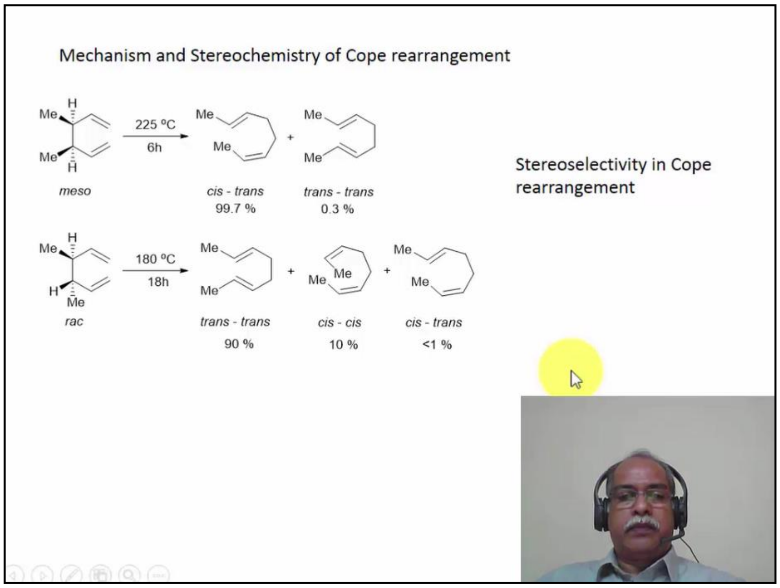

Mechanism and Stereochemistry of Cope rearrangement

Stereoselectivity in Cope rearrangement

Now, the mechanism and the stereochemistry of Cope rearrangement, is illustrated in this two example. The Dimethyl substituted Hexa-[1,5]-Diene can exist in two forms. Stereochemistry wise, this is the Meso form, or this is the Erythro form. You can say, either it is a Meso form, or Erythro form, does not matter. It implies the same thing. This is a racemic mixture, or plus or minus isomer, or the Threo form of the particular compound, that we are dealing with.

You can see here, the two Methyls, and the two Hydrogens, and the two Vinyl groups, are all Cis with respect to each other. Whereas here, it is not so. So, this is a Racemic-Threo form, whereas, this is a Meso-Erythro form. What is important here is, the stereoselectivity in the Cope rearrangement. If you look at the Meso form, which undergoes rearrangement at 225°, it exclusively, almost exclusively gives the Cis-Trans isomer of the product, that is being formed. In other words, the double bonds that are formed here, are in a very stereospecific manner.

This is a Trans double bond, and this is a Cis double bond. The Trans-Trans isomer is formed in a very, very small amount of 0.3% or so. Whereas, when the racemic or the Threo form is heated to 180°, the reaction is faster, first of all, takes place at a lower temperature. It produces almost exclusively, the Trans-Trans isomer. The Cis-Cis isomer, and the Cis-Trans isomer, are formed only in very small amount, in this particular instance. How do we explain, the formation of stereoselectivity of the product, that is being formed?

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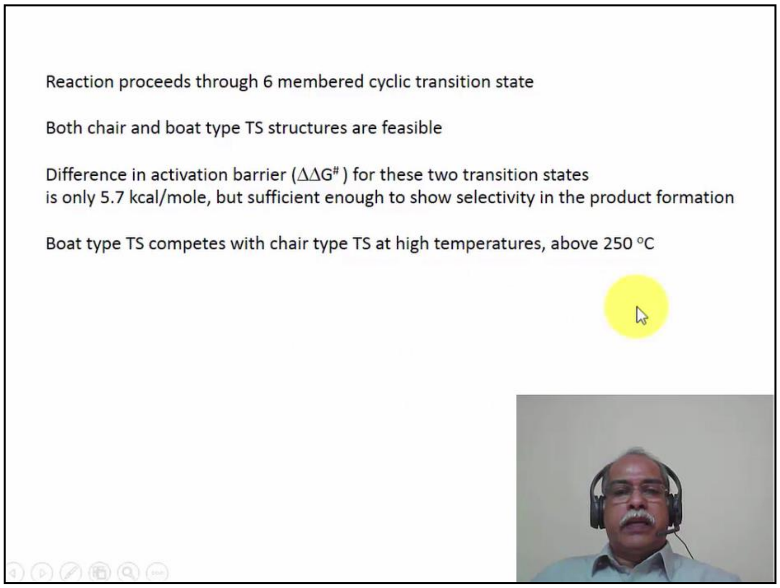

Reaction proceeds through 6 membered cyclic transition state

Both chair and boat type TS structures are feasible

Difference in activation barrier ($\Delta\Delta G^{\#}$) for these two transition states is only 5.7 kcal/mole, but sufficient enough to show selectivity in the product formation

Boat type TS competes with chair type TS at high temperatures, above 250 °C

This is by invoking, the chair type of a transition state, in all these cases. The reaction proceeds through a 6-Membered cyclic transition state. Both, chair and boat type of transition states are possible. The difference in the activation barrier, between the two-transition state, is about 5.7 kilocalories per mole. This is sufficient enough, to show a selectivity in the product formation.

The boat type of transition state, competes with the chair type of transition state, when the reaction is carried out, much about 250°. In other words, the stereoselectivity will be lost, if the temperature is very high, compared to the temperature at which, the reaction actually take place namely 200 and 180° respectively, for the Erythro and Threo isomers.

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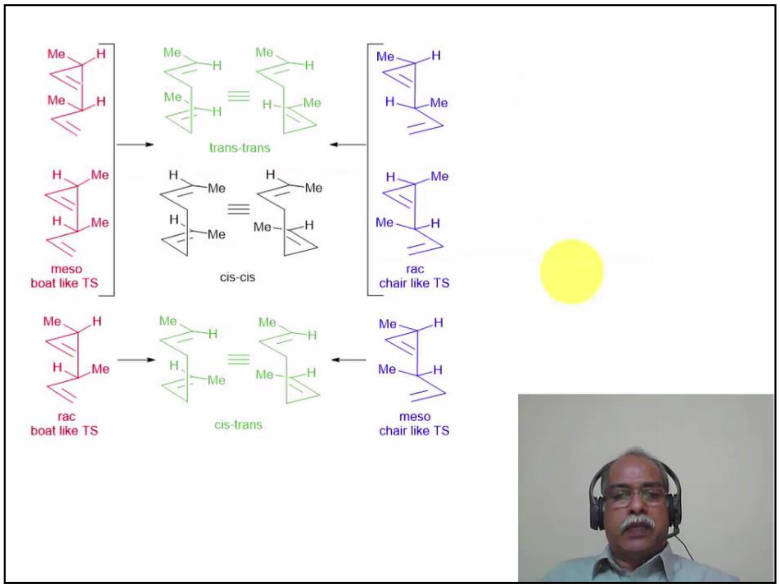

Now, the Trans-Trans isomer, or the Cis-Trans isomer formation, during the course of the rearrangement, is explained. The blue structures, are essentially chair type of structures, for the Racemic isomer, and the Meso isomer. And, the red type of transition state, the structures that are shown are, the boat type of the transition structure. This is for the Racemic isomer. And, this is for the Meso isomer.

You can tell for example, the formation of a Carbon-Carbon bond here, would result in the formation of a Carbon-Carbon double bond here, and a Carbon-Carbon double bond here. When a Carbon-Carbon double bond is formed here, this will essentially give the E isomer. Similarly, when a Carbon-Carbon bond is formed, between here and here, that will again form the E isomer, for example, the Trans-Trans isomer, is what is going to be formed. The Cis-Cis isomer can also be formed, from this.

But, that is going to be a minor process, from the Racemic isomer, of this particular compound. Whereas, from the Meso isomer, when the reaction takes place, it is a Cis-Trans isomer, that is going to be formed. This is the newly formed, Carbon-Carbon bond, that is taking place. And, the newly formed double bond, is here. And, the newly formed double bond, is here. With respect to this Methyl, it will be a Cis double bond. With respect to this Methyl, it will be a Trans double bond.

So, the Cis-Trans isomer is going to be the predominant product, for example, formed from a Meso like transition state. Whereas, the observation is that, the Meso isomer gives the Cis-Trans isomer, whereas the Racemic isomer gives the Trans-Trans isomer, which is explained on the basis of the reaction, proceeding from the chair type of a transition state. If it were proceeded by the boat type of transition state, it would have given the opposite stereochemistry, for the two Diastereo isomers, that are reacting, for example.

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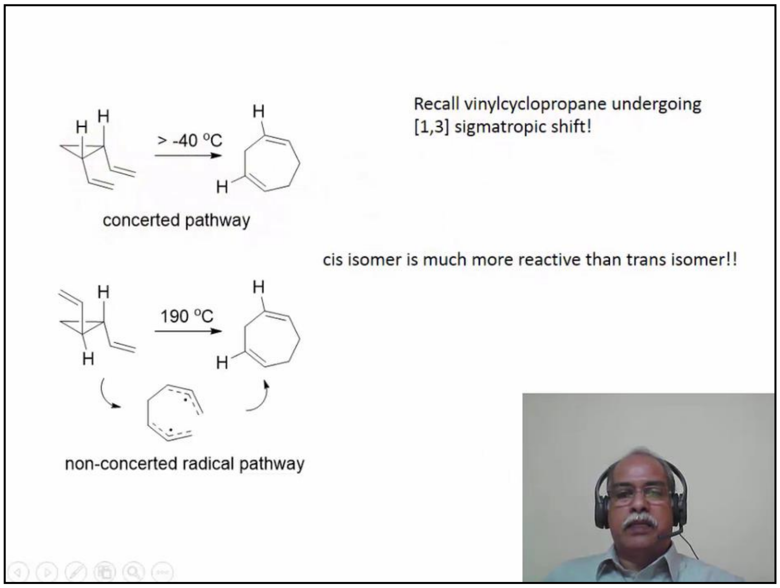

Recall vinylcyclopropane undergoing [1,3] sigmatropic shift!

cis isomer is much more reactive than trans isomer!!

Now, this is a very interesting example of a [3,3]-Sigmatropic rearrangement. This is Cis-Divinylcyclopropane. There has been a lot of attempt, to prepare the Cis-Divinylcyclopropane, but it is highly unstable, even at -740° or so. It undergoes a concerted [3,3]-Sigmatropic rearrangement, because of the close proximity of the two double bonds, as well as the release of the ring strain of the 3-Membered ring, resulting in the formation of Hexa-[1,4]-Diene kind of a system, that is being formed in the product stage.

The Cis isomer, is much more reactive, than the Trans isomer. Because, in the Trans isomer, the two Vinyl groups are further separated from each other, because of the Trans stereochemistry. So, the overlap of this Carbon, with this Carbon, is unlikely to take place in a concerted manner. So, the reaction does not proceed at -40, in the case of Trans isomer. It proceeds, at a much higher temperature of 190° or so, for example. And, this is a non-concerted pathway, is what is proposed.

It produces a diradical intermediate, by the breaking of the Carbon-Carbon bond of the Cyclopropane ring, to give Diallyl radical derivative. The Diallyl radical derivative, undergoes a ring closure reaction, to give the Cycloheptadiene as the final product. Although, the final product is same, look at the temperature, this is essentially unstable at room temperature. Whereas, this is very stable at room temperature, and reacts only around 190° or so, in this particular instance.

So, the reactivity difference between, the Cis-Divinylcyclopropane and the Trans-Divinylcyclopropane, can be explained on the basis of the close proximity of the two Vinyl groups, and the further away of the two Vinyl groups in the Trans isomer, during the course of the reaction. This will easily form a cyclic transition state, whereas, this cannot form a cyclic transition state. So, this is a concerted pathway, whereas, this is a non-concerted radical path way, is what is invoked in this particular case.

Now, you can recall the Vinyl Cyclopropane, undergoing a [1,3]-Sigmatropic rearrangement. Such a facility is not competing, in this particular process. Vinyl Cyclopropane. This impact can proceed through a [1,3]-Sigmatropic rearrangement. It does not take place. Because, the [3,3]-Sigmatropic rearrangement has a much more facile and lower energy path way, compared to the [1,3]-Sigmatropic rearrangement.

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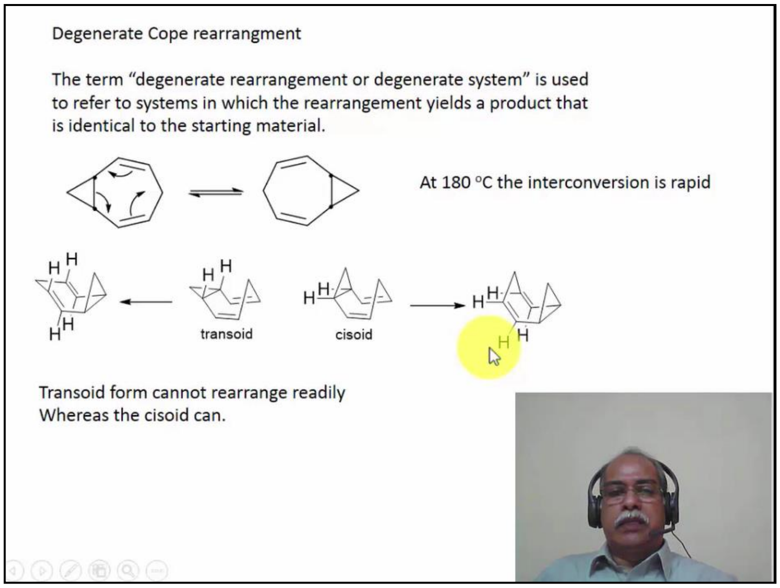

Degenerate Cope rearrangment

The term “degenerate rearrangement or degenerate system” is used to refer to systems in which the rearrangement yields a product that is identical to the starting material.

At 180 °C the interconversion is rapid

Transoid form cannot rearrange readily
Whereas the cisoid can.

We have seen the degenerate rearrangement, in many cases. The term, degenerate rearrangement, or the degenerate system, is essentially, when the starting material is same as the product. So, if you look at this particular system, this is Divinylcyclopropane derivative, except the end of the Vinyl group, are tied to a Carbon, in this particular case. So, this undergoes the [3,3]-Sigmatropic rearrangement again, to give the same starting material.

The two Carbons here, are with the thick dot is given here, indicating the stereochemistry to be Cis, with respect to the two Hydrogen. Here again, the stereochemistry is Cis, with respect to the two Hydrogen. Now, in this type of a situation, this molecule can exist either in the Transoid form, or the Cisoid form. In other words, the Cyclopropyl ring, and the two Vinyl groups, are essentially in the Transoid geometry, here.

Whereas, the Cyclopropyl group, and the two Vinyl groups, are Cisoid geometry, here. The Transoid geometry of course, cannot undergo the [3,3]-Sigmatropic rearrangement, whereas the

Cisoid can undergo the [3,3]-Sigmatropic rearrangement. So, in order to avoid this confusion, if there is an additional bridging between this Carbon and this Carbon, that would put everything in the Cisoid confirmation.

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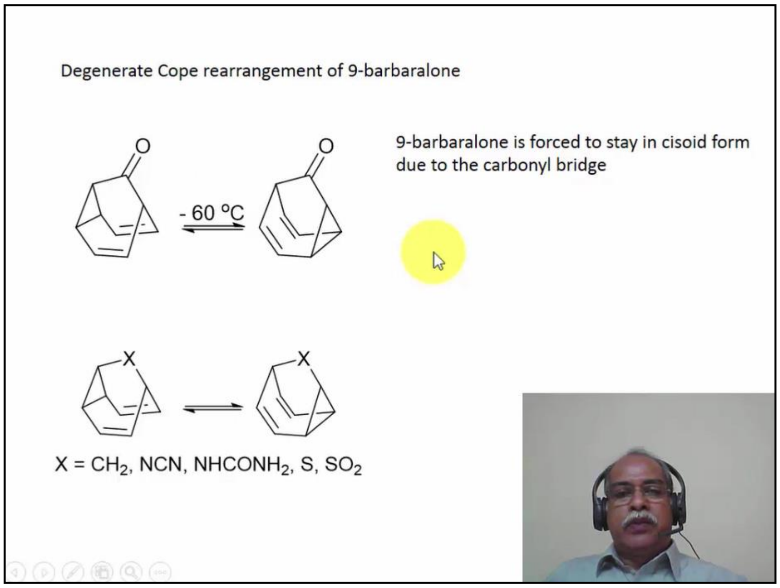

Degenerate Cope rearrangement of 9-barbaralone

9-barbaralone is forced to stay in cisoid form due to the carbonyl bridge

X = CH_2, NCN, $NHCONH_2$, S, SO_2

So, such a facility exist, in the case of 9-Barbaralone, which is this molecule, here. You can see here, this is a Cyclopropyl-Divinyl derivative. Except, the third Carbon of the Cyclopropyl is also bridged, via a Carbonyl functional group, to tie up this Carbon, and this Carbon. In other words, these two Carbon namely, this particular Carbon here, and this Carbon here, are tied together, using a Carbonyl functional group. 9-Barbaralone, undergoes the degenerate rearrangement, quite readily.

Even at -60°, this molecule undergoes a very rapid [3,3]-Sigmatropic rearrangement, which is a degenerate rearrangement. It is not specific, only to the 9-Barbaralone, there are several Heteroatoms substituted derivatives, as well as Carbon substituted derivatives, do undergo the degenerate rearrangement, quite readily, where you have the N-Cyano, or the Carbamate kind of a derivatives, here. The Sulfur X is Sulfur or Sulfur dioxide. They all undergo the [3,3]-Sigmatropic rearrangement, quite readily in the system.

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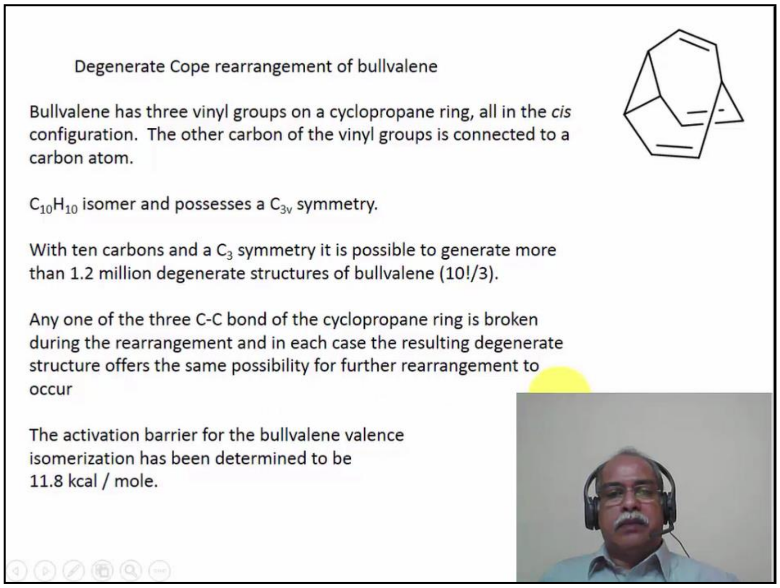

Degenerate Cope rearrangement of bullvalene

Bullvalene has three vinyl groups on a cyclopropane ring, all in the *cis* configuration. The other carbon of the vinyl groups is connected to a carbon atom.

$C_{10}H_{10}$ isomer and possesses a C_{3v} symmetry.

With ten carbons and a C_3 symmetry it is possible to generate more than 1.2 million degenerate structures of bullvalene (10!/3).

Any one of the three C-C bond of the cyclopropane ring is broken during the rearrangement and in each case the resulting degenerate structure offers the same possibility for further rearrangement to occur

The activation barrier for the bullvalene valence isomerization has been determined to be 11.8 kcal / mole.

Let us come to an interesting example of a Degenerate rearrangement of Bullvalene. This molecule is called Bullvalene. This is a most fascinating molecule, or the most fluxional molecule, in organic chemistry. So much so that, it can generate about 1.2 million degenerate structures, by means of a [3,3]-Sigmatropic rearrangement. Let us see, what is the speciality of this molecule. Bullvalene has three Vinyl groups. And, the three Vinyl groups are attached to a common Carbon, which is this particular Carbon.

And, the three Vinyl groups are also attached in a Cis fashion, to the Cyclopropyl derivative. In other words, this is a Cyclopropane, which is connected to three Vinyl groups, from all the three Carbon, in a Cis manner. The double bond geometry is Cis, and the stereochemistry of the connectivity to the Cyclopropane is also Cis, with respect to each other. In other words, this is a $C_{10}H_{10}$ Isomer. And, it possesses a C_{3v} axis of symmetry.

If you take the center of the Cyclopropane, and pass it through this particular Carbon, that axis would correspond to a C_3 axis of rotation, for this molecule. With ten Carbons, and the C_3 axis of rotation, it is possible to generate, (10! /3) number of degenerate structure, which corresponds to close to 1.2 million degenerate structure, in the case of rearrangement of the [3,3]-Sigmatropic rearrangement. All you have to do is, take anyone of the Carbon-Carbon bond of the Cyclopropane ring, break it, and connect it via the two Vinyl groups, to the opposite side.

So, if i break this particular bond, i can connect between these two bonds, which would correspond to a [3,3]-Sigmatropic rearrangement. That would be, again Bullvalene only, in terms of the geometry, that is being generated. The molecule has been studied very nicely, using NMR

Spectroscopy. And the NMR Spectroscopy, based on the NMR Spectroscopy studies, activation barrier of Bullvalene is shown to be about 11.8 kilocalories per mole.

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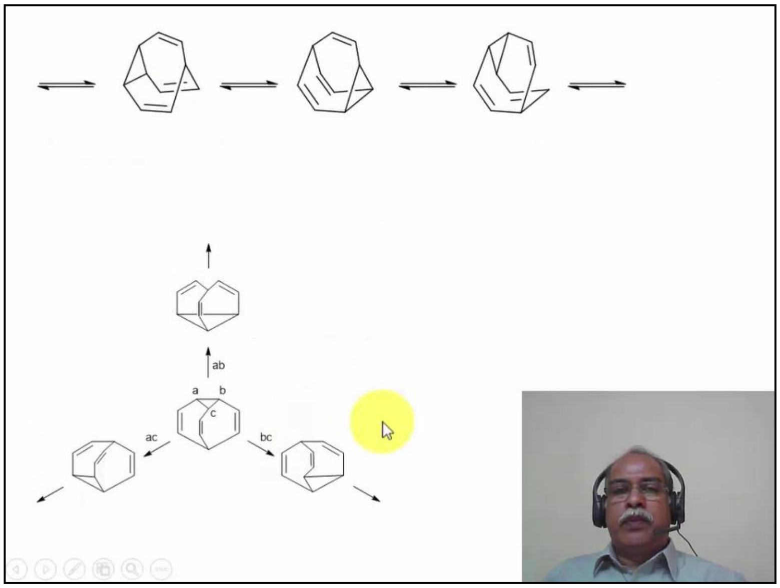

This is how, the molecule undergoes the [3,3]-Sigmatropic rearrangement. You can either break AB, BC, or AC. If you break AB, and connect it over here, then it forms another Bullvalene. If you break BC, and connect it over here, for example, it again forms Bullvalene. If you break AC, and connect it over the other two Vinyl terminal groups here, that forms again Bullvalene. So, everyone of the rearrangement produces a Bullvalene. So, it is a highly degenerate, or the most fluxional molecule, that has been known in organic chemistry. This is another way of representing, the Bullvalene rearrangement, through a [3,3]-Sigmatropic rearrangement.

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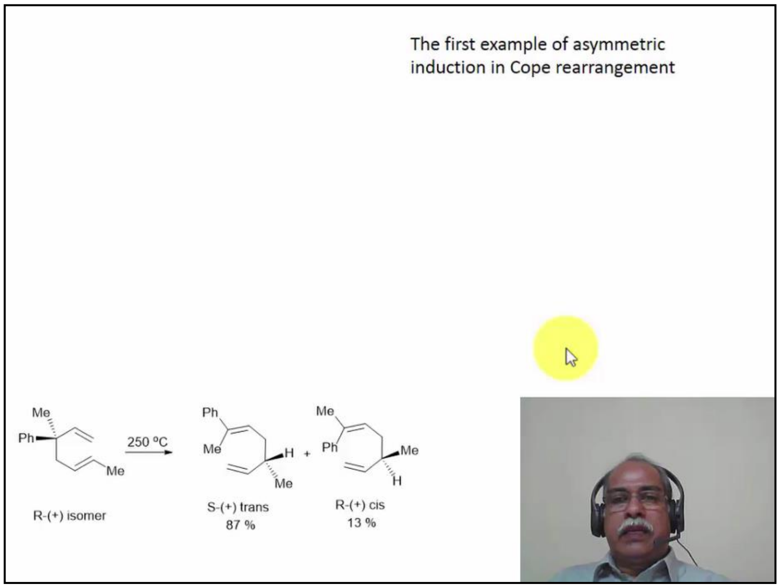

The first example of asymmetric induction in Cope rearrangement

Now, the first example of the Asymmetric induction in Cope rearrangement, is shown in this particular case. Now, before we go there, let me just illustrate the point, that the [3,3]-Sigmatropic rearrangement of Bullvalene, essentially studied by NMR Spectroscopy.

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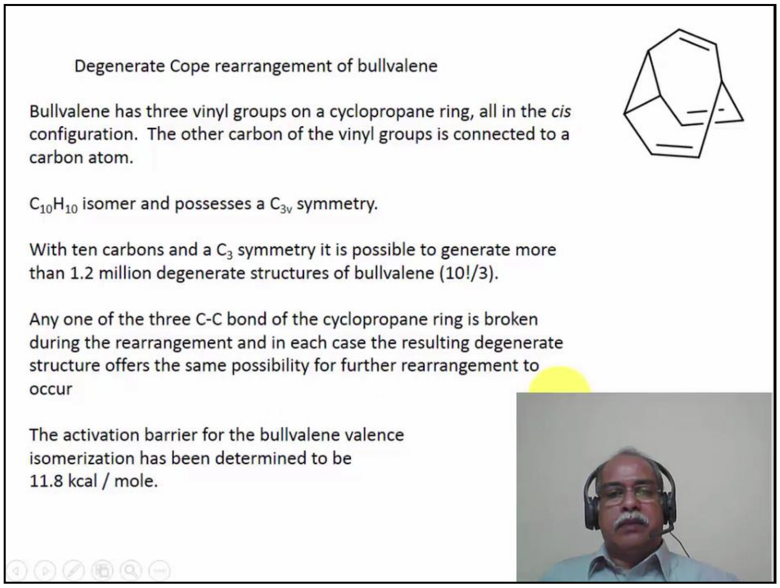

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With ten carbons and a C_3 symmetry it is possible to generate more than 1.2 million degenerate structures of bullvalene (10!/3).

Any one of the three C-C bond of the cyclopropane ring is broken during the rearrangement and in each case the resulting degenerate structure offers the same possibility for further rearrangement to occur

The activation barrier for the bullvalene valence isomerization has been determined to be 11.8 kcal / mole.

If you look at this particular structure, and look at the number of different types of Hydrogen, there are three Cyclopropyl Hydrogens, attached as a Cyclopropane ring. That is one set of Hydrogens. Then, there are three Vinyl Group Hydrogens, which are in this particular Carbon. Three Vinyl Group Hydrogens, which are in the other particular Carbon, that is shown here. Finally, there is one Hydrogen, in this. At least, there are four different types of Hydrogen in

Bullvalene, one corresponding to the Cyclopropyl Hydrogen, two types of Vinyl Hydrogen, and one type of the Methane Hydrogen.

When the reaction takes, when the molecule is studied at very low temperature, when the [3,3]-Sigmatropic rearrangement is extremely slow, one can see, all the three types, or four types of Hydrogens in the molecule, in separate chemical shift value, in the NMR Spectroscopy. But, when the reaction is very rapid, taking place around 120° are so, because the structure generates other Bullvalene.

And, when the Cyclopropyl Hydrogens, and the Vinyl Hydrogen, and the Methane Hydrogen becoming distinguishable, all the four types of Hydrogen collapsed to a singlet, for example. And, that is an illustration of study of the [3,3]-Sigmatropic Degenerate rearrangement, using proton NMR Spectroscopy, of this particular molecule.

Similarly, if one studies the Carbon-13 NMR Spectroscopy of this molecule, at various temperature, at very low temperature, one would see, 1 Carbon for the 3 Cyclopropyl Hydrogens, 1 Carbon signal for this Vinyl Hydrogens, 1 Carbon signal for other Vinyl Carbon. Finally, 1 Carbon signal for the Methane Carbon.

When the NMR study is taking place at 220°, when the rapid rearrangement takes place, all the 10 Carbon become indistinguishable, as a result of a singlet is observed, in the case of the rearrangement of the Bullvalene, studied by Carbon-13 spectroscopy. This activation barrier has been calculated, based on the Proton NMR, variable temperature Proton NMR studies, to be about 11.8 kilocalories per mole.

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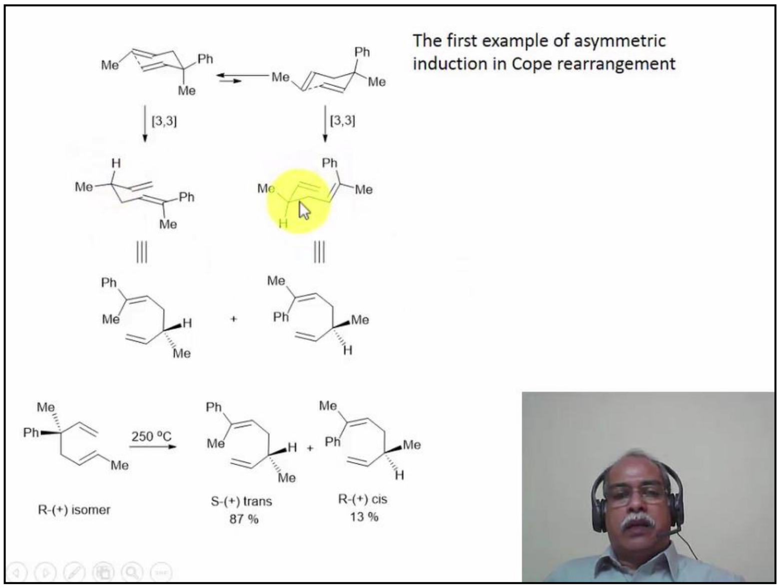

The first example of asymmetric induction in Cope rearrangement

Let us come to this example. When the R isomer-Plus isomer, of this molecule is taken and heated, it produces the S-Plus-Trans isomer. This is a Trans geometry, or R-Plus-Cis isomer. In other words, these are the two molecules, that are produced from the starting material. This highly stereospecific in the sense that, it produces S with the Trans stereochemistry, or it produces R with the Cis stereochemistry. These are the mixture of compounds, that is formed. The S Cis and the R Trans are not formed. That is why, this is highly stereospecific in nature.

How is this reaction happening? This molecule can exist in the conformational isomers, in the chair form, like this. This dotted line, is the newly formed Sigma bond, that is going to be formed during the course of the [3,3]-Sigmatropic rearrangement. If you look at this two structure, this is Axial Phenyl, and this is Equatorial Phenyl. So, the Equatorial Phenyl conformational is more preferred, compared to the Axial Phenyl conformer. See the [3,3]-Sigmatropic rearrangement, that is taking place.

A new bond is formed, between this Carbon-Carbon bond. This original Carbon-Carbon Sigma bond is broken, with the concomitant rearrangement of the PI system, to give this. And, this again gives the concomitant rearrangement, gives you this particular structure, for example, through a [3,3]-Sigmatropic rearrangement. While, writing this chair forms, you should maintain the R configuration, strictly. You should not change the configurations.

So, you can also see that, Trans stereochemistry of this double bond, is maintained here. This is Trans. This is also Trans. So, once you maintain the R stereochemistry, with the Trans double bond here, you cannot go wrong, in terms of determine the stereochemistry of the final products.

These are the two products. And, that essentially corresponds to the, Trans isomer with the S configuration here, and the Cis isomer with the R configurations here, is what is represented.

These two are same as, these two structures, that are shown here. So, what we have seen in this particular module, is the Sigmatropic rearrangement of [1,5] type, and the Suprafacial migration is illustrated by Deuterium substitution reaction, in the case of the Cyclooctatriene kind of a molecule, which specifically distributes the Deuterium, in specific places. And then, we have seen the [3,3]-Sigmatropic rearrangement, particularly the Cope rearrangement.

The stereochemistry of the Cope rearrangement, involving the cyclic transition state. And then, finally the molecule, which is a most interesting fluxional molecule in organic chemistry, namely the Bullvalene, which undergoes a series of [3,3]-Sigmatropic rearrangements, in this particular module. Thank you very much, for your kind attention. I hope, you enjoyed this particular module.