Pericyclic Reactions and Organic Photochemistry

S. Sankararaman
Department of Chemistry
Indian Institute of Technology, Madras

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Pericyclic Reactions – Tutorial session 3
Problems of Sigmatropic reactions

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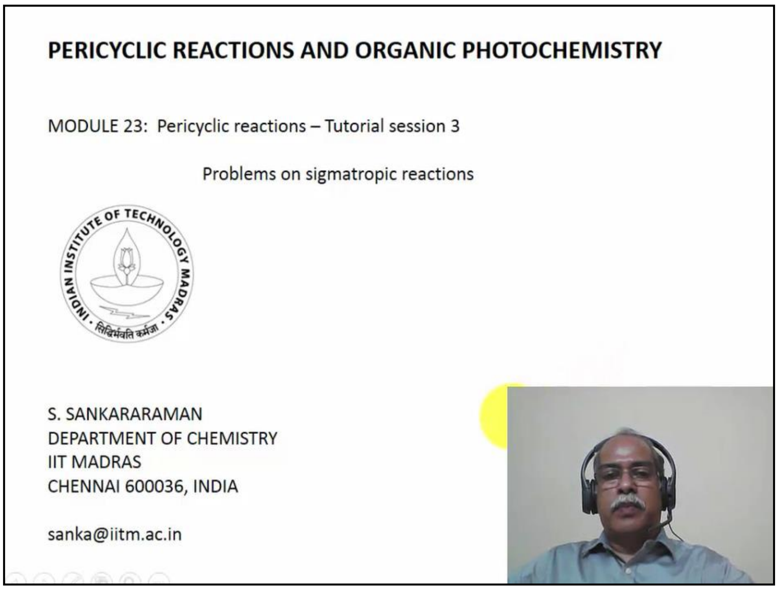

PERICYCLIC REACTIONS AND ORGANIC PHOTOCHEMISTRY

MODULE 23: Pericyclic reactions – Tutorial session 3

Problems on sigmatropic reactions

S. SANKARARAMAN
DEPARTMENT OF CHEMISTRY
IIT MADRAS
CHENNAI 600036, INDIA

sanka@iitm.ac.in

Hello, welcome to the Tutorial Session-3, of the online course on Pericyclic Reactions and Organic Photochemistry. We are in Module Number 23, of Week 5. In this particular module, we will consider, several problems involving Sigmatropic rearrangements. Problems involving Sigmatropic rearrangement can be, somewhat tricky and complex. If you are in a position, to identify the Carbon framework, or the Molecular framework, that undergoes a Sigmatropic rearrangement, it will be easy for you to identify, the rearrangement process itself.

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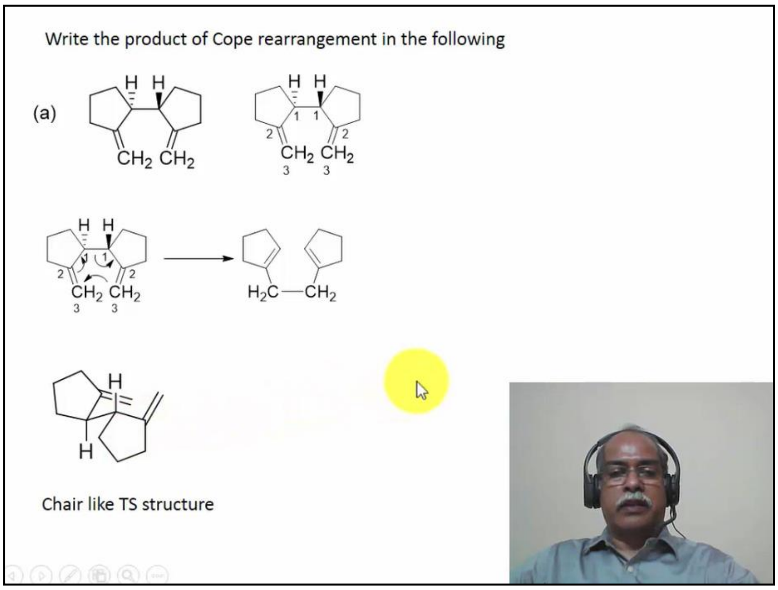

Write the product of Cope rearrangement in the following

Chair like TS structure

So, let us look at some examples of rearrangement reactions, involving Cope and Claisen rearrangement. Here is an example. Write the product of Cope rearrangement, of the following system. So, this is a molecule, that is given, with the Trans bond, between this 2 Cyclopentene Hexamethylene Cyclopentene rings. So, first thing, you need to do is, identify the [3,3]-System. Because, it is already clearly mentioned, that it is a Cope rearrangement.

So, the 3 system, essentially start from the terminus 3-2-1, 1-2-3. So, this is essentially a [3,3]-Sigmatropic rearrangement. In other words, if you look at this molecular fragment here, this is a Hexa-1,5-Diene, is what we have. Hexa-1,5-Dienes, undergo the Cope rearrangement, under thermal conditions, by a Suprafacial-Suprafacial manner. So, essentially, the connecting the [3,3]-bond, and cleaving the Carbon [1,1] bond, and rearranging the PI bond into the [1,2] position, is what this reaction is all about.

And, the rearrangement is shown, in this particular manner. The [3,3]-Sigmatropic rearrangement, is shown by means of arrows, resulting in the formation of the Methylene bridged Cyclopentene derivative, which is this particular derivative. If you want to go one step further, and show the cyclic transition state, you can do so. You can see here, the Exomethylene derivatives are forming part of the, chair form of the Cyclohexene derivative.

The chair form of 6-Membered cyclic transition state, involving the chair type of a confirmation, is what is, very clearly shown. It also shows, this 2 Hydrogens to be, Anti or Trans, with respect to each other. So, essentially, if you form a bond between this Carbon and this Carbon, and break this Carbon-Carbon bond, then you get this product, involving a [3,3]-Sigmatropic rearrangement kind of a reaction, in this particular example.

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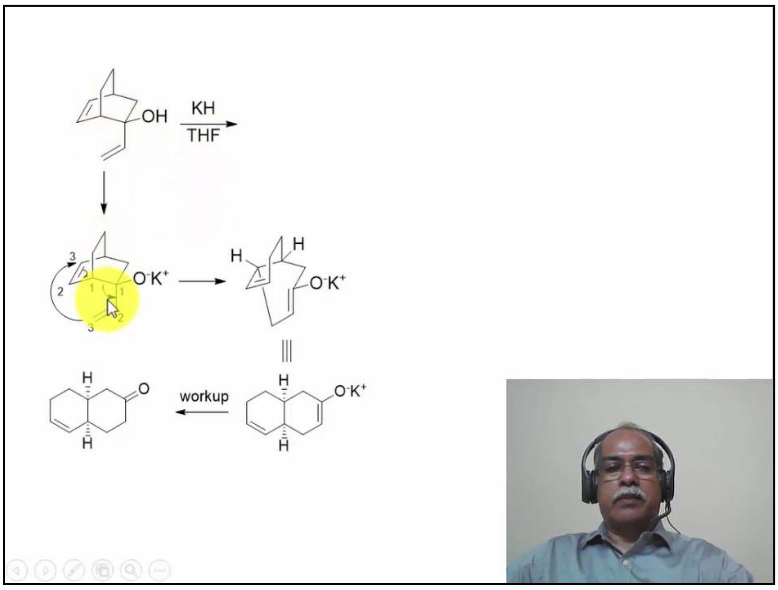

Now, here is an example. You are asked, to identify the product, of this particular reaction. The reaction essentially involves, this alcohol being treated with Potassium hydride in THF, and heated to about 50° or so, and what is the kind of a rearrangement, that is going to take place. When you treat the alcohol with Potassium hydride, you are going to get the Potassium alkoxide as the product. The Potassium alkoxide, of course, is part of a [3,3]-Anionic Oxy Cope kind of a, [3,3]-Sigmatropic rearrangement system.

This is a Sigma bond. If you look at this Carbon, 1-2-3, 1-2-3. So, this is a [3,3]-System, involving a Hexadiene kind of a system, except that, this looks like, these bonds are far away from each other. But, remember, this Vinyl group is Endo in nature. As a result of that, the Endo can approach, this particular Carbon quite readily, through a cyclic transition state. So, the [3,3]-Sigmatropic rearrangement is shown, by means of arrows, in this particular case, resulting in the formation, of this particular structure.

What is this structure? If you count the number of Carbons, in each of this ring. First of all, this is a [2,2,2]-Bridged bicyclic system. You are breaking the bridge, here. So, naturally, it becomes a fused bicyclic system, instead of a bridged bicyclic system. The fusion ring is starting from here. So, that will be 1-2-3-4-5-6. The other side also, it is 1-2-3-4-5-6. So, it is a 6 and 6 fusion, with the 2 Hydrogen being Cis, with respect to each other.

So, this molecule is nothing but, this particular Perhydro derivative of the Naphthalene. In other words, this is a Decalene kind of a system. Tetra Dihydro Decalene, you can say for example. The 2 Hydrogens are Cis, because, essentially this Hydrogen and this Hydrogen, point in the same direction, towards the back side of the skeleton. And, the Potassium alkoxide, which is an Enolate, it is generated by the [3,3]-Sigmatropic rearrangement upon workup, go to the Keto form, through the Enol formation, via the Keto Enol Tautomerism.

It results, in the formation of this particular Ketone. So, essentially, a [3,3]-Anionic Oxy Cope [3,3]-Sigmatropic rearrangement reaction, is what this molecule is capable of undergoing. And, that is illustrated by the mechanism, as well as the Stereochemistry of the rearrangement, in this particular instance.

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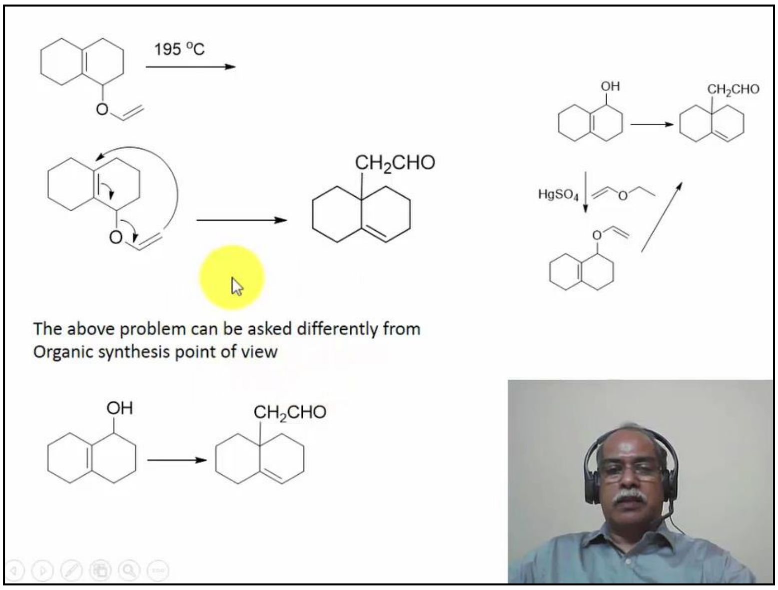


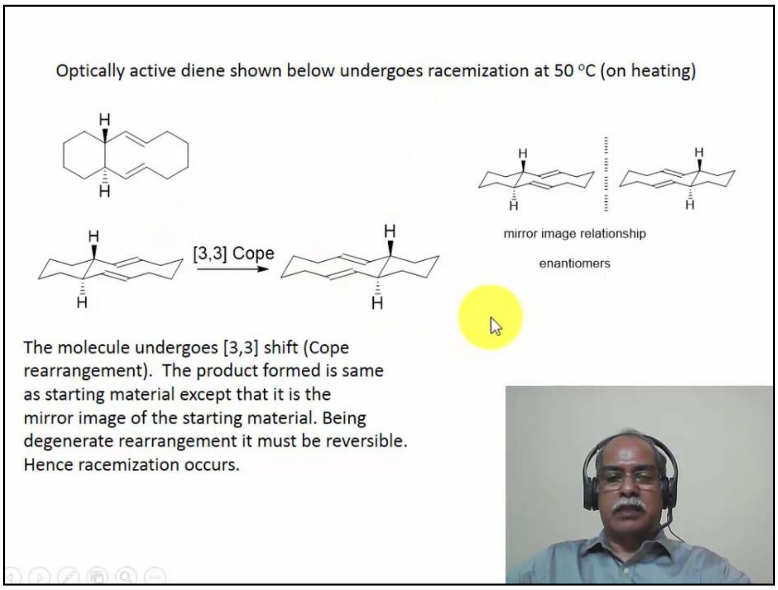
The above problem can be asked differently from Organic synthesis point of view

Now, this is another question. What, if you take this Allyl Vinyl Ether, and heat it to 195° Celsius. Because, it is an Allyl Vinyl Ether, this is clearly a Claisen system. The Claisen rearrangement is what, will take place under this condition. The Claisen rearrangement is represented, by means of mechanistic arrows, to show this transformation, in this manner. That, results in the formation of the, transfer of this Vinyl Oxy group, on to the terminal position of Allelic Ether.

In other words, the Vinyl Oxy unit is transferred on to the, terminal Carbon of the Allyl fragment of this, Vinyl Allyl Ether, resulting in the formation of an Aldehyde, which is nothing but a, Gamma Delta Unsaturated Aldehyde. Remember, the Claisen rearrangement gives a, Gamma Delta unsaturated Carbonyl derivative, depending upon, what kind of a Claisen rearrangement, it is. The above problem, can be also asked, from the organic synthesis point of view. How will you transform, this Allyl alcohol, to this particular Aldehyde?

What is easy to recognize, in this particular instance is, this is an Allyl alcohol, to start with, and this is a Gamma Delta unsaturated Carbonyl compound. These are the 2 information, that one need to gather, in this transformation. So, from the Retro synthetic point of view, if you look at, how to do this transformation. You first convert, the Allyl alcohol into Allyl Vinyl Ether, using Mercuric sulfate as a Catalyst, and the Vinyl transfer agent, namely the Ethyl Vinyl Ether.

So, the Trans Etherification reaction is carried out. Once, the Trans Etherification reaction is complete, you heat it strongly to high temperatures, to about 195° Celsius. The [3,3]-Sigmatropic rearrangement will essentially give you, this product. So, one can ask this question, as a Mechanistic question. One can also ask this question, as a Synthetic transformation question, depending upon, how the teacher, views this particular question. The question can be framed accordingly, as a Synthesis problem, or, as a Mechanistic problem.


Optically active diene shown below undergoes racemization at 50 °C (on heating)

The molecule undergoes [3,3] shift (Cope rearrangement). The product formed is same as starting material except that it is the mirror image of the starting material. Being degenerate rearrangement it must be reversible. Hence racemization occurs.

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Now, here is an interesting question. Optically active Diene, which is shown here. This is a Diene, that we are talking about, undergoes Racemization, on heating to about 50° Celsius. What is important, to recognize here is that, it is again a Hexadiene system. And, it is a Hexa-1,5-Diene system, capable of undergoing a Cope rearrangement. So, you write this, in the chair type of a confirmation. Essentially, is a Trans Decalin kind of a confirmation, is what is written here.

So, that is the Diene system, that is capable of undergoing a [3,3]-Sigmatropic Cope rearrangement. Once the Cope rearrangement takes place, the bond is formed, between these 2 Carbons. The Carbon-Carbon bond here is cleaved, and the double bond is shifted to the adjacent Carbon, resulting in the formation, of this particular molecule. What is important to recognize is that, this molecule, and these molecules, are mirror images of each other.

So, if an Optically Pure isomer of this molecule is taken, and heated, it will undergo Racemization. Because, once the reactions start to go, in the forward direction, the reverse reaction is also equally facile. Energetically, the reverse reaction has the same energy of activation, as the forward reaction. So, essentially one would, establish in equilibrium, between the starting material, and the product, that is being formed. What is important to recognize is that, the starting material, and the products are having, mirror image relationship. In other words, they are Enantiomers of each other. So, once you have 1:1 mixture of Enantiomers, then, that is essentially Racemization process. That is why, this molecule on heating, gives the mirror image product. And, hence the Racemization takes place quite readily, because of the reversibility of the Cope rearrangement, in either direction, to be favorable under.

This is a Degenerate Cope rearrangement, except that, the degeneracy is lost, because of the fact that, you get an optical antipode of the starting material, not the same configuration of the starting material. Mirror image relationship, is very clearly seen, in this diagram, where this dash line, is actually the mirror plane.

So, this is essentially reflected on the other side, as a mirror relationship, and their non-super impossible relationship, that is why, they are called Enantiomers, in this particular case. So, 1:1 ratio of Enantiomers, is what is called Racemic mixture. So, the process is known as a Racemization process.

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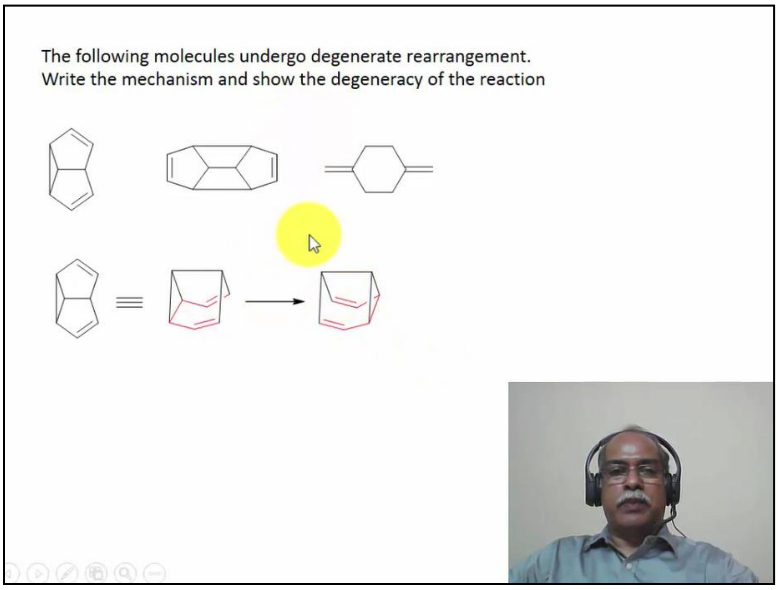

The following molecules undergo degenerate rearrangement.
Write the mechanism and show the degeneracy of the reaction

Some interesting structures, are shown here. In the Planar form, the structures are shown. They are hardly Planar molecule. One minute, we will see that, these molecules have, fairly complex geometry. The question is, the following molecules undergo, Degenerate rearrangement. Write the mechanism, and show the degeneracy of the reaction. In other words, you start with this molecule, do a rearrangement, end up with the same molecule, is what you need to show.

Now, this molecule here, is essentially a Cyclopropane, connected to 2 Vinyl group. And, the third Carbon of the Cyclopropane, is connected to a Carbon. So, Cyclopropane, with 2 Vinyl group. The third Carbon is connected to the, another Carbon, which is connected to the, that ends of the Vinyl group, for example. So, this is an actual molecule, in terms of the confirmation of the molecule, or the shape of the molecule, this molecule can. This is like a Divinyl Cyclopropane derivative.

So, it can undergo [3,3]-Sigmatropic rearrangement, with the formation of a Carbon-Carbon bond, between these 2 Carbon. The [3,3]-System is shown clearly, in the red ink color. So, the [3,3]-Sigmatropic rearrangement, is what is taking place. And, the starting material, and products, are essentially same. That is why, it is a Degenerate molecule. So, that is a purpose of this reaction, to be shown, to be a Degenerate molecule, in this particular case.

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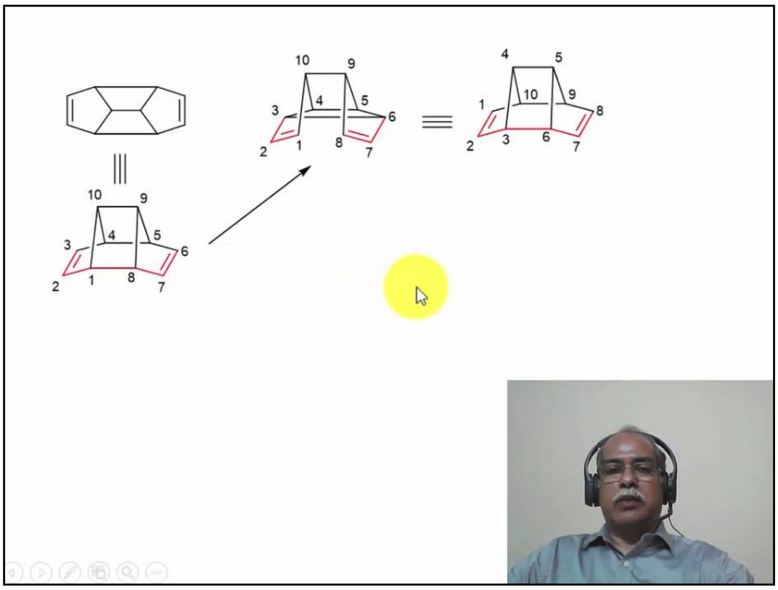

The second molecule, is this particular molecule. This molecule, has this particular geometry and shape. It is better to number these molecules, starting from here, 1,2,3,4,5, go around the ring, up to 8. 9 and 10, are the Bridging Atoms, of this particular derivative. So, what is the [3,3]-Sigmatropic component. It is very clearly shown, in the red. This, is 1,2,3. Here also, you can write this as, 1,2,3.

So, the [3,3] is going to be the connectivity between, Carbon number 3 and 6. If you connect Carbon 3 and 6, and break Carbon 1 and 8, you will get the [3,3]-Sigmatropic product. So, that is a structure, that is shown here. This structure, is essentially same as the starting material structure, which is this structure, except the numbering, has to be followed correctly. The Carbon 3 and 6 are connected.

So, you can see, Carbon 3 and 6 are connected. Carbon 4 and 5, will essentially form the bridge, which is this Methylene bridge, here. So, 4 and 5 forms the Methylene bridge. Carbon number 9 and 10, are already connected. So, they will remain connected. The double bond is shifted, between 1 and 2, and 8 and 7. So, you can see, between 1 and 2, and 8 and 7, the double bonds are shifted.

So, essentially, this is redrawn in the same way, as it is redrawn, originally. Hence, it is a Degenerate rearrangement. This molecule, is same as the starting molecule, in spite of the fact, it has undergone [3,3]-Sigmatropic rearrangement. Such rearrangements, can be studied by NMR spectroscopy, or by suitable Deuterium, or Carbon-13 Labeling, to show that, this Carbon-13 Label scrambles, during the course of the [3,3]-Sigmatropic rearrangement.

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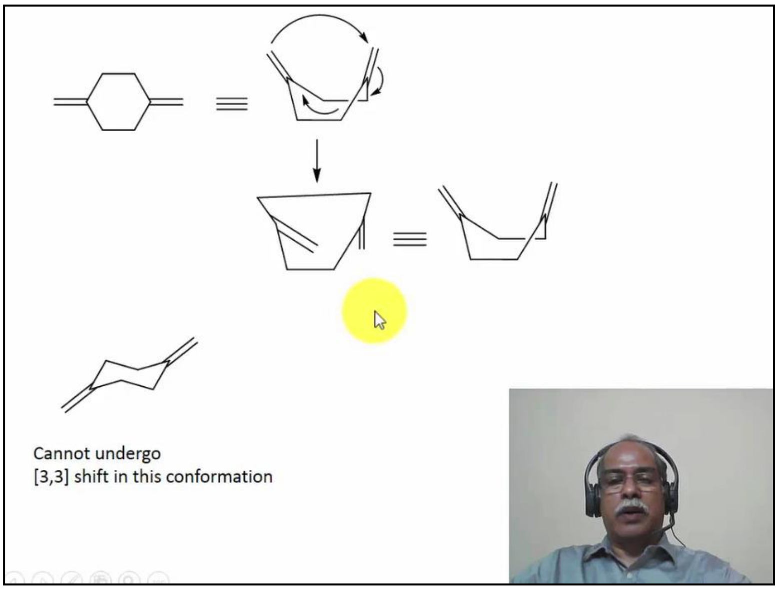


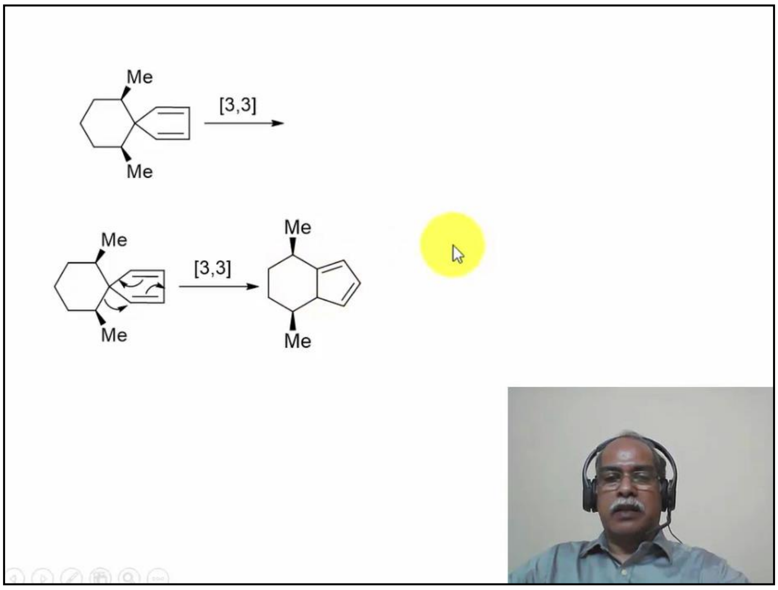
Cannot undergo
[3,3] shift in this conformation

Here is another interesting example. This molecule, essentially is a [1,4]-Hexomethylene Cyclohexane molecule. This should exist in the, boat type of a confirmation, in order to bring this Carbon number 1, and this Carbon number 6, in close proximity, to undergo a [3,3]-Sigmatropic rearrangement. You start numbering from here, 3-2-1, 1-2-3. Or, you can say, 3-2-1, 1-2-3.

So, this is actually, the Hexa-1,5-Diene system. Either, the top portion is a Hexa-1,5-Diene system, or the bottom portion is a Hexa-1,5-Diene system, connecting, either these 2 Carbons, or these 2 Carbons. So, if you write it in the boat confirmation, you can bring Carbon number 1 and 6, in close proximity. Hence, the reaction can take place, through this particular transition state, resulting in the formation, of this particular product.

The product is shown as, to be the same as starting material. In other words, if you start numbering it again, the numbering will correspond to this particular structure, being equivalent to this particular structure. Now, what cannot undergo a rearrangement, through a cyclic transition state is the, chair form of the [1,4]-Exomethylene Cyclohexane.

So, the confirmation has to be, although, this may be a favorable confirmation, there will be certain population of the boat type of a confirmation, in this molecule, which will trigger the reaction, to go in this direction, to a Sigmatropic rearrangement, which is of course a Degenerate rearrangement. Overall, you do not see any reaction. Except, if you do a Deuterium labeling, in this position, you can see the scrambling of the Deuterium labeling, in the product, to all the other positions, also.



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Here is an interesting example, to illustrate the retention of Stereochemistry, during the course of a [1,5]-Sigmatropic rearrangement. This is a [1,5]-Sigmatropic rearrangement, because of the fact, this is a substituted Cyclopentadiene molecule. So, this bond is cleaved. So, this is 1 and 1. 1,2,3,4,5.

So, this is a rearrangement, which involves [1,5]-Sigmatropic rearrangement, resulting in the formation of the product, which is this particular product. The mechanism of the rearrangement, is very clearly shown here. So, this is a Carbon-Carbon bond, that is breaking. And, it is a Suprafacial migration. So, Suprafacial migration should take place, with retention of Stereochemistry, at this particular Carbon.

So, the Stereochemistry is retained, which is inferred by the fact that, the initially you start with the Cis Dimethyl derivative, you also end up with the Cis Dimethyl derivative, which indicates the Stereochemistry here is retained, during the course of the migration. So, it is a Suprafacial component, with respect to the PI system, as well as the Suprafacial component, with respect to the Sigma system, involving a [1,5] kind of a rearrangement, involving 6-Electron rearrangement, to give this particular product.

Remember, here, there is a Hydrogen. This is also, a mono substituted Cyclopentadiene. This Hydrogens can migrate to [1,5]-Shifts. So, this can, in fact, further undergo many [1,5]-Sigmatropic rearrangement reactions, during the course of the heating of this molecule.

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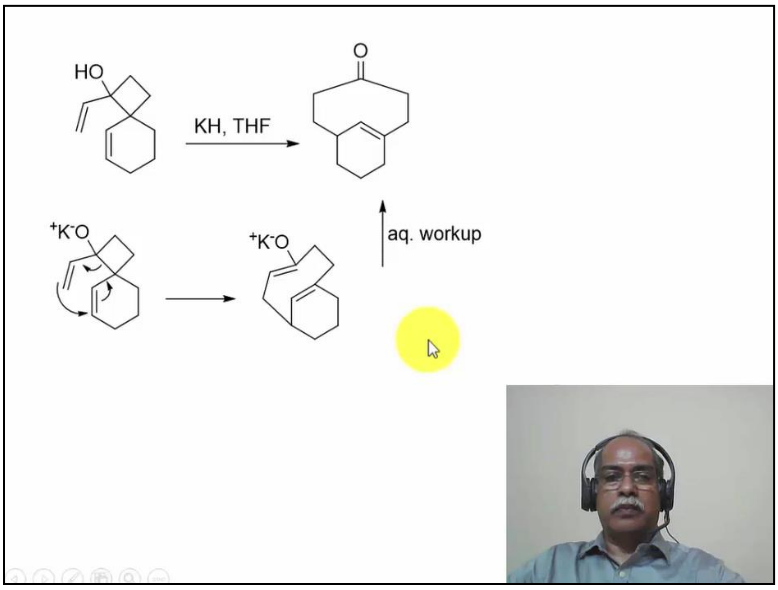

Now, here is an example of a, again an Anionic Oxy Cope rearrangement. This is a Divinyl Cyclobutene derivative. The Divinyl Cyclobutene derivative, on treatment with Potassium hydride, gives this Potassium salt of the alkoxide. This can readily undergo [3,3]-Sigmatropic rearrangement, to give this product, which on workup, essentially gives this macrocyclic Ketone. Please remember that, this is not a violation of Bredt**’s** rule.

This is actually a Bridgehead double bond. Because, this is a larger ring system. This is involving 1-2-3-4-5-6-7, 8-Membered ring system. So, this is actually 1,2,3,4,5. [5,3,1]-Bicyclic Ketone, is what is formed, in this particular case. Because of the large ring size, this double bond can be accommodated, at the Bridgehead. So, it is not a violation of the Bredt’s rule.

Because, Bredt’s rule is applicable, only to smaller bridged bicyclic ring systems, of the type [2,2,1], and type [2,2,2]-type of bicyclic ring system. So, this is essentially, an Anionic Oxy Cope rearrangement, involving the formation of the Alkoxide in the 3 position, resulting in the rearrangement, taking place at around, 50 to 60° or so. And, upon workup, this Enol essentially will go to the Ketone, resulting in the formation of this, as the final product.

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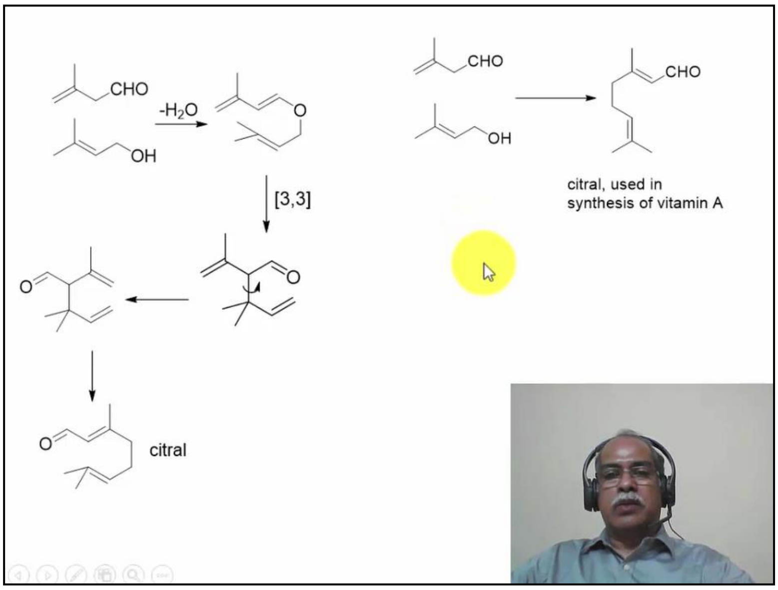

Now, here is an interesting reaction. These 2 molecules are heated together, in the presence of an acid. And, it produces Citral. Citral is a very industrially, very useful compound. This is used in fragrance industry. It is also used as a starting point, for the synthesis of Vitamin A. In fact, BASF producers are manufactures the Citral, using these 2 compounds, as starting material. What is the mechanism, that is involved in the formation of Citral, from the starting material is what?

If you add up the molecular formula of this molecule, and molecular formula of this molecule, and subtract it from, the molecular formula of this molecule, you will get, one water molecule. So, essentially, this is undergoing, some kind of a condensation reaction, followed by dehydration reaction, followed by certain molecular rearrangements, to give this particular product. What are the possible reactions, that can take place.

When this Aldehyde is treated with this alcohol, it can form a Hemiacetal. The Hemiacetal can undergo, Alpha dehydration, from the Alpha position, in this particular way, resulting in the formation of the Allyl Vinyl Ether. So, this is a Pyrinyl Vinyl Ether, is what is being formed, in this particular instance. This is a [3,3]-Sigmatropic Claisen kind of a system. So, it can undergo the [3,3]-Sigmatropic rearrangement, to give this particular product.

Once this product is formed, if you rotate this Carbon-Carbon bond, essentially you get a Cope system. So, you get a Hexadiene system, [1,5]-Diene system, which is a Cope system. So, this undergoes, this is only a conformational change, between these two structures. So, once this structure is formed, this undergoes the [3,3]-Sigmatropic rearrangement, to form this molecule. This is essentially, Citral.

And, if you see here, Gem Dimethyl Vinyl group, with a CH2, CH2. And, then a Methyl group double bond, and CHO. Gem Dimethyl group, with a Vinyl CH2, CH2, with the Methyl group, here. And, a Vinyl, and a double bond Aldehyde, is what is formed. So, this is essentially manufacturing process of Citral, starting from this to C5 molecules, that are shown as starting material, in this particular case.

So, i hope, you enjoyed this problem-Solving session. We considered, several [3,3]-Sigmatropic and [1,5]-Sigmatropic rearrangement. The essential point that, i would like to inform here is that, when the Claisen system, or Cope system is given, it is better to identify the Hexa-1,5-Diene system, or the Allyl Vinyl Ether system, and number it properly, and proceed with the [3,3]-Sigmatropic rearrangement.

In the case of [1,5]-Sigmatropic rearrangement, make sure that, the reaction proceeds with a retention of Stereochemistry, for Carbon migration. One example was shown, in this particular tutorial. And, that is all, i would like to say, in this particular module. Thank you very much, for your attention.