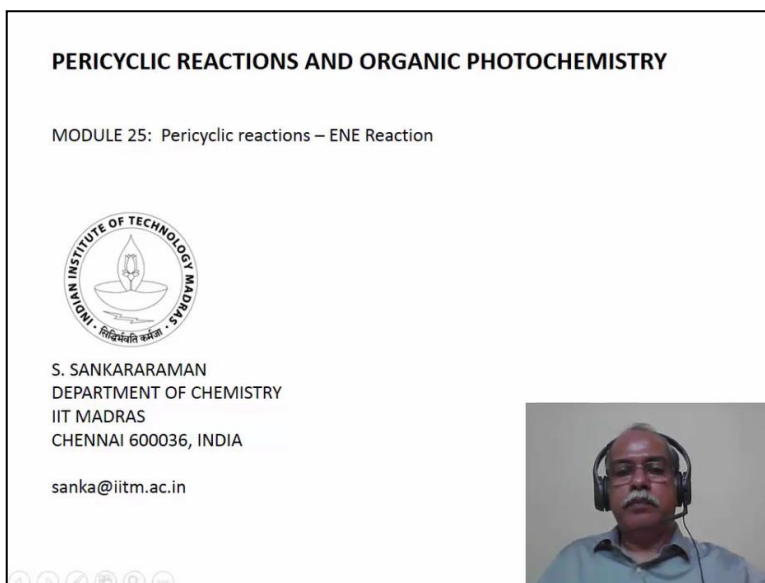


Pericyclic Reactions and Organic Photochemistry
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Module No. #06
Lecture No. #25
Pericyclic Reactions – Ene reaction

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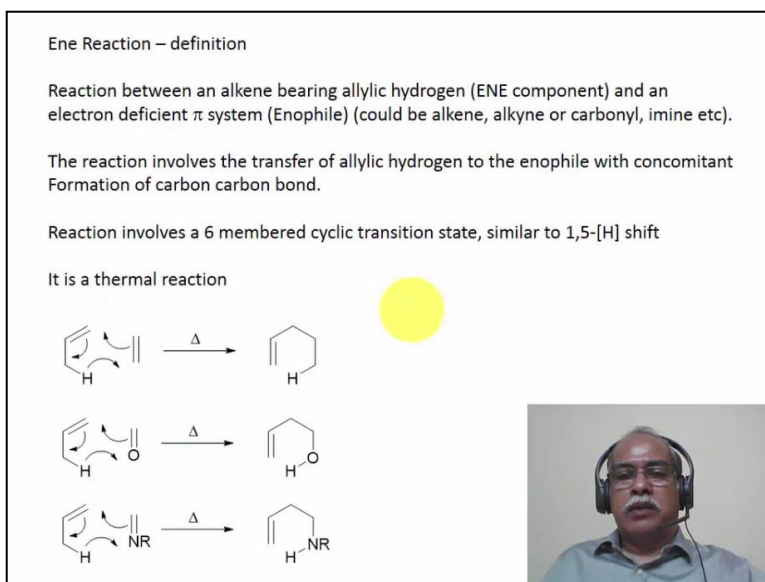
The screenshot shows a presentation slide with the following content:

- PERICYCLIC REACTIONS AND ORGANIC PHOTOCHEMISTRY**
- MODULE 25: Pericyclic reactions – ENE Reaction
- The IIT Madras logo, which is a circular emblem containing a lamp and the text "INDIAN INSTITUTE OF TECHNOLOGY MADRAS" and "विद्यया ऽ मृतमश्नुते".
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In the bottom right corner of the slide, there is a small video inset showing a man with a mustache wearing a headset, presumably the lecturer.

Hello, welcome to the online course on, Pericyclic Reactions and Organic Photochemistry. We are in, Week Number Six, and Module Number Twenty-Five. We will continue with the Pericyclic reaction. This will be the Last Module, concerning the Pericyclic reaction. From, Module Twenty-Six onwards, we will concentrate on Photochemical Reactions. Now, Ene reaction is a very important reaction, in Organic Chemistry, for the simple reason, it involves two processes.

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One is a CH activation process. Other one is a, Carbon-Carbon bond forming reaction. Both, CH activation, as well as CC-Bond forming reactions, are very vital to Organic Synthesis. And, that is a reason, Ene reaction is a important reaction. What is an Ene reaction? Let us first consider, the definition of Ene reaction. A reaction between an Alkene, bearing an Allylic Hydrogen, which is an Ene component, and an Electron deficient PI system, which is a Enophile component, is the Ene reaction.

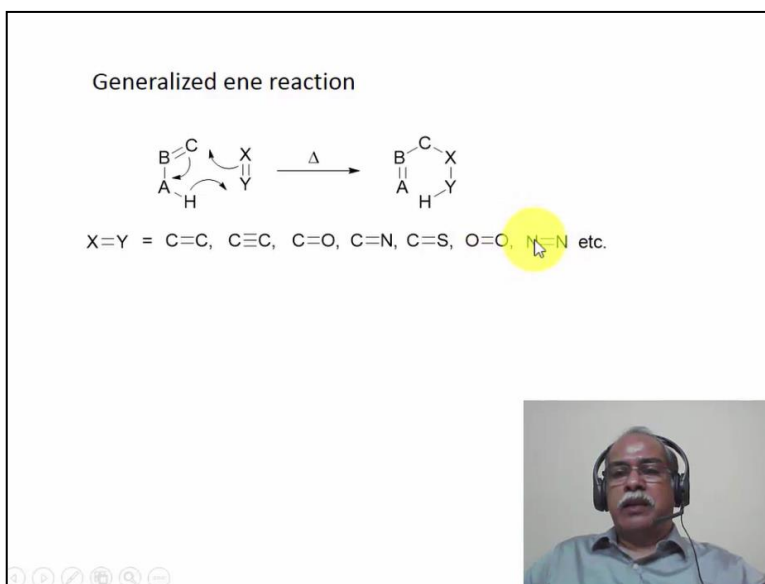
In this reaction, the Allylic Hydrogen is transferred onto the Enophile, with the concomitant formation of a Carbon-Carbon bond. The reaction involves, a 6-Membered cyclic transition state, very similar to a [1,5]-Hydrogen shift. So, if you look at this example of a Ene reaction, this is the Alkene with the Allylic Hydrogen, which is this Hydrogen, that is shown here. And, this is the Enophile, which accepts the Hydrogen.

So, you can see here, it involves a 6-Membered cyclic transition state, involving 6-Electrons also. Two of the CH-Bond Electrons, two of this PI Electron, and two of this PI Electron, all of them under the, in a cyclic transition state, this reaction undergoes a transfer of a Hydrogen, with a simultaneous formation of this Carbon-Carbon bond, with the reorganization of the PI system, towards the formation of this particular Olefin.

So, you can see here, the similarity between a [1,5]-Hydrogen shift. If you start counting from here, this will be 1 and 1. This will be, 1-2-3-4-5. In the [1,5]-Hydrogen shift, there will be already a bond existing here. Here, the new bond is being formed, in this particular reaction. Instead of having an Olefin, you can have a Carbonyl functional group, and this would be called the Carbonyl Ene reaction.

The product of a Carbonyl Ene reaction, is a Homo Allyl alcohol, which is shown here, for example. This is a Imino Ene reaction, where an Imine is acting as a Enophile, and the Allylic Hydrogen is transferred onto the Nitrogen, resulting in the formation of a Homo-Amine kind of a product, is what is formed. We will see examples of each of this type, in the due course of this particular module.

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The generalized Ene reaction, of course would be the one, which is shown here. Where, you have an Allelic Type of a Hydrogen, available in a molecule. And, typically, this will be an Alkene Type of a molecule. Whereas, the Enophile can be, either an Alkene. It can be an Alkyne. It can be a Carbonyl compound. It can be an Imine. It can be a Thiocarbonyl compound. Even, singlet Oxygen, can behave like a Enophile. We will see some example, of such reactions. And, finally, Azo compounds can act as, also as a Enophile, resulting in the formation of Hydrazine kind of a product.

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HOMO of ene

LUMO of enophile

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

Highly ordered cyclic transition state.

Similar to [1,5]-H sigmatropic shift.

Negative entropy of activation.
About $-30 \text{ cal mole}^{-1} \text{ K}^{-1}$ for intermolecular reactions.

All carbon ene reactions take place at high temperatures 400-600 °C

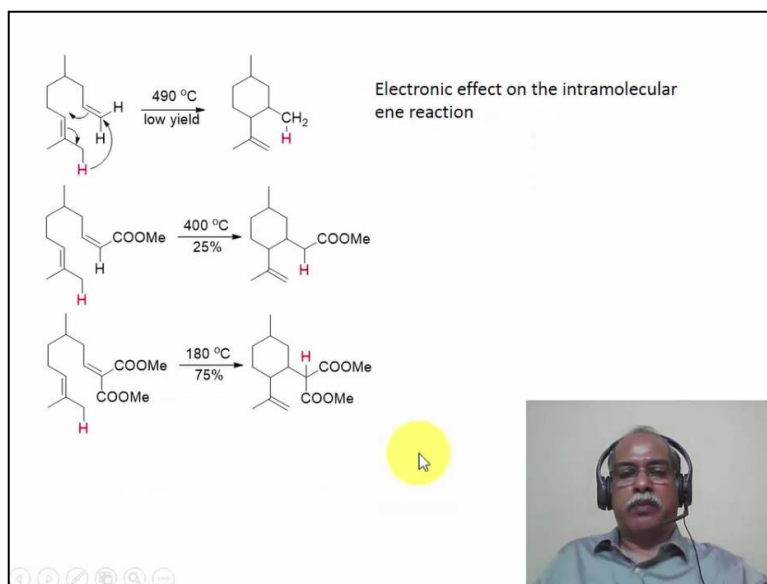
The more electron deficient the enophile, the faster the reaction and lower the temperature.

The highly ordered, cyclic transition state of the Ene reaction, is shown here. Originally, this Hydrogen is attached to the Allylic system. So, the Homo of the Ene is taken, for consideration, which interacts with the Lumo of the Enophile, which is shown in the bottom portion of this. So, essentially, the Hydrogen is transferred onto this molecule. You can see here, a Suprafacial-Suprafacial interaction is what is taking place. So, it is a 2-Sigma Suprafacial, which is this Sigma Suprafacial, 2PI Suprafacial, with respect to the PI bond here.

And, again with respect to this PI bond also, it is Suprafacial in nature. It is very similar to a [1,5]-Hydrogen shift, which occurs by a Suprafacial shift, under thermal condition. Ene reactions are always carried out under, thermal conditions only. The negative entropy of activation, is what is observed, corresponding to the proposal, that it is a highly ordered cyclic transition state. About 30 calories mole per kelvin, is the entropy of activation, for this kind of molecules, for the Intramolecular reactions of this kind.

An all Carbon Ene reaction, typically takes place at a very high temperature. In other words, it is very similar to a pyrolysis kind of a system. But, more and more of Electron deficient groups, are put in the Enophile. In other words, Electron withdrawing groups are being substituted, on the Enophile. The faster the reaction, and the lower the temperature. We will see, why that happens, in a couple of minutes.

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If you consider, the Electronic effect of the Intramolecular Ene reaction, here is an example of a Terpenoid kind of a molecule, that is undergoing Ene reaction. This Hydrogen, which is shown on the red, is what is getting transferred onto this Enophile, with the concomitant formation of a Carbon-Carbon double bond, resulting in a Cyclohexene kind of a system, here. And, the Olefin is of course rearranged, to give the Exomethylene Olefin kind of a product, in this particular case.

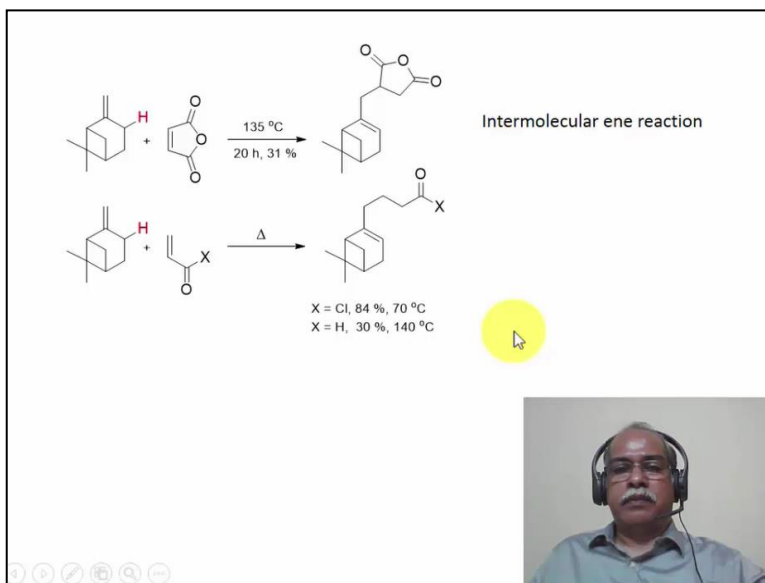
When the Enophile is substituted, with the Carbomethoxy functional group, the reaction takes place at a lower temperature, with a higher yield. This is a very low yield of the product, is what is observed, under the other pyrolysis condition. Whereas, under these conditions, the yield is slightly better. Instead of one Carboxylic acid functional group, when the both the positions are substituted with Carboxylic acid functional group, the reaction temperature is brought down dramatically, to about 180° Celsius.

And, the yield of the product, the Ene reaction product, is also very high, which is about 75% or so. So, this clearly indicates that, in the Enophile, if you have Electron withdrawing functional group, as you make it more and more of Electron deficient, the reaction occurs at a lower temperature, and the yields are also much better. This is essentially because, the Lumo level of the Enophile is brought down, closer to the Homo-level of the Ene component.

So, the Homo-Lumo gap, continuously decreases, going from this molecule, to this molecule, which is substituted with, Electron withdrawing functional group. Because of the closer nature of the Homo-Lumo gap, in the case of the Electron withdrawing substituted Enophile, the reaction

proceeds faster. Because, the activation barrier for this reaction, is much lower than the activation barrier for the, all Carbon Ene reaction of this type, without any substituents.

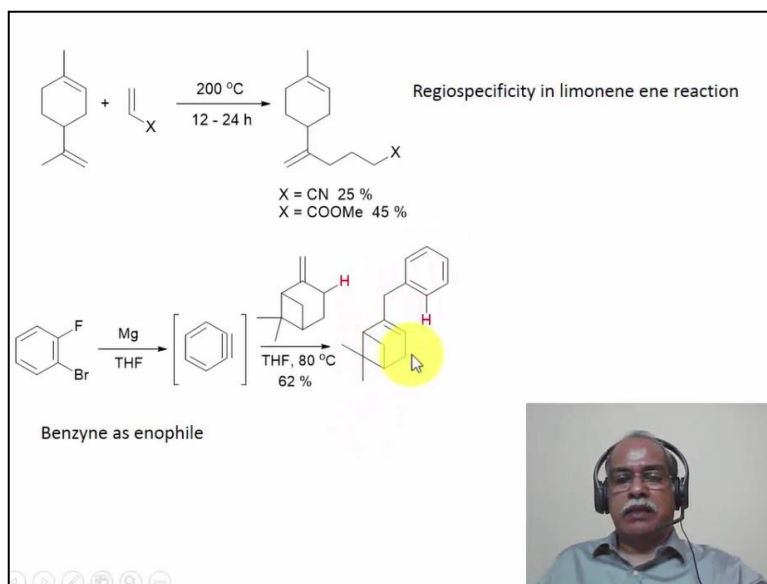
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Now, here is an example of Beta Pinene, undergoing a Ene reaction, with Maleic Anhydride in one instance, and with Acraldehyde and Acryl chloride in the next reaction, which is shown here. The Hydrogen, that is shown here is the one, that is undergoing the Ene reaction, with the formation of the Carbon Hydrogen bond, resulting in the saturation of this double bond, and the forming a Carbon-Carbon bond, between the Maleic Anhydride, and the terminal position of this particular Carbon here, resulting in the formation of the substituted Maleic Anhydride, that is formed here.

Here, the reaction is a Regio specific in the sense, the Hydrogen is transferred onto the Alpha position, and the Carbon-Carbon bond is formed between the Beta Carbon of the Enone, or the Enol chloride, and Acetyl chloride, and this particular Carbon of the Ene component, of this particular system.

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Here is another example of Limonene, undergoing reaction. There are two double bonds in Limonene. One is a disubstituted double bond, which is this double bond, which is an exocyclic double bond. It is a simple disubstituted double bond. Whereas, this is a tri-substituted double bond, which is part of a cyclic system. So, this is sterically more hindered, compared to this particular system. So, this portion of the molecule, acts as an Ene component.

Whereas, this portion of the molecule, because of probably steric hindrance of the tri-substituted system, as well as the part of the cyclic system here, this does not undergo the Ene reaction. When the reaction is carried out in the presence of acrylonitrile, or methyl acrylate, the reaction regioselectively takes place in this particular carbon.

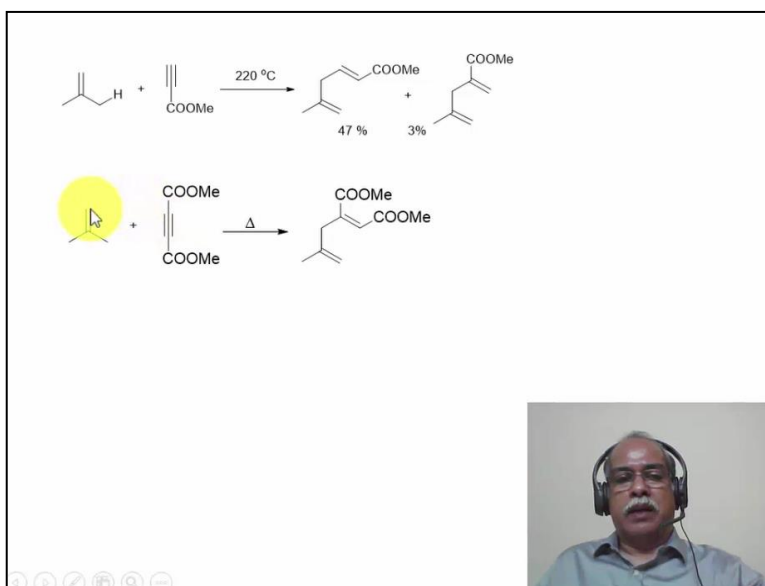
This hydrogen is transferred onto the alpha position of the acrylonitrile, or the acrylic acid ester, resulting in the formation of the carbon-carbon bond between the beta carbon and this particular methylene carbon, resulting in the chain extension that is shown here. So, here is an example of a regioselective reaction, where the limonene undergoes reaction only with the double bond which is not part of the ring system.

The ring system double bond does not undergo the reaction under this condition. Benzyne can very well be an enophile. This is an example of benzyne undergoing an Ene reaction with beta-pinene, once again. The benzyne is generated from ortho-fluorobromobenzene by treatment with magnesium. The Grignard magnesium exchange, the Grignard reagent is formed, initially here, which undergoes elimination of the fluoride, resulting in the formation of the benzyne as an intermediate.

When the reaction is carried out, in the presence of Beta Pinene, as the trapping agent. Trapping, in the sense, this is the Ene component of this reaction. The Hydrogen is transferred onto the Benzyne, resulting in the formation of Benzene, resulting in also the formation of a Carbon-Carbon bond, between this Carbon here, and one of the ortho Carbons of the Benzyne, in this particular instance. The reaction is carried out in refluxing toluene.

So, it is 80°, in about 62% yield, this particular product is formed. So, here a Enophile is Benzyne, and the Ene component is the Beta Pinene, resulting in the formation of the Alpha Pinene Substituted Benzene derivative, in this particular instance. This skeleton is Alpha Pinene, whereas this skeleton is Beta Pinene, for example.

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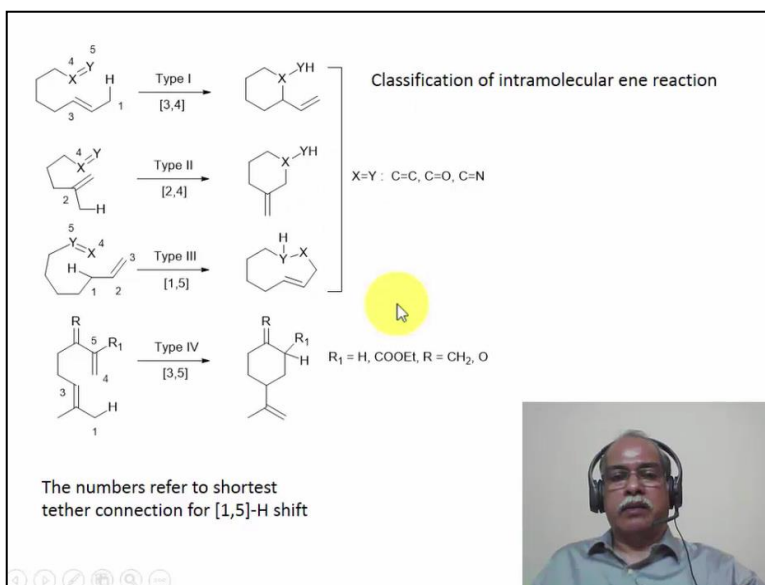
The Regio selectivity can be very poor, in the case of mono substituted Acetylenic, or Alkenic derivative, of this kind. Here is an example of Isobutylene, undergoing reaction with the Methyl propiolate, for example. The reaction is carried out around 220° Celsius. You can see here; two Regio isomers are formed.

This Hydrogen can be, either transferred to the Alpha position, which will give the major product, which is this particular product. Hydrogen can also be transferred, on to the Beta position, which case, this is a product, that is being found, which is formed in about 3% yield or so. The reaction is carried out at a much lower temperature, around 150° or so.

When the Dimethyl Acetylene Dicarboxylic acid is reacted with Isobutylene, resulting in the formation of the Hydrogen transfer, from the Methyl to this position, followed by Carbon-

Carbon bond formation, between this Carbon, and the Olefinic Carbon, which is the terminal Olefinic Carbon, resulting in the formation of this particular product, that is shown here.

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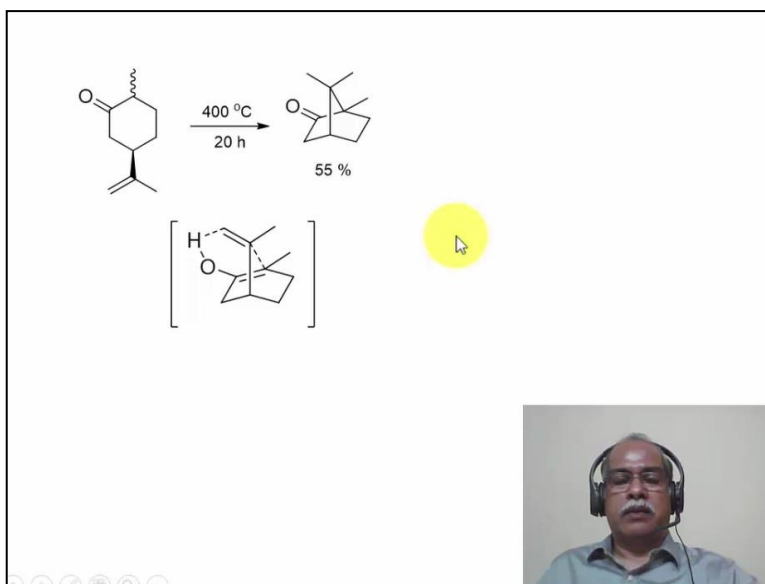
Apolsor has devised a methodology, to classify the Ene reaction. According to him, there are four types of Ene reactions, that can be classified. The numbering system, is as follows. You start with the numbering 1 from the position, which is an Allylic position, which is transferring the Hydrogen, and end up with 5 to the terminal position, where the Hydrogen actually lands at the end of the rearrangement. Now, the Tethering group, is this particular group, is what is connecting the Enophile with the Ene component.

And, this connectivity is for example, between the 3rd Carbon of the Enophile, and the 4th Atom of the Ene component-3rd Carbon, and the Enophile component-4th Carbon, are connected by this Tether. So, the Ene and the Enophile are connected by this, 4CH₂ Methylene groups, that are connecting this. That is the Tethering group. On the other hand, if you look at this molecule here, the Tethering group is connected to the 2nd position of the Ene component, and 4th position of the Enophile.

So, it is called [2,4] type. This is Type 2. This is called the [3,4] type. Because, it is a Type-1, which the Tether groups are attached, to the 3rd Carbon, and the 4th Atom, of the Ene and Enophile, respectively. Here, if you look at, this is a [1,5]-system. Because, the Hydrogen is transferred onto the Y position, here Atom Y, resulting in the formation of a YXH bond. So, this is a 5th Atom, of the cyclic transition state.

The Tethering group is attached to the 5th Atom, as well as the 1st Carbon Atom, of the Allylic system, which is the Ene component here. If you look at this system, this will be a [3,5] system. This is a Hydrogen, which is going to be transferred onto this Carbon here, resulting in the formation of a 6-Membered ring, in this this particular case. So, this corresponds to the [3,5] system. So, these systems are essentially classified with, two numbers in the square bracket, which indicates the Tethering connectivity of the Ene component, and the Enophile component. The numbering, starts from the Allylic position, which bears the Hydrogen, ends up at the position, where Hydrogen is being transferred, during the course of the Ene reaction. The shortest route of the Tether connectivity, is for the [1,5]-Hydrogen shift, is what this numbers are essentially indicative of this. And, here, we can have the XY group, as either Olefin, as Carbonyl, or as Imine, and so on, which we will see, in a minute.

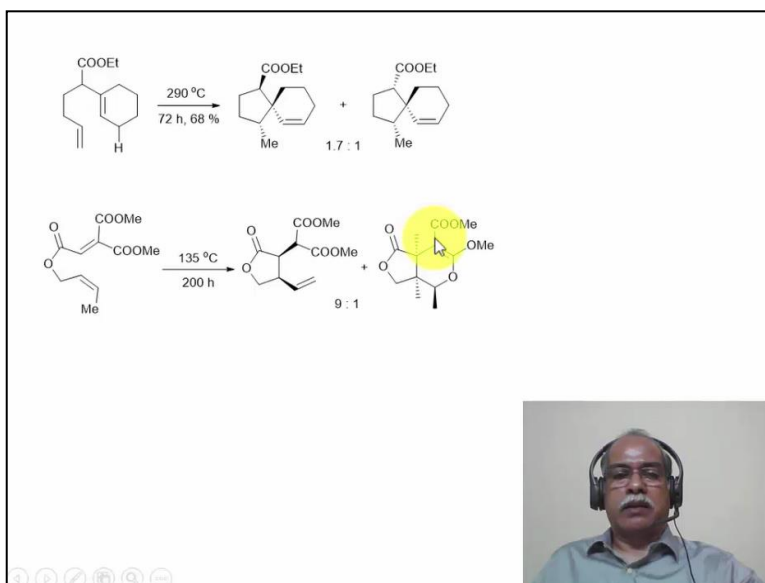
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Now, here is an example of Dihydro Carbone, undergoing an Ene reaction, under Pyrolytic condition, resulting in the formation of a [2,2,1]-Bicyclic Ketone of this kind, so, clearly, this is an Ene component, here. This Hydrogen is essentially, this is the Allylic Hydrogen, that is. This is an Enol form of these molecule, undergoing the Enolic Hydrogen transfer on to this position, resulting in the formation of a Carbon-Carbon bond, between this Carbon, and this Carbon. So, this has to undergo a boat kind of a transition state, in order for the connectivity. The dashed lines are the Carbon-Carbon bond connectivity, and the Hydrogen transfer connectivity. So, the Enolic Hydrogen is transferred onto this position, and this Carbon is connected on to the Beta position of the Enol, in this particular case, resulting in the formation of a [2,2,1]-Bicyclic

Ketone, which is shown here. The transition state structure, is shown in this particular structure, within the square bracket, here.

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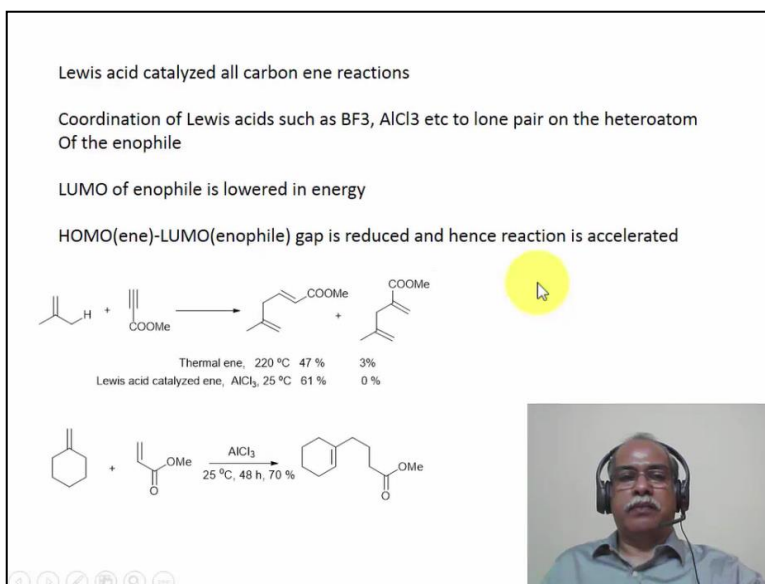


Spirocyclic compounds have been synthesized by Ene reaction, using this kind of a Carbon skeleton, where the Ene component, is clearly shown to be this particular component, and the Enophile component, is this particular component, resulting in the formation of Hydrogen migration, in a [1,5]-manner, which pushed this Methyl group here, because of the Hydrogen transfer. This Methylene, becomes a Methyl group here. You can see, some amount of Diastereo selectivity, in terms of the formation of the Cis and Trans isomers, of this two molecule.

Here, there are two reactions, that is taking place. The first product, that is formed, is a major amount in 9:1 ratio. The major product is formed, is the Ene product. The Ene product is arising from the Hydrogen, from this Methylene, transferred onto this position here, the Alpha position, with the concomitant formation of the bond, between these two system. So, this will be essentially, 1-2-3-4 kind of a, Type-1 kind of a Ene reaction, is what we are referring to here.

And, that takes place around 135° Celsius, in 200 hours of the reaction, this reaction is taking place, for example. This product was formed. This is a by-product. If you consider the Carbonyl functional group, and this double bond, this will be a Diels-Alder Diene kind of a system. So, this will be a Dienophile. So, a 4+2 Cycloaddition products is what is, one can visualize, as far as the product formation, which is a minor product concerned, in this particular reaction.

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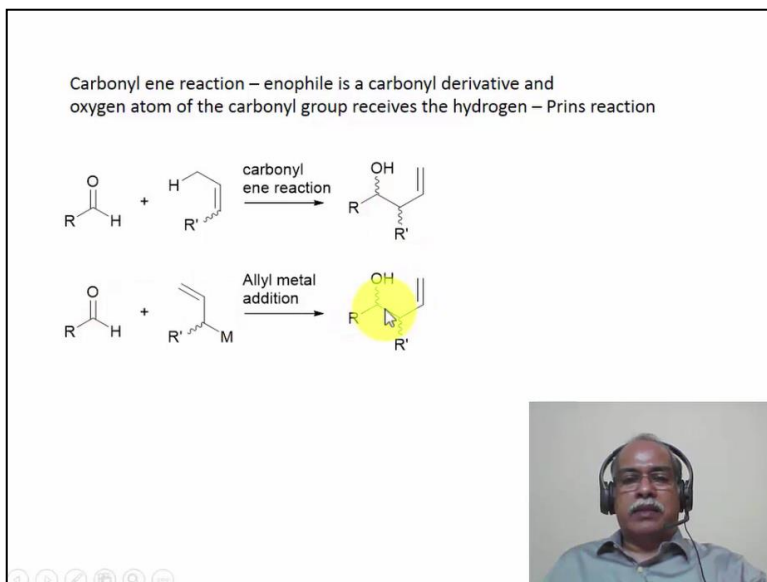


Lewis acid catalyze, the all Carbon reaction, just like the Lewis acid catalysis of the Diels-Alder reaction, and other reactions, were discussed earlier. Coordination of the Lewis acid, such as BF₃ and Aluminium chloride, to the lone pair of the Hetero Atom of the Enophile, is what normally takes place. As usual, because of the Electron deficiency being increased, by the coordination of the Lewis acid, the LUMO of the Enophile, are lowered in energy.

So, therefore, the Homo-Lumo gap, between the Ene and the Enophile, is reduced. And, rate is hence accelerated, very much. Now, imagine this reaction, we already consider under thermal condition, the mixture of Regio isomers are formed, in this reaction. However, under the Lewis acidic conditions, only one Regio isomer is formed. The other Regio isomer is completely absent, during the course of the reaction. That is not a important point here. The important point is, the rate acceleration. The uncatalyzed reaction, takes place around 220° Celsius.

Whereas, the catalyzed reaction, in the presence of Aluminium chloride, takes place at room temperature, around 25°. So, that is the most important aspect of this particular reaction. Similarly, in the case of Acrylate also, Regio isomeric products can be formed. However, under Lewis acidic conditions, the only one isomer is formed, where the Ene Hydrogen is transferred onto the Alpha position, and the Beta position of the Enophile is connected to the terminal position of the Olefin, which is a Ene component, in this particular case.

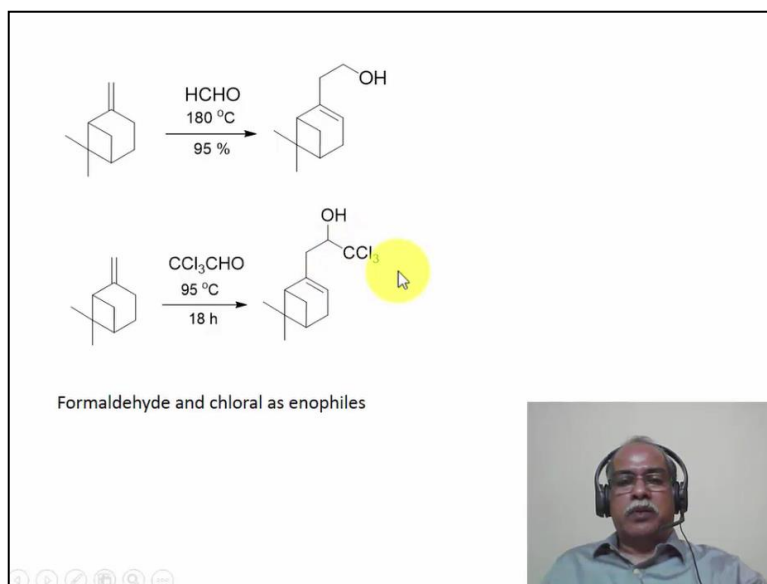
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A Carbonyl Ene reaction is the one, where Enophile is a C-double bond-O. So, you can see here, this Hydrogen is essentially transferred onto the Oxygen, resulting in the formation of a Carbon-Carbon bond, resulting in the Homo Allylic kind of a product. Essentially, this reaction is equivalent to adding an Allyl Magnesium Bromide kind of a reagent, to a Carbonyl functional groups.

So, it is an equivalent to that particular, in terms of the product formation, that is formed, in this reaction, which is a Carbonyl Ene reaction. In this reaction, which is an equivalent reaction, which is a Grenard addition reaction. Essentially, the equivalence is, what is being shown, by this two equations, that are shown here.

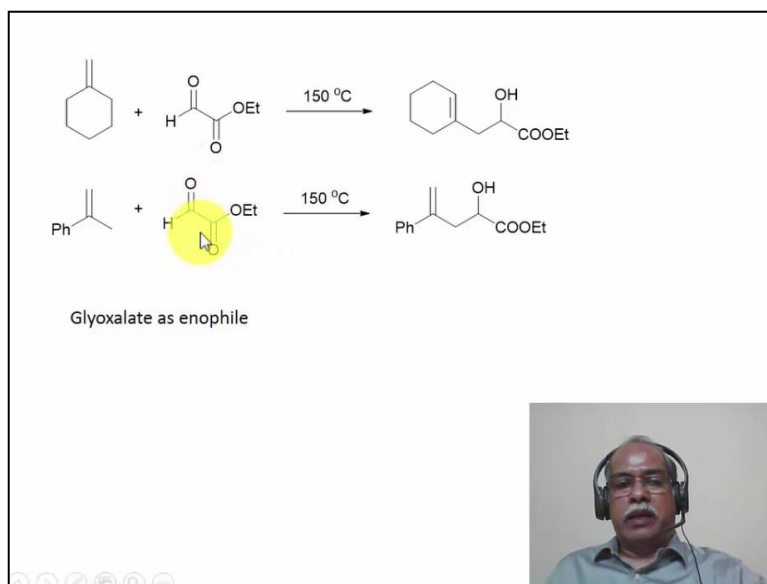
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Formaldehyde is a very reactive Enophile. Formaldehyde can undergo reaction, with Beta Pinene, in a Ene reaction manner. The Hydrogen from the Allylic position, is transferred onto the Carbonyl, resulting in a CH₂OH formation, with a simultaneous formation of the Carbon-Carbon bond, with the terminal position of the Olefin, resulting in the formation of the Homo Allylic alcohol, in this particular system. The same example is shown with Chloral.

Chloral is also a highly reactive Enophile, because of the Electron deficient nature of the Enophile. The Trichloro Acetaldehyde, is more reactive than the Formaldehyde, itself. As you can see here, this is carried out at 180° Celsius, whereas, this is at a low temperature of 95° Celsius or so, resulting in the formation of a Homo Allylic alcohol system, which is substituted with the Trichloro Methyl group, in this instance.

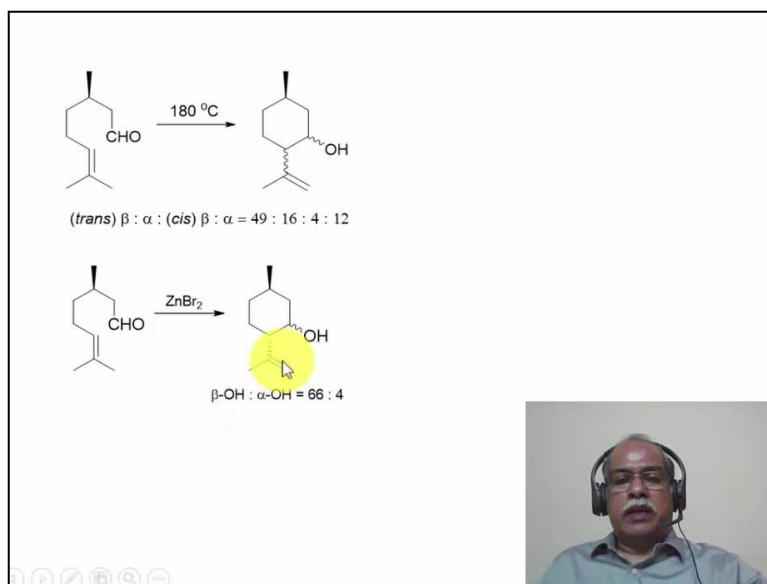
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Glyoxalates are also very excellent Enophiles. The reaction is carried out around 150° Celsius. In the case of Exomethylene Cyclohexane, the product formed is the Cyclohexene, which is substituted in the 1-Position, in this particular case. Whereas, Alpha Methyl styrene is undergoing the reaction, to give the Alpha Methyl styryl derivative, of the Homo Allyl alcohol, of this product. In other words, this Hydrogen is transferred onto the Oxygen.

A Carbon-Carbon bond is formed, between this Carbon, and this particular Carbon, during the course of the reaction, with the Glyoxalate. So, Glyoxalates undergo, highly Regio specific [1,5]-Hydrogen shift. The Hydrogen shift is always, on to the Aldehydic Oxygen. Aldehydic Oxygen is a more reactive enophilic Oxygen, compare to the Ester functional group, which is inactive, in this particular instance.

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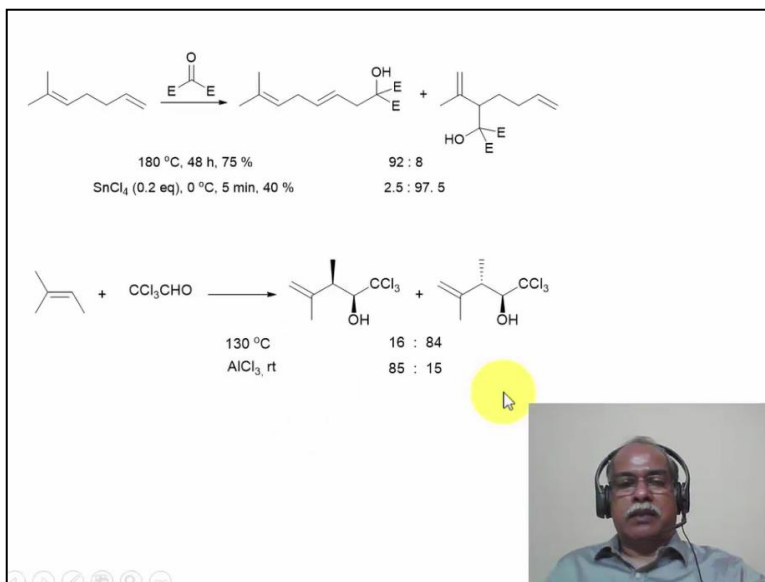


Here are some examples of Intramolecular Carbonyl Ene reaction. In the case of the, this Aldehyde, which is a Terpene Aldehyde, the reaction takes place at 180° Celsius. A mixture of both, the Cis and the Trans-compounds, are formed. We are talking about, the relative stereochemistry between this Carbon here, and the newly formed Carbon, which is this particular Carbon, which is the stereo center. This can be, either Cis or Trans. Both, Cis and Trans are formed.

The Trans isomer, is a major product. And, between these two con stereo centers, it can be either Alpha or Beta, depending upon, whether the Hydroxy is up or down, with respect to the [1,4]-Stereochemistry. So, the Cis and Trans, refers to the [1,4]-Stereochemistry. Alpha, Beta, refers to the Hydroxy functional group, being either Alpha or Beta, with respect to the Methyl group. So, all the four possible isomers are formed. The Trans Beta is the major product, in this particular case.

In other words, the Methyl group, and the Hydroxy group, are Cis with respect to each other, and the Methyl group, and the Isopropenyl group, are Trans with respect to each other, is a product, that is the major product. When the reaction is catalyzed by Zinc Bromide, essentially, predominantly, only one product is formed. The Trans isomer is formed. The Cis isomer is absent, in this particular reaction. In the Trans isomer, the Beta isomer is a major product formed, in about 66% yield, in this case.

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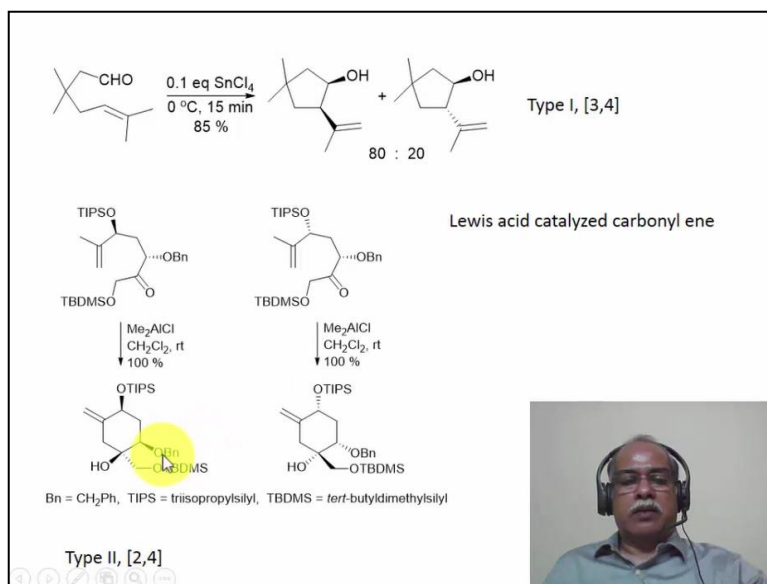


Here is a competition, between a Tri-Substituted Olefin, and the Mono-Substituted Terminal Olefin, for example. Under, normal thermal Ene reaction, the sterically least hindered Olefin, is what is undergoing the Ene reaction. The hydrogens from this Allylic position, are transferred onto the Keto Diester, in this particular case. However, when Tin chloride is added, the reversal of the Regio chemistry takes place.

The Hydrogen from this position, is what is undergoing the Ene reaction, resulting in the formation of a Carbonyl Carbon bond forming reaction at this position, in a very high yield of 97.5%, in this particular case. Chloral, again, can be catalyzed using Aluminium chloride, in terms of the Carbonyl Ene reaction. The two isomers, that are formed. These are Diastereo isomers, that are formed. We will see in a minute, how the Diastereo isomers are formed, in an Ene reaction.

For the time being, take it that, the thermal reaction gives a particular Diastereomeric ratio. The Diastereomeric ratio is reversed, when the Aluminium chloride is added. Essentially, because in the transition state, you can have either Endo or Exo transition state, with respect to Ene and the Enophile, which is reversed, because of the Aluminium chloride attachment, to the Carbonyl functional group.

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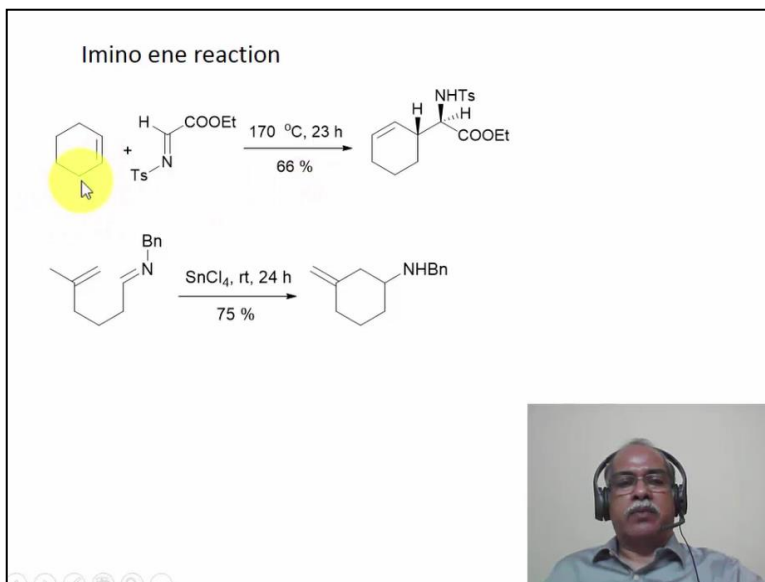
Lewis acid catalyzed, Intramolecular Carbonyl Ene reaction, is shown here. This is a [3,4]-Type-1 kind of an Ene reaction. Tin, essentially coordinates to the, Oxygen of the Carbonyl functional group. And, the Hydrogen from this Methyl group, is transferred onto the Oxygen, resulting in the formation of a Carbon-Carbon bond, between these two Carbons, resulting in a Cyclopentanol kind of a structure, Cis-Trans isomers are formed, Diastereo isomers are formed, in about 80:20 ratio, in this particular case.

And, this is an example of a highly-substituted derivative, being produced by a Type-2, [2,4] Type of Ene reaction. [2,4] connectivity, essentially because, this is the Tether, which is connected to the 2nd position, and to the 4th position, which is this particular position. Because, the 5th position is the one, that is receiving the Hydrogen, in this particular case. So, the Hydrogen from this Allylic position, is transferred onto the Oxygen.

So, this is 1-2. And, this is 3-4 and 5. The [1,5]-Hydrogen shift, is from this position, to this position, in this particular instance, resulting in the formation of an Exomethylene Cyclohexene derivative, which is highly substituted, in terms of the stereo selectivity of the reaction. This is highly stereo selective in the sense that, this is the only product, that is formed in about 100% yield, in each of this Diastereo isomers that are formed, as starting material.

The Diastereo isomer, in this particular case, is a Trans isomer. Whereas here, it is a Cis isomer, giving us stereoselective product formation, in terms of the Diastereo selectivity, with respect to this newly formed chiral center, in this particular instance.

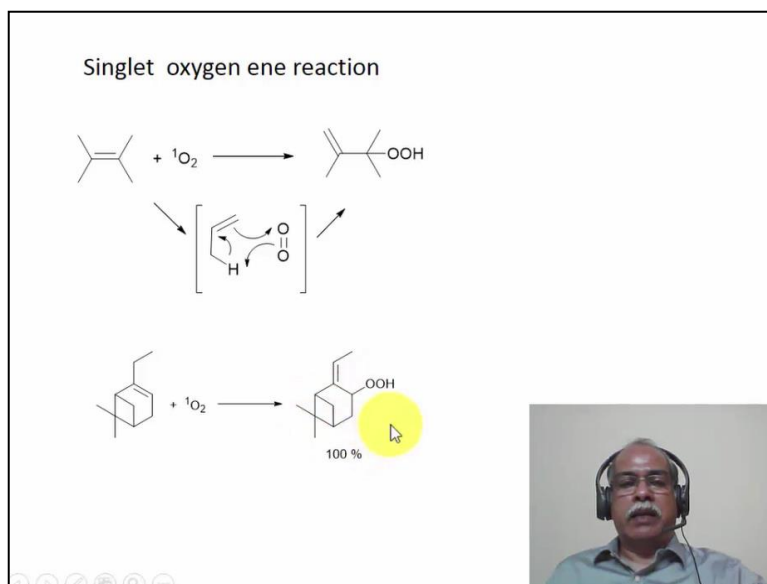
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Imino Ene reactions are the ones, where the Enophile component is an Imine. Here, a Tosyl Imine of the Glyoxaldehyde is taken, and it is reacted with Cyclohexene, resulting in the formation of the product, which is shown here, by a transfer of a Hydrogen from this position to Nitrogen, and resulting in the Carbon-Carbon bond formation to the Beta position, to give this product. This is a Benzyl Imine of Aldehyde. Originally, this was an Aldehyde.

The Benzyl Imine is formed, which is undergoing a Lewis acid catalyzed Ene reaction, even at room temperature, for example, resulting in the formation of a Carbon-Carbon bond, between these two Carbons here. The Hydrogen from this position, is transferred onto the Nitrogen, to give the secondary Amine, which is a Benzyl Amine, in this particular case.

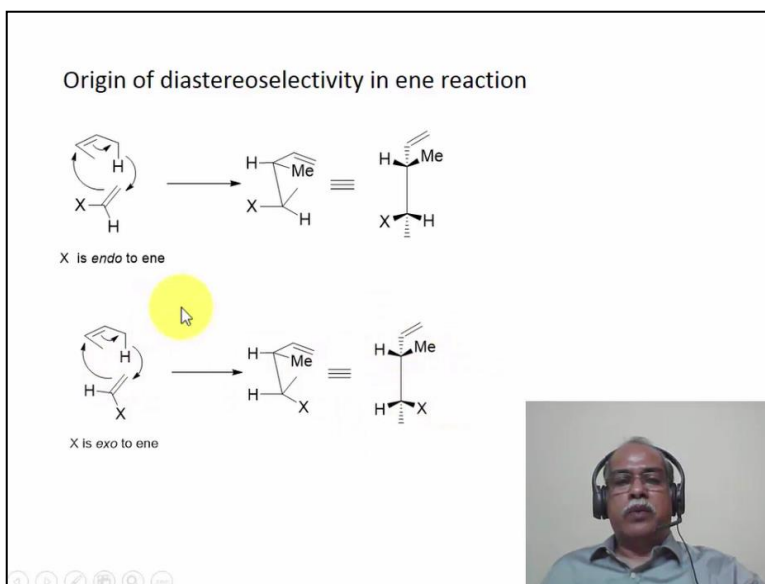
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Singlet Oxygen is almost, as reactive as Benzynes, in terms of the Ene reaction. Singlet Oxygen can be produced, under photochemical condition. In the photochemistry, we will see this, once again, this particular reaction. When, Methylene Blue kind of a dye is irradiated, it forms the excited triplet state, which transfers the energy onto the triplet Oxygen, which is a normal Oxygen, producing in the singlet Oxygen, in the process.

The Singlet Oxygen is essentially a, O=O double bond configuration, is what we have. So, this is essentially, the Hydrogen is transferred onto the Oxygen. And, there is an Oxygen Carbon bond is formed, leading to the formation of Peroxides. So, here again, the Beta Pinene derivative is undergoing a Singlet Oxygen Ene reaction, to produce the corresponding Hydroperoxide, in about quantitative yield, in this particular case.

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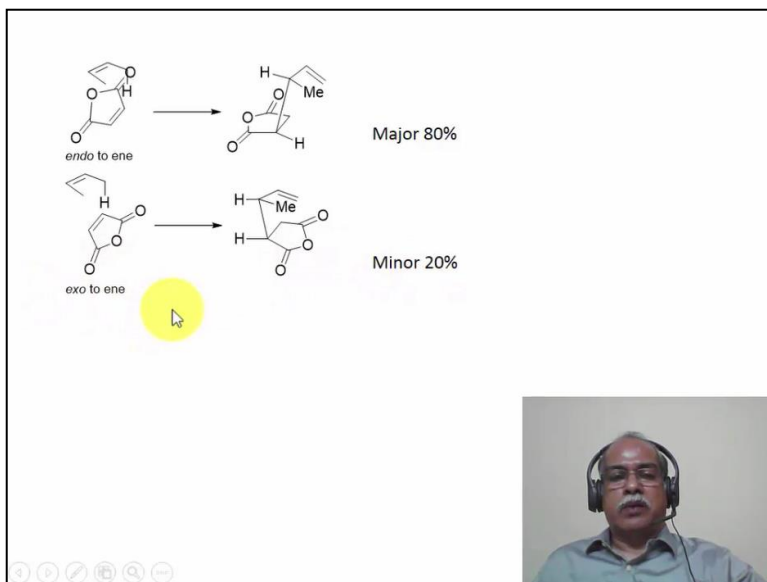


We will see, more examples of the Oxygen Ene reaction, in the photochemical reaction, when we consider Singlet Oxygen reaction. Now, we will explain the, origin of Diastereo selectivity, in the Ene reaction. Remember, early on, we saw the formation of a Diastereo isomers, in the Ene reaction. What causes the formation of selectively one, or the other Diastereo isomer, in an Ene reaction, is explained here. There are two transition state, that are possible.

The Hydrogen, the X-group in the Enophile can be Endo, with respect to the Ene, or it can be Exo, with respect to the Ene. Here, you can see here, the CX bond is Exo, with respect to the Ene. The CX bond is Endo, with respect to the Ene. The Hydrogen is transferred onto the Beta position here, with the concomitant formation of the Alpha position, with this particular Carbon here, resulting in the formation of this two products. This product is similar to a Threo kind of an Endo product, whereas, this is similar to an Erythro kind of a product.

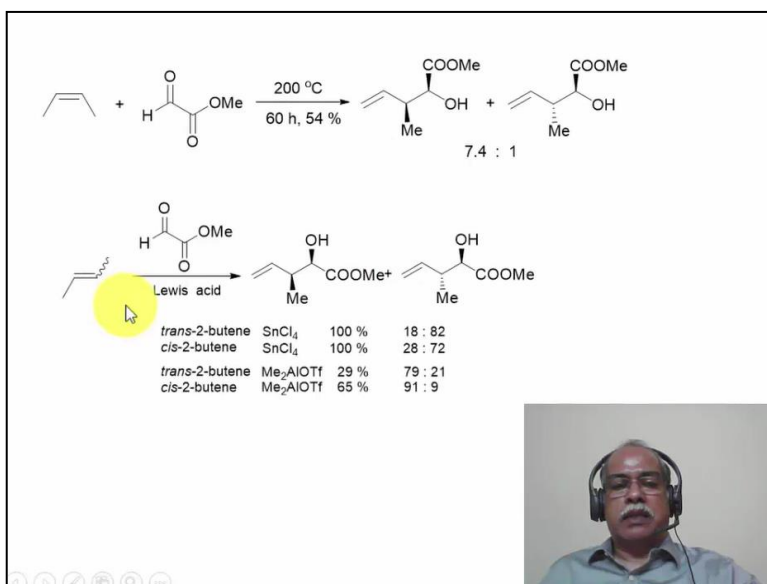
So, the transition state is, what is clearly shown here. The X is Exo to Ene, X is Endo to Ene, that will result in the Carbon-Carbon bond formation, resulting in the Diastereomeric form. If the Endo transition state is a favorable transition state, this will be a major product. If the Exo transition state is a favorable transition state, then, this will be a product. It would depend upon, the bulky nature of the X-group. It will also depend upon, whether X is coordinated to a Lewis acid, and so on.

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So, there are several factors, which are involved in the reaction. Normally, if you consider the All Thermal Ene reaction, without any kind of a Lewis acid catalysis, it seems that, the Endo Ene reaction is the most favorable reaction. Perhaps, there is some kind of a secondary orbital interaction, between this Carbonyl, and this Carbonyl over here, resulting in the formation of, this as a major product. The minor product, which is shown, is formed only in about 20% yield, arising from the Exo Type of a transition state in the Ene.

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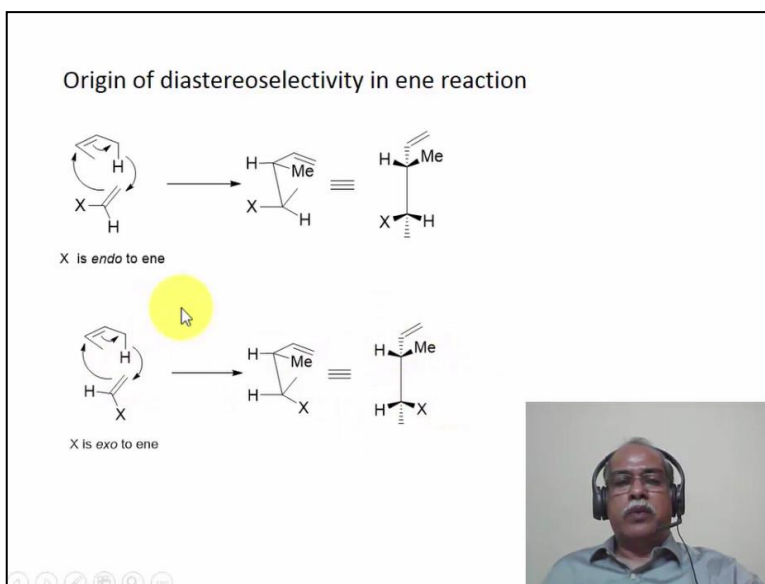


these are examples of the Diastereo selectivity, in the Ene reaction. when, Methyl Glyoxalate is used as the Enophile, and Cis-2-Butene is used as the Ene component, the Diastereo isomers are formed in about 7.5:1 ratio. this is a thermal reaction, uncatalyzed Ene reaction, is what is shown

here. when you do a catalysis, using either Tin chloride or Methyl triflate, depending upon the Lewis acid catalyst, the stereoselectivity changes, for example.

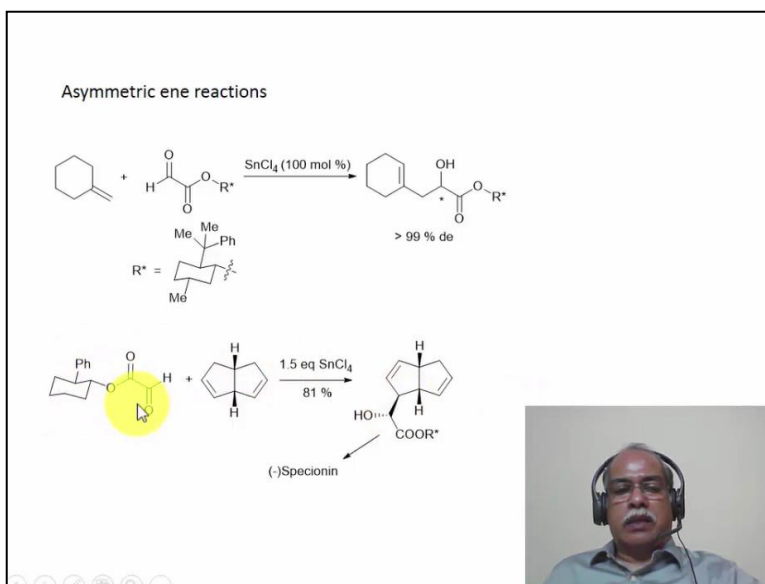
when Tin chloride is used, Trans-2-Butene is used, or Cis-2-Butene is used, the product, that is formed here, is the major product, which arises from the Endo selectivity. Whereas, when Cis-2-Butene, or Trans-2-Butene is used, with the Methyl triflate as the Lewis acidic reagent, the product arising out of the Exo Tricyclic transition state, is what is major product, in this case.

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So, the Diastereoselectivity can be explained, by looking at this picture here, with the bulky group, if it is attached to the X-group, for example, by a Lewis acid catalyst. This maybe a crowded transition state, in which case, this is a preferred transition state. Normal thermal Ene reaction, probably, this transition state is favored. And, that is why, that particular Diastereo isomer is formed, as a major product.

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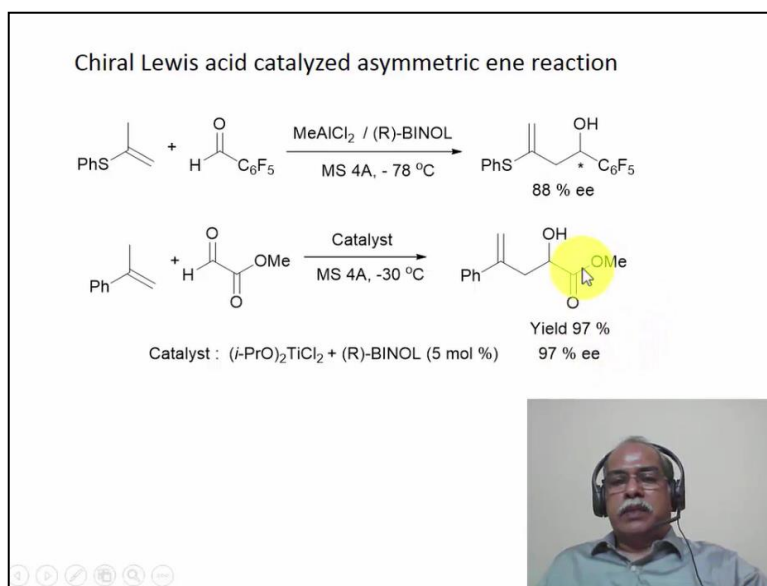


In the process of generating the Ene reaction, you also generate chiral centers, because of C-C Bond forming reactions, that are taking place. So, one can also imagine an Asymmetric Ene reaction. In this particular case, this pendant group is attached as an auxiliary, to the Glyoxylate. In other words, the Glyoxylate Ester is a chiral Ester, arising from a Menthol kind of a derivative, in this particular case. Ene reaction, produces the Diastereo isomer, in 99% yield. Once, this is cleaved, the particular Enantiomer will be formed, in 99% yield.

So, this is a Lewis acid catalyzed. Not catalyzed, this is almost, stoichiometric amount of Lewis acid is taken. Because, in the product also, you have Oxygens present. So, the Lewis acid will be tied up to the product Oxygens, also. And, that is why, the excess amount of the Tin chloride is taken, although the role of Tin chloride is only catalytic, in this particular instance. Here is an example of Alpha Phenyl Cyclohexanol, which is an optically pure compound, which is esterified to the Glyoxylate, Ester is formed, in this particular case.

This is a chiral auxiliary. So, used for inducing the chirality, for the newly generated chiral center, that is formed. The Ene reaction, essentially this Hydrogen is removed, transferred onto the Glyoxylate Oxygen here, resulting in the migration of this double bond, over to this position, forming this particular product. This is a starting material, for a natural product called Specionin. So, this is essentially stereoselectivity synthesized, by an Asymmetric transformation, by generating this two-chiral center, simultaneously, during the course of the reaction, by taking a chiral auxiliary, in this case.

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Lewis acid catalyzed, Asymmetric Ene reactions, are also known. This is a chiral Lewis acid is generated, by reacting the Methyl Aluminium chloride, with R-Binal. Binal is an optically active Diphenol. When Aluminium chloride reacts with the Binal, the corresponding Aluminium Phenoxy derivative, is what is found. So, that undergoes the Ene reaction. This is the Ene component, with Allylic Hydrogen. And, this is the Enophile, which is an Electron deficient Enophile. Because, it is Pentafluorobenzaldehyde, which is a highly Electron deficient Aldehyde. The efficient Ene reaction, takes place even at -78° Celsius, resulting in the formation of Enantiomerically Pure One isomer of this formed, because of the chiral induction from the R-Binal, results in the chirality, this particular position. So, here is, this is an example of a Chiral Lewis acid catalyzed, Asymmetric Ene reaction. Another example of a Chiral Lewis acid catalyzed, Ene reaction is, using Titanium Isopropoxide, and Binal. Here, the Titanium Isopropoxide, essentially exchanges with a Binal, to give the Binal Titanium Enolate kind of a product, is what is formed.

Methyl Glyoxylate is the Enophile, and the Alpha Methyl styrene is the Ene component, resulting in the formation of 97% chemical yield of this compound, with 97% Enantiomerically Pure Homo Allylic alcohol is produced, in this particular instance. So, what we have seen in this particular module, is a very important reaction, which is essentially a [1,5]-Hydrogen shift kind of a reaction, taking place either Intermolecularly, or Intramolecularly. And, it is classified as the

Ene reaction. And, the Carbonyl Ene is the one, where the Carbonyl group is used as the Enophile.

There are two components in an Ene reaction, the Ene component, and the Enophile component. The Ene component is invariably a compound, having an Allylic Hydrogen. The Enophile can be either, Carbon-Carbon double bond, Carbon-Oxygen double bond, Carbon-Nitrogen double bond. A variety of Ene reaction, we have seen. Asymmetric version, as well as the Diastereo selective nature of the Ene reactions, are explained in this particular module. I hope, you enjoyed this module. Thank you very much, for your kind attention.